THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL

Department of Pathology

ANNUAL REPORT

1 JULY 1997 - 30 JUNE 1998

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LIST OF FACULTY

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Name	Rank	Institutional Affiliation
Abell, Murray R	Professor Emeritus	The University of Michigan
Abrams, Gerald D.	Professor	The University of Michigan
Afify, Alaa M. –1	Clinical Assistant Professor	The University of Michigan
Al-Khafaji, Basim M. –1	Clinical Assistant Professor	The University of Michigan
Annesley, Thomas M.	Professor	The University of Michigan
Appelman, Henry, D.	Professor	The University of Michigan
Arend, Lois J.	Assistant Research Scientist	The University of Michigan
Baker, James R.	Associate Professor	The University of Michigan
Barr Jr., Mason	Professor+	The University of Michigan
Beals, Theodore F.	Assistant Professor	Veterans Affairs Medical Center
Blaivas, Mila	Clinical Associate Professor	The University of Michigan
Bonadio, Jeffrey	Associate Research Scientist	The University of Michigan
Brawn, Peter	Assistant Professor	Veterans Affairs Medical Center
Capps, Rodney D.	Assistant Professor	The University of Michigan
Chamberlain, Priscilla	Clinical Instructor II	Veterans Affairs Medical Center
Chensue, Stephen W.	Associate Professor	Veterans Affairs Medical Center
Cho, Kathleen R. -2	Associate Professor*	The University of Michigan
D'Amato, Constance J.	Assistant Professor	The University of Michigan
Davenport, Robertson	Associate Professor	The University of Michigan
de la Iglesia, Felix	Adjunct Research Scientist**	Warner-Lambert; Parke Davis
Dressler, Gregory R.	Assistant Professor	The University of Michigan
Elner, Victor M.	Assistant Professor++	The University of Michigan
England, Barry G.	Associate Professor	The University of Michigan
Fantone, Joseph C.	Professor and Director, Anatomic Pathology	The University of Michigan
Fearon, Eric R.	Professor*	The University of Michigan
Flint, Andrew	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 Emeritus	The University of Michigan
Giordano, Thomas J.	Assistant Professor	The University of Michigan
Gordon, David	Associate Professor	The University of Michigan
Greenson, Joel	Associate Professor and Director, Surgical Pathology	The University of Michigan
Headington, John T.	Professor Emeritus	The University of Michigan
Heidelberger, Kathleen P.	Professor	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Judd, W. John	Professor	The University of Michigan
Keren, David F.	Clinical Professor	Warde Medical Laboratories
Killeen, Anthony A.	Assistant Professor	The University of Michigan
Killen, Paul D.	Associate Professor	The University of Michigan
Kunkel, Steven L.	Professor and Co-Director, Division of General Pathology	The University of Michigan
Lieberman, Richard W.	Visiting Lecturer+++	The University of Michigan
Lowe, Lori	Clinical Assistant Professor	The University of Michigan
Lowe, John B.	Professor	The University of Michigan
Lukacs, Nicholas	Assistant Research Scientist	The University of Michigan
McKeever, Paul E.	Associate Professor	The University of Michigan
Michael, Claire W.	Clinical Assistant 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
Mosley, R. Lee	Assistant Research Scientist	The University of Michigan
Murphy, Hedwig S.	Assistant Professor	The University of Michigan
Naylor, Bernard	Professor Emeritus	The University of Michigan
Nunez, Gabriel	Associate Professor	The University of Michigan
Oberman, Harold A.	Professor	The University of Michigan
Paulino, Augusto F. -1	Clinical Assistant Professor	The University of Michigan
Phan, Sem H.	Professor	The University of Michigan
Pierson, Carl L.	Assistant Professor	The University of Michigan
Polverini, Peter J.	Professor**	The University of Michigan
Ramsburgh, Stephen R. -1	Clinical Instructor II	The University of Michigan
Rasche, Rodolfo	Clinical Assistant Professor	The University of Michigan
Remick, Daniel G.	Associate Professor	The University of Michigan
Ross, Charles W.	Associate Professor	The University of Michigan
Rowe, Nathaniel H.	Professor*	The University of Michigan
Rubin, Mark A. -2	Assistant Professor#	The University of Michigan
Schmidt, Robert W.	Professor Emeritus	The University of Michigan
Schnitzer, Bertram	Professor	The University of Michigan
Shanberge, Jacob N.	Clinical Professor	William Beaumont Hospital
Sheldon, Susan	Assistant Professor	The University of Michigan
Silverman, Eugene M.	Clinical Associate Professor	The University of Michigan
Singleton, Timothy P.	Assistant Professor	The University of Michigan
Stoolman, Lloyd M.	Associate Professor	The University of Michigan
Su, Lyndon -1	Clinical Assistant Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Till, Gerd O.	Professor	The University of Michigan
Varani, James	Professor	The University of Michigan
Ward, Peter A.	Professor and Chairman	The University of Michigan
Warren, Jeffrey S.	Associate Professor and Director, Clinical Pathology	The University of Michigan
Wojno, Kirk	Assistant Professor	The Universit of Michigan

1 Faculty appointed 1 July 1998
2 Faculty appointed 1 September 1998
* Joint Appointment, Department of Internal Medicine.
** 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 Obstetrics and Gynecology
\# Joint Appointment, Department of Urology

Faculty, Residents and Fellows
Department of Pathology
October, 1997

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DEPARTMENTAL OVERVIEW

DEPARTMENTAL OVERVIEW
1997/1998

Introduction

Major institutional changes within the University of Michigan Health System (UMHS) have been a challenge for the clinical departments but these have provided a number of opportunities. Establishment of an integrated relationship among the faculty, the Medical School and the Hospital via the Clinical Delivery System (CDS) agreement and the Faculty Group Practice (FGP) has allowed implementation of innovative strategies designed for more efficient and cost effective functions. Cost per hospital case and average length of stay for the UMHS have decreased. The number of M-Care enrollees and the number of ambulatory care patients have grown. The Hospitals are operating at capacity. The Department of Pathology cost-efficiency plan, which called for several laboratory consolidations and administrative reorganizations, was realized and new attention has been directed towards enhancement of operations (see Clinical Service Activities below). Consistent with the changes outlined above, the Department implemented its new Risk II Incentive program, distributed CDS margin revenue to individual faculty, distributed FGP professional development funds, and has increased the academic discretionary funds for the Department.

During the past academic year, the Department has completed a record recruitment of faculty, filling eight faculty slots: two in cytopathology, three in surgical pathology, one in general pathology and surgical pathology, one in dermatopathology and one in hematopathology. Each new faculty member possesses excellent credentials and comes from an institution of renown. This infusion of "new blood" into the Departmental faculty ranks will greatly enhance the Department as we approach the millennium. The Department continues to develop innovations in its undergraduate medical and graduate medical programs, and the research programs and their funding are thriving.

Teaching Activities

Faculty members continue to fill leadership roles as course directors, sequence coordinators, and serve as Associate Dean for Medical Education in the Medical School curriculum. Several faculty members continue to be recognized as recipients of outstanding teaching awards and selection as graduation class marshals. Pathology laboratories continue to be a strength within the histology course and second year organ system sequences. Fourth year clerkships in Pathology and Laboratory Medicine are elected by approximately one fifth of the Medical School class each year and receive exceptional evaluations. The summer program for first year medical students enrolled 8 students this year. The Department continues to present a semester-long Dental Pathology course and a summer semester course to Medical Illustration students. Both courses continue to focus on the specific educational needs of these students and engage them in more inter-active learning activities, including the implementation of Web-based instruction. The Pathology graduate program was successful in recruiting three new students and graduating two students this past academic year. One Pathology student received a University of Michigan Outstanding Dissertation Award for his work. This was one of four such awards within the University. The Department faculty are actively involved in the Medical Scientist Training Program (MD/PhD) and combined graduate student recruitment activities associated with the Program in Biomedical Sciences (PIBS). The Pathology residency and fellowship programs continue to prosper despite declining national student interest in pathology residency training. The program consists of 25 house officers and fellows of whom 11 are women and 4 under-represented minorities. Last year all graduates of the house officer program found desirable positions, in both academia and private practice,

including fellowships at Cornell Medical School (NYC), University of New Mexico and positions at the Cleveland Clinic and Indiana University (Indianapolis).

Clinical Service Activities

The Anatomic and Clinical Pathology Laboratories continue to provide excellent, full-spectrum service as the UMHS has experienced a dramatic expansion in ambulatory care activities, growth in several major clinical programs and continued expansion of M-Labs activities. Efforts have been directed towards the improvement of phlebotomy, central distribution and laboratory operations as we emerged from the first full year following implementation of vigorous institutionally-mandated cost reductions and the opening of the Cancer and Geriatrics Center. In 1997-98 the Laboratories performed more than 3 million laboratory analyses and nearly 40,000 surgical pathology cases. The maintenance of high quality service, in the face of increasing complexity of demands, is a testimony to the professionalism of the staff as well as the management capabilities of laboratory directors and senior laboratory personnel. The Laboratories successfully completed the biannual on-site College of American Pathologists (CAP) self-inspection. Maintenance of the delicate balance among quality service, cost-effective testing, utilization control and research and development, which characterizes an academic institution, will be a continuing challenge.

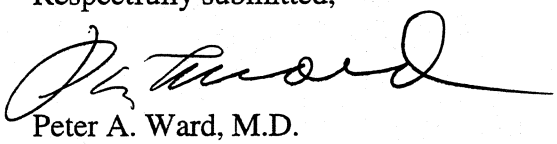
1997-98 was marked by several major initiatives. In response to pressures to reduce our cost/unit of laboratory service and to improve operating efficiency, a comprehensive plan for laboratory reorganization was realized. Reorganization entailed a nearly 10% reduction in operating budget, consolidation of several laboratories and reorganization of inpatient phlebotomy services. This reorganization entailed the consolidation of the Immunopathology, Ligand Assay, Toxicology/Therapeutic Drug Monitoring and Chemistry Laboratories into a single unit; consolidation of the Hematology, Flow Cytometry and Coagulation Laboratories (formerly Internal Medicine) into a single unit; incorporation of histopathology, immunohistochemistry and cytopathology into coordinated units; and streamlining of the administrative structure of these and other laboratories. Second, the Laboratories continued to reallocate resources needed to meet the continuing and marked increase in transplantation activity (especially bone marrow) experienced in 1997-98. Augmentation of the capabilities of the Molecular Diagnostics, Blood Bank, Tissue Typing and Cytogenetics Laboratories was contributory to this process. Finally, as alluded to above, the Laboratories have responded to the institutional initiative to expand primary care capabilities within the region. This activity has been coupled with expansion of on-site point-of-care testing and data handling activities. The Laboratories continue to support the growing M-Labs outreach program, to forge strong collaborative relationships with local and regional reference laboratories and to intensify our role in institutional utilization management.

Research Activities

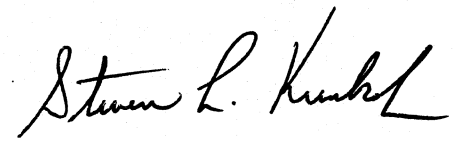
Research activities in the Department of Pathology remain a strong and active component of our academic mission. The faculty in the Department of Pathology continues to publish in highly visible, peer-reviewed scientific journals, attract numerous graduate and postdoctoral fellows from national and international locales, and successfully compete for extramural research support. This latter aspect is exemplified by the expenditures of active grants and contracts credited to Pathology research efforts of nearly $10 million. This total includes approximately $7 million in direct expenditures and $3 million in indirect expenditures. Presently in the Department there are in excess of 72 individual research grants from the National Institutes of Health, with additional grants originating from the National Science

Foundation, American Heart Association, American Lung Association, the Army and various industrial sources. Many faculty play important roles in support of institutional initiatives associated with the University of Michigan Cancer Center, Urologic SPORE, Breast Cancer Program and Interstitial Lung Disease SCORE. Faculty members in the Department of Pathology actively publish in both the experimental and clinical arena and cover diverse research interests, such as anatomical pathology, clinical pathology and basic cellular and molecular mechanisms of disease. In the past year, faculty members in the Department have collectively published hundreds of scholarly articles in numerous scientific journals, with many of these articles appearing in journals with a high citation index impact. Our faculty participate in peer review of submitted scientific articles for diverse journals, as well as serve on a large number of Editorial Boards. An additional index of the academic research activities of the faculty is the large number of postdoctoral fellows in the various laboratories, nearly 40 postdoctoral fellows from diverse backgrounds are presently engaged in research activities and clinical fellowships in the Department. These postdoctoral scholars have actively sought research positions in the Department of Pathology to enhance their research and clinical careers. Our faculty members continue to provide expertise for both internal and external program review processes, which include serving as ad hoc and permanent members of various National Institutes of Health study sections, serving as committee members for site visits and reverse site visits, providing expertise on Government special emphasis panels, and either organizing or chair/co-chairing various clinical and experimental scientific meetings and conferences.

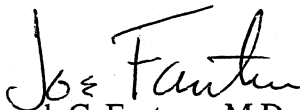
Respectfully submitted,



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



Steven L. Kunkel, Ph.D.
Co-director, Division of General Pathology



Joseph C. Fantone, M.D.
Director, Division of Anatomic Pathology

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

INDIVIDUAL FACULTY REPORTS

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

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Services - 5 1/4 months.
B. Necropsy Service - on call for consultation.
C. Pathologist, Cardiac Transplant Team. Transplant biopsies - 9 months.
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 - 8 contact hours.
   3. Introductory Histopathology Sequence, Sequence Director, Lecturer, Lab Instructor - 28 contact hours (7 lectures, 21 lab hours).
   4. Pathologic correlation in Gross Anatomy Labs - 6 contact hours.

B. Sophomore Medical Class:
   1. Cardiovascular Sequence - Pathology Lab Coordinator.
   2. Pathology Lab Instructor - all sequences, 50 contact hours.

C. Senior Medical Class:
   1. Clinical Radiology, Pathology Correlations, Elective Course, Co-director and discussion leader - 12 contact hours.

D. Dental School:
   1. Sophomore Dental Class (Path 580) - 2 lecture hours

E. Undergraduate LS&A/Graduate:
   1. Biology 224 - 1.5 lecture hours.
   2. Nuclear Engin. 582 - 1.5 lecture hours.

F. Hospital Conferences:
   1. Cardiovascular Pathology Conference - monthly.
   2. Internal Medicine, Morbidity, Mortality Conference/CPC - monthly

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

H. Invited Lectures:
   1. Keynote Address, Medical School White Coat Ceremony - August, 1997.
   2. Research Responsibility Program, December, 1997.

I. Production of Teaching Materials:
   1. Development of website for Pathology 500.
   2. Development of website for Histopathology Lab.

J. Continuing Medical Education
   1. Cardiology update - August, 1997.
   2. Northern Michigan Summer Conference - June, 1998.

K. Honors:
   1. Elected Class Marshall, Medical Class of 1998.
   2. Recipient - "Medical Student Award for Teaching Excellence," 1997-1998.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Pathologic-Radiologic correlation in aortic disease, with D. Williams.
B. Pilot studies of chemo-embolization with Degra Bloc, with K. Henley.
C. Tissue reactions to vena caval filters, with L. Greenfield.
D. Compidex 7227 as MRI agent to evaluate lymph nodes, with I. Francis.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member, Pathology House Officer Selection Committee.

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

A. Member, Historical Center for the Health Sciences Liaison Committee.
B. Member, Component I Committee.
C. Ombudsperson, Medical Faculty.
D. Chair, Panel of Inquiry into Federally Sponsored Human Radiation Research at U of M (OVPR).
E. Member, Medical School Executive Committee.
F. Member, Sesquicentennial Celebration Committee.
G. Member, Ad Hoc Search Committee for Associate Dean for Medical Education.

REGIONAL AND NATIONAL:

A. Editorial Board, Modern Pathology.
B. Manuscript Reviewer for Cancer, Gastroenterology.

V. PUBLICATIONS:

BOOKS/CHAPTERS IN BOOKS:

1. Abrams, G.D. in Ming, S.C. and Goldman, H. (eds) Pathology of the Gastrointestinal Tract, 2nd ed. Williams & Wilkins, 1998. Chapter 28: Infectious Disorders of the Intestines, 651-672.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Biochemistry Section, Clinical Pathology Laboratories.
   1. Administered consolidation and move of Drug Analysis Laboratory into Chemical Pathology space and structure.
   2. Development of assay for Lamotrigine in-house. Savings to hospital ~ $11,000.
   3. Development of assay for Homocysteine in-house. Savings to hospital ~ $75,000.

B. Consultant to Veterans Administration Hospital, Ann Arbor, Michigan.
C. Laboratory Director, Chelsea Family Practice, M-Care Facility.
D. Laboratory Director, Briarwood Medical Group, M-Care Facility.
E. Laboratory Director, Briarwood Family Practice Facility.
F. Laboratory Director, Chelsea Internal Medicine Associates.
G. Laboratory Director, West Ann Arbor Health 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. Lecturer, Minority Students Clerkship in Pathology.

B. House Officers:
   1. Lecturer, Clinical Pathology Grand Rounds.
   2. Lecturer, Clinical Pathology Didactic Lecture Series.
   3. Daily sign-out and interpretation of Laboratory Results.
   4. Clinical Pathology Curriculum Committee.
   5. Coordinator, Clinical Pathology Block B.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Analysis of Cyclosporine by Specific Monoclonal Antibody", Co-Investigator: Donald Giacherio, Abbott Diagnostics Corporation.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Biochemistry Section, Clinical Pathology Laboratories.
B. M-Labs Technical Group.
C. M-Labs Support:
   1. Provided lecture at M-labs Symposium "Current Concepts in Clinical Pathology", October 1997.
   2. Provided CME review article for Spectrum entitled "Monitoring Anticonvulsant Drug Therapy", January 1998.
   3. Provided M-Labs CME lecture at Hurley Hospital entitled "Monitoring of Anticonvulsant Drugs", April 1998.
D. Clinical Pathology Laboratory CME Committee.
E. Clinical Pathology Discretionary Incentive Funds Committee.

REGIONAL AND NATIONAL:

A. Board of Directors, American Board of Clinical Chemistry.
B. Clinical Chemistry Examination Committee, American Board of Clinical Chemistry.
C. Task Force on Postdoctoral Training and Certification, American Board of Clinical Chemistry.
D. Nominating Committee, Therapeutic Drug Monitoring Division of the American Association for Clinical Chemistry.
E. Executive Committee/Journal Management Group, Clinical Chemistry Journal.
F. Task Force on Journal Operations, American Association for Clinical Chemistry.
G. Member, Academy of Clinical Laboratory Physicians and Scientists.
H. Member, Clinical Ligand Assay Society.
I. Member, American Association for Advancement of Sciences.
J. Member, Association of Clinical Scientists.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

OTHER:

A. Clinical Chemistry, Reviewer.
B. Biomedical Chromatography, Reviewer.
C. Therapeutic Drug Monitoring, Reviewer.

INVITED LECTURES/SEMINARS:

1. "Monitoring Anticonvulsant Drug Therapy", University of Michigan Symposium on Current Concepts in Clinical Pathology, October 1997.
2. "Update on Anticonvulsant Drugs", Hurley Hospital, Flint MI, April 1998.
3. "Pharmacokinetics and Monitoring of Fosphenytoin", Ohio State University Children's Hospital, Columbus OH, May 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kugler, A.R., Olson, S.C., Annesley, T.M., Nordblom, G.D., and Koup, J.R.: Cross-reactivity of fosphenytoin in two human plasma phenytoin immunoassays. Clin. Chem. 1998;44:1474-80.
2. Roberts, W.L., De, B.K., and Annesley, T.M.: False elevations of immunoassay measurements of phenytoin in critically ill uremic patients receiving fosphenytoin. Clin. Chem. 1998;44:A89.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. Pathology 600 - 2 full class lectures.
   2. Pathology 630 (dental) - one full class lectures.

B. House Officers:
   1. Surgical pathology diagnosing room instruction for assigned house officer - 4 months.
   2. Gastrointestinal and hepatic pathology tutoring - full time.

C. Interdepartmental:
   1. G-I Tumor Conference - Every other Wednesday (three hours/month).
   2. Liver Biopsy Conference - one hour per month.
   3. Gastrointestinal Biopsy Conference for Gastrointestinal fellows and staff, 2 hours.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. National Study of Thymosin Treatment of Chronic Hepatitis B with Milton Mutchnick (Wayne State), and others. Manuscript submitted.
B. The changing appearance of ulcerative colitis in biopsies with time and treatment, with Celina Kleer. Manuscript in press.
C. Stromal tumors of the abdominal colon and anorectum, with Joe Tworek, Joel Greenson, Sharon Weiss, and John Goldblum (Cleveland Clinic) manuscripts submitted.
D. The effect of diet on recurrence rates of colonic adenomas, with Klaus Lewin (UCLA) and Arthur Schatzkin and others (National Cancer Institute, Chemoprevention Branch).

E. Clinical trial of difluoromethylornithine in Barrett's esophagus, with Dean Brenner of the U of Mich., Gary Stoner of Ohio State Univ, Stuart Spechler, and Edward Lee of University of Texas-Southwestern, and Anil Rustgi of Harvard.
F. What gastric stromal tumors are always benign"? with Carolyn Misick.
G. Lymphocyte colitis, a comprehensive clinical/endoscopic/histologic study, with Rachel Vidal and members of the division of Gastroenterology.
H. Anaplastic, lymphoma-like carcinoma arising in Barrett's mucosa, with BJ McKenna, T Nazeer, and A del Rosario, of Albany Medical Center.
I. Neoplasms of the small intestines, a survey, with BJ McKenna of Albany Medical Center.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Coordinator for Pathology, Randomized Therapeutic Trail in Cancer of the Esophagus, International Organization for Statistical Studies of Diseases of the Esophagus, Paris, France.
B. 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.
C. Central Pathologist, Polyp Prevention Trial, National Cancer Institute, Washington, DC.
D. Member, Editorial Board, Human Pathology.
E. Member, Editorial Board, Modern Pathology.
F. Member, Editorial Board, American Journal of Surgical Pathology.
G. Reviewer of manuscripts for Archives of Pathology and Laboratory Medicine, Cancer, Gastroenterology, Annals of Internal Medicine, and American Journal of Gastroenterology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Half-day-lecture course on gastrointestinal pathology: 1. "A whirlwind tour through esophagogastric inflammations". 2. "Precancers, dysplasias, in situ cancers and intramucosal cancers from esophagus to anus". Pathology Update for Practicing Pathologists: Recent

Advances and Selected Topics. American Society of Clinical Pathologists course, Vancouver, BC, July, 22, 1998.

2. Lecture: Stromal tumors of the small intestine; can we afford them in a managed care environment? Companion meeting, Gastrointestinal Pathology Society, Annual Fall Meeting, American Society of Clinical Pathologists, Philadelphia, September 20, 1997.
3. Half day course with BJ McKenna: Practical approaches to gastrointestinal biopsy pathology: how much clinical data is essential? Presented at the annual meeting of the American Society of Clinical Pathologists, Philadelphia, PA, September 21, 1998 and Weekend of Pathology, New York NY, June 27, 1998.
4. Microscopic tutorial: Mundane cases in GI pathology--even the non-interesting can be exciting., Annual Fall Meeting, American Society of Clinical Pathologists, Philadelphia, September 22, 1997.
5. Lecture: Can we tell benign from malignant stromal tumors, and if we can, what do we do with the information from a clinical standpoint? Presented at the Fall Symposium of the Flemish Society of Gastroenterology (Vlaamse Vereniging voor Gastro-Enterologie), Leuven, Belgium, November 28, 1997.
6. Seminar (full day) with BJ McKenna: Gastrointestinal pathology in the real world and other monkey business. Presented at the annual fall meeting of the Virginia Society for Pathologists, Richmond, VA, November 22, 1997.
7. Seminar (2 half days) with BJ McKenna: Gastrointestinal biopsy pathology in the real world—between them (gastroenterologists) and us (pathologists), it's amazing we ever get anything right! and other monkey business. Presented at the 24th Annual Anatomic Pathology Conference, Florida Society of Pathologists, Orlando, FL, Jan 31-Feb 1, 1998.
8. Lecture: The adenoma-carcinoma sequence in the colon. Department of Pathology and Laboratory Medicine, Albany Medical College, Albany NY, March 18, 1998. Lecture: Annoying gut biopsies: They are painful but potentially informative, so I refuse to lose any sleep over them. Division of Gastroenterology, University of Washington, Seattle, WA, May 8, 1998.
9. Half day course: "Neoplastic diseases of intestine", American Society of Clinical Pathologists, Newport RI, FL June 5, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. MacDonald GM, Greenson JK, DelBuono EA, Grady WM, Merion RM, Frank TS, Lucey MR, Appelman HD. Mini-microabscess syndrome in liver transplant recipients. Hepatology. 26:192-197, 1997.
2. Fig, LM, Brown RS, von Moll L, Appelman HD, et al. Immunolymphoscintography in breast cancer: evaluation using 131-I labeled monoclonal antibody B72.3. Nucl Med Biol 25:251-260, 1998.
3. Prabhu RM, Medieros LJ, Kumar D, Drachenberg C, Papadimitriou J, Appelman HD, et al. Primary hepatic low-grade B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) associated with primary biliary cirrhosis. Mod Pathol 11:404-410, 1998.
4. Kleer CG, Appelman HD. Ulcerative colitis: patterns of involvement in colorectal biopsies and

changes with time. Am J Surg Pathol, in press.

5. MacDonald GA, Greenson JK, Saito K, Cherian S, Appelman HD, Boland CR. Microsatellite instability and loss of heterozygosity at DNA mismatch repair loci occurs during hepatic carcinogenesis. Hepatology, 28:90-97, 1998.
6. Appelman HD, McKenna BJ. Editorial: A rose is a rose is a rose, but what exactly is a gastric adenocarcinoma? J Surg Oncol, in press.

CHAPTERS and BOOKS:

1. Antonioli DA, Appelman HD: Anus and Perianal Area. Chapter 36 in Sternberg Stephen S, ed. Diagnostic Surgical Pathology, Raven Press, Ltd, New York, 3rd Edition, 1998 or 1999, in press.
2. Appelman HD: Mesenchymal tumors of the GI tract. Chapter 15 in Pathology of the Gastrointestinal Tract, Ming S-G and Goldman H., Eds. Second edition, Williams & Wilkins, Baltimore, 1998.

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

1. Dignan CR, Ladabaum U, Scheiman JM, Appelman HD, Greenson JK. Fundic gland polyps are associated with Omeprazole use. Mod Pathol. 11:63A, 1998.
2. Valdez R, Appelman HD, Greenson JK. Diffuse duodenitis associated with ulcerative colitis. Mod Pathol. 11:72A, 1998.
3. McKenna BJ, Appelman HD, del Rosario AD, et al. Lymphoma-like anaplastic carcinoma of the esophagus, a Barrett's-associated tumor. Gastroenterol. 114:A222, 1998.
4. Carethers JM, Lopez BM, Zigman AF, Jo W-S, Lavine JE, Jones MC, Chauhan DP, Chang CL, Appelman HD, Boland CR. Presence of microsatellite instability (MIN) in the normal-appearing epithelium of familial juvenile polyps. Gastroenterol. 114:A574, 1998.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Director, Histocompatibility and Immunogenetics Laboratory.

II. TEACHING ACTIVITIES:

A. Director, Basic Immunology Course for Allergy Fellows-In-Training.
B. Instructor, Host Defense Course, First-Year Medical School Students.
C. Attending, General Internal Medicine Service.
D. Instructed Pathology Residents, Renal Fellows and Allergy Fellows in HLA typing
E. Supervised undergraduate students in research: Ellen Phelps.
F. Supervisor for:
Allergy Fellows: Drs. Kunhee Chung, Michael DiCello, Anna Dobracki
Postdoctoral Fellows: Drs. Marie Anderson, James Bretz, Jonathan Eichman, Su He Wang.
G. Director, Allergy Training Program.

III. RESEARCH ACTIVITIES

SPONSORED SUPPORT:

A. NIAID National Institutes of Health, R01 AI 37141, "Immune Responses to Thyroid Peroxidase" J. Baker, Principal Investigator, 1/1/95-12/31/98, (budget approximately $653,708).
B. DARPA, MDA972-97-1-0007, "Nanomolecule-Based Agents for Pathogen Counter Measure" J. Baker, Principal Investigator, 3/1/97-2/28/2001, (budget approximately $10,890,561).
C. NIAID-National Institutes of Health, RO1 AI40286-01 A1, "Mucosal Gene Transfer Using Dendrimer Polymers" (J. Baker, Principal Investigator), 5/1/97-4/30/00, (budget approximately $720,784).
D. University of Michigan-MAC, National Institutes of Health, D. Fox, Principal Investigator, 2 PO AR20557-15 "Hybridoma Core", J. Baker, Principal Investigator, 1/1/98-12/31/03, (budget approximately $276,765).

E. NIH-NIDDK, Greene D.E., M.D., Principal Investigator, 5 P60 DK20572-16, Michigan Diabetes Research and Training Center, Hybridoma Core, J. Baker, Principal Investigator, 12/1/97-11/30/02, (budget approximately $171,413).
F. NIH/MIAMS, "Gene Therapy for Rheumatic and Skin Disease, B.J. Roessler, M.D., Principal I Investigator, 9/30/96-2/29/01, (budget approximately $1,913,825.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Executive Board, Michigan Diabetes Research and Training Center.
B. Hybridoma Core Director and Sterlings Committee.
C. Chief, Division of Allergy, Department of Internal Medicine.
D. Medical School Faculty Representative, University of Michigan Faculty Senate.

REGIONAL AND NATIONAL:

1. Editor, JAMA Primer.
2. Editorial Board, Endocrinology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Transfection with Dendritic Polymers." Isis Pharmaceuticals, Carlsbad, CA, July 1997.
2. "Transfection with Dendritic Polymers." Chiron Technologies, Viagen Division, San Diego, CA, July 1997.
3. "Programmed Cell Death in the Thyroid." Endocrine Division, University of Cincinnati, Cincinnati, OH, October 1997.
4. "Programmed Cell Death in Thyroiditis." The American Thyroid Association Annual Meeting, Colorado Springs, CO, October 1997.
5. "Autoimmune Disease in Women." Office on Research on Women's Health, NIH, Bethesda, MD, November 1997.
6. "The Future of Biologic Nanotechnology." IBC Nanotechnology Conference, LaJolla, CA, December 1997.
7. "The Interaction of Plasmid DNA with Polyamidoamine Dendrimers: Mechanism of complex Formation and Analysis of Alterations in Nuclease Sensitivity and Transcriptional Activity of Complexed DNA." AAPS Eastern Regional Meeting, Parsippany, NY, May 1998.
8. "Polymer Transfection of the Lung for Anti-inflammatory Gene Therapy." Asthma & Allergy Utilizing Pharmacogenetics and Cost-Effective Approaches for Target Validation." Baltimore, MD, May 1998.

SCIENTIFIC ACTIVITIES:

A. Reviewer, Journal of Clinical Endocrinology and Metabolism.
B. Reviewer, Annals of Internal Medicine.
C. Reviewer, Journal of Clinical Investigation.
D. Reviewer, Journal of Leukocyte Biology.
E. Reviewer, Autoimmunity.
F. Reviewer, Thyroid.
G. Reviewer, Journal of Biological Chemistry.
H. Reviewer, The New England Journal of Medicine.
I. Reviewer, Journal of Endocrinological Investigation.
J. Reviewer, The American Journal of Medicine.

VI. PUBLICATIONS:

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

1. Bielinska AU, Kukowska-Latallo JF, Baker JR Jr. The interaction of plasmid DNA with polyamidoamine dendrimers: Mechanism of complex formation and analysis of alterations induced in nuclease sensitivity and transcriptional activity of the complexed DNA. Biochimica et Biophysica Acta 1997;1353:180-190.
2. Arscott PL, Knapp J, Rymaszewski M, Bartron JL, Bretz JD, Thompson NW, Baker JR Jr. Fas (AP0-1, CD95)-mediated apoptosis in thyroid cells is regulated by a labile protein inhibitor. Endocrinology 1997;138:5019-5027.
3. Baker JR Jr. Autoimmune Endocrine disease. JAMA 1997;278:1931-1937.
4. Qin L, Pahud DR, Din Y, Bielinska AU, Kukowska-Latallo JF, Baker JR Jr, Bromberg JS. Efficient transfer of genes into murine cardiac grafts by Starburst polyamidoamine dendrimers. Human Gene Therapy 1998;9:553-560.
5. Stokes TA, Rymaszewski M, Arscott PL, Wang SH, Bretz JD, Bartron JR, Baker JR Jr. Technical Comment: An examination of the expression of Fas and its ligand on thyrocytes. Science 1998;279:2015-2016.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Arscott PL, Baker JR Jr, Apoptosis and thyroiditis. Clinical Immunology and Immunopathology, in press.
2. Raczka E, Kukowska-Latallo JF, Rymaszewski M, Chen C, Baker JR Jr. The effect of synthetic surfactant Exosurf® on gene transfer in lung primary cells *in vitro* and in mouse lung *in vivo*. Gene Therapy, in press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Wang SH, Koenig RJ, Giordano T, Thompson NW, Baker JR jr. 1α,25-dihydroxyvitamin D3 up-regulates Bcl-2 expression and protects normal human thyrocytes from programmed cell death.

BOOKS AND CHAPTERS IN BOOKS:

None.

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

1. Arscott PL, Knapp J, Rymaszewski M, Bretz JD, Bartron JL, Thompson NW, Giordano T, Baker JR Jr. Induction of apoptosis through the Fas death pathway is blocked by a labile inhibitor in thyrocytes. The American Thyroid Association, Colorado Springs, CO, October 1997.
2. Rymaszewski M, Arscott PL, Knapp J, Bretz JD, Thompson NW, Bartron J, Baker JR Jr. An examination of Fas ligand expression on thyrocytes. The American Thyroid Association, Colorado Springs, CO, October 1997.
3. Bretz JD, Rymaszewski M, Baker JR Jr. IL-1ß induction of the BCL-2 gene family member BFL-1 is associated with protection against cell death in thyrocytes. The American Thyroid Association, Colorado Springs, CO, October 1997.
4. Dobracki AT, Bielinska AU, Baker JR Jr. The effect of phophodiester oligonucleotides on mediator release from mast cells. Annual Meeting, American Association of Allergy Asthma and Immunology, Washington, DC, March 1998.
5. Hayes MM, Cao Z, Chung Y, Wright DC, Brisker J, Baker JR Jr. Biocidal effect of unique lipid surfactants on *Bacillus* spores. Annual Meeting, American Society for Microbiology, Atlanta, GA, May 1998.
6. Hamouda T, Wright DC, Brisker JM, Baker JR Jr. Microbicidal effects of liposome-like microemulsions on pathogenic gram negative bacteria. Annual Meeting, American Society for Microbiology, Atlanta, GA, May 1998.
7. Reuter J, Hayes M, Roy R, Baker JR Jr. sialic acid conjugated dendritic polymers inhibit influence virus binding to target cells in a structural and virus strain-specific manner. Annual Meeting, American Society for Microbiology, Atlanta, GA, May 1998.
8. Wang SG, Koenig RJ, Giordano T, Thompson NW, Baker JR Jr. 1α,25-dihydroxyvital D3 up-regulates Bcl-2 expression and induces protection from the induction of programmed cell death in normal thyrocytes. Annual Meeting, The Endocrine Society, New Orleans, LA, June 1998.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Diagnostic Electron Microscopy, Veterans Affairs Medical Center; Director of Electron Microscopy Center of Excellence.
B. Cytopathology, Veterans Affairs Medical Center, Director Center of Excellence.
C. Surgical Pathology, Veterans Affairs Medical Center.
D. Fine Needle Aspiration, Veterans Affairs Medical Center.
E. Autopsy Pathology, Veterans Affairs Medical Center.
F. Tumor Board, Veterans Affairs Medical Center.
G. Chief Pathology and Laboratory Medicine, Ann Arbor and Toledo OPC, Veterans Affairs Health Systems.

II. TEACHING ACTIVITIES:

A. Pathology House Officer elective: Diagnostic Electron Microscopy and Cytopathology.
B. Diagnostic Electron Microscopy Case Conferences.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Tumor suppressor gene loci on chromosome 18 and prognosis in squamous cell carcinoma. (Co-investigator, Thomas E. Carey PI)
B. Head and Neck Oncology Program Project. (G.T.Wolf)

PROJECTS UNDER STUDY:

A. Clinical relevance of ultrastructural characteristics of small cell carcinoma of lung.
B. Utilization of plastic embedded cell blocks and electron microscopy in fine needle aspiration cytology.
C. DNA content as a predictor of chemotherapeutic response and prognosis in squamous cell carcinoma of the larynx. (with C.Bradford).
D. Differentiation of isolated renal tubular epithelial cells in culture (with D. Humes).
E. Apoptosis in lung injury (with J.L.Curtis).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Electron Microscopy Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Clinical Executive Committee, Veterans Affairs Medical Center.
B. Professional Standards Board, Veterans Affairs Medical Center.
C. Invasive Procedures Review Committee, Veterans Affairs Medical Center.
D. Electron Microscopy Committee, Veterans Affairs Medical Center.
E. Information Management Committee, Veterans Affairs Medical Center.
F. Cancer Committee, Veterans Affairs Medical Center.
G. Coordinator of Data Processing for Pathology and Laboratory Medicine Service, Veterans Affairs Medical Center.
H. Dean's Committee, Veterans Affairs Medical Center.
I. Faculty Management Committee, VISN#11, Department of Veteran Affairs.

REGIONAL AND NATIONAL:

A. Department of Veteran Affairs, Veterans Health Administration, Patient Care Services, Chief Consultant Officer, Diagnostic Services Strategic Healthcare Group.
B. Department of Veterans Affairs, Veterans Health Administration, Director Pathology and Laboratory Medicine.
C. National Veterans Affairs Pathology Field Advisory Board.
D. Armed Forces Institute of Pathology, Scientific Advisory Board.
E Association of Pathology Chairs, Veterans Affairs Committee, Consultant.
F. National Veterans Affairs Cytopathology Committee, Chair.
G. National Veterans Affairs Surgical Pathology Committee, Chair.
H. National Veterans Affairs Diagnostic Electron Microscopy Ad Hoc Advisory Group.
I. Laboratory Medicine Committee, Veterans Health Administration/Department of Defense/National Institutes of Health/Indian Health Service.
J. Interagency Coordinating Committee for Minority Health Care Careers, VHA/DOD/HHS/Commerce/DOE/NASA.
K. Department of Veterans Affairs, Veterans Health Administration, Office of Information Technology, Clinical Applications Requirement Group.
L. Department of Veterans Affairs, Veterans Health, Administration, Office of Information Technology, Laboratory Expert Panel.
M. National Committee for Clinical Laboratory Standards, Delegate.
N. Department of Veterans Affairs, Veterans Health Administration, Telemedicine Field Advisory Group.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Beals, T.F., VA/DOD Cooperative Review of Veteran's Tissue Specimens. The 1997 Edward Rhodes Stitt Lecture, Nashville.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Milik, A.M., Buechner-Maxwell, V.A., Sonstein, J., Kim, S., Seitzman, G.D., Beals, T.F., Curtis, J.L.. Lung lymphocyte elimination by apoptosis in the murine response to intratracheal particulate antigen. J. Clin. Invest. 99:1082-1091, 1997.
2. Su, L., Beals, T., Bernacki, E.G., Giordano, T.J.. Spindle epithelial tumor with thymus-like differentiation: A case report with Cytologic, histologic, Immunohistologic and ultrastructural findings. Mod. Pathol. 10:510-514,1997.
3. Jones, J.W., Raval, J.R., Beals. T.F., Worsham, M.J., VanDyke, D.L., Esclamado, R.M., Wolf,G.T., Bradford,C.R., Miller,T., Carey, T.E.. Frequent loss of heterozygosity on chromosome 18q in squamous cancers: Identification of two regions of loss – 18q11.1-12.3, and 18q21.1-23. Arch Otolaryn Head Neck Surg. 123:610-614, 1997.

BOOKS AND CHAPTERS IN BOOKS:

None.

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

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Six and a half months of Neuropathology Service.
B. Three weeks of Autopsy Service and seven weekends autopsy calls.
C. Muscle and nerve biopsies at the UMHS and referred by other hospitals in- and out-of-state throughout the year.
D. Consultations on brain biopsies, autopsied brains and rheumatology cases.

II. TEACHING ACTIVITIES:

A. Taught residents, fellows and staff in Neurology, Rheumatology and Pediatrics and medical and dental students on muscle, nerve and brain biopsies.
B. Taught Pathology Residents how to perform and read-out autopsies.
C. Lectures on muscle, nerve and brain pathology to residents in Pathology, Neurology, and Neurosurgery.
D. Conferences on muscle and nerve cases with Neurology Department.
E. Neuropathology cases review with Pathology Residents.
F. Weekly Conferences with Neuromuscular staff.
G. Conferences and lectures for Neurosurgery Residents and staff.
H. Monthly conferences for Rheumatology residents and staff.
I. Personal tutoring of neurology and pathology residents on Neuropathology – 7 persons

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Histology of animal models of rheumatoid arthritis with Arthritis and Rheumatology with Blake Roessler and Timothy Laing.
B. Urethral musculature in aging and incontinence, with John DeLancey group, Obstetrics/Gynecology.
C. Rat model in brain tumors growth and treatment, with Donald Ross, Neurosurgery and Philip Kish. (Grant application submitted.)
D. Genetic treatment of hemophilia in mice model, with Kotoku Kurachi's group in the Department of Genetics.
E. Neurochemical anatomy of human temporal lobe in epilepsy, with D. Ross and N. Selden, Neurosurgery.

F. Primary CNS vasculitis, with J. Trobe and A. Alrawi, Ophthalmology.
G. Evaluation of temporal lobectomy/hippocampectomy cases with epilepsy group.
H. Several projects with the epilepsy Division of Neurology.
I. Collaboration with EMG group, Radiology (S. Gebarski, M.D.), neurosurgery, pulmonary/internal medicine and ophthalmology on various projects.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL:

A. Member of the Admissions Committee.

REGIONAL AND NATIONAL:

A. Neuropathology conferences for pathology residents, St. John Hospital in Detroit.
B. Consulting with outside pathologists, neurologists and family practitioners on muscle and nerve biopsies performance and interpretation, brain biopsies.
C. Member, American Association of Neuropathologists, IAP, and AAN.
D. Attended the meeting of American Association of Neuropathologists and Swiss Society of Neuropathology XVII International Winter meeting with posters and platform presentation.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Tworek, J., Mikhail, A. and Blaivas, M.: Meningioma: Local recurrence and metastasis diagnosed by fine needle aspiration. Acta Cytol., 41, 3:946-947, 1997.
2. Robertson, P.L., Pavkovic, I., Donovan, C. and Blaivas, M.: Immature teratoma of the leptomeninges in an 8-year-old child: unusual presentation with recurrent transient oculomotor nerve pulses and rapid progression to diffuse brain ischemia. J. Child Neurology 13(3):143-145, March 1998.
3. Wang, J.M., Zheng, H., Blaivas, M. and Kurachi, K: Persistent systemic production of human factor IX in mice by skeletal myoblast-mediated gene transfer: feasibility of repeat application to obtain therapeutic levels. Blood 90:1075-1082, 1997.
4. Levy, R.A. and Blaivas, M.: Desmoplastic medulloblastoma: magnetic resonance imaging findings. AJNR 18:1364-1366, 1997.

5. Robertson, P.L., Muraszko, K.M., Blaivas, M. and Brunberg, J.A.: Symptomatic leptomeningeal fibrosis: association with delayed diagnosis of an intracranial PNET. Pediatric Neurology, 16, 1:74-78.
6. Sorenson, E.J., Sima, A.A.F., Blaivas, M., Sawchuk, K. and Wald, J.J.: Clinical features of perineuritis. Muscle and Nerve 20:1153-1157, 1997.
7. Cemeroglu AP, Blaivas M, Muraszko KM, Robertson PL, Vasquez DM. Lymphocytic hypophysitis presenting with diabetes insipidus in a 14-year old girl. Case report and review of the literature. Eur. J. Pediatric, 156:684-688, 1997.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Ross DA, Kish P, Muraszko KM, Speed G, Blaivas M, Strawderman M: Chemoprevention of ethylnitrosourea-induced rat gliomas by retinoic acid. Accepted To: Neurosurgery.
2. Schuh LA, Henry TR, Fromes G, Blaivas M, Ross DA, Drury I: Epilepsy predisposition and outcome following anterior temporal lobectomy. Accepted To: The archives of Neurology.
3. O'Brien A, Blaivas M, Albers J, Wald J, Watt C: A case of respiratory muscle weakness due to cytochrome C oxidase enzyme deficiency. Accepted To: European J. of Pulmonary Medicine.
4. Mikhail AA, Yamini B, McKeever PE, Blaivas M: MIB-1 proliferation index predicts survival among patients with grade II astrocytoma. Accepted To: J. Neuropathol. Exp. Neurol (in press).
5. Rodas RA, Fenstermaker RA, McKeever , Blaivas M, Dickinson L, Papadopoulos S, Hoff J, Hopkins LN, Fronckowiak MD, Greenberg H. Intraluminal thrombosis in brain tumor vessels correlates with post-operative deep vein thrombosis. Accepted To: J. Neurosurgery.

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

1. Sant S, Kaplan MJ, Stafford Johnson DB, Blaivas M, Ike RW: Myositis is not reliably predicted by magnetic resonance imaging in patients with suspected inflammatory myopathy. Presented at the American College of Rheumatology fall meeting. 1997..
2. Gebarski SS, Blaivas M: Five germinal matrices, not one: a unifying scheme for understanding migrational disorders. Presented at Swiss Society of Neuropathology XVII International Winter Meeting, St. Moritz, March 14-18, 1998.
3. Blaivas M, Gebarski S: Heterogeneity of the temporal lobe neoplasms. J. of Neuropathol and Experimental Neurol 1998, 57,5:504. Platform presentation at the AANP meeting, June 18-21, Minneapolis, MN.
4. Blaivas M: Role of Neuropathologist is Neurologist Education. Will be presented at the 3rd EFNS Congress, Seville, Spain, September 19-25, 1998.
5. Carney PR, Blaivas M, Drury I: Histopathological findings in a familial form of medically refractory temporal lobe epilepsy. To be presented at the American Epilepsy Society meeting in Fall 1998.
6. Thomas DA, Courblath WT, Blaivas M: Comitant strabismus in an older woman. Presented at the Frank B. Walsh meeting, 1998.
7. Minecan D, Blaivas M, Muraszko KM, Robertson PL: Progressive neurobehavioral encephalopathy, leptomeningeal fibrosis, hydrocephalus and multi-cystic brain lesions: An

unusual presentation of diffuse low-grade glial neoplasm. Will be presented at the 27th annual meeting of the Child Neurology Society, October 22-24, 1998.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Graduate Students: None.
B. Post-doctoral Fellow: Jianming Fang, M.D.
C. Undergraduate Students: NA
D. Courses:
   1. Anatomy and Cell Biology 680, University of Michigan Medical School, 1998.
   2. Pathology (Laboratory Section), University of Michigan, Medical School, 1988-1998.
   3. Molecular Cell Biology, University of Michigan, School of Medicine (Wound Healing Section, 1993-1998.
   4. Pathology 581, University of Michigan, Graduate School (Course Director), 1994-1998.
E. Continuing Medical Education: None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

1. Sponsored Research Agreement with Matrigen, Inc., DRDA 953008, "Direct Osteoinductive Gene Transfer", 1995-.
2. NIDR, National Institutes of Health, 1 P20 DE12387-01, "Center for Restoration of Oral Health", 1997-1998.
3. NIDR, National Institutes of Health, 1 R01 DK53904-01, "Anabolic Mechanisms of PTH Action in Bone", 1998-2002.
4. NIDR, National Institutes of Health, 1 R01 HL60473-01, "Regulated Osteoinductive Plasmid Gene Transfer Via Gene Activated Matrices", 1998-2003.
5. NIDR, National Institutes of Health, 1 R01 HL60473-01, "Mechanically Guided Tissue Regeneration", 1998-2003.
6. NIDR, National Institutes of Health, P60DE13062, "Center for Biorestoration of Oral Health", 1999-2004 (Pending approval).

PROJECTS UNDER STUDY:

1. Molecular cloning of activins, members of the TGF-β superfamily
2. Direct gene transfer in vivo

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

None.

DEPARTMENTAL:

Oversight Committee, Graduate Program, 1989 - 1998

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Ad-hoc Reviewer:
American Journal of Pathology
Orthopedic Research and Education Fund
Journal of Clinical Investigation
American Journal of Human Genetics
Spine
Experimental Cell Research
NIH, NIAMSD (Special Study Section), Teleconference, 1998.

B. Consultant Editor:
European Journal of Experimental Musculoskeletal Research, 1991 -

C. Member:
U-M Multipurpose Arthritis Center
Michigan Cancer Center
U-M Bioengineering Program

INVITED LECTURES AND SEMINARS:

1. "Pharmaceutical gene delivery for bone repair". NMHCC Conference: Orthopedic Tissue Engineering: Rebuilding Bone, Cartilage, Ligament, and Tendon, Boston, MA, August 1997.
2. "GAM plasmid gene delivery for tissue repair and regeneration". Sprout Group, Menlo Park, CA, September 1997.
3. "GAM plasmid gene delivery for tissue repair and regeneration". Institutional Venture Partners, Menlo Park, CA, September 1997.

4. "GAM plasmid gene delivery for tissue repair and regeneration". U.S. Venture Partners, Menlo Park, CA, September 1997.
5. "GAM plasmid gene delivery for tissue repair and regeneration". Robertson Stephens & Company, San Francisco, CA, September 1997.
6. "GAM plasmid gene delivery for tissue repair and regeneration". Weiss, Peck & Greer Venture Partners, L.P., San Francisco, CA, September 1997.
7. "GAM plasmid gene delivery for tissue repair and regeneration". Domain Associates, Costa Mesa, CA, September 1997.
8. "GAM plasmid gene delivery for tissue repair and regeneration". Atlas Venture, Boston, MA, September 1997.
9. "GAM plasmid gene delivery for tissue repair and regeneration". Highland Capital Partners, Boston, MA, September 1997.
10. "GAM plasmid gene delivery for tissue repair and regeneration". Johnson & Johnson Professional, Inc., Raynham, MA, September 1997.
11. "GAM plasmid gene delivery for tissue repair and regeneration". Genetics Institute, Cambridge, MA, October 1997.
12. "GAM plasmid gene delivery for tissue repair and regeneration". Creative BioMolecules, Hopkinton, MA, October 1997.
13. "Pharmaceutical gene delivery for tissue repair / regeneration", (Session Chair). Keystone Symposium on Tissue Engineering, Copper Mountain, CO, January 1998.
14. "GAM plasmid gene delivery for tissue repair and regeneration". Novartis Pharma AG, Summitt, NJ, April 1998.
15. "GAM plasmid gene delivery for tissue repair and regeneration". U.S. Surgical Corporation, Norwalk, CT, June 1998.
16. "GAM plasmid gene delivery for tissue repair and regeneration". Ortho-McNeil, Summitt, NJ, June 1998.
17. "Gene therapy for wound healing: DNA as a pharmaceutical". Scios Nova, Mountain View, CA, January 1996.
18. "GAM plasmid gene delivery for tissue repair and regeneration". Johnson & Johnson, Corporate Office of Science and Technology, New Brunswick, NJ, June 1998.
19. "Gene activated matrices: tissue engineering implants for bone regeneration". The Wound Healing Society Eighth Annual Meeting, Salt Lake City, UT, June 1998.
20. "Gene therapy applications for orthopaedic tissue engineering". NMHCC Bio/Technology Division, 2nd Annual Orthopaedic Tissue Engineering Conference, Boston, MA, August 1998.
21. "Gene activated matrices: tissue engineering implants for bone regeneration". Euroconference: Tissue and Cell Engineering, Park Hotel Suisse, Santa Margherita Ligure (Italy), September 1998.
22. "New activins: expression and action". 189th meeting of the Society for Endocrinology, Royal College of Physicians, London, England, November 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Jepsen, K.J., Schaffler, M.B., Kuhn, J.L., Goulet, R.W., Bonadio, J., and Goldstein, S.A. (1997) Type I collagen mutation alters the strength and fatigue behavior of Mov13 cortical bone. J. Biomechanics 30, 1141-1147.
2. Fang, J., Li, X., Smiley, E., Francke, U., Mecham, R.P., and Bonadio, J. (1997) Mouse latent TGF-β binding protein-2: molecular cloning and developmental expression. Biochim. Biophys. Acta 1354, 219-230.
3. Yin, W., Smiley, E., and Bonadio, J. (1998) Alternative splicing of LTBP-3. Biochem. Biophys. Res. Comm. 245, 655-661.
4. Pezzuti, J.A., Morris, M.D., Bonadio, J., and Goldstein, S.A. (1998) Hyperspectral Raman imaging of bone growth and regrowth chemistry. Proc. SPIE 3261, 270-276.
5. Yin, W., Fang, J., Smiley, E., and Bonadio, J. (1998) 8-cysteine TGF-bp structural motifs are the site of covalent binding between mouse LTBP-3, LTBP-2, and latent TGF-β1. Biochim. Biophys. Acta 1383, 340-350.
6. Adami, R.C., Collard, W.T., Gupta, S.A., Kwok, K.Y., Bonadio, J., and Rice, K.G. (1998) Stability of peptide-condensed plasmid DNA formulations. J. Pharm. Sci. 87, 678-683.

BOOKS/CHAPTERS IN BOOKS:

1. Bonadio, J., Goldstein, S.A., and Levy, R.J. Gene therapy for tissue repair and regeneration. Advanced Drug Delivery Reviews, in press.

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

1. Bonadio, J. Pharmaceutical Gene Delivery for Tissue Repair / Regeneration, Invited presentation, Keystone Symposium on Tissue Engineering. Copper Mountain, CO, January 1998.
2. Adami, R.C., Collard, W.T., Gupta, S.A., Kwok, K.Y., Bonadio, J., and Rice, K.G. Stability of peptide condensed plasmid DNA formulations. Midwest Regional American Association of Pharmaceutical Scientists meeting, Chicago, IL, May 1998.
3. Lau, A.L., Quixia, G., Bonadio, J., and Matzuk, M.M. In vivo functions of liver-specific TGF-β superfamily members. 57th Annual meeting of the Society for Developmental Biology, Stanford University, Palo Alto, CA., June 1998.
4. Bonadio, J. Gene Activated Matrices: Tissue Engineering Implants for Bone Regeneration. The Wound Healing Society Eighth Annual Meeting, Salt Lake City, UT, June 1998.
5. Bonadio, J. New activins: Expression and Action. 189th meeting of the Society for Endocrinology, Royal College of Physicians, London, England, November 1998.

PRISCILLA CHAMBERLIN, M.D.
CLINICAL INSTRUCTOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Surgical Pathology sign out – 6 months
B. Director of Cytology with primary sign out responsibilities

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Sophomore pathology lab
      b. Pathology residents

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

PENDING:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Medical Director of Microbiology, Immunology and Chemistry labs at VA Hospital
B. Lab Reorganization Committee Chair

MEDICAL SCHOOL/HOSPITAL:

A. Admissions Committee

UNIVERSITY OF MICHIGAN:

None.

REGIONAL AND NATIONAL:

None.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

None.

HONORS AND AWARDS

None.

PATENTS:

None.

INVITED LECTURES/SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

None.

BOOKS/CHAPTERS IN BOOKS:

None.

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

None.

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

ANNUAL DEPARTMENT REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Director, Clinical Laboratories, Veterans Affairs Medical Center, responsibilities include, equipment and methodology evaluation, review and consultation regarding quality management programs, personnel evaluation, counseling and grievance procedures.
B. Hematology, daily evaluation of pathologist referred blood smears, bone marrow smears, Veterans Affairs Medical Center.
C. Surgical/Frozen Section Diagnosis and Quality Control, (4 months in 1997, approx. 2000 cases).
D. Autopsy Service, rotational basis, on call 13 weeks/year (staffing 15-20 cases/year).
E. Special Chemistry/Immunology, daily interpretation of protein electrophoreses, isoenzyme studies, and problem ligand studies (approx. 1000 cases/year), Veterans Affairs Medical Center.
F. Blood Bank, consults and investigations, full time as needed, Veterans Affairs Medical Center.

II. TEACHING ACTIVITIES:

A. Pathology house officers, Surgical Pathology/Autopsy supervision and instruction, (5 months/year).
B. Technologists, technicians and hospital staff, ongoing continuing medical education instruction on clinical laboratory topics.
C. Graduate students, mentor training toward doctoral degrees.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, Cytokine Cascades in Granuloma Formation VAMC Merit Review Grant, ($93,000 direct costs annually, 1997-2000).
B. Principal Investigator, Chemokine Receptor Dynamics in Granuloma Formation, NIH AI43460 ($115,000 direct costs annually, 1998-2001)
C. Principal Investigator, Prostate Carcinoma Bone Metastasis in a SCID-hu Mouse Model, VERAM ($5,000, annually 1998)

PROJECTS UNDER STUDY:

A. Cytokine manipulation of mycobacterial (Th1) and schistosomal (Th2) Ag mediated forms of hypersensitivity granuloma formation.
B. Regulation of chemokine receptor expression during Th1 and Th2 immune and inflammatory responses.

