

**THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL**

Department of Pathology

ANNUAL REPORT



1 JULY 1998 - 30 JUNE 1999

THE UNIVERSITY OF MICHIGAN

MEDICAL SCHOOL

Department of Pathology

ANNUAL REPORT



1 JULY 1997 - 30 JUNE 1998

LIST OF FACULTY

LIST OF FACULTY

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
Abell, Murray R	Professor Emeritus	The University of Michigan
Abrams, Gerald D.	Professor	The University of Michigan
Afify, Alaa M.	Clinical Assistant Professor	The University of Michigan
Al-Khafaji, Basim M.	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
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.	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 Professor**	Warner-Lambert; Parke Davis
Dressler, Gregory R.	Assistant Professor	The University of Michigan
Elnor, Victor M.	Associate 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	Adjunct 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

Department of Pathology Annual Report

<u>Name</u>	<u>Rank</u>	<u>Institutional Affiliation</u>
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.	Clinical Assistant Professor+++	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
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.	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.	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.	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	Clinical Assistant Professor	The University of Michigan

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

* Joint Appointment, Department of Internal Medicine

** Joint Appointment, Dental School

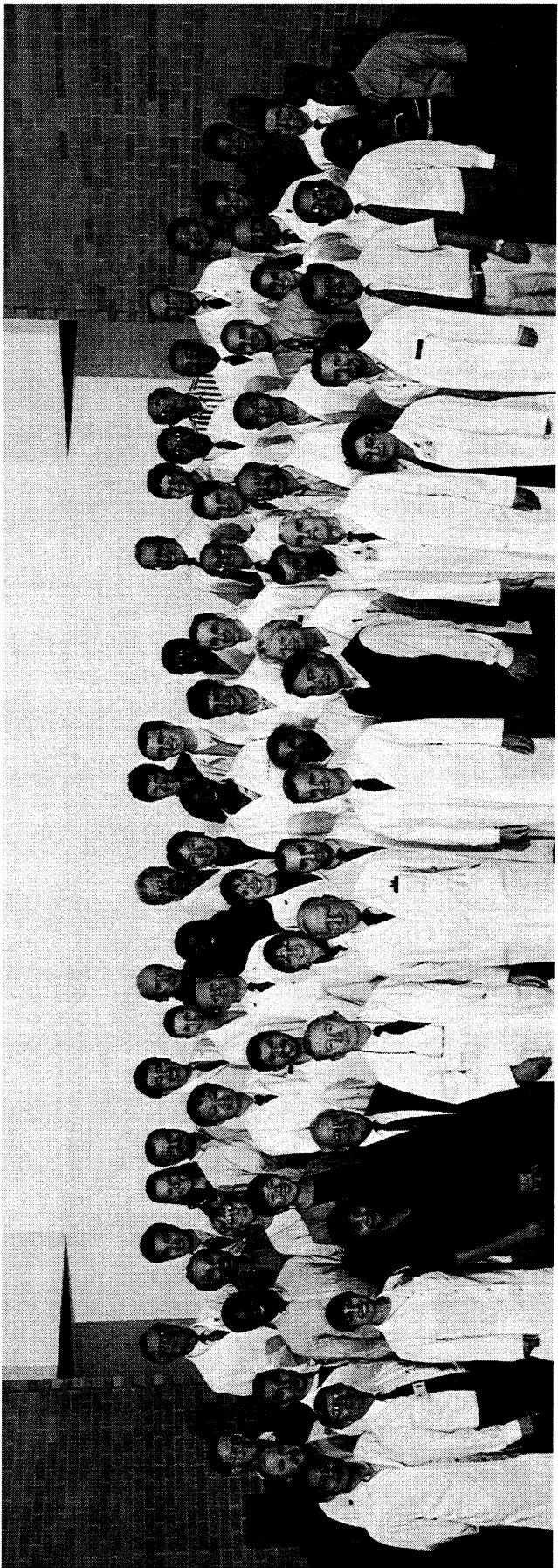
*** Clinical Appointment, Warner-Lambert, Parke Davis

+ 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, 1998

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DEPARTMENTAL OVERVIEW

**DEPARTMENTAL OVERVIEW
1998/1999**

Introduction

As described below, there has been a large influx of faculty into the Department, primarily involving replacements for open positions in Anatomic Pathology but also in response to greatly increased demands in diagnostic clinical areas (e.g. cytopathology and dermatopathology). Several of the new diagnostic faculty have also brought research expertise that has direct applications to surgical pathology. The dental/medical student teaching programs of the Department have been enhanced by development of websites that students have found to be very accessible and convenient. The research enterprise of the Department continues to be very healthy, with a continued emphasis on basic and clinically relevant mechanisms of inflammation, apoptosis and neoplasia. Federal funding for these programs continues to exceed projections. At the current time, the Department is undergoing Internal Review, which is being directed by Dr. Dan Remick. As has been the case for many years, the Department is short on space for faculty offices and for research laboratories. It should be noted that our research space has not increased for nearly 15 years in spite of very robust growth of the research enterprise of the Department. We continue to work actively with the Hospital to define options for relocation (out of the Pathology Building) of the Clinical laboratories.

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 five new students and graduating two students this past academic year. 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 two under-represented minorities. Graduates found desirable employment including fellowships at Johns Hopkins Hospitals and University of Minnesota as well as faculty positions at Ohio State University Hospitals, University of Michigan Hospitals and Piedmont Hospital in Atlanta, Georgia.

Clinical Service Activities

The Anatomic and Clinical Pathology Laboratories continue to provide excellent, full-spectrum service as the UMHS has continued to experience growth in ambulatory care activities and in several major clinical programs. Efforts continue to be directed toward the improvement of phlebotomy, central distribution and laboratory operations. Particular attention was directed toward improvement of compliance with the HCFA-mandated documentation rules. In 1998-99 the Laboratories performed more than 3 million laboratory analyses and more than 50,000 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) 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.

1998-99 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 fully 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 experienced in 1998-99. 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

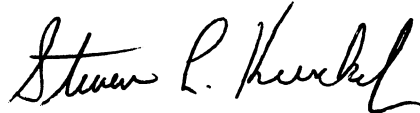
Research activities in the Department of Pathology remain a strong and active component of our academic mission. The faculty in the Department of Pathology continues to publish in highly visible, peer-reviewed scientific journals, attract numerous graduate and postdoctoral fellows from national and international 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 SCOR. 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 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Services - 4 1/2 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 - 6 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 - 4 contact hours.
- B. Sophomore Medical Class:
 - 1. Cardiovascular Sequence - Pathology Lab Coordinator.
 - 2. Musculo-skeletal Sequence - Pathology Lab Coordinator, lecturer - 2 contact hours.
 - 3. Pathology Lab Instructor - all sequences, 50 contact hours.
- C. Senior Medical Class:
 - 1. Clinical Radiology, Pathology Correlations, Elective Course, Co-coordinator, cardiovascular sequence.
- 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.
 - 3. Macy Summer Science Academy - 1 lecture hour.
- 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, 1998.
- I. Production of Teaching Materials:
 1. Development of website for Pathology 500.
 2. Development of website for Histopathology Lab.
- J. Continuing Medical Education
 1. Spring Family Practice Review, March 1999.

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. Effects of high intensity ultrasound on cardiac tissues, with A. Ludomirsky

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Member, Pathology House Officer Selection Committee

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

- A. Member, Historical Center for the Health Sciences Liaison Committee
- B. Member, Component I Committee
- C. Ombudsperson, Medical Faculty
- D. Member, Medical School Executive Committee
- E. Member, Sesquicentennial Celebration Committee
- F. Chair, Medical Affairs Advisory Committee

REGIONAL AND NATIONAL:

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

V. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Kim MH, Abrams GD, Pernicano PG, Eagle KA. Sudden death in a 55-year old woman with systemic lupus erythematosus. *Circulation* 98; 271-275, 1998.

**ALAA M. AFIFY, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998-30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Cytopathology sign-out (in-house Gynecologic & Non-gynecologic cases)-10 months.
- B. Sign-out transfer cytology cases (TC)- 5 months.
- C. Performance and interpretation of fine needle aspirates at Cancer Center Clinic- 5 months
- D. Rapid interpretation of fine needle aspirations performed by Clinicians and Radiologists- 5 months.
- E. Intradepartmental cytology consultations- 12 months.
- F. Evaluation of immunohistochemistry control slides-12 months.
- G. Necropathy Service: 4 weekends.

II. TEACHING ACTIVITIES:

- A. Residents and Cytopathology Fellow-12 months:
 - 1. Instruction in the evaluation, work-up and sign out of Gynecologic and Non-gynecologic cytopathology cases.
 - 2. Supervision and instructing in the performance, evaluation and interpretation of fine needle aspirates from patients at the Cancer Center Clinic.
 - 3. Supervision and instructing in the evaluation and interpretation of the assisted invasive deep-seated fine needle aspirates
- B. Interdepartmental teaching lectures:
 - 1. Didactic Cytopathology lectures and microscopic oriented teaching lectures (6/year).
 - 2. Cytotechnologists: Cytopathology Conferences.
 - 3. Immunohistochemistry laboratory technologists: weekly teaching sessions.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- 1. Endoscopic Ultrasound-Guided fine needle aspiration biopsy of the pancreas, clinicopathology correlation. In collaboration with the Gastroenterology Department at University of Michigan.
- 2. Expression of CD44 in mesothelioma and in adenocarcinoma in malignant cells obtained from body fluid cytologic specimen.
- 3. Hyaluronic acid in mesothelioma and in adenocarcinoma in malignant cells obtained from body fluid cytologic specimen. In collaboration with University of California in San Francisco.
- 4. Oncogenes expression in serous ovarian tumors. In collaboration with University of Cincinnati.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Immunohistochemistry laboratory, anatomic pathology laboratory.

V. PUBLICATIONS:

ARTICLES PUBLISHED IN REFERRED JOURNALS:

1. Afify AM, Davila RM. Pulmonary Fine Needle Aspiration Biopsy, the negative diagnosis. Acta Cytologica 1999;43:601-604.
2. Werness B, Afify AM, Bielat KL, Eltabbakh GH, Piver MS. Altered surface epithelium of ovaries removed prophylactically from women with a family history of ovarian cancer. Human Pathology 1999;30(2):151-157.
3. Mark HFL, Stephen B, Ci-Lin Sun, and Afify AM: Fluorescent in-situ hybridization detection of HER-2/neu gene amplification in rhabdomyosarcoma. Pathobiology 1998;66:59-63.
4. Quddus MR, Henley JD, Afify AM, Dardick I, Gnepp DR. Basal cell adenocarcinoma of the salivary gland: An ultrastructural and immunohistochemical study. Oral Surgery Oral Medicine Oral Pathology 1999;87:485-492.

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

SCIENTIFIC POSTERS/ABSTRACT PRESENTATIONS:

1. Afify AM, Werness BA, Mark HFL. Prevalence of HER-2/neu amplification and trisomy 8 In stage I And stage III ovarian papillary serous carcinomas. Poster Presentation at USCAP Meeting, 1999.
2. Afify AM, Davila RM, Allen H, Werness BA. Expression of CD44v5 is more common in Stage III than in Stage I ovarian carcinomas. Poster Presentation at USCAP Meeting, 1999.
3. Afify AM, Davila RM, Block AMW, Loree T, Werness BA. High rate of tetraploidy in the tall cell variant of papillary thyroid carcinoma. Poster Presentation at USCAP Meeting, 1999.
4. Michael CW, McConnell J, Afify AM, Al-Khafaji B, Pecott J. Comparison of the ThinPrep and AutoCyte Liquid Based Preparations in the non-gynecologic specimens. Poster Presentation at USCAP Meeting, 1999.
5. Werness B, Afify AM, Bielat KL, Eltabbakh GH, Piver MS. P53, c-erbB2 and Ki-67 expression in ovaries removed prophylactically from women with a family history of ovarian cancer. Platform Presentation at USCAP Meeting, 1999.
6. Afify AM and Mark HFL. Trisomy 8 and HER-2/neu oncogene amplification in rhabdomyosarcoma studied by FISH. Poster Presentation at The American Society of Human Genetics, 1998.
7. Afify AM, Mangala S, Mark HFL. Trisomy 8 in papillary serous carcinoma of the ovary studied by FISH. Annual Clinical Genetics Meeting, 1998.
8. Hsu P, Sun L, Afify AM, Mark HFL. Her2/neu oncogene amplification in ovarian cancer. Poster Presentation at The American Society of Human Genetics, 1998.