C. Role of chemotactic cytokines in granulomatous inflammation and Th1 and Th2 cell expression.
D. Regulation of chemotactic cytokine production by leukocytes and stromal cells.
E. Analysis of eosinophil recruitment factors in type 2 granulomatous inflammation.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Graduate Program Exam Committee
B. Member of graduate student thesis committees.
C. Interviewing and evaluation of residents and faculty.

MEDICAL SCHOOL/HOSPITAL:

A. Blood Utilization Review Committee, Veterans Affairs Medical Center, Chairman.
B. Ambulatory Care Committee, Veterans Administration Medical Center.
C. Research Animal Use Committee, Veterans Administration Medical Center.
D. Personnel employment and annual evaluations.
E. Anatomic Pathology Quality Assurance evaluation and reporting
F. Editor, VA Labs Newsletter.

REGIONAL AND NATIONAL:

A. Editorial Review:
   1. American Journal of Pathology.
   2. Journal of Immunology.
   3. Inflammation Research, Section Editor.
   4. American Journal of Respiratory Cell and Molecular Biology.
   5. Journal of Clinical Investigation.
   6. Parasitology.
B. Medical Advisory Committee, American Red Cross, SMBSR.

V. OTHER RELEVANT ACTIVITIES:

A. Case presentations at Tumor Board and Morbidity and Mortality Conferences.
B. Tissue evaluation for clinical researchers.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chensue, S. W., Warmington, K.S., Ruth, J.H., N. Lukacs and S.L. Kunkel. Mycobacterial and Schistosomal antigen-elicited granuloma formation in interferon-g and interleukin 4 knockout mice: Analysis of local and regional cytokine and chemokine networks. J. Immunol. 1997, 159:3565-3573.

2. Cameron, M. J., Arreaza, A., Zucker P., Chensue, S.W., Strieter R. M., Chakrabarti, S., and Delovitch, T.L. IL-4 prevents insulitis and IDDM in nonobese diabetic mice by potentiation o regulatory Th2 cell function. J. Immunol. 1997, 159:4686-4692.
3. Arreaza, A., Cameron, M. J., Jaramillo, A., Gill, B.M., Hardy, D., Laupland K.B., Rapoport M.J., Zucker P., Chensue, S.W., Chakrabarti, S, Qin, H.Y. Singh, B. and Delovitch, T.L.Neonatal activation of CD28 signaling overcomes T cell anergy and prevents autoimmune diabetes by an IL-4 dependent mechanism. J. Clin. Invest. 1997 100(9):2243-53.
4. Boring, L., Gosling, J., Chensue, S.W., Kunkel, S.L., Farese, R.V., Broxmeyer, H.E., and Charo, I.F. Impaired monocyte migration and defects in type 1 cytokine (Th1) responses in CCR2 knockout mice. J.Clin. Invest. 1997, 100:2552-2561.
5. Hogaboam, C. M., Chensue, S. W., Steinhauser, M. L., Huffnagle, G. B., Lukacs, N. W., Strieter, R. M. and Kunkel, S. L. Alteration of the cytokine phenotype in an experimental granuloma model by inhibiting nitric oxide. J. Immunol. 1997, 159:5585-5593.
6. Hogaboam C. M., Lukacs N. W., Chensue S. W., Strieter R.M. ,Kunkel SL. Monocyte chemoattractant protein-1 synthesis by murine lung fibroblasts modulates CD4+ T cell activation. J. Immunol. 1998, 160:4606-4614.

BOOKS AND CHAPTERS IN BOOKS:

1. Hogaboam, C.M., Chensue S.W., and Kunkel, S.L. Role of C-C chemokines in Th1- and Th2-type pulmonary Inflammation models. *In,* The Role of Chemokines in the Progression of Chronic Inflammatory Disease, Human Press 1998.

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

1. Chensue, S.W., Boring, L., Warmington, K.S., Ruth, J.R., Charo, I.F. and Kunkel, S.L. Effect of C-C chemokine receptor 2 knockout on schistosomal egg antigen-elicited granuloma formation and the regional lymphoid response. FASEB J. 1998, 12:A3757.
2. Hogaboam, C.M., Bone-Larson, C., Lipinski, S., Lukacs, N.W., Strieter, R.M., Chensue, S.W., and Kunkel, S.L. Differential MCP-1 and CCR2b expression by murine lung fibroblasts derived from Th1-type and Th2-type pulmonary granuloma models. FASEB J. 1998, 12:A3756.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Occasionally work with house officers and staff in Pathology and other departments in the gross and microscopic examination of dementia brains from autopsies at University Hospital.
B. Occasionally attend and instruct house officers in the removal and gross examination of brains from autopsies at University Hospital.
C. Work with Neuropathology Staff on autopsy brain material sent for consultative study from University-associated hospitals, other hospitals, and institutions.
D. Work with house officers in planning Dementia 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 every two months for the Neurology Department, and occasionally for their Grand Rounds.
F. Continuous review of quality control of diagnostic techniques, and autopsy neuropathology, and search for improved and new methods.
G. Co-coordinator, Neuropathology Core Laboratory, MADRC.

II. TEACHING ACTIVITIES:

A. Neuroscience Sequence, Neuropathology for Second Year Medical Students, two-one hour lectures, eight hours laboratory, and sequence coordinator for the eight week sequence.
B. Neuropathology for Pathology house officers. This exercise is integrated with Clinical Activities A, B, and D.
C. Neuropathology 858. Intensive laboratory-lecture course for house officers and fellows, in Pathology and in the several clinical services concerned with the nervous system, and medical students, graduate students, and faculty; implement, plan, and teach the course. Annual, 8 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 (MADRC).

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Co-Investigator with Dr. Anders Sima on Michigan Alzheimer Disease Research Center Project, The Pathology of Diffuse Lewy Body Disease. June, 1994 -.
B. The Pathologic Examination of Human Autopsy Brains From Patients With Clinical Diagnosis of Alzheimer's, Huntington's, Pick's and Other Dementing Diseases is being done in collaboration with Dr. Roger Albin, in the Michigan Alzheimer Disease Research Center.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Anatomic Pathology Committee.
B. Organize and teach the Neuropathology 858 Course.

MEDICAL SCHOOL/HOSPITAL:

A. Coordinator for the Neuroscience Sequence, 2nd year medical students.
B. Neuroscience Curriculum Committee, Chairman.
C. Coordinator for Neuropathology, Neuroscience Sequence.
D. Neuroscience Examination Committee, Chairman.
E. Admissions Committee, the University of Michigan Medical School.
F. Curriculum Policy Committee (Elected).

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

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

VI. PUBLICATIONS:

ARTICLES ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS, BOOK CHAPTERS:

1. Sima AAF, D'Amato, CJ: Dementias and other neurodegeneration diseases. In: Neuropathology: The Diagnostic Approach, J. Garcia (ed.), Philadelphia, Mosley. Pp 637-668, 1997.

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

1. Erickson SL, Gao W-O, Shinsky N, Kljavin I, Gerlai R, D'Amato CJ, O'Shea KS: Neurological examination of heregulin, ErbB2, and ErbB3 heterozygous null mice: nerve conductivity velocity measurements, nerve crush analysis and behavior. Society for Neuroscience 23:865, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Associate Medical Director, Blood Bank and Transfusion Service, University of Michigan Hospitals.
B. Cytopathology, consultation and staff coverage.

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. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
   1. Presented workshop entitled: "Coagulation Review for Blood Bankers".
   2. Presented talk entitled: "Role of Cytokines in Transfusion Medicine".
D. Clinical Pathology Grand Rounds: "Transfusion Reactions", May 15, 1998.
E. Teleconference: "Transfusion Reactions", University of Texas Teleconference Network of Texas. February 10, 1997.
F. Invited lecture: "Cytokines in Transfusion Reactions", Blood Bank Supervisors Association of New York, April 4, 1997.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "A Murine Model of Hemolytic Transfusion Reactions", National Blood Foundation.

PROJECTS UNDER STUDY:

A. Cytokine production in hemolytic transfusion reactions.
B. Cytomegalovirus reactivation by blood transfusion.
C. Enzyme converted red blood cells.
D. Mechanisms of action of leukoreduction filters.
E. Mechanisms of hypotensive transfusion reactions.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Transfusion Committee.

V. OTHER RELEVANT ACTIVITIES:

A. President-elect, Michigan Association of Blood Banks.
B. Executive Committee, Michigan Association of Blood Banks.
C. Program Committee, Michigan Association of Blood Banks.
D. Scientific Section Coordinating Committee, American Association of Blood Banks.
E. Editorial Board, Transfusion.
F. Reviewer, Transfusion.
G. Reviewer, Chest.
H. Reviewer, American Journal of Clinical Pathology.
I. Reviewer, Journal of Clinical Investigation.

VI. PUBLICATIONS:

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Davenport RD, Penezina OP: Cleavage of high molecular weight kininogen induced by filtration of platelet concentrates. Submitted to Transfusion.

ABSTRACTS, AND PRESENTED PAPERS:

1. Penezina OP, Fomovskaia GN, Haddock TF, Davenport RD: Specific adhesion of human leukocytes to magnetic polyester beads, modifies with Ca2+ independent ligands to L-selectin. FASEB J 11:A1093, 1997.
2. Davenport RD, Kunkel SL: Characterization of a murine model of hemolytic transfusion reactions. Transfusion 37:1S, 1997.
3. Davenport RD, Penezina OP: Cleavage of high molecular weight kininogen induced by filtration of platelet concentrates. Transfusion 37:104S, 1997.
4. Judd WJ, Davenport R. On the high probability that a perceived lack of value of obtaining a p value will be detrimental to patient care! (letter) Transfusion 37:866, 1997.

CHAPTERS IN BOOKS:

1. Davenport RD: Management of transfusion reactions. In: Mintz PD (ed):Practice Guidelines for Transfusion Therapy. AABB Press, Bethesda, MD (in press).
2. Davenport RD: The immune system: an overview. In: Vamvakas S, Blajchman MD (eds): Immunomodulatory Effects of Blood Transfusion. AABB Press, Bethesda, MD (in press).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997-30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Co-Director, Genomic Pathology Laboratory

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. None

REGIONAL AND NATIONAL:

A. Member, Scientific Advisory Committee, NSF Center for Light Microscopy, Carnegie Melon University, Pittsburgh, PA

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Editorial Board Member, Drug Metabolism Reviews

INVITED LECTURES/SEMINARS:

1. "Genotyping and Primer Extension Preamplification Applications in Preclinical and Clinical Pathology Testing", San Diego, CA, August 1997.
2. "Cellular Changes in Intestinal Mucosa of Wistar Rats After Epidermal Growth Factor 1-48", Society of Toxicology, Cincinnati, OH, March 1997.
3. "Phenobarbital Modulation of Cobalt Mesoporphyrin Effects on Cytochrome P450 in Rat Liver", Society of Toxicology, Seattle, WA, March 1998.
4. "Absence of P53 Inactivation in Mouse Vascular Tumors", Society of Toxicology, Seattle, WA, March 1998.
5. "Carcinogenicity Study of the Antidiabetic Troglitazone in Wistar Rats", Society of Toxicology, Seattle, WA, March 1998.
6. "Carcinogenicity Study of the Antidiabetic Troglitazone in B6C3F1 Mice", Society of Toxicology, Seattle, WA, March 1998.
7. "Chronic Toxicity Study of the Antidiabetic Troglitazone in Wistar Rats", Society of Toxicology, Seattle, WA, March 1998.
8. "Differential Effects of epidermal Growth Factor in Intestinal Mucosa From Non-Human Primates", American Society of Pathology Investigative, San Francisco, CA, April 1998.
9. "Effects of Troglitazone on Adipocyte Populations in Mice, Rats, and Monkeys", American Society of Investigative Pathology, San Francisco, CA, April 1998.
10. "In Vitro Subcellular Changes by Acridines in Human Hepatocytes", American Society of Investigative Pathology, San Francisco, CA, April 1998.
11. "Approaches to Understanding Species Differences in Hepatotoxic Responses to Therapeutic Agents", Japanese Society of Toxicology, Nagoya, Japan, June 1998

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. D.K. Monteith, J.C. Theiss, J.R. Haskins and F.A. de la Iglesia. Functional and Subcellular Organelle Changes in Isolated Rat and Human Hepatocytes induced by Tetrahydroaminoacridine Arch. Toxicol. 72: 147-156, 1998

2. D. G. Robertson, T. K. Braden, E. R. Urda, N. D. Lalwani and F. A. de la Iglesia. Elucidation of Mitochondrial Effects by Tetrahydroaminoacridine (Tacrine) in Rat, Dog, Monkey and Human Hepatic Parenchymal Cells. Arch. Toxicol. 72: 362-371, 1998
3. J. Sims, F. de la Iglesia. Designing Non-Clinical Safety Evaluation Programmes for Colony Stimulating Factors, Growth Factors and Hormones: Recommendations and the Way Forward. Human Exper Toxicol 17: 63-83, 1998
4. D.R. Plymale and F. A. de la Iglesia. Acridine-Induced Subcellular and Functional Changes in Isolated Human Hepatocytes In Vitro. J. Appl. Toxicol.(In press, 1988)

ARTICLES SUBMITTED FOR PUBLICATION:

1. F. A. de la Iglesia, C. J. Di Fonzo, R. A. Martin, E. J. McGuire and G. Feuer. Quantitative Microscopic Changes of the Functionally Impaired Hepatic Endoplasmic Reticulum in a Proposed Cholestasis Rat Model. Drug Chem. Tox. (submitted 1998).
2. M.A. Breider, A.W. Gough, J.R. Haskins, G. Sobocinski and F.A. de la Iglesia Effects of Troglitazone on Cell Proliferation in Murine Cardiac and Adipose Tissue.(Submmitted, 1998)
3. J.C. Theiss, S. Bulera, T. Festerling and F.A. de la Iglesia In Vitro Photogenotoxic Activity of Clinafloxacin: A Paradign Predicting Photocarcinogenicity. Tox. Appl. Pharm. (Submmitted, 1998)
4. D.R. Plymale and F.A. de la Iglesia Coherent, Multiparameter, real-Time Fluorescence for Monitoring Subcellular Toxicity of Hepatocytes In Vitro. Nature Medicine (Submmitted, 1988)
5. S.K. Duddy, R.F. Parker, M.R. Bleavins, A.W. Gough, P.E. Rowse, S. Gorospe, L.A. Dethloff and F.A. de la Iglesia P53 is not inactivated in B6C3F1 Mouse Vascular Tumors Arising Spontaneously or Associated with Long-term Administration of the Thiazolidindione, Troglitazone. (Submitted, 1998)
6. N.D. Lalwani, D.G. Robertson, R.E. Sigler, W. tefera, M.R. Bleavins, A. W. Gough and F.A. de la Iglesia. H-ras DNA Methylatiuon Pattern and Genomic Instability in the Pancreas of Rats Fed Soybean Diets and Gabapentin. (Submitted)
7. F.A. de la Iglesia, R. Walker, C.J. DiFonzo, R.A. Martin, E.J. McGuire and G. Feuer. Metabolic Effects of Antiinfective Agents on the Liver of Common Marmosets (Callithrix jacchus) Arch. Toxicol. (Submitted 1998)
8. G. Feuer, M.S.I. Dhami, and F.A. de la Iglesia. Changes by Progestrone Derivatives in Fatty Acids from Phosphatidylcholine and Phosphatidylethanolamine Fractions in Rat Liver Endoplasmic Exp. Toxicol. Path. (Submitted)
9. E.J. McGuire and F.A. de la Iglesia Hypolipidemic. Effects on Rat Liver Mitochondria Studied by Quantitative Microscopy. Human Exper. Toxicol. (Submitted)

BOOKS/CHAPTERS IN BOOKS:

1. A. L. Metz, A. W. Gough, D. G. Robertson, F. A. de la Iglesia and S. P. Bishop. Agents Associated with the Development of Cardiac-Hypertrophy and/or Cardiac Failure. In: Comprehensive Toxicology, Volume 6: Cardiovascular Toxicology. Editors: Sipes, I.G., McQueen C.A. and Gandolfi A.J. Elsevier, Oxford, UK. P385-407, 1997

2. F. A. de la Iglesia, D. G. Robertson and J. R. Haskins. Morphofunctional Aspects of the Hepatic Architecture: Functional and Subcellular Correlates. In: Handbook of Drug Metabolism. T. Woolf (Ed.) Marcel Dekker (in press 1998).
3. F.A. de la Iglesia. Approaches to Understanding Species Differences in Hepatotoxic Responses to Therapeutic Agents. Proceedings, Ann. Mtg. Japan. Soc. Tox. p1-5, 1998

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

1. D.R. Plymale, R. Rahjbari, J.R. Haskins, F.A. de la Iglesia. In Vitro subcellular Changes by Acridines in Human Hepatocytes. FASEB Journal, 12:A798, 1998
2. M.R. Bleavins, J.D. Haskins, S.K. Duddy, E.J. McGuire, F. A. de la Iglesia. Effects of Troglitazone on adipocyte Populations in Mice, Rats, and Monkeys. FASEB Journal, 12:A376, 1998
3. J.R. Haskins, J.F.Reindel,M.R. Bleavins, F.A. de la Iglesia. Differential Effects of epidermal growth Factor in intestinal Mucosa From Non-Human Primates. FASEB Journal, 12:A376, 1998
4. R.M.Walker,Z.W.Wojcinski,L.M.King,F.A. de la Iglesia. Phenobarbital Modulation of cobalt Mesoporphyrin Effects on Cytochrome P450 in Rat Liver. Toxicological Sci., 42: 369, 1998
5. S.K. Duddy, R.F. Parker, M.R. Bleavins, A.W. Gough, P.E. Rowse, L.A. Dethloff, F. A. de la IglesiaAbsence of P53 Inactivation in Mouse Vascular Tumors. Toxicological Sci.,42: 319-320, 1998
6. J.R. Herman, E.J. McGuire, F. A. de la Iglesia, K.M. Walsh, H. Masuda. Carcinogenicity Study of the Antidiabetic Troglitazone in Wistar Rats42: 71, 1998
7. E.J. McGuire, L.A. Dethloff, R.S. Parker, F.A. de la Iglesia, A.W. Gough and H. Masuda. Carcinogenicity Study of the Antidiabetic Troglitazone in B6C3F1 Mice. Toxicological Sci., 42: 50, 1998
8. F.A. de la Iglesia, J.R.Herman, E.J. McGuire, A.W. Gough and H. Masuda. Chronic Toxicity Study of the Antidiabetic Troglitazone in Wistar Rats. . Toxicological Sci., 42: 50, 1998
9. M. Bleavins, T. Gipson, S. Duddy, F. de la Iglesia. Genotyping and Primer Extension Preamplification Applications in Preclinical and Clinical Pathology TestingClinical Chem. 43:2214,1997
10. F. de la Iglesia, A. W. Gough, R. E. Sigler Letter to Editor: a2u-Globulin Nephropathy and Ravens: Letter to the Editor: Do Ravens of a Different Feather Flock Together? Environmental Health Perspectives.
11. L.A. Dethloff and F.A. de la Iglesia Chemically-Induced Ploidy Changes. Letter to the Editor. Tox. Appl. Pharm. 150: 443, 1998

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Second Year Medical Students - Renal Section, one full lecture.
B. Graduate Students Supervised - Martin Powers, MSTP.
C. Post-doctoral Trainees Supervised - Mark Lechner, Ph. D.; Eun Ah Cho, Ph. D., Julie Martin, Ph. D.
D. Ph. D. Thesis Committee Member - Laura Post, Dept. of Genetics; Kris Coulter, Dept. of Genetics.

MEDICAL SCHOOL/HOSPITALS:

None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, Howard Hughes Medical Institute - 001819, "Analysis of Mammalian Developmental Control Genes", (50%), October 1, 1994-September 30, 1998. Approximately $250,000 current year (including staff salaries, supplies and travel) excluding PI's salary and benefits. The actual budget is negotiated yearly.
B. Principal Investigator, "PAX-2 in Normal and Cystic Epithelium Development", NIH/NIDDK - R01 DK51043-02, (25%), September 30, 1995-August 31, 2000. Direct costs approximately $100,000 requested annually.
C. Sponsor, WELLCOME TRUST, "Regulation of PAX-2 in Normal and Cystic Epithelium", Fellowship recipient: Julie Martin, Awardee, Gregory Dressler, Sponsor, (5%), March 1, 1996-February 28, 1998. Direct costs/year (supplies only)-$5,400.

PROJECTS UNDER STUDY:

A. The identification of co-factors required for Pax protein mediated transcription activation.
B. The development of novel methods for identifying genes regulated by Pax proteins.

C. The role of Pax-2 in the initiation and progression of polycystic kidney disease.
D. The GDNF/RET signaling pathway in the developing kidney.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A Department of Pathology - Preliminary Exam Committee.
B. Center for Organogenesis - Interim Co-Director, Steering Committee, Training Grant Review Committee, Advisory Committee.

REGIONAL AND NATIONAL:

NIH Study Section, General Medicine B, Ad-hoc reviewer.
NIDDK, Renal Program Project Grants, Site visit reviewer.
American Journal of Physiology, Editorial Reviews Board.

Reviewer for: Mechanisms of Development, Development, Proceedings of the National Academy of Sciences, Developmental Dynamics, Journal of Biological Chemistry, Nature, American J. of Physiology, Journal of Clinical Investigation, Molecular and Cellular Biology, Genes & Development.

V. OTHER RELEVANT ACTIVITIES:

A. Membership in the American Society of Nephrology.
B. Membership in Society for Developmental Biology.
C. Membership in University of Michigan Comprehensive Cancer Center.
D. Membership in the Center for Organogenesis, University of Michigan.

INVITED LECTURES/SEMINARS:

1. International Society of Developmental Biology, annual meeting, Snowbird, UT, (speaker & session chair), July 5-10, 1997.
2. NIDDK Workshop on Polycystic Kidney Disease, Crystal City, VA, Sept. 9-10, 1997.
3. HHMI Annual Meeting, Chevy Chase, MD, Nov. 1997.
4. Experimental Biology 98, San Francisco, CA, April 18-21, 1998.
5. Division of Biological Sciences, University of Edinburgh, Edinburgh, UK, May 14, 1998.
6. Dept. of Biochemistry, University of Virginia Medical center, Charlottesville, VA, May 28, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Valentini, R., Brookhiser, W.T., Park, J., Yang, T., Briggs, J., Dressler, G.R. and Holzman, L.B. (1997). Post-translational processing and renal expression of mouse indian hedgehog cDNA. J. Biol. Chem. 272:8466-8473.
2. Lechner, M.S., and Dressler, G.R. (1997). The molecular basis of embryonic kidney development. Mechanisms of Development. 62:105-120.
3. Cho, E. A., Patterson, L.P., Brookhiser, W.T., Mah, S., Kintner, C. and Dressler, G.R. (1998) Expression and function of cadherin-6 in the developing kidney. Development 125, 803-812.
4. Cho, E.A. and Dressler, G.R. (1998) Mouse Tcf-4 binds β-catenin and is expressed in distinct regions of the developing brain and limbs. Mech. Develop. in press.
5. Tang, M.J., Worley, D., Sanicola, M. and Dressler, G.R. (1998) Migration and chemoattraction of RET expressing epithelial cells in response to GDNF. J. Cell Biol. in press.
6. Yang, Y., Jeanpierre, C., Dressler, G.R., Lacoste, M., Niaudet, P. and Gubler, M.-C. (1998) WT1 and Pax-2 podocyte expression in Denys-Drash syndrome and isolated diffuse mesangial sclerosis. Am. J. Pathol. in press.

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Schwarz, M., Alvarez-Bolado, G., Urbanek, P., Busslinger, M., Dressler, G.R., and Gruss, P. (1998) The forebain/midbrain boundary formation depends on the interaction between Pax6 and Pax2/5.
2. Leavey, S.F., Arend, L.J., Dare, H., Dressler, G.R., Briggs, J.P., Margolis, B.L. (1998) Expression of the growth factor receptor signaling protein Grb7 in kidney development and in the adult kidney.
3. Lechner, M.S. and Dressler, G.R. (1998) PTIP: A novel BRCT-domain protein interacts with the Pax family of transcription factors.

BOOK CHAPTERS:

None.

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

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Director, Ligand Assay Laboratory.

II. TEACHING ACTIVITIES:

A. Instructor for Pathology House Offices Laboratory Rotation.
B. Instructor for Nuclear Medicine Residents Laboratory Rotation.
C. Participant, Clinical Pathology Grand Rounds.
D. Instructor for Medical Student (M-4) rotation through Chemistry Laboratories.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH: P60 DK 20572 (D. Greene) 12/01/97 - 11/30/02
Michigan Diabetes Research and Training Center
$123,404 Direct Costs (Clinical Implementation Core)
Consultant with 5% Effort.
1. The major goals of this project provide laboratory support for diabetes related research conducted by the Michigan Diabetes Research and Training Center investigators.

B. NIH/NIA: U01 AG 12495 (AR Midgley) 09/30/94 - 05/31/99.
Study of Women's Health Across the Nation: Menopause and Aging in Women
$694,405 Direct Costs (Central Laboratory)
Associate Lab. Director with 10% Effort.
1. The major purpose of this Central Laboratory for the U01 Cooperative Agreement on Menopause and Health in Aging Women will provide participating Clinical Sites with assistance, service, and state of the art assays for markers of ovarian aging that are reliable, accurate and precise.

C. Chiron Diagnostic Corporation (BG England) 11/01/97 - 10/31/99.
CCD Chemical Pathology Fellowship
$30,000 Direct Costs
Principle Investigator with 0% Effort.
1. The major goals of this project are to provide postdoctoral training in the general area of Endocrinology and Immunoassay Methodologies.

D. NIH/NIA U01 AG 12495 (AR Midgley) 06/01/99 - 05/31/03 (Pending)
Study of Women's Health Across the Nation: Menopause and Aging in Women
$768,462 Direct Costs (Central Laboratory)
Associate Lab. Director with 10% Effort.
1. The major purpose of the Central Ligand Assay Satellite Services (CLASS) laboratory is to continue supporting the Study of Women's Health Across the Nation (SWAN) through state-of-the-science, automated assays for all major reproductive axis hormones, adrenal markers of aging, other endocrine markers, and new ovarian markers which have the potential to allow us to hormonally define the menopausal transition and the postmenopause with greater precision.

SCIENTIFIC COLLABORATIONS:

A. University of Michigan; Reproductive Science Program: A. Rees Midgley Jr. M.D., and Daniel S. McConnell, Ph.D.: The major purpose of the Central Ligand Assay Satellite Services (CLASS) laboratory at the University of Michigan is to support the Multicenter National Study of Women's Health Across the Nation (SWAN) through state-of-the-science, automated assays for all major reproductive axis hormones, selected markers of aging, other endocrine markers, and new ovarian markers which have the potential to define more accurately the menopausal transition and the characterize the postmenopause with greater precision.

B. University of Mississippi: Hamed Benguzzi, Ph.D. and University of Dayton: P.K. Bajpai, Ph.D.: Long-term drug delivery is of considerable research and clinical interest, particularly if the rate and length of delivery time can be accurately controlled. This collaborative effort has focused on the use of immunologically inert biomaterial similar to bone in composition (ceramics) that has proven capable of delivering a wide variety of steroids, protein hormones, therapeutic drugs, vitamins, autocrine and paracrine factors, etc. collectively referred to as "drugs". These delivery devices have proven capable of constant release of biological compounds into the circulation for as many as 12 months. These studies are continuing permitting increasingly tighter control in the rate and length of "drug" delivery.

C. University of Missouri: Mark Flinn, Ph.D.: We have monitored several biochemical markers of growth, puberty, stress and immunological function in the salivary excretions of children in a small isolated Caribbean village for approximately 8 years. We have examined several markers in saliva samples obtained from children between the ages of 2 and 21. Samples and a detailed history of relevant physical and emotional events are collected daily over a 2 - 3 month period each year throughout the multiyear study. Salivary levels of adrenal and gonadal steroid hormones provide good estimates of the concentration of biologically active hormone in the peripheral circulation on a twice-daily

basis throughout the collection interval. This study has lead to a variety of new insights into the interaction between emotional and environmental stress and normal growth and development in human subjects.

D. University of Michigan: Jonathon A. Ship, D.M.D.: In the preceding study hormone concentrations in salivary secretions from children have provided invaluable information into the developmental physiology of children under natural conditions. Salivary flow rates are not different in healthy young and older adults although histomorphometric studies clearly show a decrease in acinar salivary producing cells across the human life span. It would be of interest to compare salivary hormone excretion patterns in subjects of advancing age. We are attempting to determine if a secretory reserve exists early in life, by determining if there is a difference in the ability of healthy human subjects' salivary glands to respond to an anticholinergic medication (glycopyrrolate).

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Director, Central Ligand Assay Laboratory.

MEDICAL SCHOOL/HOSPITAL:

A. Consultant, Chemistry Core Facility, Diabetes Research and Training Center.
B. Co-Director, Standards and Reagents Core Facility, Reproductive Sciences Program.
C. Associate Director, CLASS laboratory in the SWAN study, Reproductive Science Program.
D. Associate Research Investigator of Reproductive Biology, Reproductive Science Program.

V. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. England BG, and England RL: Clinical Utility and Measurement of Estradiol-17_. American Association of Clinical Chemistry: Diagnostic Endocrinology and Metabolism. Vol 15(11): 333-351, 1997.
2. Henricks WH, England BG, Giacherio DA, Oesterling JE, and Wojno KJ: Serum percent-free PSA does not predict extra-prostatic spread of prostate cancer. American Journal of Clinical Pathology 109:533-539, 1998.
3. Flinn MV, Baerwald C, Decker SD, and England BG. Evolutionary functions of neuroendocrine response to social environment. Behavioral and Brain Sciences 20(1):xxx June, 1998.
4. Cason Z, Tucci M, England BG, and Benghuzzi H: Pathophysiological Changes Associated with Sustained Delivery of Estrogen and Estrogen Plus Progesterone by TCPL Devices; Biomed. Science Instrumentation, (Paper #98-005 ISA), Vol. 34, pp 24-29, 1998.

ABSTRACTS AND PAPERS AT MEETINGS:

1. Benghuzzi HA, England BG and Possley RM: Sustained release of dihydrotestosterone by means of TCPL delivery system in adult wethers. FASEB Journal Vol 11, Iss 3, pp 2401 – 2401, 1997.
2. Cason Z, Tucci M, England BG, and Benghuzzi H: Pathophysiological Changes Associated with Sustained Delivery of Estrogen and Estrogen Plus Progesterone by TCPL Devices; Biomed. Science Instrumentation, (Paper #98-005 ISA), Vol. 34, pp 23-29, 1998.
3. Cason Z, Tucci M, England BG, Butler K, and Benghuzzi H: Sequential Endometrial Changes associated with Sustained Deliver of Ovarian Hormones in Adult Female Rats. 17th Southern Biomedical Engineering Conference, San Antonio, TX, February 7-8, 1998.
4. Beduschi R, Beduschi MC, Wojno K, Giacherio DA, and England BG. Free PSA And Total PSA Significantly Correlates With The Serum Concentration Of Free Testosterone, Albumin-Bound Testosterone And Dihydrotestosterone In A Normal Male Population. 14th International Medical Sciences Student Congress, May 6-9, 1998, Istanbul, Turkey. Abs. #55.
5. Beduschi MC, Beduschi R, Wojno K, Giacherio DA, and England BG. The Use Of A Super Sensitive PSA Assay And IGF-1 For The Early Diagnosis Of Recurrent Prostate Cancer. 14th International Medical Sciences Student Congress, May 6-9, 1998, Istanbul, Turkey. Abs. #59.
6. Vallorosi CJ, Giacherio DA, Beduschi MC, England BG, Montie JE and Wojno KJ. The use of a third generation chemiluminescent PSA assay for the early detection of recurrent prostate cancer. Clin. Chem. 44(S6): A38, 1998.
7. Beduschi MC, Beduschi R, Vashi A, Putzi MJ, Giacherio DA, , England BG, Wojno KJ, Montie JE, Yurgalevitch SM, and McKinla J. Percent free PSA distribution in male populations with normal and abnormal prostate evaluations: Determination of reference ranges. J. Urol. 159:234, 1998.
8. Flinn MV and England BG 1997. Individual differences in endocrine and immune response to stress among children in a rural Caribbean village. Abstracts of the American Anthropological Association Meetings, 1997.
9. Turner MT, Flinn MV and England BG: Stress, immune function, and health among children in a Caribbean village. (abstract). American Journal of Physical Anthropology Supplement 23:xxx. 1997.
10. Decker SA, Flinn MV and England BG. Social support, affluence, and stress among adult male Dominican horticulturists. Abstracts of the American Anthropological Association Meetings, 1997.

ARTICLES SUBMITTED TO REFEREED JOURNALS:

1. Flinn MV and England BG. Health condition and glucocorticoid stress response among children in a rural Caribbean village. Submitted to Proceedings of the National Academy of Sciences.
2. Decker SA, Flinn MV and England BG. Male cortisol and testosterone profiles are associated with social events and status. Submitted to American Journal of Human Biology.
3. Turner M, Flinn MV and England BG. Variation of mother and infant salivary and breast milk cortisol levels. Submitted to American Journal of Human Biology.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Autopsy Service.

II. TEACHING ACTIVITIES:

A. Director, Resident Training Program.
B. Graduate Program Committee (Chair).
C. Course Director - Pathology Teaching Laboratories.
D. Laboratory Instructor, M1 Histopathology Sequence.
E. Laboratory Instructor:M2 Pathology Labs.
F. Laboratory Instructor: Dental Labs.
G. Lecturer, M1 Host Defense Sequence.
H. Lecturer, Medical Illustration course.
I. Coordinator, Department of Pathology Summer Clinical Program for Minority Medical Students.
J. Pulmonary Pathology Conference (six per year to Pulmonary Division, Department of Internal Medicine).
K. Graduate Student Ph.D. Thesis Committee (two).
L. Medical Student Advisor (3rd and 4th year).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Investigator, "Pulmonary Immune Responses to Inhaled Pathogens". NIH-R01-HL5531601 (1998-2002)
B. Co-Investigator, "Regulation of IL-Gene Expression", NIH GM50401 (1996-1999).

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Associate Dean of Medical Education.
B. CD/ACD Education Committee (Chair).
C. Curriculum Policy Committee (Chair).
D. Medical Student Basic Science Academic Review Board (Chair).
E. Medical Student Clinical Academic Review Board (Chair).
F. Medical School Academic Hearing Committee (Chair).
G. Medical School Information Technology Advisory Committee.
H. University of Michigan Distance Learning Committee.

REGIONAL AND NATIONAL:

A. ALA of Michigan, Grant Review Committee.
B. USMLE, Pathology Test Committee (Chair - designee).

V. OTHER RELEVANT ACTIVITIES:

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Brieland JK, Fantone JC, Remick DG, LeGendre M, Engleberg NC: Legionella pneumophila-infected protozoa: an infectious particle in a murine model of Legionnaires' disease. Infect Immun 1998; 65:5330-3.
2. Brieland JK, Remick DG, LeGendre ML, Engleberg NC, Fantone JC: In vivo regulation of replicative Legionella pneumophila lung infection by endogenous interleukin-12. Infect Immun 1998; 66:65-9.
3. Crockett-Torabi, E., and Fantone, J.C.: L-selectin-dependent canine neutrophil stimulation initiates Ca^{2+} signal secondary to tyrosine kinase activation. Am J Physiol 1997; 272:1302-8.
4. Robins, L.S., Wolf, F.M., Alexander, G.L., Fantone, J.C., and Davis, W.K. Development and evaluation of an instrument to assess medical students' multicultural comfort. Journal of the American Medical women's Association (in press).

5. Robins, L.S., Fantone, J.C., Alexander, G.L., Hermann, J., Zweifler, A.J. Improving cultural awareness and sensitivity training in medical school. Academic Medicine, (accepted for publication in the 1998 Academic Medicine supplement).

WILLIAM G. FINN, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997- 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Clinical Hematology Laboratory.
B. Diagnostic Hematopathology (Bone marrow biopsies, lymph nodes, blood smears, body fluids).
C. Clinical Flow Cytometry Laboratory.
D. Clinical Molecular Diagnostics Laboratory.
E. 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.
   4. Hematopathology case conferences (2).

B. Hematopathology teaching:
   1. Leukemia conference/biweekly.
   2. Lymphoma conference/weekly.
   3. Hematology conference/biweekly.
   4. Clinical Pathology Grand Rounds (one lecture).
   5. Clinical Pathology Case Conference/weekly.

C. "Bone Marrow Pathology - An Update": 11th Annual M-Labs Symposium, April 25, 1998.

D. Regional/National:
   1. Faculty member: 11th Annual Clinical Course in Flow Cytometry and Image Analysis. Flow Cytometry Educational Association. Chicago, Illinois, July 24-26, 1998.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

PROJECTS UNDER STUDY:

A. Clonal evolution and biologic diversity in B-cell chronic lymphocytic leukemia.
B. Clonal expansion of cytotoxic T-cell subsets in B-cell chronic lymphocytic leukemia.
C. Central nervous system involvement in mantle cell lymphoma.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Diagnostic Hematology Laboratory.
B. Clinical Pathology Resident Training.

REGIONAL/NATIONAL:

A. Appointed to Editorial Board, Cytometry (Communications in Clinical Cytometry).
B. Ad hoc manuscript reviewer, Human Pathology.
C. Ad hoc manuscript reviewer, American Journal of Clinical Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Lecturer, "Low Grade Lymphoma of Ocular Adnexa". Society for Hematopathology, Fourth Slide Workshop. Pittsburgh, PA, October 1997.
2. Lecturer, "Analysis of Leukemias": Laboratory Session. 11th Annual Clinical Course in Flow Cytometry and Image Analysis. Flow Cytometry Educational Association. Chicago, Illinois. July 25-26, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kroft SH, Finn WG, Singleton TP, Ross CW, Sheldon SS, Schnitzer B: Follicular large cell lymphoma with immunoblastic features in a child with Wiscott-Aldrich Syndrome: an unusual immunodeficiency-related neoplasm not associated with Epstein-Barr virus. Am J Clin Pathol 110: 95-99, 1998.
2. Finn WG, Peterson LC, James C, Goolsby CL: Enhanced detection of malignant lymphoma in cerebrospinal fluid by multiparameter flow cytometry. Am J Clin Pathol (in press).
3. Huang JC, Finn WG, Variakajis D, Goolsby CL, Peterson LC: CD5 negative small B-cell leukemias are rarely classifiable as chronic lymphocytic leukemia. Am J Clin Pathol (in press).
4. Finn WG, Kroft SH: New classifications for non-Hodgkin lymphoma. Cancer Treat Res (in press).

5. Finn WG, Kay NE, Kroft SH, Church S, Peterson LC: Secondary abnormalities of chromosome 6q in B-cell chronic lymphocytic leukemia: a sequential study of karyotypic instability in 51 patients. Am J Hematol (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Fang JM, Finn WG, Hussong JW, Cubbon AR, Goolsby CL, Variakojis D: CD10 antigen expression correlates with the t(14;18) major breakpoint region in diffuse large B-cell lymphoma.

BOOKS AND CHAPTERS IN BOOKS:

None.

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

1. Finn WG, Goolsby CL: CD4 expression in acute non-lymphocytic leukemia (letter). Am J Clin Pathol 108:699-700, 1997.
2. Fang JM, Finn WG, Hussong JW, Cubbon AR, Variakojis D: CD10 antigen expression correlates with the t(14;18) in diffuse large B cell lymphoma. Platform presentation; United States and Canadian Academy of Pathology annual meeting, 1998. Mod Pathol 1998; 11(1):128A. Lab Invest 78:128A, 1998.
3. Kuchnio M, Finn WG, Goolsby CL, Peterson LC: Clonal expansion of cytotoxic/suppressor T cells in B-cell chronic lymphocytic leukemia. Platform presentation; United States and Canadian Academy of Pathology annual meeting, 1998. Mod Pathol 11(1): 134A, 1998. Lab Invest 78:134A, 1998.
4. Peterson L, Marcelli A, Arthur D, Burt R, Kwaan H, Finn W, Frizzera G: Systemic polyclonal immunoblastic proliferation: a distinct atypical lymphoproliferative disorder. Poster presentation; United States and Canadian Academy of Pathology annual meeting, 1998. Mod Pathol 11(1):138A, 1998. Lab Invest 78:138A, 1998.
5. Pooley RJ, Finn WG, Peterson LC, Kroft SH: Morphologic detection of cytomegalovirus (CMV)-infected endothelial cells in routinely prepared peripheral blood smears. Poster presentation; American Society of Clinical Pathology spring meeting, 1998. Am J Clin Pathol 109:473, 1998.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Rotations, July (1/4), August (2/4), September (1/4), December (4/5), January (3/4), February (3/4), March (3/4), April (3/4), May (2/4), June (1/4).
B. Estrogen and progesterone receptor analysis of paraffin embedded breast carcinomas.
C. Ophthalmic Pathology Service.

II. TEACHING ACTIVITIES:

A. Pathology 600 Lectures:
   1. Obstructive Lung Disease - November, 1997.
   2. Pulmonary Neoplasms - November1997.
   3. Pathology of ARDS - November1997.
   4. Tissue Reactions to Infectious Agents - November 1997.
   5. Pulmonary Pathology Review for Medical Students - November, 1997.
   6. Gynecologic Pathology Review for Medical Students - April, 1998.
   7. General Pathology Review for Medical Students - June, 1997.
   8. Laboratory Instructor, September, 1997 - May,1998.
   9. Medical student question and answer sessions, October, 1997 - May, 1998.

B. Pathology 630:
   1. Respiratory Disease I - October, 1997.
   2. Respiratory Disease II - November, 1997.

C. Residency Training:
   1. Diseases of the Chest I - January, 1998.
   2. Diseases of the Chest II - January, 1998.
   3. Diseases of the Chest III - January, 1998.
   4. Surgical Pathology Consultant's Conference, December, 1997; June, 1998.

D. Inteflex 211
   1. The Physician as Scientist - November, 1997.

E. Other educational activities:
   1. M4 student elective mentor, February, 1998, May, 1998.
   2. Center for Research on Learning and Teaching Workshops Public Speaking Skills I, II.
   3. Member, M-2 Respiratory Sequence Committee, 1997-1998.
   4. Course Director, M-4 Student Pathology Clerkships.
   5. Participant, Thoracic Surgery Residents Core Curriculum, 1997 – 1998.
   6. Medical Education Scholars Program, February 1998 - February 1999.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Interstitial Lung Diseases - Specialized Center of Research (1 P50 HL- 46487-01), Galen Toews, M.D. (Principal Investigator), Andrew Flint, M.D. (Co-Investigator).
B. Promoting Interactive Teaching in the Pathology Laboratory (Faculty Development Fund, Center for Research on Learning and Teaching, 1997 -1998).
C. Medical Education Scholars Program.

PROJECTS UNDER STUDY:

A. Histologic predictors of obliterative bronchiolitis in lung transplant patients.
B. Histologic prognostic indicators of survival in ARDS patients treated with ECMO.
C. The cytopathologic features of vitreous fluids.
D. The clinical, radiographic, and pathophysiological manifestations of nonspecific interstitial pneumonitis.
E. The pathologic and clinical features of the "accelerated" form of usual interstitial pneumonitis.
F. The pathologic manifestations of ocular involvement by Wegener's granulomatois.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interviewer of Pathology House Officer Candidates 1997.
B. Member, Admissions Committee of the University of Michigan Medical School, 1995 – present.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

1. Invited Reviewer, American Journal of Pathology.
2. Member, Abstract Review Board, USCAP.

INVITED LECTURES/SEMINARS:

1. "The Physician as Scientist", Inteflex 211, University of Michigan, Ann Arbor, MI, May, 1997.

VI. PUBLICATIONS:

1. Michael CW, Flint A: Cytologic features of Wegener's granulomatosis: a retrospective review. Am J Clin Path 110:10 -15, 1998.

2. Brown RS, Leung JY, Zasadny KR, Flint A, Wahl RL: Initial evaluation of the importance of glucose transporters, proliferating cells and macrophages to FDG uptake in human non-small cell lung cancer as assessed by PET. Chest (in press).
3. Lynch JP, Belperio J, Flint A, Martinez F: Bronchiolar complications of connective tissue disorders. Clinics in Chest Medicine (accepted).
4. Gay SE, Kazerooni EA, Toews GB, Lynch JP, Gross BH, Cascade PN, Spizarny DL, Flint A, Schork MA, Whyte RI, Popovich J, Hyzy R, Martinez FJ: Idiopathic pulmonary fibrosis. Predicting response to therapy and survival. Am J Respir Crit Care Med 157:1063 - 1072, 1998.

SUBMITTED PUBLICATIONS:

1. Zisman DA, Lynch JP, Toews GB, Strieter RB, Kazerooni EA, DiGiovine B, Flint A, Martinez FJ: Cyclophosphamide in the treatment of idiopathic pulmonary fibrosis.
2. Martinez FJ, Lynch JP, Hariharan K, Strawderman R, Kazerooni E, Flint A, Toews GB: Risks of high dose steroids in idiopathic pulmonary fibrosis: is it worth the benefit?
3. Brown RS, Leung JY, Flint A, Wahl RL: Expression of glucose transporters in human lung cancer.
4. Brown RS, Leung JY, Kison PV, Zasadny KR, Flint A, Wahl RL: The importance of glucose transporters to FDG uptake in untreated primary human non-small cell lung cancer as assessed by PET.
5. Flint A, Williams BC: Interactive teaching in the Pathology Laboratory.

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

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Director, Pathology Data Systems.
B. Director, Ancillary Information Systems (Pathology, Radiology, Pharmacy, Radiation Oncology, Nuclear Medicine, HomeMed), University of Michigan Health System.

II. TEACHING ACTIVITIES:

DEPARTMENTAL:

A. Co-Director of laboratory section for Pathology 600.
B. Two-week pathology informatics course for two pathology house officers, May 11-18.

MEDICAL SCHOOL/HOSPITALS:

A. Director of the Sixteenth Annual Symposium on Automated Information Management in the Clinical Laboratory (AIMCL), Ann Arbor, Michigan, May 27-29, 1997. The symposium attracted approximately 260 registrants and 28 exhibitors.
B. Director of a new conference (Executive Briefing: Pitfalls and Opportunities in Pathology and Laboratory Medicine) held May 26-27 in conjunction with AIMCL. This conference, devoted to futuring and strategic planning for the entire clinical laboratory industry, attracted 75 registrants and will be repeated in 1999.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. The development of a virtual clinical laboratory and academic pathology department.
B. Applications for Personal Digital Assistants (e.g., Palm III) for residents and staff physicians.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Clinical Laboratory Directors Committee.

HOSPITAL:

A. Chief Information Officer Executive Committee (CIOEC).
B. Chairman, GroupWise Steering Committee and GroupWise Executive Committee.
C. Chairman, Ancillary Information Systems Managers' Committee
D. Chief Information Officer Search Committee.
E. Chairman, Diagnostic Imaging Advisory Committee (DIAC)

UNIVERSITY:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. *Pathology Informatics and the Emergence of the Virtual Academic Pathology Department.* A lecture presented under the sponsorship of UAREP in conjunction with the Association of Pathology Chairmen annual meeting, Lake Tahoe, Nevada, July 24, 1997.
2. *The Virtual Clinical Laboratory: A New Organizational Structure Enabled by Information Technology.* A luncheon lecture delivered at the CAP Fall meeting, Philadelphia, Pennsylvania, September 21, 1997.
3. *The Virtual Clinical Laboratory: A Rapidly Changing IT-Enabled Organization.* A lecture delivered at a conference entitled "Adapting Laboratories to Integrated Delivery Systems" and sponsored by the American Hospital Association, Chicago, Illinois, October 16, 1997.
4. *The Pathologist as a Model for the Information-Savvy Medical Specialist.* A lecture delivered at the second annual conference entitled "Anatomic Pathology, Informatics, Imaging, and the Internet," Pittsburgh, Pennsylvania, October 17, 1997.
5. *The Future of Pathology and Laboratory Medicine: An Info-Centric Perspective.* Keynote speaker at the fifth biennial meeting of the A. James French Society of Pathologists, Ann Arbor, Michigan, October 18, 1997.
6. *Regionalization and Consolidation of Clinical Laboratories: An Information Technology Perspective.* A lecture delivered at the CLMA Hot Topics Seminar, Charlotte, North Carolina, April 25, 1998.
7. *The Evolution of the Clinical Information System: W(h)ither the LIS?.* A lecture presented at the 16th annual Automated Information Management in the Clinical Laboratories (AIMCL) symposium, Ann Arbor, Michigan, May 27, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Friedman, B.A.. Integration of Laboratory Processes into Clinical Processes, Web-Based Laboratory Reporting, and the Emergence of the Virtual Clinical Laboratory. Clinical Laboratory Management Review. (Clinical Laboratory Management Review; In Press)

BOOKS/CHAPTERS IN BOOKS:

1. Friedman, B.A. and Mitchell, W.: Community Health Information Networks (CHINS) and Their Relationship to Telemedicine. pp.53-76, In: Telemedicine, Theory and Practice, Edited by Rashid L Bashshur, Jay H Sanders, Gary W Shannon, Charles Thomas Publishers, Springfield IL., 1997

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Director, Chemistry Laboratory.
B. Daily sign-out and interpretation of electrophoresis results.
C. Direct the operation of blood gas/electrolyte analyzers, coagulation testing meters, and hematology analyzers in the Emergency Department and the operating rooms of Main , Mott, and Kellogg Hospitals.
D. Direct the workgroup overseeing the quality assurance programs for bedside blood glucose testing in the Medical Center.
E. Planning group for the establishment of alternate site testing programs.
F. Technical Director for laboratories at U-M Health Centers off-site clinics.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Pathology House Officers:
   1. Clinical Pathology Rounds (1 lecture).
   2. Coordinator, Pathology House Officer rotation through Chemistry Lab.
   3. Review daily sign-out and interpretation of electrophoresis results.
   4. Review of selected topics in Clinical Chemistry.

B. Postgraduate:
   1. Ph.D. Thesis Committees, Michael Ducey (5/95 to present) and Aaron Smith (5/96 to present), Department of Chemistry.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

1. Evaluation of assays for Troponin I as an early marker of myocardial injury.
2. Evaluation of portable analyzers for the measurement of coagulation testing parameters PT, aPTT, and ACT in alternate testing sites.
3. Evaluation of automated immunoassay for cyclosporine. (funded by Abbott Laboratories).
4. Evaluation of an immunoassay for Phenobarbital on the Vitros 250 Chemistry analyzers (funded by Ortho Clinical Diagnostics).
5. Evaluation of the performance and clinical utility of percent free PSA determinations.

6. Development of an HPLC assay for plasma homocysteine.
7. Evaluation of a sensitive PSA assay for the detection of recurrence of prostate cancer after radical prostatectomy.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

1. Incentive Committee.
2. Quality Assurance Committee.
3. Chemistry Lab Renovation Project Work Group.
4. M Labs / Central Distribution Work Group.
5. Director, Chemistry Laboratory.
6. Director, Point of Care Testing.

MEDICAL SCHOOL /HOSPITAL:

1. Ambulatory Care Operations and Planning Council.
2. Brighton Health Center Expansion Project Planning Group.
3. Emergency Department Expansion Project Work Group.

REGIONAL AND NATIONAL:

1. Executive Committee, Michigan Section AACC.
2. Chair, Program Committee, Michigan Section AACC.
3. Lipids and Lipoproteins Division Member, AACC.
4. Pediatric Clinical Chemistry Division Member, AACC.
5. Consultant, Parke-Davis.
6. Reviewer, Clinical Chemistry.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Troponin I as a marker of myocardial injury." Coldwater Community Hospital Medical Staff, Coldwater, MI. September 15, 1997.
2. Issues in implementing new laboratory tests." M Labs Symposium, Current Concepts in Clinical Pathology, Ann Arbor, MI , October 30, 1997.
3. "Homocysteine: A new marker of risk for coronary disease." Michigan Society for Clinical Laboratory Scientists Annual Meeting, Lansing, MI. April 22, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Henricks, W.H., England, B.G., Giacherio, D.A., Oesterling, J.E., and Wojno, K.J.: Serum percent-free PSA does not predict extraprostatic spread of prostate cancer. Am. J. Clin. Pathol. 1998; 109:533-539.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Mosca, L., Jahnige, J., and Giacherio, D.A.: Beneficial effect of combination hormone replacement therapy on lipoprotein (a) levels in postmenopausal women. Annals of Internal Medicine (submitted for publication).

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

1. Nicklas, J.M., Bleske, B.E., Brown, M., Stemmer, K., Waidley, M.R., Das, S.K., and Giacherio, D.A.: Nocturnal hypokalemia in patients with congestive heart failure treated with diuretics. Presented at American Heart Association 71st National Meeting, 1998.
2. Giacherio, D.A., Stern, S.C., and Matz, K.: Evaluation of the performance of the Abbott AxSYM Troponin I assay: Comparison with the Dade Stratus II assay. Clin. Chem. 1998; 44 (S6):A134.
3. Vallorosi, C.J., Giacherio, D.A., Beduschi, M.C., England, B.G., Montie, J.E., and Wojno, K.J.: The use of a third generation chemiluminescent PSA assay for the early detection of recurrent prostate cancer. Clin. Chem. 1998; 44 (S6):A38.
4. Beduschi M., Beduschi, R., Vashi, A., Putzi, M.J., Giacherio, D.A., England, B.G., Wojno, K.J., Montie, J.E., Yurgalevitch, S.M., and McKinlay, J.: Percent free PSA distribution in male populations with normal and abnormal prostate evaluations: Determination of reference ranges. J. Urol. 1998; 159:234.
5. Beduschi R., Beduschi, M., Wojno, K.J. , Giacherio, D.A., and England, B.G.: Free PSA and total PSA significantly correlates with the serum concentration of free testosterone, albumin-bound testosterone, and dihydrotestosterone in a normal male population. 14th International Medical Sciences Student Congress, May 6-9, 1998, Istanbul, Turkey.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

Autopsy Service one week (May 11-15).

II. TEACHING ACTIVITIES:

A. One week in May – Autopsy with residents.
B. Histopathology Lab Section for medical students.

III. RESEARCH ACTIVITIES:

None.

PROJECTS UNDER STUDY:

None.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

MEDICAL SCHOOL/HOSPITAL:

A. Interviewed medical school applicants for Admissions Committee.

REGIONAL AND NATIONAL:

A. NCAA Drug Testing Crew Chief.
B. Chairman, Board of Directors, Public Citizen, Inc. (Ralph Nader, Initial Chairman and Founder).
C. Reviewer for the Journal of Urology.

V. OTHER RELEVANT ACTIVITIES:

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

NATIONAL:

A. American Society of Clinical Pathologists, Anatomic Pathology Workshop, "Practical Endocrine Surgical Pathology", National Fall Meeting, Philadelphia, PA

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. Sequence Coordinator – Component II Endocrine Sequence
   2. Component II Endocrine Sequence - 2 lectures on Endocrine Pathology.
   3. Endocrine Pathology Laboratories - preparation of course materials.
   4. Pathology Laboratories - 10 sessions.
   5. Component IV Pathology Elective mentor – one month.

B. House Officers:
   1. General Surgical Pathology - 5 months.
   2. Endocrine Surgical Pathology - 12 months as needed.
   3. Consultation Conferences - four.
   4. Molecular Pathology lecture.
   5. Endocrine Pathology lectures – two.

C. Dental and Graduate Students:
   1. Endocrine Pathology lecture.

D. Interdepartmental:
   1. Endocrine Conference, Department of Surgery - monthly.
   2. Endocrinology and Metabolism Clinical Conference - occasional case presentations.
   3. Adrenal Cancer Conference - monthly.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Investigator with Dr. Liz Petty, "Analysis of Genetics Events in the Progression of Adrenocortical Carcinomas, Tumor Progression", ($20,000 Renewal), Schembechler Adrenal Cancer Research Program, The University of Michigan Comprehensive Cancer Center

B. Department of Defense, "Human Breast Cancer Cell/Tissue Bank and Database"; 10-94 - 09-98 (1,300,000), 15% effort as Pathology Director

PROJECTS UNDER STUDY:

A. Principal Investigator, "Genetic Analysis of Adrenal Cortical Neoplasms."
B. Co-Investigator, "Squamous cell carcinoma of the thyroid."
C. Principal Investigator, "Proliferation and Apoptosis Studies of Papillary Thyroid Carcinoma during Pregnancy."
D. Co-Investigator, "Molecular comparison of adenocarcinomas of the esophagus, gastroesophageal junction and stomach".
E. Co-Investigator, "Preclinical Studies on New Drugs for Adrenal Cancer," with Dr. David Schteingart, Department of Internal Medicine.
F. Co-Investigator, "Molecular analysis of ovarian and concurrent peritoneal serous borderline tumors".
G. Co-Investigator, "Studies of apoptosis and fas in thyrocytes and thyroid neoplasms".
H. Co-Investigator, "Chemokine-secreting adrenocortical carcinoma".
I. Co-Investigator, "Genetic changes in chromosome 1p and 17p in thyroid progression".