**BASIM AL-KHAFAJI, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Cytopathology { 10 months }
 - 1. Review & Signout of in-house cytology, Transfer cytology (TC), and intradepartmental cytology consultations. (Gynecologic & Non-Gyn).
 - 2. Performance of Fine Needle Aspiration (FNA), at Cancer Center Clinic, University Hospital, and Motts Children Hospital, to include rapid interpretation and assessment of FNAs performed by Clinicians and Radiologists (including CT, Ultrasound, Medical Procedures Unit, and outpatient clinics).
- B. Review & Signout of Genitourinary (TS) cases. { 1 month }
- C. Performance, review, and signout of Autopsies. { 4 weekends }

II. TEACHING ACTIVITIES:

- A. Cytopathology Fellow: {Full time }
 - 1. Microscopic sessions involving review of cytology preparations (Gyn & Non-Gyn).
 - 2. Supervision and instructing on performance of FNA.
 - 3. Supervision and instructing on rapid assessment of cytology preparations.
 - 4. Discussion and review of pertinent cytology literature with emphasis on diagnostic applications.
- B. Pathology Residents: {Full time }
 - 1. Introduction to the basic concepts of cytopathology through microscopic interaction.
 - 2. Instruction on FNA performance, and principles of cytopathology preparations.
- C. Medical Students: {2 months }
 - 1. Interaction through their pathology rotation with emphasis on explaining the role of cytopathology and its interaction with the other specialties.
- D. Interdepartmental teaching lectures to include:
 - 1. Didactic Cytopathology lectures directed towards the pathology fellows and pathology residents. {three sessions }
 - 2. Microscopic oriented teaching lectures involving the residents and fellows. {three sessions }
 - 3. Cytotechnologist cytologic/histologic correlation conference (two/year)

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

1. Assessment of Cytologic/Histologic correlation of Salivary gland Neoplasm, with emphasis on the role of the Thin Prep technique
2. Diagnostic utility of Image morphometry in the follow-up of patients with TCC
3. AGUS (Atypical glandular cells of undetermined significance), identifying cytologic parameters based on cytologic/histologic and clinical follow-up.
4. Development of Web based, and Multimedia tools for cytopathology teaching, and cytopathology intra and interdepartmental consultations.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

1. Cytopathology Division Quality assurance & control.
2. Cytopathology Fellowship Training

V. INVITED LECTURES/SEMINARS:

1. Lecturer “ FNA of Salivary Gland Neoplasms” Annual MLab symposium, Ann Arbor, MI, October 13,1998.

VI. ABSTRACTS:

1. Al-Khafaji, B., Pasco-Miller, L., Zhang H. Z., Katz, RL. Chromosomal Aberrations in Renal cell Carcinoma: A Diagnostic & Prognostic Role for Cytopathology. Acta Cytologica 42(5): 1217, 1998.
2. Michael CW, McConnell J, Afify A, Al-Khafaji B, Pecott J. Comparison of the ThinPrep and AutoCyte Liquid Based Preparations in nongynecological specimens. Mod Pathol;12:49A, 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Biochemistry Section, Clinical Pathology Laboratories.
- 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:

None

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Biochemistry Section, Clinical Pathology Laboratories.
- B. M-Labs Technical Group.
- C. Coordinator, Clinical Pathology Laboratory CME Program.
- D. Clinical Pathology Discretionary Incentive Funds Committee.

REGIONAL AND NATIONAL:

- A. Board of Directors, National Academy of Clinical Biochemistry.
- B. House of Delegates, American Association for Clinical Chemistry.
- C. Membership Committee, American Association for 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. Member, Academy of Clinical Laboratory Physicians and Scientists.
- G. Member, National Academy of Clinical Biochemistry.
- H. Member, Association of Clinical Scientists.
- I. Member, American Society for Mass Spectrometry.

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.

OTHER:

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Roberts, W.L., De, B.K., and Annesley, T.M.: Falsely increased immunoassay measurements of total and unbound phenytoin in critically ill uremic patients. Clin. Chem. 1999;45: 829-37.
- 2. De, B.K., Annesley, T.M., Juenke, J.M., Moulton, L., and Roberts, W.L.: Effects of diminished renal function on three immunoassay methods for free phenytoin measurement. Clin. Chem. 1999;45: A126-7.

BOOKS PUBLISHED:

- 1. Warner, A., and Annesley, T.M. (eds.): Standards of Laboratory Practice: Guidelines for Therapeutic Drug Monitoring Services. Franklin, TN: Durick Publishing Inc., 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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 and laboratory 2-4 hours per week
 - 2. Pathology 630 (dental) - one full class lectures.
 - 3. Senior Elective in Pathology: mentor, 4 weeks with daily conferences
- B. House Officers:
 - 1. Surgical pathology diagnosing room instruction for assigned house officer - 4 months
 - 2. Gastrointestinal and hepatic pathology tutoring - full time.
 - 3. Lectures in gastrointestinal and liver pathology, 2 hours
 - 4. Consult conferences, 4-5 hours
- 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, 4 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 effect of diet on recurrence rates of colonic adenomas, with Klaus Lewin (UCLA) and Arthur Schatzkin and others (National Cancer Institute, Chemoprevention Branch)
- C. 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.
- D. What gastric stromal tumors are always benign"? with Carolyn Misick and members of the pathology department at the Cleveland Clinic
- E. Lymphocyte colitis, a comprehensive clinical/endoscopic/histologic study, with Rachel Vidal and members of the division of Gastroenterology.

- F. Anaplastic, lymphoma-like carcinoma arising in Barrett's mucosa, with BJ McKenna, T Nazeer, and A del Rosario of Albany Medical Center
- G. 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. Member, Scientific Advisory Committee, 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. Ad hoc reviewer for Archives of Pathology and Laboratory Medicine, Cancer, Gastroenterology, Annals of Internal Medicine, and American Journal of Gastroenterology.
- H. Member of the Council, member of the Ad hoc Nominating Committee, member of the Young Investigator's Committee, United States and Canadian Academy of Pathology, Inc.

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". "Annoying gastrointestinal biopsies". Pathology Update for Practicing Pathologists: Recent Advances and Selected Topics. American Society of Clinical Pathologists course, Montreal Quebec, July, 22, 1998.
2. "Gastric polyps and neoplasms, including GISTs and carcinoma"; "The pathology of idiopathic inflammatory bowel disease"; "The role of the pathologist in the diagnosis and management of inflammatory bowel disease"; "Annoying gut biopsies"; "Neoplasms of the appendix and anus"; "What is wrong with this report?" Diagnostic Problems in Gastrointestinal Pathology, sponsored by Stanford University Medical Center, Hawaii, October 5-8, 1998.

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, Washington DC, October 21, 1998.
4. "Inflammatory fibroid polyp of the stomach" presented during the Slide Seminar on "Gastrointestinal polyps and polyposis, XXII International Congress of the International Academy of Pathology, Nice FR, October 22, 1998.
5. "The role of the pathologist in the diagnosis and management of inflammatory bowel diseases", presented during the Long Course: Inflammatory diseases of the gastrointestinal tract, Appelman HD and Dixon MF, co-directors, XXII International Congress of the International Academy of Pathology, Nice FR, October 23, 1998.
6. "Stromal tumors of the gastrointestinal tract", Department of Pathology and, Laboratory Medicine, Albany Medical College, Albany NY, December 3, 1998.
7. "The role of the pathologist in the diagnosis and management of inflammatory bowel diseases, especially the colitides." Allegheny University Hospitals, Pittsburgh, PA, March 17, 1999.
8. Inflammations of the Esophagus and Stomach. Pittsburgh Pathology Society, Pittsburgh, PA, March 17, 1999.
9. "Carcinomas at the junction: where is the cardia anyway?" Annual Scientific Meeting of the Gastrointestinal Pathology Society, San Francisco, CA, March 21, 1999.
10. "A nihilistic approach to the gastritides---does it really make a difference what we call them?" and "The pathologist's role in the diagnosis and management of the inflammatory bowel diseases, especially the colitides." Presented at the Eighteenth Annual Current Issues in Surgical Pathology, sponsored by the University of Texas Southwestern Medical School, Dallas, TX, May 13, 1999.
11. Half day course: "Neoplastic diseases of intestine", American Society of Clinical Pathologists, Scottsdale AZ, May 26, 1999.
12. "Annoying gastrointestinal biopsies" and "The role of the pathologist in the diagnosis and management of inflammatory bowel diseases." Presented at The Second Annual Current Issues in Anatomic Pathology-1999, sponsored by Stanford University and the University of California at San Francisco, San Francisco, May 29, 1999.
13. "Inflammations of the squamous esophagus", Department of Pathology and Laboratory Medicine, Albany Medical College, Albany, NY, June 10, 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. 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.
2. Kleer CG, Appelman HD. Ulcerative colitis: patterns of involvement in colorectal biopsies and changes with time. *Am J Surg Pathol*, 22:983-989, 1998.
3. Macdonald GA, Greenson JK, Saito K, Cherian S, Appelman HD, Boland CR. Microsatellite instability and loss of heterozygosity at DNA mismatch repair gene loci during hepatic carcinogenesis. *Hepatology*, 28:90-97, 1998.
4. Appelman HD, McKenna BJ. A "rose is a rose is a rose is a rose," but exactly what is a gastric adenocarcinoma? Guest Editorial, *J Surg Oncology*. 68:141-143, 1998.
5. Schoen RE, Corle D, Cranston L, Weissfeld JL, Lance P, Burt R, Iber F, Shike M, Kikendall JW,

- Hasson M, Lewin KJ, Appelman HD, et al. Is colonoscopy needed for the nonadvanced adenoma found on sigmoidoscopy? *Gastroenterol.* 115:533-541, 1998.
6. Appelman HD. Editorial: The Carney trial: a lesson in observation, creativity and perseverance. *Mayo Clin Proc* 74:638-640,1999.
 7. Tworek JA, Goldblum JR, Weiss SW, Greenson JK, Appelman HD. Stromal tumors of the abdominal colon: a clinicopathologic study of 20 cases. In press, *Am J Surg Pathol.*
 8. Tworek JA, Goldblum JR, Weiss SW, Greenson JK, Appelman HD. Stromal tumors of the anorectum: a clinicopathologic study of 22 cases. In press, *Am J Surg Pathol.*
 9. Kim B, Barnett JL, Kleer CG, Appelman HD. Endoscopic and histologic patchiness in treated ulcerative colitis. Accepted for publication, *Am J Gastroenterol.*

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, 1999.

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

1. Kim B, Barnett JL, Kleer CG, Appelman HD. Endoscopic and histologic patchiness in treated ulcerative colitis. *Am J Gastroenterol* 93:1691, 1998.
2. McKenna BJ, Appelman HD, del Rosario AD, et al. Anaplastic carcinoma of the esophagus resembling lymphoma, a Barrett's-associated tumor. *Mod Pathol* 12:80A, 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Diagnostic Electron Microscopy, Veterans Affairs Medical Center; Director of Electron Microscopy Center of Excellence.
- B. Cytopathology, Veterans Affairs Medical Center.
- C. 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.
- C. M2 Pathology Laboratory, Medical School

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 1998 - 30 JUNE 1999**

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.
- E. Coverage of muscle and nerve biopsies for MSU.

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 and fellows 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 – 8 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 Neurosurgery Department (Philip Kish, grant application submitted.)
- D. Genetic treatment of hemophilia in mice model, with Kotoku Kurachi's group in the Department of Genetics.
- E. Changes in limb muscle in patients with HTN & DM. With HTN Division of the Internal Medicine Department.
- F. Primary CNS vasculitis, with J. Trobe and A. Alrawi, Ophthalmology.

- G. Evaluation of temporal lobectomy/hippocampectomy cases with Erasmo Passaro, M.D., and the 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.
- J. Supervision of histology/immunohistochemistry projects for residents, fellows and researchers in Neurosurgery, Neurology and Neuroscience labs.

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.
- C. Improvements in immunoperoxidase stainings.

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. Invited lecture for Psychiatrists, Kalamazoo, MSU Campus.
- D. Invited lecture to Medical College of Ohio Neurology.
- E. Member, American Association of Neuropathologists, IAP, and AAN.
- F. Attended the meeting of American Association of Neuropathologists and VI European Neuropathology Congress with poster presentation.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Ross DA, Kish P, Muraszko KM, Speed G, Blaivas M, Strawderman M: Chemoprevention of ethylnitrosourea-induced rat gliomas by retinoic acid. *J of Neuro-Oncology*, 1998, 40:29-30.
2. Schuh LA, Henry TR, Fromes G, Blaivas M, Ross DA, Drury I: Epilepsy predisposition and outcome following anterior temporal lobectomy. *Archives of Neurology*, 1998, 55:1325-1328.
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. *European J. of Pulmonary Medicine*, 1998, 12:742-744.

4. 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. *J. Neurosurgery*, 1998, 89:200-205.
5. Mikhail AA, Yamini B, McKeever PE, Blaivas M: MIB-1 proliferation index predicts survival among patients with grade II astrocytoma. *J. Neuropathol. Exp. Neurol.*, 1999, 57:10-931-936.
6. Boulis NM, Bhatia V, Brindle TI, Holman HT, Krauss DJ, Blaivas M, Hoff JT: Adenoviral nerve growth factor and beta-galactosidase transfer to spinal cord: a behavioral and histological analysis. *J Neurosurgery*, 1999, 90:99-108.
7. Harrigan MR, Gebarski SS, Messe SR, Blaivas M, McGillicuddy JE: Metastatic adenocarcinoma to the brain mimicking hemorrhage: Case report. *Surgical Neurology*, 1999, 52:46-49.
8. Greenfield LA, Jr., Blaivas M, Drury I: Denovo status epilepticus due to multiple cerebral hamartomas. *Neurology*, 1999, 53:231-238.
9. Alrawi A, Trobe JD, Blaivas M, Musch DC: Brain biopsy in primary angiitis of the central nervous system. To: *Neurology*.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Pandit M, DeLance OL, Iyengar J, Blaivas M, Ashton-Miller JA: Development of techniques to quantify urethral nerve size and distribution: histological methods. To: *Neurology*.
2. Smith AG, Blaivas M, Russel JR, Urbanits S, Grisold W, Feldman EL: The clinical and pathologic features of focal myositis. To: *Neurology*.
3. Galasso JM, Stegman LD, Blaivas M, Harrison JK, Ross BD, Silverstein FS: Transplanted 9L gliosarcomas induce expression of the monocyte chemoattractant protein-1 receptor, CCR2, in rat brain. To: *J Neuropathol Exp Neurol*.

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

1. Blaivas M: Role of Neuropathologist is Neurologist Education. Presented at the 3rd EFNS Congress, Seville, Spain, September 19-25, 1998.
2. Carney PR, Blaivas M, Drury I: Histopathological findings in a familial form of medically refractory temporal lobe epilepsy. Presented at the American Epilepsy Society meeting in Fall 1998.
3. 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. Presented at the 27th annual meeting of the Child Neurology Society, October 22-24, 1998.
4. Gebarski SS, Blaivas M: Tentorial sinuses: patterns of venous occlusive disease. *Supplement to Radiology*, 1998, 209 (P): 787. Presented at the 84th Scientific Assembly and Annual Meeting of RSNA, November 4 – December 4, 1998, Chicago, IL.
5. Gebarski SS, Blaivas M: Five germinal matrices, not one: a unifying scheme for understanding migrational disorders. *Supplement to Radiology*, 1998, 209 (P):927. Presented at the 84th Scientific Assembly and Annual Meeting of RSNA, Nov 4 – Dec 4, 1998, Chicago, IL.
6. Blaivas M, Wald JJ: Key enzymes in histochemical diagnosis of subtle dermatomyositis. Presented at the VI European Congress of Neuropathology, Barcelona, Spain, May 5-8, 1999.

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7. Gebarski SS, Blaivas M: Adult primary brain neoplasms: the role of the germinal matrices. To be presented at RSNA 85th Scientific Assembly and Annual Meeting, 1999.
8. Pandit M, DeLancey JOL, Iyenger J, Blaivas M, Ashton-Miller J: Quantification of circular and longitudinal smooth muscle in the ventral wall of the female urethra. To be presented at the American Urogynecology Society fall meeting, 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology sign out – 6 months
- B. Director of Cytology with primary sign out responsibilities
 - 100% of Pap Smears
 - 75% of non-gynecological cases

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: Diagnosis of Non-gynecological cytology specimens by digital images sent over the Internet – Oklahoma VAMC.

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
- C. Ancillary Committee Chair
- D. Toledo VA Laboratory Director

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 1998 - 30 JUNE 1999**

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 (approx 300 cases/1998).
- C. Surgical/Frozen Section Diagnosis (approx 250 cases/1998)
- D. Surgical Case Diagnosis (4 months in 1998, approx. 1800 cases) Veterans Affairs Medical Center.
- E. Autopsy Service, rotational basis, on call 13 weeks/year (staffing 11 cases in 1998).
- F. Special Chemistry/Immunology, daily interpretation of protein electrophoreses, isoenzyme studies, and problem ligand studies (approx 900 cases/1998), Veterans Affairs Medical Center.
- G. 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. Medical Students, Pathology 600 laboratory (26 contact hours).
- C. Technologists, technicians and hospital staff, ongoing continuing medical education instruction on clinical laboratory topics.
- D. 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)
- D. Coinvestigator, Molecular Mechanisms of Lung Host Defense, VA REAP Grant (250,000 annually, 1998-2003).

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.
- E. Personnel employment and annual evaluations.
- F. Anatomic Pathology Quality Assurance evaluation and reporting
- G. Editor, VALabs 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

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. Ruth, J. H., Lukacs, N. W., Warmington, K.S., Polak, T.J., Burdick, M., Kunkel, S. L., Strieter, R. M., and Chensue, S. W.: Expression and participation of eotaxin during mycobacterial (type 1) and schistosomal (type 2) antigen-elicited granuloma formation. *J. Immunol.* 1998, 161:4276-4282.
2. Lukacs N.W., Hogaboam, C.M., Kunkel S.L., Chensue S.W., Burdick M.D., Evanoff H.L., Strieter R.M.: Mast cells produce ENA-78, which can function as a potent neutrophil chemoattractant during allergic airway inflammation. *J. Leuk. Biol.* 1998, 63:746-751.
3. Hogaboam, C.M., Steinhauser, M.L., Chensue, S.W., and Kunkel, S.L.: Novel roles for chemokines and fibroblasts in interstitial fibrosis. *Kidney Intl.* 1998, 54:2152-2159.
4. Kunkel, S.L. Lukacs, N.W., Strieter, R.M., Chensue, SW.: Animal models of granulomatous inflammation. [Review] *Seminars in Respiratory Infections* 1998, 13:221-228.
5. Hogaboam, C.M., Simpson, K.J., Chensue, S.W., Steinhauser, M.L., Luckacs, N.W., Gauldie, J., Strieter, R.M., and Kunkel, S.L. Macrophage inflammatory protein-2 gene therapy attenuates adenovirus- and acetaminophen-mediated hepatic injury. *Gene Therapy* 1999, 6:573-584.
6. Warmington, K.S., Boring L., Ruth, J.H., Sonstein, J., Hogaboam, C.M., Curtis, J.L., Kunkel, S.L., Charo, I.R. and Chensue, S.W.: Effect of C-C Chemokine Receptor 2 (CCR2) Knockout on Type-2 (Schistosomal Antigen-Elicited) Pulmonary Granuloma Formation: Analysis of Cellular Recruitment and Cytokine Responses. *Am. J. Pathol.* 1999, 154:1407-1416.
7. Chensue, S.W., Warmington, K.S., Allenspach, E.J., Lu, B., Gerard, C., Kunkel, S.L. and Lukacs, N.W.: Differential Expression and Crossregulatory Function of RANTES during Mycobacterial (Type-1) and Schistosomal (Type-2) Antigen-Elicited Granulomatous Inflammation. *J. Immunol.* 1999, 163:165-173.

BOOKS AND CHAPTERS IN BOOKS:

1. Kunkel, S.L., Lukacs, N.W., Strieter, R.M., and Chensue, S.W. The role of chemokines in the immunopathology of pulmonary disease. *In, FORUM Trends in Experimental and Clinical Medicine.* In press. 1999.

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

1. Chensue, S.W. Chemokine participation in types-1 and 2 pulmonary granulomatous inflammation. *Keystone Symposium-Type 2 Cytokines in Allergy and Helminth Infections.* January 9-15, 1999. Incline Village, Lake Tahoe, NV.
2. Chensue, S.W., Warmington, K.S., Lincoln, P., Evanoff, H., Kunkel, S.L. and Ruth, J.R. Multiparameter analysis of IL-4 and IL-13 participation in mycobacterial (type-1) and schistosomal (type-2) antigen-elicited granuloma formation. *FASEB J.* 1999, 13:A253.3

3. Bone-Larson, C.J., Hogaboam, C.M., Steinhauser, M.L., Lukacs, N.W., Strieter, R.M., Chensue, S.W. and Kunkel, S.L. The multiple protective roles of SCF in a murine model of fecal peritonitis. *FASEB J.* 1999, 13:A750.6.

**KATHLEEN CHO, M.D.
ASSOCIATE PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Gynecological pathology consultation services – five months.

II. TEACHING ACTIVITIES:

- A. Postdoctoral Fellows:
1. Responsible during the current academic year for the following:
a. Denise C. Connolly, Ph.D.
b. Rong Wu, M.D.
c. Donald Schwartz, Ph.D.
- B. Medical students (Work-Study):
1. Edward Chang
- C. House Officers:
1. Two consultation conferences
2. One didactic lecture on molecular biology of endometrial cancer
- Interdepartmental:
1. Multidisciplinary Gynecologic Oncology tumor board – one hour twice per month
- E. National:
1. Course Faculty: Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, The Given Institute, Aspen, Colorado.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Studies of the Molecular Pathogenesis of Cervical Cancer", NIH R29 CA64466 (50% effort), \$73,743 annual direct costs (\$350,000/five years), April 1, 1995 – March 31, 2000.
- B. Principal Investigator, "FHIT Gene Alterations in Cervical Cancer Pathogenesis", NIH RO1 CA81587 (30% effort), \$171,441 annual direct costs (\$482,884/three years), September 1, 1998 - August 31, 2001.
- C. Sponsor of postdoctoral fellow (Dr. Donald Schwartz) in the Cancer Biology Training Program, University of Michigan Comprehensive Cancer Center, NIH 5T32CA09676-08, salary support to commence July 1, 1999.

PENDING:

- A. U19 Program Project – “Toward A Molecular Classification of Tumors”, Project #2 Principal Investigator "Ovarian Tumors", (15% effort), \$106,887 Project #2 annual direct costs (\$570,372/five years), with S. Hanash, M.D., Ph.D., Principal Investigator.
- B. Coinvestigator – “CDX2 Tumor Suppressor Pathway Defects in Colon Cancer”, NIH RO1 CA82223 (10% effort), \$995,080/five years (requested direct costs). Principal Investigator: Eric Fearon, M.D., Ph.D.
- C. Coinvestigator – “The Role of β -catenin/Tcf Pathway Defects in Cancer”, NIH – number to be assigned (10% effort), \$1,000,000/five years (requested direct costs). Principal Investigator: Eric Fearon, M.D., Ph.D.

PROJECTS UNDER STUDY:

- A. Evaluation of loss of Fhit protein expression as a tumor progression and/or prognostic marker for cervical cancer.
- B. Identification and characterization of cellular genes differentially expressed in human keratinocytes with and without expression of human papillomavirus oncoproteins (E6 and E7).
- C. Molecular profiling of ovarian epithelial tumors using 2-D gel approaches and DNA microarray technologies.
- D. Identification and characterization of novel genes amplified in ovarian carcinomas.
- E. Characterization of genetic alterations in poorly differentiated (anaplastic) colorectal carcinomas.