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. House Officer Candidate Interviews.
B. Faculty Candidate Interviews.
C. Director, Anatomic Pathology Molecular Diagnostics Laboratory
D. Sequence Coordinator – Component II Endocrine Sequence
E. Director, Pathology Portion of Breast Cancer Core Facility

NATIONAL:

A. Editorial Board, *Endocrine Pathology*

V. OTHER RELEVANT ACTIVITIES:

A. Consultant, U.S. Surgical Corporation.

INVITED LECTURES/SEMINAR:

1. Invited Speaker, "Evaluation of Thyroid Nodules. Are They Cancer?", Endocrinology and Diabetes Update 1997, Grand Traverse Resort, given with Dr. James Sisson
2. Invited Speaker, "Molecular Pathology: Potential and Challenges", Robert Wood Johnson University Hospital, New Brunswick, NJ
3. Invited Speaker, "Thyroid Pathology", Allegheny University of the Health Sciences, Allegheny General Hospital, Pittsburgh, P.A.

VI. PUBLICATIONS:

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

1. Angelos P, Thompson NW, Giordano TJ. Spontaneous vocal cord paresis and return to normocalcemia: An unusual presentation of parathyroid adenoma with concomitant abscess. Surgery 1997:121;704-707.
2. Fogt, F, Vortmeyer AO, Goldman H, Giordano TJ, Merino MJ, Zhuang Z. Loss of heterozygosity in the development of dysplasia and carcinoma in ulcerative colitis: A genetic characterization. Hum Path 29:131-6, 1998.
3. Sisson JC, Jamadar DA, Kazerooni EA, Giordano TJ, Carey JE, Spaulding SA. Treatment of micronodular metastases of papillary thyroid cancer: Are the tumors too small for effective irradiation from radioiodine? Thyroid 1998:8;215-221.
4. Montgomery EA, Devaney KO, Giordano TJ, Weiss SW. Inflammatory myxohyaline tumor of distal extremities with virocyte or Reed-Sternberg-like cells: A distinctive lesion with features simulating inflammatory conditions, Hodgkin's disease, and various sarcomas. Mod Pathol 1998:11;384-391.
5. Tworek JA, Giordano TJ, Michael CW. Comparison of intraoperative cytology with frozen sections in the diagnosis of thyroid lesions. In press to Am. J. Clin. Pathol.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Richards ML, Thompson NW, Giordano TJ. Spontaneous Infarction of a Parathyroid Adenoma in Primary Hyperparathyroidism.
2. Pawlik TM, Richards ML, Burney R, Giordano TJ, Thompson NW. Intravagal Parathyroid Adenoma: Report of Two Cases.
3. Wang SH, Koenig RJ, Giordano TJ, Thompson NW, Baker, JR Jr. Up-regulation of Bcl-2 expression and protection from programmed cell death in normal thyrocytes by 1alpha,25 dihydrooxyvitamin D3.

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

1. Arscott, PL, Knapp J, Rymaszewski M, Bretz JD, Bartron JL, Thompson NW, Giordano TJ, and Baker JR Jr.. Induction of apoptosis through the fas death pathway is blocked by a labile inhibitor in thyrocytes. Presented at the 1997 Annual Meeting of the American Thyroid Association.
2. Devaney, S, Svoboda-Newman S, Thompson NW, and Giordano TJ. Proliferation, apoptosis, and hormone receptor expression in papillary thyroid carcinoma during pregnancy - an immunohistochemical study. Presented at the 1997 Annual Meeting of the American Thyroid Association.
3. Ferguson AW, Kuznicki DL, Giordano TJ, and Greenson JK. Molecular comparison of adenocarcinomas of the esophagus, gastroesophageal junction and stomach. Presented at the 1998 Meeting of the United States and Canadian Academy of Pathology.
4. Kleer CG, Bryant BR, Giordano TJ, Sobel M, and Merino MJ. Genetic changes in chromosome 1p and 17p in thyroid cancer progression. Presented at the 1998 Meeting of the United States and Canadian Academy of Pathology.
5. Kleer CG, Giordano TJ, and Merino MJ. Squamous cell carcinoma of the thyroid: An aggressive tumor associated with tall cell variant of papillary thyroid carcinoma. Presented at the 1998 Meeting of the United States and Canadian Academy of Pathology.
6. Petty EM, Bondor JA, Svoboda-Newman SM, Giordano TJ. Analysis of sporadic adrenal cortical carcinomas (ACC) suggests inactivation of MEN1 is an important event. Proc Amer Assoc Cancer Res. 39, March 1998.
7. Schteingart DE, Strieter RM, Giordano TJ, Benitez RS. Chemokine-secreting adrenocortical carcinoma. A novel clinical syndrome. Presented at 1998 Meeting of the Endocrine Society.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

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

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

C. House Officers:
   1. Surgical pathology diagnosing room instruction for house officers - four months.
   2. Two didactic lectures on gastrointestinal pathology - May, 1998.
   3. Gastrointestinal and hepatic pathology tutoring - six months.
   4. Four consultation conferences.

D. Interdepartmental:
   1. Liver biopsy conference - one hour per month.
   2. Multidisciplinary GI tumor board - 1-1/2 hours every other week.
   3. GI pathology teaching sessions with GI fellows - one hour/week.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-investigator R01CA66560-01 ($5,180,000) "Staging Breast Cancer with Positron Emission Tomography", 5% salary support, Richard L.Wahl, M.D. Principal investigator.
B. Co-investigator R01ES07129- 01A2 ($1,153,536) "DDT and Related Compounds and Pancreas Cancer", 5% salary support, David H. Garabrant, M.D. Principal investigator.

PROJECTS UNDER STUDY:

A. Study of COX-2 expression in H. pylori gastritis with Division of Rheumatology.
B. Study of molecular mechanisms in barretts cancers, G-E junction cancers, and H. pylori cancers with Amy Fergueson and Tom Giordano.
C. Study of MALT lymphomas arising in Helicobacter pylori gastritis with Eric Hsi and Charlie Ross.
D. Study of LOH of the DCC gene in Dukes B colon cancers with Richard Boland and John Carruthers, Division of Gastroenterology, UC San Diego.
E. Study of ischemic colitis with Caroline Dignan.
F. Study of colonic stromal tumors with Joseph Tworek and Henry Appelman.
G. Study of PET scans in detecting metastases in breast cancer with Richard Wahl, Division of Nuclear Medicine.
H. Study of etiology of pancreas cancer with David Garabrandt, School of Public Health.
I. Study of fundic gland polyps with Caroline Dignan.
J. Study of telepathology with Alberto Marchevsky at Cedars-Sinai Medical Center.
K. Study of adenovirus in graft vs host disease patients with Neil Bavakatty.
L. Study of diffuse duodenitis and UC with Riccardo Valdez.
M. Study of Barretts dysplasia grading with GI Study Group.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Surgical Pathology.
B. Director, Surgical Pathology Fellowship Program.
C. Member, Residency Selection Committee.
D. Member, Departmental Incentive Committee.

REGIONAL AND NATIONAL:

A. Reviewer, Cancer.
B. Reviewer, Archives of Pathology and Laboratory Medicine.
C. Reviewer, Gastroenterology.
D. Reviewer, Human Pathology.
E. Reviewer, American Journal of Surgical Pathology.
F. Reviewer, American Journal of Pathology.
G. Reviewer, Modern Pathology
H. Webmaster, Hans Popper Hepatopathology Society.
I. Abstract reviewer, GI section of USCAP meeting.
J. Chairperson, Education Committee of the Gastrointestinal Pathology Society.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Visiting Professor, The University of Vermont Medical School, Pathology Grand Rounds, Burlington, Vermont, July 1997.
2. Invited speaker, Atlanta Society of Pathologists/Georgia Medical Society, Atlanta, Georgia, November 1997.
3. Co-director of USCAP course entitled "Infectious Diseases of the GI tract," March, 1998.
4. Chairperson of Proffered Papers, Gastrointestinal Pathology section, USCAP Meeting, March 1998.
5. Moderator, GI Pathology Society Companion Meeting at USCAP meeting, March 1998.
6. Moderator, GI Pathology Society Companion Meeting at DDW meeting, May, 1998.
7. Invited Speaker, ASCP Teleconference on Colitis given to >100 hospitals, May, 1998
8. Faculty Member, ASCP Workshop - Surgical Pathology of the Gastrointestinal Tract, Newport, Rhode Island, June 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. MacDonald GA, Greenson JK, DelBuono EA, Grady W, Frank TS, Lucy MR, Appelman HD: "Mini"-microabscess Syndrome in Liver Transplant Recipients. Hepatology 26:192-197, 1997.
2. Hsi ED, Greenson JK, Singleton TP, Eisbruch A, Ross CW, Schnitzer B: Classification of Primary Gastric Lymphomas According to Histologic Features Am J Surg Pathol 22:17-27,1998.
3. Greenson JK. The use of the Polymerase Chain Reaction and In-Situ Hybridization in Detecting Infections of the Gastrointestinal Tract. Acta Endoscopica 27:145-153, 1997.
4. Hedderwick SA, Greenson JK, McGaughy VR, Clark NM: Adenovirus Cholecystitis in a Patient with AIDS. Clinical Infectious Diseases 26:997-999, 1998.
5. Friis-Hansen L, Sundler F, [Li Y, Gillespie PJ, Saunder TL, Greenson JK, Owyang C, Rehfeld JF, Samuelson LC: Impaired gastric acid secretion in gastrin-deficient mice.. Am J Phys 274:G561-G568, 1998.
6. Macdonald GA, Greenson JK, Saito K, Cherian S, Appelman HD, Boland CR: Microsatellite instability and loss of heterozygosity at DNA mismatch repair gene loci occurs during hepatic carcinogenesis. Hepatology 28:90-97, 1998.
7. Carethers JM, Hawn MT, Greenson JK, Hitchcock CL, Boland CR. Prognostic Significance of Allelic Loss of Chromosome 18q for Stage II Colorectal Cancer. Gastroenterology 114:1188-1195, 1998.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Tworek JA, Goldblum JR, Weiss SW, Greenson JK, Appelman, HD. Stromal Tumors of the Colon. Modern Pathology (submitted).

2. Tworek JA, Goldblum JR, Weiss, SW, Greenson, JK, Appelman HD. Stromal Tumors of the Rectum and the Anus. Modern Pathology (submitted).
3. Shureiqi I, Wojno K, Poore J, Reddy R, Moussalli MJ, Spindler S, Greenson JK, Normolle D, Brenner DE: Decreased 13-S-hydroxyoxoctadecadienoic acid (13-S-HODE) tissue levels and 15-lipoxgenase (15-Lox) expression in human colon cancers. Journal of Clinical Investigation (submitted).

BOOKS/CHAPTERS IN BOOKS:

1. Eckhauser FE, Yahanda AM, Greenson JK. Gastric Smooth Muscle Tumors. In: Current Surgical Therapy, Sixth Edition. Ed: Cameron, JL, Mosby Electronic Production, Philadelphia, PA, 1998, p. 114-117.

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

1. Hatton C, Woods J, Dhir R, Bastacky S, Epstein J, Miller G, Greenson J, Wojno K, Becich M. Proceedings/AMIA Annual Fall Symposium 420-3, 1997.
2. Valdez R, Appelman HD, Greenson JK. Diffuse Duodenitis Associated with Ulcerative Colitis. Platform Presentation, USCAP Meeting, 1998, Modern Pathol 11:72A, 1998.
3. Dignan CR, Ladabaum U, Scheiman JM, Appelman HD, Greenson JK. Fundic Gland Polyps are Associated with Omeprazole Use. Poster Presentation at USCAP Meeting, 1998, Modern Pathol 11:63A, 1998.
4. Singson R, Natarajan S, Greenson JK, Marchevsky AM. High Resolution Digital Microphotography and the Internet as Telepathology Consultation Tools: A Study of Gastrointestinal Biopsies. Poster Presentation at USCAP Meeting, 1998, Modern Pathol 11:70A, 1998.
5. Hsi ED, Singleton TP, Swinnen L, Greenson JK, Alkan S. Mucosa-Associated Lymphoid Tissue Type Lymphomas Occurring in Posttransplantation Patients: A Form of Posttransplantation Lymphoproliferative Disorder? Poster Presentation at USCAP Meeting, 1998, Modern Pathol 11:131A, 1998.
6. Ferguson AW, Kuznicki DL, Giordano TJ, Greenson JK. Molecular Comparison of Adenocarcinomas of The Esophagus, Gastroesophageal Junction, and Stomach. Poster Presentation at USCAP Meeting, 1998, Modern Pathol 11:63A, 1998.
7. Fontana RJ, Greenson J, Punch JD, Brown NK, Lok ASF. Long Term Outcome of Hepatitis B Patients Treated with Lamivudine Before and After Liver Transplantation. Abstract submitted to the 17th Annual Scientific Meeting, 1998.
8. Lacourse KA, Gillespie PJ, Swanberg LJ, Lay JM, Greenson JK, Samuelson LC. Cholecystokinin-Deficient Mice are Viable and Exhibit Pancreatic Adaptation to Dietary Protein. Abstract submitted to Experimental Biology, 1998

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Pediatric Necropsies, daily, twelve months.
B. Pediatric Surgical Consultation Cases, intra and extra mural, daily, twelve months.
C. Placental Pathology, daily twelve months.
D. Heart biopsy service, regular back-up for Dr. Gerald Abrams.
E. Adult Necropsy Service, staff, fourteen weeks.
F. Regular coverage for Dan Remick, M.D. as Director of Autopsy Service
G. Continued to organize and maintain the Michigan Cardiac Registry, twelve months.
H. Teratology Unit, histology, as necessary, approximately 40 cases per year.
I. Children's Cancer Study Group, coordinate pathological material and data necessary for all children registered in national tumor protocols. (Collaborating investigator, NCI #2-U10-CA-02971-33, CCSG, R. Hutchinson, M.D., P.I.).

II. TEACHING ACTIVITIES:

A. M2: Pathology 600, three hours with class as part of joint (with Pediatric Cardiology-Dennis Crowley, M.D.) Congenital Heart Sequence.
B. M4: Pathology clerkship mentor, two students.
C. House Officers in Pathology, daily consultation on Pediatric cases in surgical reading rooms, twelve months.
D. House Officers in Pathology, gross and microscopic supervision of most pediatric necropsies, twelve months, and adult cases, fourteen weeks plus on-call weekends.
E. Lecture on Pediatric Necropsy Pathology in Orientation for new House Officers in Pathology.
F. Core curriculum lectures for House Officers in Pediatric Pathology, two.
G. Individual gross and microscopic resident teaching in Placental Pathology.
H. Gross Necropsy Conference, one hour/week, twelve months.
I. Supervised Pediatric Hematology Fellows (two) for Pediatric Pathology elective period.
J. Coordinate three core curriculum lectures in placenta: Pathology and OB/GYN residents.
K. Consult conference (2), pediatric cases for pathology residents.
L. Conferences: Faculty, house staff and students:
    1. Pediatric Cardiology Death Conference, monthly, twelve months.
    2. Pediatric Tumor Conference, twice monthly, twelve months.
    3. Pediatrics CPC/General Death Conference, quarterly (approximately).
    4. Pediatric Liver-GI Conference, twice monthly, twelve months.
    5. Pediatric General Surgery Conference monthly, twelve months.

III. RESEARCH ACTIVITIES:

A. Continued review of effects of various congenital heart defects on the pulmonary vasculature.
B. Histopathological component of lung changes associated with various cardiopulmonary therapeutic support mechanisms.

C. Collaborative project with pediatric surgeons (Joseph Lelli, M.D., lead) on the correlation of the frozen section results in biliary atresia with post operative bilirubin levels and recovery.
D. Continuing correlation of histopathologic classification of neuroblastoma cell/tumor maturity with different tissue gene expressions. (Valerie Castle, M.D., PI.)
E. Project with Pediatric surgeons (C. Harmon, M.D.) on CD 36 Expression in Neuroblastoma.

PROJECTS UNDER STUDY:

A. Review of predictive value of heart biopsies for death in pediatric transplant patients. (Manuscript submitted.)
B. Collaborative project with pediatric surgeons (Dan Teitelbaum, M.D., lead) on the mechanisms of the effects of total parenteral nutrition on the gastrointestinal tract and liver in a mouse model. (See abstracts.)
C. Continued follow-up (with Mason Barr, M.D. and Aileen Sedman, M.D.) of the abnormal kidney development and function in surviving twin(s) in twin transfusion syndrome.
D. Continuing study/evaluation of normal pediatric heart measurements of Triangle of Koch with Caren Goldberg, M.D. and M. Dick, M.D. for use in electrophysiology therapy of infants and children.
E. Correlation project with pediatric surgeons (Joseph Lelli, M.D. lead) on clinical diagnosis/management of perforated appendicitis in children (see abstracts).

ONGOING RESEARCH:

A. Co-investigator, with Robert Bartlett, Principal Investigator (NIH); study to further develop and research life support systems (Extra Corporeal Life Support Systems).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Departmental ACAPT.
B. Administrative coverage for Dan Remick as Director of Autopsy Service in his absence.

MEDICAL SCHOOL/HOSPITAL:

A. Executive Committee for Mott/Women's/Holden/Psychiatric Hospitals.
B. Interviewing Pediatric Cardiology fellowship candidates.
C. Interviewing faculty candidates:
   1. Pediatric G.I.
   2. Pediatric Cardiology
   3. Pathology

REGIONAL AND NATIONAL:

A. Women's Liaison Officer, American Association of Medical Colleges.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Barr M, Sedman AB, and Heidelberger KP: Renal Tubular Dysgenesis in Twins. (Accepted, Pediatric Nephrology.)

2. Goldberg, C.S., Caplan, M.J., Heidelberger, K.P. and Dick, M.: The Dimensions of the Triangle of Koch in Children. (Accepted Am J Cardiol.)

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

1. Lelli, J.L., Wilke, L., Heidelberger, K.P., Drongowski, R.A.and Coran, A.G.: Perforated Versus Non Perforated Appendicitis in Children (Abstract submitted.)
2. Lelli, J.L., Wilke, L., Heidelberger, K.P., Drongowski, R.A.and Coran, A.G.: The Impact of Early Discharge on the Medical Outcome of Children with Perforated Appendicitis. (Abstract submitted.)
3. Forbush, B., Kiristioglu, I., Teitelbaum, D.H., Eisenbraun, M.D. and Heidelberger, K.P.: Multi Drug Resistance 2 Gene Expression in the Murine Liver: Relevance to the Development of Parenteral Nutrition - Associated Cholestasis. (Abstract submitted.)

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Oxidants and Protease Interaction in Acute Lung Injury", National Institutes of Health, $834,625, 12/94 - 11/98.
B. Co-Principal Investigator, "Pathophysiology of Aspiration Pneumonitis", with Paul Knight, Anesthesia , R01, National Institutes of Health - Budget - $720,866; $187,518 annual, 08/96 - 07/99.
C. Principal Investigator, "Oxidants and Glomerular Injury", Project V, Renal Center Grant, National Institutes of Health, $246,585/five years.
D. Principal Investigator, "Mechanisms of Glomerular and Tubular Injury", Core B, Renal Center Grant, National Institutes of Health, $147,795.
E. Principal Investigator, "Inflammatory Cells and Lung Injury", Core C, National Institutes of Health, $291,025.
F. Co-Investigator, "DNA Methylation and SLE", with Bruce Richardson, Rheumatology, National Institutes of Health.

PENDING SUPPORT:

A. Co-Principal Investigator, "A New Approach to Treat Lupus Nephritis" NIH.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

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

V. INVITED LECTURES AND SEMINARS:

1. Visiting Professor, Metro Health Center, Cleveland, Ohio, 1997.
2. Visiting Professor, SUNY Buffalo, NY, Department of Anesthesiology, Buffalo, New York, 1997.
3. Visiting Professor and Lecture, University of Florida, Gainesville, Florida, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Huber, A.R., Ellis, S., Johnson, K.J., Dixit, V.M. and Varani, J.: Monocyte diapodesis through an in vitro vessel wall construct: inhibition with monoclonal antibodies to thrombospondin. J. Leuk. Biol., In Press.

2. Johnson, K.J., Sulavik, C. and Rehan, A.: Role of oxygen radicals in autologous anti-GBM nephritis. Inflammation, In Press.
3. Mulligan, M.S., Sulavik, C., Ward, P.A., Kunkel, R.G. and Johnson, K.J.: The delayed phase of anti-GBM nephritis is deferoxamine sensative but catalase insensitive. Inflammation, In Press.
4. 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.
5. Yung, R., Chang, S., Hemati, N., Johnson, K. and Richardson, B.: Mechanisms of drug-induced lupus. IV. Comparison of procainamide and hydralazine with analogs in vitro and in vivo. Arthritis and Rheumatism. 40, 1997.
6. Yung, R., Williams, R., Johnson, K.J., Stoolman, L., Change, S. and Richardson, B.: Mechanisms of drug-induced lupus. III. Sex-specific differences in splenic T cell homing may explain increased severity in female mice. Arthritis and Rheumatism. 40, 1997.
7. Nader-Djalal, N., Knight, P.R., Davidson, B.A., Johnson, K.J.: Hyperoxia exacerbates microvascular lung injury following acid aspiration. Chest. (In Press), 1997.
8. Nader-Djal, N., Knight, P. R., Bacon, M. F., Tait, A. R., Kenedy, T. P., and Johnson, K. J.: Alterations in the course of acid-induced lung injury in rats after general anesthesia: Volatile anesthetics versus ketamine. Anesth. Analg. 1998;86:1-6.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Ward, P.A., Till, G.O., Kunkel, R.G. and Johnson, K.J.: Protection against neutrophil-mediated lung injury by platelet depletion. Submitted for publication.
2. Hirschl, R.B., Tooley, R., Parent, A., Johnson, K.J. and Bartlett, R.H.: Evaluation of gas exchange, pulmonary function and lung injury during total and partial liquid ventilation in the setting of severe respiratory failure. Submitted for publication.
3. Lebedovych, L.M., Johnson, K.J., McMorris, M.S., Gilardy, A.K., Hirschl, R.B., Ward, P.A. and Baker, J.R.: Characteristics of the late allergic responses in rats previously sensitized with monoclonal IgE antibodies. Submitted for publication.
4. Varani, J., Hirschl, R., Dame, M. and Johnson, K.J.: Neutrophil infiltration is reduced during liquid ventilation: II. In Vitro analysis. Amer. J. Respir. & Crit. Care Med., Submitted.
5. Colton, D.M., Hirschl, R.B. Till, G.O., Johnson, K.J, Dean, S.B., Patel, S. and Bartlett, R.H.: Neutrophil infiltration is reduced during liquid ventilation: 1. In vivo analysis. Amer. J. Respir. & Crit. Care Med., Submitted.
6. Hirschl, R.B., Tooley, R., Parent, A., Johnson, K.J. and Bartlett, R.H.: Evaluation of gas exchange, pulmonary compliance, and lung injury during total and partial liquid ventilation in the acute respiratory distress syndrome. J. Crit. Care Med., Submitted.
7. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K.J, Ichiba, S. and Bartlett, R.H.: Liquid ventilation decreases pulmonary hemorrhage and vascular permeability. Submitted for publication.
8. Annis, K., Sigler, C. Johnson, K.J., Berman, S., Haber, H, Bonalsky, J., Luscombe, F. and Van de Carr, S.: Predictors of angioedema associated with angiotensin converting enzyme inhibitor. Submitted for publication.

9. Hirschl, R.B., Tooley, R., Parent, A., Johnson, K. and Bartlett, R.H.: Evaluation of gas exchange, pulmonary compliance, and lung injury during total and partial liquid ventilation in the acute respiratory distress syndrome. Journal of Critical Care Medicine, Submitted.
10. Sonda, P., Ellis, J.H., Kunkel, R., Platt, J.F., Faerber, G.J., Rubin, J.M. and Johnson, K.J.: Chronic partial renal obstruction in dogs: resistive indices and ratios by duplex doppler sonography. Submitted for publication.
11. Colton, D.M., Till, G.O., Johnson, K.J., Dean, S.B. and Hirschl, R.B.: Neutrophil accumulation is reduced during partial liquid ventilation. Submitted to Critical Care Med.
12. Gipson, T.S., Shanley, T.P., Gibbs, D.F., Jones, M.L., Bleavins, M.R., McConnell, P., Mueller, W., Johnson, K.J., and Ward, P.A.: Role of endogenous rat tissue inhibitor of metalloproteinase-2 in acute lung inflammatory injury. Submitted to Am J of Pathology
13. Nader-Dajal, N., Knight, P.R., Thusu, K., Davidson, B.A., Aljada, A., Holm, B.A., Johnson, K.J., Dandona, P.: The role of reactive oxygen species in oxygen-related lung injury following acid aspiration. Submitted to Chest.
14. Nader-Djalal, N., Knight, P.R., Tait, A.R., Kennedy, T.P. and Johnson, K.J.: Alterations in the course of acid-induced lung injury in rats following general anesthesia: Volatile anesthetics vs ketamine. Submitted to Anesthesia and Analgesia.

BOOKS AND CHAPTERS IN BOOKS:

1. Warren, J.S., Johnson, K.J. and Ward, P.A.: Phagocytes and reactive oxygen substances as mediators of acute lung injury, in, Hyers, T. (ed), Diffuse Alveolar Damage and Respiratory Failure, Futura Press, New York, In Press.
2. Till, G.O., Johnson, K.J. and Ward, P.A.: Oxygen free radicals in inflammation, in, Messmer, K. and Hammersen, F. (eds), Prog. Appl. Microcirc., Volume 9, Karger, Basel, In Press.
3. Ward, P.A., 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.
4. 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.
5. 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, 1997.

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

1. O'Shea, S., Johnson, K.J.J., Moore, M., and Erickson, S.: Heregulin, ErbB2, and ErbB3 heterozygous mice: histological analysis and response to heregulin challenge. Submitted to AACE, 1997.
2. Crouch, L.D., Lentsch, A.B., Warner, R.L., Johnson, K.J., and Ward, P.A.: Regulatory effects of adrenal gland products in IgG immune complex acute lung injury. Submitted to FASEB, 1997.
3. Gipson, T.S., Shanley, T.P., Bleavins, M.R., Tefera, W., Johnson, K.J., and Ward, P.A.: Molecular cloning and in vivo transcriptional expression of rat SLPI in lung inflammation. FASEB, 1997.

4. Sawyer, R., Chenault, R., Merion, R., Johnson, K., Kutz, E., and Hebert, C.: Antibody to interleukin-8 (IL-8) decreases systemic and pulmonary sequelae of sepsis in porcine bacteremia. Submitted to Society of Critical Care Society, 1997
5. Gipson, T. S., Shanley, T.P., Bleavins, M. R., Wongelawit, T., Johnson, K. J., and Ward, P. A.: Regulation of proteinase inhibitors in acute inflammatory lung injury in rats. FASEB J. 12(4):4595, 1998.
6. Gibbs, D. F., Varani, J. J., and Johnson, K. J.: Role of matrix metalloproteinases in macorphage-dependent acute alveolitis in the rat. FASEB J. 12(4):4506, 1998.
7. Younkin, E. M., Warner, R. L., Varani, J. J., and Johnson, K. J.: Matrix metalloproteinase expression by rat pulmonary parenchymal cells. FASEB J. 12(4):4594, 1998.
8. Johnson, KJ., Dame, M. K., Wojno, K., and Varani, J.: Human prostate in organ culture morphological features, epithelial cell growth and motility and elaboration of matrix metalloproteinases Presented at Proteases and Protease Inhibitors in Cancer. Nyborg, Denmark, June, 1998.
9. Dame, M. K., Wojno, K., and Johnson, K. J.and Varani, J: Human prostate in organ culture morphological features, epithelial cell growth and motility and elaboration of matrix metalloproteinases. 6th SPORE Conference Nat. Int. Health., July, 1998.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Director, Blood Bank Reference Laboratory.
   1. Procedural change implemented in October, 1997:
      a) Discontinued repeat antibody identification studies on alloimmunized patients except when there is serological or clinical evidence of a new antibody.
      b) This change, reduced reference laboratory case-load by 40%.
      c) Initiated monitor to verify case-load reduction and impact on patient care.

B. Consultant, Veteran's Administration Medical Center, Ann Arbor.

II. TEACHING ACTIVITIES:

A. Clinical Pathology Grand Rounds:
   1. Program Director.
   2. Presented lectures on:
      a) Immune hemolysis
      b) The Rh blood group system

B. Anatomical Pathology Conferences:
   1. Program Coordinator.

C. Core-Lecture Series in Blood Banking for 1st-year Pathology House Officers:
   1. Program Coordinator.
   2. Presented lectures on:
      a) Pretransfusion testing.
      b) Prenatal/perinatal testing.
      c) Immune hemolysis.
      d) Antibody identification.

D. Clinical Pathology Case Study Conference:
   1. Program Coordinator.
   2. Participant.

E. Fellows:
   1. Hematology/Oncology - Provided instruction in immunohematology to Drs. Huber, Smith, Grino, Aziz and Reynolds (25 hours contact).
   2. Pediatric Hematology - Provided instruction in immunohematology to Drs. Nadwami and Mody.

F. Pathology Residents:
   1. Residency Training Review Committee.

2. Coordinated Blood Bank/Immunology/Coagulation and HLA block rotations for house-officer training in clinical pathology.
3. Provided instruction in immunohematology to house-officers during their Blood Bank Rotation (100 contact hours).

G. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
1. Program Director - Planned and coordinated the June, 1998 Current Topics in Blood Banking Symposium and Preconference Workshops.
2. Presented Workshop entitled: "Issues in implementing an electronic crossmatch."
3. Presented talk entitled: "Repeat antibody identification studies. How? When? Ever?"
4. Moderated morning session on Transfusion Management.

III. RESEARCH ACTIVITIES:

A. Judd WJ, Steiner EA, Fullen DR, Knafl PC. Revisiting the issue: can the reading for serologic reactivity following 37°C incubation be omitted? Transfusion: *Submitted.*
B. Evaluated commercially prepared 0.8% cell suspension for use with ID-MTS gel cards.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL/NATIONAL/INTERNATIONAL:

A. Michigan Association of Blood Banks:
1. Co-Chairman, Special Lecture Series Committee - coordinated a series of 60 lectures medical technologists seeking Certification as a Specialist in Blood Banking.
2. Presented lectures on Rh and MN systems, lectins and polyagglutination (10.5 contact hours) as part of Special Lecture Series.
3. Planned and directed Current Practices in Immunohematology Workshop, William Beaumont Hospital, Troy, MI, April, 1998.
4. Member, Annual Meeting Program Committee.

B. American Association of Blood Banks:
1. Member, Awards Committee.
2. Member, Scientific Abstract Review Committee.

C. Member, Editorial Board, Transfusion.
D. Reviewer of articles submitted for publication in Transfusion, Immunohematology, and Transfusion Medicine.
E. International Society of Blood Transfusion

1. Member, WHO Committee on Blood Group Nomenclature

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

1. Fetal-Maternal Immunohematology. Annual Meeting of the Michigan Association of Blood Banks, Troy, September, 1997.
2. Issues in implementing an electronic crossmatch. American Association of Blood Banks Annual Meeting, Denver, CO, October, 1997.
3. Session Moderator - Red Cells and Serological Methods. American Association of Blood Banks Annual Meeting, Denver, CO, October, 1997.
4. Immune hemolysis. Michigan Association of Blood Banks' Current Topics in Immunohematology Workshop, William Beaumont Hospitals, Troy, MI, April, 1998.
5. Prenatal-perinatal testing. Michigan Association of Blood Banks' Current Topics in Immunohematology Workshop, William Beaumont Hospitals, Troy, MI, April, 1998.
6. Issues in implementing an electronic crossmatch. United Blood Services, Scottsdale, AZ, March, 1998.
7. Modern approaches to pretransfusion testing. Ohio Association of Blood Banks Annual Meeting, Covington, KY, April, 1998.
8. Requirements for the electronic crossmatch. Blood Group Serology 1998, Institute of Biomedical Sciences, Durham, England, April, 1998.
9. Modern approaches to pretransfusion testing. Retirement Seminar in Honor of Dr. Peter D. Issitt, Washington, DC, May, 1998.
10. Repeat antibody identification studies: How? When? Ever? Annual Meeting of the American Cross Blood Group Reference Laboratories, Washington, DC, May, 1998.
11. Requirements for the electronic crossmatch. XXV Congress of the International Society of Blood Transfusion, Oslo, Norway, June, 1998.

PUBLICATIONS:

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

1. Judd WJ. Two or three reagent red cells for antibody detection? Immunohematology 1997;13:90-92.
2. Judd WJ, Steiner EA, Knafl PC. The gel test: sensitivity and specificity for unexpected antibodies to blood group antigens. Immunohematology 1997;13:132-135.
3. Judd WJ, Steiner EA, Knafl PC, Masters C. The gel test: use in the identification of unexpected antibodies to blood group antigens. Immunohematology 1998;14:59-62.
4. Judd WJ. 'New' blood bank technologies. Clin Lab Sci 1998;11:106-113.
5. Judd WJ. Requirements for the electronic crossmatch. Vox Sanguinus 1998;74(S2):409-407.

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

1. Judd WJ, Davenport RD. On the high probability that a perceived lack of value in obtaining a p value will be detrimental to patient care! Transfusion 1997;37:877.
2. Steiner EA, Judd WJ. Detection of ABO incompatibility in gel. Transfusion 1997;37(S):29.
3. Judd WJ, Fullen DR, Steiner EA, Knafl PC. Omitting the 37 C reading. Transfusion 1997;37(S):65.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Lectures to House Staff on Block B, Clinical Pathology.
B. Protein Sign-Out in Immunology Laboratory with 1-2 residents for 4-6 hours biweekly.
C. Molecular Diagnostics Sign-Out with Fellow, weekly.
D. Lectures to Pathology House Staff and Faculty at Clinical Pathology Rounds.
E. Research advisor to undergraduates: Ms. Renee Jiddou, Mr. J. Zelmanovich, UROP.
F. Research co-advisor to post-doctoral fellow: Dr. J. Srinivasan, Dept. of Chemistry, University of Michigan.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Molecular Genetics of CYP21 (Steroid 21-hydroxylase).
B. Quantitative analytical technologies for nucleic acids.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Molecular Diagnostics Laboratory.
B. Director, Clinical Chemistry Section.
C. Member, Pathology Resident Selection Committee.
D. Director, Fellowship Program in Chemical Pathology
E. Member, Web Editors Task Force for Departmental Home Page.

REGIONAL AND NATIONAL:

A. Chair-Elect, Molecular Pathology Subdivision of American Association for Clinical Chemistry (as of July, 1998).
B. Member, Publications Committee, Association for Molecular Pathology.
C. Editor of ACLPS Newsletter.
Chair, ACLPS Taskforce on Networking.
D. Member, AACC, ASHG, CAP, ACLPS, AMP.
E. Manuscript Reviewer, Clinical Chemistry, Molecular Diagnosis, and Biotechniques.
F. Consultant in Molecular Biology to Michigan Governor's Task Force on Genetic Privacy.
G. Testified before Michigan Legislature on Bills regarding human cloning.

V. INVITED LECTURES AND SEMINARS:

1. "Genetics of Alzheimer's Disease", Association for Medical Laboratory Immunologists annual meeting, San Francisco, July, 1997.
2. "Basic Genetics". Lecture to the Michigan Association of Blood Banks, March 1998.

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

1. Srinivasan JR, Liu Y, Venta PJ, Siemieniak D, Killeen AA, Zhu Y, Lubman DM: MALDI TOF-MS as a rapid screening method to detect mutations causing Tay-Sachs disease. *Rapid Communications in Mass Spectrometry*, 11: 1144-1150, 1997
2. Srinivasan JR, Kachman MT, Killeen AA, Akel N, Siemieniak D, Lubman DM: Genotyping of apolipoprotein E by matrix assisted laser desorption, ionization time of flight mass spectrometry (MALDI MS). *Rapid Communications in Mass Spectrometry* (In Press).
3. Killeen AA, Jiddou R, Sane KS: Characterization of frequent polymorphisms in intron 2 of CYP21. Application to analysis of segregation of CYP21 alleles. (Revision submitted to *Clinical Chemistry*).
4. Wei WL, Killeen AA: Analysis of 4 common salt-wasting mutations in CYP21 (steroid 21-hydroxylase) by CFLP, and characterization of a frequent polymorphism in intron 6. *Molecular Diagnosis* (In Press).

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

1. Wei WL, Killeen AA: Identification of a frequent RsaI polymorphism in intron 6 of CYP21. *Clinical Chemistry* (In Press).
2. Killeen AA, Jiddou R, Sane KS: Identification of polymorphisms in intron 2 of the CYP21 gene. *American Journal of Pathology*, 151:1490, 1997.

PAUL D. KILLEN, M.D., PH.D.
ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Board Certification, Anatomic Pathology.
B. Autopsy Pathology (3 days).
C. Diagnostic Renal Biopsy Service (32 weeks).
D. Chief Renal Consultant.

II. TEACHING ACTIVITIES:

A. M2 Pathology Lecture - Renal Sequence (3 hours).
B. M2 Pathology Laboratory- Renal Sequence (20 hours).
C. Co-Coordinator - Renal Sequence (40 hours).
D. Curriculum Development -Renal Sequence (80 hours).
E. Gross Pathology Conference.
F. Renal Pathology for Pathology Residents (five hours).
G. Renal Pathology for Nephrology Fellows (nine hours).
H. Renal Pathology Fellows - Lois Arend - (30 hours).
I. Dissertation Committees (one).
J. Graduate Program Oral Examiner (two)
K. Post Doctoral Fellows (one).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, Project VI, "TGF-β Induced Collagen IV Gene Transcription", NIH-P50-DK39225, (10% Effort) $49,822/year, 8/1/92-7/30/97.
B. Co-Investigator, "Renal Fibrosis", NIH-RO1, (5% Effort) $198,213/ year, 4/1/93-3/30/98.
C. Co-Investigator, "Role of EDRF in the Juxtaglomerular Apparatus", NIH-RO1-DK40042, (5% Effort) $164,666/year, 12/1/93-11/30/98.
D. Core Consultant, Molecular Biology Core, "Michigan Diabetes Research and Training Center", NIH-P60-DK20572, (5% Effort) $100,000 direct costs/year, 4/1/93-3/31/98.

PENDING SUPPORT:

A. Co-Investigator, "Altered Neural Myo-Inositol Metabolism in Diabetes", NIH-R01-DK38304, (20% Effort) $225,547 direct costs/year.

B. Co-Investigator, "IGF-I is an Osmoprotectant in Neuroglial Cells", NIH-R01-DK38304, (5% Effort) $103,045 direct costs/year.
C. Director, Morphology Core B, George M. O'Brien Renal Center, NIH-P50-DK39225, (5% Effort) $55,603 direct costs/year.

PROJECTS UNDER STUDY:

A. Regulation of collagen IV gene expression.
B. Structure and assembly of collagen IV chains.
C. Regulation/expression of hypertonicity stress proteins.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Anatomic Pathology Accessioning Committee.
B. Digital Imaging Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Faculty recruitment, Department s of Internal Medicine, Pediatrics.
B. Member, Biomedical Research Council.
C. Curriculum development, M2 Urinary System.
D. Assistant Director, Diagnostic Renal Biopsy Service.
E. Supervisory Committee, U of M Multipurpose Arthritis Center, Molecular Biology Core.

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. American Journal of Physiology.
    4. Journal of Clinical Investigation.
    5. Journal of Biological Chemistry.
    6. Journal of American Society of Nephrology.
E. Program Committee, Annual Meeting of the American Society of Nephrology.

V. INVITED LECTURES AND SEMINARS:

1. Program organizer and Chairman, "Organic Osmolytes and Osmotic Stress" Annual meeting of the American Society of Nephrology, San Antonio, October 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lee SK, Goyal M, de Miguel M, Thomas P, Wharram B, Dysko R, Phan S, Killen PD, Wiggins RC,: Renal biopsy collagen I mRNA predicts scarring in rabbit anti-GBM disease: Comparison with conventional measures of function and histology. Kidney Int 52:1000-1015, 1997.
2. Wu K, Setty S, Mauer SM, Killen P, Nagase H, Michael AF, Tsilibury EC: Altered kidney matrix gene expression in experimental diabetes. Acta Anat 158:155-165, 1997.
3. Bergijk EC, Van Alderwegen IE, Baelde HJ, de Heer E, Funabiki K, Miyai H, Killen PD, Kalluri RK, Bruijn JA: Differential expression of collagen IV isoforms in experimental glomerulosclerosis. J Pathol 184:307-315, 1998.
4. Porcellati F, Hlaing T, Togawa M, Stevens M, Larkin D, Hosaka Y, Glover TW, Henry DN, Greene DA, Killen PD: The human Na^+-myo-inositol cotransporter gene: Alternate splicing generates diverse transcripts. Am J Physiol, 274:C1215-1225, 1998.
5. Minto AW, Kalluri R, Togawa M, Bergijk EC, Killen PD, Salant DJ: Augmented Expression of Glomerular Basement Membrane Specific Type IV Collagen Isoforms (α3-α5) in Experimental Membranous Nephropathy. Proceedings of the Association of American Physicians, 110:207-217, 1998.
6. Van Vliet AI, Van Alderwegen IE, Baelde HJ, de Heer E, Killen PD, Kalluri RK, Bruijn JA, Bergijk EC: Differential Expression of Collagen Type IV Subchains in Experimental Renal Interstitial Fibrosis, in press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Todd-Turla KM, Schnermann JB, Briggs JP, Killen PD: Regulation of Renal Mineralocorticoid and Glucocorticoid Receptor mRNA in Response to Adrenalectomy and Corticosteroid Hormone Replacement. Submitted 1998.
2. Porcellati F, Hosaka Y, Hlaing T, Togawa M, Larkin D, Stevens M, Killen PD, Greene DA: Alternative splicing of human Na^+-myo-inositol cotransporter transcripts predicts multiple isoforms: Implications for tissue-specific regulation of myo-inositol transport and metabolism. Submitted 1998.
3. Schieren G, Gattone VH, Killen PD: Aberrant expression of extracellular matrix genes is prominent in slowly progressive polycystic kidney disease in *pcy/pcy* mouse. Submitted 1998.

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

1. Lu W, Phillips CL, Overbeek P, Meisler MH, Killen PD: A New Model of Alport's Syndrome, J Amer Soc Nephrol 8:393A, 1997.
2. Bergijk EC, van Griensven M, de Heer E, Bruijn JA, Killen PD: Promoter-flanking Sequences Modulate Transcription Regulation of Collagen Type IV Genes. J Amer Soc Nephrol, 8:512A, 1997.
3. Karihaloo A, Smith SS, Dawson DC, Killen PD, Greene DA: Protein Kinase A (PKA) Agonists Enhance *myo*-Inositol (MI) Uptake in Oocytes Expressing Alternative Sodium-dependent MI Co-Transporter (SMIT) Isoforms. J Amer Soc Nephrol (submitted) 1998.
4. Pop-Busui R, Town T, Larkin DA, Killen PD, Greene DA: Anti-peptide Antibodies Detect Distinct Sodium-dependent myo-Inositol (MI) Co-transporter (SMIT) isoforms in human retinal pigment epithelial (RPE) cells. J Amer Soc Nephrol (submitted) 1998.

ESPERANZA B. KINTANAR, M.D.
LECTURER
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Cytopathology - twelve months.
B. Cytology transfer cases - twelve months.
C. Cytology outside consult cases – occasional.
D. Cytology intradepartmental consult cases - twelve months.
E. Surgical head and neck transfer cases - September 1997 to June 1998.
F. Autopsy service - six weekends.

II. TEACHING ACTIVITIES:

A. Residents and Cytopathology Fellow (and on a sporadic basis, clinical fellows and medical students):
   1. Instruction and supervision in the performance, evaluation and interpretation of fine needle aspirates from patients in-house and at the Cancer Center.
   2. Instruction and supervision in the evaluation and interpretation of assisted invasive, deep-seated fine needle aspirates.
   3. Instruction in the evaluation, work-up and signing out of gynecologic and non-gynecologic cases.
   4. Instruction in the evaluation, work-up and signing out of cytology transfer cases.
   5. Monthly Residents Cytopathology Conference - comprehensive organ systems review with surgical correlation, glass slide and/or kodachrome sessions with handouts.
   6. Consult Case Conference for residents- three a year.
   7. Instruction and supervision in the performance, presentation and sign-out of autopsy cases.

B. Other Education Activities:
   1. Cytopathology Conference for Cytotechnologists - six/year.
   2. Current concepts update in the practice of Cytology - residents, fellow and cytotechnologists.
   3. Cytohistologic correlation - fellow, residents and cytotechnologists.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-investigator with Thomas E. Carey, Ph.D., IRBMED archive #1991-335 and -337, "Molecular and Biological Studies of Head and Neck Tumors", University of Michigan (NIH funded).

PROJECTS UNDER STUDY:

A. Endoscopic Ultrasound-Guided Fine Needle Aspiration Biopsy of the Pancreas, Clinico-Pathologic Correlation, with James M. Scheiman, M.D. and Byungki Kim, M.D.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None.

MEDICAL SCHOOL/HOSPITAL:

None.

UNIVERSITY OF MICHIGAN:

None.

REGIONAL AND NATIONAL:

None.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Immature Squamous Metaplasia", University of Michigan M-Labs Symposium, Ann Arbor, Michigan, October 4, 1997.
2. "Urine Cytology: Update on Current Concepts and Controversies", University of Michigan, Department of Pathology, Ann Arbor, Michigan, November 19, 1997.
3. "Diagnostic Pitfalls and Mimics of HGSIL, platform presented at the 45th Annual Meeting of the American Society of Cytopathology, Boston, Massachusetts, November, 1997.
4. "Cytologic Criteria for High-Grade Transitional Cell Neoplasia: Analysis of Single Cells in Thinprep Slides", platform presented at the 87th Annual USCAP Meeting, Boston, Massachusetts, March, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

None.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Kintanar EB, Giordano TJ, Thompson NW, Michael CW: Granular Cell Tumor of Trachea Masquerading as Hurthle Cell Neoplasm on Fine Needle Aspirate: A Case Report and Review of Literature. Diagnostic Cytopathology.

BOOKS/CHAPTERS IN BOOKS:

None.

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

1. Kintanar EB, Michael CW.: Diagnostic Pitfalls and Mimics of HGSIL. Acta Cytol 1997; 41:5,1544-1545.
2. Kintanar EB, Tworek JA, Putzi M, Wojno K.: Cytologic Criteria for High-Grade Transitional Cell Neoplasia: Analysis of Single Cells in Thinprep Slides. Mod Pathol 1998; 11:39A.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Epidemiology 570.
B. Host Defense Sequence, First Year Medical School.
C. Lecture in didactic seminar series for Pediatrics.
D. Member, Pathology graduate program committee.
E. Member, Lung Immunopathology Post-doctoral Training Program (Pathology).
F. Member, Experimental Immunopathology Training Program (Pathology).
G. Member and Co-Director, Pulmonary Cellular and Molecular Biology Training Program.
H. Chair, Pathology Graduate Examination committee.
I. Member, Graduate Teaching Award Review Committee.
J. Member, Task force for Medical School Graduate Program for Joint recruitment Joint Admissions.
K. Supervised the following postdoctoral fellows and graduate students: fellows, Drs. Betsy Parks, Cory Hogaboam, Bruno DiGiovine, Akihiro Matsukawa, Sandra Oliveira.
L. Undergraduate students: Matt Steinhauser, Eric Strieter, Scott Lipinski, Carrie Zickus.
M. Doctoral Thesis Committee Member/Orals Committee for the following graduate students: Andrew Merry (Pathology), Jim Parks (Pharmacology), Jeffrey Ruth (Public Health), Mei-Chen Kuo (Public Health), Joyce J. Lai (Public Health), Shimin Hu (Pathology), Wannee Asavaroengchai (Pathology), Sara Cheng (CMB), Cindi Bone-Larson (Pathology).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH - Macrophage/MonocyteSignals in Lung Granuloma Formation; HL-RO1-35276; Principal Investigator.
B. NIH - Monokine Gene Expression/Regulation in Lung Injury HL-RO1-31237; Principal Investigator.
C. NIH - Inflammatory Cells and Lung Injury; Program Project HL-31963; Principal Investigator for Section II.

D. NIH - The role of TNF and ICAM-1 in Lung Allograft Rejection, Co-Investiagator HL-50057.
E. NIH-RO1, The role of C-X-C chemokines in lung cancer, Co-Investigator.
F. SCOR Occupational and Immunological Lung Disease, P50HL-46487 Principal Investigator for Project 3.

PATENTS:

"CXC Chemokines as Regulators of Angiogenesis" Notice of Allowance U.S. Serial #08/468,819.

PROJECTS UNDER STUDY:

A. Role of cytokines in acute inflammation.
B. Regulation of chemokine gene expression.
C. Macrophage-lymphocyte interactions in the initiation, maintenance, and resolution of chronic inflammation.
D. Role of cytokines in angiogenesis/tumorgenesis.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Operating committee Pathology graduate program.
B. Space utilization and research committee.
C. Interview candidates for residency/graduate program.
D. Divisional Co-Director of General Pathology.
E. Chair, Graduate program's Examination committee.

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

A. Member, Committee on medical student research.
B. Member, search committee for the Robinson and Huetwell Professor of Rheumatology.
C. Medical school admission interview committee.
D. Medical scientist training program interviewer.
E. Member, Research Council of the Office of the Vice President for Research.
F. Member, Michigan cancer center.
G. Grant reviewer, Biomedical Research Council.
H. Member, Advisory Committee Cancer Center Animal Core.
I. Member, Panel of Inquiry into Federally-Sponsored Human Radiation Research at the University of Michigan in the Post-World War II Era.
J. Associate Dean, Rackham Graduate School.
K. Task Force for Medical School's Joint Recruitment/Joint Admissions Committee.
L. The University of Michigan medical school LCME self-study Graduate education in the basic medical sciences committee.

M. Search Committee, Vice President for Research university of Michigan.
N. Co-Chair Immunology Task Force Group.

REGIONAL AND NATIONAL:

A. Master of the College of Math and Science (Outstanding alumni for 1998) North Dakota State University.
B. Associate Editor, Journal of Clinical Investigation.
C. Senior Associate Editor, American Journal of Pathology.
D. Associate editor, American Journal of Respiratory Cell and Molecular Biology.
E. Associate Editor, Pathobiology.
F. Associate Editor, Shock.
G. Editorial board, Mediators of Inflammation.
H. Co-chair, 1998 Gordon Conference on Chemotactic Cytokines.
I. Chair, 2000 Gordon Conference on Chemotactic Cytokines.
J. Co-Chair, 1999 Keystone Conference on Chemokines.
K. Co-Chair, 1999 Keystone Conference on Inflammatory Paradigms and the Vasculature.
L. Reviewer for the following journals: American Journal of Pathology, American Review of Respiratory Disease, Circulation, Infection and Immunity, Laboratory Investigation, Science, Journal of Immunology, American Journal of Respiratory Cell and Molecular Biology.
M. Grant Reviewer, The Arthritis Society.
N. Grant Reviewer, Veterans Administration.
O. National Institutes of Health Study Section, Lung Biology and Pathology.
P. National Institutes of Health Study Section, Biological and Physiological Sciences special emphasis panel.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Invited Speaker, Chemokine Symposium, DNAX, Palo Alto, CA, September 1997.
2. Keynote Address, "1997 British Liver Trust Lecture", British Association for the Study of the Liver, London, England, September 1997.
3. Visiting Professor, Department of Immunology, University of Pennsylvania, September, 1997.
4. Invited Speaker, Division of Pulmonary and Critical Care Medicine, University of Pennsylvania, September 1997.
5. Invited Speaker, Northwestern University, CMIER, October, 1997.
6. Invited Participant, NIH Workshop on Interstitial Lung Disease, October, 1997.
7. Visiting Professor, University of Tennessee, November, 1997.
8. Visiting Professor, Michigan State University, February, 1998.
9. Invited Speaker, Keystone Conference, Lake Tahoe, NV Leukocyte trafficking March 1998.
10. Invited Speaker, National Immunology Investigator Meeting, Bodega Bay, CA March 1998.
11. Invited Speaker, Masters Week, North Dakota State University, Fargo, ND, March 1998.
12. Plenary Lecture, European Peritoneal Dialysis Meeting, Edinburgh, Scotland, April 1998.

13. Invited Speaker, American Thoracic Society, Chicago, IL April, 1998.
14. Invited Speaker, Duke University's Eleventh Annual Rheumatology Symposium, Durham, NC, May, 1998.
15. Invited Speaker, American Society for Transplant Physicians, Chicago, IL, May , 1998.
16. Invited Speaker, National Conference on Medical Chemistry, Richmond, VA, June 1998.
17. Co-chair, session chairman, and speaker, Gordon Conference on Chemotactic Cytokines, NH, June, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Shanley, T.P., Foreback, J.L., Remick, D.G., Ulich, T.R., Kunkel, S.L., Ward, P.A. Regulatory effects of Interleukin-6 in IgG immune complex-induced lung injury. Am. J. Pathol.1997; 151:193-202.
2. Keane MP, Arenberg DA, Lynch JP, Whyte RI, Iannettoni MD, Burdick MD, Wilke CA, Morris SB, Glass MC, DiGiovine B, Kunkel SL, Strieter RM. The CXC chemokines, IL-8 and IP-10, regulate angiogenic activity in idiopathic pulmonary fibrosis. J. Immunol. 1997; 159:1437-1443.
3. Walley KR, Lukacs NW, Standiford TJ, Strieter RM, Kunkel SL. Elevated macrophage inflammatory protein-2 in severe murine peritonitis increases neutrophil recruitment and mortality. Infect Immunity 1997; 65: 3847-3851.
4. Chensue, S.W., Warmington, K., Ruth, J.H., Lukacs, N. Kunkel, S.L. Mycobacterial and schistosomal antigen-elicted granuloma formation in IFN-gamma and IL-4 knockout mice. Analysis of local and regional cytokine and chemokine networks. J. Immunol. 1997; 159: 3565-3573.
5. Lin, H., Gastman, B.R., Wei, R.Q., Kunkel, S.L., Gordon, D., Bolling, S.F. Phase-directed therapy and cardiac xenograft survival. J. Sur. Research. 1997; 72: 84-88.
6. Smith, R.E., Hogaboam, C.M., Strieter, R.M., Lukacs, N.W., Kunkel. Cell-to-cell and cell-to-matrix interactions mediate chemokine expression: An important component of the inflammatory lesion. J. Leuk. Biol. 1997; 62:612-619.
7. Teixeira, M.M., Wells, T.N.C., Lukacs, N.W., Proudfoot, A.E.I., Kunkel, S.L., Williams, T.J., Hellewell, P.G. Chemokine-induced eosinophil recruitment. Evidence of a role for endogenous eotaxin in an in vivo allergy model in mouse skin. J. Clin. Invest. 1997; 100:1657-1666.
8. Huffnagle GB, Strieter RM, McDonald RA, McNeil LK, Burdick MD, Kunkel SL, Toews GB. Macrophage inflammatory protein-1 (MIP-1) required for the efferent phase of pulmonary cell-mediated immunity to a *Cryptococcus neoformans* infection. J. Immunol. 1997;159:318-327.
9. Chensue, S.W., Warmington, K., Ruth, J.H., Kunkel, S.L. Effects of slow release IL-12 and IL-10 on inflammation, local macrophage function and the regional lymphoid response during mycobacterial (Th1) and schistosomal (Th2) antigen-elicited pulmonary granuloma formation. Inflamm. Res. 1997;46:86-92.
10. Boorstein SM, Elner SG, Bian ZM, Strieter RM, Kunkel SL, Elner VM. Selective IL-10 inhibition of HLA-DR expression in IFN-• -stimulated human retinal pigment epithelial cells. Curr. Eye Res 1997;16:547-555.
11. Zisman DA, Kunkel SL, Strieter RM, Tsai WC, Bucknell K, Wilkowski J, Standiford TJ. MCP-1 protects mice in lethal endotoxemia. J. Clin. Invest. 1997;99:2832-2836.