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

- A. Member, Oral Biology and Medicine 1 Study Section, National Institutes of Health.
- B. Member, Special Emphasis Panel, National Cancer Institute (RFA CA-98-008) for SPORE in Ovarian Cancer. Silver Spring, Maryland, June 1999.
- C. Program Subcommittee Co-Chairperson, Organ Site-Specific Studies I: Preclinical Research, American Association for Cancer Research, 1999 Annual Meeting.
- D. Member, National Comprehensive Cancer Center Panel for establishment of endometrial and cervical cancer treatment guidelines, 1997-present.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Member, Editorial Board, Human Pathology
- B. Member, Editorial Board, International Journal of Gynecological Pathology
- C. Associate Editor, Clinical Cancer Research

- D. Consulting Reviewer for Science, Molecular and Cellular Biology, Journal of the National Cancer Institute, Journal of Clinical Investigation, Gynecologic Oncology, Cancer Research, American Journal of Pathology

INVITED LECTURES/SEMINARS:

1. Molecular Genetics of Gynecological Tumors. Molecular Biology in Clinical Oncology Workshop, American Association for Cancer Research, The Given Institute, Aspen, Colorado, July 1998.
2. 9th Annual Review Course on Gynecologic Oncology and Pathology. Lectures on "Fundamentals of Molecular Biology and Cancer Genetics", "Molecular Biology of Cervical Cancer" and "Molecular Biology of Endometrial Cancer". Kyoto, Japan, November 1998.
3. Hematology/Oncology Research Conference. "Studies on the Molecular Pathogenesis of Cervical Cancer". University of Alabama, Birmingham, Alabama, April, 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Katabuchi, H., Tashiro, H., Cho, K.R., Kurman, R.J., and Hedrick, L. Micropapillary Serous Carcinoma of the Ovary: An Immunohistochemical and Mutational Analysis of p53. International Journal of Gynecological Pathology 17:54-60, 1998.
2. Kendall, B.S., Ronnett, B.M., Isacson, C., Cho, K.R., Hedrick, L., Diener-West, M., and Kurman, R.J. Reproducibility of the diagnosis of endometrial hyperplasia, atypical hyperplasia, and well differentiated carcinoma. American Journal of Surgical Pathology 22:1012-1019, 1998.
3. Geng, L., Connolly, D.C., Isacson, C., Ronnett, B.M., and Cho, K.R. Atypical Immature Metaplasia (AIM) of the Cervix: Is It Related to High Grade Squamous Intraepithelial Lesion (HSIL)? Human Pathology 30:345-51, 1999.
4. Szych, C., Staebler, A., Connolly, D.C., Wu, R., Cho, K.R., and Ronnett, B.M. Molecular Genetic Evidence Supporting the Appendiceal Origin of Pseudomyxoma Peritonei in Women. American Journal of Pathology 154:1849-55, 1999.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Wu, R., Connolly, D.C., Ren, X., Fearon, E.R., and Cho, K.R. Somatic Mutations of the *PPP2R1B* Candidate Tumor Suppressor Gene at Chromosome 11q23 are Infrequent in Ovarian Carcinomas. Submitted.
2. Wu, R., Connolly, D.C., and Cho, K.R. Restoration of Fhit Expression Does Not Suppress Growth or Tumorigenicity of Cervical Carcinoma Cells. Submitted.
3. Connolly, D.C., Katabuchi, H., Scully, R.E., Cliby, W.A., Lei, R.Y., and Cho, K.R. Absence of STK11/LKB1 Gene Mutations in Sporadic Forms of Rare Tumor Types Associated with Peutz-Jeghers Syndrome (in preparation).

BOOKS/CHAPTERS IN BOOKS:

1. Cho, K.R. Cervical Cancer. The Genetic Basis of Human Cancer, eds. B. Vogelstein and K. Kinzler, McGraw-Hill, Inc., New York, New York, 1998.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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. Plan and present Dementia Brain Cutting Conference for house officers, students and faculty, 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 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.
- C. 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.
- D. Teach laboratory techniques and basic neuroanatomy and neuropathology to our laboratory technologist (MADRC).

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. The Pathologic Examination of Human Autopsy Brains From Patients With Clinical Diagnosis of Alzheimer's, Huntington's, Pick's and Other Dementing Diseases is being

done in collaboration with Drs. Roger Albin, Sid Gilman, and Norman Foster 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. Kluin, K.J., Gilman, S., Foster, N.L., Sima, A.A.F., D'Amato, C.J., et al: Neuropathologic correlates of dysarthria in progressive supranuclear palsy. Submitted to *Neurology*, May, 1999.
2. Dickson, D.W., Liu, W.K., Hardy, J., Farrer, M., Mehta, N., Utti, R., Mark, M., Zimmerman, T., Golbe, L., Sage, J., D'Amato, C.J., et al: Widespread alterations in alpha-synuclein in multiple system atrophy. Submitted for publication, 1999.

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

1. O'Shea, K.S., Alton, S., D'Amato, C.J., Gratsch, T.E.: Embryonic stem cell derived neuroepithelial progenitor cells. Society for Neuroscience, October, 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Associate Medical Director, Blood Bank and Transfusion Service, University of Michigan Hospitals.

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.
- D. Thoracic Surgery Teaching Conference: "Blood Transfusion".
- E. Clinical Pathology Grand Rounds: "Adverse Responses to Transfusion".
- F. Invited lecture: "Options for Transfusion", Michigan Association of Blood Banks.
- G. Invited Lecture: "Transfusion Reactions", Teleconference Network of Texas.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "A Murine Model of Hemolytic Transfusion Reactions", National Blood Foundation.
- B. Principal Investigator, "Postmarketing Pharmacovigilance of SD-Plasma", V. I Technologies, Inc.

PROJECTS UNDER STUDY:

- A. Cytokine production in hemolytic transfusion reactions.
- B. Mechanisms of action of leukoreduction filters.
- C. Mechanisms of hypotensive transfusion reactions.
- D. Value of autologous blood donation.
- E. Isoagglutinin-depleted plasma.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Transfusion Committee.

V. OTHER RELEVANT ACTIVITIES:

- A. President, 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. Medical Advisory Committee, American Red Cross Southeastern Michigan Region.
- F. Editorial Board, Transfusion.
- G. Reviewer, Transfusion.
- H. Reviewer, Chest.
- I. Reviewer, American Journal of Clinical Pathology.
- J. 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.
2. Judd WJ, Fullen DR, Steiner EA, Davenport R, Knafl PC. Revisiting the issue: can the reading for serologic reactivity following 37°C incubation be omitted? Transfusion 39:295-9, 1999.

ABSTRACTS, AND PRESENTED PAPERS:

1. Davenport R, Haddock T, Penezina O, Fomovskaia G: L-selectin expression on peripheral blood leukocytes over 48 hr. in stored blood. Transfusion 38:17S, 1998.

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 PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998-30 JUNE 1999**

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. Research activities 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 Mellon University, Pittsburgh, PA

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Editorial Board Member, Drug Metabolism Reviews

INVITED LECTURES/SEMINARS:

1. Cardiac Enlargement and Cellular Proliferation Induced in B6C3F1 Mice by Troglitazone. Proceedings, Keystone Symposium, Molecular Biology of the Cardiovascular System Angiogenesis and Remodeling. Steamboat Springs, CO, March 1998.
2. Pancreatic Acinar Cell Tumors in Wistar Rats Treated with Tacrine, A Cognition Activator, for 104 Weeks. Society of Toxicology, New Orleans, LA, March 1999.
3. Phenotypic and Genotypic Variation in Serum Lipid Parameters in Cynomolgus Monkeys. Society of Toxicology, New Orleans, LA, March 1999.
4. High-Throughput Genotyping for Single Nucleotide Polymorphism Detection in NAD(P)H-Quinone Oxidoreductase (DT-Diaphorase) using Taqman Probes. Experimental Biology Conference, Washington DC, April 1998.
5. High-Throughput Genotyping Method for Glutathione S-Transferase Theta and Mu Gene Deletion Using Taqman Probes. Experimental Biology Conference, Washington DC, April 1998.
6. Ex Vivo Functional Assessment of Mitochondrial Transmembrane Potential from Lean and Diabetic Zucker Rats with or without Troglitazone. American Diabetes Association - 59th Scientific Sessions, San Diego, CA, June 1999

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. 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.(Toxicol. Pathol. In press, 1999)
2. 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.
3. 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.
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.* 19:31-38, 1999
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. *Tox. Appl. Pharm.* 156, 106-112 (1999).
 6. S. J. Bulera, J.C. Theiss, T. A. Festerling and F.A. de la Iglesia. In Vitro Photogenotoxic Activity of Clinafloxacin: A Paradigm Predicting Photocarcinogenicity. *Tox. Appl. Pharm.* 156, 222-230 (1999).
 7. D.R. Plymale, J.R. Haskins and F.A. de la Iglesia. Monitoring simultaneous subcellular events in vitro by means of coherent multiprobe fluorescence. *Nature Medicine.* 5: 351-355,1999.
 8. M. Shi, S. Myrand, F.de la Iglesia and M. Bleavins. High Throughput Genotyping for the Detection of Single Nucleotide Polymorphism in NAD(p)H-Quinone Oxidoreductase (DT-Diaphorase) Using TaqMan Probes. *Mol. Path.* 1999 (In press).
 9. S.K. Duddy, S.M. Gorospe, J.M. Bleavins, F.A. de la Iglesia. Spontaneous and Thiazolidinedione-Associated B6C3F1 Mouse Hemangiosarcomas Exhibit Low *ras* Oncogene Mutation Frequencies *Tox. Appl. Pharm.* (In Press) 1999.

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 1999).
2. 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 Methylation Pattern and Genomic Instability in the Pancreas of Rats Fed Soybean Diets and Gabapentin. (Submitted)
3. 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)
4. G. Feuer, M.S.I. Dhami, and F.A. de la Iglesia. Changes by Progesterone Derivatives in Fatty Acids from Phosphatidylcholine and Phosphatidylethanolamine Fractions in Rat Liver Endoplasmic Exp. *Toxicol. Path.* (Submitted)
5. E.J. McGuire and F.A. de la Iglesia Hypolipidemic. Effects on Rat Liver Mitochondria Studied by Quantitative Microscopy. *Human Exper. Toxicol.* (Submitted)
6. M.M. Shi, Myrand, S., Bleavins, M.R. and F.A. de la Iglesia. High Throughput Genotyping for the Detection of Single Nucleotide Polymorphism in NAD(P)H-Quinone Reductase (DT-Diaphorase) Using TaqMan Probes. *Mol. Pathol* (submitted 1999).
7. M.M. Shi, Myrand, S., Bleavins, M.R. and F.A. de la Iglesia. Genotyping for the Functionally Important Human CYPD6*4 (B) Mutation Using TaqMan Probes. *Mol. Pathol. Protocols.* (Submitted 1999).
8. M.M. Shi, Bleavins, M.R. and F.A. de la Iglesia. Technologies for Detecting Genetic Polymorphisms in Pharmacogenomics. (Submitted, 1999).
9. H. Masuda, M.J. Adams, R.C. Secker, E. J. McGuire, J.R. Herman, D. Bailey and F.A. de la Iglesia. Reproductive Toxicology Studies with the Thiazolidindione Antidiabetic Agent Troglitazone. *J. Tox. Sci.* (Submitted, 1999)

10. L. Dethloff, B. Barr, L. Bestervelt, S. Bulera, R. Sigler, M. LaGattuta and F.A. de la Iglesia. Gabapentin-Induced Mitogenic Activity in Rat Pancreatic Acinar Cells. *Pancreas* (Submitted, 1999)

BOOKS/CHAPTERS IN BOOKS:

1. 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.) M. Dekker Publ., New York, (3) 81-107, 1999.
2. F.A. de la Iglesia. Approaches to Understanding Species Differences in Hepatotoxic Responses to Therapeutic Agents. *Proceedings Annual 25th Meeting, Japanese Society of Toxicology*. p1-5, 1998.

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

1. L.A. Dethloff and F.A. de la Iglesia. Chemically-Induced Ploidy Changes. *Letter to the Editor. Tox. Appl. Pharm.* 150: 443, 1998.
2. M.A. Breider, A. W. Gough, J. Haskins, F.A. de la Iglesia. Cardiac Enlargement and Cellular Proliferation Induced in B6C3F1 Mice by Troglitazone. *Proceedings, Keystone Symposium. Molecular Biology of the Cardiovascular System: Angiogenesis and Remodeling*, page 41, 1998.
3. M. Shi, S. Myrand, M. Bleavins, F. de la Iglesia. High-Throughput Genotyping for Single Nucleotide Polymorphism Detection in NAD(P)H-Quinone Oxidoreductase (DT-Diaphorase) Using Taqman Probes. *FASEB Journal* 13: A426, 1999.
4. M. Shi, S. Myrand, M. Bleavins, F. de la Iglesia. High-Throughput Genotyping Method for Glutathione S-Transferase Theta and Mu Gene Deletion Using Taqman Probes. *FASEB Journal* 13: A812, 1999.
5. J.R. Haskins, J.H. Johnson, F. A. de la Iglesia. Ex Vivo Functional Assessment of Mitochondrial Transmembrane Potential from Lean and Diabetic Zucker Rats with or without Troglitazone. *American Diabetes Association - 59th Scientific Session. Diabetes* 48 (suppl. 1) A262, 1999.
6. Z. Wojcinski, L. Lillie, N. Gragtmans, R. Walker, D. Welty, J. Herman, F. de la Iglesia. Pancreatic Acinar Cell Tumors in Wistar Rats Treated with Tacrine, a Cognition Activator for 104-Weeks. *Toxicol. Sci.* 48: 320, 1999.
7. D. Robertson, T. Gipson, W. Tefera, S. Knight, M. Bleavins, F. de la Iglesia. Phenotypic and Genotypic Variation in Serum Lipid Parameters in Cynomolgus Monkeys. *Toxicol. Sci.* 48: 271, 1999.
8. S.J. Bulera, J.C. Theiss, T.A. Festerling and F. de la Iglesia. In Vitro Photogenotoxic Activity of Clinafloxacin: A Paradigm Predicting Photocarcinogenicity. *Toxicol. Sci.* 48: 122, 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Rotation Students Supervised - Martin Powers, MSTP; Jingmei Lin, Dept. of Pathology
- B. Post-doctoral Trainees Supervised - Mark Lechner, Ph.D.; Eun Ah Cho, Ph.D.; Yi Cai, M.D., Ph.D.
- C. Ph. D. Thesis Committee Member - Laura Post, Dept. of Genetics; Kris Coulter, Dept. of Genetics. Hoonkyo Soo, Dept. of Genetics.