12. Boring, L., Gosling, J., Chensue, S.W., Kunkel, S.L., Farese, R.V., Broxmeyer, H.E., Charo, I.F. Impaired monocyte migration and reduced type 1 (TH1) cytokine responses in C-C chemokine receptor 2 knockout mice. J. Clin. Invest. 1997; 100:2552-2561.
13. Arenberg DA, Polverini PJ, Kunkel SL, Shanafelt A, Hesselgesser J, Horuk R, Strieter RM. The role of CXC chemokines in the regulation of angiogenesis in non-small cell lung cancer. J. Leuk. Biol. 1997; 62:554-562.
14. Hogaboam, C.M., Chensue, S.W., Steinhauser, M.L., Huffnagle, G.B., Lukacs, N.W., Strieter, R.M., Kunkel, S.L. Alteration of the cytokine phenotype in an experimental lung granuloma model by inhibiting nitric oxide. J. Immunol 1997; 159:5585-5593.
15. Simpson, K.J., Lukacs, N.W., Colletti, L., Strieter, R.M., Kunkel, S.L. Cytokines and the liver. J. Hepatol. 1997; 27:1120-1132.
16. Elner, V.M., Burnstine, M.A., Strieter, R.M. Kunkel, S.L., Elner, S.G. Cell-associated human retinal pigment epithelium interleukin-8 and monocyte chemotactic protein-1: Immunochemical and in-situ hybridizationa analyses. Exp. Eye Res. 1997; 65:781-789.
17. Zisman, D.A., Kunkel, S.L., Strieter, R.M., Gauldie, J., Tsai, W.C., Bramson, J., Wilkowski, J.M., Bucknell, K.A., Standiford, T.J. Anti-interleukin-12 therapy protects mice in lethal endotoxemia but impairs bacterial clearance in murine Escherichia coli peritoneal sepsis. Shock 1997; 8:349-356.
18. Standiford, T.J., Kunkel, S.L., Strieter, R.M. Role of chemokines in antibacterial host defense. Methods Enzymol 1997; 288:220-241.
19. Arenberg, D.A., Polverini, P.J., Kunkel, S.L., Shanafelt, A., Strieter, R.M. In vitro and in vivo systems to assess the role of C-X-C chemokines in regulation of angiogenesis. Methods Enzymol. 1997; 288:190-220.
20. Verma, M.J., Lloyd, A., Rager, H., Strieter, R.M., Kunkel, S.L., Taub, D., Wakefield, D. Chemokines in acute anterior uveitis. Curr Eye Res. 1997; 16:1201-1208.
21. Hogaboam, C.M., Steinhauser, M.L., Schock, H., Lukacs, N., Strieter, R.M., Standiford, T., Kunkel, S.L. Therapeutic effects of nitric oxide inhibition during experimental fecal peritonitis: Role of interleukin-10 and monocyte chemoattractant protein 1. Infect Immun 1998; 66:650-655.
22. Karpus, W.J., Kennedy, K.J., Kunkel, S.L., Lukacs, N.W. Monocyte chemotactic protein 1 regulates oral tolerance induction by inhibition of T helper cell 1-related cytokines. J. Exp. Med. 1998, 187: 733-741.
23. Lu, B., Rutledge, B.J., Gu, L., Fiorillo, J., Lukacs, N.W., Kunkel, S.L., North, R., Gerard, C., Rollins, B.J. Abnormalities in monocyte recruitment and cytokine expression in monocyte chemoattractant protein-1 deficient mice. J. Exp. Med. 1998 187:601-608.
24. Hogaboam, C.M., Lukacs, N.W., Chensue, S.W., Strieter, R.M., Kunkel, S.L. Monocyte chemoattractant protein-1 synthesis by murine lung fibroblasts modulates CD4+ T cell activaiaton. J. Immunol 1998; 160: 4606-4614.
25. Parks, E.P., Strieter, R.M., Lukacs, N.W., Gauldie, J., Hitt, M., Graham, F.L., Kunkel, S.L. Transient gene transfer of IL-12 regualtes chemokine expression and disease severity in experimental arthritis. J. Immunol. 1998; 160:4615-4619.
26. Dipietro, L.A.,Burdick, M., Low, Q. E., Kunkel, S.L., Strieter. MIP-1alpha as a critical macrophage chemoattractant in murine wound repair. J. Clin. Invest. 1998; 101:1693-1698.
27. Bolin, L.M.,Murray, R., Lukacs,N.W., Strieter, R.M.,Kunkel, S.L.,Schall, T.J., Bacon, K.B. Primary sensory neurons migrate in response to the chemokine RANTES. J. Neuroimmunol. 1998; 81:49-57.

28. Bian Z.M., Elner, S.G., Strieter, R.M., Kunkel, S.L., Elner, V.M. Synergy between glycated serum albumin and tumor necrosis factor-alpha for interleukin-8 gene expression and protein secretion in human retinal pigment epithelial cells. Lab. Invest.1998; 78:335-344.
29. Parks, E., Lukacs, N.W., Strieter, R.M., Kunkel, S.L. Chemokines expression in endothelial cells and monocytes is differentially regulated. Pathobiology 1998; 66:64-70.

BOOKS AND CHAPTERS IN BOOKS:

1. Kunkel, S.L., Chensue, S.W.,Colletti, L., Standiford, T.J., Lukacs, N., Strieter, R.M. Cytokine networks dictate leukocyte recruitment. in: Cytokines in pulmonary infectious disease: Pathogenesis and therapeutic strategies. edited by S. Nelson and T. Martin, Marcel Dekker, New York, N.Y.

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

1. Ruth JH, Lukacs NW, Warmington KS, Pollack T, Burdick M, Strieter RM, Kunkel SL, Chensue SW. Expression and participation of eotaxin during TH_1 and TH_2 cytokine-mediated granuloma formation. Presented at the first AAAAI/AAI/CIS Joint Meeting, San Francisco, CA, February 21-26, 1997.
2. DiPietro LA, Rahbe SM, Burdick M, Kunkel SL, Strieter RM. MIP-1 is an essential macrophage chemoattractant in wound repair. J. Allergy Clin. Immunol. 99:S247, 1997.
3. Lukacs NW, Strieter RM, Glass M, Taub DD, Kunkel SL. Mast cell-fibroblast interaction induces histamine release and C-C chemokine production. J. Allergy Clin. Immunol. 99:S387, 1997.
4. Simpson KJ, Lukacs NW, Evanoff H, Strieter RM, Kunkel SL. Production of angiogenic and chemoattractant chemokines during monocyte:hepatoma cell adhesion. GUT 40: TH116, 1997.
5. Keane MP, Arenberg DA, Burdick MD, Wilke CA, Morris SB, Glass MC, Kunkel SL, Strieter RM. The angiostatic CXC chemokines, IP-10 and MIG, are reduced during the pathogenesis of bleomycin-induced pulmonary fibrosis. FASEB J. 11:A228, 1997.
6. Lukacs NW, Addison C, Gauldie J, Simpson K, Strieter RM, Chensue SW, Kunkel SL. Transgene-induced production of IL-4 alters the development and collagen expression of TH1-type pulmonary granulomas. FASEB J. 11:A229, 1997.
7. Arenberg D, DiGiovine B, Morris S, Burdick M, Kunkel S, Polverini P, Strieter RM. Angiogenesis mediated by ENA-78 promotes growth of human non-small lung cancer (NSCLC). FASEB J. 11:A544, 1997.
8. Lukacs NW, Kunkel SL, Chensue SW, Strieter RM. Role of chemokines in allergic airway inflammation and airway reactivity. Presented at the Keystone Symposia on "The role of chemokines in leukocyte trafficking and disease", Copper Mountain, CO, March 31-April 5, 1997.
9. Hogaboam CM, Lukacs NW, Strieter RM, Chensue SW, Kunkel SL. Nitric oxide contributes to TH1-type lung granuloma formation and chemokine generation. FASEB J. 11:A125, 1997.
10. DiGiovine B, Whyte RI, Iannettoni MD, Arenberg DA, Burdick MD, Glass MC, Morris SB, Kunkel SL, Strieter RM. CXC chemokine composition of stage I adenocarcinoma of the lung correlates with clinical outcome. Am. J. Respir. Crit. Care Med.155:A37, 1997.
11. Zisman DA, Kunkel SL, Strieter RM, Tsai WC, Wilkowski JM, Bucknell KA, Standiford TJ. The role of interleukin-12 in sepsis. Am. J. Respir. Crit. Care Med.155:A467, 1997.
12. Arenberg D, Kunkel SL, Polverini PJ, Burdick MD, Glass M, Morris S, Strieter RM. Interferon-inducible protein 10 (IP-10) prolongs survival in a mouse model of non-small cell lung cancer (NSCLC). Am. J. Respir. Crit. Care Med.155:A500, 1997.

13. Arenberg D, Kunkel S, Keane M, Glass M, Morris S, Burdick M, Strieter R. Human lung cancers recruit macrophages via expression of CC chemokines. J. Invest. Med. 45:332A, 1997.
14. Zisman DA, Kunkel SL, Strieter RM, Tsai WC, Bucknell K, Wilkowski J, Standiford TJ. MCP-1 protects mice in lethal endotoxemia. J. Invest. Med. 45:332A, 1997.
15. Chen B, Xue YY, Burdick MD, Kunkel SL, Strieter RM. The CC chemokines RANTES, MCP-1, and MIP-1 are expressed and MIP-1 is suppressed during lung allograft rejection. . J. Invest. Med. 45:349A, 1997.
16. Koch AE, Halloran MM, Szekanecz Z, Woods JM, Volin MV, Hosaka S, Haines III GK, Kunkel SL, Burdick MD, Walz A, Strieter RM. The role of epithelial neutrophil activating peptide-78 in rat adjuvant-induced arthritis, a model for human rheumatoid arthritis. Arthritis Rheum. 40: 268, 1997.
17. Parks E, Strieter RM, Gauldie J, Lukacs NW, Kunkel SL. Cytokine gene transfer modifies inflammation and regulates cytokine and chemokine production in murine arthritis. Arthritis Rheum. 40: 1137, 1997.
18. Koch AE, Halloran MM, Szekanecz Z, Woods JM, Volin MV, Hosaka S, Haines III GK, Kunkel SL, Burdick MD, Walz A, Strieter RM. The role of epithelial neutrophil activating peptide-78 in rat adjuvant-induced arthritis, a model for human rheumatoid arthritis. Arthritis Rheum. 40: 268, 1997.
19. Campbell EM, Kunkel SL, Strieter RM, Lukacs NW. A murine model of cockroach antigen-induced airway inflammation. FASEB J. 12:A645, 1998.
20. Keane MP, Wilke CA, Moore BB, Kunkel SL, Burdick MD, Glass MC, Strieter RM. MIP-2 regulates angiogenic activity in a murine model of bleomycin-induced pulmonary fibrosis. FASEB J. 12:A646, 1998.
21. Hogaboam CM, Bone-Larson C, Lipinski S, Lukacs NW, Strieter RM, Chensue SW, Kunkel SL. Differential MCP-1 and CCR2b expression by murine lung fibroblasts derived from Th1-type and Th2-type pulmonary granuloma models. FASEB J. 12:A646, 1998.
22. Steinhauser ML, Hogaboam CM, Kunkel SL, Lukacs NW, Strieter RM, Standiford TJ. Interleukin-10 is a major mediator of sepsis-induced impairment in lung antibacterial host defense. FASEB J. 12:A807, 1998.
23. Arenberg D, Keane M, Kunkel S, Glass M, Morris S, Burdick M, Strieter R. Tumor associated macrophages and CC chemokines in lung cancer. FASEB J. 12:A890, 1998.
24. Moore B, Chen B, Xue Y, Burdick M, Kunkel S, Strieter R. Differential expression of CC chemokines during lung allograft rejection. Am J. Respir. Crit. Care Med. 157:A331, 1998.
25. Arenberg D, DiGiovine B, Keane M, Morris S, Burdick M, Kunkel S, Strieter R. Inhibition of epithelial neutrophil activating peptide (ENA-78) reduces growth and angiogenesis of human non-small cell lung cancer. Am J. Respir. Crit. Care Med. 157:A756, 1998.
26. Elner SG, Strieter RM, Elner VM, Bian ZM, Kunkel SL. Differential production of retinal pigment epithelial (RPE) IP-10 and IL-8 induced by pro-inflammatory cytokines. Invest Ophthal. Vis. Sci. 39:S735, 1998.

RICHARD W. LIEBERMAN, M.D.
VISITING LECTURER
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Gynecologic Pathology Consultation - twelve months.
B. Gynecologic Oncology Semimonthly Tumor Planning Conference - twelve months.
C. Dermatopathology – four months, January – April, 1998.
D. Autopsy service – six weeks coverage, April – June, 1998

II. TEACHING ACTIVITIES:

A. Residents:
   1. Sign-out - Gynecologic Pathology and Dermatopathology cases.
   2. Instruction in the Gross Examination, frozen section diagnosis, and processing of Gynecologic Surgical specimens, October 1997.
   3. Instruction and supervision in the performance, presentation and sign-out of autopsy cases.
   4. Teaching Conferences- lectures in Gyn Pathology, two weeks, May 1998.
   5. Consult Case Conference - two/year.
   6. Miscellaneous resident evening conferences in Gyn Path

B. Medical Students:
   1. M2, Obstetrics & Gynecology Sequence: Four hours Gynecologic Pathology lectures; preparation of examination questions.
   2. M2, Obstetrics & Gynecology Sequence: Laboratory instruction.

C. Ob/Gyn Residents and Gynecologic Oncology Fellow:
   1. Semimonthly Tumor Planning Conference – twelve months.
   2. Lectures in Gynecologic Pathology to Gyn Oncology Service – two/year
   3. Gyn Pathology Rotation for 3rd year Gyn Oncology Rotation – one month

D. Cytopathology Fellow:
   1. Review cases and supervise presentation of semimonthly Gynecologic Oncology Tumor Planning Conference – twelve months.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

PROJECTS UNDER STUDY:

A. "Web Based Teaching in Gynecologic Oncology". An unrestricted Educational Grant from the Association of Professors in Gynecology and Obstetrics (APGO). Dr. James Lilja (2nd year Gyn Oncology Fellow), Dr. Richard W. Lieberman (Gynecologic Pathology), and Dr. Kevin Reynolds (Chief, Gynecologic Oncology Division).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member, Pathology Informatics Planning Committee, Department of Pathology.
B. Member, Pathology Informatics Exchange Program (PIX) with University of Michigan & University of Pittsburgh.

MEDICAL SCHOOL/HOSPITAL:

None.

UNIVERSITY OF MICHIGAN:

None.

REGIONAL AND NATIONAL:

A. Co-Chairperson, Medical Informatics Committee, Gynecologic Oncology Group.
B. Member, Pathology Committee, Gynecologic Oncology Group.
C. Member, Tissue Utilization Committee, Gynecologic Oncology Group.
D. Member, National Comprehensive Cancer Network (NCCN) Cervical/Endometrial Cancer Screening Panel.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Non-neoplastic Endometrial Biopsy: Clinical Correlation with Microscopic Findings". Guest speaker; M-Labs Symposium, Ann Arbor, Michigan, October 4, 1997.
2. "FlashPix: A New Imaging Technology for Pathology." Electronic Poster Presentation, Anatomic Pathology Informatics, Imaging, and the Internet (APIII) Meeting in Pittsburgh, Pennsylvania. October 16-18, 1997.
3. "Highlights in Gynecologic Pathology: Clinical-Pathologic Correlation of Selected Cases at the University of Michigan." Grand Rounds for the Department of Obstetrics and Gynecology, maternal and Child health Center Auditorium at the University of Michigan Hospitals. March 19, 1998.
4. "The Utility of the FlashPix Image Format in Pathology and Laboratory Medicine." Information Technology Demonstration, presented over the Internet from the Armed Forces Institute of Pathology, Washington, D.C. to the Automated Information Management in the Clinical Laboratory (AIMCL) 16th Annual Symposium at Chrysler Center, The University of Michigan. May 29, 1998.

VI. PUBLICATIONS:

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lieberman RW, Henry MR, Laskin W, Walenga JF, Buckner S, O'Connor DM. "Colposcopically directed brush cytology in pregnant patients with abnormal PAP smears." Submitted to *Obstetrics & Gynecology.*

2. Taylor RT, Lieberman RW, O'Connor DM. "An analysis of two versus three grades for endometrial carcinoma." Submitted to *Gynecologic Oncology.*

BOOKS/CHAPTERS IN BOOKS:

None.

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

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Supervision of five postdoctoral fellows (Steven Domino, M.D., Ph.D., Jonathon Homeister, M.D., Ph.D., Moonjae Cho, Ph.D., Glennda Smithson, Ph.D., and Hedwig Murphy, M.D., Ph.D.)
B. Lecturer - Postdoctoral Research Training Program.
C. Member of five Ph.D. thesis committees (Stephanie M. Alt, Stacey Arnold, Hangjun Duan, George Pipia, and Vance H. Thomas).
D. Oral prelim committees; Department of Pathology, Ph.D. Program.

III: RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Oligosaccharide function during murine embryogenesis". Source of award: Howard Hughes Medical Institute.
B. Program Project - Project #2 Principal Investigator, "Carbohydrate-dependent adhesion of normal and tumor cells", NIH - CA71932 (25% effort), $732,109/five years direct cost, 07/08/96 - 04/30/2001.
C. Program Project - Project #1 Principal Investigator, "Oligosaccharides as Anti-Inflammatory Agents", NIH AI33189, (15% effort), $647,684/five years direct cost), 09/01/92 - 08/31/2000.
D. Sponsor, Reproductive Scientist Development Award, "Cell surface molecules that mediate blastocyst implantation", Steven E. Domino, M.D., Ph.D., 07/01/94 - 06/30/99.
E. Sponsor, Physician Scientist Award, "Structure and function of recombinant selectin ligands", Hedwig Murphy, M.D., Ph.D., 09/01/94-08/31/99.

PROJECTS UNDER STUDY:

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

mammalian gene transfer techniques, and on characterization of immune defects in glycosyltransferase knock-out mice.

IV: ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chair, Ad-Hoc Research Faculty Search Committee.
B. Chair, Neuropathology Faculty Search Committee.

REGIONAL AND NATIONAL:

A. President, The Society for Glycobiology.
B. Deputy Editor, The Journal of Clinical Investigation.
C. Member, Scientific Advisory Board, The Ara Parseghian Medical Research Foundation (Niemann-Pick disease type C).
D. Member, Pathobiochemistry Study Section, National Institutes of Health.
E. Member, Editorial Board of Glycobiology.
F. Member, Editorial Board of Archives of Biochemistry and Biophysics.
G. Consulting Reviewer for Proceedings of the National Academy of Sciences USA, Journal of Cell Biology, Journal of Experimental Medicine, Biochemistry, European Journal of Biochemistry, Journal of the American Chemical Society, Journal of Histochemistry and Cytochemistry, Journal of Immunology, Glycoconjugate Journal, and Transfusion.

V. OTHER RELEVANT ACTIVITIES:

A. Howard Hughes Medical Institute, Investigator.

VI. INVITED LECTURES AND SEMINARS:

1. Selectin ligand defects in fucosyltransferase mutant mice. 1997 Gordon Conference on epithelial differentiation and keratinization. Tilton, NH, July 1997.
2. Exploring mammalian oligosaccharide function through targeted ablation of glycosyltransferase genes. 17th International Congress of Biochemistry and Molecular Biology, San Francisco, CA, August 1997.
3. Leukocyte trafficking defects in fucosyltransferase-mutant mice. Conference on the molecular mechanisms in leukocyte traffic. Ringberg, Germany, September 1997.
4. Selectin ligands and fucosyltransferases. Eos Biotechnology, Inc. South San Francisco, CA. October 1997.
5. Immune defects in glycosyltransferase knock out mice. The San Diego Glycobiology Symposium, La Jolla, CA. January 1998.
6. Leukocyte trafficking defects in fucosyltransferase mutant mice. University of Chicago, Chicago, IL. March 1998.
7. Fucosyltransferases and selectin ligands. Keystone Symposium on Mechanisms of Leukocyte Trafficking, Lake Tahoe, CA. March 1998.

8. Phenotypic consequences of glycan alterations via glycosyltransferase gene ablation in the mouse. International Glycobiotechnology Meeting, Braunschweig, Germany. May 1998.
9. Immune deficiencies and selectin ligand defects in glycosyltransferase-mutant mice. Finnish Medical Society Duodecim International Symposium on Cellular Interactions in Inflammation and Cancer. Helsinki, Finland. June 1998.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Domino S, Hiraiwa N, and Lowe JB. Structure and tissue-specific expression of a murine α(1,2) fucosyltransferase gene. Biochem J 327:105-115, 1997.
2. Frenette PS, Moyna C, Hartwell DQ, Lowe JB, Hynes RO, and Wagner DD. Platelet-endothelial interactions in inflamed mesenteric venules. Blood 91:1318-1324, 1998.
3. Niemela R, Natunen J, Majuri M-L, Maaheimo H, Helin J, Lowe JB, Renkonen O, and Renkonen R. Complementary acceptor and site specificities of Fuc-TIV and Fuc-TVII allow effective biosynthesis of sialyl-triLex and related polylactosamines present on glycoprotein counterreceptors of selectins. J Biol Chem 273:4021-4026, 1998.
4. Ohyama C, Smith PL, Angata K, Fukuda MN, Lowe JB, and Fukuda M. Molecular cloning and expression of GDP-D-mannose-4,6-dehydratase, a key enzyme for fucose metabolism defective in Lec13 cells. J Biol Chem 273:14582-14587, 1998.
5. Mulligan MS, Warner RL, Lowe JB, Suzuki Y, Miyasaka M, Yamaguchi S, Ohta Y, Tsukada Y, Kiso M, Hasegawa A, and Ward PA. In vitro and in vivo selectin-blocking activities of sulfated lipids and sulfated sialyl compounds. Int Immunol 10:569-575, 1998.
6. Homeister JW, Zhang M, Frenette PS, Hynes RO, Wagner DD, Lowe JB, and Marks RM. Overlapping functions of E- and P-selectin in neutrophil recruitment during acute inflammation. Blood, 1998, in press.
7. Knibbs RN, Craig RA, Maly P, Thall AD, Smith PL, Wolber F, Lowe JB, and Stoolman LM. Fucosyltransferase Fuc-TVII-dependent synthesis of P-selectin ligands on human and murine lymphoblasts. J. Immunol., 1998, in press.
8. Wolber FM, Curtis JL, Maly P, Smith PL, Kelly RJ, Lowe JB, and Stoolman LM. Endothelial selectins and α4 integrins regulate independent pathways of T-lymphocyte recruitment in the pulmonary immune response. J Immunol, 1998, in press.
9. Swarte VR, Joziasse DH, van den Eijnden DH, Petryniak B, Lowe JB, Kraal G, and Mebius RE. Regulation of fucosyltransferase-VII expression in peripheral lymph node high endothelial venules. Eur J Immunol, 1998, in press.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Thall A, Maly P, Cheng G, Smith PL, Rogers C, Askari S, Saunders T, Petryniak B, von Adrian UH, and Lowe JB. The α(1,3)fucosyltransferase Fuc-TIV/ELFT controls leukocyte trafficking by tuning the affinities of E-, P, and L-selectin ligands. In preparation.
2. Hiraiwa N, Domino S, Saunders T, and Lowe JB. Dominant pre-implantation lethality in mice directed by aberrant expression of an α(1,2)fucosyltransferase cDNA. In preparation.

3. Smith PL, Phillips ML, Etzioni A, Ketchum K, Sullivan FX, Kumar R, Paulson JC, and Lowe JB. A biochemical lesion interacting with GDP-D-mannose 4,6-dehydratase accounts for defective selectin ligands in Leukocyte Adhesion Deficiency II syndrome. In preparation.

BOOKS AND CHAPTERS IN BOOKS:

None.

LORI LOWE, M.D.
CLINICAL ASSISTANT PROFESSOR OF PATHOLOGY AND DERMATOLOGY
DEPARTMENTS OF PATHOLOGY AND DERMATOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Dermatopathology Service.
B. Dermatopathology Consultation Service (including MLabs and Veterans Administration Hospital) – twelve months.

II. TEACHING ACTIVITIES:

A. Medical Students:
   1. Lecturer, MS II Dermatology Sequence.
   2. Dermatopathology, Pathology Clerkship, MS I and MS IV students (3 students).
B. House Officers:
   1. Dermatopathology signout.
   2. Review of dermatopathology consultation material.
   3. Dermatopathology teaching conference/weekly.
   4. Anatomic Pathology Conference, dermatopathology/2 per year.
C. Diagnostic Conference, Department of Dermatology (weekly).
D. Hospital Conferences:
   1. Multidisciplinary Melanoma Conference (twice monthly).
   2. Cutaneous Lymphoma Conference (twice monthly).
E. Visiting Scientists
   1. Yukari Hatori, M.D., Ph.D., Tokyo, Japan.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Effectiveness of Biobrain versus adhesive dressing in guinea pigs (James Quinn, M.D., Department of Surgery and Emergency Medicine).
B. Bcl-2 Expression in basaloid follicular hamartoma (Anj Dlugosz, M.D., Department of Dermatology).
C. Basaloid proliferation in dermatofibroma (Anj Dlugosz, M.D., Department of Dermatology).
D. Incidence of nodal nevi in lymph nodes from melanoma versus breast carcinoma patients (V. Sondak, M.D., A. Yohanda, M.D., A. Chang, M.D., and T. Johnson, M.D.).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Dermatopathology Service.

REGIONAL AND NATIONAL:

A. Member, Dermatopathology Test Committee, American Board of Pathology.
B. Member, Dermatopathology Test Committee, American Board of Dermatology.
C. Member, North American Melanoma Pathology Study Group.
D. Ad hoc manuscript reviewer, Journal of Cutaneous Pathology.
E. Ad hoc manuscript reviewer, The American Journal of Dermatopathology.
F Ad hoc manuscript reviewer, Journal of the American Academy of Dermatology.
G. Ad hoc manuscript reviewer, Archives of Dermatology.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Editor, Off-Center Fold Section, Archives of Dermatology.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Burns, R.L., Lowe, L.: Xanthomonas maltophilia infection presenting as erythematous nodules. J Am Acad Dermatol 37:836-838. 1997.
2. Saluja, A., Peters, N.T., Lowe, L., Johnson, T.M.: A surgical wound infection due to Mycobacterium chelonae successfully treated with clarithromycin. J Dermatol Surg Oncol 23:539-543, 1997.
3. Johnson, T.M., Headington, J.T., Baker, S., Lowe, L.: Usefulness of the staged excision for lentigo maligna and lentigo maligna melanoma: The "square" procedure. J Am Acad Dermatol 37:758-764, 1997.
4. Wittenberg, G.P., Douglass, M.C., Azam, M., Lee, M.W., al-Vjayli, B., Lowe, L.: Cutaneous malacoplakia presenting in a patient with the acquired immune deficiency syndrome. Arch Dermatol 134:244-245, 1998.
5. Johnson, T.M., Dolan, O.M., Hamilton, T.A., Lu, M.C., Swanson, N.A., Lowe, L.: Clinical and histologic trends of melanoma. J Am Acad Dermatol 38:681-686, 1998.
6. Dolan, O.M., Lowe, L., Orringer, M.B., Rinck, M., Johnson, T.M.: Basal cell carcinoma arising in a sternotomy scar: A report of three cases. J Am Acad Dermatol 38:491-493, 1998.
7. Wang, T.S., Lowe, L., Smith, J.W., Francis, I.R., Sondak, V.K., Dworzanian, L., Finkelstein, S., Johnson, T.M.: Complete spontaneous regression of pulmonary metastatic melanoma: A case report. J Dermatol Surg Oncol (in press).

8. Johnson, T.M., Hamilton T.A., Lowe, L.:Multiple primary melanomas. J Am Acad Dermatol (in press).

BOOKS/CHAPTERS IN BOOKS:

1. Lowe, L.: Basal cell carcinoma: Histology, in: Miller, S.J., Maloney, M.E. (eds), Cutaneous Oncology (Cambridge, MA: Blackwell Science, Inc), 1998.

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

ANNUAL DEPARTMENT REPORT
1 JULY 1997-30 JUNE 1998

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. "Immune mechanisms of Disease", Epidemiology 570, Course Instructor, Fall, 1997.
B. "Immunopathologic responses in Disease", Pathology 643, Course Instructor, Winter, 1998.
C. Undergraduate students - Matt Steinhauser, Scott Lipinski.
MSTP Students- Sara Chang and Cindi Bone-Larson.
Post-doctoral fellows- Emma Campbell and Sandra Oliveira.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

ACTIVE:

A. Principal Investigator, "Role of C-C chemokines in eosinophil airway inflammation", R-29 FIRST Award, 7/1/96-6/30/01, National Institutes of Health.
B. Co-Investigator, "Inflammatory lung disease, Section II-Granulomatous lung inflammation" NIH Program Project, with Steven L. Kunkel, Ph.D. P.A. Ward, M.D., Program Director 3/1/94-2/28/99.
C. Consortium/Co-Investigator, "The role of chemokines in autoimmune encephalomyelitis", NIH RO1 NS34510-01, with William J. Karpus, Ph.D. Microbiology/Immunology, Northwestern University, Chicago, Ill., 9/1/95 to 8/30/99.
D. Co-Investigator, "Fibrotic cytokine phenotypes in interstitial lung disease" Project 3, NIH Special Centers of Research (SCOR) grant, with Steven L. Kunkel, Ph.D. Galen B. Towes, M.D. SCOR Director.

PENDING:

A. Principal Investigator, "SCF and mast cells in allergic airway inflammation", NIH R01.
B. Principal Investigator, "Cockroach allergen-induced airway inflammation" NIH Program Project, Project IV with P.A. Ward, M.D., Program Director 3/1/99-2/28/04.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Departmental representative- Curriculum Committee for Joint Medical School Graduate program.

REGIONAL AND NATIONAL:

A. Associate Editor.
   1. Journal of Immunology.
B. Reviewer for the following Journals:
   1. Journal of Immunology.
   2. American Journal of Pathology.
   3. American Journal of Respiratory Cell and Molecular Biology.
   4. Infection and Immunity.
   5. Immunology Today.
   6. European Respiratory Journal.
   7. Journal of Experimental Medicine.
   8. Hepatology.
   9. Shock.
   10. Journal of Leukocyte Biology.
   11. Cellular Immunology.
   12. BLOOD.
   13. Journal of Clinical Investigation.
   14. Journal of Clinical Allergy.
C. Adhoc Grant Review Activities:
   1. The Israel Science Foundation Grants.
   2. The Veterans Administration MERIT Grants.
   3. The Canadian Medical Research Council.
   4. Welcome Trust Fund Grants (United Kingdom).
   5. Onterio Lung Grants.
D. Task Force recommendation on NIH Funding 1997.
   1. Immediate hypersensitivity and Allergy with K. Frank Austen.
      a. Section on Animal models.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Cytokines in allergic airway inflammation. 60th Annual Sheldon Society Meeting. Ann Arbor, MI July 11-13, 1997.
2. The dynamic interactions between cytokines, chemokines, and adhesion molecules maintains leukocyte recruitment and dictates the evolution of chronic inflammation. XIX Annual Meeting of International Society For Heart Research. July 25, 1997, Vancouver, Canada.
3. Cytokines and chemokines in allergic airway inflammation. 1rst International meeting on MIF. Picower Institute. Roslyn, N.Y. Nov. 14th, 1997.
4. The role of chemokines in Disease and Animal models. AVCP annual meeting, Albe, N.M. Nov. 21, 1997.
5. The role of chemokines in allergic airway inflammation. 2nd international conference on Chemokines in disease models and pathogenesis. Washington, D.C. Dec. 15-16, 1997.
6. Role of chemokines in acute inflammation. Inflammation and the Surgical Patient: Trauma and Burn. Snowbird, Utah, Jan 30-Feb 4, 1998.
7. Asthma, allergy, and chemokines. Schering Plough. Feb. 9, 1998.
8. Cytokines, chemokines, and leukocyte accumulation in development of inflammatory disease. Department of Burn and Trauma, Loyola University, Chicago, IL. March 18th, 1998.
9. Role of chemokines on leukocyte recruitment, airway reactivity and lymphokine profiles. The molecular asthma: Fundamental processes with potential genetic and therapeutical targets. March 29th to April 1, 1998. Banbury Center at Cold Spring Harbor.
10. Mini symposium Co-chair- Chemokines and Inflammation. Experimental Biology '98, San Francisco, CA April 18th-23rd, 1998.
11. Cytokines, chemokines, and leukocyte recruitment in allergic lung inflammation. NIOSH Conference: Occupational Asthma: In and Out of the Work Place" Morgantown, WV. April 29 to May 2, 1998.
12. Chemokines in infectious diseases. ASM Meeting. Symposium talk. Atlanta, GA. May 20, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERREED JOURNALS:

1. Chensue, S.W., K. Warmington, J.H. Ruth, N.W. Lukacs, and S.L. Kunkel. 1997. Mycobacterial and schistosomal antigen-elicited granuloma formation in interferon-g and interleukin-4 knockout mice: Analysis of local and regional cytokine and chemokine networks. J.Immunol. 159:3565-3573.
2. Teixeira, M.M., T.N.C. Wels, N.W. Lukacs, A.E.I. Proudfoot, S.L. Kunkel, T.J. Williams, and P.G. Hellewell. 1997. Chemokine-induced eosinophil recruitment: Evidence of a role for endogenous eotaxin in an in vivo allergy model in mouse skin. J. Clin. Invest. 100:1657-1666.

3. Smith, R.E., C.M. Hogaboam, R.M. Strieter, N.W. Lukacs, and S.L. Kunkel. 1997. Cell-to-cell and cell-to-matrix interactions mediate chemokine expression: an important component of the inflammatory lesion. J. Leuk Biol. 62:612-620.
4. Karpus, W.J., R.M. Strieter, S.L. Kunkel, and N.W. Lukacs. 1998. Monocyte chemotactic protein-1 regulates oral tolerance induction by inhibition of T helper cell 1-related cytokines J. Exp. Med. 187:733-741.
5. Hogaboam, C.M., S.W. Chensue, M.L. Steinhauser, N.W. Lukacs, R.M. Strieter, and S.L. Kunkel. 1997. Alteration of the cytokine phenotype in an experimental lung granuloma model by inhibiting nitric oxide. J. Immunol. 159:5585-5593.
6. Hogaboam, C.M., M.L. Steinhauser, H. Schock, N.W. Lukacs, R.M. Strieter, T.J. Standiford, and S.L. Kunkel. Therapeutic effects of nitric oxide inhibition during fecal peritonitis. Role of interleukin 10 and monocyte chemoattractant protein-1. Infect. Immun.66:650-655.
7. Bolin, L.M., R. Murray, N.W. Lukacs, R.M. Strieter, S.L. Kunkel, T.J. Schall, and K.B. Bacon. 1998. Primary sensory neurons migrate in response to the chemokine RANTES. J Neuroimmunol. 81:49-57.
8. Hogaboam, C.M., N.W. Lukacs, R. M. Strieter, and S.L. Kunkel. 1998. Monocyte chemoattractant protein-1 synthesis by lung fibroblasts modulates T cell activation. J. Immunol. 160:4606-4614.
9. E. Parks, R.M. Strieter, N.W. Lukacs, J. Gauldie, M. Hitt, F.L. Graham, and S.L. Kunkel. 1998. Transient gene transfer of IL-12 regulates chemokine expression and disease severity in experimental arthritis. J. Immunol. 160:4615-4621.
10. Carr, DJJ, S. Noisadran, WP Halford, N. Lukacs, V. Asensio, and IL Campbell. Cytokine and chemokine production in HSV-1 latently infected trigeminal ganglion cell cultures: Effects of hyperthermic stress. J. Neuroimmunology (In Press).
11. Lukacs, N.W. and S.L. Kunkel. Chemokines and their role in disease. Intern. J. Clin. Lab. (In Press).
12. B. Lu, B.J. Rutledge, L. Gu, J. Fiorillo, N.W. Lukacs, S.L. Kunkel, R. North, C. Gerard, and B.J. Rollins. Abnormalities in monocyte recruitment and cytokine expression in monocyte chemoattractant protein 1-deficient mice. J Exp. Med. 187:601-608.
13. Lukacs, N.W., C.M. Hogaboam, S.L. Kunkel, S.W. Chensue, M.D. Burdick, H.L. Evanoff, and R.M. Strieter. Mast cell-derived ENA-78 functions as a potent neutrophil chemoattractant during allergic airway inflammation. J. Leuk. Biology 63:746-751.
14. Hogaboam, C., S.L. Kunkel, R.M. Strieter, D.D. Taub, P. Lincoln, T.J. Standiford, and N.W. Lukacs. Novel role of transmembrane SCF for mast cell activation and eotaxin production in mast cell-fibroblast interactions. J. Immunol. (In Press).
15. Zickus, C., S.L. Kunkel, H. Evanoff, M. Glass, R.M. Strieter, and N.W. Lukacs. 1997. Differential regulation of CC chemokines during fibroblast-monocyte interactions: Adhesion vs. inflammatory cytokine pathways. Mediators of Inflammation (In Press).
16. Steinhauser, M.L., S.L. Kunkel, C.M. Hogaboam, H. Evanoff, R.M. Strieter, and N.W. Lukacs. Macrophage/fibroblast coculture induces macrophage inflammatory protein-1alpha production mediated by intracellular adhesion molecule-1 and oxygen radicals. Journal of Leukocyte Biology (In Press).

BOOKS/CHAPTERS IN BOOKS:

1. Simpson, K.J., N.W. Lukacs, L. Colletti, R.M. Strieter, and S.L. Kunkel. 1997. Cytokines and the liver. J. Hepatology 27:1120-1132.

ABSTRCTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFFEREED JOURNALS:

1. Waldhauser, L.K., N.W. Lukacs, X-F. Lei, M. Jordana, J. Gauldie, and Z. Xing. 1998. Adenovirus-mediated gene transfer of interleukin-4 in mouse lung induces marked airways eosinophilia. ATS International Meeting.
2. Wang, J., N.W. Lukacs, H. Liang, D. Snider, and Z. Xing. 1998. GM-CSF transgene expression in mouse lung induces macrophage activation, dendritic cell differentiation and cytokine/chemokine responses. ATS International Meeting.
3. Campbell, E.M., S.L. Kunkel, R.M. Strieter, and N.W. Lukacs. 1998. A murine model of cockroach antigen-induced airway inflammation. Exp. Biology '98. #3751.
4. Hogaboam, C.M., C. Bone-Larson, S. Lipinski, N.W. Lukacs, R.M. Strieter, S.W. Chensue, and S.L. Kunkel. 1998. Differential MCP-1 and CCR2 expression by murine lung fibroblasts derived from Th1-type and Th2-type pulmonary granuloma models. Exp. Biology '98. #3756.
5. M.L. Steinhauser, C.M. Hogaboam, S.L. Kunkel, N.W. Lukacs, R.M. Strieter, and T.J. Standiford. 1998. Interleukin 10 is a major mediator of sepsis-induced impairment in lung antibacterial host defense. Exp. Biology '98. #4675.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Daily surgical neuropathology and electron microscopic neuropathology, weekly Brain Tumor Board, review of neurosurgical, neuroradiologic, neuropathologic and clinical-pathologic correlation shared with Dr. Blaivas.
B. Consultations on surgical neuropathology from other hospitals.
C. Diagnostic neuropathology consultant, Veterans Administration Hospital.
D. Examination of all University Hospital autopsy neuropathologic material - all duties previously done by Dr. Sima except peripheral nerve and ADRC: brain cutting, sampling, microscopic examination, and special stains.

II. TEACHING ACTIVITIES:

DEPARTMENTAL:

A. Neuroscience Sequence, Neuropathology for Second Year Medical Students. Prepared and taught two laboratories and two lectures on brain tumors: toxic, metabolic, demyelinating and infectious diseases. Taught two laboratories on ischemic and degenerative diseases.
B. House Officers:
   1. Brain cutting, sampling, microscopic examination and special stain instruction of pathology house officers.
   2. Individual instruction of Pathology House Officers on neurosurgical biopsy material over microscope shared with Dr. Blaivas.
   3. Review all neurosurgically removed material in this hospital in CME-approved biweekly conference shared with Dr. Blaivas.
   4. Shared consultations in QA/QC and individual conferences.
   5. Invited presentations of neuropathologic observations at joint clinical conferences.
   6. Pathology Resident's Tuesday AP Conference rotated with other faculty.
   7. One month House Officer Electives for Neurosurgery, Neurology, and Pathology.
C. Teach laboratory techniques to Research Assistant Erin Loyer.

REGIONAL AND NATIONAL:

A. Faculty, "New Methods of Brain Tumor Analysis": 36th Annual AFIP Kenneth M. Earle Memorial. Neuropathology Review, Armed Forces Institutes of Pathology, Rockville, Maryland, February 22, 1997.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Nycomed Pharmaceuticals. "Transferin Receptor Gene Therapy" 07/01/96 - 04/30/98 ($35,000 for project).

B. National Institutes of Health, Principal Investigator, "Glioma Markers of Potential Diagnostic and Prognostic Value" ($562,806 for entire cost of project).

PROJECTS UNDER STUDY:

A. Growth, spread and antigenicity of ENU-induced gliomas in rats with Constance D'Amato and Dr. Terry Hood.
B. Extracellular matrix products and plasminogen activators of gliomas with Drs. James Varani, Robert Sitrin, Dario Caccamo and Suzanne Fligiel.
C. Magnetic resonance diffusion and cross relaxation of brain tumors with Drs. James Brunberg, Thomas Chenevert and Brian Ross.
D. Characterization of Rosai-Dorfman disease in brain with Drs. Michael Boland and Karin Muraszko.
E. Viral vectors in glioma therapy with Drs. Julian Hoff, Brian Ross and Donald Ross.
F. Effects of BCNU on histopathology and MRI signals in experimental rat brain tumors with Drs. Brian Ross and Thomas Chenevert.
G. Roberson PL, Ten Haken RK, McKeever PE, Ensminger WD: Nonuniform liver dose for yttrium-90-microsphere therapy in a rabbit model.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chief, Section of Neuropathology.
B. Director, Neuropathology Residency. Full accreditation from the Accreditation Council for Graduate Medical Education obtained in 1996.
C. Member, Photography Committee.
D. 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. Interaction with Chiefs and Staff of other clinical services, particularly Neurosurgery, Neurology, Nuclear Medicine, Radiation Oncology, Neuro-oncology and Neuro-radiology.
D. Quality control of microscopic, ultrastructural and immunodiagnostic neuropathology. This included QA/QC meetings and various ad hoc reviews requested by faculty.

REGIONAL AND NATIONAL:

A. Editorial Board, Journal of Neuro-Oncology, Primarily reviewed, found referees for and reviewed decisions on approximately 12 manuscripts.
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 neuro-oncology journals.
D. M-Labs Neuropathology Services.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

A. Faculty of Graduate Program of Department of Pathology.
B. Member of the University of Michigan Cancer Center.
C. Member, International Academy of Pathology, 1972--.
D. Member, Alpha Omega Alpha, Eta Chapter, 1972--.
E. Member, American Association of Neuropathologists, 1978--.
F. Member, Society of Neuroscience, 1983--.
G. Member, American Association of Pathologists, 1984--.
H. Member, Children's Cancer Study Group, 1985--.
   1. Pathology Committee, 1989--.
      Decide on policies regarding handling of tumor specimens at annual meetings.
   2. Primary Review Pathologist for astrocytoma study, 1991--.
      Review and determine correct diagnoses on cases put on study protocol.
I. Member, Histochemical Society, 1989--.
   1. Publication Committee 1995-1998.
      Monitor the Journal of Histochemistry and Cytochemistry and other HCS publications.
   2. Future Directions Committee 1994-1998.
   3. Constitution Advisor 1996--.
      Make certain Council functions in accord with constitution.
   4. Councilor, 1994-1998.
      Review and vote upon policies regarding the Society's journal, annual meetings, membership, new directions, etc., at annual meetings and all during the year.
J. Lieutenant Colonel, U.S. Army Reserve Medical Corps, 1997--.

INVITED LECTURES/SEMINARS:

1. Speaker, "Assessment of Grade of Malignancy and Transferrin Receptor Staining of Astrocytomas," Nycomed Research Conference, Hamilton, Bermuda, 1998.
2. Speaker, The Histochemical Society Presidential Symposium, "Insights about Brain Tumors Gained through Immunohistochemistry and In Situ Hybridization of Nuclear and Phenotypic Markers", Microscopy and Microanalysis '97, Cleveland, Ohio, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. McKeever PE, Ross DA, Strawderman MS, Brunberg JA, Greenberg HS, Junck L: A comparison of the predictive power for survival in gliomas provided by MIB-1, bromodeoxyuridine and proliferating cell nuclear antigen with histopathologic and clinical parameters. J. Neuropathol. Exp. Neurol. 7:798-805, 1997.
2. Kamchonwongpaisan S, McKeever P, Hossler P, Ziffer H, Meshnick SR. Artemisinin neurotoxicity: Neuropathology in rats and mechanistic studies in vitro. Am. J. Trop. Med. Hyg. 56(1)7-12, 1997.
3. McKeever PE: Insights about brain tumors gained through immunohistochemistry and in situ hybridization of nuclear and phenotypic markers. J. Histochem. Cytochem. 46:585-594, 1998.

4. Rodas RA, Fenstermaker RA, McKeever PE, Blaivas M, Dickinson L, Papadopoulos SM, Hoff JT, Hopkins LN, Fronckwiak MD, Greenberg HS. Intraluminal thrombosis in brain tumor vessels correlates with postoperative thrombotic complications. J. Neurosurg. 89:200-205, 1998.
5. McKeever PE, Strawderman MY, Yamini B, Mikhail A, Blaivas M. MIB-1 Proliferation index predicts survival among patients with Grade II astrocytoma. J. Neuropathol. Exp. Neurol. (in press).
6. Chenevert TL, McKeever PE, Ross BD: Monitoring early response of experimental brain tumors to therapy using diffusion magnetic resonance imaging. Clinical Cancer Research 3:1457-1466, 1997.

BOOKS/CHAPTERS IN BOOKS:

1. McKeever PE: Molecular neuropathology in tumor diagnosis. In: Kornblith PL and Walker MD, (Eds): Advances in Neuro-Oncology II, 2nd Edition, Futura, New York, 1997 pp. 139-178.
2. McKeever PE: Glial cell pathology. In: Smith BH and Adelman A, eds.: Encyclopedia of Neuroscience, Elsevier Science, 1997 (in press).
3. Greenberg HS, Chandler WF, Ensminger WD, Junck L, Page MA, Gebarski SS, Hood TW, Stetson PL, Diaz RF, Hegarty T, Thornton A, Lichter AS, McKeever PE, Tankanow R: Radiosensitization with constant intra-arterial infusion of bromodeoxyuridine (BUDR) and focal external beam radiation in the treatment of malignant astrocytoma. In: Infusion Systems in Medicine. (in preparation).
4. McKeever PE, Lloyd RV: Tumors of the pituitary region. In: Garcia JH, Budka H, McKeever PE, Sarnat HB, Sima AAF (Eds.): Neuropathology: The Diagnostic Approach, Mosby, St. Louis, 1997 pp. 219-261.
5. McKeever PE, Blaivas M, Nelson JS: Tumors: Applications of light microscopic methods. In: Garcia JH, Budka H, McKeever PE, Sarnat HB, Sima AAF (Eds): Neuropathology: The Diagnostic Approach, Mosby, St. Louis, 1997 pp. 31-95.
6. McKeever PE, Blaivas M, Gebarski SS: Pituitary Tumors. In: Thapar K, Kovacs K, Scheithauer BW, Lloyd RV (Eds.): The Humana Press Inc., Totowa, New Jersey, 1997 (in press).

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

1. McKeever PE: Insights about brain tumors gained through immunohistochemistry and *in situ* hybridization of nuclear and phenotypic markers. Microscopy and Microanalysis, August 11, 1997.

CLAIRE W. MICHAEL, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Cytopathology - six months.
B. Breast Cancer Clinic, Cytopathology and back-up Histopathology - twelve months.
C. Consultation Service, Department of Pathology:
    1. Cytopathology - twelve months.
    2. Breast pathology - back up, twelve months.
D. Necropsy Service - six weekends.

II. TEACHING ACTIVITIES:

A. Medical School Students: Laboratory instructor, September 1997 - May 1998 (38 contact hours).
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. Consult Case Conference - three/year.
C. Other Education Activities:
    1. Cytotechnologists - Cytopathology Conferences - three/year.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Investigator 1 UO1 CA68291-01 ($2,610,213-direct cost) "Retinoids and Intermediate Biomarkers for CIN II and III", 9% effort, National Institute of Health.

PROJECTS UNDER STUDY:

A. Genomic deletions in tumors from families with breast and ovarian cancer. In collaboration with Sofia D. Merajver, M.D., Ph.D.
B. The cytologic spectrum of mesothelioma in situ, in collaboration with Dr. C.Bedrossian, C.W.M., Northwestern University.
C. Can true papillary neoplasms and their mimickers be distinguished cytologically?, in collaboration with Buschmann, B., University of South Alabama.
D. The differential diagnosis of Psammoma bodies on cervical smears.

E. Breast carcinoma mimicking fibroadenoma or fibrocystic changes.
F. The cytologic evaluation of vitreous fluids in collaboration with Andrew Flint, M.D. and Victor Elner, M.D.
G. The cytologic features of neoendocrine lesions of the lung: differential diagnosis and mimics with Andrew Flint, MD.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Cytopathology Laboratory.
B. Director, Cytopathology Fellowship.

MEDICAL SCHOOL/HOSPITAL:

None.

REGIONAL AND NATIONAL:

A. Reviewer, Diagnostic Cytopathology.
B. Reviewer, Cancer Cytopathology.
C. Reviewer, CAP Check Sample.
D. Member, Quality Control Committee, Papanicolaou Society of Cytopathology.
E. Member, Nomination Committee, Papanicolaou Society of Cytopathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Pregnancy Related Changes on Cervical Smears," invited seminar, Department of Pathology, University of Maryland, Baltimore, MD, August 1997.
2. "Confocal Laser Scanning Microscopy and its Application in Pathology," invited seminar, New York Medical Hospital (Cornell School of Medicine), New York, August 1997.
3. "Fine Needle Aspiration of the Breast, A Pattern Recognition," invited seminar, Saint Louis University Hospital, St. Louis, MO, August 1997.
4. "Pap smears in the 90's and Beyond", in Women's Health Care: State of the Art Symposium. St. Joseph Medical Center, Towson, MD, February 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Michael CW, King J, Hester R: Confocal laser scanning microscopy (CLSM) and three-dimensional reconstruction of serous fluids. Diagn Cytopathol 1997;17:272-279.

2. Michael CW and Esfahani FM: Pregnancy related changes: A retrospective review of 278 patients. Diagn Cytopathol 1997; 17:99-107.
3. Stastny FJ, Geisinger KR, Michael CW, Raab SS, Powers CN, Davila MR. Another quality assurance issue. Amended reports: What do we really know about them. Diagn Cytopathol 1998; 18:67-70.
4. Michael CW, Flint A: Cytologic features of Wegeners Granulomatosis. Am J Clin Path 1998; 110:10-15.
5. Tworek J, Giordano T, Michael CW. Comparison of intraoperative cytology with frozen sections in the diagnosis of thyroid lesions. Am J Clin Path (in press).
6. Rock CL, Michael CW, Reynolds RK, Ruffin MT. Prevention of cancer cervix. In critical reviews on oncology and hematology (accepted for publication).

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Tworek JA, Michael CW. Fine needle aspiration cytology of lymphocyte rich parotid lesions (submitted to Am J Clin Path).

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

1. King J, Elkhalifa M, Michael CW. Malignant lymphoma identified on a cervical cytologic smear with immunophenotypic analysis. (Letter to the Editor) Acta Cytol 1997; 41:1228-29.
2. Kintanar EB, Michael CW. Diagnostic pitfalls and mimics of HGSIL. Acta Cytol 1997; 41:5, 1554-1545.
3. Michael C, Naylor B. Amyloid in cytologic specimens: Differential diagnosis and diagnostic pitfalls. Acta Cytol 1997; 41:5, 1621.
4. Michael CW, Georgy B, Elhosseiny A. The cytologic spectrum and diagnostic pitfalls of apocrine lesions of the breast. Acta Cytol 1997; 41:5, 1588.
5. Hunter B, Michael CW. Cytologic artifacts and pitfalls in fine needle aspirates processed by thinprep technique. Accepted for a platform presentation, American Society of Cytopathology, 1998.
6. Michael CW, Tworek JA, Wojno KJ. The use of newly marketed antibodies in conjunction with the routine panel in the evaluation of serosal fluids. Accepted for poster presentation in the American Society of Cytopathology, 1998.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Program Director, "Experimental Immunopathology Training Grant."
   2. Ph.D. Dissertation Committees, University of Michigan:
      a. Anne Jackson.
      b. Pamela Bennett-Baker.
   3. Ph.D. Dissertation Advisor:
      a. Michael Eisenbraun.
      b. Chris Kirk.
      c. Annavelys Ortiz-Suarez.
      d. Allen Harrison.
      e. Boqin Qui.
      f. Laura Mancino.
   4. Undergraduate students:
      a. Aaron Freilich, CLA III.

B. Postdoctoral Fellows:
   1. Dong-Li Yang, M.D.
   2. Ami Tamir, Ph.D.
   3. Gonzalo Garcia, Ph.D.

C. Assistant Research Scientists:
   1. R. Lee Mosley, Ph.D.
   2. Igor Dozmorov, Ph.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Activation Defects in Aging T Cells", NIH AG-09801 (15%), $170,741 direct costs/year, 8/1/90 - 7/31/98. MERIT award.

B. Principal Investigator, "Immune and Muscle Function Assays as Biomarkers of Aging", NIH AG-11067 (8%), $162,629 direct costs/year, 4/1/93 - 3/31/99.

C. Principal Investigator, "Genetic Control of Longevity in Mice", NIH AG-11687 (8%), $258,077 direct costs/year, 9/1/93 - 8/31/98.

D. Principal Investigator, "New T Cell Subsets Defined by P-glycoprotein in Aging Mice", NIH R01-AG03978 (15%), $156,266 direct costs year, 12/1/95 - 11/30/98.
E. Director, "Core Facility for Aged Rodents", NIH AG-08808 (5%), $64,627 direct costs/year, 9/1/94 - 8/31/99. (Component of Claude Pepper Older Americans Independence Center, J. Halter, Program Director).
F. Director, "Research Development Core", NIH AG-08808 (15%), $155,270 direct costs/year, 9/1/94 - 8/31/99. (Component of Claude Pepper Older Americans Independence Center, J. Halter, Program Director).
G. Project Director, "Prevention of Disease by Immunotonic Agents in Mice", NIH AG-08808 (5%), $50,235 direct costs/year, 9/1/94 - 8/31/99. (Component of Claude Pepper Older Americans Independence Center, J. Halter, Program Director).
H. Program Director, "Research Training in Experimental Immunopathology", NIH T32-AI-07413 (5%), $243,644 direct costs/year, 5/1/93 - 4/30/98.
I. Co-Director, "Breast Cancer in Elderly Women", (M. Wicha, PI), NIH/NCI P20-AG13094 (5%), $25,000 direct costs/year, 9/30/94 - 8/31/98.
J. Course Director, "Summer Training Courses in Experimental Aging Research", NIH/NIA R13-AG12917 (0%), $31,537 direct costs/year, 4/1/95 - 3/31/98.
K. Principal Investigator, "Wild Derived Mouse Stocks: New Models for Aging Research," NIH R01-AG13711 (5%), $112,102 direct costs/year, 9/1/96 - 8/31/99.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Graduate Education Committee.
B. Qualifying Examination Committee.
C. Director, Experimental Immunopathology Training Program.
D. Representative to Executive Committee, Program in Biomedical Sciences.

MEDICAL SCHOOL/HOSPITAL:

A. Geriatrics Center: Research Development Core Director.
B. Geriatrics Center: Director, Core Facility for Aged Rodents.
C. Member, Geriatrics Center Research Operating Committee.
D. Associate Director for Research, Geriatrics Center.
E. Member, Executive Committee, Cell and Molecular Biology Training Program.
F. Member, Rheumatology Training Program.
G. Co-director, Breast Cancer in Elderly Women Project, UM Cancer Center.
H. Member, Cancer Biology Training Program.

REGIONAL AND NATIONAL:

A. Board of Scientific Advisors, Buck Center for Research on Aging.
B. Fellow, Gerontological Society of America.
C. Research Committee, American Federation for Aging Research.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Journal of Gerontology: Biological Sciences.
B. Journal of the American Geriatrics Society. (Section Editor).
C. Journal of Immunology Primary Reviewer Pool.

INVITED LECTURES/SEMINARS:

1. President's Cancer Panel: Cancer in the Aging Population. University of Michigan. "Molecular Biologic Questions: Animal Models." July 31.
2. International Symposium on Psychoneuroendocrine and Immunological Correlates of Aging, Pavia, Italy. "The Aging Immune System: Subsets, Signals, Survival." September 17 – 20.
3. Rochester Conference on Health: Successful Aging and the New Millennium. University of Rochester, NY. "Genetics of Longevity, Disease, and Immunity in Aging Mice." September 24-26.
4. Rotary Club of Hamtramck Luncheon Meeting. "Immune Decline in Old Age." Hamtramck, MI. October 2.
5. Gerontology Society of America Annual Meeting, Cincinnati, OH. "Finding Genes for Aging and Longevity." November 14.
6. International Conference on Biomedical Aspects of Aging Research, Venice (Italy). Discussant: Immunosenescence. December 10 – 13.
7. International Symposium on Selected Issues in Kidney Transplantation, Zürs, Austria. "The Aging Immune System." January 9 – 11.
8. Department of Biology, Wright State University, Dayton, OH. "T Cells in Old Mice: Subsets, Signals, and Survival." January 16.
9. North Shore University Hospital, Manhasset, NY. "T Cells in Old Mice: Subsets, Signals, and Survival." February 10.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Gorgas, G., Butch, E.R., Guan, K. and Miller, R.A.: Diminished activation of the MAP kinase pathway in CD3-Stimulated T lymphocytes from old mice. Mechanisms of Ageing and Development, 94:71-83, 1997.
2. Miller, R.A.: Age-related changes in T cell surface markers: a longitudinal analysis in genetically heterogeneous mice. Mechanisms of Ageing and Development, 96:181-196, 1997.
3. Telford, W.G., Nam, S.Y., Podack, E.R. and Miller, R.A. CD30-mediated apoptosis in murine CD8 T cells after cessation of TCR signals. Cellular Immunology 182:125-136, 1997.
4. Dozmorov, I.M. and Miller, R.A.: In vitro production of antigen-specific T cells from unprimed mice: role of dexamethasone and anti-IL-10 antibodies. Cellular Immunology 178:187-196, 1997.
5. Dozmorov, I. and Miller, R.A.: Generation of antigen-specific Th2 cells from unprimed mice in vitro: effects of dexamethasone and anti-IL-10 antibody. J. Immunol. 160:2700-2705,1998.
6. Miller, R.A., Chrisp, C. and Galecki, A.: CD4 memory T cell levels predict lifespan in genetically heterogeneous mice. FASEB Journal 11:775-783, 1997.
7. Miller, R.A., Chrisp, C., Jackson, A.U., and Burke, D.: Marker loci associated with lifespan in genetically heterogeneous mice. J. Gerontology: Medical Sciences, in press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Garcia, G.G., and Miller, R.A.: Increase in Zap-70 association with CD3ζ in CD4 T cells from old mice. Submitted for publication.
2. Kirk, C.J., and Miller, R.A.: Analysis of Raf-1 activation in response to TCR activation and co-stimulation in murine T-lymphocytes: effect of age. Submitted for publication.