MEDICAL SCHOOL/HOSPITALS:

- A. Second Year Medical Students - Renal Section, one full lecture

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, Howard Hughes Medical Institute - 001819, "Analysis of Mammalian Developmental Control Genes", (50%), October 1, 1994- December 31, 1998.
- B. Principal Investigator, "PAX-2 in Normal and Cystic Epithelium Development", NIH/NIDDK R01 DK51043-02, (20%); September 30, 1995-August 31, 2000. Direct costs approximately \$90,000 requested annually.
- C. Principal Investigator, "Cell Migration, Chemoattraction and the RET/GDNF Pathway", NIH/NIDDK. 1 R01 DK54723-01 (30% effort), 1/1/99 - 12/31/03, Annual Direct Costs \$158,840.
- D. Principal Investigator, "PAX2 Interacting Proteins in Development and Disease", NIH/NIDDK 1 R01 DK54740-01 (30% effort), 1/1/99 - 12/31/02, Annual Direct Costs \$158,840.
- E. Principal Investigator, Project #3 (20% effort), "Functional Analysis of RET Signaling in Renal Epithelial Cells", NIH/NIDDK, 2 P50 DK39255-11A1, O' Brien Renal Center Grant, "Mechanisms of Glomerular and Tubular Injury", Dr. Roger C. Wiggins, PI. 9/1/98 - 8/31/03, \$76,066 Initial Budget Period.

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.
- E. Wnt and Frizzled signaling in the developing kidney

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Dept. of Pathology - Preliminary Exam Committee, Curriculum Committee
- B. Center for Organogenesis - Interim Co-Director, Steering Committee, Training Grant Review Committee, Advisory Committee, Seminar Committee (Chair)
- C. Program in Biomedical Sciences (PIBS) - Admissions Committee

REGIONAL AND NATIONAL:

- A. NIH Study Section, General Medicine B, Ad-hoc reviewer
- B. NIDDK, Renal Program Project Grants, Site visit reviewer
- C. American Journal of Physiology, Editorial Reviews Board
- D. 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, Science, International Journal of Developmental Biology, Kidney International

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. Lecturer/Teacher, "Experimental Genetics of the Laboratory Mouse", The Jackson Labs, Bar Harbor, ME, 8/23/98-9/2/98
2. HHMI Annual Meeting, Chevy Chase, MD, 10/98.
3. 23rd Annual Argenteuil Symposium, Princess Lillian Foundation, "Kidney Development has Clinical Impact", Brussels, Belgium, 10/26/98-10/27/98.
4. Dept. of Biochemistry, LSU Medical Center, New Orleans, LA, 3/8/99.
5. Dept. of Anatomy, University of Kansas Medical School, Kansas City, KS, 4/22/99.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Leavey, S.F., Arend, L.J., Dare, H., Dressler, G.R., Briggs, J.P. and Margolis, B.L. (1998) Expression of Grb7 growth factor receptor signaling protein in kidney development and in the adult kidney. *Am. J. Physiol.* 275, F770-F776.
2. 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.
3. Cho, E.A. and Dressler, G.R. (1998) Mouse Tcf-4 binds • -catenin and is expressed in distinct regions of the developing brain and limbs. *Mech. Develop.* 77, 9-18.
4. Tang, M.J., Worley, D., Sanicola, M. and Dressler, G.R. (1998) The RET-Glial Cell-derived Neurotrophic Factor (GDNF) pathway stimulates migration and chemoattraction of epithelial cells. *J. Cell Biol.* 142, 1337-1345.
5. Weiss, J.B., Von Ohlen, T., Mellerick, D.M., Dressler, G., Doe, C.Q. and Scott, M.P. (1998). Dorsoroventral patterning in the Drosophila central nervous system: the intermediate neuroblasts defective homeobox gene specifies intermediate column identity. *Genes & Dev.* 12, 3591-3602.
6. Yang, Y., Jeanpierre, C., Dressler, G.R., Lacoste, M., Niaudet, P. and Gubler, M.-C. (1999) WT1 and Pax-2 podocyte expression in Denys-Drash syndrome and isolated diffuse mesangial sclerosis. *Am J. Pathol* 154, 181-192.
7. Dressler, G.R. (1999) Kidney development branches out. *Dev. Genetics* 24, 189-193.
8. Schwarz, M., Alvarez-Bolado, G., Dressler, G., Urbanek, P., Busslinger, M., and Gruss, P. (1999) Pax2/5 and Pax6 subdivide the early neural tube into three domains. *Mech. Dev.* 82, 29-39
9. Dressler, G. R. and Woolf, A. S. (1999) Pax2 in development and renal disease. *Int. J. Dev. Biol.* In press.

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lechner, M.S. and Dressler, G.R. (1999) PTIP: A novel BRCT-domain protein interacts with the Pax family of transcription factors.
2. Mah, S.P., Saueressig, H., Goulding, M., Kintner, C., and Dressler, G.R. (1999) Regulation of the mesenchyme-epithelial transition during mouse kidney development by Cadherin-6.

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 1998 - 30 JUNE 1999**

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.: 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 collaboration with Dr. Flinn, 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). We have developed an enzyme immunoassay for glycopyrrolate that is

capable of measuring this drug in serum at the level of 0.5 ng/ml and are currently processing samples collected in a pharmacokinetic study involving 36 patients.

- E. University of Michigan: Daniel S. McConnell, Ph.D., A.Rees Midgley, M.D., Samir Hanash, M.D., Ph.D., Dean Brenner, M.D., Anthony Killeen, M.D., Ph.D., Donald Giacherio, Ph.D., and Cyrenius M. Jone, Ph.D.: The discovery, measurement and clinical evaluation of cancer biomarkers are the goals of this collaborative study. We recently submitted a proposal, in response to a request for proposal from the National Cancer Institute, to develop a laboratory for the analysis of new cancer biomarkers obtained through discovery in Biomarkers Development Laboratories associated with a proposed U24 Cooperative Agreement. The Cooperative Agreement is expected to establish a national Network for the development, evaluation, and validation of biomarkers for early cancer detection and risk assessment. We will develop automated, high quality assays for the analysis of biomarkers provided by the Biomarkers Development Laboratories, and will provide participating Clinical/Epidemiological Centers with assistance, service, and state-of-the-art assays for cancer detection.

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. Nunnery M*, Zizzi T, Tucci M, Cason Z, Benghuzzi H, and England BG: Fertility Regulation of Femal Rats Exposed to Sustained Delivery of Dehydroepiandrosterone Independently or in Combination with Estrogen by Means of TCPL Delivery Devices. *Biomed. Sciences Instrumentation* 35: 79-84, 1999.
2. Cason Z. Tucci M. England BG. Benghuzzi H: TCPL Delivery Devices: Endometrial Changes Associated with Exogenous Sustained Release of Ovarian Hormones. *Biomed. Sciences Instrumentation* 35:205-210, 1999.
3. Flinn M. Baerwald C. Decker S. England BG. Evolutionary Functions Of Neuroendocrine Response To Social Environment. *Behavioral & Brain Sciences*. 21(3):372, 1998.
4. Flinn MV, DV Leone & BG England. Fluctuating asymmetry, stress, and health among children in a Caribbean village. *American Journal of Physical Anthropology Supplement* 27:103-104, 1999.

5. Kaplan JS. Iqbal S. England BG. Zawacki CM. Herman WH. Is pregnancy in diabetic women associated with folate deficiency? *Diabetes Care*. 22(7): 1017-1021, 1999.
6. Bagavandoss P. England B. Asirvatham A. Bruot BC. Transient Induction Of Polycystic Ovary-Like Syndrome In Immature Hypothyroid Rats. *Proceedings of the Society for Experimental Biology & Medicine*. 219(1): 77-84, 1998 Oct.

ABSTRACTS AND PAPERS AT MEETINGS:

1. Nunnery M. Zizzi T. Tucci M. Cason Z. Benghuzzi H. England BG: The Effect of Sustained Delivery of Dehydroepiandrosterone Independently or in Combination with Estrogen on the Reproductive and Vital Organs of Adult Female Rats. *Journal of Mississippi Academy of Sciences Annual Meeting, Tupelo, MS, February 25-26, 1999.*
2. Cason Z, Tucci M, England BG, and Benghuzzi H: TCPL Delivery Devices: Endometrial Changes Associated with Exogenous Sustained Release of Ovarian Hormones, Abstract accepted for presentation and invited for full-length manuscript submission at the 36th annual Rocky Mountain Bioengineering Symposium and 36th International ISA Biomedical Sciences Instrumentation Symposium, Copper Mountain, CO, April 16-18, 1999.
3. Nunnery M, Zizzi T, Tucci M, Cason Z, Benghuzzi H, and England BG: Fertility Regulation of Femal Rats Exposed to Sustained Delivery of Dehydroepiandrosterone Independently or in Combination with Estrogen by Means of TCPL Delivery Devices. Abstract accepted for presentation and invited for full-length manuscript submission at the 36th annual Rocky Mountain Bioengineering Symposium and 36th International ISA Biomedical Sciences Instrumentation Symposium, Copper Mountain, CO, April 16-18, 1999.
4. Benghuzzi H, Puckett A, Tucci M, Tsao A, and England BG: Estradiol TCP Delivery System and the Regulation of Fertility in Males. *Rocky Mountain Bioengineering Symposium 36th and 36th International ISA Biomedical Sciences Instrumentation Symposium, Providence, RI, April 28-May 2, 1999.*
5. Benghuzzi H, Possley R, and England BG: The Use of TCPL Delivery System to Mimic the Ovarian Cycle in Ewes, *Transaction, Published and presented at 25th Annual Meeting of the Society for Biomaterials, Rhode Island, Providence, April 22-26, 1999.*
6. Benghuzzi H, Puckett A, Tucci M, Tsao A, and England BG: The Use of Estradiol TCPL Delivery System to Regulate Fertility in Males, *Transaction, Published and presented at 25th Annual Meeting of the Society for Biomaterials, Rhode Island, Providence, April 22-26, 1999.*
7. Flinn MV, Leone DV, and England BG, Fluctuating asymmetry, stress, and health among children in a Caribbean village. *American Association of Physical Anthropologists Annual Meeting, Columbus OH, April, 29, 1999.*
8. Flinn MV and England BG, Family environment, health and stress responses in children. Keynote talk for "Stress responses in infants and children" Conference at Children's Hospital, University of Utrecht, Netherlands, March 4, 1999

ARTICLES SUBMITTED TO REFEREED JOURNALS:

1. Growth and fluctuating asymmetry of stepchildren. Flinn MV, McClusky F, and England BG, submitted to *Evolution and Human Behavior*.
2. Health and psychological development of stepchildren. Flinn MV, McClusky F, and England BG, submitted to *Evolution and Human Behavior*.

3. Ensuring reliability of assay results in a large, longitudinal, multiethnic, multicenter, cooperative study of the menopausal transition. Midgley AR, McConnell DS, England BG, et al. Submitted to *Clinical Chemistry*.
4. Serum thyroglobulin levels in patients with low risk papillary thyroid carcinoma. Sisson JC, England BG, et al. Submitted to *Thyroid*.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Autopsy Service.

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator, "Pulmonary Immune Responses to Inhaled Pathogens". NIH-R)1-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.
- C. Assessment of Professional Values in Medical Student Education

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 for 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.
- I. Medical School Strategic Planning Committee.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

- 1. Invited speaker: Workshop on Medical Curriculum Reform, NYU Medical School, N.Y. 1999.
- 2. Invited speaker: Plenary Session on Professional Development in Medical Education, AAMC, Washington, D.C., 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

- 1. 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.
- 2. 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*, 1998, 1998: S31-34.
- 3. 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*, 1998, 53: 124-127.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998- 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Medical Director, 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. Medical Students:
 - 1. M-2 Hematology Sequence: Section leader for laboratory sessions (4 hours).
 - 2. M-2 Hematology Sequence: Administered practical examination (2 hours).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None.