3. Jackson, A.U., Fornés, A., Galecki, A., Miller, R.A., and Burke, D.T.: Multiple trait QTL analysis using a large mouse sibship. Submitted for publication.
4. Mosley, R.L., Koker, M.M. and Miller, R.A.: Idiosyncratic alterations of TCR size distributions affecting both CD4 and CD8 T cell subsets in aging mice. Submitted for publication.

BOOKS/CHAPTERS IN BOOKS:

1. Miller, R.A.: When Will the Biology of Aging Become Useful? Future Landmarks in Biomedical Gerontology. J. American Geriatrics Soc. 45:1258-1267, 1997.
2. Miller, R.A.: DHEA – Brass ring or red herring? J. American Geriatrics, Soc. 45:1402-1403, 1997.
3. Miller, R.A., Garcia, G., Kirk, C. J., and Witkowski, J. M.: Early activation defects in T lymphocytes from aged mice. Immunological Reviews 160:79-90, 1997.
4. Miller, R.A.: The biology of aging and longevity. In: Principles of Geriatric Medicine and Gerontology, 4th Edition, W. R. Hazzard et al., (eds), McGraw-Hill, Inc., NY, In Press.
5. Kirk, C. J., and Miller, R.A.: Raf-1 protein kinase activity in T cells from aged mice. In: Methods in Molecular Medicine: Aging Methods and Protocols, Y. Barnett and C. Barnett, (eds), Humana Press, In Press.
6. Miller, R.A.: Aging and Immune Function, in, Paul, W.E. (ed), : Fundamental Immunology, Fourth Edition, Lippincott-Raven, New York, In Press.
7. Miller, R.A. and Schneider, E.: Anti-Aging Interventions. In: Textbook of Geriatric Medicine, Fifth Edition, J.C. Brockelhurst, R. C. Tallis, and H. M. Fillit, (eds), Churchill Livingstone, New York, In Press.

HEDWIG S. MURPHY, M.D., Ph.D.
ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Surgical Pathology and Frozen Section Diagnosis (6 months/year)
B. Autopsy Service, rotational basis, on call 13 weeks/year (staffing 15-20 cases/year).
C. Case presentations at Tumor Board
D. Case presentations at Morbidity and Mortality Conferences.
E. Case presentations at weekly Urologic Pathology Conferences

II. TEACHING ACTIVITITES:

A. Post-Doctoral Fellows:
   1. Research co-advisor to post-doctoral fellow: Dr. Matthew Adams, Dept. of Rheumatology, University of Michigan.supported by Arthritis Foundation of Michigan
B. House Officers:
   1. Pathology house officers, Autopsy supervision and instruction (13 weeks /year)
   2. Pathology house officers, Surgical Pathology supervision and instruction, (6 months/year)
   3. Lecture and Case presentations at Biweekly Urologic Pathology Conferences
C. Graduate students:
   1. Pathology 585, Lecture and Laboratory course for Medical Illustration students, 1997.
D. Undergraduate students:
   1. Research advisor to undergraduate student: Jennifer Woodside supported by Lupus Foundation Gina Finzi Memorial Student Fellowship
   2. Human anatomy and pathology, Cranbrook-Kingswood (High School Biology Classes).

III. RESEARCH ACTVITIES:

SPONSORED SUPPORT:

A. Principle Investigator, NHLBI Clinical investigator Development Award K08 HL03181-01: Structure and Function of Recombinant Selectin Ligands. 09/01/94-08/31/99. ($402,916/five years).

B. Principal Investigator, Biological Responses of Vascular Endothelial Cells. American Heart Association, Michigan Affiliate MHA#03GB978 7/01/97-6/30/98 ($30,000.00/one year).
C. Collaborator. Lung Injury by Oxygen Metabolites NIH/NIGMS R37 GM29507. National Institute of Health (Peter A. Ward, Principal Investigator). ($1.123,824/four years) 7/1/97-6/30/01.
D. Mentor, Jennifer Woodside, recipient, Lupus Foundation Gina Finzi Memorial Student Fellowship, $2000.00 and OSBRP award for summer student research.
E. Co -mentor, Matthew Adams, M.D., Arthritis Foundation, Michigan Chapter. 1/1/98-12/31/98 ($20,000/one year).

PENDING:

A. Co-Investigator, "Gender-specific T cell homing and autoimmunity" (B. Richardson, Internal Medicine, PI), NIH $1,760,000 12/98 – 11/03
B. Co-Investigator, "Host Defense of the Lung" Research Enhancement Award Program (REAP)Veteran's Administration $1,350,00011/98-10/03
C. Principal Investigator "Effect of Estrogen on Vascular Endothelial Cells" Lupus Foundation of America, Inc.$30,000 10/98 - 09/00

PROJECTS UNDER STUDY:

A. Heterogeneity of endothelial cell responses in inflammation
B. Gender-specific effects of hormones on T cell and endothelial cells in autoimmunity
C. Sources and function of endothelial cell oxidants

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None.

MEDICAL SCHOOL/HOSPITAL:

None.

REGIONAL AND NATIONAL:

A. Manuscript Review for:
Clinical Immunology and Immunopathology
Biochemical pharmacology
Shock
Free Radical Biology and Medicine

B. Membership in National Organizations:
American Association for the Advancement of Science, New York Academy of Science, American Society for Investigative Pathology
American Society of Clinical Pathologists, American Association of University Women, The A. James French Society of Pathologists

V. OTHER RELEVANT ACTIVITIES:

A. Case presentations at Tumor Board.
B Case presentations at Morbidity and Mortality Conferences.
C Case presentations at Urologic Pathology Conferences
D. Tissue evalulation for clinical researchers.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

None.

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

1. Effects of estrogen on endothelial cell adhesion molecule expression and function. J Huo, M Adams, HS Murphy, BD Richardson, RR Mo, JK Eisenbraum, R Yung. AFMR Regional Scientific Meeting, 1998.
2. The effects of β-Estradiol on T cell adhesion molecule expression and function MD Adams,RL Yung, HS Murphy, BC Richardson. AFMR Regional Scientific Meeting, 1998.
3. Effects of estrogen on endothelial cell adhesion molecule expression and function. R Yung. J Huo, M Adams, BD Richardson, RR Mo, JK Eisenbraum, HS Murphy. American College of Rhematology Annual Meeting, 1998.
4. The effects of β-Estradiol on T cell adhesion molecule expression and function. R Yung. J Huo, M Adams, BD Richardson, RR Mo, JK Eisenbraum, HS Murphy. American College of Rhematology Annual Meeting, 1998.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Consultation Service: Cytopathology, gynecologic pathology and pulmonary pathology - 12 months.

II. TEACHING ACTIVITIES:

A. Pathology residents – Diagnostic consultations, autopsy supervision, and seminars.
B. Dental and graduate students - Lectures (Dermatopathology).

III. RESEARCH ACTIVITIES:

A. Cytopathology, with particular reference to serous fluids.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Advisory Committee on Appointments and Promotions.

REGIONAL AND NATIONAL:

A. American Society of Cytopathology:
Long Range Planning Committee.
B. Cytopathology, Editorial Advisory Board.
C. Acta Cytologica, Editorial Advisory Board.
Associate Editor, North American Review Board.
D. Diagnostic Cytopathology, Consulting Editor.
E. International Academy of Cytology:
International Board of Cytopathology, Member.
Editorial and Ethics Committee, Member.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Naylor, B.: Cytology of serous fluids: Technical approaches and diagnostic problems. Workshop, Annual Scientific Meeting of American Society of Cytopathology, Boston, Massachusetts, November, 1997.
2. Naylor, B.: a). Mesothelioma, b). Transthoracic fine needle aspiration cytology, c) Histology of cytopathology. Lectures, Cytotechnology Training Program, Henry Ford Hospital, Detroit, Michigan, 1998.

HONORS AND AWARDS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

None.

BOOKS/CHAPTERS IN BOOKS:

1. Naylor, B.: Cytopathology of the Uterus: Historical Perspectives. In: Cytopathology of the Uterus, A. Meisels, C. Morin eds, Second Edition, Chicago, ASCP Press, 1997, 1-28.

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

1. Michael CW, Naylor B. Poster presentation. Amyloid in cytologic specimens: Differential diagnosis and diagnostic pitfalls. American Society of Cytopathology, Annual Scientific Meeting, Boston, Massachusetts, November, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Supervised Luis Del Peso, Daryoush Ecketerae, Maribel Gonzalez-Garcia, Victor Gonzalez-Muñoz, Yuanming Hu, Naohiro Inohara, Takeyoshi Koseki, Rebecca Liu, Dayang Wu, Postdoctoral Fellows.
B. Supervised Mary Benedict, Andrew Merry, Tom Hlaing, Tania Gourley, graduate students.
C. Laboratory Instructor, Pathology 630/631. Full semester, two hours/week.
D. Department of Pathology, Graduate Program Course 581, University of Michigan, Ann Arbor, Michigan.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Genetic regulation of apoptotic cell death," National Institutes of Health, $813,000 (total direct costs).
B. Principal Investigator, Research Career Development Award, "genetic regulation of apoptotic cell death," National Institutes of Health, $315,000 (total direct costs).
C. Principal Investigator, "Bcl-x_s-mediated apoptosis of Kaposi's sarcoma cells," National Institutes of Health, $1,292,048 (total direct costs).
D. Principal Investigator, "Molecular analysis of Bcl-x_s-induced apoptosis in breast cancer," US Army Medical Research and Material Command, Fort Detrick, Frederick, MD $801,917 (total).
E. Principal Investigator, "HRK, A novel apoptosis regulatory gene," National Institutes of Health, $116,826 (total annual direct costs).
F. Principal Investigator, "Regulation of apoptosis in hematopoietic progenitors," fellowship for Daryoush Ekhterae, Research Fellow. National Institutes of Health, $29,500.00.
G. Principal Investigator, "Molecular interactions of Bcl-2 family members," US Army Medical Grant; fellowship for Mary Benedict, Graduate Student Research Assistant. $51,000.

PROJECTS UNDER STUDY:

A. Molecular characterization of the programmed cell death pathway in mammals and *C. elegans.*
B. Molecular regulation of Bcl-2 family members.
C. Gene therapy using Bcl-2 proteins as targets for cancer cell killing.

IV. DEPARTMENTAL:

A. Member, University of Michigan Cancer Center, Ann Arbor, MI.
B. Member, Transgenic Core Committee, Multipurpose Arthritis Center, University of Michigan, Ann Arbor, MI.
C. Member, Comprehensive Examination Committee, Pathology Graduate Program, University of Michigan, Ann Arbor, MI.
D. Member, Admissions Committee, Molecular and Cellular Biology, Graduate Program, University of Michigan, Ann Arbor, MI.
E. Member, Hybridoma Core Committee, Multipurpose Arthritis Center, University of Michigan, Ann Arbor, MI.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Molecular and Cellular Biology Program.
B. Member, University of Michigan Cancer Center.
C. Member, Transgenic Core Facility Committee, Multipurpose.
D. Member, Faculty Search Committee, Rheumatology Division, and Department of Microbiology/Immunology.
E. Reviewer, Departmental Grants and Summer Student Scholarship Program.
F. Member, Search Committee to find Chairman of Department of Radiation Oncology, University of Michigan Medical School, Ann Arbor, MI.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

A. Reviewer for the following journals: American Journal of Pathology; Cancer Research; Cell; Cell Death and Differentiation; Immunity; Journal of Biological Chemistry; Journal of Cell Death and Differentiation; Journal of Immunology; Oncogene; Journal of Cell Biology; Laboratory Investigation; Proceedings of National Academy of Science USA; Science.

INVITED LECTURES AND SEMINARS:

University Of Michigan:

1. Invited Speaker, "Regulation of Apoptosis in Red Blood Cell," Organogenesis of Red Blood Cells Symposium, University of Michigan Medical Center, January 20, 1998.
2. Invited Speaker, "Regulation of Programmed Cell Death," Comprehensive Cancer Center Grand Rounds, University of Michigan Medical Center, February 13, 1998.
3. Invited Speaker, "Regulation of Apoptosis," University of Michigan RARU Seminar, April 2, 1998.

National and International:

1. Invited Speaker and Session Co-chair, Cold Spring Harbor meeting on Programmed Cell Death, September 14-18, 1997.
2. Invited Speaker, "Regulation of Programmed Cell Death," University of Texas Southwest Medical Center, September 30, 1997.
3. Invited Speaker, "Regulation of Programmed Cell Death," Case Western Reserve University, Cleveland, Ohio, October 20, 1997.
4. Invited Speaker, "Regulation of Programmed Cell Death," National Institute on Aging, Gerontology Research Center, Baltimore, Maryland, October 30, 1997.
5. Invited Speaker, Signal Transduction Seminar Series, "Regulation of Apoptosis by the Bcl-2 Family," Parke-Davis, Ann Arbor, Michigan, November 4, 1997.
6. Invited Speaker and Session Chair, "Protein-Protein and Protein-Lipid Interactions in Signal Transduction: Use of Small Synthetic Molecules as Probes and Therapeutic Agents," NATO Advanced Research Workshop at H. Lee Moffitt Cancer Center and Research Institute, University of South Florida, Tampa, Florida, December 5-9, 1997.
7. Invited Speaker, "Regulation of Programmed Cell Death," University of Seville, December 29, 1997.
8. Invited Speaker, "Molecular Regulation of Programmed Cell Death," Nagoya University Medical School, Nagoya, Japan, March 9, 1998.
9. Invited Speaker, "Molecular Regulation of Apoptotic Cell Death," Aichi Cancer Center Research Institute, Nagoya, Japan, March 10, 1998.
10. Invited Speaker, "Regulation of Programmed Cell Death," National Cancer Center, Tokyo, Japan, March 11, 1998.
11. Invited Speaker, "Regulation of Programmed Cell Death," Osaka University Medical School, Osaka, Japan, March 18, 1998.
12. Invited Speaker, "Regulation of Apoptosis," Albert Einstein College of Medicine, Yeshiva University, April 6, 1998.
13. Invited Speaker, "Apoptosis," New York University, April 7, 1998.
14. Invited Speaker, "Regulation of Programmed Cell Death," University of Pennsylvania, Philadelphia, May 11, 1998.
15. Invited Speaker, "Regulation of Programmed Cell Death," Pfizer, Inc., Groton, Connecticut, May 12, 1998.

16. Invited Speaker, "Regulation of Programmed Cell Death," Vertex Pharmaceuticals, Cambridge, Massachusetts, May 13, 1998.
17. Invited Speaker, "Regulation of Programmed Cell Death," Manitoba Institute of Cell Biology, Winnipeg, Manitoba, Canada, May 28, 1998.
18. Invited Speaker, "Regulation of Programmed Cell Death," FASEB Summer Research Conference, Vermont Academy, Saxtons River, VT, June 23, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNAL:

1. Bojes HK, Datta K, Xu J, Chin A, Simonian P, Nuñez G, Kehrer JP: Bxl-ZL overexpression attentuates glutathione depletion in FL 5.12 cells following interleukin-3 withdrawal. Biochem J. 325:15:315-319 (1997).
2. Simonian PL, Grillot DAM, Nuñez G: Bcl-2 and Bcl-x_L can differentially block chemotherapy induced cell death. Blood. 90:1208-1216 (1997).
3. Wu D, Wallen, HD, Inohara N, Nuñez G: Interaction and regulation of the C. Elegans death protease CED-3 by CED-4 and CED-9. J Biol Chem. 274:21449-21454 (1997).
4. Simonian PL, Grillot DAM, Nuñez, G: Bak can accelerate chemotherapy-induced cell death independently of its heterodimerization with Bcl-x_L and Bcl-2. Oncogene. 15:1871-1875 (1997).
5. Inohara N, Koseki T, Hu Y, Chen S, Nuñez, G: CLARP, a novel DED-containing protein interacts with Caspase-8 and regulates apoptosis. Proc Natl Acad Sci USA. 94:10717-10722 (1997).
6. del Peso L, Gonzalez-Garcia M, Page C, Herrera R, Nuñez G: Interleukin-3-Induced Phosphorylation of BAD through the Protein Kinase Akt. Science. 278:687-689 (1997).
7. Packham G, White EL, Yang H, Eischen CM, Parganas E, Ihle JN, Nuñez G, Cleveland JL: Bcl-x_L is selectively regulated by haemopoietins and activated in murine haemopoietic malignancies. Nature Genetics. (In press).
8. Fulda S, Friesen C, Los M, Scaffidi C, Mier W, Benedict M, Nuñez G, Krammer PH, Peter ME, Debatin KM: Betulinic acid triggers CD95 (APO-1/Fas)- and p53-independent apoptosis via activation of caspases in neuroectodermal tumors. Cancer Research. 57(21):4956-4964 (1997).
9. Schneider TJ, Grillot D, Foote LC, Nuñez G, Rothstein TL: Bcl-x protects primary B cells against Fas-mediated apoptosis. J Immunol. 159(10):4834-4839 (1997).
10. Petschner F, Zimmerman C, Strasser A, Grillot D, Nuñez G, Pircher H: Constitutive expression of Bcl-x_L or Bcl-2 prevents peptide antigen-induced peripheral T cell deletion but does not influence memory T cell survival. Eur J Immunol. 28(2):560-569 (1998).
11. Akifusa S, Ohguchi M, Koseki T, Nara K, Semba I, Yamato K, Okahashi N, Merino R, Nuñez G, Hanada N, Takehara T, Nishihara T: Increase in bcl-2 level promted by CD40 ligation correlates with inhibition of B-cell apoptosis induced by vacuolar type H^+ -ATPase inhibitor. Exp Cell Research. 238:82-89 (1998).
12. Solvason N, Wu W, Kabra N, Lund-Johansen F, Grazia-Roncarolo M, Behren T, Grillot D, Nuñez G, Lees E, Howard M: Transgene expression of bcl-x_L permits anti-immunoglobulun (Ig)-induced proliferation of xid B cells. J Exp Med. 187(7):1081-1091 (1998).

13. Stoll S, Benedict M, Mitra R, Hiniker A, Elder JT, Nuñez G: EGF receptor signaling inhibits keratinocyte apoptosis: evidence for mediation by bcl-x_L. Oncogene. 16:1493-1501 (1998).
14. Inohara N, Ekhterae D, Garcia I, Carrio R, Merino J, Merry A, Chen S, Nuñez G: Mtd, a Novel Bcl-2 Family Member Activates Apoptosis in the Absence of Heterodimerization with Bcl-2 and Bcl-X_L. J Biol Chem. 273(15):8705-8710 (1998).
15. Hu Y, Benedict M, Wu D, Inohara N, Nuñez G: Bcl-x_L interacts with Apaf-1 and inhibits Apaf-1-dependent Caspase-9 activation. Proc Natl Acad Sci USA. 95:4386-4391 (1998).
16. Koseki T, Inohara N, Chen S, Nuñez G: ARC, an inhibitor of apoptosis expressed in skeletal muscle and heart that interacts selectively with caspases. Proc Natl Acad Sci USA. 95(9):5156-5160 (1998).
17. Inohara N, del Peso L, Koseki T, Chen S, Nuñez G: RICK: a novel protein kinase containing a caspase recruting domain interacts with CLARP and regulates CD95/Fas/Apo-1-mediated apoptosis. J Biol Chem. 273(20):12296-12300 (1998).
18. Inohara N, Koseki T, Chen S, Wu X, Nuñez G: CIDE, a novel family of cell death activators with homology to the 45 kDa subunit of the DNA fragmentation factor. EMBO J. 17(9):2526-2533 (1998).
19. Lam M, Bhat MB, Nuñez G, Ma J, Distelhorst CW: Regulation of Bcl-x_L channel activity by calcium. J Biol Chem. 273(28):17307-17310 (1998).
20. Han JS, Nuñez G, Wicha MS, Clarke MF: Targeting Cancer Cell Death with a bcl-x_S adenovirus. Springer Seminars in Imm*unopathology*. 19(3):279-88 (1998).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

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 U.S.
E. Medical direction of Transfusion Service.
F. Member, University of Michigan Breast Care Center.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Lectures on breast pathology and transfusion medicine to sophomore class in system sequences. (six contact hours).
B. Lecture on breast neoplasia in clinical oncology sequence (one contact hour).
C. Laboratory course for sophomore medical students (Pathology 600).
D. Daily case review with pathology house officer assigned to blood bank.
E. Weekly lecture/discussion on Transfusion Medicine for Pathology, Hematology and Pediatric hematology house officers.
F. Postgraduate course, "Current Topics in Blood Banking", Planning Committee.
G. Lectures on Transfusion Medicine presented to Pathology and Hematology/Oncology House Officers.
H. Seminars and lectures on Pathology of Breast to Pathology House Officers.
I Lectures on Transfusion Medicine to Pharmacology and Therapeutics senior student elective course. February 5, 1998.
J. Planning committee for curriculum in hematology for sophomore medical students.
K. Presentation of consultation slide conferences (4) on pathology of the breast to pathology house officers.
L. Current use of blood components. Lecture to Section of Thoracic Surgery, Department of Surgery. June 11, 1998.

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. Microinvasive carcinoma of the breast (with L Pierce).
D. Evaluation of diseases of the breast and premalignant significance. Tecumseh project (with D. Schottenfeld).
E. Correlation between histopathology and molecular pathology with prognosis of cystosarcoma phyllodes (with C. Kleer).
F. Inter-institutional study of ductal carcinoma in situ (with L. Pierce).
G. Phase II evaluation of primary chemotherapy with doxorubicin/docetaxel in operable stage I and II breast cancer (L. Baker and A. Schott, P.I.).

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

A. American Association of Blood Banks.
   1. Transfusion Practices Committee.
   2. Transfusion medicine research strategies committee.
   3. Liaison to College of American Pathologists.
B. American Society of Clinical Pathologists.
C. College of American Pathologists.
D. Michigan Society of Pathologists.
E. Southeastern Michigan Region Red Cross Blood Program.
   1. Board of Directors.
   2. Medical Advisory Committee.
F. Consultant, Veteran's Administration Hospital, Ann Arbor.
G. Breast Cancer Advisory Committee, Michigan Department of Public Health.
H. Referee, Canadian Red Cross Society Research and Development Proposal Evaluations, 1997-8.

DEPARTMENTAL:

A. Director, Transfusion Medicine program.
B. Director, training program in Blood Banking/Transfusion Medicine.

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

A. Transfusion Committee, Chairman.
B. Breast Care Center.
C. Bone marrow homotransplantation task force.
D. Executive Committee on Clinical Affairs of University Hospital.
E. Hematology sequence advisory committee, M-2 year.

V. OTHER RELEVANT ACTIVITIES:

HONORS:

EDITORIAL BOARDS:

A. Associate Editor, TRANSFUSION.
B. Editorial Board, American Journal of Surgical Pathology.
C. Editorial Board, American Journal of Clinical Pathology.
D. Editorial Board, Modern Pathology
E. Reviewer, Journal of the American Medical Association.
F. Reviewer, Blood.
G. Reviewer, Cancer.
H. Reviewer, Human Pathology.

INVITED LECTURES/PAPERS/SEMINARS:

1. Oberman HA.: The pathological assessment of breast cancer. Breast and Cervical Cancer Control Program, Michigan Public Health Institute. Traverse City Michigan September 18, 1997.
2. Oberman HA, Silverberg S.: Diagnostic problems in surgical pathology of the breast. Course presented at annual meeting of American Society of Clinical Pathologists. Philadelphia PA. September, 1997.
3. Oberman HA.: Transfusion of platelets and plasma. Workshop presented at annual meeting of American Association of Blood Banks. Denver, CO October, 1997.
4. Oberman HA: The Standards of the AABB. Lecture presented at annual meeting of American Association of Blood Banks. Denver, CO October, 1997.
5. Oberman HA: Rudolph Virchow, pathologist afield. Victor Vaughn Society. University of Michigan. January 12, 1998.
6. Problem solving in the blood bank. Workshop. Current Topics in Blood Banking. 22nd annual symposium. University of Michigan. June 3, 1998.
7. Oberman HA, Goldman EB. Legal aspects of transfusion medicine. Current Topics in Blood Banking. 22nd annual University of Michigan. June 4, 1998.

VI. PUBLICATIONS:

1. Benson K, Popovsky MA, Hines D, Hume H, Oberman HA, Glassman AB, Pisciotto PT, Thurer RL, Stehling L, Anderson KC. Nationwide survey of home transfusion practices. Transfusion. 1998;38:90-96.
2. Butch SH, Oberman HA. The computer, or electronic, crossmatch. Transfusion Medicine Reviews. 1997;11:256-264.
3. Patterson SK, Tworek JA, Roubidoux MA, Helvie MA, Oberman HA. Metaplastic carcinoma of the breast: Mammographic appearance with pathologic correlation. Am J Radiol. 1997;169:709-712.

4. Kleer C, Oberman HA. Adenoid cystic carcinoma of the breast. Am J Surg Pathol 1998;22:569-575.
5. Salas AP, Helvie MA, Wilkins EG, Oberman HA, Possert PW, Yahanda AM, Chang AE. Is mammography useful in screening for local recurrences in patients with TRAM flap breast reconstruction following mastectomy for multifocal DCIS? Ann Surg Oncol. (in press)

BOOK REVIEWS, LETTERS TO THE EDITOR:

1. Oberman HA. Review of Silverstein MJ. Ductal carcinoma in situ. Am J Surg Pathol.
2. Henson DE, Oberman HA, Hutter RVP. Breast examination protocol: why the nipple? Arch Pathol Lab Med 1997;121:1238.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Autopsy Service.

II. TEACHING ACTIVITIES:

A. Lecturer, Pathology 580/630.
B. Hong-yu Zhang, M.D., Ph.D., Postdoctoral Fellow.
C. Sujata G. Roy, Ph.D., Postdoctoral Fellow.
D. Kazuo Hatano, Ph.D., Postdoctoral Fellow.
E. Yasuhiro Nazaki, M.D., Ph.D., Postdoctoral Fellow.
F. Mehrnaz Gharaee-Kermani, D.V.M., Ph.D., Postdoctoral Fellow.

III. RESEARCH ACTIVITES:

A. Principal Investigator, "Mechanisms of pulmonary fibrosis," NIH, RO-1, HL28737, (20% effort). 1996-2001 (years 14-19). Total direct costs: $811,365).
B. Principal Investigator, "Myofibroblasts in pulmonary fibrosis," NIH, RO-1, HL 52285, (25% effort. 1994-1998 (years 01-04), (Total direct costs: $906,614).
C. Project Leader, Project IV, "Macrophage function in lung injury and fibrosis," (P.A. Ward, Principal Investigator), NIH, PO-1, HL 31963, (25% effort), 1994-1999, (Total direct costs: $512,859), Project IV only.
D. Co-investigator, Project 1, "Cytokine networks regulating inflammation of pulmonary fibrosis," (G.B. Toews, Principal Investigator), SCOR NIH, P-50 HL 46487, SCOR in Occupational and Immunologic Lung Diseases, Project 1 (5% effort), 1992-1996, (Total direct costs $828,155).
E. RO-1, DK 46469, (10% effort), 1993-1998, (Total direct Costs: $499,644).

PROJECTS UNDER STUDY:

A. Mechanisms of lung injury and fibrosis.
B. Cytokine regulation of fibroblast function.
C. Regulation of the α-smooth muscle actin promoter and gene expression.
D. Myofibroblast differentiation and its regulation by cytokines.
E. Regulation of cytokine expression by fibroblasts and eosinophils.
F. Regulation and cellular localization of cytokine gene expression in fibrotic tissues.

G. Mechanisms of eosinophil recruitment.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Member, Medical Scientist Training Program Operating Committee.
B. Member, Immunology Program Planning Committee.

REGIONAL AND NATIONAL:

A. Associate Editor, American Journal of Pathology.
B. Reviewer for the following journals:
   1) American Journal of Respiratory and Critical Care Medicine.
   2) American Journal of Pathology.
   3) Journal of Immunology.
   4) American Journal of Physiology.
   5) American Journal of Respiratory Cell and Molecular Biology.
   6) Journal of Clinical Investigation,
   7) Experimental Cell Research.
   8) Journal of Applied Physiology.
C. Reviewer for VA grant proposals.

INVITED LECTURES/SEMINARS:

1. Co-Chair, session on "Cytokines and pulmonary fibrosis," at the 1998 International Conference of the American Thoracic Society, Chicago, IL, 1998.
2. Invited Speaker, 1998 International Conference of the American Thoracic Society, Chicago, IL, 1998.
3. Invited speaker and session chair at the NATO Advanced Study Institute on ARDS, Corfu, Greece, 1997.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Zhang H, Gharaee-Kermani M, and Phan SH: Regulation of lung fibroblast α-smooth muscle actin expression, contractile phenotype and apoptosis by IL-1β. J. Immunol. 1997;158:1392-1399.
2. Gharaee-Kermani M, and Phan SH: Lung interleukin-5 expression in murine bleomycin-induced pulmonary fibrosis. Am. J. Resp. Cell Molec. Biol. 1997;16-438-447.
3. Lee S-K, Wiggins RC, de Miguel M, Goyal M, Wharram B, Thomas P, Dysko R, Phan SH, Killen PD: Renal biopsy collagen I mRNA predicts scarring in rabbit anti-GBM disease: Comparison with conventional measures of function and histology. Kidney International, 1997, 52:1000-1015.
4. Gharaee-Kermani M, and Phan SH: The role of eosinophils in pulmonary fibrosis. Int. J. Molec. Med. 1998, 1:43-53.

BOOKS/CHAPTERS IN BOOKS:

1. Phan SH: Interaction between cellular sources of cytokine and collagen gene expression in pulmonary fibrosis. In: Relationships between respiratory disease and exposure to air pollution. Eds.: Dungworth DL, Brain JD, Driscoll KE, Grafstrom RC and Harris CC. ILSI Press, Washington, D.C. 1998, pp. 172-182.
2. Phan SH, Gharaee-Kermani M, and Zhang H: Cellular sources of cytokines in pulmonary fibrosis. In: Acute respiratory distress syndrome; cellular and molecular mechanisms and clinical management. Eds.: Matalon S, and Sznajder JI. Plenum Press, New York, NY. 1998, pp. 235-244.

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

1. Warner R, Gharaee-Kermani M, Fisher GJ, Phan SH, Voorhees JJ, Varani J: Retinoid treatment increases expression of collagen III in 80^{+} year old individuals. FASEB J. 1998;12:A630.
2. Zhang H, Phan SH: Transforming growth factor β1 protects myofibroblasts from apoptosis. FASEB J. 1998;12:A795.
3. Nozaki Y, Hatano K, Gharaee-Kermani M, Phan SH: Telomerase activity of fibroblasts from bleomycin-injured rat lungs. Am. J. Resp. Crit. Care Med. 1998;157:A246.
4. Guha Roy S, Phan SH: Regulation of α-smooth muscle actin promoter activity by transforming growth factor β1 in rat lung fibroblasts. Am. J. Resp. Crit. Care Med. 1998;157:A429.
5. Gharaee-Kermani M, Hatano K, Nozaki Y, McGarry B, Phan SH: Gender-based differences in the response to bleomycin-induced lung injury. Am. J. Resp. Crit. Care Med. 1998;157:A494.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Director, Clinical Microbiology/Virology Laboratories.
B. Director, UMHC Saline Health Center Clinical Laboratory
C. Director, UMHC Ypsilanti Family Practice Health Care Center Clinical Laboratory.
D. Coordinator, Infectious Disease Microbiology Laboratory Rounds.
E. Technical Consultant - M-Labs.
F. New clinical test development, verification and implementation.

II. TEACHING ACTIVITIES:

A. Instructor, Pathology House Officer Microbiology/Virology Program.
B. Lecturer, Clinical Pathology Grand Rounds.
C. Coordinator, Clinical Microbiology/Virology In-service Program.
D. Instructor, Infectious Disease Laboratory Rounds.
E. Lecturer, Epidemiology 680, "Hospital Epidemiology"
F. Host/Instructor, ASM Seminar/Workshop for Michigan Community College Biologists
G. Host/Organizer, special seminar: " Infection control problems associated with antimicrobial resistance." Crowne Plaza Hotel, Ann Arbor, MI.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Trends in Antimicrobial Resistance for Clinical Isolates of *Bacteroides sp.*", Principal Investigator: D. R. Snydman, New England Medical Center, Boston, Massachusetts.
B. "The incidence of sexually transmitted diseases among women in Bali", Principal Investigator: Barbara Reed, School of Public Health, University of Michigan.
C. "Evaluation of novasomes and dendrimers as barrier molecules for the prevention and treatment of infectious disease", Principal Investigator: James Baker, Jr., Dept. of Pathology, University of Michigan.
D. Study of amoxicillin administration protocols for the optimal treatment of acute otitis media", Principal Investigator: Richard Linsk, Dept. of Pediatrics, University of Michigan.
E. Comparative Study of quinolone susceptibility among ICU isolates of *Pseudomonas aeruginosa*. Bayer Pharmaceutical Division, Bayer Corporation.

F. Assessment of quinolone activity against clinical isolates of *Haemophilus influenzae, Streptococcus pneumoniae* and *Moraxella catarrhalis*. Medical Reference Laboratories.

PROJECTS UNDER STUDY:

A. Evaluation of NASBA to detect CMV pp67 mRNA in whole blood.
B. Detection of the mecA resistance gene in staphylococci growing in blood culture bottles.
C. Epidemiologic studies of *Pseudomonas aeruginosa* comparing pulse-field gel electrophoresis and Cleavase.
D. Activity of LY333328, a new glycopeptide, against vanA-expressing *Enterococcus faecium.*
E. Quantitation of HIV in plasma using the Roche Amplicor HIV-1 Monitor Ultra Sensitive System.
F. Evaluation of the automated Cobas System for the detection of *Chlamydia* and *Neisseria gonorrhoeae* in urine.
G. Verification of the Meridian *Helicobacter pylori* stool antigen assay.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Clinical Pathology Laboratory Directors Committee.
B. Chair, Clinical Microbiology/Virology Senior Staff meeting.
C. Chair, Clinical Microbiology/Virology Advisory Committee.
D. UMHC Health Care Centers Laboratory Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Hospital Infection Control Committee.
B. Antimicrobial Use subcommittee of the Pharmaceutical & Therapeutics Committee.
C. Group B Streptococcus protocol committee.

REGIONAL/NATIONAL:

A. Executive Board, South Central Association for Clinical Microbiology.
B. Co-Chair, Michigan Microbiology Laboratory Directors Association.
C. Co-Chair, TriCounty Clinical Microbiology Association.
D. Councilor, American Society for Microbiology.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

A. American Society for Microbiology.
B. European Congress for Clinical Microbiology and Infectious Diseases.

C. Infectious Disease Society of America.
D. South Central Association for Clinical Microbiology.
E. TriCounty Clinical Microbiology Association.

INVITED LECTURES/ SEMINARS:

1. M-Labs Inservice Program on the laboratory diagnosis of *Chlamydia trachomatis* and *Neisseria gonorrhoea.*
2. "Emerging infectious diseases", Annual Meeting, Michigan Community College Biologists, Ann Arbor, MI.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Pearlman, MD, Pierson, CL, and Faix, RG: Frequent resistance of clinical group B streptococci isolates to clindamycin and erythromycin. 1998. Obstetrics & Gynecology. in press.
2. Boubeau, P., Riley, J., Heiter, B., Master, R., Young, C., and Pierson,C.: Use of the BacT/Alert for culture of sterile body fluids other than blood. 1998. Amer. J. Clinical Microbiol. in press.
3. Faix, RG, Perzigian, RW, Adams,JT, Weiner, GM, DiPietro, MA, Blythe, LK and Pierson, CL: *Ureaplasma urealyticum* and chronic lung disease in very low birth weight infants during he exogenous surfactant era. 1998. The Pediatric Infectious Disease J. in press.
4. Marinella, MA, Pierson, C, Chenoweth, C: The stethoscope. A potential source of nosocomial infection? 1997. Arch. Intern. Med. 157 (7):786-790.

BOOKS/ CHAPTERS IN BOOKS:

1. Pierson, CL: "Collection and transport of gynecologic microbiology specimens". In Emergency Care of the Woman. Ed.s, M. D. Pearlman and J. E. Tintinalli, McGraw Hill, 1997.

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

1. Pierson C: Comparative susceptibility of *Staphylococcus* sp., *Enterobacter* sp. and *Pseudomonas aeruginosa* to quinolone antimicrobics. Abstracts, Interscience Conference on Antimicrobial Agents and Chemotherapy. 1998

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

OVERVIEW:

Most of my efforts continued to be devoted to the M-Labs program. In addition, I also continued my commitments to help the Cytopathology and the Autopsy Services. In Cytopathology I performed Pap-smear interpretations and intermittent full-service coverage while this Service was short staffed. Surgical pathology sign-out for M-Labs cases (including outside consults from client hospitals) constituted another significant portion of my activity.

This past year we continued to see a significant trend in the hospital market towards consolidation and networking between hospitals. As a result, we have been re-directing our marketing strategies. Instead of only targeting individual hospitals , we continue our involvement in the two main developing hospital networks, the Great Lakes Network and the Joint-Venture Hospital Laboratory Network (which includes W. Beaumont, Oakwood, St. John , Mt. Clemens General and others). Some attempts at forming networks failed or changed their objectives. We continue to devote efforts to the hospital market and have responded to a few request-for-proposals. More details of these activities can be found in M-Labs' Annual Report .

Revenue levels continued to increase due to a higher volume of testing from our current hospital clients and from the acquisition of physician practices by our Medical Center. We also continued taking advantage of our potential as an alternative to the independent commercial laboratories.

The group of client pathologists continues to increase as more hospitals send us reference lab work and so does my involvement in our support to them. The M-Labs Symposium for pathologists continues to be successful. The eleventh was held in April, 1998. The volume in surgical pathology cases continues at the same level , with the cases from the satellite clinics or acquired physician offices in addition to the cases from Trillium and Addison Hospitals.

I. CLINICAL ACTIVITIES:

A. Reading surgicals for M-Labs' clients (Albion and Addison Hospitals and selected offices). This activity is predominantly performed by E.M. Silverman, M.D. Reporting on consultation cases from our clients.

B. Stat outside surgical pathology consults for M-Labs client hospitals. These stat-consults rely on our courier service and provide fast turnaround times. Most of these cases are shown in consultation to other faculty.

C. Cytopathology: reviewing and verifying Pap smears one day-a-week with the Cytopathology fellow and residents . Intermittent full coverage for this Service was also provided.

D. Autopsy coverage at the University Hospitals approximately two weeks a year and six week-ends a year.

E. Pathologist, on site coverage for Albion and Addison Community Hospitals.

F. Frozen sections at Livonia SurgiCenter, Livonia (frequency: up to 10 cases / year)

II. TEACHING ACTIVITIES:

A. Read out autopsies with house officers.

B. Organize and lecture at the M-Labs Symposium, a one day-long event with lectures and case presentations for pathologists . Discussions also include Managed Care and Utilization. Held twice a year (October/April).
C. In-service teaching to laboratory staffs at Albion Community Hospital and the University of Michigan Health Service.
D. Colposcopy meetings held once-a-month with the Gyn medical staff at the University of Michigan Health Service .

III. RESEARCH ACTIVITIES:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Associate Director, M-Labs Program. Participate in planning, marketing and implementation.
B. Problem solving with laboratory directors and supervisors.
C. Intra-departmental meetings (faculty, cytopathology, etc.)

OTHER:

A. Director of Laboratory, University of Michigan Health Service.
B. Medical staff member at Albion and Addison Hospitals.

V. OTHER RELEVANT ACTIVITIES:

A. Continued enhancement of the M-Labs version of the Spectrum, a newsletter sent to our clients and their medical staff.
B. Inspector for College of American Pathologists Inspection and Accreditation Program.
C. Quality Assurance program in Surgical Pathology , for M-Labs client pathologists .

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Director, Autopsy Service.
B. Director, Electron Microscopy Service.
C. Supervision of Autopsies-8 weeks, signed out 54 autopsies.
D. Coordinator, Trauma/burn autopsy conference monthly.
E. Coordinator of Senior Staff Autopsy Call Schedule.
F. Coordinator, Medical Examiner Investigators, University of Michigan.
G. Deputy Medical Examiner for University Hospitals.

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, 1 contact hour.
D. Pathology 600, Provided written critiques of student autopsy write-ups (167).
E. Laboratory Instructor, Histopathology Laboratory for M1 students, 20 contact hours.
F. Laboratory Instructor, Pathology 600 (M2 pathology course), year long.
G. Mentor, Michael Shillingford, U of Michigan Post-baccalaureate student, now admitted to medical school.
H. Thesis Committee - Andrew Merry, Jami Foreback.
I. Directed research of Michael O'Reilly, M.D. (Department of Anesthesiology), Stewart Wang, M.D., Ph.D., Susan Stern, M.D., Richard Klein, M.D. (Department of Surgery), Postdoctoral fellows, Samuel Ebong, Ph.D. Doug Call, Ph.D., Jean Nemzek, D.V.M. Graduate Students - Jami Foreback.
Medical Students - Liza Green, Hilliary Cohen, Undergraduate Students - David Newcomb, Rob Cohen.

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.
4. 2 hit model of acid aspiration induced lung injury.

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, mIL-18, mIL-1ra.
F. Oxidant regulation of chemokine gene expression.
G. Mechanisms of nosocomial pneumonia, and association with IL-8.
H. Medical Examiner practices in the State of Michigan.

SPONSORED SUPPORT:

A. Principal Investigator, "The Role of Cytokines in Sepsis and Trauma", GM44918 $906,182, 1990-2000.
B. Principal Investigator, "Regulation of IL-8 gene expression: four years, GM50401 $870,822, 1995-1999.
C. Principal Investigator, "Chemokines in the Pathogenesis of Asthma", ES09589, project #3, $1,180,00, 1998 – 2002.
D. Principal Investigator, "Keratinocyte Growth Factor Regulation of Acid Induced Lung Injury" Amgen Inc. 1997-1998 $25,000.
E. Principal Investigator, "Sulfazalazine modulation of cytokine production", Pharmacia-Upjohn, $76,800, 1998 – 2000.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director - Autopsy Service.
B. Director, Electron Microscopy Service.
C. Interviewer - Candidates for faculty, house officer, postdoctoral, and graduate student positions.
D. Coordinator of call schedule, both weekend and weekday, autopsy service.
E. Coordinator, medical examiner investigator call schedule, University of Michigan.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Faculty Senate.
B. Member, Medical School Admissions Committee.
C. Member, Biomedical Research Council Undergraduate Research council.
D. Academic Credentials, Appointments and Promotions and Tenure, Instructional Tract, 1997 – 2001.
E. University Committee on Use and Care of Animals, 1997 – 2001.
F. Chair, University Committee on Use and Care of Animals, 1998 – 1999.
G. Reviewer, Biomedical Research Council grants.

H. Reviewer, Department of Surgery grants.

REGIONAL AND NATIONAL:

A. Chair, Michigan Association of Medical Examiners.
B. Chair, Michigan Department of Public Health Postmortem Examination Workgroup.
C. Member, Executive Committee, Dementia Subcommittee, Chronic Disease Advisory Committee to the Michigan Department of Public Health.
D. Deputy Medical Examiner for Washtenaw County.
E. Ad hoc reviewer, National Institutes of Health, Surgery, Anesthesiology and Trauma, Feb, Jun 1998.
F. Reviewer, Special emphasis panel, National Institutes of Health, February 1998.
G. Reviewer, Program Project, Alden Harkin, M.D. Principal Investigator, University of Colorado, Dec 1997.
H. Member, Michigan Coalition on Donation.
I. Member, Michigan Association of Medical Examiners, Shock Society, American Association of Immunologists, A. James French Society, American Society of Investigative Pathologists, United States-Canadian Academy of Pathology.

V. OTHER RELEVANT ACTIVITIES:

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

INVITED LECTURES/SEMINARS:

1. Amgen Seminar on G-CSF, Santa Monica CA, Apr 1998.
2. Michigan Public Health Institute, Medical Examiner Database project, Okemos, MI, July, August 1997.
3. Michigan Public Health Institute, Medical Examiner Database project, Jackson, MI Feb, 1998.
4. Michigan Public Health Institute, Medical Examiner Database project, Ann Arbor, MI, May, 1998.
5. Speaker, Shock Society, June, 1998.
6. Upjohn-Pharmacia Seminar on Inflammatory Mediators, June, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Zhang, K., M. Gharaee-Kermani, B. McGarry, D. Remick, S. H. Phan. (1997) TNF-alpha-mediated lung cytokine networking and eosinophil recruitment in pulmonary fibrosis. J.Immunol. 158: 954-959.
2. Villarete, L. H., D. G. Remick. (1997) Nitric oxide regulation of interleukin-8 gene expression. Shock. 7: 29-35.
3. Wang, H., X. Tan, H. Chang, F. Gonzalez-Crussi, D. G. Remick, W. Hsueh. (1997) Regulation of platelet-activating factor receptor gene expression in vivo by endotoxin, platelet-activating factor and endogenous tumour necrosis factor. Biochem.J. 322 (Pt 2): 603-608.
4. Shanley, T. P., J. L. Foreback, D. G. Remick, T. R. Ulich, S. L. Kunkel, P. A. Ward. (1997) Regulatory effects of interleukin-6 in immunoglobulin G immune-complex-induced lung injury. American Journal of Pathology. 151: 193-203.
5. Brieland, J. K., J. C. Fantone, D. G. Remick, M. LeGendre, M. McClain, N. C. Engleberg. (1997) The role of Legionella pneumophila-infected Hartmannella vermiformis as an infectious particle in a murine model of Legionnaire's disease. Infection & Immunity. 65: 5330-3.
6. Foreback, J. L., D. G. Remick, E. Crockett-Torabi, P. A. Ward. (1997) Cytokine responses of human blood monocytes stimulated with Igs. Inflammation. 21: 501-17.
7. Wang, H., X. D. Tan, X. W. Qu, H. Chang, D. G. Remick, F. Gonzalez-Crussi, W. Hsueh. (1997) Platelet-activating factor (PAF) up-regulates plasma and tissue PAF-acetylhydrolase activity in the rat: effect of cycloheximide. Pediatric Research. 42: 597-603.
8. Remick, D. G. (1997) The adrenal response to sepsis [editorial]. Shock. 8: 146.
9. Hunter, B., D. French, J. Warner, D. Remick. (1998) Correlation of body mass index with thoracic and abdominal panniculus. Journal of Forensic Sciences. 43: 427-30.
10. Remick, D. G., S. J. Garg, D. E. Newcomb, G. Wollenberg, T. K. Huie, G. L. Bolgos. (1998) Exogenous interleukin-10 fails to decrease the mortality or morbidity of sepsis [see comments]. Critical Care Medicine. 26: 895-904.
11. Evans, C. A., J. Jellis, S. P. Hughes, D. G. Remick, J. S. Friedland. (1998) Tumor necrosis factor-alpha, interleukin-6, and interleukin-8 secretion and the acute-phase response in patients with bacterial and tuberculous osteomyelitis. Journal of Infectious Diseases. 177: 1582-7.
12. Brieland, J. K., D. G. Remick, M. L. LeGendre, N. C. Engleberg, J. C. Fantone. (1998) In vivo regulation of replicative Legionella pneumophila lung infection by endogenous interleukin-12. Infection & Immunity. 66: 65-9.

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

1. High systemic IL-8 does not prevent local inflammation. D. Remick, G. Bolgos, L. Green, & S. Garg, International Cytokine Society, Lake Tahoe, Nevada, June, 1997.
2. IL-1ra +TNF-SR fails to improve sepsis survival. G. Bolgos, D. Call, S. Ebong, D. Newcomb & D. Remick, Experimental Biology, San Francisco, California, April, 1998.

3. The effect of sulfasalazine treatment on IGG induced cytokine production. P. Nybom & D. Remick, Experimental Biology, San Francisco, California, April, 1998.
4. Development of a sandwich ELISA for measurement of picogram quantities of murine granulocyte colony stimulating factor. J. Granger, M. O'Reilly & D. Remick, Experimental Biology, San Francisco, California, April, 1998.
5. Glucocorticoid modulation of LPS inflammation. D. Newcomb, G. Bolgos & D. Remick, Experimental Biology, San Francisco, California, April, 1998.
6. Low molecular weight heparin is associated with greater cytokine production in a stimulated whole blood model. D.R. Call & D. Remick, Experimental Biology, San Francisco, California, April, 1998.
7. Inflammatory changes in non-lethal sepsis. S. Ebong, G. Bolgos, D. Call, P. Nybom & D. Remick, Experimental Biology, San Francisco, California, April, 1998.
8. TNF-SR + IL-1ra fail to decrease sepsis mortality. D. Remick, D. R. Call, S. Ebong, D. Newcomb & G. Bolgos, TNF Congress, Hyannis, Massachusetts, May, 1998.
9. CD11b AND CD18 are unregulated on murine neutrophils following intraabdominal infection in mice. M. O'Reilly, J.P. Smith, J. Granger, L. Mayo-Bond, M. KuKuruga & D. Remick, International Anesthesiology Research Society, Orlando, Florida, March, 1998.
10. The effect of anti-g-csf antiserum on the expression of CD11b and CD18 in mice M. O'Reilly, J.P. Smith, T. Millican, J. Granger, L. Mayo-Bond, M. KuKuruga & D. Remick, International Anesthesiology Research Society, Orlando, Florida, March, 1998.
11. Granulocyte colony stimulating factor mRNA production following severe infection in mice M. O'Reilly, R. Klein, S. Wang, J. Granger, T. Millican, & D. Remick, International Anesthesiology Research Society, Orlando, Florida, March, 1998.
12. The role of chemokines in a 2 hit model of pulmonary injury. D. Remick, L. Green, G. Bolgos, Dept. of Pathology, Univ. of Michigan, Shock Society, San Antonio TX, June 1998.

BOOKS AND CHAPTERS IN BOOKS:

1. Remick, D.G. L. Villarete, and DeForge, L.E.: Oxidant regulation of cytokine gene expression in Clerch, L.B and Massaro, D.J (eds) Oxygen, Gene Expression and Cellular Function Marcel Dekker, Inc, 1997, 243 - 278.
2. Remick, D.G. Quantitation of cytokines, in Remick, D.G. and Friedland, J.F. (eds) Cytokines in Health and Disease, second edition Revised and expanded, Marcel Dekker, Inc. 1997, 281-298.
3. Editor, Cytokines in Health and Disease, second edition Revised and expanded, Marcel Dekker, Inc. 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997- 30 JUNE 1998

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

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

C. Hematopathology teaching:
   1. Leukemia conference/biweekly.
   2. Lymphoma conference/weekly.
   3. Hematology conference/biweekly.
   4. Cutaneous Lymphoma Conference/biweekly.
   5. Clinical Pathology Grand Rounds (one lecture).
   6. Clinical Pathology Case Conference/weekly.
   7. Hematology/Oncology Fellows Teaching Conference (one lecture).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

PROJECTS UNDER STUDY:

A. Immunophenotyping in acute and chronic leukemias.
B. Histopathology, immunophenotyping, and genotyping of possible precursor lesions for lymphoma of mucosa-associated lymphoid tissue.
C. Histopathology, immunophenotyping, and clinical features of anaplastic large cell lymphoma and mantle cell lymphoma.
D. Radioimmunotherapy for B-cell lymphoma.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Clinical Flow Cytometry Laboratory.
B. Coordinator, CP resident teaching program.
C. Clinical Pathology Incentive Distribution Committee.
D. Pathology Faculty Incentive Committee.

REGIONAL/NATIONAL:

A. Pathology reviewer, multicenter study of I^{131} anti-B1 radioimmunotherapy for B-cell lymphoma, Coulter Pharmaceutical.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Lecturer, "Hematologic Coups: A practical approach to challenging cases in hematolymphoid diagnosis", American Society of Clinical Pathologists National Meeting, April, 1998.
2. Lecturer, "Basic Principles of Flow Cytometry – Clinical Flow Cytometry", M-Labs CME for clinical laboratory staff and medical technology students, Towsley Center, Ann Arbor, October 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Su LD, Schnitzer B, Ross CW, Vasef M, Mori S, Shiota M, Mason DY, et. al. The t(2;5)-associated P80 NPM/ALK fusion protein in nodal and cutaneous CD30+ lymphoproliferative disorders. J Cutan Pathol 24:597-603, 1997.
2. Kroft SH, Singleton TP, Dahiya M, Ross CW, Schnitzer B, Hsi ED. Ruptured spleens with expanded marginal zones do not reveal occult B-cell clones. Mod Pathol 10:1214-1220, 1997.
3. Krishnan K, Ross CW, Bockenstedt PL, Adams PT. Successful treatment of autoimmune neutropenia with recombinant human granulocyte-colony stimulating factor (R-metHuG-CSF). Clin Lab Haem 19:105-109, 1997.
4. Hsi ED, Eisbruch A, Greenson JK, Singleton TP, Ross CW, Schnitzer B. Classification of primary gastric lymphomas according to histologic features. Am J Surg Pathol 22:17-27, 1998.
5. McCarthy CJ, Sheldon S, Ross CW, McCune WJ. Cytogenetic abnormalities and therapy-related myelodysplastic syndromes in rheumatic disease. Arthritis and Rheumatism (in press).

6. Kroft SH, Finn WG, Singleton TP, Ross CW, Sheldon S, Schnitzer B. Follicular large cell lymphoma with immunoblastic features in a child with Wiskott-Aldrich Syndrome: An unusual immunodeficiency-related neoplasm not associated with Epstein-Barr virus. Am J Clin Pathol (in press).
7. Tworek JA, Singleton TP, Schnitzer B, Hsi ED, Ross CW. Flow cytometric and immunohistochemical analysis of small lymphocytic lymphoma, mantle cell lymphoma, and plasmacytoid small lymphocytic lymphoma (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Singleton TP, Anderson MM, Ross CW, Sheldon S, Schnitzer B. Leukemic phase of mantle cell lymphoma, blastoid variant.
2. Wahl RL, Zasadny KR, McFarlane D, Francis IR, Ross CW, et al. Iodine-131 anti-B1 antibody for B-cell lymphoma: An update on the Michigan Phase I Experience.
3. Hsi ED, Singleton TP, Svoboda S, Schnitzer B, Ross CW. Characterization of the lymphoid infiltrate in Hashimoto's thyroiditis by immunohistochemistry and polymerase chain reaction for immunoglobulin heavy chain gene rearrangement.
4. Kroft SH, Hsi ED, Ross CW, Schnitzer B, Singleton TP. Evaluation of CD23 expression in paraffin-embedded gastric MALT lymphoma.

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

1. Massarani-Wafai R, Hsi ED, Singleton TP, Schnitzer B, Kroft S, Ross CW. Classification of primary thyroid lymphoma according to histologic features. Am J Clin Pathol 108:350, 1997.
2. Kroft SH, Hsi ED, Ross CW, Schnitzer B, Singleton TP. CD23 expression in paraffin-embedded gastric MALT lymphoma. Am J Clin Pathol 109:477, 1998.
3. Iravani S, Ross CW, Schnitzer B, Singleton TP. Ocular adnexal lymphomas: lack of CD23 in nonfollicular small B-cell lymphoma supports marginal zone type. Mod Pathol 11:132A, 1998.
4. Iravani S, Singleton TP, Ross CW, Schnitzer B. B-cell lymphoblastic lymphoma presenting as lytic bone lesions: a clinicopathological study. Mod Pathol 11:132A, 1998.
5. Ross CW. Basic Principles of Flow Cytometry. M-Labs Spectrum, Volume 12, No. 1, January 1998.

ALVIN SCHMAIER, M.D.
PROFESSOR
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Professor of Internal Medicine.
B. Professor of Pathology.
C. Director, Coagulation Laboratory

II. TEACHING ACTIVITIES (Department of Pathology):

A. Pathology House Officers:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Residents participated in weekly sign-out rounds by laboratory direct of specialized coagulation testing.
      b. Formal lecture for 4th year medical student elective clinical pathology course.

III. RESEARCH ACTIVITIES:

1. The research efforts of this laboratory are directed in three areas. A major effort is being made to develop a new class of selective inhibitors of α-thrombin activation of platelets and other cells. An agent termed "thrombostatin" is being developed as an inhibitor of α-thrombin cleaving the cloned thrombin receptor, PAR1. Investigations show that this agent binds to PAR1 to prevent thrombin's cleavage of it. It also directly interacts with the active site of a-thrombin itself, although at a 100-fold less affinity than interacting with PAR1. Our first proof-of-concept animal studies show that our model agent prevents coronary thrombosis in dogs. More potent thrombostatins are being designed by second generation combinational libraries and rational drug design. Dr. Schmaier's start-up biotechnology company (Thromgen, Inc.) to foster the development of these agents is in its second year with a Phase II SBIR from the NHLBI. It should be noted that thrombostatin biology has a much wider potential use than just prevention of coronary thrombosis. It could be used to treat stroke, inhibit growth and proliferation of various cells, and could possibly influence cancer metastasis mediated by a-thrombin. Current projects related to this area include defining the protein-peptide mechanism of thrombostatin's inhibition, in vivo studies to prevent coronary thrombosis, design of more potent inhibitors, and examine the influence of thrombostatins on fibroblast and smooth muscle cell growth and proliferation.

A second investigative effort is Dr. Schmaier's work on the kallikrein/kinin system. The Schmaier laboratory has had the privilege of making a fundamental discovery this year, which should change everyone's notions about this field. When prekallikrein assembles on its cell receptor, high molecular weight kininogen, a cell-associated cysteine protease activates prekallikrein to kallikrein. This pathway is independent of factor XII. In fact, factor XII is activated secondarily by kallikrein formation. Our work has allowed us to propose a new hypothesis, the first one in 25 years, on how this system assembles and becomes activated. Current projects include the discovery of a new mechanism for factor XI activation based upon the above, mapping the kininogen binding domain on cytokeratin 1, characterizing the regulation of expression of the kininogen receptor on cells, determining the enzyme(s) that activates prekallikrein, characterizing the factor XII receptor on endothelial cells.

Last, this laboratory has a development project on the role of the Kunitz protease inhibitory domain of the amyloid β-protein precursor as an anticoagulant (AβPP). A preliminary project is in-progress to determine the effects of overexpression of AβPP in cells and in a transgenic mice on vascular hemostasis and endothelial cell biology. At present we have a second generation transgenic mouse colony of overexpression of AβPP in cerebral vasculature. The goals of these studies are to determine a molecular cause for intracerebral hemorrhage. Further investigations have examined the role of the isolated KPI domain as an anticoagulant in a rabbit model of extracorporeal circulation.

SPONSORED SUPPORT:

A. Principal Investigator, "Regulation of Kinin Delivery on HUVEC", RO1-HL52779, ($21,496,751 total costs), 1996 - 2001.
B. Co-Investigator, "Markers and Mechanisms of Macrovascular Disease in IDDM", T. Garvey, P.I., RO1-HL55782, ($52,773 total costs), 1996 - 2001.
C. Principal Investigator, "Thrombostatin – A Selective Antithrombin", RO1-HL56415, ($969,398 total costs), 1997 – 2000.
D. Co-Investigator, "Thrombostatin – A Thrombin Receptor Inhibitor", A.A.K. Hasan P.I., Award to Thromgen, Inc., R44-HL55907 ($703,000 total cost), 1997 – 1999.
E. Co-Investigator, "Molecular Genetics of Coagulation Disorders", D. Ginsburg, P.I., Core A., PO1-HL57346, ($296,000 direct costs to Dr. Schmaier), 1997 – 2002.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Coagulation Laboratory.

REGIONAL AND NATIONAL:

A. Member, Research Committee of the Midwest Consortium, American Heart Association.

V. OTHER RELEVANT ACTIVITIES:

A. NIH Study Section:

NHLBI: Hematology-2 Special Emphasis Panel, 1998.

EDITORIAL BOARDS:

None.

HONORS AND AWARDS:

A. Association of American Physicians – Elected 1998.

INVITED LECTURES/SEMINARS:

1. Chairman, Contact Activation Subcommittee of the SSC of the ISTH, Florence, Italy, June 6, 1997.
2. Invited State-of-the-Art Lecture: International Society of Thrombosis and Hemostasis: "Contact Activation – A Revision", Florence, Italy, June 8, 1997.
3. Lecturer, INSERM. "A New Approach to Selective Inhibition of Thrombin", Paris, France, June 16, 1997
4. Lecturer: "The Kininogen Receptor", Henry Ford Hospital, Hypertension Research Group, Detroit, MI, June 28, 1997.
5. Lecturer, "New Anticoagulants – 1997; A Description and Mechanism of Action", Overlook Hospital, Summit, N.J., Hemostasis, Thrombosis, and Stroke, Annual Symposium, October 21, 1997.
6. Lecturer, "Contact Activation – A Revised Hypothesis", Medical University of South Carolina, Department of Pharmacology, Charleston, S.C., November 11, 1997.
7. Lecturer, "Contact Activation – A Revision", Wayne State University, Department of Pharmacology, Detroit, MI, December 17, 1997.
8. Lecturer, "Contact Activation – A Revision", 32nd Penner Conference on Haemostatis, Las Vegas, NE, May 11, 1998.
9. Lecturer, "Thrombostatin: A Platelet Inhibitor Directed to the Thrombin Receptor", Beyond Heparin: Cambridge Healthtech Institute Conference, San Diego, CA, May 29, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Motta G, Rojkjaer R, Hasan AAK, Cines DB, Schmaier AH. High molecular weight kininogen regulates prekallikrein assembly and activation on endothelial cells: A novel mechanism for contact activation. Blood 91:516-528, 1998.

2. Hasan AAK, Zisman T, Schmaier AH. Identification of cytokeratin 1 as a binding protein and presentation receptor for kininogens on endothelial cells. Proc Natl Acad Sci 95:3615-3620, 1998.
3. Spalding A, Vaitkevicius H, Scott D, Mackenzie S, Schmaier A, Lockette W. Mechanisms of epinephrine-induced platelet aggregation. Hypertension 31:603-607, 1998.
4. Gitlin SD, Deeb GM, Yann C, Schmaier AH. Intraoperative monitoring of danaparoid sodium (Orgaran) anticoagulation during cardiovascular surgery. J Vasc Surg 27:568-575, 1998.
5. Musial J, Gluszko P, Undas A, Mahdi F, Kang S, Szczeklik A, Schmaier AH. Gamma interferon administration to patients with atopic dermatitis inhibits fibrinolysis and elevates C1 inhibitor. Thromb Res 89:253-261, 1998.
6. Rojkjaer R, Hasan AAK, Motta G, Schousboe I, Schmaier AH. Factor XII does not initiate prekallikrein activation on endothelial cells. Thromb Haemost 80:74-81, 1998.

ARTICLES SUBMITTED FOR PUBLICATION/REVIEW ARTICLES:

1. Colman RW and Schmaier AH. Contact sytem: A vascular biology modulator with anticoagulant, profibrinolytic, anti-adhesive, and proinflammatory attributes. Blood 90:3819-3843, 1997.
2. Schmaier AH. Contact Activation. In: Thrombosis and Hemorrhage. Ed: Loscalzo J. and Schafer A.I. Second Edition. Williams & Wilkins, Baltimore, 1998.
3. Schmaier AH. Contact Activation – A Revision. Ed: G. de Gaetano. In 1997 State of the Art, Thrombosis and Haemostasis, 78:101-105, 1997.
4. Schmaier AH. Contact Activation – A revised hypothesis. In: Biological Research, Eds. McGiff JC and Vio CP (in press).
5. Schmaier AH. Plasma kallikrein\kinin system: A newly recognized mechanism for its physiologic activation. Thrombose (in press).
6. Wakefield TW and Schmaier AH. Vascular thrombosis due to hypercoagulable states. Vasc Surg. Ed: Rutheford RB, Johnston W (in press).
7. Wakefield TW and Schmaier AH. Hematologic factors in recurrent venous thrombosis. Prac Vasc Surg, Eds: Yao JST, Pearce WH (in press).
8. Wakefield TW and Schmaier AH. Prothrombotic states and vascular thrombosis. Current Therapy in Vascular Surgery. Eds: Ernst CB and Stanley JC (in press).
9. Wakefield TW and Schmaier AH. Warfarin-induced skin necrosis. Current Therpy Vascular Surgery. Eds: Ernst CB and Stanley JC (in press).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Director, Clinical Hematology Laboratory.
B. Diagnostic Surgical Pathology, Hematopathology (12 months).
C. Diagnostic Hematopathology Consultant, Veterans Administration Hospital.
D. Diagnostic Hematopathology of M-Labs clients.
E. Consultant for external and transfer Hematopathology cases.
F. Review of Southwest Oncology Group (SWOG) cases (circa 150/year).
G. 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.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITALS:

A. Clinical Hematology Laboratory, Director.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

A. Human Pathology. Designated reviewer.
B. American Journal Clinical Pathology. Designated reviewer.

INVITED LECTURES/SEMINARS:

1. "A Practical Approach to the Diagnosis of Extranodal Lymphomas", ASCP Workshop, Philadelphia, Pennsylvania, September, 1997.
2. Schnitzer, B.: Videomicroscopy Workshop, "Interesting Lymphoid Lesions", ASCP Workshop, Philadelphia, Pennsylvania, September, 1997.
3. Schnitzer, B.: Microscopy Tutorial Workshop, "Lymph Node Pathology", ASCP Workshop, Philadelphia, Pennsylvania, September, 1997.
4. Schnitzer, B.: Non-Hodgkin's lymphomas, classifications; Hodgkin's disease; Flow cytometry in diagnosis of leukemias and lymphomas; Extranodal lymphomas; Acute lymphoblastic leukemia. A Practical Approach to Hematologic Problems, ASCP Educational Course, Las Vegas, Nevada, November, 1997.
5. "Reactive Lymphadenopathies", Tutorial on Neoplastic Hematopathology, Department of Laboratory Medicine and Pathology, Cornell University, Miami, Florida, February, 1998.
6. Schnitzer, B., Ross, C.W. and Singleton, T.: "Hematologic Coups", ASCP Workshop, Los Angeles, California, April, 1998.
7. Schnitzer, B.: Videomicroscopy Workshop, "Interesting Lymphoid Lesions", ASCP Workshop, Los Angeles, California, April, 1998.
8. Schnitzer, B.: Microscopy Tutorial Workshop,: "Lymph Node Pathology", ASCP Workshop, Los Angeles, California, April, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kroft SH, Singleton TP, Dahiya M, Ross CW, Schnitzer B, Hsi ED: Ruptured spleens with expanded marginal zones do not reveal occult B-cell clones. Mod Pathol 10:1214-1220, 1997.

2. Su LD, Schnitzer B, Ross CS, Vasef M, Mori S, Shiota M, Mason DY, Pulford K, Headington JT, Singleton TP: The t(2;5)-associated p80 NPM/ALK fusion protein in nodal and cutaneous CD30+ lymphoproliferative disorders. J. Cutan Pathol 23:597-603, 1997.
3. Hsi ED, Eisbruch A, Greenson JK, Singleton TP, Ross CW, Schnitzer B: Classification of primary gastric lymphomas according to histologic features. Am J Surg Pathol 22:17-27, 1998.
4. Singleton, TP, Anderson, MD, Ross, CW, Sheldon, S and Schnitzer, B: Leukemic phase of mantle cell lymphoma, blastoid variant. Am J Clin Pathol.
5. Kroft SH, Hsi ED, Ross CW, Schnitzer B, Singleton TP: CD23 expression in paraffin embedded gastric MALT lymphoma. Mod Pathol.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Tworek, J.A., Singleton, T.P., Schnitzer, B., Hsi, E.D., Ross, C.W.: Flow cytometric and immunocytochemical analysis of small lymphocytic lymphoma, mantle cell lymphoma and plasmacytoid small lymphocytic lymphoma. Am J Clin Pathol.
2. Kroft, S.H., Finn, W.G., Singleton, T.P., Ross, C.W., Sheldon, S., Schnitzer, B.: Follicular large cell lymphoma with immunoblastic features in a child with Wiskott-Aldrich syndrome: An unusual immunodeficiency-related neoplasm not associated with Epstein-Barr virus. Am J Clin Pathol.

BOOKS AND CHAPTERS IN BOOKS:

1. Reactive Lymphadenopathies. In: Knowles, D. (ed). Neoplastic Hematopathology, 2nd Ed. Williams & Wilkins, 1999.

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

1. Massarani-Wafai R, Hsi Ed, Singleton TP, Schnitzer B, Kroft S, Ross CW: Classification of primary thyroid lymphoma according to histologic criteria. Am J Clin Pathol 108:350-351, 1997.
2. Izban KF, Hsi ED, Schnitzer B, Alkan S: Immunohistochemical analysis of nodular lymphocyte predominance Hodgkin's disease for the expression of the ICE/CED-3 family protease CPP32. Lab Invest 78:132A, 1998; Mod Pathol 11:132A, 1998.
3. Iravani S, Ross CW, Schnitzer B, Singleton TP: Ocular adnexal lymphomas (OAL). Lack of CD23 in non-follicular small B-cell lymphoma supports marginal zone type. Lab Invest 78:132A, 1998; Mod Pathol 11:132A, 1998.
4. Iravani S, Singleton TP, Ross CW, Schnitzer B: B-cell lymphoblastic lymphoma presenting as lytic bone lesions. A clinicopathologic study. Lab Invest 78:132A, 1998; Mod Pathol 11:132A, 1998.
5. Kroft SH, Hsi ED, Ross CW, Schnitzer B, Singleton TP: CD23 expression in paraffin embedded gastric MALT lymphoma. Am J Clin Pathol 109, 477, 1998.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Weekly conferences on Coagulation, Thrombosis and Component Therapy for Blood Bank Residents, University of Michigan.
B. Weekly conferences on Bone Marrow Aspiration Techniques for Pathology Residents, University of Michigan.
C. Grand Rounds, "Vascular Abnormalities as the Cause of Bleeding," April 3, 1998.
D. Eight lectures on Hemostasis and Thrombosis, School of Allied Health, Eastern Michigan University, April 1998.

III. RESEARCH ACTIVITIES:

None.

IV. PUBLICATIONS:

A. Shanberg JN: Hematology in Philately, 3:209-218, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Clinical Cytogenetics Laboratory.

II. TEACHING ACTIVITIES:

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

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

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

D. Clinical Pathology Grand Rounds, two lectures.

E. Pediatric Genetics Rounds, weekly participant, one lecture.

F. Leukemia Conference, biweekly.

G. Genetic Counseling graduate students:
   1. Two lectures.
   2. Individual tutorials.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

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

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

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

D. Correlation of ploidy with expression of differential function.

E. Role of chromosome abnormalities in eosinophilia.

F. Fluorescence *in situ* hybridization for identification of marker chromosomes.

G. Fluorescence *in situ* hybridization as "interphase cytogenetics".

H. Role of chromosome abnormalities in treatment-resistant low grade lymphoma.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Clinical Cytogenetics Laboratory.

REGIONAL AND NATIONAL:

None.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. USCAP Short Course, "FISH, ISH and RISH", Boston, March, 1998.
2. Medical Technologists Association of Central Michigan "Basic Cytogenetics"; April 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Innis, JW, Asher, JH, and Sheldon S: Autosomal dominant microcephaly without mental retardation, short palpebral fissures, and digital anomalies. Am. J. Med. Genet. 71:150, 1997.
2. Innis, JW, Asher, J, Liang, Y, Wike, C, Dietick, H, Kazen-Gillespie, K, Sheldon, S, Glover, T, and Friedman, T: Exclusion of BMP6 as a candidate gene for cleidocranial dysplasia. Am. J. Med. Gen. 71:292, 1997.
3. McDonald, MT, Flejter, W, Sheldon, S, Putzi, M and Gorski, J.: XY sex reversal and gonadal dysgenesis due to 9p24 monosomy; Am. J. Med. Genet 73:321, 1997.
4. McCarthy, C, Sheldon, S, Ross, C, and McCune, J.: Myelodysplastic syndromes in rheumatic diseases after immunosuppressive therapy: a cytogenetic study; Amer. J. Rheum. In press.

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

1. Weidmer-Mikhail, E., Sheldon, S, and Ghaziuden, M. A study of chromosome abnormalities in autism/pervasive developmental disorders. Abstract, Genetics and Psychiatry Meeting, San Diego, CA, March 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

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

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

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

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

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

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

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

II. TEACHING ACTIVITIES:

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

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

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

III. RESEARCH ACTIVITIES:

None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Michigan Health Corporation representative to Joint Venture Hospital Labs (JVHL).

B. Director, M-Labs:
   1. Provide leadership for and participate in planning, marketing, and implementation of M-Labs programs.
   2. Expansion of M-Labs.
      a. We have now improved our Quality Assurance activities and monitor errors and problems in a systematic way with a more organized effort to resolve problems.

b. We have our third fully operational interface between the University of Michigan laboratory computer system and a client hospital's computer system. One more is planned.

3. Growth. FY 98 was a good year for M-labs. We experienced a 20.2% increase in net billing for clinical pathology activities and an 8.8% increase in net billing for anatomic pathology activities. Although some of this increased work came from existing hospital clients who have increased their outreach efforts, most of the increase in our business has come from the addition of physician office practices, including the Health System's contracts with IHA practices. We have added these 31 offices to our client base in the last fiscal year.
Our contract was terminated with one hospital client after that client became affiliated with another hospital which is a competitor in the lab outreach business. We have 2 proposals submitted to potential hospital clients and await the outcome of these.

4. Managed Care Activities. M-Labs has implemented our agreement with M-Care to supply outpatient laboratory services for that portion of the enrollees in its new Medicare (Senior Plan) subscribed to 4 of M-Care's hospital group providers. In order to accomplish this task, M-labs developed and implemented processes for claims transfer from and means of distribution of capitated revenue among the subcontracted laboratory providers, and developed and implemented a Quality Assurance plan to meet with M-Care's and HCFA's requirements for this product. This year, M-Labs has contracted with M-Care for provision of outpatient laboratory services for its HMO, POS, and Medicaid products. We are subcontracting these services to M-Care's provider hospital laboratories. We have begun implementing this arrangement and are adding IDNs in an orderly fashion.

5. Networks. We are still working with a group of Michigan hospital laboratories to form Great Lakes Laboratory Network, which will have the capability to negotiate for statewide and, eventually, regional managed care contracts for laboratory services. M-Labs personnel now work in key committees of this group.
   a. We have joined JVHL, a network of major hospital laboratories in the Detroit area. I have been appointed as one of 2 representatives of the Michigan Health Corporation to JVHL. We have actively urged that the network rationalize its esoteric laboratory testing within the group and we are working towards M-Labs being a significant reference laboratory for some of this esoteric testing.

C. Member Department of Pathology Incentive Committee.
D. Member, University of Michigan Networking Leads Committee.
E. Department of Pathology representative to Managed Care Committee.
F. Director, Laboratory at Trillium Hospital, Albion, Michigan.
G. Director of Laboratories, Addison Community Hospital, Addison, Michigan.
H. Chair, Tissue/Transfusion and Infection Control Committees, Trillium Hospital, and Addison Community Hospital.
I. Member, Surgical and Medicine/Family Practice Committees, Trillium Hospital.
J. Member, Executive Committee and Peer Review Committee, Addison Community Hospital.
K. Plan and review Laboratory QA and CQI at Trillium and Addison Community Hospitals.
L. Review Quality Control of Clinical Pathology tests at Trillium and Addison Community Hospitals.

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Assistant Director, Clinical Hematology Laboratory.
B. Director, Anatomic Pathology's Special Studies Laboratory (Clinical Immunohistochemistry, Immunofluorescence and Neural and Muscular Studies).
C. Diagnostic Hematopathology.
D. Diagnostic Flow Cytometry.
E. Consultant, Hematopathology (M-Labs, Veterans Administration Hospital).

II. TEACHING ACTIVITIES:

A. Medical Students
   1. Lecturer, Second Year Medical Students (four contact hours).
   2. Laboratory Instructor, Second Year Medical Students (eight contact hours)
B. Dental Students
   1. Lecturer, Second Year Dental Students (one contact hour).
C. House Officers
   1. Sign-out bone marrows, lymph nodes, blood smears, body fluids, joint crystals, leukemias, lymphomas and extramedullary myeloid cell tumors.
   2. Sign-out flow cytometry.
   3. Clinical pathology case conference, weekly.
   4. Hematopathology case conference, bimonthly.
   5. Immunohistochemistry conference, bimonthly.
D. Clinical Pathology Grand Rounds (one lecture)
E. Interdepartmental Conferences
   1. Lymphoma conference (weekly).
   2. Leukemia conference (biweekly).
   3. Hematology conference (biweekly).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Director, Cancer Center Core Laboratory for Research Histology and Research Immunohistochemistry (5% effort).

PROJECTS UNDER STUDY:

A. Cutaneous B-cell lymphoma.
B. Bone marrow biopsies after treatment with radioactive anti-CD20.
C. Detection of CD10 in paraffin-embedded leukemias: Comparison with flow cytometry.
D. Mantle cell lymphoma involving cerebrospinal fluid.
E. CD15-negative Hodgkin's disease.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Assistant Director, Clinical Hematology Laboratory.
B. Director, Anatomic Pathology's Special Studies Laboratory (Clinical Immunohistochemistry, Immunofluorescence and Neural and Muscular Studies).

MEDICAL SCHOOL/HOSPITAL:

None.

UNIVERSITY OF MICHIGAN:

None.

REGIONAL AND NATIONAL:

None.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

1. Lecturer, Hematological Coups: A practical approach to challenging cases in hematolymphoid diagnosis. Four hour course with Drs. Ross and Schnitzer, at the American Society for Clinical Pathology, April, 1998.

VI. PUBLICATIONS:

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

1. Hsi ED, Singleton TP, Svoboda SM, Schnitzer B and Ross CW. Characterization of the lymphoid infiltrate in Hashimoto's thyroiditis by immunohistochemistry and polymerase chain reaction for immunoglobulin heavy chain gene rearrangement. (in press, Am J Clin Pathol)

2. Tworek JA, Singleton TP, Schnitzer B, Hsi ED and Ross CW. Flow cytometric and immunohistochemical analysis of small lymphocytic lymphoma, mantle cell lymphoma and plasmacytoid small lymphocytic lymphoma. (in press, Am J Clin Pathol)
3. Kroft SH, Finn WG, Singleton TP, Ross CW, Sheldon S, Schnitzer B: Follicular large cell lymphoma with immunoblastic features in a child with Wiscott-Aldrich syndrome: an unusual immunodeficiency-related neoplasm not associated with Epstein-Barr virus. Am J Clin Pathol 110:95-99, 1998.
4. Kroft SH, Singleton TP, Dahiya M, Ross CW, Schnitzer B, Hsi ED. Ruptured spleens with expanded marginal zones do not reveal occult B-cell clones. Mod Pathol 10(12):1214-20, 1997.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Singleton TP, Anderson MM, Ross CW, Sheldon S, Schnitzer B: Leukemic phase of mantle cell lymphoma, blastic variant.
2. Izban KF, Singleton TP, Alkan S, Hsi ED. Multiparamter immunohistochemical analysis of the cell cycle proteins cyclin D1, Ki-67, p21WAF1, p27KIP1 and p53 in mantle cell lymphoma.

ABSTRACTS IN UNREFEREED JOURNALS:

1. Iravani S, Ross CW, Schnitzer B and Singleton TP. Ocular adnexal lymphomas (OAL). Lack of CD23 in nonfollicular small B-cell lymphoma supports marginal zone type. Mod Pathol 11(1): 132A, 1998.
2. Hsi Ed, Singleton TP, Swinnen L, Greenson JK and Alkan S. Mucosa-associated lymphoid tissue (MALT) type lymphomas occurring in posttransplantation patients: A form of posttransplantation lymphoproliferative disorder (PTLD)? Mod Pathol 11(l): 131A, 1998.
3. Iravani S, Singleton TP, Ross CW and Schnitzer B. B-cell lymphoblastic lymphoma presenting as lytic bone lesions: a clinicopathological study. Mod Pathol 11(l): 132A, 1998.
4. Kroft SH, Hsi ED, Ross CW, Schnitzer B and Singleton TP. CD23 expression in paraffin-embedded gastric MALT lymphoma. Am J Clin Pathol 109(4):477, 1998.
5. Kleer CG, Singleton TP and Wojno KJ. Estrogen receptor expression in paraffin-embedded carcinomas of the breast: Comparison of two monoclonal antibodies using an automated stainer. Am J Clin Pathol 109(4): 488, 1998.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. **Flow Cytometry Diagnostic Service** - interpretation of cell surface marker studies 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, post-doctoral and research-track investigators:**

1.1. **Katie Phillips, junior undergraduate (Nov 1995-present):** Ms. Phillips worked ~10 hours/week during the academic year on a variety of ongoing projects. Her research and academic productivity (top 5% of her class) culminated in the award of an OSRBP summer research grant for study of T-cell trafficking during the adoptive immunotherapy of metastatic cancer (10 awards for 100 applicants). Ms. Phillips will determine the adhesion receptor phenotype of the tumor-reactive T-cells that develop in lymphnodes draining experimental murine sarcomas. The phenotype will then be used to isolate these cells before expansion in vitro. The tumor-suppressive activity of fractionated and unfractionated cells will then be compared in vivo. Preliminary findings indicate that tumor suppression via adoptive immunotherapy can be significantly enhanced through this novel approach.

1.2. **Keishi Tanigawa, M.D., post-doctoral fellow (April 1998-present):** Dr. Tanigawa is jointly supported by the L.M. Stoolman (Pathology) and A.E. Chang laboratories (Surgical Oncology) for work on T-cell trafficking during the adoptive cellular immunotherapy of metastatic cancer. Previous work from the Stoolman Larboratory indicated that the ex-vivo expansion of tumor reactive T-cells generates lymphoblasts expressing high levels of selectin-ligands. These cells suppress experimental lung sarcoma and melanoma metastases despite the fact that recruitment into tumor-bearing lungs is minimally above baseline. Preliminary experiments indicated that the recruitment of adoptively transferred tumor-reactive T-lymphoblasts and suppression of tumor growth increased when selectins (the counter-receptors for selectin-ligands) were induced on the lung microvasculature prior to treatment. Dr. Tanigawa will determine whether adjuvant therapy with pro-inflammatory cytokines and chemokines augments the suppression of metastatic disease by adoptive T-cell immunotherapy.

1.3. **Randall Knibbs, Ph.D., Research Scientist (January, 1994-present)** - Dr. Knibbs continued his investigation of selectin-ligand synthesis. A recently accepted manuscript proves that the fucosyltransferase FucT-VII regulates the synthesis of both P- and E-selectin ligands on human and murine T-lymphoblasts. Furthermore, P-selectin ligand synthesis requires significantly lower levels of enzymatic activity than synthesis of E-selectin ligands. Consequently, P-selectin ligands reach physiologically active levels on T-cells before E-selectin ligands

during blast transformation. These ligands are essential for the entry of T-cells into both normal and pathologic immune lesions in the skin, lung and elsewhere. These discoveries provide the first specific target for development of agents which suppress selectin-mediated T-cell recruitment in immune mediated diseases. Dr. Knibbs efforts now focus on the structure of the carbohydrate portion of the selectin ligands on T-cells and on the signalling pathways controlling FucT-VII activity.

B. **Director, General Pathology Laboratory Course for Dental Students (Pathology 631) and co-director, General Pathology Lecture Course (Pathology 630):** A major new effort this year was the development, dissemination across campus and management of a first generation Website for the General Pathology Laboratory Sequence. The site incorporates high resolution (1900 X 1300 pixel) photographs of gross and microscopic specimens into an on-line version of the laboratory syllabus. An NT-Server in the Pathology Department houses the Livepicture Image Server dedicated to this project. The Livepicture Server software allows one to pan across a low-power image and then magnify selected regions. Focus is maintained to the limits of photographic resolution. This "active" learning modality allows students to interact with specimens and slides much as they will in the laboratory. Consequently, it provides a unique approach to preview and review of laboratory material. Current efforts focus on ungrades of hardware, server software and courseware.

C. **Co-director and lecturer, Hematology Sequence in Component II (Medical School 2nd year curriculum)**- designed/administered pathology component of sequence and co-directed course with Roland Hiss, M.D. (Department of Internal Medicine). A major new effort this year was the development, dissemination across campus and management of a Hematopathology Website for the M2-course. This site utilizes the image server and general approach outlined above for the General Pathology Laboratory Website. The sequence, particularly the laboratory component, continues to enjoy one of the highest ratings (both student and faculty) for any sequence in Component II.

D. **General Pathology laboratory instructor, Component II**- one of ten permanent faculty in the laboratory component. We are currently the only instructors in any department with teaching activities throughout the entire 2nd year curriculum. The group provides sequence-specific laboratory instruction, general reviews at intervals throughout the year and quality-control for laboratory examinations in all sequences.

E. **Section leader, Hematopathology Section of Component II**- several sequences use specialists to cover pertinent laboratories. This is in addition to serving as an instructor in the general pathology laboratories of Component II.

F. **Lecturer, Host Defense Sequence of Component I.**

G. **Attending, Flow Cytometry Service.**

H. **Attending, Autopsy Service.**

III. RESEARCH ACTIVITIES:

ACTIVE SUPPORT:

A. **Principal Investigator- T Cell Trafficking in Adoptive Cellular Immunotherapy-** NIH, RO1, CA73059-01A1, 30% effort, $583,278, 1 April 1998- 31 March 2001. ***(NEW)***

B. **Principal Investigator, project 3- "Structure of selectin-ligands synthesized by human T-lymphoblasts"**, NIH, PO1AI33189 (Oligosaccharides as Anti-inflammatory Agents; PA Ward, Program Director), 15% effort, $347,950; 9 September 1996- 31 August 2001.

C. **Principal Investigator, project 5- "Mononuclear Leukocyte Adhesion and Recruitment in Chronic Inflammatory Lung Disease"** - NIH, P01, HL31963 (Inflammatory Cells and Lung Injury; PA Ward, M.D., Program Director), 20% effort, $500,000; 1 Mar 1994 - 28 February 1999.

PENDING APPLICATIONS:

A. **Co-investigator (with B. Richardson, Rheumatology Division, University of Michigan)- "Gender specific T-cell homing and autoimmunity", NIH, RO1, 15% effort, re-submitted 3/1/98:** This project builds on the observation that female gonadal steroids markedly increase the trafficking or auto-reactive T-lymphoblasts to the spleen. This increased recruitment is associated with development of a lupus-like syndrome in genetically susceptible mice. Autoimmune diseases generally occur with greater frequency in females. Consequently, gender-specific differences in trafficking/accumulation of auto-reactive T-cells may be a contributing factor. This project will determine whether differential regulation of vascular/lymphocytic adhesion receptors by gonadal steroids explains the observed differences in T-cell trafficking to the spleen. Furthermore, it will determine whether trafficking and the development of the lupus-like syndrome are causally related.

B. **Co-investigator (with Gregory Plautz, M.D., Center for Surgery Research, Cleveland Clinic Foundation)- "Adoptive Immunotherapy for Intracranial Tumors":** This project will evaluate the contribution of selectins and other adhesion receptors to the suppression of experimental CNS malignancies by adoptively transferred tumor-reactive T-lymphoblasts.

PROJECTS UNDER STUDY:

A. **Regulation of selectin-ligand synthesis by T-cells:** This projects builds on the discovery that pre-translational regulation of a single fucosyl-transferase, FucT-VII, controls the synthesis of selectin ligands on T-cells. The synthesis of these ligands, in turn, enhance the trafficking of T-cells into both normal and pathologic immune lesions. The signalling pathways responsible for the regulation of the FucT-VII gene are currently under investigation. It is anticipated that these studies will identify novel targets for therapy in auto-immune and chronic inflammatory diseases.

B. **Selectin-mediated T-cell recruitment into inflammatory/immune responses in non-lymphoid organs:** The selectins mediate T-cell entry in delayed-type hypersensitivity lesions in the skin. However, there is currently no direct evidence that the selectins contribute to T-cell recruitment during immune responses in other organs as well. Furthermore, recent studies imply that selectins mediate the recruitment of T-cells with the T-1 cytokine profile primarily. Mice with targeted deletions in one or both selectins, direct measurment of T-lymphoblast trafficking and concurrent analysis of cytokine and adhesion receptor profiles will be used to investigate these issues in several chronic inflammatory models in vivo.

C. **T-cell recruitment during adoptive immunotherapy of malignant gliomas:** A collaboration with Gregory Plautz, M.D. and Suyu Shu, Ph.D. (Surgical Reserarch Division, Cleveland Clinic Foundation) will examine the molecular mechanism of T-cell trafficking into primary and metastatic CNS malignancies

IV. ADMINISTRATIVE ACTIVITIES:

A. **Director of Research Flow Cytometry Laboratory and Co-Director of Clinical Flow Cytometry Laboratory**- managed the development of new software to interface clinical flow cytometry instruments with the Laboratory Information System (Cerner V300).

Participated in the consolidation of Clinical Flow Cytometry and Hematology Laboratories. Managed the operation of the research flow cytometry instruments (provided access for departmental investigators with grant support for flow cytometry).

B. **Co-Director, Hematology Sequence in Component II and General Pathology 580/630/631**- see educational activities.
C. **Member, Learning Resources Center Oversight Committee**
D. **Member, Medical School InfoTech Committee**
E. **Member, Medical School and MD/PhD Admissions Committees**
F. **Member, Pathology/Immunology Graduate Program Admissions Committee**
G. **Participant, Retreat on Medical School Evaluations and Advancement**
H. **Member, Pathology Website Committee**

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL ACTIVITIES:

A. Journal of Clinical Investigation.
B. Journal of Biological Chemistry.
C. Journal of Laboratory Investigation.
D. Nature.
E. Cell.
F. Journal of Experimental Medicine.
G. American Journal of Pathology.
H. Journal of Immunology (Associate Editor).

INVITED LECTURES AND SEMINARS:

A. Molecular Mechanisms of Leukocyte Trafficking, Keystone Symposium at Incline Village, NV., March 22-28, 1998.
B. Imunotherapy of Cancer IV, Satellite Symposium of AAI at Experimental Biology '98, San Franscisco, CA., April 18. 1998.
C. Leukocyte Trafficking, Block Symposium for AAI at Experimental Biology '98, San Francisco, CA., April 21, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN PEER REVIEWED JOURNALS:

1. F.M. Wolber, J.L. Curtis, A.M. Milik, K.L. Fields, S. Kim, J. Sonstein and L.M. Stoolman. 1997. Lymphocyte recruitment and the kinetics of adhesion receptor expression during the pulmonary immune response to particulate antigen. Am. J. Path. 151(6): 1715.
2. Snapp K.R., Wagers AJ, Craig R, Stoolman L.M., Kansas GS. 1997. P-selectin glycoprotein ligand-1 (PSGL-1) is essential for adhesion to P-selectin but not E-selectin in stably transfected hematopoietic cell lines. Blood: 89, 896.
3. A.J. Wagers, L.M. Stoolman, R. Craig, R. Kannagi and G.S. Kansas. 1997. Expression of leukocyte fucosyltransferases regulates binding to E-selectin: relationship to previously implicated carbohydrate epitopes. J. Immunol. 159: 1917.
4. F.M. Wolber, J.L. Curtis, P. Mály, R.J. Kelly, P. Smith, J.B. Lowe, L.M. Stoolman. 1998. Endothelial selectins and α4-integrins regulate independent pathways of T-lymphocyte recruitment in the pulmonary immune response. J. Immunol. (in press)

5. R.N. Knibbs, R.A. Craig, P. Maly, A. Thall, P. Smith, F. Wolber, J.B. Lowe and L.M. Stoolman. 1998. Fucosyltransferase-VII dependent synthesis of P-selectin ligands on human and murine lymphoblasts. J. Immunol. (in press).
6. K.R. Snapp, R. Craig, M. Herron, R.D. Nelson, L.M. Stoolman and G.S. Kansas. 1998. Dimerization of P-selectin glycoprotein ligand-1 (PSGL-1) required for optimal recognition of P-selectin. J. Cell Biol. (in press).

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

1. Kansas GS, Snapp KR, Wagers AJ, Craig R, Knibbs R, Stoolman LM. 1997. Glycosyltransferase and glycoprotein requirements for recognition of vascular selectin. Glycobiology 7 (7): 7.
2. RN Knibbs, R Craig, P Mály, P Smith, FM Wolber, N Faulkner, JB Lowe and LM Stoolman. α (1,3) fucosyltransferase-VII dependent synthesis of P- and E-selectin ligands on cultured T-lymphoblasts- Keystone Symposium on Molecular Mechanisms of Leukocyte Trafficking 1998, Lake Tahoe, CA.
3. LM Stoolman, FM Wolber, RN Knibbs, P Maly, R Craig, JB Lowe and J Curtis. Synthesis and function of selectin-ligands on T-lymphocytes. Keystone Symposium on Molecular Mechanisms of Leukocyte Trafficking 1998, Lake Tahoe, CA.
4. LM Stoolman, JL Curtis, RJ Kelly, P. Maly, P. Smith, TA Yednock, JB Lowe and FM Wolber. 1998. Endothelial Selectins and a4-integrins mediate indipendent pathways of T-lymphoblast recruitment in the pulmonay immune response. FASEB J. 12 (4): A580.
5. KR Snapp, R Craig, M Herron, RD Nelson, LM Stoolman and GS Kansas. 1998. Dimerization of P-selectin glycoprotein ligand-1 (PSGL-1) is required for optimal recognition of P-selectin. FASEB J. 12(4): A581.
6. K Zhang, HE Chuluyan, D Hardie, D-C Shen, R Larsen, L Stoolman and AC Issekutz. 1998. Novel antibodies recognize carbohydrate epitopes and inhibit selectin binding. FASEB J. 12(4): A581.
7. LM Stoolman. 1997. The Virtual Microscope- Interactive Hematology Syllabus. URL= http://141.214.5.223/virtualheme/.
8. LM Stoolman. 1997. The Virtual Microscope- Interactive Pathology 631 Syllabus. URL= http://141.214.5.223/cyberscope631/

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Lecturer in General Pathology for Dental Students and Graduate Students (Pathology 630/580).
B. Faculty Research Partner in the Undergraduate Research Opportunity Program (UROP).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Role of Cytokines and Adhesion Molecules in Thermal Injury", (NIH GM-48477), Principal Investigator.
B. "Lung Injury Produced by Oxygen Metabolites", (NIH GM-29507), Co-Principal Investigator with Dr. P.A. Ward.

PENDING SUPPORT:

A. None.

PROJECTS UNDER STUDY:

A. Role of leukocytes, inflammatory mediators, and adhesion molecules in thermal trauma-related cell and tissue injury.
B. Pathomechanisms of ischemia-reperfusion injury.
C. Pathophysiologic role of complement activation products in secondary lung injury.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Course Co-Director Pathology 580/630/631.
B. Member Medical School Committee on Student Biomedical Research Programs.
C. Interviewed candidates for faculty positions.
D. Consultant for clinical research programs.
E. Reviewer of intra-departmental grant proposals.

REGIONAL AND NATIONAL:

None.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Member Editorial Board Immunopharmacology.
B. Reviewer for the following scientific journals:
   1. American Journal of Pathology.
   2. American Journal of Physiology: Gastrointestinal and Liver Physiology.
   3. Free Radical Biology and Medicine.
   4. Journal of Clinical Investigation.
   5. Journal of Leukocyte Biology.
   6. Shock.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Schmid, E., Warner, R.L., Crouch, L.D., Friedl, H.P., Till, G.O., Hugli, T.E., Ward, P.A. Neutrophil chemotactic activity and C5a following systemic activation of complement in rats. Inflammation 21:325-333, 1997.
2. Schmid, E., Piccolo, M.-T.S., Friedl, H.P., Warner, R.L., Mulligan, M.S., Hugli, T.E., Till, G.O., Ward, P.A. Requirement for C5a in lung vascular injury following thermal trauma to rat skin. Shock 8:119-124, 1997.
3. Lai, J.C., Johnson, M.W., Martonyi, C.L., Till, G.O. Complement-induced retinal arteriolar occlusions in the cat. Retina 17:239-246, 1997.
4. Younger, J.G., Taqi, A.S., Till, G.O., Hirschl, R.B. Partial liquid ventilation protects the lung during resuscitation from shock. J. Appl. Physiol. 83:1666-1670, 1997.
5. Espana A., Diaz, L.A., Mascaro, J.M., Giudice, G.J., Fairley, J.A., Till, G.O., Liu, Z. Mechanisms of acantholysis in pemphigus foliaceus. Clin. Immunol. Immunopathol. 85:83-89, 1997.
6. Liu, Z., Giudice, G.J., Zhou, X., Swartz, S.J., Trov, J.L. Fairley, J.A., Till, G.O., Diaz, L.A. A major role for neutrophils in experimental bollous pemphigoid. J.Clin.Invest. 100:1256-1263, 1997.

7. Colton, D.M. Till, G.O., Johnson, K.J., Dean, B.S., Bartlett, R.H., Hirschl, R.B. Neutrophil accumulation is reduced during partial liquid ventilation. Crit. Care.Med. (in press).
8. Schlag, G. Redl, H., Till, G.O., Davies, J. Anti-L-selectin antibodies treatment of traumatic shock in baboons. Crit. Care.Med. (in press).
9. Younger, J.G., Taqi, A.S., Jost, P.F. Till, G.O., Johnson, K.J., Stern, S.A., Hirschl, R.B. The pattern of early lung parenchymal and airspace injury following acute blood loss. Acad.Emerg.Med. (in press).
10. Colton, D.M., Till, G.O., Johnson, K.J., Gater, J.J., Hirschl, R.B., Partial liquid ventilation (PLV) decreases pulmonary hemorrhage and albumin leak in the setting of acute lung injury. Chest (in press).
11. Winn, W.C., Davis, G.S., Durda, J.P., Till, G.O.: The effect of neutropenia on experimental Legionella pneumonia. Infec. Immun. (in press).
12. Seekamp, A., Hultquist, D.E. Till, G.O.: Protection by vitamin B2 against oxidant-mediated acute lung injury. Inflammation. (in press).

BOOKS AND CHAPTERS IN BOOKS:

1. Till, G.O.: Chemotactic Peptides. pp266-278, In: The Complement System; Rother K. O., Till G. O., Hänsch G. M. (Eds.) Springer-Verlag Berlin Heidelberg, 1998.
2. Rother, K., Till, G.O. Introduction: Phases of complement research and nomenclature. XIII-XVI, In: The Complement System; Rother K. O., Till G. O., Hänsch G. M. (Eds.) Springer-Verlag Berlin Heidelberg, 1998.
3. Rother, K.O., Till, G.O. Hänsch, G.M. (Eds.). The Complement System. 2nd revised edition. Springer-Verlag Berlin Heidelberg, 1998.

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

1. Watkins, S.A. Ravage, Z.B., Till, G.O. Inflammatory mediators in burn wound edema formation. UROP Research Conference, December 1997.
2. Ravage, Z.B. Watkins, S.A. Till, G.O. Pathogenesis of microvascular damage in second-degree burn wounds in the rat. Shock (Suppl.) 9:5, 1998.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Member, Dissertation Committee of Douglas F. Gibbs (Pathology).
B. Member, Dissertation Committee of Shemin Hu (Pathology).
C. Mentor for students who worked in my laboratory over the past year three post-doctoral fellows, one pathology graduate student, and three undergraduate students.
D. Member, University of Michigan Minority Student Research Opportunities Program.
E. Member, University of Michigan Student Research Opportunities Program.
F. Lecturer, Oncology sequence for M2 students.
G. Lecturer, Graduate Cancer Biology Course
H. Member, Cancer Biology Training Grant Steering Committee.
I. Member, Dermatological Sciences Training Grant Steering Committee

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Squamous Epithelial Invasion in Organ Culture," NIH CA60958, 3/1/95-6/30/98.
B. Principal Investigator, "High Density Cell Growth in Microcarrier Aggregate," NIH. CA 61616, 7/1/96-6/30/98.
C. Principal Investigator on Project 10, "Retinoic Acid and Cells of the Skin," Johnson and Johnson Corporation, 7/1/91- 6/30/2006.
D. Co-Investigator, "Erb-b-2 Expression and Resistance to TNF Killing," NIH CA 64803, 9/01/94-8/30/98.
E. Co-Investigator, "Protease-Oxidant Interactions in Lung Inflammation," NIH HL42607, 7/1/94-6/30/98.
F. Principal Investigator, "Co-polymer - Trimethylamine microcarriers for high-density cell growth under serum-free conditions," HIH CA 74595, 7/1/97-12/31/97.
G. Principal Investigator, "Organ culture of Human Prostate", NIH SPORE 8/1/97-7/31/98.

PROJECTS UNDER STUDY;

A. The development of substrates for optimum growth of cells in large-scale culture.
B. The biology of human squamous carcinoma cell invasion.
C. Biological basis of photoaging and natural aging in skin.
D. Biology of prostate cancer 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.
F. Member, University Committee on Use and Care of Animals (UCUCA).
G. Member, Curriculum Committee of the combined biomedical sciences graduate program

UNIVERSITY:

A. Member, Graduate School Task Force on Non-Academic Misconduct

REGIONAL AND NATIONAL:

A. Editorial Board of Invasion and Metastasis.
B. Manuscript Review for:
    1. American Journal of Pathology.
    2. Cancer Research.
    3. Experimental Cell Research.
    4. International Journal of Cancer.
    5. Journal of Investigative Dermatology.
    6. Laboratory Investigation.
    7. Invasion and Metastasis.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/PRESENTATIONS:

1. 46th Symposium on Biology of the Skin, Aspen, Colorado, July 26, 1997.
2. Molecular Design International., Memphis, TN, Jan 6, 1998.
3. Genentech, Jan 8, 1998.
4. Departments of Pathology and Biochemistry, Univ. of Manitoba. Winnipeg, Man., Jan 16, 1998.
5. Cell Culture Engineering, VI, San Diego, California, Feb. 8-12, 1998.
6. Keystone Symposium on Breast and Prostate Cancer, Copper Mountain, CO., Feb 21-25, 1998.
7. Experimental Biology, San Francisco, April 18-23, 1998.
8. Johnson & Johnson Retinoid Symposium, Short Hills, New Jersey, June 11,12, 1998.
9. National Cancer Institute National SPORE meeting; Rockville, MD. July 11-14, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS.

1. Ginsburg, I., Yedgar, S. and Varani, J.: Diethylcarbamate and nitric oxide synergize with oxidants and with membrane-damaging agents to injure mammalian cells. Free Rad. Res. 27:143-164, 1997.
2. Varani, J., Zeigler, M.E., Perone, P., Carey, T.E. and Datta, S.C.: Human squamous carcinoma cell invasion in organ-cultured skin. Cancer Lett., 11:51-57, 1997.
3. Varani, J.: Human skin in organ culture: A model for the study of normal and pathological responses of skin. Histology and Histopathology (In Press).
4. Varani, J., Chi, Y. Zeigler, M.E., Elaboration of matrix metalloproteinases (MMPs) and MMP inhibitors by human skin in organ culture during invasion. Invasion and Metastasis (In Press).
5. Fisher, G.J., Wang, Z-Q,., Datta, S.C., Varani, J., Kang, S. and Voorhees, J.J. Pathophysiology and retinoic acid prevention of sun-induced premature skin aging. New Eng. J. Med. 337:1419-1428.
6. Varani, J., Kang, S., Warner, R., Wang, Z-Q., Datta, S.C., Fisher G.J. and Voorhees, J.J. Molecular mechanisms of intrinsic skin aging and retinoid-induced repair and reversal. J. Invest. Dermatol. (In Press).
7. Varani, J., Perone, P., Chi, Y., Schmidt, T., Johnson, T., Zeigler, M.E.; Elaboration of matrix metalloproteinases and matrix metalloproteinase inhibitors by basal cell and squamous cell carcinomas of skin. Int. J. Cancer (in press).
8. Varani, J., Piel, F., Josephs, S., Beals, T.F., Hillegas, W.J.; Attachment and growth of anchorage-dependent cells on a novel, charged-surface microcarrier under serum-free conditions. Cytotechnology (in press).
9. Varani, J., Kang, S., Stoll, S., Elder, J.T.; Human psoriatic skin in organ culture: Comparison with normal skin exposed to exogenous growth factors and effects of an antibody to the EGF receptor. Pathobiology (in press).

10. Murphy, H.S., Bakopoulos, N., Dame, M.K., Varani, J., Ward, P.A.; Heterogeneity of vascular endothelial cells: differences in susceptibility to neutrophil-mediated injury. Microvascular Res. (in press).
11. Murphy, H.S., Warner, R.O., Dame, M.K., Varani, J., Ward, P.A.; Nitric oxide protects endothelial cells from oxidant injury. Free. Rad. Biol. Med. (in press).

BOOKS AND CHAPTERS IN BOOKS:

1. Varani, J. and Ward, P.A.: Activation of the inflammatory response-asbestos and mineral dusts, in, Wallace, K.B. (ed), *Free Radical Toxicology*, Second Edition, Raven Press, New York, pp 295-304, 1997.
2. Varani, J. and Ward, P.A.: The Biology of Endothelial Cells, in, Middleman, E. et al (eds), *Allergy: Principals and Practices,* Fifth Edition, Mosbey, St. Louis, Missouri, In Press.

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

1. Zeigler, M.E., Chi, Y. and Varani, J.: MAP kinase signaling during growth factor-induced epidermal invasion of the dermis in organ culture. AACR Proceed. 1997.
2. Varani, J., Kang, S., Wang, Z-Q,., Datta, S.C., Fisher G.J. and Voorhees, J.J. Molecular mechanisms of intrinsic skin aging and retinoid-induced repair and reversal. J. Invest. Dermatol, 1997.
3. Warner, R.O., Kang, S. and Varani, J. Expression of nitric oxide from cultured human skin cells and punch biopsies in response to retinoic acid and cytokines. FASEB J., 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

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. Jacqueline Jordan, Ph.D., Postdoctoral Fellow.
   b. J. Eric McDuffie, Ph.D., Postdoctoral Fellow.
   c. Nicolas Bless, M.D., Postdoctoral Fellow.
   d. Larry Crouch, Ph.D., Postdoctoral Fellow.
   e. Boris Czermak, M.D., Postdoctoral Fellow.
   f. Jami Foreback, Pathology Graduate Program Student (MSTP student) (mentor).
   g. Alex Lentsch, Ph.D., Postdoctoral Fellow.
   h. Hagen Schmal, M.D., Postdoctoral Fellow.
   i. David Tung, Ph.D., Postdoctoral Fellow.
   j. Roscoe Warner, Ph.D., Postdoctoral Fellow.
   k. UROP Undergraduate Students:
      - Hillary Cohen, Senior.
      - Karen Rosner, Sophomore.
      - Richard Carter, Freshman.
   l. Morgan Althoen, Medical Student.
2. Supervision of four Research Scientists.
3. Gross Autopsy Conference, 25 hours.
4. Clinical Pathology Grand Rounds Lecture, Reflections on the Pathology Board Examination.

B. Undergraduate students:

1. Lecture, College Honors Seminar 250 (LS&A), three hours.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Lung Immunopathology" (Training Grant), NHLBI-NIH-HL-07517 (5%), $218,805/year, 6/1/86-5/31/01.
B. Principal Investigator, "Lung Injury by Oxygen Metabolites", NIGMS-NIH-GM-29507 (20%), $272,284/year ($1,123,824/four years), 7/1/97-6/30/01.
C. Principal Investigator, "Inflammatory Cells and Lung Injury", NHLBI-PO1-HL-31963 (25%), $189,794/year (Proj. I) $630,840 (all projects), 3/1/84-2/28/99.
D. Principal, Investigator, "Oligosaccharides as Inflammatory Agents", PO1-AI-33189 (10%), $93,443/year (Proj. II) $26,853/year (Core A), 9/30/96-08/31/99.
E. Co-Investigator, "The Role of Cytokines and Adhesion Molecules in Thermal Injury", GM48477 (5%), $178,772/year ($1,384,651/five years), with G.O. Till, Principal Investigator.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Division of General Pathology.

MEDICAL SCHOOL/HOSPITAL:

A. Advisory Committee for the Howard Hughes Medical Institute.
B. Clinical Council.
Conflict of Interest Committee.
C. Technology Transfer Committee
D. Dean's Advisory Council.
E. Geriatric Center Executive Committee.
F. Howard Hughes Medical Institute Dean's Advisory Committee.
G. Internal Medicine Advisory Committee for the University of Michigan George M. O'Brien Renal and Urologic Center.
H. Michigan Eye Bank Research Review Committee.
I. Undergraduate Research Opportunity Program, University of Michigan.
J. University of Michigan Cancer Center Executive Committee.

UNIVERSITY OF MICHIGAN:

A. Senate Assembly, September, 1995-present.
1. Chair, Medical Affairs Advisory Committee, Chair, September, 1996-present.
B. Senate Advisory Committee on University Affairs, 1998 – present.
C. Michigan League Board of Governors, September, 1997 – present.

REGIONAL AND NATIONAL:

A. American Association of Immunologists.
B. American Board of Pathology, effective January 1, 1988:
   1. Immediate Past President, 1997.
   2. President, 1996.
   3 Vice-President, 1995.
   4. Trustee, 1980-present.
   5. Immunopathology Test Committee, 1980-present.
   6. Anatomic Pathology Examination Committee, 1988-present.
   7. By-Laws Committee, 1988-present.
   8. Examination Evaluation Committee, 1988-present.
   9. Professional Qualification/Competence Committee, 1988-present.
   10. ABP/ABPRF Research Committee, 1989-present.
   11. Residency Review Committee for Pathology.
   12. Building Committee, 1992-present.
   13. Planning and Development Committee, 1992-present.
   14. Test Committee for Molecular Pathology, 1993-present.
C. American Society for Clinical Investigation.
D. Association of American Physicians.
E. American Society of Investigative Pathologists, President 1979-80, member since 1967.
F. American Pathology Foundation.
G. American Thoracic Society.
H. Association of Pathology Chairmen.
I. A. James French Society of Pathologists, 1988-present.
J. Health Policy Agenda for the American People, Advisory Committee.
K. Institute of Medicine, National Academy of Sciences, July, 1990-present.
L. Michigan Society of Pathologists.
M. Michigan Thoracic Society, 1988-present.
N. National Research Council.
   1. Institute of Laboratory Animal Resources.
   2. Committee on Human Rights, Correspondent.
O. The Oxygen Society, 1988-present.
P. United States and Canadian Academy of Pathology, Inc.
   1. Council Member, April, 1986-1989.
   2. Member, Finance Committee, April, 1986-1990.
   3. Vice-President, 1990.
   4. President-Elect, 1991.
   5. President, 1992.
   6. Past-President, 1993.
Q. 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-present.
B. American Review of Respiratory Diseases, Consulting Editor, 1977-present.
C. Biological Signals, Consulting Editor.
D. Clinical Immunology and Immunopathology, Consulting Editor, 1977-present.
E. CRC Critical Reviews in Free Radical Research, Advisory Board, 1986-present.
F. CRC Critical Reviews in Toxicology, Advisory Board, 1986-present.
G. Free Radical Biology & Medicine, Editorial Board, 1995-present.
H. Journal of Clinical Investigation, Consulting Editor.
I. Toxicologic Pathology, Editorial Board, 1988-present.

HONORS AND AWARDS:

None.

PATENTS:

None.

INVITED LECTURES/SEMINARS:

1. Invited Speaker and Chair, "Regulation of Chemokine Expression by Complement, 2nd World Congress on Advances in Oncology, Athens, Greece, October 17, 1997.
2. Invited Speaker and Moderator, "Modern Biology as Applied to Pulmonary Edema", Councils on Cardiology and Critical Cardiology, American Heart Association 70th Annual Scientific Sessions, Orlando, Florida, November 10, 1997.
3. Invited Speaker, "Role of Complement Activation Products in Lung Inflammatory Injury", 3rd World Congress on Inflammation, Tokyo, Japan, November 16, 1997.
4. Invited Speaker, "Complement Chemokines and Acute Lung Injury", Society for Leukocyte Biology 32nd National Meeting, Baltimore, Maryland, December 5, 1997.
5. Invited Speaker, "P-Selectin and Complement in Inflammation", NeXstar Pharmaceuticals, Inc. Scientific Advisory Committee, Boulder, Colorado, February 23, 1998.
6. Invited Speaker, "Intrinsic Regulation of the Lung Inflammatory Response", Eighth Medical Symposium: Research Day, Ross University School of Medicine, Portsmouth, Dominica, West Indies, March 7, 1998.
7. Invited Speaker, "How Lung Inflammatory Responses are Regulated", Glaxo Welcome Research Papers Competition, Brigham & Women's Hospital, Boston, Massachusetts, March 28, 1998.
8. Invited Speaker, "Regulation of the Lung Inflammatory Response", Northwestern University Medical School, Chicago, Illinois, April 6, 1998.
9. Invited Speaker, "Activation and Regulation of the Lung Inflammatory Response", Harvard Medical School, Boston, Massachusetts, April 14, 1998.