PROJECTS UNDER STUDY:

- A. Adhesion molecule expression in B-cell lymphoproliferative disorders.
- B. Prognostic significance of CD10 expression in large cell lymphoma.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Medical Director, Diagnostic Hematology Laboratory.
- B. Clinical Pathology Resident Training.
- C. Interviewer of residency candidates.

REGIONAL/NATIONAL:

- A. Editorial Board, Cytometry (Communications in Clinical Cytometry).
- B. Manuscript reviewer, Human Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. "Lymphadenopathy Associated with Reactive Processes and its Clinical Significance." Teleconference Network of Texas, August 18, 1998.
- 2. "Hematopathology as a Model for the Integration of Laboratory Medicine with Clinical Practice." 17th Annual Symposium on Automated Information Management in the Clinical Laboratory, Ann Arbor, Michigan, May 28, 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Finn WG, Peterson LC, James C, Goolsby CL: Enhanced detection of malignant lymphoma in cerebrospinal fluid by multiparameter flow cytometry. *Am J Clin Pathol* 110:341-346, 1998.
- 2. 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* 59:223-229, 1998.
- 3. Huang JC, Finn WG, Variakojis D, Goolsby CL, Peterson LC: CD5 negative small B-cell leukemias are rarely classifiable as chronic lymphocytic leukemia. *Am J Clin Pathol* 111:123-130, 1999.
- 4. 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. *Mod Pathol* 12(3):295-300, 1999.
- 5. Pooley Jr. RJ, Peterson L, Finn WG, Sharma B, Kroft S: Cytomegalovirus-infected cells in routinely prepared peripheral blood films of immunosuppressed patients. *Am J Clin Pathol* 112:108-112, 1999.
- 6. Kroft SH, Finn WG, Schnitzer B, Dawson DB, Singleton TP, Ross CW: Precursor B-lymphoblastic transformation of grade I follicle center lymphoma. *Am J Clin Pathol* (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

None

BOOKS AND CHAPTERS IN BOOKS:

1. Finn WG, Kroft SH: New classifications for non-Hodgkin's lymphoma. In: Diagnostic and Therapeutic Advances in Hematologic Malignancies. Tallman MS, Gordon LI, eds. Boston, MA: Kluwer Academic Publishers, 1999:1-26.

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

1. Padmore RF, Finn WG, Singleton TP, Ross CW, Schnitzer B: Fascin expression in immunophenotypic variants of classical Hodgkin's disease. Poster presentation, United States and Canadian Academy of Pathology annual meeting, 1999. Lab Invest 1999; 80:144A. Mod Pathol 1999; 12(1): 144A.
2. Valdez R, Kroft SH, Schnitzer B, Ross CW, Singleton TP, Peterson LC, Finn WG: Cerebrospinal fluid (CSF) involvement by mantle cell lymphoma. Poster presentation, United States and Canadian Academy of Pathology annual meeting, 1999. Lab Invest 1999; 80:147A. Mod Pathol 1999; 12(1): 147A.
3. Finn WG, Sheldon S, Ross CW, Singleton TP, Schnitzer B: Philadelphia chromosome-positive acute lymphoblastic leukemia (CLL). Accepted for presentation. 2nd Joint Meeting, Society for Hematopathology and European Association of Hematopathology, Barcelona, Spain, September 1999.
4. Petricek C, Ross CW, Graham DM, Singleton TP, Finn WG, Schnitzer B: Grade II nodular sclerosis Hodgkin's lymphoma with rapid recurrence of widespread refractory disease after therapy. Accepted for presentation. 2nd Joint Meeting, Society for Hematopathology and European Association of Hematopathology, Barcelona, Spain, September 1999.
5. Valdez R, Petricek CM, Finn WG, Singleton TP, Ross CW, Schnitzer B: Simultaneous occurrence of nodular lymphocyte predominant Hodgkin's disease and large cell non-Hodgkin's lymphoma. Accepted for presentation. 2nd Joint Meeting, Society for Hematopathology and European Association of Hematopathology, Barcelona, Spain, September 1999.
6. Schnitzer B, Singleton TP, Ross CW, Sheldon S, Finn WG: Extramedullary myeloid cell tumor of differentiated monocytic cells followed by development of acute myelogenous leukemia, FAB M5b. Accepted for presentation. 2nd Joint Meeting, Society for Hematopathology and European Association of Hematopathology, Barcelona, Spain, September 1999.
7. Bavikatty NR, Finn WG, Schnitzer B, Ross CW, Singleton TP: Expression of CD99 and terminal deoxynucleotidyl transferase in acute myeloid leukemia. Accepted for presentation to American Society of Clinical Pathologists Fall Meeting, New Orleans LA, September 1999. Am J Clin Pathol 1999 (in press).
8. Bavikatty NR, Ross CW, Finn WG, Schnitzer B, Singleton TP: CD10 detection in acute leukemia by immunohistochemistry in paraffin sections. Accepted for presentation to American Society of Clinical Pathologists Fall Meeting, New Orleans LA, September 1999. Am J Clin Pathology 1999 (in press).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology Rotations, July (4/5), August (1/4) September (1/4), October (3/4), November (2/4), December (2/5), January (1/4), February (1/4), March (2/4), April (1/4), May (1/4), June (2/4)
- B. Ophthalmic Pathology Service

II. TEACHING ACTIVITIES:

- A. Pathology 600
 - 1. Pathology of Valvular Disease, October, 1998
 - 2. The Vasculitides, October, 1998
 - 3. Obstructive Lung Disease - November, 1998
 - 4. Pulmonary Neoplasms - November 1998
 - 5. Pathology of ARDS - November 1998
 - 6. Tissue Reactions to Infectious Agents - November 1998
 - 7. Pulmonary Pathology Review for Medical Students - November, 1998
 - 8. Gynecologic Pathology Review for Medical Students- April, 1998
 - 9. General Pathology Review for Medical Students - June, 1999
 - 10. Laboratory Instructor, September, 1998 - May, 1998
 - 11. Medical student question and answer sessions, October, 1998 - May, 1999
- B. Pathology 630:
 - 1. Respiratory Disease I - October, 1998
 - 2. Respiratory Disease II - October, 1998
- 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 - May, 1999
 - 4. Surgical Pathology Consultant's Conference, December, 1998; June, 1999
- D. Other educational activities:
 - 1. M4 student elective mentor, August, 1998, September, 1998
 - 2. Provost's Seminar on Teaching, November, 1998
 - 3. Center for Research on Learning and Teaching Workshops: Making Large Classes Interactive, October, 1998; How Many People Did the Reading?, November, 1998; Strategies for Active Learning in Large Classes, November, 1998
 - 4. Member, M-2 Respiratory Sequence Committee, 1997-1998
 - 5. Course Director, M-4 Student Pathology Clerkships

6. Radiology - Pathology Correlation Course Co-Director, April, 1999
7. "One-to-One Teaching: In the Clinic and the Studio", New Faculty Orientation, Michigan League, September, 1998
8. Medical Education Scholars Program, February 1998 - February 1999
9. Lab Instructor, M1 Pathology Course, Spring, 1999
10. Nominated for American Association of Medical Colleges Humanism in Medical Education Award, 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, 1998 - 1999

PROJECTS UNDER STUDY:

- A. The separation of usual interstitial pneumonitis from nonspecific interstitial pneumonitis
- B. The cytopathologic features of vitreous fluids
- C. The clinical, radiographic, and pathophysiological manifestations of nonspecific interstitial pneumonitis
- D. The pathologic manifestations of ocular involvement by Wegener's granulomatosis
- E. Interactive Teaching in Pathology

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

Interviewer of Pathology House Officer And Surgical Pathology Fellowship Candidates 1998 - 1999

V. OTHER RELEVANT ACTIVITIES:

Member, Admissions Committee of the University of Michigan Medical School, 1995 - present
Member, Rules Committee, Senate Advisory Committee on University Affairs, 1999 - 2000

EDITORIAL BOARDS:

Abstract Review Board, USCAP

INVITED LECTURES/SEMINARS:

The Physician as Scientist, November, 1998 Inteflex 211, University of Michigan, Ann Arbor, MI, May, 1997

VI. PUBLICATIONS:

1. Brown RS, Leung JY, Flint A, Wahl RL: Expression of glucose transporters in human lung cancer. *J. Of Nuclear Medicine*
2. Gay SE, Kazerooni EA, Toews GB, Lynch III JP, Gross BH, Cascade PN, Spizarny DL, Flint A, Whyte RI, Popovich J, Hyzy R, Martinez FJ: Idiopathic pulmonary fibrosis: Predicting response to therapy and survival. *Am J Respir Crit Care Med* 1998; 157:1063-1072
3. Lynch III JP, Belperio J, Flint A, Martinez FJ: Bronchiolar complications of connective tissue disorders. *Sem Respir Crit Care Med* 1999; 20: 149-68
4. Flaherty KR, Toews GB, Lynch III JP, Kazerooni EA, Strawderman III RL, Hariharan K, Flint A, Martinez FJ: Steroids in idiopathic pulmonary fibrosis: Prospective comparative study of varying dosage regimens. *Am J Respir Crit Care Med* (in revision)

SUBMITTED PUBLICATIONS:

1. Zisman DA, Lynch III JP, Toews GB, Strieter RM, Kazerooni EA, Flint A, DiGiovine B, Martinez FJ: Cyclophosphamide in the treatment of idiopathic pulmonary fibrosis. A prospective study in patients who failed corticosteroids. *Chest* (submitted)

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

1. Kazerooni EA, Gross BH, Flint A, Colby TV, Flaherty K, Martinez FJ: Non-specific interstitial pneumonitis versus usual interstitial pneumonitis: Comparison of semi-quantitative HRCT scoring

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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:

MEDICAL SCHOOL/HOSPITALS:

- A. Director of the Seventeenth Annual Symposium on Automated Information Management in the Clinical Laboratory (AIMCL) and the Executive Briefing, Ann Arbor, Michigan, May 27-29, 1999.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Use of the GroupWise Messaging System for support of clinical activities (clinical email) and clinic work processes.
- B. Policy development regarding confidentiality and security of email.
- C. Direct wireless and email transmission of laboratory test results to clinicians.
- D. Evolution of clinical laboratory web portals; e-commerce and the clinical laboratory.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Clinical Laboratory Directors Committee.

HOSPITAL:

- A. Chief Information Officer Executive Committee (CIOEC).
- B. Applications Management Committee.
- C. Various executive level Y2K readiness and operations committees.
- D. Chairman, GroupWise Operations Committee.
- E. Chairman, Email Policy and Oversight Committee.
- F. Chairman, Ancillary Information Systems Managers' Committee

G. 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. *Future Directions for Informatics in Transfusion Medicine.* A lecture presented at the 25th annual symposium, Current Topics in Blood Banking, Ann Arbor, Michigan, 5 June, 1998.
2. *An Info-Centric Model for the Pathology Department of the Future.* A lecture presented to the annual meeting of the Association of Pathology Chairs, Pasadena, California, September 26, 1998.
3. *Integrated Clinical Information Systems: W(hither) the LIS? Information-System Based Virtual Pathology Departments.* A workshop and seminar presented at the Fall Meeting of the College of American Pathologists, Washington, D.C., October 18-18, 1998.
4. *Y2K Readiness in the Clinical Laboratory.* Two one-hour teleconferences as part of the Georgia Hospital Association (GHA) TELNET Audioconference Series to a national audience, October 21, 1998.
5. *The Technology of the Efferent Information Loop in Complex Lab Organizations.* A lecture presented the Anatomic Pathology Informatics, Imaging, and the Internet (APIII) Conference sponsored by the Division of Pathology Informatics, Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, PA, November 6, 1998.
6. *Y2K: Your Laboratory, Your Hospital, Your World.* A lecture sponsored by the Western Ohio Chapter of the Clinical Laboratory Management Association, Toledo, Ohio, March 18, 1999.
7. *The Digital and Virtual Radiology Department: An Organizational and Technical Viewpoint.* A lecture presented at a symposium entitled "Practical PACS: Evaluation, Acquisition, and Implementation" at the University of Michigan Medical School, March 26, 1999, Ann Arbor, Michigan.
8. *A Fresh Look at Lab Reporting Strategies and the LIS Architecture.* A lecture presented at the 17th annual symposium on Automated Information Management in the Clinical Laboratories (AIMCL) and Executive Briefing, Ann Arbor, Michigan, May 27, 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Friedman, B.A. Integrating laboratory processes into clinical processes, web-based laboratory reporting, and the emergence of the virtual clinical laboratory. *J. Clin. Lab. Man. Assoc.* 1998, 12:333-338.