10. Invited Speaker, "Role of Integrins in Inflammatory Lung Injury", Integrin Meeting, Garda, Verona, Italy, May 8, 1998.
11. Invited Speaker, "Intrinsic Regulation of the Lung Inflammatory Response", Mario Negri Institute, Milano, Italy, May 13, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ward, P.A.: Editorial Review: Neutrophils and adjuvant arthritis. Clin Exp Immunol, 1997;107(2):225-226.
2. Lowe, J.B. and Ward, P.A.: Therapeutic inhibition of carbohydrate-protein interactions *in vivo*. J Clin Invest, 1997;99(5):822-826.
3. Shanley, T.P., Schmal, H., Warner, R.L., Schmid, L., Friedl, H.P. and Ward, P.A.: Requirement for C-X-C chemokines (macrophage inflammatory protein-2 and cytokine-induced neutrophil chemoattractant) in IgG immune complex-induced lung injury. J Immunol, 1997;158:3439-3448.
4. Beck-Schimmer, B., Schimmer, R.C., Warner, R.L., Schmal, G., Nordblom, G., Flory, C.M., Lesch, M.E., Friedl, H.P., Schrier, D.J., and Ward, P.A.: Expression of lung vascular and airway ICAM-1 after exposure to bacterial lipopolysaccharide. Am J Resp Cell and Mol Bio, 1997;17:344-352.
5. Mulligan, M.S., Schmid, E., Till, G.O., Hugli, T.E., Friedl, H.P., Roth, R.A. and Ward, P.A.: C5a-dependent upregulation in vivo of lung vascular P-selectin. J of Immunol, 1997;1857-1861.
6. Eppinger, M.J., Deeb, G.M., Bolling, S.F. and Ward, P.A.: Mediators of ischemia-reperfusion injury in rat lung. Am J Path, 1997;150:1773-1784.
7. Kilgore, K.S., Schmid, E., Shanley, T.P., Flory, C.M., Maheswari, V., Tramontini, N.L., Cohen, H., Ward, P.A., Friedl, H.P. and Warren, J.S.: Sublytic concentrations of the membrane attack complex (MAC) of complement induce endothelial interleukin 8 (IL-8) and monocyte protein 1 (MCP-1) through nuclear factor kappa-B (NF-kB) activation. Am J Path, 1997;150(6): 2019-2031.
8. Ward, P.A.: Recruitment of inflammatory cells into lung: Roles of cytokines, adhesion molecules, and complement. J Lab Clin Med, 1997;129(4):400-404.
9. Shanley, T.P., Foreback, J.L., Remick, D.G., Ulich, T.R., Kunkel, S.L. and Ward, P.A.: Regulatory effects of IL-6 in IgG immune complex-induced lung injury. Am J Path, 1997;151(1):193-203.
10. Schmid, E., Warner, R.L., Crouch, L.D., Friedl, H.P., Till, G.O., Hugli, T.E., Ward, P.A.: Neutrophil chemotactic activity and C5a following systemic activation of complement in rats. Inflammation, 1997;21(3):325-333.
11. Foreback, J.L., Remick, D.G., Crockett-Torabi, and Ward, P.A.: Cytokine responses of human blood monocytes stimulated with Ig's. Inflammation, 1997;21(5):501-517.
12. Schmid, E., Piccolo, T.S., Friedl, H.P., Warner, R.L., Mulligan, M.S., Hugli, T.E., Till, G.O. and Ward, P.A.: Requirement for C5a in lung vascular injury following thermal trauma to rat skin. Shock, 1997;8(2);119-124.

13. Mulligan, M.S., Warner, R.L., Foreback, J.L., Shanley, T.P., Ward, P.A.: Protective effects of IL-4, IL-10, IL-12 and IL-13 in IgG immune complex-induced lung injury: Role of endogenous IL-12. J Immunol, 1997;159:3483-3489.
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15. Schimmer, R.C., Schrier, D.J., Flory, C.M., Dykens, J., Tung, D., Jacobson, P.B., Friedl, H.P., Conroy, M.C., Beck-Schimmer, B. and Ward, P.A.: Streptococcal cell wall-induced arthritis: requirements for neutrophils, P-selectin, ICAM-1 and MIP-2. J Immunol, 1997;159:4103-4108.
16. Bless, N.M., Smith, D., Charlton, J., Czermak, B.J., Schmal, H., Friedl, H.P., and Ward, P.A.: Protective effects of an aptamer inhibitor of leukocytic elastase in lung inflammatory injury. Curr Biol, 1997;7(11):877-880.
17. Warner, R.L., Glovsky, M.M., Pangburn, M.K. and Ward, P.A.: Effects of polymeric C3, C3b and iC3b on neutrophil expression of CD11b and CD18. Int Arch Allergy Immunol, 1997;113(1-3):368-369.
18. Ding, Z., Kawashima, H., Suzuki, T., Ward, P.A., and Miyasaka, M.: A sulfatide receptor distinct from L-selectin is involved in lymphocyte activation. FEBS Lett, 1997;418(3):310-314.
19. Schmid, E., Friedel, H.P., Till, G.O., and Ward, P.A.: Anti-C5a suppresses post-traumatic permeability damage of the lung after severe burn trauma. Langenbecks Arch Chir suppl Kongressbd, 1997;114:631-634.
20. Shanley, T.P., Warner, R.L., Crouch, L.D., Dietsch, G.N., Clark, D.L., O'Brien, M.M., Gallatin, W.M. and Ward, P.A.: Requirements for αd in IgG immune complex-induced rat lung injury. J Immunol, 1998;160:1014-1020.
21. Schimmer, R.C., Schrier, D.J., Flory, C.M., Laemont, K.D., Tung, D., Metz, A.L., Friedl, H.P., Conroy, M.C., Warren, J.S., Beck, B. and Ward, P.A.: Streptococcal cell wall-induced arthritis: requirements for IL-4, IL-10, Interferon-γ and MCP-1, J Immuno, 1998;160:1466-1471.
22. Schrier, D.J., Schimmer, R.C., Flory, C.M., Tung, D.K., and Ward, P.A.: Role of chemokines and cytokines in a reactivation model of arthritis in rats induced by injection with streptococcal cell walls. J Leukoc Biol, 1998;63:359-363.
23. Ward, P.A., and Hunninghake, G.W.: Lung inflammation and fibrosis. Am J Respir Cell Mol Biol, 1998;157(4):S123-S129.
24. Mulligan, M.S., Lentsch, A.B., and Ward, P.A.: In vivo recruitment of neutrophils: consistent requirements for L-arginine and variable requirements for complement and adhesion molecules. Inflammation, 1998;22(3):327-339.
25. Ward, P.A.: Thematic review series I: Lung biology of chemokines and cytokines. PAAP, 1998;110(4):287-287.
26. Mulligan, M.S., Lentsch, A.B., Shanley, T.P., Miyasaka, M., Johnson, K.J., and Ward, P.A.: Cytokine and adhesion molecule requirements for lung injury induced by anti-glomerular basement membrane antibody. Inflammation, 1998;22(4):403-417.
27. Czermak, B.J., Friedl, H.P., and Ward, P.A.: Complement, cytokines and adhesion molecule expression in inflammatory reactions. PAAP, 1998;110(5):306-312.
28. Mulligan, M.S., Lentsch, A.B., Miyasaka, M., and Ward, P.A.: Cytokine and adhesion molecule requirements for neutrophil recruitment during glycogen-induced peritonitis. Inflamm, 1998,47:251-255.

29. Foreback, J.L., Sarma, V., Yeager, N.R., Younkin, E.M., Remick, D.G., and Ward, P.A.: Blood mononuclear cell production of TNFα and IL-8: engagement of different signal transduction pathways including the p42 MAP kinase pathway. J Leuk Biol, 1998;64:124-133.
30. Lentsch, A.B., Czermak, B.J., Bless, Nicolas, M., and Ward, P.A.: NF-κB activation during IgG immune complex-induced lung injury: requirements for TNFα and IL-1β but not complement. Am J Pathol, 1998;152:1327-1336.
31. Czermak, B.J., Lentsch, A.B., Bless, N.M., Schmal, H., Friedl, H.P., and Ward, P.A.: Role of complement in *in vitro* and *in vivo* lung inflammatory reactions. J Leukoc Biol, 1998,64:40-48.
32. Mulligan, M.S., Warner, R.L., Lowe, J.B., Smith, P.L., Suzuki, Y., Miyasaka, M., Yamaguchi, S., Ohta, Y., Tsukada, Y., Kiso, M., Hasegawa, A. and Ward, P.A.: *In vitro* and *in vivo* selectin-blocking activities of sulfated lipids and sulfated sialyl compounds. International Immunol, 1998;10(5)569-575.
33. Anaya-Prado, R., Toledo-Pereyra, L.H., Collins, J.T., Smejkal, R., McClaren, J., Crouch, L.D., and Ward, P.A.: Dual blockade of P-selectin and beta2-integrin in the liver inflammatory response after uncontrolled hemorrhagic shock. J Am Coll Surg, 1998;187(1):22-31.
34. Schmal, H., Czermak, B.J., Lentsch, A.B., Bless, N.M., Schimmer, B., Friedl, H.P., and Ward, P.A.: Soluble ICAM-1 activated lung macrophages and enhances lung injury. Inflamm. In press.
35. Bless, N.M., Tojo, S.J, Kawarai, H., Natsume, Y., Lentsch, A.B., Padgaonkar, V., Czermak, B.J., Schmal, H., Friedl, H.P. and Ward, P.A.: Differing patterns of P-selectin expression in lung injury. Am J Pathol. In press.
36. Beck-Schimmer, B., Schimmer, R.C., Schmal, H., Flory, C.M., Friedl, H.P., Pasch, T., and Ward, P.A.: Characterization of rat lung ICAM-1. Inflamm Res. In press.
37. Lentsch, A.B. and Ward, P.A.: NF-kB activation and lung inflammatory injury. Curr Trends Immunol. In press.
38. Kilgore, K.S., Ward, P.A. and Warren, J.S.: Neutrophil adhesion to human endothelial cells is induced by the membrane attack complex: The roles of P-selectin and platelet activating factor. Inflammation. In press.
39. Lentsch, A.B., Czermak, B.J., Bless, N.M., Van Rooijen, N., and Ward, P.A.: Essential role of alveolar macrophages in intrapulmonary activation of NF-κB. Am J Respir Cell Mol Biol. In press.

BOOKS/CHAPTERS IN BOOKS:

1. Ward, P.A.: Phagocytes and the lung. Paoletti R. (eds). Phagocytes: Biology, Physiology, Pathology, and Pharmacotherapeutics. N.Y. Academy of Sciences, New York, In Press, 1997.
2. Varani, J., and Ward, P.A.: Role of the endothelium in lung inflammation. Chapter 25 in Biology of Endothelial Cells, In Press, 1998.

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

1. Schmal, H., Bless, N., Czermak, B.J., Friedl, H.P., Ward, P.A.: Regulation of macrophage inflammatory protein 1 β (MIP-1 β) in a rat model of acute lung injury. Submitted for the 4th International Congress on the Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches, 1997.

2. Bless, N., Czermak, B.J., Schmal, H., Friedl, H.P., Ward, P.A.: Upregulation of Airway ICAM-1 in Acute Lung Injury and Its Role for the Expression of Chemokines. Submitted for the 4th International Congress on the Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches, 1997.
2. Czermak, B.J., Bless, N., Schmal, H., Friedl, H.P., Ward, P.A.: In *vivo* regulation of chemokine expression in acute lung injury in Rats. Submitted for the 4th International Congress on the Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches, 1997.
3. Ward, P.A., Czermak, B.J., Bless, N. and Friedl H.P.: Regulation of chemokine production by complement. Experimental Biology '98 Conference, 1997.
4. Gipson, T. S., Shanley, T.P., Bleavins, M. R., Wongelawit, T., Johnson, K. J., and Ward, P. A.: Regulation of proteinase inhibitors in acute inflammatory lung injury in rats. FASEB J. 12(4):4595, 1998.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. CLINICAL ACTIVITIES:

A. Director, Division of Clinical Pathology/Clinical Laboratories, May 1993-present.
B. Director, Clinical Immunopathology Service; September 1989-present.
C. Microbiology Laboratory; review of malaria smears; July 1996-present.
D. Molecular Diagnostics Laboratory; signout of cases (3 weeks/year); July 1997-present.

II. TEACHING ACTIVITIES:

A. "Current Topics in Immunopathology" series: pathology residents, M4 students; (29 contact hours).
B. Clinical Pathology Grand Rounds:
   1. "Cases and images in immunopathology" (12/12/97).
   2. "Disorders of the complement system" (12/19/97).
   3. "Laboratory evaluation of vasculitis" (01/09/98).
C. Immunopathology journal club: EMU medical technology students, medical technologists (6 contact hours).
D. Immunopathology signout: pathology residents, M-4 medical students, EMU medical technology students (three times/week; 26 weeks/year).
E. Immunopathology component of Block C (Clinical Pathology); ad hoc topical reviews: pathology residents (53 contact hours).
F. M-1 Histopathology sequence; 1st year medical students; (16 contact hours).
G. M-1 Host Defense sequence; "Immunologic testing and diagnosis" (5/29/98); (1 contact hour).
H. Supervision of Research activities for:
   1. Karen Powers (Undergradate, University of Michigan); (9/1/95-present), (sponsored in Student Biomedical Research Program).
   2. Anjali Desai, Ph.D. (Postdoctoral Fellow); (6/15/96-present).
   3. Hernan Gomez, M.D. (Assistant Professor; Emergency Medicine, University of Michigan); (6/1/96-present).
   4. Mark Miller, Ph.D. (Postdoctoral Fellow); (8/15/96-present).
   5. Leah Thurm (Undergraduate, University of Michigan); (4/15/96-12/5/97); (sponsored in UROP).
   6. Soldrea Roberts (Undergraduate, Hope College, Holland, MI, 1998 University of Michigan – Hope College Scholar, sponsored by Office of Student Biomedical Research Programs (6/1/98-8/15/98).
I. Ph.D. Thesis Committees:
   1. James Park, Department of Pharmacology, University of Michigan Medical School (6/2/95-8/1/97).
   2. Jennifer Bowen, Department of Physiology and the Reproductive Biology Program, University of Michigan Medical School (2/5/97-present).
   3. Shimin Hu, Department of Pathology, University of Michigan Medical School (6/1/97-present).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Oxidant-Induced Beta Chemokines in Granuloma Formation", NIH (RO1-HL48287), (40% effort), $877,511; direct costs, 7/1/96-6/30/01.
B. Co-Investigator, "Monocyte Chemoattractant Protein 1 in Corpus Luteum", NIH (RO1-HD33478), (10% effort), $651,215; direct costs, 5/1/96-4/30/00 (Landis Keyes, Ph.D., Department of Physiology, University of Michigan, Principal Investigator).

PROJECTS UNDER STUDY:

A. Role of cellular redox status and neutrophil-derived mediators in MCP-1-mediated pulmonary granulomatous vasculitis.
B. Modulation of proinflammatory endothelial cell functions by the membrane attack complex (MAC) of complement.
C. Role of MCP-1 in luteolysis (collaboration with Landis Keyes, Ph.D., Department of Physiology, University of Michigan Medical School).
D. Ischemia-reperfusion injury in perinatal rat brain (collaboration with Faye Silverstein, M.D., Departments of Pediatrics and Neurology, University of Michigan Medical School).
E. MCP-1 in arterialized vein grafts (collaboration with John Hoch, M.D., Department of Surgery, University of Wisconsin, Madison, Wisconsin).
F. P-selectin antagonists in glucan-induced granulomatous vasculitis (collaboration with Mark Anderson, Ph.D., GlycoMed Corp., Alameda, California).
G. Pathogenesis of Loxosceles reclusa venom-induced cell activation (collaboration with Hernan Gomez, M.D., Department of Surgery, Section of Emergency Medicine, University of Michigan, Ann Arbor, Michigan).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

A. Dean's Advisory Committee (ad hoc substitute for Dr. Ward), 1994-present.
B. Finance Subcommittee, advisory to Faculty Group Practice Executive Committee, 1997-present.
C. Member, Standardization and Product Evaluation Committee, 1996-1998.
D. Clinical Council (ad hoc substitute for Dr. Ward), 1996-present.

DEPARTMENTAL:

A. Interviewer of Pathology Residency Candidates, 1989-present.
B. Interviewer of Pathology Graduate Program Candidates, 1990-present.
C. Chairman, Laboratories Communications Committee, 1993-present.
D. Chairman's Advisory Committee, 1993-present.
E. Chairman, Department of Pathology Quality Assurance Committee, 1993-present.
F. Clinical Associate and Advisory Committee for Medical Technology Program, Eastern Michigan University, 1993-present.
G. Chairman, Utilization Management Committee, Department of Pathology, 1995-present.
H. Chairman, Category Risk II Faculty Salary Planning Committee, Department of Pathology, 1996-present.

REGIONAL AND NATIONAL:

A. Ad hoc referee for:
1. American Journal of Pathology.
2. Laboratory Investigation.
3. Human Pathology.
4. Journal of Applied Physiology.
5. Lung.
6. Blood.
7. Journal of Laboratory and Clinical Medicine.
8. Pediatric Research.
9. Journal of Leukocyte Biology.
10. American Review of Respiratory Disease.
11. Chest.
12. Journal of Pharmacology and Experimental Therapeutics.
13. Circulation.
14. Ophthalmology.
15. American Journal of Respiratory Cell and Molecular Biology.
16. Clinical Immunology and Immunopathology.
17. Circulation Research.
18. Journal of Immunology.
19. Surgery.
20. Reviews of Infectious Diseases.
21. Infection and Immunity.
22. Experimental Lung Research.
23. Journal of Rheumatology.
24. Clinical Infectious Diseases.
25. Journal of Clinical Investigation.
26. Cytometry.
27. Biological Signals.
28. Metabolism.
29. Molecular Medicine Today.
30. American Journal of Respiratory and Critical Care Medicine.
31. The Cancer Journal.

B. Preparation of Immunopathology Subspecialty Exam Questions, American Board of Pathology, 1990-present.

C. Preparation of Clinical Pathology Exam Questions, American Board of Pathology, 1991-present.

D. Representative, National Committee for Clinical Laboratory Standards, 1996-present.

E. Member, Area Committee on Clinical Immunology and Ligand Assays, National Committee for Clinical Laboratory Standards, 1998-present.

F. Member, Council for Diagnostic Immunology and Molecular Pathology, American Society of Clinical Pathologists, 1998-present.

V. INVITED LECTURES/SEMINARS:

1. Warren JS: Monocyte chemoattractant protein-1 the pathogenesis of human diseases: potential therapeutic targets for β-chemokine antagonists. Glycomed, Alameda, CA, August 17, 1997.
2. Warren JS: Update in immunopathology: Antinuclear antibody testing and autoimmune diseases. ASCP Workshops, Seattle, WA, October 23, 1997.
3. Warren JS: Disorders of the complement system. ASCP Workshops, Boston, MA, March 18, 1998.

4. Warren JS: The role of intracellular redox status in the development of pulmonary granulomatous vasculitis. American Society of Investigative Pathology, San Francisco, April 20, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kilgore KS, Imlay MM, Szaflarski JP, Silverstein FS, Malani AN, Evans VM and Warren JS: Neutrophil and reactive oxygen intermediates mediate glucan-induced pulmonary granuloma formation through the local induction of MCP-1. Lab. Invest. 76:191-202, 1997.
2. Kilgore KS, Schmid E, Shanley TP, Flory CM, Maheswari V, Tramontini NL, Cohen H, Ward PA, Friedl, HP and Warren, JS: Sublytic concentrations of membrane attack complex (MAC) of complement induce endothelial interleukin 8 (IL-8) and monocyte chemoattractant protein 1 (MCP-1) through nuclear factor kappa-B (NF-κB) activation. Am J Pathol 150:2019-2032, 1997.
3. Tang WW, Qi M, Warren JS, Yan GY: Chemokine expression in tubulointerstitial nephritis. J Immunol 159:870-876, 1997.
4. Ivacko J, Szaflarski J, Malinak, C Flory CM, Warren JS. and Silverstein FS.: Hypoxic-ischemic injury induces monocyte chemoattractant protein-1 expression in neonatal rat brain. J. Cerebral Blood Flow Metabolism 17:759-770, 1997.
5. Kilgore KS, Imlay MM, Malani A, Allen DI., Beyer JT, Anderson MB and Warren JS: The carbohydrate sialyl Lewis glycomimetic GM2941 attenuates glucan-induced pulmonary granulomatous vasculitis in the rat. J Pharmacol and Exper Therapeutics (in press).
6. Szafarski J, Ivacko J, Liu XH, Warren JS, Silverstein FS: Excitotoxic injury induces monocyte chemoattractant protein-1 expression in neonatal rat brain. Molec Brain Res (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Szaflarski J, Liu XH, Warren JS and Silverstein FS: Treatment with antibody to monocyte chemoattractant protein-1 attenuates excitotoxic brain injury in perinatal rats. J Neuroscience (submitted).
2. Schimmer RC, Schrier DJ, Beck B, Flory CM, Laemont KD, Metz AL, Friedl HP, Conroy MC, Warren JS and Ward PA: Streptococcal cell wall-induced arthritis: requirements for IL-4, IL-10, interferon-γ and MCP-1. J Immunol (submitted).
3. Desai A, Miller MJ, Gomez HF, Warren JS: Loxosceles deserta spidervenom induces NF-κB-dependent chemokine production by endothelial cells. Am J Pathol (submitted).
4. Bowen JM, Towns R, Warren JS, Keyes PL: Luteal regression in the normally cycling rat: apoptosis, monocyte chemoattractant protein-1, and inflammatory cell involvement. Biol Reproduction (submitted).
5. Miller MJ, Gomez HF, Snyder R, Warren JS: Detection of Loxosceles venom in lesional hair shafts and skin: application of a specific immunoassay to identify dermonecrotic arachnidism in the northcentral United States. Annals of Int Med (submitted).
6. Kilgore KS, Ward PA, Warren JS: Neutrophil adhesion to human endothelial cells is induced by the membrane attack complex: the roles of P-selectin and platelet activating factor. Inflammation (submitted).

BOOKS/CHAPTERS IN BOOKS:

1. Warren JS and Ward, PA: Immunoglobulin and complement mediated immune injury, in Crystal RG, West JB, Weibel ER and Barnes PJ (eds.) The Lung: Scientific Foundations, Second Edition, Lippincott-Raven Publishers, Philadelphia, PA 2411-2419, 1997.
2. Warren JS and Ward, PA.: Consequences of oxidant injury, in Crystal RG,West JB, Weibel ER and Barnes PJ (eds.) The Lung: Scientific Foundations, Second Edition, Lippincott-Raven Publishers, Philadelphia, PA 2279-2288, 1997.
3. Warren JS: Cytokines in autoimmune disease, in Keren, DF and Nakemura, RM (eds.) Progress and Controversies in Autoimmune Disease Testing, First Edition, Saunders, Inc., Philadelphia, PA 547-558, 1997.
4. Warren JS: Role of cytokines in lung injury, in Remick, DG and Friedman, J (eds.) Cytokines in Health and Disease, Second Edition, Marcel Dekker, Inc., New York, NY 519-531, 1997.
5. Keren DF and Warren, JS: Immunodeficiency disorders and their effects on the gastrointestinal tract, in Ming, S-C and Goldman, H. (eds.) Pathology of the Gastrointestinal Tract, Second Edition, Williams and Wilkins, Baltimore, MD 323-338, 1998.
6. Warren JS, Ward PA: The inflammatory response, in Beutler E, Lichtman MA, Coller BS, Kipps TJ and Seligsohn U (eds.) Williams' Hematology, 6th Edition, McGraw-Hill, New York, NY, (in press).

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

1. Silverstein FS, Galasso JM and Warren JS: Monocyte chemoattractant protein-1 exacerbates NMDA-induced striatal neurotoxicity in neonatal rats. Society for Neuroscience. New Orleans, LA, October 25-30, 1997.
2. Gomez H, Miller M, Desai A and Warren JS. *Loxosceles* venom induces endothelial cell production of multiple chemokines, Journal of Toxicology-Clinical Toxicology 35,5:557; 1997.
3. Desai A, Miller MJ, Warren JS and Gomez HF. *Loxosceles* venom induces NF-κB activation in endothelial cells, Journal of Toxicology-Clinical Toxicology 35,5:568; 1997.
4. Miller MJ, Gomez HF, Huang X, Desai A and Warren JS. In vivo analysis of loxosceles evenomation and mediators of dermonecrotic lesion development. American Society of Investigative Pathology, San Francisco, April 18-22, 1998.
5. Desai A, Miller MJ, Huang X and Warren JS. The role of intracellular redox status in the development of pulmonary granulomatous vasculitis. American Society of Investigative Pathology, San Francisco, April 18-22, 1998.
6. Whetstone W, Gomez HF, Ernsting J and Warren JS. Inhibition of dermonecrotic arachnidism with 6 hour delayed-dose interleukin-8 (IL-8) monoclonal antibody (MAB). Society for Academic Emergency Medicine, May 17-20, 1998.
7. Gomez HF, Miller MJ, Tracy J, Desai A and Warren JS. Inhibition of dermonecrotic arachnidism with intradermal polyclonal anti-Loxosceles venom Fab fragments. Society for Academic Emergency Medicine, May 17-20, 1998.

SECTION REPORTS

ANATOMIC PATHOLOGY

DIVISION OF ANATOMIC PATHOLOGY

ANNUAL REPORT
1 JULY 1997 - 30 JUNE 1998

The Division of Anatomic Pathology continues to enjoy a strong national and international academic reputation while providing a breadth of expertise in support of the clinical and educational programs of the University of Michigan Medical Center, Medical School, and University. This past year has been one of transition with the recruitment of seven new faculty to the division and the departure of Drs. Caplan, Devaney, Kintinar, Weiss and Wojno. Drs. Alaa Affify (Barnes Hospital, St. Louis, Missouri) and Basim Al-Khaffagi (M.D. Anderson Hospital, Houston, Texas) have joined the section of Cytopathology. We also welcome Drs. Kathleen Cho (Johns Hopkins Hospitals, Baltimore, Maryland) Augusto Paulino (Memorial Sloan Kettering Cancer Center, N.Y., N.Y.), Mark Rubin (Columbia University, N.Y., N.Y.) Steven Ramsburgh (University of Michigan), and Lyndon Su (Stanford University, Palo Alto, Calif.) to the division. These faculty bring additional expertise in general surgical pathology as well as sub-specialty expertise in gynecologic pathology, head and neck pathology, bone and soft tissue pathology, urologic pathology and dermatopathology. Extramural support for faculty academic programs continues to increase especially in programmatic areas associated with the Cancer Center and SPORE in Urologic Disease.

During the past year we had strong support by Drs. Kintinar and Goldman in cytopathology and dermatopathology, respectively, and we greatly appreciated their efforts.

Three senior residents completed surgical pathology fellowships. Four additional house officers completed fellowship training in cytopathology, urologic pathology, soft tissue pathology and hematopathology.

Overall, the clinical activity in surgical pathology and cytolopathology increased by approximately 8% with marked increases especially in the intramural fine needle aspiration service and dermatopathology. While implementation of the Medical Center Cost Efficiency Program (CEP) resulted in consolidation of laboratory functions and enhanced productivity in several areas, significant additional reductions in laboratory support in the context of increasing service volumes and demands to decrease turnaround times are requiring additional support and restructuring of work activity. Renovations to faculty office space and the frozen section diagnostic area have been initiated with future (2-3 years) re-design of the entire frozen section area projected. The autopsy suite is currently undergoing renovations and a new program to enhance turnaround times has been successful. The efforts of Kathy Smiezney (Anatomic Pathology Laboratory Supervisor), Jim Pecott (Cytology Laboratory Supervisor) and all laboratory staff continue to be instrumental in successfully implementing the CEP and preparing the Anatomic Pathology laboratory for the upcoming JCAHO inspection.

The Division is well positioned to continue as one of the pre-eminent academic divisions in the country provided the Medical Center clinical programs continue to thrive. There is currently an excellent

balance of senior and junior faculty with expanding academic programs. It will be critical, in the face of increasing clinical demands, that the academic programs of the faculty especially junior faculty continue to be supported.

Joseph C. Fantone, M.D.
Director, Anatomic Pathology

AUTOPSY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

I. Timely Completion of Autopsy Reports:

We have continued to struggle with timely completion of our autopsy reports. With the upcoming JCAOH inspections it has become imperative to ensure that our autopsies are completed within the mandated time frame. Beyond complying with the guidelines, it is our professional responsibility to complete our work. Our clinical colleagues want to know the information and the families want to know what was found at autopsy. Close observation of autopsies which are not completed is now being done on a weekly basis, and the pathologists who have not completed their work are being phoned. With this protocol in place we have begun to realize the goal of completing all of our cases in 60 days. Since April of 1998, the final report on all autopsies was completed within the 60 day time frame. This standard must continue to be followed so that we can continue to fulfill our professional commitments.

Listed below are the times for completion of our autopsies, starting in 1995. We need to continue to ensure that all cases are completed within the mandated 60 day time frame.

Time Interval	% completed in 60 days	% completed in 90 days
1995	29	48
1996	49	76
1997	65	83
Jan – Mar, 1998	65	100
Apr, 1998	100	100
May, 1998	100	100
June, 1998	100	100

II. Medical Examiner Contract:

Our contract for forensic services has been re-negotiated with the Washtenaw County Medical Examiners Office. Starting October 1, 1997, the University of Michigan provides only a facility for autopsies and does not provide for professional services. The only medical examiner autopsies that are performed at the University are those patients who die at the University. Cases from other hospitals and cases from the scene are now sent to St. Joseph Mercy Hospital.

III. Statistics:

All of these are for the time period July 1, 1996 to June 30, 1997.

Total number of autopsies performed	412
Total hospital autopsies	265
Total number of medical examiner cases	147

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

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1997 - 30 JUNE 1998

This year has been very eventful to the laboratory with the appointment of Dr. C. Michael as the Director of Cytopathology and the successful recruitment of Dr. Alaa Afify and Dr. Basim Al-Khafaji as the two new Cytopathology faculty.

Total gynecologic specimens for the year were 38,012, representing an 8.6% increase over the previous year. Non-gynecologic specimens numbered 5697; a 5.6% increase from last year; and reversing the decline that began in 1991 when 7,592 specimens were processed. Fine needle aspirations performed by the cytopathologists (an indicator of FNA clinic usage in the Cancer Center) totalled 243 for the current year, a 49.1% increase over the previous fiscal year. Despite the stability the lab enjoyed this year, we continued to strive to maintain the turnaround time for non-gynecologic specimens within 24 to 48 hours and the gynecologic specimens within the promised 5-7 working days as a result of the increase in the number of specimens and marginal technical staffing.

Mr. James Pecott was appointed Assistant Chair on the National Anatomic Pathology Special Interests Group and the Chair of the Regional Anatomic Pathology Special Interests Group. He attended the Cerner Healthcare Conference in Kansas City, Missouri in May of 1998.

The following steps were taken to address the cost containment, case volume increase and "turnaround time" issues:

- The moving of the Cytopathology Department, and the consolidation into the Anatomic Department was completed. Lab assistants were cross-trained, allowing a more efficient utilization of personnel.

- The new screening area for cytotechnologists removed them from most of the distractions of the previous location.

- Cerner's V500 files were completely built. We are optimistic that the QA/QC module can replace the approximate 5-7 days per month of manual counting and record keeping that is currently a necessity to meet CAP standards (CLIA 88). This time can be better utilized by cytotechnologists for screening.

- New criteria were established for the re-screening of pap smears that lacked an endocervical component, eliminating approximately 90% of that re-screening.

- New criteria were established for the screening of fine needle aspirates, so that not all slides of a grossly-positive specimen need to be screened.

- Cytotechnologists have less interaction with the 1st year residents rotating through the department.

- We purchased a new coverslipper and a new automated stainer which reduced the labor intensity of specimen preparation, allowed smoother flow of work, and eliminated the need to depend on cytotechnologists to fill in the gaps for specimen preparation.

- We have begun an evaluation of the autocyte specimen processor as a replacement to the thin prep. The cost per specimen would be approximately half that of the current supply. If diagnostically on par with thin prep, a change to the system will be made. FDA approval of the liquid-based GYN method is anticipated by the end of the summer with the same cost savings. The anticipated potential of screening volume could increase by 25-30% per tech with this system.

Dr. Michael and Dr. Brian Hunter completed their study on the morphologic changes that occur with the new thinprep technology. Dr. Hunter will be presenting the results of this study in the upcoming American Society of Cytology meeting in Nashville, Tennessee.

Cytofocus and Cytopass were purchased as electronic image training tools for the residents rotating through the department. Changes were also made for the first rotation to make it more meaningful and flexible for the individual residents.

In the 12th year of our Cytopathology Fellowship Program, Dr. Joe Tworek completed his training with distinction.

Mr. Pecott and Ms. Gyrnek attended the national Cytology meeting. Dr. Michael, Dr. Naylor and Dr. Kintanar have presented papers and workshops in national meetings, cytologic societies and cytotechnology schools.

Claire W. Michael, M.D.
Director, Cytopathology Laboratory

DERMATOPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 – 30 JUNE 1998

The Dermatopathology Service receives diagnostic case material from six different sources: (1) UMMC (ID) cases; (2) outside contractual (MD) cases; (3) personal consultation (HE and LO) cases; (4) outside slides reviewed for referred patients (TD) cases; (5) miscellaneous intramural referrals (IE, IF, IS, ME, SC, TS) cases; (6) and informal consultations (intramural, VAH and MU).

Workload volume is as follows:

	1995-1996	1996-1997	1997-1998
ID	4,440	4,491	5,225
MD	2,957	3,832	4,138
TD	653	815	919
LO		126	428
HE	641	555	45

The Dermatopathology Service is very appreciative of the assistance provided by Dr. Robert Goldman during our transitional period following the retirement of John T. Headington, M.D. Dr. Goldman will be retiring July 31, 1998. We are pleased to have Dr. Lyndon Su join the faculty, effective July 1, 1998.

A noteworthy ongoing trend is the increasing workload of the Dermatopathology Service. The volume continues to be significantly impacted by the growth of Cutaneous Oncology services. The number of new patients seen in the Multidisciplinary Melanoma Clinic has increased from 473 in 1995-1996 to over 700 this year. This growth is reflected in the increased TD cases and represents a substantial volume of difficult pigmented lesions.

Overall, there has been a 16% increase in ID cases, a 13% increase in TD cases and an 8% increase in MD cases this year. The total number of cases for 1997-1998 was 10,755 and was seen by 1.0 FTE.

Dermatopathology teaching in the Department of Dermatology includes weekly formal didactic sessions. Formal presentations were made to both medical and dental students.

Correlative activities include active participation in:

1. Multidisciplinary Melanoma Conference (bi-weekly)
2. Cutaneous Lymphoma Conference (bi-weekly)
3. Dermatology Diagnostic Conference (Grand Rounds) (weekly)

Lori Lowe, M.D.
Director, Dermatopathology Service

NEUROPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
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1 JULY 1997 - 30 JUNE 1998

Neuropathology continues to have three interrelated functions: Diagnostic service, teaching, and research. Dr. Mila Blaivas, Ms. Constance J. D'Amato, and Dr. Paul E. McKeever contributed to the Neuropathology Service.

I. CLINICAL ACTIVITIES:

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

1. There were 860 neurosurgical cases examined this year, with 93 of these cases coming from outside hospitals in consultation.
2. The Diagnostic Unit of the Neuropathology Core Laboratory of the MADRC processed 65 dementia brain cases. Of these 65 brains, 44 were MADRC hospital cases, 12 were neurology hospital patients, and 9 were from the Michigan Dementia Network Program.
3. There were 273 muscle biopsies, 15% with electron microscopy. There were 95 peripheral nerve biopsies. There were 20% teased fiber preparations,all processed in plastic 60% with electron microscopy; Buffy coat, skin and other tissues for EM – 13 cases,.
4. The Brain Tumor Board of the University of Michigan Cancer Center and Hospitals, supported weekly by a neuropathologist, reviewed neuropathology and clinical aspects of more than 130 difficult neuro-oncology cases.
5. There are two neuropathology quality assurance meetings scheduled each month, and attended as necessary. Attendees include neuropathologists from nearby institutions in Michigan and Ohio.

II. TEACHING ACTIVITIES:

1. Medical Students: This year the neuropathology faculty taught in the eight week Neuroscience Sequence for our second year medical school curriculum. There were fourteen hours of neuropathology taught: six hours of lecture and eight hours in the laboratory.
2. Dental Students: 4 lectures
3. House Officers, Graduate Students, Postgraduate and other students and faculty. :These include periodic conferences with Neurology, monthly CME accredited Rheumatology Pathology Grand Rounds and occasional CPC conferences, twice monthly Continuing Medical Education (CME) accredited conferences with all biopsies are presented and interpreted; a weekly conference where abnormal brains are examined (including one week for dementia cases) with all clinicians invited; weekly nerve and muscle conferences accredited for CME, monthly nerve and muscle biopsy conference accredited for CME; individual instruction on autopsies and biopsy material; Neuropathology 868, an 8-hour laboratory course; bimonthly conferences with Neuroradiology,

Neurosurgery and Neuroradiology House Staff and every third month microscopic conference for dementia brain cases. Weekly seminars are provided to neurological and neurosurgical house staff on clinico-pathological correlations.

4. Electives: Two Pathology Residents, one Neurosurgery, four Neurology Residents and one M-4 student chose elective rotations on the Neuropathology Service.

III. RESEARCH ACTIVITIES:

1. Dr. Sima and Ms. D'Amato provided neuropathology support for MADRC. Ms. D'Amato is Core Coordinator of the Diagnostic Neuropathology Unit of the Neuropathology Core of MADRC. Ms. D'Amato is also Co-Investigator with Dr. Anders Sima on the MADRC Project: The Pathology of Diffuse Lewy Body Disease.
2. Dr. Blaivas is working on the histology of animal models of rheumatoid arthritis with Arthritis and Rheumatology Section with Blake Roessler and Timothy Laing; Urethral musculature in aging and incontinence, with John DeLancey group, Obstetrics/Gynecology; Rat model in brain tumors growth and treatment, with Donald Ross, Neurosurgery and Philip Kish. (Grant application submitted); Genetic treatment of hemophilia in mice model, with Kotoku Kurachi's group in the Department of Genetics; Neurochemical anatomy of human temporal lobe in epilepsy, with D. Ross and N. Selden, Neurosurgery; Primary CNS vasculitis, with J. Trobe and A. Alrawi, Ophthalmology; Quantitative evaluation of temporal lobectomy/hippocampectomy cases with Erasmo Passaro group; Collaboration with EMG group, Radiology (S. Gebarski, M.D.), pulmonary/internal medicine and ophthalmology on various projects.
3. Dr. McKeever and associates are determining the extent and cause of differences in gene product expression in brain tumors. These differences may result from a separate population of cells within brain tumors or from genetic instability in neoplastic cells. They are assessing the prognostic value of DNA content, specific chromosomal markers by in situ hybridization and Ki-67, PCNA and BUDR labeling indices in brain tumor specimens. He is principal investigator on an NIH funded project studying the prognostic potential of MIB-1 proliferation marker on brain tumors. He is the study pathologist for a multi-institutional transferrin receptor targeted glioma treatment protocol, and for a multi-institutional study of treatments of low grade astrocytoma. He is studying treatments of low grade astrocytomas as study pathologist for the Children's Cancer Group.
4. Groups in the University of Michigan Cancer Center faculty and staff with clinical research interests in brain tumors, met and generated a number of project considerations from Pathology, Neurosurgery, Nuclear Medicine, Neuropathology, Neurology and Neuroradiology collaborations.
5. Collaboration with Neurology, Michigan State University, The Alzheimer's Association, Henry Ford Hospital, Butterworth and Blodgett Hospitals, and Wayne State University has established a registry for Alzheimer's disease and other dementias and degenerative diseases.

SPECIAL STUDIES LABORATORY
ANATOMIC PATHOLOGY
(CLINICAL IMMUNOHISTOCHEMISTRY, IMMUNOFLUORESCENCE AND NEURAL AND MUSCULAR STUDIES)

DEPARTMENT OF PATHOLOGY
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INTRODUCTION

There have been extensive changes to meet the cost containment guidelines established with the Department of Pathology. Technologists have been cross-trained between the different areas of the laboratory. Developmental efforts are being considered to adapt the Ventana automated immunostainer to manual imunofluorescence tests. And the laboratory has moved to the hospital from Medical Science Building 1.

Unfortunately, Dr. Kirk Wojno will no longer be the Medical Director of this laboratory, since he has left for another hospital. Although I have been an Assistant Director or Co-Director of Clinical Immunohistochemistry for the past four years, this makes the fourth change in Medical Directors over the last six years. In my opinion, this rapid turnover in Directors is an indication of the enormous demands placed on this laboratory. Since there is little formal regulation of immunohistochemistry, it is left to the expertise of the Medical Director(s) to determine all aspects of the protocols and tests.

LABORATORY MOVES TO HOSPITAL

The laboratory moved from Medical Science Building 1 to the hospital next door to histology. Now sections cut by histology are easily passed to immunohistochemistry. The entire laboratory is located in one room. Also, the histology and special studies laboratories now have one supervisor, Kathy Smiezny. This change in structure may facilitate improved efficiency.

Cross-training has been extensive between the different areas of the laboratory: clinical immunohistochemistry, immunofluorescence for kidney and skin biopsies and neural and muscular studies. Immunofluorescence studies for kidney and skin biopsies has been transferred from the Immunology Laboratory to the Special Studies Laboratory in an attempt to improve efficiency, with eventual plans to perform these manual techniques on the Ventana automated immunostainers. Electron microscopy has not been integrated for various reasons, including its spatial distance.

CLINICAL IMMUNOHISTOCHEMISTRY

The laboratory performed 10,368 immunohistochemical stains, including 5,667 antibody stains on patient tissues, 2,349 negative controls on patient tissues and 2,352 positive controls on selected control tissues. The number of negative controls has been reduced recently by using the same control for both monoclonal and polyclonal antibodies.

Immunohistochemistry is in the midst of an exponentially increasing medical literature. The Clinical Immunohistochemistry Laboratory is attempting to balance cost efficiency and the rapidly expanding number of antibodies. Almost every month there are demands to provide new antibodies. Over the last year, the following antibodies have been added to the menu: CD1a, CD5, CD23, CD56, CD79a, adenovirus, fascin, HER-2/*neu*, HBME, ubiquitin, etc. Other antibodies are in developmental stages. The menu has expanded despite the enormous work involved with moving the laboratories and cross-training personnel.

However, not all antibodies are appropriate for a clinical laboratory. Two criteria have been developed which must be fulfilled before adding an antibody for clinical use: (1) There should be published peer-reviewed literature that supports the clinical utility of the antibody. (2) There should be published peer-reviewed literature that demonstrates the specificity and sensitivity of the commercially available antibody.

It is not clear whether the volume of immunohistochemical stains will decrease with the recent loss of Dr. Weiss, who left for Emory University. To assess the impact of Dr. Weiss' leaving, the laboratory conducted an audit of a randomly chosen month. During January 1998, Dr. Weiss' requests accounted for 20% of the immunohistochemical stains. However, it is not clear to what extent the loss of these cases might be offset by the addition of new antibodies and by the addition of several pathology staff who will be starting over the next year. For example, new guidelines from the National Comprehensive Cancer Network (NCCN) advocate testing breast carcinomas for HER-2/*neu*.

IMMUNOFLUORESCENCE

Immunofluorescence for skin and kidney biopsies was moved from Immunology to Anatomic Pathology's Special Studies Laboratory. Plans to adapt these techniques to the Ventana automated immunosainers are in the developmental stages. There has been extensive cross-training between immunofluorescence and the other areas of this laboratory. Dr. Paul Killen handles the technical aspects of this laboratory.

NEURAL AND MUSCULAR STUDIES

There has been extensive cross-training between neural and muscular studies and the other areas of this laboratory. Some of the laboratory manuals have been updated. However, Dr. Blaivas handles the technical aspects of this laboratory.

CONCLUSION

There have been extensive changes in attempts to meet the containment guidelines established with the Department of Pathology. These include cross-training between recently merged laboratories, early developmental efforts to adapt the Ventana automated immunostainer to manual tests and moving the laboratory to the hospital and next to histology.

Timothy Singleton, M.D., Medical Director

SURGICAL PATHOLOGY SERVICE

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The Surgical Pathology Division remains an active University Hospital service despite dramatic changes in personnel. This year, the Division saw nearly 32,000 in-house surgical specimens, over 6,000 personal consults, and 8,000 M-Lab cases. These numbers indicate over an 8% increase in volume, despite having one less surgical pathologist for most of the year. The Division will greatly miss Drs. Kenneth Devaney, Kirk Wojno and Sharon W. Weiss, who have all left to pursue different opportunities. These three individuals were superb surgical pathologists and wonderful colleagues. We have been fortunate to recruit Augusto Paulino, M.D. as our new head and neck, bone, and soft tissue pathologist. In addition, we anticipate the arrival of Mark Rubin, M.D. as our new GU pathologist, and Kathleen Cho, M.D. in OB/GYN pathology later this year.

With the help of Kathy Davis and Paulette Dozier, we have implemented a new turnaround time monitoring system. This will enable us to closely follow turnaround times on a wide variety of individual specimens. In addition, we continue to track our turnaround time and look for ways to improve it.

The Histopathology Laboratory has now completed its integration with Cytology and Immunohistochemistry. This has resulted in increased cross training of individuals and a marked improvement in efficiency within the laboratories. Ms. Kathy Smieszny is to be congratulated on a fine job in this regard. The laboratory has become much more efficient in the turnaround time of special stains, further helping our cost-efficiency program.

Our fellowship programs continue to be highly successful. This year's soft tissue fellow, Dr. Tamara Smith has returned to the Cleveland Clinic as an attending pathologist. Dr. Stephen Ramsburgh, a second year surgical pathology fellow will remain here at Michigan as an attending surgical pathologist. Dr. Stephanie Dillard, another surgical pathology fellow has gone on to private practice in Alabama. We would also like to welcome back a previous surgical and cytopathology fellow, Dr. Lyndon Su, as a new attending in dermatopathology. We welcome Dr. Peter Lucas, Dr. Carolyn Misick, and Dr. Celina Kleer as this year's new surgical pathology fellows. In addition, we would like to welcome the new uropathology fellow, Dr. Bassily from Brown University.

Despite our increasing service commitments and decreasing numbers, the Surgical Pathology Division has maintained its superb productivity at national meetings. At this year's USCAP meeting, our faculty presented 17 abstracts, directed 2 short courses, and chaired several subspecialty sessions. In addition, Dr. Sharon Weiss presided as the President of USCAP.

As always, it is an honor to work with such outstanding faculty members.

Joel K. Greenson, M.D.
Director, Surgical Pathology

CLINICAL PATHOLOGY

DIVISION OF CLINICAL PATHOLOGY

DEPARTMENT OF PATHOLOGY
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The Clinical Laboratories have continued to provide excellent, full-spectrum service as the institution has experienced expansion of ambulatory care activities, growth in several major clinical programs, and the expansion of M-Labs activities. Efforts have been directed towards the improvement of phlebotomy, central distribution, and laboratory operations as we emerged from the first full year following implementation of vigorous institutionally-mandated cost reductions and the opening of the Cancer and Geriatrics Center. In 1997-98 the Clinical Laboratories performed more than 3 million billable analyses. The maintenance of high quality provided by the Clinical Laboratories, in the face of increasing complexity of demands, is a testimony to the professionalism of the staff and the management capabilities of the laboratory directors and senior laboratory personnel. The Clinical Laboratories successfully completed the biannual on-site College of American Pathologists (CAP) self-inspection. 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.

1997-98 was marked by several major initiatives. In response to pressures to reduce our cost/unit of laboratory service and to improve operating efficiency, a comprehensive plan for laboratory reorganization was realized. Reorganization entailed a nearly 10% reduction in operating budget, consolidation of several laboratories, and reorganization of inpatient phlebotomy services. This reorganization entailed the consolidation of the Immunopathology, Ligand Assay, Toxicology/Therapeutic Drug Monitoring, and Chemistry Laboratories into a single unit, consolidation of the Hematology, Flow Cytometry, and Coagulation Laboratories (formerly Internal Medicine) into a single unit, and streamlining of the administrative structure of these and other laboratories. Second, the Clinical Laboratories continued to reallocate resources needed to meet the continuing and marked increase in transplantation activity (especially bone marrow) experienced in 1997-98. Augmentation of the capabilities of the Molecular Diagnostics, Blood Bank, Tissue Typing, and Cytogenetics Laboratories was contributory to this process. Finally, as alluded to above, the Clinical Laboratories have responded to the institutional initiative to expand primary care capabilities within the region. This activity has been coupled with expansion of on-site point-of-care testing and data handling activities. The Clinical Laboratories continue to support the growing M-Labs outreach program, to forge strong collaborative relationships with local and regional reference laboratories, and to intensify our role in institutional utilization management.

Faculty and laboratory staff participated in a wide variety of intramural and extramural educational programs during 1997-98. For instance, the 25th annual Blood Bank/Transfusion Medicine course and the 16th Laboratory Information Systems (LIS) course were each well attended, making them among the most visible courses of their kinds in the United States. Ten pathology residents from around the nation received scholarships to attend the May LIS course. This program, coupled with a burgeoning

collaborative relationship with the Informatics Program in the Department of Pathology at the University of Pittsburgh, and establishment of a Departmental website on the Internet, along with several pending Departmental and Institutional initiatives promise to further enhance the Department's leadership role in this important area. The May LIS course was linked for the first time to a highly successful Executive Briefing which brought together leaders from a variety of instituions and laboratory information technology fields to discuss the future of clinical pathology practice. These courses, along with the M-Labs educational programs, are prominent examples of educational outreach activities. The revised clinical pathology residency training format (July, 1993), which organizes pathology residents into teams that rotate through three blocks of clinical laboratories that are grouped according to "relatedness of discipline" will be updated in 1998. In keeping with a modern thematic approach, the 1998 update will entail the establishment of four rotation blocks and will place greater emphasis on molecular diagnostics, coagulation, informatics, statistics, and management. The continued high quality of trainees in the Hematopathology Fellowship program has enhanced the service, educational, and academic missions of the Hematopathology group and the Department.

The academic achievements of faculty members within the Clinical Pathology Division have been outstanding. As a group, the CP faculty had approximately 100 articles published in peer-reviewed journals. Most faculty members played highly visible leadership roles in national organizations, courses, symposia, as well as on editorial boards, examining committees, and research review study sections; an illustration of their high levels of recognition throughout the United States (see individual reports). Numerous faculty members received extramural funding that supported a variety of scholarly activities (see individual reports).

The Clinical Pathology Division is faced with numerous challenges in the future. In addition to its ongoing academic enterprises, educational issues, leadership and development in quality assurance, and laboratory resource utilization in the context of the hospital cost efficiency program, the Division plans to continue to expand its attention to informatics, its clinical molecular diagnostics program and, in cooperation with the M-Labs program, to optimize its position in the regional clinical laboratory market. Achievement of these objectives will require the continued commitment, professionalism, and hard work of the faculty, laboratory staff, administration, and house officers.

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

UNIVERSITY HOSPITALS BLOOD BANK AND TRANSFUSION SERVICE

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1997 - 30 JUNE 1998

PATIENT CARE:

Careful monitoring of blood component use and excellent support by the medical staff allowed blood component utilization to remain at approximated 100,000 units. However, clinical growth, especially in the areas of bone marrow transplantation and cardiovascular surgery, resulted iin increased stress on the laboratory to meet clnical requirements.

The support of bone marrow transplantation related to the increased desire for peripheral blood progenitor cells rather than bone marrow, as this necessitated a focus on the capablity of the transfusion and apheresis area and on the main laboratory of the blood bank. The inadequate space for both functions is currently being discussed with hospital administration, as solutions to the problem must be defined to adequately support the program.

The transfusion and apheresis area requires additional space for additional cell separators as well as for patient accomodation. The current space compromises patient privacy and patient safety. The main laboratory space also is inadequate for bone marrow or stem cell processing, as the technical staff of the area has tripled and the number of liquid nitrogen storage tanks has increased in relation to the number of harvesting procedures.

The preadmission blood typing program was enhanced by expanding the number of patients eligible for the program and coupling this with an educational videotape for use by patients. In addition, the Reference Laboratory procedures were modified to improve efficiency and turn-around time. This was done by eliminating some of the testing which proved to be superfluous.

Members of the staff actively supported interdepartmental functions. Mrs. Hoffman worked closely with the Bone Marrow Transplantation Program and also coordinated orders for HLA-matched Single Donor Platelets from our blood suppliers. The reference laboratory section supported the Department of Obstetrics and Gynecology, attending their weekly high-risk pregnancy conference, and playing a vital role in PUBS procedures. Ms. Butch led the Quality Management program of the clinical laboratories of the Department of Pathology and Mrs. Stoe chaired the Department's Laboratory Safety Committee. Both Mrs. Stoe and Ms. Butch enhanced patient care by implementation of the Pre-Admission Type and Screen video program for patient use. In anticipation of the institution's new laboratory information system, Mrs. Stoe was active in developing a data base for the Cerner Millennium system.

EDUCATIONAL ACTIVITIES:

As in previous years, the medical, technical and nursing staffs of the Blood Bank/Transfusion Service were actively involved in educational programs within the institution and at regional and national meetings. The long-standing two-week Blood Bank orientation program for House Officers at University Hospital was presented on two occasions during the year so that this information would be provided in proximity to the lab rotation. Three hours of lecture were provided for the sophomore medical class in the context of the hematology portion of the Department of Pathology course, and a presentation on Transfusion Medicine was provided for the medical student senior elective course in Pharmacology and Therapeutics. Senior medical students partaking of a month-long pathology elective, spent three to five days in the laboratory, and hematology fellows in both pediatrics and internal medicine rotated through the laboratory. In addition, the laboratory supported the medical technology training program of Eastern Michigan University.

The 25th annual postgraduate course, "Current Topics in Blood Banking", was held on June 3-5, 1998. The course, under the direction of Mr. Judd, attracted well over 200 technologists and physicians from throughout the United States. It continues to be one of the most popular postgraduate courses in the country devoted to blood bank topics, and was the first to be presented by a medical center rather than by a national blood program. Members of the Blood Bank and Transfusion Service staff presented Workshops on a variety of topics, and Ms. Butch, Mr. Judd, Mr. Meade and Drs. Oberman and Davenport participated in the plenary sessions of the symposium.

Members of the Blood Bank and Transfusion Service faculty and staff participated in the annual meeting of the American Association of Blood Banks, providing poster presentations, courses and lectures covering a variety of topics. In addition, members of the laboratory, including Mr. Judd, Ms. Butch, Mrs. Stoe, Ms. Steiner and Drs. Davenport and Oberman, presented invited lectures to a variety of regional and national blood banking organizations and state societies.

Aside from the lectures and presentations noted in the individual faculty reports of Mr. Judd and Drs. Davenport and Oberman, Mrs. Stoe, Mrs. Hoffman, Mrs. Dates and Ms. Butch were active in educational programs of the Michigan Association of Blood Banks. Ms. Butch was particularly active on the national scene, lecturing and authoring papers on computer utilization in the blood bank, quality management and the use of the electronic crossmatch. Mrs. Hoffman provided a workshop on stem cell processing at our annual postgraduate course. Mrs. Stoe chaired the Cerner SIG users group, and authored a chapter in the text, Immunohematology Principles and Practice.

PROFESSIONAL ACTIVITIES:

Members of the Blood Bank and Transfusion Service medical and technical staffs were active at the regional and national levels. Dr. Oberman served as Associate Editor of TRANSFUSION and was a member of the Transfusion Practices Committee of the American Association of Blood Banks. Ms. Butch also served on the Information Systems Committee and on the Chief Technologist's Forum of the American Association of Blood Banks. Dr. Davenport serves on the Scientific Section of the American Association of Blood Banks. In addition, members of the technical staff participated in the Inspection

and Accreditation program of the American Association of Blood Banks. Dr. Oberman's, Dr. Davenport's, and Mr. Judd's activities are further noted in their individual faculty reports.

RESEARCH ACTIVITIES:

The individual reports of Drs. Oberman, Davenport and a Mr. Judd record their publications and investigative efforts related to blood banking and Transfusion Medicine.

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

CHEMICAL PATHOLOGY LABORATORY

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The focus of the Chemistry Section this past year was on continued automation of manual assays and the implementation of new assays which were previously sent out. Considerable time and effort was spent on a renovation project that allowed the consolidation of the Drug Analysis and Toxicology Laboratory (DATL) into Chemistry. The complex move of equipment, personnel, and sample workflow was accomplished in December of 1997. All involved staff of the Chemistry, Ligand Assay, Immunology, and Drug Analysis and Toxicology sections should be congratulated for their efforts at making this project go smoothly. The Chemistry Section experienced an approximate 9 % increase in overall test volume this year. Included in this was a 13% increase in the more manual testing areas of Special Chemistry, Drug Analysis, Immunology, and Ligand Assay.

The Chemistry Section made a series of changes aimed at increasing the number of tests performed on automated, random access analyzers. ACTH, PTH, and Growth Hormone assays were moved from manual RIA's to the more automated Immulite chemiluminescent immunoassay analyzer. C-peptide and insulin assays, previously done in the Diabetes Research and Training Center were evaluated and set up in Chemistry. Ca-125 , Troponin I, and Valproic acid analyses were moved from more manual assays to the Abbott AxSYM automated immunoassay analyzer. The assay for thyroglobulin was switched from RIA to the Immulite analyzer. The Sebia semi-automated system for serum protein electrophoresis and immunofixation was evaluated and put into routine service in the Immunology lab. These changes have allowed the laboratories to save personnel time, which has been applied to implementing new tests and increasing the frequency at which other batch tests are performed. The efforts and cooperation of the staff of Chemistry, DATL, Ligand Assay, and Immunology were critical in making these changes possible.