BOOKS/CHAPTERS IN BOOKS:

1. An Analysis of Point-of-Care Testing in Relationship to the Shift from the Centralized Laboratory Model to the Virtual Clinical Laboratory. In: Point-of-Care Testing: Principles, Management, and Clinical Practice, Gerald J. Kost, Editor. (In preparation)

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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.
- G. Sign out of Triple Marker Screen results from maternal serum testing.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

- A. Pathology House Officers:
 - 1. Clinical Pathology Rounds (2 lectures)
 - 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 9/98) and Aaron Smith (5/96 to present), Department of Chemistry.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Evaluation of assays for Troponin I as an early marker of myocardial injury.
- B. Evaluation of portable analyzers for the measurement of coagulation testing parameters PT, aPTT, and ACT in alternate testing sites.
- C. Development and refinement of an HPLC assay for plasma homocysteine.
- D. Evaluation of the RIBA assay for confirmation of antibodies to Hepatitis C.
- E. Development of an assay for gamma hydroxy butyrate (GHB)
- F. Evaluation of methods for the rapid measurement of PTH in surgical cases.
- G. Evaluation of new meters and data management systems for point of care whole blood glucose monitoring.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Incentive Committee
- B. Quality Assurance Committee
- C. Chemistry Lab New Instrumentation Work Group
- D. M Labs / Central Distribution Work Group
- E. Director, Chemistry Laboratory
- F. Director, Point of Care Testing

MEDICAL SCHOOL /HOSPITAL:

- A. Ambulatory Care Operations and Planning Council
- B. Brighton Health Center Expansion Project Planning Group
- C. Emergency Department Expansion Project Work Group

REGIONAL AND NATIONAL:

- A. Executive Committee, Michigan Section AACC.
- B. Treasurer, Michigan Section AACC.
- C. Lipids and Lipoproteins Division Member, AACC
- D. Pediatric Clinical Chemistry Division Member, AACC
- E. Reviewer, Clinical Chemistry

V. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

- 1. Mosca, L., Jahnige, J., and Giacherio, D., Christman, G., and Johnson, T.: Beneficial effect of combination hormone replacement therapy on lipoprotein (a) levels in postmenopausal women. Preventive Cardiology 1999; 2: 51-58

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

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Histopathology Lab Section for medical students.

III. RESEARCH ACTIVITIES:

None.

PROJECTS UNDER STUDY:

None.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

MEDICAL SCHOOL/HOSPITAL:

A. Member of Medical School Admission Committee.

REGIONAL AND NATIONAL:

A. Chairman, Board of Directors, Public Citizen, Inc. (Ralph Nader, Initial Chairman and Founder).

B. Reviewer for the "Journal of Urology" and "Urology".

V. OTHER RELEVANT ACTIVITIES:

None.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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, 1999.
 - 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.

- C. Co-Investigator R01CA81488-01 (\$4,547,772) “Molecular Epidemiology of Colorectal Cancer”, 20% Salary Support, years 1-4, Stephen Gruber, M.D., Ph.D. Principal Investigator.
- D. Co-Investigator N01-DK-9-2323 (\$1,433,559) “Hepatitis C Clinical Trial”, 7% Salary Support, Anna Lok, 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 Ferguson and Tom Giordano.
- C. NIH study of HCV with Anna Lok in Division of Gastroenterology.
- D. NIH study of the Molecular Epidemiology of Colon Cancer in Israel.
- E. Study of PET scans in detecting metastases in breast cancer with Richard Wahl, Division of Nuclear Medicine.
- F. Study of etiology of pancreas cancer with David Garabrandt, School of Public Health.
Study of Granulomatous Appendicitis with Laura Lamps at the University of Arkansas.
Study of telepathology with Alberto Marchevsky at Cedars-Sinai Medical Center.
Study of Enterohemorrhagic E. coli with Riccardo Valdez.
Study of diffuse duodenitis and UC with Riccardo Valdez.
Study of Barretts dysplasia grading with GI Study Group.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Surgical Pathology
- B. Director, Surgical Pathology Fellowship Program.
- C. Quality Assurance Officer for Surgical Pathology
- D. Member, Residency Selection Committee.
- E. Member, Departmental Incentive Committee
- F. Member, University Hospital Tissue Committee
- G. Member, University Hospital Operating Room Committee

REGIONAL AND NATIONAL:

- A. Reviewer, Cancer.
- B. Reviewer, Archives of Pathology and Laboratory Medicine.
- C. Reviewer, Gastroenterology.
- D. Reviewer, Human Pathology.
- E. Reviewer and Editorial Board member, 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.

- K. Judge for Resident Abstract competition, Hans Popper Hepatopathology Society
- L. Editorial Board member, The Online Journal of Digestive Diseases

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Faculty Member, Long Course in Gastrointestinal Pathology, IAP meeting, Nice, France October, 1998.
2. Invited speaker, Ohio Society of Pathologists. "GI Pathology for the new millennium", Columbus, Ohio Feb. 1999.
3. Co-director of USCAP course entitled "Infectious Diseases of the GI tract," March, 1999.
4. Invited Panelist, Gastrointestinal Pathology Specialty Conference, USCAP Meeting, March 1999.
5. Moderator, GI Pathology Society Companion Meeting at USCAP meeting, March 1999.
6. Moderator, GI Pathology Society Companion Meeting at DDW meeting, May, 1999.
7. Faculty Member, ASCP Workshop - Surgical Pathology of the Gastrointestinal Tract, Scottsdale, Arizona, May 1999.
8. Faculty Member, University of Michigan Postgraduate Course: An Update on Common Clinical Concerns in Primary Care. Bellaire, Michigan, June 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Singson RPC, Natarajan S, Greenson JK, Marchevsky AM. Virtual microscopy and the Internet as telepathology consultation tools: a study of gastrointestinal biopsies. *Am J Clin Pathol* 1999;111:792-795.
2. McCarthy CJ, Crofford LJ, Greenson JK, Scheiman JM. Cyclooxygenase-2 expression in gastric antral mucosa before and after eradication of *Helicobacter pylori* infection. *Am J Gastro* 1999;94:1218-1223.
3. Tworek JA, Goldblum JR, Weiss SW, Greenson JK, Appelman, HD. Stromal Tumors of the Colon. *American Journal of Surgical Pathology* (In Press).
4. Tworek JA, Goldblum JR, Weiss, SW, Greenson, JK, Appelman HD. Stromal Tumors of the Rectum and the Anus. *American Journal of Surgical Pathology* (In Press).

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Shureiqi I, Wojno K, Poore J, Reddy R, Moussalli MJ, Spindler S, Greenson JK, Normolle D, Brenner DE: Decreased 13-S-hydroxyoctadecadienoic acid (13-S-HODE) tissue levels and 15-lipoxygenase (15-Lox) expression in human colon cancers. *Journal of Clinical Investigation* (submitted).

BOOKS/CHAPTERS IN BOOKS:

None.

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

1. Montgomery E, Bronner M, Goldblum J, Greenson J, et al. Reproducibility of the Diagnosis of Dysplasia in Barrett's Esophagus: A Multicenter Study of 125 Mucosal Biopsies by 12 Observers. Poster presentation at USCAP meeting, 1999. *Modern Pathol* 12:81A, 1999.
2. Valdez R, Kuznicki DL, Lamps LW, Greenson JK, Giordano J. Polymerase chain reaction detection of enterohemorrhagic *E. coli* shiga-like toxins in archival human colonic tissue. Platform presentation at USCAP meeting, 1999, *Modern Pathol* 12:86A; 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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, thirteen 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. House Officers in Pathology, daily consultation on Pediatric cases in surgical reading rooms, twelve months.
- C. House Officers in Pathology, gross and microscopic supervision of most pediatric necropsies, twelve months, and adult cases, thirteen weeks plus on-call weekends.
- D. Lecture on Pediatric Necropsy Pathology in Orientation for new House Officers in Pathology.
- E. Core curriculum lectures for House Officers in Pediatric Pathology, two.
- F. Individual gross and microscopic resident teaching in Placental Pathology.
- G. Gross Necropsy Conference, one hour/week, twelve months.
- H. Supervised Pediatric Hematology Fellows (two) for Pediatric Pathology elective period.
- I. Coordinate three core curriculum lectures in placenta: Pathology and OB/GYN residents.
- J. Consult conference (2), pediatric cases for pathology residents.
- K. 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.
- L. Participant in Cardiology Section of joint Radiology-Pathology correlation course.

- M. Lectures to Pediatric Hematology/Oncology Section on Logistics of Pathologic Classification and Diagnoses.

III. RESEARCH ACTIVITIES:

- A. Continued study of effects of various congenital heart defects on the pulmonary vasculature.
- B. 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.
- C. Project with Pediatric surgeons (C. Harmon, M.D.) VEGF (vascular endothelial growth factor) and thrombospondin expression in neuroblastoma.

PROJECTS UNDER STUDY:

- A. 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; manuscript submitted.)
- B. 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.
- C. Correlation project with pediatric surgeons (Joseph Lelli, M.D. lead) on clinical diagnosis/management and outcome of appendicitis in children (see abstracts and publications).
- D. Study within Drs. Graziano and Ludomirsky (Pediatric Cardiology) on pulmonary venous wall properties in hypoplastic left ventricle syndrome with premature closure of foramen ovale.
- E. Study with James Geiger, M.D. (Pediatric surgery) on dendritic cell (and other) markers in ganglioneuroma and ganglioneuroblastoma.

ONGOING RESEARCH:

- A. Continuing correlation as co-investigator of histopathologic changes in neuroblastoma associated with cell/tumor maturity with different tissue gene expressions. (Valerie Castle, M.D., PI.)

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 Surgery

REGIONAL AND NATIONAL:

- A. Women's Liaison Officer, American Association of Medical Colleges.
- B. Appointed to Distinction and Awards Committee, Society for Pediatric Pathology.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Barr M, Sedman AB, and Heidelberger KP: Renal Tubular Dysgenesis in Twins. *Pediatric Nephrology*: 12:408-413, 1998.
- 2. Goldberg CS, Caplan MJ, Heidelberger KP and Dick M: The Dimensions of the Triangle of Koch in Children. *Am J Cardiol* 83:117-120, 1999.
- 3. Lelli, J, Drongowski R, Raviz S, Wilke L, Heidelberger KP and Hirschl R: Historical changes in the postoperative treatment of appendicitis in children: Impact on medical outcome. (Accepted, *Journal of Pediatric Surgery*)

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

- 1. Lelli J, Drongowski R, Raviz S, Wilke L, Heidelberger KP and Hirschl R: Historical changes in the post-operative treatment of appendicitis in children: Impact on medical outcome. Paper presented at Am. Pediatric Surg. Assn. Annual meeting. May, 1999. Palm Springs, CA.,
- 2. Forbush B, Kiristioglu I, Teitelbaum DH, Eisenbraun MD and Heidelberger KP: Multi Drug Resistance 2 Gene Expression in the Murine Liver: Relevance to the Development of Parenteral Nutrition - Associated Cholestasis. *Surgical Forum*, 1998, XLIX 569-570.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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 - 12/99.
- 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, "Inflammatory Cells and Lung Injury", Core C, National Institutes of Health, \$291,025.
- D. 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.
- B. Co-Principal Investigator, "MMPs in Prostate Cancer" 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.
 - 3. American Journal of Respiratory Cell and Molecular Biology
- C. Consultant/Grant reviewer for the Veteran's Administration.
- D. NIH NHLBI Study Section.

V. INVITED LECTURES AND SEMINARS:

- 1. Visiting Professor and Lecture, University of Florida, Gainesville, Florida, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. 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.