Several new tests were developed, evaluated, and put into routine service this past year. An HPLC assay for Lamotrigine, a new anticonvulsant drug was developed by the Drug Analysis and Toxicology lab staff. An HPLC assay for homocysteine, a risk factor for coronary disease and thrombotic disorders was developed in the Chemistry lab. Savings from offering these two new assays in-house versus sending them out to a reference lab should be over $ 60,000 a year. The automated chemistry area initiated testing for percent free PSA, a determination which helps to differentiate prostate cancer and benign prostatic hyperplasia in men with elevated total PSA levels. The Ligand Assay area began offering a 3rd generation PSA test for evaluating residual disease in men following radical prostatectomy. The Chemistry Lab initiated a rapid HIV1 antibody test to be used solely by the employee health service for exposure cases. This assay is available on a STAT basis 24 hours a day. Chemistry also began offering the Abbott Fetal Lung Maturity assay (FLM) on a STAT basis.

The laboratory directors and laboratory staff participated in a significant number of evaluations and research studies. These included:

1. Evaluation of methods for measuring the free fraction of PSA and the use of percent free PSA as an improved marker of prostate cancer.
2. Evaluation of the performance of phenobarbital and determinations by the Ortho Clinical Diagnostics Vitros 950 immunorate dry slide technology.
3. Evaluation of the Abbott AxSYM assay for Troponin I as a marker of myocardial injury
4. Comparison of HPLC versus immunoassay for the determination of whole blood cyclosporine concentration.
5. Evaluation of myoglobin and troponin I assays on the Chiron ACS-180.
6. Evaluation of a 3rd generation sensitive PSA assay for detection of recurrence of prostate carcinoma.

The Chemistry Laboratory continued its active role in Point of Care (POC) testing both within the hospitals and at the off-site health care centers. The laboratory at East Ann Arbor Medical Center has expanded its scope of testing with the growth of patient visits at that site. Additional Pathology personnel have been added at Brighton and Plymouth Health Care Centers. Hemoglobin A1c testing was added to the menu of testing at the Ypsilanti Health Center. Laboratory staff have participated in the planning of new health care facilities at Brighton and Livonia. As the University has acquired more physician office practices, Chemistry point-of-care coordinators have played an active role in setting up laboratories and managing specimen and data flow back to University Hospital from these locations. All off site centers have successfully passed COLA accreditation with no deficiencies.

The lab has continued its active role in the supervision of bedside blood glucose monitoring programs at University Hospitals. The lab maintains quality control, linearity, and proficiency testing records on 75 whole blood glucose meters stationed throughout the institution. Lab staff have worked with nursing personnel to standardize training and record keeping in preparation for a JCAHO inspection of the institution. Several new glucose meters are being evaluated by the Point of Care Testing group, and the Chemistry Lab continues to actively pursue options for the computerized collection and analysis of quality control data from these meters. In addition, Chemistry POC group has been charged with bringing all CLIA waived testing in the institution up to JCAHO accreditation standards.

Chemistry lab personnel also took on the additional task of result entry for all sendout tests for the Clinical Laboratories. In addition to result entry, Chemistry personnel monitor all pending reports and call reference laboratories on overdue reports. In conjunction with Pathology Data Systems and Central Distribution, Chemistry staff worked on developing an improved interface for sendout results, leading to substantial improvements in turnaround time for results.

Donald Giacherio, Ph.D.

CLINICAL CYTOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY
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The Clinical Cytogenetics Laboratory has seen an increase in volume in most areas, some more than others. In the area of prenatal diagnosis, 850 amniotic fluid specimens, an increase from 760 last year, 110 (vs 85 in 1996) chorionic villus biopsy, and 70 tissues were analyzed. Of interest is the increase in the number of cases that are seen solely for the purpose of growing fibroblasts with the ultimate aim of DNA or biochemical diagnosis; these cases are in addition to the 50 enumerated above. Approximately 50 tissues were rejected as inappropriate specimens ie. blood clots instead of placenta, of little use clinically, or already fixed in formalin.

The bone marrow specimens continue to skyrocket, from under 400 five years ago, to 914 in the last year to 1140 in the current fiscal year. These requests are scrutinized more carefully due to staffing problems and our active program of utilization review. The increased volume does not include the approximately 250 requests which were declined for one or more reasons. In addition, 498 peripheral blood specimens were analyzed. Approximately 50 of these tests were for high resolution karyotypes. Much of the increase was accounted for by repeat analyses requested by physicians whose patients had had studies performed at commercial laboratories.

Cytogenetic analysis of solid tumors has remained steady. Pediatric sarcomas and "small round, blue cell tumors" remain the specimens most commonly submitted. Although there are descriptions of various other tumors with specific cytogenetic abnormalities, often the clinical significance is unclear.

The demand for molecular Cytogenetic analysis has increased from one request a month to 2 or more per week. The Laboratory is currently offering a number of specific gene probes for fluorescence in situ hybridization on a research basis including those for Prader-Willi, Angelman's, Williams, and DiGeorge syndromes. Marker chromosomes are characterized. A probe for the so-called minor breakpoint cluster region in the bcr/abl gene rearrangement in CML and ALL are being developed as a potential supplement to cytogenetic analysis, as has nMYC amplification for neuroblastoma. In situ hybridization is performed on at least a weekly basis.

I would comment that while our volume increased dramatically in some areas, increased staffing has not been allotted to the laboratory. Despite this, we were able to decrease the turn around time for prenatal specimens by a concerted effort on the part of the group. We maintained our improved turn around times until we were forced to deal with a dramatic turnover in personnel in the latter part of this year, often working with 20-30% fewer technologists than has been approved for this laboratory. This, of course, impacts turn around time in a negative fashion.

Susan Sheldon, Ph.D.
Director, Clinical Cytogenetics

COMBINED LABORATORY
(HEMATOLOGY, BONE MARROW, FLOW CYTOMETRY, COAGULATION)

DEPARTMENT OF PATHOLOGY
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I. HEMATOLOGY AND BONE MARROW

A. Improved cost efficiency

1. Consolidated clinical Hematology/Bone Marrow, Coagulation and Flow Cytometry into one Combined Hematology Laboratory.
   a. The new laboratory is administered by one Chief Technologist.
   b. Hematology/Bone Marrow, Coagulation and Flow Cytometry are all located adjacent to each other in the hospital, after renovations to the laboratory space.
   c. Flow cytometry moved from Medical Science Building I to the hospital, next to Coagulation and Bone Marrows. Flow cytometry is functional in its new facilities, but cross-training has not yet begun.
   d. Routine hematology and coagulation tests have been incorporated into a Main Laboratory, with cross-training of all shifts in general hematology and routine coagulation.
   e. Coagulation's specialized tests are performed by a core group of technologists.
2. The new generation Coulter Gen-S is operational with a bidirectional interface in both the Main Laboratory and the new Cancer Center Laboratory.
3. Beta-testing an automated slide spreader which interacts with the new generation Coulter Gen-S, for those blood smears which need manual review.

B. Increased volume of work

1. The hematopathology staff review abnormal peripheral blood smears, body fluids, joint crystals and the morphology, immunohistochemistry, immunophenotyping by flow cytometry, cytochemical stains and molecular diagnostics (gene rearrangement) for tissue biopsies of lymph nodes, spleens, bone marrows, lymphomas/leukemias and extramedullary myeloid cell tumors.
2. The volume of cases signed out by hematopathologists has increased dramatically since 1992.
   a. The number of transfer cases (599) is 219% of the 1992 volume. This number excludes flow cytometry, peripheral blood smears, and body fluids.
   b. The number of inside cases (1209) is 171% of the 1992 volume.
   c. The number of consult cases (453) is 128% of the 1992 volume.

3. Since 1992 the number of staff hematopathologists signing out these cases (#2, above) has increased from 3 to 4 FTE's; however, the hematopathology fellow can no longer verify reports, with the new reimbursement guidelines.
4. The number of bone marrow aspirates (3100) increased by 15% compared to last year.
5. The number of other laboratory tests in the hematology laboratory has changed slightly over the prior year.

	Test	1998 volume	Percentage change from last year
a.	Complete blood counts	274,000	+8%
b.	Differential counts on blood	47,500	+3%
c.	Fluids	6,000	-2%
d.	Urines	44,600	-13%

II. FLOW CYTOMETRY

The Clinical Flow Cytometry section processed about 4500 specimens, a volume increase of 8% from the previous year. The percentage change in volume (relative to 1996-97) is listed below for each of the major test categories:

Test Category	Change from 1996-97
Immunodeficiency monitoring	+12%
CD34 stem cell counts	+0%
Chronic leukemia/lymphoma phenotyping	+24%
Acute leukemia phenotyping	+15%
T-cell subset monitoring in organ transplant recipients	-41%
Antiplatelet and antineutrophil antibody testing (antineutrophil antibody testing discontinued this year)	-31%

M-Labs referrals continue to comprise a substantial part of the work volume, including 47% of all acute leukemia immunophenotyping panels, 32% of all chronic leukemia/lymphoma panels, and 44% of all immunodeficiency monitoring.

Attending staff continue to triage all requests for leukemia/lymphoma immunophenotyping, with cancellation of unwarranted requests. Of the 1225 specimens submitted for leukemia/lymphoma immunophenotyping, pathologist review lead to cancellation of 472 of these requests.

In addition to moving the laboratory facilities to the main hospital, the laboratory completed the transition to new Coulter XL instruments and software. A new computer interface and Oracle database was developed to read, transfer, and store data generated by the Coulter instruments.

III. COAGULATION LABORATORY

A. Laboratory Consolidation:

1. The laboratory was moved from its traditional space in the clinical labs into smaller space to make room for Flow Cytometry.
2. 3 FTEs perform all specialized coagulation studies: This group consists of one full-time individual and 3 part-time individuals.
3. Much effort was expended to train multiple technologists from the Hematology Laboratory to perform routine coagulation tests which include PT, APTT, TT, Fibrinogens, FSP, D-Dimer, Factor V, Factor VIII assays.
4. All scheduling for the laboratory is now done by the Hematology Supervisor.
5. Ordering of specialty reagents divided between Hematology Supervisor and one Senior Clinical Technologist in Coagulation Laboratory.

B. New Programs in the Laboratory:

1. A new ELISA assay was established to monitor heparin-induced thrombocytopenia and thrombosis syndrome.
2. One new Amelung Coagulation instrument was set-up to monitor TCT, Reptilase Times, Lupus Anticoagulant Tests, Fibrinogens, etc. in specialized Coagulation Laboratory.
3. Training has begun to have anti-factor Xa assays for heparin and any low molecular weight heparin be performed on a routine basis, 24 h/day for needed patients.

C. Laboratory Growth:

1. University of Michigan Hospitals System.

There was an overall 4.9% decrease in revenue for fiscal year '98 compared to fiscal year '97 ($3,879,373 from $4,082,610). This decrease in revenue reflects a change in activity in three tests: the prothrombin time (PT), activated partial thromboplastin (APTT), and thrombin clotting time (TCT). The decrease in activity was 5% for both the PT and APTT and 50% for the TCT. The decrease in tests performed can almost fully account for the decrease in overall revenue. This decreased activity probably results from two reasons: (1) income from Point-of-Care testing of PTs and APTTs has been removed from the Coagulation Laboratory category and placed in another category. Second, there may be a change in test ordering practice as result of the use of low molecular weight heparin anticoagulation. This latter assessment is reflected in the decrease in TCT testing and a rise in anti-factor Xa assays.

Overall, there was a rise in demand for specialty coagulation laboratory testing. In particular, testing for prothrombotic states continues to show growth in the Coagulation laboratory. For example, the activated protein C resistance ratio grew 91% from the previous year. Antithrombin II, protein C activity, and free protein S antigen all grew 15% from fiscal year '97.

2. M-Labs Activity:

There was 107% increase in net M-Labs activity in specialized coagulation testing from fiscal year '96 to '97. In fiscal year '96, combined net patient and client income from work performed was $62,299. In fiscal year '97, combined net patient and client incomes

were $129,013. The revenue distribution was equalized over the breadth of assays performed in the laboratory.

IV. TEACHING AND RESEARCH ACTIVITIES: Hematology/Flow Cytometry

A. Pathology house officers, hematopathology fellows and fellows from Pediatrics and Hematology/Oncology participated in the following activities:

1. Daily review of abnormal blood smears, body fluids, joint crystals, bone marrow smears, bone marrow biopsies, lymph node biopsies, splenectomies, lymphomas/leukemias and extramedullary myeloid cell tumors.
2. Correlation of morphology with cytochemical stains, immunohistochemistry, flow cytometry, gene rearrangement and electron microscopy.
3. Formal teaching conferences.
4. Review of cases for the Southwestern Oncology Group.
5. Weekly review of cases for Lymphoma Conference.
6. Biweekly review of cases for Leukemia Conference.
7. Biweekly review of cases for Non-Neoplastic Hematology Conference.
8. Biweekly review of cases for Cutaneous Lymphoma Conference.

B. Accredited Hematopathology Fellowship

C. Training and continuing education for medical technologists

D. Formal lectures and laboratories for freshman and sophomore medical students

TEACHING AND RESEARCH ACTIVITIES: Coagulation Laboratory

A. Pathology House Officers: Residents participated in weekly sign-out rounds by laboratory direct of specialized coagulation testing.

B. Formal lecture for 4th year medical student elective clinical course.

V. GOALS FOR 1998-99: Hematology/Flow Cytometry

A. Cross-train technologists in Flow Cytometry and Bone Marrows, while maintaining specialized expertise.

B. Incorporate the automated slide spreader into routine hematology with the new generation Coulter Gen-S, for those blood smears which need manual review.

C. Develop new procedure manual and QC program for new Coulter flow instruments.

D. Continue collaboration with Coulter and Pathology Data Systems to enhance reporting and databasing of flow cytometry results.

GOALS FOR 1998-99: Coagulation Laboratory

A. Continue integration of coagulation laboratory into the combined hematology laboratory.

1. Train more personnel in routine coagulation testing.
2. Recruit an individual from current laboratory personnel to be trained in specialized coagulation testing.

B. Assay development.
1. Set-up anti-factor Xa assay as a routine coagulation test.
2. Establish a factor Xa enzymatic assay as a specialized assay.
3. Evaluate additional ELISA assays for heparin-induced thrombocytopenia.
4. Establish an Amelung coagulation testing instrument in routine coagulation.
5. Evaluate instruments and reagents for routine coagulation testing.

C. Teaching.
1. Redesign the clinical pathology resident's role and activity in the Specialized Coagulation Laboratory to integrate them in the work activity.

Bertram Schnitzer, M.D.
Director, Hematology Laboratory

Timothy P. Singleton, M.D.
Co-Director, Hematology Laboratory

Charles W. Ross, M.D.
Director, Flow Cytometry

Lloyd M. Stoolman, M.D.
Co-Director, Flow Cytometry

Alvin Schmaier, M.D.
Director, Coagulation Laboratory

HISTOCOMPATIBILITY AND IMMUNOGENETICS LABORATORY

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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.

CLINICAL ACTIVITIES:

Clinical activity of the Histocompatibility Laboratory stabilized over the prior year. The Laboratory had expanded to 18 individuals to accommodate prior increases in activity and has had to streamline all areas of its function. Average numbers of tissue typings per month are in the 400 range for Class I and Class II typings whereas cross matches are in the 600 per month range. This activity is remarkable and makes the Laboratory one of the ten busiest in the country.

More importantly, high resolution Class II DNA typing has become our primary technique and achieved excellent results. In conjunction with the DNA Sequencing Core for the University, essentially any polymorphism in Class II HLA DRß can now be identified by the Laboratory within 72 hours.

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 in ASHI and presented at the National Meeting. Ms. Cynthia Schall, the Laboratory Supervisor, was involved in teaching review courses at ASHI, 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 goal for the Laboratory is to continue to deal with the increasing activity and demand for more complex services from the transplant programs. We have internalized the DNA sequencing and evaluated assays for the determination of class I MHC polymorphism by DNA analysis. The transplant programs appear to be more active in clinical and basic research although currently and the transplantation laboratory is interested in supporting this activity.

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

CLINICAL IMMUNOPATHOLOGY LABORATORY

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I. OVERVIEW:

The Immunopathology Laboratory performed more than 50,000 analyses in 1997-98. Anthony A. Killeen, M.D., Ph.D. and John Lowe, M.D. provided invaluable service to the laboratory in the interpretation of protein electrophoresis studies. Kent Johnson, M.D., Paul Killen, M.D., Ph.D., and Dr. Killeen also provided coverage of anti-neutrophil cytoplasmic antibody (ANCA) and anti-GBM studies.

II. CLINICAL SERVICES:

There was the continued growth in several specialized assays; most notably the ANCA test and the anti-GBM indirect immunofluorescence test. Neutrophil cytoplasic antibody determinations increased from approximately 150/month to more than 175/month. New procedures were also implemented in the protein electrophoresis area; in hemolytic complement assays, and in the measurement of antibodies to extractable nuclear antigens. We have recently evaluated and initiated a series of new utilization control measures in the laboratory. Finally, laboratory personnel continued cross-training programs with the Chemistry Laboratory. This was one of the chief goals of the Chemistry Section consolidation.

III. RESEARCH AND DEVELOPMENT:

The Laboratory supported clinical studies of the effects of cytotoxic/immunosuppressive drugs on IgG, IgA and IgM as well as IgG subclass concentrations in lupus patients in conjunction with Dr. Joseph McCune (Department of Medicine, University of Michigan). Several commercially-financed methods and instrument evaluations were also carried out. These studies involved new protein electrophoresis instrumentation, anti-streptolysin O and anti-cardiolipin antibody measurements, and several nephelometric assays.

IV. QUALITY ASSURANCE:

The laboratory participated in the department-wide utilization management program..

V. 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 4 times during the academic year. Clinical Pathology Grand Rounds included immunopathology presentations by Dr. David Keren (Warde Medical Laboratory, Ann

Arbor), and Dr. Warren (see individual faculty report). Drs. Warren and Keren continued the weekly series of didactic sessions entitled "Current Topics in Immunopathology". Other professional activities of faculty and staff in the laboratory are summarized under individual reports.

Jeffrey S. Warren, M.D.
Director, Clinical Immunopathology Laboratory

CLINICAL MICROBIOLOGY / VIROLOGY LABORATORIES

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I. CLINICAL ACTIVITIES:

The primary goals for the year were to continue to assess proper test utilization and to evaluate and implement tests that allow for rapid, direct detection of infectious agents in body fluids and tissues. Such tests may be more expensive to perform but should be clinically beneficial to the patient (more rapid diagnosis) and be more cost-effective when assessing total hospitalization costs (shortened hospitalization stay). To meet these goals several discussions were held with clinical services to review test ordering practices which usually resulted in a decrease in selected test ordering. Other changes were made to streamline our specimen and identification work-ups and improve our test reports to clinicians. Commercial tests to directly detect toxins produced by enterohemorrhagic serotypes of *Escherichia coli* (e.g. O157:H7) and to detect *Human papillomavirus* in appropriate patient specimens were evaluated and added to the test menu. Recent FDA approval allowing the use of blood culture media to be used for detecting organisms in other selected body fluids has shortened detection time and increased assay sensitivity. A section of the Laboratory was renovated to accommodate current and future expansion of testing using molecular methods.

The Laboratories continue to work with Infection Control & Epidemiology Services to monitor for evolving antimicrobial resistance and nosocomial spread of infections. Unfortunately vancomycin-resistant enterococci (VRE) continue to be a serious threat to our patients and Laboratory personnel serve as a front line in detecting and reporting patients who are either infected or colonized with such organisms. The recent reports of increased resistance of the staphylococci to vancomycin is a major concern; the Laboratory developed a screening method to serve as an early warning for the possible emergence of such strains within the UMHS. Dr. Pierson serves on the new UMHS Antibiotic Subcommittee of the P&T Committee and updates the Subcommittee members on developing antimicrobical resistance and the activity of new antimicrobics on clinical isolates.

II. RESEARCH ACTIVITIES:

Laboratory personnel have actively assisted clinical investigators from other departments. Over 600 endocervical specimens collected in Indonesia were tested for STDs in the Laboratory using molecular methods as part of an study being conducted by investigators at the SPH. A PCR method for the detection of *Pneumocystis carinii* in pulmonary specimens was developed by Susan Salo, a Sr. Technologist, and implemented as a clinical test due to requests by members of the Infectious Disease section. The BioMIC was used to assess the degree of resistance to selected quinolone antimicrobics. A "research" drug panel was developed and used for three months to evaluate a panel of new antimicrobics for relative activity against clinical isolates. The Laboratories continue to collect selected isolates for submission to designated reference laboratories as part of national collaborative investigations.

III. TEACHING ACTIVITIES:

All Laboratory personnel continue to provide instruction to Pathology House Officers and Infectious Disease residents on diagnostic procedures used in the Laboratories. Infectious Disease "rounds" are conducted daily in the Laboratories where demonstrations are performed by assigned Pathology House Officers. Numerous informal contacts were made during the year during which Laboratory personnel worked with residents from other services to explain and demonstrate laboratory procedures. Dr. Pierson participated in an M-Labs Inservice Program for M-Labs clients and, with assistance by staff volunteers, conducted an on-site Seminar/Workshop in clinical microbiology for Jr. College science instructors within the state. Dr. Pierson also hosted a UMHS seminar for Infectious Disease, Infection Control and Clinical Microbiology specialists to address the problems of controlling the spread of resistant organism within patient care facilities.

IV. PROFESSIONAL DEVELOPMENT:

Both supervisors and most of the Sr. Technologists attended one or more national or regional scientific meetings and actively participated in one or more workshops associated with these meetings. In addition, several staff technologists attended advanced training programs in diagnostic mycology, parasitology and molecular diagnostics. The Laboratories also subscribed to two audioconference series that were well attended by laboratory staff members as part of our CME program.

Carl L. Pierson, Ph.D.
Director, Clinical Microbiology & Virology Laboratories

MOLECULAR DIAGNOSTICS LABORATORY

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The volume of testing in Molecular Diagnostics continued to grow during the year to approximately 2500 tests per annum, an increase of 500 tests over the previous academic year. An important area of growth continues to be related to the monitoring of bone marrow engraftment following bone marrow transplantation. This service has become a routine activity for the BMT program, and we are gratified that this assay has been so favorably received by our clinical colleagues. There was also significant growth in the area of detecting genetic abnormalities that predispose to thrombosis. We are currently offering testing for the factor V Leiden and prothrombin 20210A mutations. We are planning to bring up testing for one other mutation in this area.

There were no new major items of equipment purchased this year, however our hope is that a new venture with Parke-Davis Laboratories will enable us to use state-of-the-art equipment in a shared facility with that company. The limitation on access to the darkroom in Biological Chemistry has heightened the need for access to a Departmental darkroom for developing autoradiograms.

With the relocation of the laboratory to new space in Medical Science I, we will have more room for test performance and for clerical functions, something which has been limited in the past.

Residents have continued to participate in signout of cases in the Laboratory. These opportunities have been welcomed, especially because of the apparent increase in questions related to molecular pathology on the Board exams. We maintain our accreditation for fellowship training in Clinical Molecular Genetics, although owing to financial constraints, we have not been able to recruit a fellow.

The Medical Technologists, some of whom were hired in the past 2 years, performed an exceptional job during the year. The dedication of Ms. Akel, Sr. Medical Technologist was invaluable.

Anthony A. Killeen, M.D., Ph.D.
Assistant Professor
Director, Clinical Chemistry/Molecular Diagnostics

PHLEBOTOMY SERVICES AND CENTRAL DISTRIBUTION

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The following are the major achievements for Phlebotomy and Central Distribution during 1997-1998:

- Continued adjustment to the reengineering services due to the downsizing of 35.7 FTEs in 1996.
- Upgrade of minimum salaries of Phlebotomists and Lab Assistants
- Change of titles to Clinical Lab Associate from Phlebotomists and Lab Assistants
- Second level of responsibility and performance for the Lab Assistants called Clinical Lab Associate II. The Phlebotomist II level was converted to this Clinical Lab Associate II level.
- Employees in the Taubman area were trained so that Indwelling access for blood draws could be offered in Taubman. From July 1, 1997 to June 30, 1998, 84,106 patients were drawn in the second and third floor blood drawing stations. Five people took early retirement in 1997 from July and September. The hours in the third floor blood drawing station are 7:30 a.m.- 6 p.m. and the hours in the second floor blood drawing station were expanded to 8:30 a.m. – 3:30 p.m. The number of FTEs used to provide these services is 15.7.
- Cancer Geriatric Center, which opened May 6, 1997, has had increasing workload during the past year. The number of patients drawn from July 1, 1997 to June 30, 1998 was 40,024. In June of 1997, 2,598 patients were drawn and in June of 1998, 3,417. A significant achievement has been the receipt of orders through the computer systems instead of storing requisitions. It is the first area to receive their orders in this fashion. This allows the area to have up to date orders on this very sick population. Indwellings account for about 10% of all draws. Fast turn around for hematology tests has occurred because of the direct line for the pneumatic tube and the effort of personnel in Phlebotomy and the Hematology Stat Lab. Nine FTEs are used to provide these services from 7 a.m. to 6 p.m., Monday through Friday.
- Inpatient Phlebotomy coped with the uncertainty of level of service from April 1997 to June 1998. The work was accomplished by adding temporary employees for positions that were being held. The area suffered from high turn over due to the uncertainty and the opening of the Cancer Geriatric Center where experienced Phlebotomists went to insure their jobs. With the reinstatement of the 200 temporary hours, 29.1 FTEs are used to provide blood drawing and specimen pick up services in UH and Mott. The number of patients drawn in Mott was 22,204; and the number in UH was 121,605.
- Central Distribution has recovered from an unusually high turn over of employees after the downstaffing of 8.5 FTEs in 1996. Hiring and training has occurred and workflow is achieving experience and efficiency needed for this complex area. To handle specimens for the hospitals, clinics, Mcare sites, and Mlabs clients as well as sendout clinical specimens to reference labs, a total of 34.6 FTEs are used in this area. An additional person was added to do the quality assurance for the Mlab area.
- The Inpatient area training supervisor provided the Inpatient, Outpatient, and Central Distribution areas with a superb roll out of training for "Putting Patients and Families First" with multiple inservices on all shifts on a monthly basis from January 1998 to the present. Topics included Critical

Behaviors, "It's a Dog World" video, Putting Patients and Families First part 2, "Difficult Guest" video, reflective "where are we now", and telephone etiquette.

- The personnel currently in positions in each area which were not working here before July, 1997 are:
  Central Distribution 21.6 FTE/34.8 FTE
  Outpatient Phlebotomy 11.5 FTE/24.1 FTE
  Inpatient Phlebotomy 13.7 FTE/29.1 FTE
  This does not include positions hired as temporaries to support Inpatient during the transition, or positions that have vacated and refilled more than once. It does include those that retired.

Suzanne Johnson

GENERAL PATHOLOGY

ELECTRON MICROSCOPY SERVICE

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The electron microscopy service continues to provide important diagnostic services to the University of Michigan. The facility provides high quality diagnostic work for the nephropathologists, neuropathologists, hematopathologists, and the general pathologists. On a limited basis, electron microscopy service is available to researchers through a recharge arrangement.

The EM service has continued its strong growth which began in the recent past with a substantial increase in the number of cases submitted and processed into the lab. A temporary employee Ethan Booker, was hired to assist with the workload and allow the EM technicians sufficient time to take their vacations. Toby Booker has started medical school this fall but we were able to clear the backlog of cases with his help.

We have received authorization of funds to purchase a new electron microscope. After an exhaustive evaluation of all available systems (Hitachi, Zeiss, Jeol and Philips) we have selected the Hitachi. The specific unit that we will be purchasing is the Hitachi 7500 with an integrated digital photography system. The digital system is integrated into the microscope and will work in conjunction with the standard plate film. It is possible to have either the plate film, or the digital image. Discussions with other institutions indicate that they have been very pleased with the performance of the Hitachi system with the digital photography apparatus. We anticipate that much of the standard photography and darkroom work will no longer be needed since the images may be printed on a high quality printer as soon as the image is captured. The next step is to send the images directly to the pathologist without the prints, but that process is at least 2 years away.

Renovations for the new microscope have already started on the third floor of Med Sci I building. The entire EM suite will be renovated to provide upgraded facilities for all aspects of electron microscopy.

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

M-LABS

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I. GOALS:

1. To generate increased revenue and decreased unit operating cost of the University of Michigan Hospitals Clinical Laboratory System by outreach testing for:

   - Reference laboratory services to hospitals.
   - Group Practices.
   - Physicians offices.
   - Managed care organizations.
   - Specific esoteric services such as renal biopsies, molecular diagnostics, cytogenetics, and flow cytometry, and other "centers of excellence".
   - Clinical trials for clinical research organizations and pharmaceutical firms.

2. Develop and participate in hospital laboratory networks to:

   - Compete effectively for managed care laboratory testing.
   - Reduce costs through test sharing and consolidation.

3. Through our outreach efforts, to build bridges to other institutions that will facilitate working arrangements between these institutions and other branches of the University of Michigan Health System.

4. To support the mission of the University of Michigan Hospital System by providing for outpatient laboratory services to M-Care through a network or networks of hospital laboratories which will be potential M-Labs clients.

II. M-LABS EXPANSION:

M-Labs is on target for revenues generated in FY98 as compared to projected revenue for this time period in our 1994 business plan which resulted in an expansion of M-Labs operations.

III. GROWTH:

- Total CP net billing increased 20.2% over FY 97.
- Billing for AP surgical pathology cases increased by 8.8% over FY97.
- M-Labs has added 31 new physician's office clients in FY98. One hospital client's contract terminated when that hospital formed an affiliation with another hospital system. No new major hospital clients were added in FY98.

IV. INTERFACES:

Interfaces have now become requisite to obtaining contracts for reference laboratory services for all large hospitals.

Through the efforts of PDS, we now have interfaces between the University of Michigan laboratory computer system and three hospital laboratories (Mount Clemens General Hospital, Botsford Hospital and Hurley Hospital).

An interface is also planned for another client hospital.

V. MANAGED CARE ACTIVITIES:

M-Labs has implemented our agreement with M-Care to supply outpatient laboratory services for that portion of the enrollees in its new Medicare (Senior Plan) subscribed to 4 of M-Care's hospital providers.

In order to accomplish this task, M-labs developed and implemented processes for claims transfer from and means of distribution of capitated revenue among the subcontracted laboratory providers, and developed and implemented a Quality Assurance plan to meet with M-Care's and HCFA's requirements for this product.

In FY98 M-Labs has contracted with M-Care for provision of outpatient laboratory services for its HMO, POS, and Medicaid products. We are subcontracting these services to M-Care's provider hospital laboratories.

VI. NETWORKS:

In order to provide geographic coverage for managed care products, and to compete with the large national laboratories which are now dominant in that arena, hospital laboratories are now increasingly banding together in networks. M-Labs has joined JVHL, a network of major hospital laboratories in Southeastern Michigan formed to do laboratory work for Select Care and other managed care organizations.

We are still working with another network of Michigan hospital laboratories (GreatLakes Laboratory Network) which will have the capacity to negotiate for statewide managed care contracts for laboratory services.

VII. PROSPECTS:

The developing shift from indemnity insurance to managed care as well as the trend to reduced reimbursement by payors for each unit of laboratory testing can be expected to lead to reduced revenue from current clients. The effects of these trends may be countered by increased outreach efforts of our client hospitals which may increase reference testing from these sources.

In addition alliances, purchases, and consolidation of health care delivery systems which do not include the University of Michigan will put some of our current clients at risk and put potential new clients into other camps and out of M-Labs' reach.

We propose to maintain our market share and continue growing by the following means:

1. Participate in developing hospital laboratory networks to contact for managed care laboratory work and position our labs to benefit from possible future rationalization of laboratory testing among network members.
2. Assist in the identification of potential "centers of excellence" in our laboratories and marketing of these to networks, managed care entities, and other potential clients.
3. Continue our efforts to contract with M-Care for all of its outpatient laboratory testing which would be subcontracted to its provider hospital laboratories and who would become potential clients of M-Labs.
4. Work with Pathology Data Systems to implement the most efficient information transfer of data to our clients. Information system support has become the single most important concern to many of our potential and current clients.
5. Explore and develop non-core activities such as clinical trials laboratory testing.

VIII. CLINICAL TRIALS LABORATORY TESTING:

Clinical trials laboratory testing represents a very small part of the M-Labs operation but billing of this service to a large local pharmaceutical firm has remained about constant for FY98.

IX. IMPEDIMENTS TO GROWTH:

- **External:**

- Revenues can be expected to decrease from:
  - Increased penetration of managed care.
  - Continued erosion of pricing.
  - Outpatient DRGs.
  - Alliances, consolidations, and purchases of hospitals not involving the University of Michigan put existing clients at risk and other potential clients out of reach.

- **Internal:**

- Maintaining a broad test menu and rapid turnaround times in spite of internal demands for cost reduction.
- Continued demands for more and more esoteric testing as technology advances bring more and more tests within the reach of smaller hospitals.

Prepared by Eugene M. Silverman, M.D.

PATHOLOGY DATA SYSTEMS

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The following is a bulleted list of some of the major accomplishments of Pathology Data Systems during the past academic year, July 1997 through June 1998:

Continuing efforts to install Cerner PathNet V.500 (Millennium product)

- Pathology Data Personnel have been actively working for more than a year to prepare for the installation of the Cerner client-server LIS called Millennium. Most recently, efforts have been devoted to the cross-loading and validation of the current two-year on-line database that is in a proprietary format to the Oracle database that will constitute the backend of the new Millennium system. Extensive efforts have also been devoted to the co-development with Cerner of the web browser that will be the primary means to access test results by hospital residents and staff physicians with the new LIS.
- Hardware upgrade to two DEC model 8400 CPUs in preparation for the Millennium conversion.

Machine room and server consolidation

- Worked actively with MCIT personnel toward the goal of machine room and server consolidation. Lloyd Suter was recruited from Pathology Data System to MCIT/Operations and Technical Services to pursue this goal and oversee machine room operations. Hospital servers have been installed in the PDS machine room as part of this integration effort.

Co-developmental efforts with Cerner

- Launch of new project to with Cerner to capture digital images of surgical pathology cases and integrate them with textual surgical pathology reports. Emphasis is being placed on minimal disruption of workflow and also foolproof identification of the stored and integrated images.

Network support and PC deployment

- Approximately 120 new PCs have been deployed in the department in preparation for the Millennium installation and also to replace aging equipment for departmental personnel.
- Continuing refinements to the pathology network and to increase storage space on database servers

Interface engine (hub) enhancements and deployment of new interfaces to "foreign" systems

- Host-to-host interface through the hub (interface engine) to Bottsford Hospital, an important MLabs client.
- Interface between PathNet and the OPTS system running in the Burn/Trauma unit. This activity involved extensive validation of the data transferred across the interface.

- Extensive efforts to validate test data that is replicated near-real time to the enterprise Clinical Data Repository (CDR) and that is extensively accessed by hospital physicians using the enterprise web browser called CareWeb which is the front-end to the CDR..

Investigation of an order-entry application for the clinical laboratory and other ancillary systems

- Extensive investigation of a PC-based order-entry application that meets compliance needs for medical necessity justification of test orders and can also generate an advanced beneficiary notification (ABN) prior to test ordering. A product called Dr. Chart, manufactured by Advanced Healthcare Technologies, that runs on both a fat client and browser is seriously being considered for deployment in ambulatory care settings as well as at MLabs outreach client settings. This product may ultimately be rolled out to other ancillary departments.

Web-based initiatives

- Launching of a new departmental web site containing such diverse information as faculty biographies, faculty annual reports, descriptions of clinical laboratories, and synchronized PowerPoint/RealAudio lectures as a byproduct of the AIMCL and Executive Briefing CME activities sponsored by the department.

GroupWise (word processing and calendaring) activities

- GroupWise 5.0 was installed across the entire department and then upgraded during the year to V. 5.2.
- Bruce Friedman served as the chairman of the GroupWise Steering Committee and Executive Committee that has been actively deploying the software across the entire health system. Approximately 13,000 accounts will have been created by the end of 1998.

Ancillary-wide and enterprise-wide information technology activities

- PDS and pathology are actively supporting a project, funded through the Y2K initiative, to deploy a software product called SMS that can be used to identify software running on PCs and to remotely install PC software. The relationship to the Y2K initiative is that PC can also be made Y2K-compliant with the software. Pathology has donated laboratory space on a temporary basis to house the SMS project team.

Educational and committee activities

- The sixteenth annual Symposium on Automated Information Management in The Clinical Laboratory (AIMCL) was presented at the Chrysler Center and Media Union on the North Campus May 27-29, 1998. There were 28 vendors in attendance at the meeting and about 260 paid registrants.
- Bruce Friedman continued as a member of the CIO Executive Committee which is composed of all of the information technology directors for the enterprise. He also provided a two-week pathology informatics course for two house officers in May.
- Steve Gendler continued to participate in the Cerner User Group Executive Committee

Year 2000 Activities

- Pathology Data Systems and the entire department are ramping up quickly to deal with the so-called "Year 2000" bug. This is a software bug that incapacitates computers in the year 2000.

The Cerner Millennium product will be Y2K compliant. Extensive effort has already been expended analyzing Y2K compliance in the departmental servers, PCs, clinical laboratory instruments, and also analytical instruments in the various departmental research labs.

Bruce A. Friedman, M.D.
Laboratory Director

DEPARTMENT OF PATHOLOGY EDUCATIONAL PROGRAMS

ANNUAL REPORT
1 JULY 1997 - 30 JUNE 1998

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 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 continuing medical education programs, workshops and seminars offered through The University of Michigan, and professional organizations including the United States and Canada Association of Pathologists (USCAP), and American Society of Clinical Pathologists (ASCP).

Medical Student Education:
Pathology faculty continue to provide outstanding leadership (e.g. course directors, sequence coordinators, Associate Dean of Medical Education) and excellent teaching in the first two years of the medical student curriculum. Faculty continue to be recognized as recipients of student teaching awards and selection as graduation class marshall. Efforts to increase student active learning experiences in a web-based teaching format continue. The elective fourth year clerkships in General Pathology and Laboratory Medicine continue to be highly evaluated by students and meet important curriculum educational goals. The special topics clinical elective rotation has been successful, meeting specific student career needs especially those with a subspecialty orientation. The summer program for M-1 students is popular and has resulted in a significant increase in the number of these students entering pathology.

Residency Training:
The Department offers combined residency training in Anatomic and Clinical Pathology as well as fellowships in Cytopathology, Hematopathology, Surgical Pathology, Urologic Pathology and Medical Informatics. Approximately 27 residents and fellows receive training annually. Residents continue to be very academically active, with multiple presentations at national meetings and first author publications. Several residents continue to provide strong support to the medical student educational programs through their involvement as laboratory instructors, mentors and tutors to students. Four house officers and four fellows completed training this past year. Graduates found desirable employment and fellowships at institutions such as Cornell University, Universit of New Mexico, Indiana University and the Cleveland Clinic.

Graduate Program:
The Department's doctoral graduate program is a small program (approx. 8 students) with a focus on providing excellent training in preparation for student's careers as scientific investigators. The quality of the faculty and training offered is reflected by the continued interest of MSTP students and the completion of doctoral theses by two students this past year. A pathology graduate student was selected

as one of four recipients from the entire University for an Outstanding Discertation Award. Two training grants within the Department continue to serve as important sources of support for graduate students and post-doctoral fellows. The Department of Pathology is participating with other basic science departments in the Program in Biomedical Science (PIBS), a joint recruitment effort.

University / CME: Programs:
Department faculty continue to offer high quality laboratory research opportunities to both undergraduate and medical students, a Dental student pathology course with lab, CME programs , and individual teaching in the other schools of the University including Public Health. The course in general pathology offered to Medical Illustration students and implemented in 1997 continues to meet an important educational need within the University. The Pathology Informatics and Blood Bank CME courses continue to be recognized as foremost programs in the country.

Joseph C. Fantone, M.D.
Associate Dean of Education

ANN ARBOR VA HEALTH SYSTEM
PATHOLOGY AND LABORATORY MEDICINE SERVICE

DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

INTRODUCTION:

The Ann Arbor VA Health System (AAVAHS) is a tertiary health care provider for veterans partnered with the University of Michigan. It is one of three tertiary medical centers in the Veterans Integrated Service Network (VISN) #11 serving the veteran population of Michigan, and portions of Ohio, Indiana and Illinois. The AAVAHS Pathology and Laboratory Medicine Service maintains a close relationship with the University Department of Pathology at every level. All pathologists in the AAVAHS have medical school appointments and participate in university activities in a manner similar to other departmental sections. Recruitment for AAVAHS pathologists are a joint activity 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. Two and 1/2 resident training positions in the Department's program are supported with funds from the Department of Veterans Affairs. All residents serve monthly rotations in Surgical Pathology, Autopsy Pathology, and a number of arranged electives including Diagnostic Electron Microscopy and special study programs in Surgical Pathology, Cytopathology and Digital Imaging. The Chief, Pathology and Laboratory Medicine Service at the AAVAHS is a voting member of the Dean's Committee. The AAVAHS laboratory was inspected in 1998 and retains full accredited by the College of American Pathologists. The AAVAHS was inspected by the JCAHO in 1997 and is currently fully accredited. The medical center's Decentralized Hospital Commuter System (*VistA*) is recognized as the most fully integrated medical information system. It combines all of the clinical management of the patient and is moving toward a totally computerized patient medical record by 2000. Data storage for all components of pathology and the clinical laboratories contains full patient information for more than a decade. Starting this year digital images of selective patient surgical, cytopathology, autopsy and ultrastructural specimen are stored as part of the patient medical record and are accessible to clinicians within minutes of case review.

Two major reorganization thrusts are underway at the AAVAHS. 1) The facility is refocusing its mode of healthcare delivery, down sizing inpatient care and greatly expanding its ambulatory care. In keeping with this change, a substantial capital improvement program is currently in progress. A Research Building and two additional parking structures have been built. A clinical addition is nearly completed. This 340,000 sq. ft building attached to the current hospital provides space for ambulatory care, new surgical suites, vascular cath facilities, intensive care units and a floor for diagnostic services (Pathology, Clinical Labs, Radiology and Nuclear Medicine). This includes 23,000 sq. ft for the complete relocation of Pathology and Laboratory Medicine. Relocation is scheduled for August 1998. The severe space restrains that have hindered functional changes will be removed with this move. Current discussions concern a complete functional restructuring of the clinical labs. 2) The VISN is

moving toward an integrated health delivery system. Diagnostic Services will be a target for networking/consolidation among the current 8 independent facilities. This will result in additional sharing of service responsibilities, decrease in fee basis (send-out) testing to nonVA clinical labs and increase the workload in Ann Arbor AAVAHS's anatomic pathology and the clinical labs.

ANATOMICAL PATHOLOGY:

A. **Surgical Pathology**: 5014 surgical cases have been accessioned and reported during this period of time. This represents an 29% increase over the prior reporting period. 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 mentoring by the staff pathologists. The resident interacts with the clinical teams. Monthly Morbidity and Mortality Conferences are held jointly by Pathology and Medicine Service. The residents assigned to autopsy and surgical pathology are primary presenters in these clinical conferences. The residents obtain a broad educational experience and aid in providing high quality medical care. There is an extensive quality improvement program within Anatomical 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, surgical appropriateness, turnaround times and follow-up of positive diagnoses, within the medical center. The surgical and cytology readout stations are fully integrated into a hospital digital imaging system. Routine images are captured on cases of interest. These are particularly useful in presentations to clinical teams reviewing specimens from their patients with the pathology staff and residents.

B. **Autopsy Pathology**: 42 autopsies were performed during this year that is a rate of approximately 26% of in-patient deaths. Assigned residents perform the autopsies, prepare the pathologic diagnosis, and present the case in conference to the staff pathologists and other residents. The resident cuts and otherwise prepares the tissue for the preparation of slides and then reviews them and makes a microscopic diagnosis. These steps are supervised by staff pathologists who permit a gradual increase in independence for the resident with increased experience. Several autopsies performed at the VAMC are also presented at the extended Gross Conference at the University.

C. **Cytology**: 2732 cases were examined and diagnosed during this period. This is an increase of 200 over the last reporting year. Nearly all of the cytology specimens are of a diagnostic type, with very few screening cytologies. Although there is not a formal rotation in cytology within the VAMC the cytological material is readily available and is used as correlative information for surgical and autopsy pathology. This laboratory is a "Center of Excellence" in cytology.

D. **Electron Microscopy**: 323 electron microscopy cases were processed. Ultrastructural diagnosis is provided through sharing agreements with several Michigan hospitals. The unit also serves several AAVAHS research investigators. 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 electron microscopy seminars at the University of Michigan. This VAMC is a "Center of

Excellence" in electron microscopy and serves as consultant to other VA Medical Centers, to the University of Michigan Medical Center and to other hospitals by contract.

CLINICAL PATHOLOGY:

During the period of this report 862,903 clinical pathology procedures were performed in the laboratory. In Chemistry there were 707,260; in Hematology 105,818; in Microbiology 26,756, and in Blood Bank 23.069. These figures represent productivity (billable) rather than weighted test numbers. Each of these numbers has declined during this year, with the exception of the blood bank procedures which increased by 2,200. The reasons for the declines is complex, but is primarily the effect of the shift from inpatient to ambulatory care. A formal clinical pathology rotation has not been available for pathology residents although the residents may participate or observe clinical pathology procedures when this activity is appropriate in relation to their other rotations. Drs Chensue and Chamberlain oversee the clinical laboratory and make available interesting and pertinent clinical laboratory information available to residents as desired. Clinical Pathology data is available to pathology 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 mentoring 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. Residents join in continuing educational activities in histopathology and cytopathology from the AFIP, CAP, and ASCP. 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 physically close to the University, the residents are expected to attend the appropriate teaching conferences at the University as well. The staff contribute to the laboratory and lecture portions of the second year medical students at the University of Michigan. 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. Both Dr. Beals and Dr. Chensue have made presentations at international pathology conferences.

RESEARCH:

The specific efforts of the pathology staff are included on individual reports. Dr. Stephen Chensue has a strong funded research program that was renewed during this reporting period. He also participates in cooperative studies with other investigators at the University of Michigan. Dr. Murphy carries a full investigative program. She and Dr. Chensue have research laboratories in the Research Building of the VAMC. Staff participate in various clinical studies and collaborate with a variety of investigators. The laboratory in general serves the VAMC research program by providing considerable technical support for clinical research and in some cases for more basic research in both anatomic and clinical pathology. The staff also serves as consultants and advisors for a number of research programs.

ADMINISTRATION:

Dr. Beals serves as Chief of Service. 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 as well as other graduate course in the medical, dental schools and the shool of public health. At VA Medical Center the pathology staff members serve on all major committees involved with institutional policies and procedures. Dr. Beals has been designated by the National Veterans Administration to oversee anatomic pathology within Department of Veterans Affairs Medical Centers. He has been instrumental in developing policies and procedures related to anatomic pathology within the Department of Veterans Affairs. Dr. Beals has been permanently appointed Director of Pathology for the VA nationally. He designated the Chief Consultant Officer for the Diagnostic Service Strategic Healthcare Group. In this capacity serving as the leader of the Veteran Health Administration National Headquarters' administrative oversight of: Pathology, Clinical Laboratories, Radiology and Nuclear Medicine.

The VA's National Cytopathology Proficiency Program's administrative offices are located in the AAVAHS. All VA pathologists privileged in cytopathology are required to participate in a 16 glass slide comprehensive proficiency review annually. This is the largest comprehensive cytopathology proficiency program in the nation. It has entered its fourth year with more than 320 circulating glass cytology smears and 399 participating pathologist.

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 the veteran patients as its first and highest responsibility. There is close supervision of resident activities as they are involved with patient care. All staff members are privileged and evaluated in accordance with their training, experience, continuing education and participation in quality improvement activities. Within the service there is an extensive quality improvement program that integrates with that of the hospital as a whole. The Pathology and Laboratory Medicine Service has maintained accreditation by the College of American Pathologists since the early 1960's. The Blood Bank approved by the Federal Drug Administration. The partnership with the University of Michigan serves to strengthen and improve the quality of patient care to our veterans. The teaching effort involving both residents and medical students is of benefit to the two institutions. The newly constructed Clinical Addition will house: Ambulatory Care, Surgical Suites, the Intensive Care Units, Nuclear Medicine, Radiology and the full Clinical and Anatomic Pathology laboratories. Move to the new structure is scheduled for August 1998.

Ted F. Beals, M.D.
Chief, Pathology and Laboratory Medicine Service
Ann Arbor VA Health System

FINANCE AND ADMINISTRATION

DIVISION OF FINANCE AND ADMINISTRATION

DEPARTMENT OF PATHOLOGY - UNIVERSITY OF MICHIGAN
ANNUAL DEPARTMENTAL REPORT
1 JULY 1997 - 30 JUNE 1998

INTRODUCTION:

The Division of Finance and Administration, which is under the auspices of the Office of the Chairman and directed by Mr. Eugene J. Napolitan, Department Administrator is comprised of four units as follows:

A. ADMINISTRATIVE SUPPORT CENTER - PATHOLOGY LABORATORIES

Nancy A. Coray, Financial Analyst and Billing Coordinator
Deborah Day Jansen, Administrative Coordinator for Pathology Laboratories
Thomas D. Morrow, Assistant Administrator for Finance and Administration
Beverly J. Smith, Administrative Assistant, personnel and payroll functions

Clinical Faculty Offices & Surgical Pathology Transcription, University Hospitals:

Deborah Day Jansen, Administrative Coordinator
Paulette Dozier, Office Manager, Surgical Pathology Transcription
Janice Kitley, Office Manager, Clinical Faculty Offices

B. OFFICE OF ACADEMIC AND BUSINESS AFFAIRS - MEDICAL SCHOOL:

David R. Golden, Clinical Department Associate
Joseph L. DeJohn, Student Services Assistant
John E. Harris, Administrative Assistant
Susan M. Hunter, Administrative Assistant

C. OFFICE OF THE CHAIRMAN

Laura D. Blythe, Staff Assistant
Carol N. Galofaro Executive Secretary

D. PATHOLOGY PHOTOGRAPHY AND IMAGING CENTER:

Mark V. Deming, Photographer

This Division is responsible for the business, operational and fiscal affairs of the Department of Pathology as mandated by the policies of the Chairman, Clinical Delivery System (CDS), Medical

School and University. In addition to directing this division, Mr. Napolitan serves on various departmental, CDS, Medical School and University Committees, several professional society committees and as a board director for non-profit organizations.

A major reorganization of this division was accomplished in Fiscal Year 1997. With the departure of Mrs. Maydis Caldwell Skeete, Research and Education Administrator, the Education and Research Administration Office was consolidated into the Finance Unit under the direction of Mr. David R. Golden. This new unit, the Office of Academic and Business Affairs - Medical School, has resulted in cost savings in personnel, space and commodities. Administrative support staff formerly located on the fourth level of the Pathology Building have been relocated to the fifth level sharing space with staff from the former Finance Unit. This reorganization also allowed us to vacate space that is vital to the academic programs of the Department.

In addition to the management of daily activities, each of the units has completed major projects which are summarized as follows:

ADMINISTRATIVE SUPPORT CENTER/PATHOLOGY LABORATORIES:

This unit is directed by Mr. Thomas Morrow, Assistant Administrator and is responsible for the business, operational and fiscal affairs of the Anatomic and Clinical Pathology Laboratories. This includes preparation and monitoring of all Hospitals laboratories revenue, expense and capital budgets, and personnel and payroll systems. Mr. Morrow assisted with the planning, development and implementation of the Cost Efficiency Program for the Pathology Laboratories as mandated by CDS Administration and the Redesign Coordinating Group (RCG). For Fiscal Year 1996/1997, the fifth year of the University Hospitals Cost Efficiency Plan, our RCG mandated staff reduction, based upon MECON data, was 20FTEs - equal to $622,359. The majority of the staff reductions, as targeted by the CDS, were in the Blood Drawing and Central Distribution Unit. Mr. Morrow was responsible for analyzing the MECON data for comparison of our laboratory productivity with similar academic institutions. A reorganization of these units including re-definition of phlebotomy services provided to the Hospitals is being proposed. Key administrative support in addition to the Assistant Administrator include:

Administrative Coordinator: This individual, Mrs. Deborah Day Jansen, assists with the coordination of intra and inter laboratory activities for the anatomic and clinical pathology laboratories which include coordination of required proficiency tests; coordination of inspections required for continuing certification or licensure by the JCAH, CAP and MDPH; serving as departmental representative on the Safety Committee, Disaster Committee and as United Way Chairperson. In addition, the Administrative Coordinator acts as the liaison with the Hospital for renovation projects and coordinates the publication of the Pathology Laboratories Handbook (including on-line version) and the SPECTRUM Newsletter; and is responsible for all requisition modifications. This individual also manages the Surgical Transcription Unit and has assumed responsibility for the Faculty Office Suite in the Hospitals. With the opening of the Cancer and Geriatrics Center in April 1997, Mrs. Jansen was responsible for coordinating the move of the Hematology and Phlebotomy services to this facility. Additionally, expansion of our Autopsy Suite including planning and design of a multipurpose room for viewing of bodies, chaplain and police services, etc., and the installation of a new refrigeration unit was completed. Renovation to

the Pathology Laboratories as outlined in last year's CEP has been initiated and is targeted for completion in Spring 1998.

Billing Coordinator: This individual, Ms. Nancy Coray, is responsible for processing and auditing all laboratory charges (gross charges of approximately $142,000,000), ensuring the accuracy of the daily billing files, correction of all errors with the appropriate Hospital department and responding to all questions regarding interdepartmental, MLabs or Hospital patient billings (technical portion). This position is also responsible for our billing system related to the MLabs Program.

Administrative Assistant: This individual, Mrs. Beverly Smith, oversees the clerical support staff assigned to the Administrative Support Center and coordinates personnel and payroll paperwork for all Pathology Laboratories staff (approximately 370 FTE staff). The Administrative Assistant is responsible for the compilation of the Pathology Telephone Directory (on-line and hard copy) and serves as lead for the Departmental Orientation Program. Responsibility for the implementation of the new Paid Time Off system and the development of Department of Pathology guidelines were coordinated by Mrs. Smith.

OFFICE OF ACADEMIC AND BUSINESS AFFAIRS - MEDICAL SCHOOL:

This unit, which is managed by Mr. David Golden, is responsible for the Medical School all funds budget preparation and variance reporting; tracking of all Medical School expenditures, professional fee billing operations; general funds and teaching and administration funds; departmental renovation and remodeling; and management of the Word Processing Center. In addition, the responsibilities formerly administered in the Office of Research and Education Administration were assumed by this unit in March 1997.

All business and administrative functions associated with our sponsored research and education programs including coordination of the application process, receipt of grant awards, establishment of budgets, monitoring of expenditures and acting as liaison between the Principal Investigators, research sponsors and other University departments are now performed by staff in this unit. In addition, personnel and payroll paperwork associated with non-instructional staff (Medical School paid), house officers and post-doctoral fellows is coordinated in this office.

This unit also assists the Coordinator of the Pathology Education Programs with Medical School courses, the Pathology Graduate Program and the House Officer Training Program.

Mr. John Harris has assumed responsibility for oversight of the staff supporting our Research Programs and Mrs. Susan Hunter is responsible for the payroll and personnel issues for staff in the Medical School (approximately 150 FTEs) and our House Officer Program (24 FTEs).

OFFICE OF THE CHAIRMAN:

In addition to providing support to the Chairman, Mrs.Carol Galofaro is responsible for processing faculty appointments and promotions through our ACAPT, the Medical School and University. She also assists the Division Directors with coordinating schedules for faculty recruits.

Mrs. Laura Blythe provides staff support to the Administrator, Mr. Eugene J. Napolitan. In addition, she is responsible for the supervision of faculty support staff, the Chairman's Office Receptionist and temporary office staff. Additional responsibilities include payroll and personnel issues, and travel and dues reimbursements for faculty.

PATHOLOGY PHOTOGRAPHY AND IMAGING UNIT:

Mr. Mark Deming is the photographer assigned to this service. He is responsible for a variety of photography and imaging services including those requested by our clinical and research faculty and house officer staff.

SUMMARY OF FINANCIAL DATA:

1. Grants and Contracts:

225 active grants, contracts and other accounts

Total Direct Expenditures:	$ 6,981,980
Indirect Research Expenditures:	$ 2,693,743
Total Sponsored Projects:	$ 9,674,722

2. Faculty Group Practice Plan - Pathology:

Number of charge entries:	107,452
Gross Billings - Anatomic and Clinical Pathology:	$ 15,166,943
CDS Payment	$ 4,050,000
Part A Payment:	$ 2,572,000
M-Labs Net Transfer:	$ 786,000

3. Pathology Laboratories:

Number of billed tests reported to MECON:	2,499,487
Total Gross Revenue - Pathology Laboratories:	$142,026,778
Total Direct Expenses Pathology Laboratories:	$ 29,171,811

Respectfully submitted,

Eugene J. Napolitan
Administrator