2. Nader-Dajal, N., Knight, P.R., Thusu, K., Davidson, B.A., Aljada, A., Holm, B.A., Johnson, K.J., Dandona, P.: Reactive oxygen species contribute to oxygen-related lung injury after acid aspiration. *Anesth Analg.* 1998, 87(1);127-133.
3. 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.
4. Colton, D.M., Till, G.O., Johnson, K.J., Gater, J.J., and Hirschl, R.B.: Partial liquid ventilation decreases albumin leak in the setting of acute lung injury. *J. Crit. Care* 1998, 13;136-139.
5. Younger, J. G., Taqi, A.S., Jost, P. F., Till, G. O., Johnson, K. J., Stern, S. A., and Hirschl, R. B.: The pattern of early lung parenchymal and airspace injury following acute blood loss. *Acad. Emergency Med.*, 1998, 5(7)659-665.
6. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K.J., Dean, S.B., Patel, S., and Bartlett, R.H.: Neutrophil accumulation is reduced during partial liquid ventilation. *Crit. Care Med.*, 1998, 26(10):1716-1724.
7. Smoyer, W.E., Gregory, M.J., Bajwa, R.S., Johnson, K.J., Bunchman, T.E.: Quantitative morphometry of renal biopsies prior to cyclosporine in nephrotic syndrome. *Pediatr. Nephrol.* 1998, 12(9):737-743.
8. Gipson, T.S., Bless, N.M., Shanley, T.P., Crouch, L.D., Bleavins, M.R., Younkin, E.M., Sarma, V., Gibbs, D.F., Wongelawit, T., McConnell, P.C., Mueller, W.T., Johnson, K.J., and Ward, P.A.: Regulatory effects of endogenous protease inhibitors in acute lung inflammatory injury. *J. Immunol.*, 1999, 162:3653-3662.
9. Gibbs, D.F., Apel, I.J., Weiss, S.J., Johnson, K.J., and Varani, J.: Characterization of matrix metalloproteinases produced by rat alveolar macrophages. *Am. J. Respir. Cell Mol. Biol.*, 1999, 20:1136-1144.
10. Gibbs, D.F., Shanley, T.P., Warner, R.L., Murphy, H.S., Varani, J. and Johnson, K.J.: Role of matrix metalloproteinases in models of macrophage-dependent acute lung injury. *Am. J Respir. Cell Mol. Biol.*, 1999, 20:1145-1154.
11. Varani, J., Dame, M.K., Wojno, K., Schuger, L., and Johnson, K.J.: Characteristics of non-malignant and malignant human prostate in organ culture. *Lab. Invest.* 199,79(6):723-731.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Kershaw, D.B., Bunchman, T.E., Johnson, K.J., Sedman, A.B., Kelsch, R.C.: Crescentic glomerulonephritis with subsequent hemolytic uremic syndrome in a child. Submitted for publication.
2. Varani, J., Hirschl, R., Dame, M. and Johnson, K.: Neutrophil infiltration is reduced during liquid ventilation: II. In Vitro analysis. Submitted for publication to *Amer. J. Respiratory & Critical Care Medicine*.
3. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K.J., Ichiba, S., Bartlett, R.H.: Liquid ventilation decreases pulmonary hemorrhage and vascular permeability. Submitted to *Clin. Immuno and Immunopathol.* 1996.
4. Annis, K., Sigler, C., Johnson, K.J., Berman, S., Haber, H., Bonalsky, J., Luscombe, F., Van de Carr, S.: Predictors of angioedema associated with angiotensin converting enzyme inhibitor. Submitted for publication.
5. Sawyer, R.G., Chenault, R.H., Merion, R.M., Johnson, K.J., Kuta, E.G., and Hebert, C.A.: Antibody to interleukin-8 decreases systemic and pulmonary sequelae of sepsis: evidence for

- early chemokine regulation of cytokine activity in a porcine model of bacteremia. Submitted for publication.
6. O'Shea, K.S., Johnson, K.J., Gordon, D., Sliwkamski, M.X., and Erickson, S.L.: Effects of heregulin treatment on adult wild-type and ErbB2, ErbBC and heregulin heterozygous null mice. Submitted for publication.
 7. O'Shea, S., Johnson, K.J., Gordon, D., Pisacane, P., Clark, R., Sliwkowski, M.X. and Erickson, S.L.: Effects of heregulin on adult breast and other epithelial tissues: an in vivo study of wild-type, heregulin, ErbB2 and ErbB3 heterozygous null mice. Submitted for publication.
 8. Hamouda, T., Hayes, M.M., Cao, Z., Tonda, R., Johnson, K., Wright, D.C., Brisker, J., and Baker, J.R.: A novel surfactant nanoemulsion with broad-spectrum sporicidal activity against *Bacillus* species. Submitted for publication.
 9. Shanley, T.P., Davidson, B.A., Nader, N.D., Bless, N., Vasi, N., Ward, P.A., Johnson, K.J., and Knight, P.R.: The role of macrophage inflammatory protein-2 (MIP-2) in aspiration-induced lung injury. Submitted for publication.
 10. Reuter, J.D., Myc, A., Cao, Z., Johnson, K.J., Wright D.C., Brisker, J., and Baker, J.R.: Prevention of influenza A virus infection by non-ionic surfactant nanoemulsions in a murine model. Submitted for publication.

BOOKS AND CHAPTERS IN BOOKS:

1. Warren, J.S., Johnson, K.J. and Ward, P.A.: Phagocytes and reactive oxygen substances as mediators of acute lung injury, in, Hyers, T. (ed), Diffuse Alveolar Damage and Respiratory Failure, Futura Press, New York, In Press.
2. Till, G.O., Johnson, K.J. and Ward, P.A.: Oxygen free radicals in inflammation, in, Messmer, K. and Hammersen, F. (eds), Prog. Appl. Microcirc., Volume 9, Karger, Basel, In Press.
3. Ward, P.A., 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.
6. Johnson, K.J., Chensue, S.W., Kunkel, S.L. and Ward, P.A.: Immunopathology, in, Rubin, E. and Farber, J.L. (eds) Textbook of Pathology, Third Edition, J.B. Lippinott Inc., New York, NY, Philadelphia, Pennsylvania, pp. 104-153, 1998.

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

1. 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.
2. Gibbs, D. F., Varani, J. J., and Johnson, K. J.: Role of matrix metalloproteinases in macrophage-dependent acute alveolitis in the rat. FASEB J. 12(4):4506, 1998.

3. 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.
4. Johnson, K.J., 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.
5. 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.
6. Varani, J., Gibbs, D. F., Apel, I. J., Warner, R. L., Weiss, S. J., Johnson, K. J.: Characterization of matrix metalloproteinases produced by rat alveolar macrophages. Keystone Symposium, Macrophage Biology, January 1999.
7. Johnson, K. J., Gibbs, D. F., Shanley, T. P., Warner, R. L., and Varani, J.: The role of matrix metalloproteinases in models of acute lung injury: evidence for the alveolar macrophage as the source of the proteinases. Keystone Symposium, Macrophage Biology, January 1999.
8. Lake, K.D., Leavey, S.F., Ojo, A.O., Johnson, K.J., Punch, J.D., Bromberg, J.S., Campbell, D.A., Magee, J.C., Merion, R.M., Turcotte, J.G. and Leichtman, A.B.: The successful use of sirolimus in transplant recipients with hemolytic uremic syndrome. American Society of Transplant Surgeons, 1999.
9. Younkin, E.M., Warner, R.L., Bless, N.M., Varani, J., and Johnson, K.J.: In vitro effects of catalase on the production of matrix metalloproteinases (MMPs) by alveolar macrophages and neutrophils. *FASEB J.* 13(5)748.6, 1999.
10. Warner, R.L., Bless, N.M., Younkin, E.M., Varani, J., and Johnson, K.J.: Time-dependent effects of catalase administration on the reduction of matrix metalloproteinase (MMP) activity in acute lung alveolitis. *FASEB J.* 13(5)639.15, 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Clinical Pathology Grand Rounds:
 - 1. Program Director.
 - 2. Presented lectures on:
 - a) Streamlined pretransfusion testing – are our patients at risk?
 - b) Red cell polyagglutination
- 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 Eric Carson, MD.
 - 2. Pediatric Hematology - Provided instruction in immunohematology to Matt Hansen, MD and Angela Busch-Thompson, MD.
- F. Pathology Residents:
 - 1. Residency Training Review Committee.
 - 2. Coordinated Blood Bank/Coagulation block rotations for house-officer training in clinical pathology.
 - 3. Provided instruction in immunohematology to house-officers during their Blood Bank Rotation (over 100 contact hours).
 - 4. Developed and submitted application for accreditation of a Transfusion Medicine Fellowship Training Program to the Accreditation Council for Graduate Medical Education.

- G. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
 - 1. Program Director - Planned and coordinated the June, 1999 Current Topics in Blood Banking Symposium and Preconference Workshops.
 - 2. Presented Workshop entitled: "Tricks of the trade."
 - 3. Presented talk entitled: "What is a clinically significant antibody?"
 - 4. Moderated afternoon session on Controversies/Future Horizons.

III. RESEARCH ACTIVITIES:

- A. Judd WJ, Storry J, Annesley T, Reid ME, Bensette M, et al. The first example of a Paraben-Dependent Anti-Rh. Abstract Submitted to AABB.
- B. Judd WJ, Robertson D, Downs T, Chin S, Hammond D, Pehta JC. In vitro analysis of isoagglutinin-depleted solvent detergent plasma: a "universal" plasma for transfusion. Abstract Submitted to AABB.

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, Michigan Community Blood Center, March, 1999
 - 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, Transfusion Medicine and Vox Sanguinis.
- E. International Society of Blood Transfusion
 - 1. Member, WHO Committee on Blood Group Nomenclature

OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

1. Immune hemolysis. Michigan Association of Blood Banks' Current Topics in Immunohematology Workshop, Michigan Community Blood Center, March, 1998.
2. Repeat antibody identification studies: How? When? Ever? Wisconsin Association of Blood Banks Annual Scientific Meeting, Milwaukee, WI, September, 1998.
3. Modern approaches to pretransfusion testing. Wisconsin Association of Blood Banks Annual Scientific Meeting, Milwaukee, WI, September, 1998.
4. What is a clinically significant antibody. South Central Gel User's Seminar, Ortho Clinical Diagnostics, Dallas, TX, September, 1998.
5. Modern approaches to pretransfusion testing. South Central Gel User's Seminar, Ortho Clinical Diagnostics, Dallas, TX, September, 1998.
6. Issues in implementing an electronic crossmatch. American Association of Blood Banks Annual Meeting, Philadelphia, PA, November, 1998.
7. Session Moderator - Red Cells and Serological Methods. American Association of Blood Banks Annual Meeting, PA, November, 1998.
8. Streamlined pretransfusion testing: have we placed patients at risk? NEQAS Meeting, Sheffield, UK, November, 1999.
9. Modern approaches to pretransfusion testing. Distinguished Speaker Series, South Texas Blood and Tissue Center, San Antonio, TX, December, 1998.
10. Casting swine before pearls. Retirement Seminar for John C Case, Houston, TX, December, 1998
11. Polyagglutination: or fruits and nuts I have known and loved. Retirement Seminar for Malcolm L. Beck, Kansas City, MO, January, 1999.
12. Prenatal-perinatal testing. Michigan Association of Blood Banks' Current Topics in Immunohematology Workshop, Michigan Community Blood Center, March, 1998.
13. Immune hemolysis. Michigan Association of Blood Banks' Current Topics in Immunohematology Workshop, Michigan Community Blood Center, March, 1998.
14. Visiting Lecturer in Transfusion Medicine. PathCentre, Queen Elizabeth Hospital, Perth, Western Australia, April, 1999.
15. The electronic crossmatch. Western Australian Society for Blood Transfusion, Margaret River, Western Australia, April, 1999,
16. The electronic crossmatch, Victoria Blood Group Discussion Group, Melbourne, Victoria, May, 1999.
17. The electronic crossmatch. Brisbane Area Antibody Club, Brisbane, Queensland, May, 1999.
18. The electronic crossmatch. NSW Antibody Group. Sydney, NSW, May, 1999.
19. Modern approaches to pretransfusion testing. Ortho Clinical Diagnostics, Raritan, NJ, May, 1999.
20. Modern approaches to pretransfusion testing. Ortho Clinical Diagnostics, Philadelphia, PA, May, 1999.
21. Modern approaches to pretransfusion testing. Ortho Clinical Diagnostics, Washington, DC, May, 1999.

PUBLICATIONS:

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

1. Judd WJ. 'New' blood bank technologies. *Clin Lab Sci* 1998;11:106-13.
2. Judd WJ. Requirements for the electronic crossmatch. *Vox Sanguinis* 1998;74(S2):409-407.
3. Judd WJ. The electronic crossmatch: an alternative to the immediate-spin crossmatch to detect ABO incompatibility. *Advance* 1998;10(15):16-23.
4. Judd WJ, Fullen DR, Steiner EA, Knafl PC. Revisiting the issue: can the reading for serologic reactivity following 37°C incubation be omitted? *Transfusion* 1999;39:295-299.
5. Judd WJ. Modern approaches to pretransfusion testing. *Immunohematology* 1999;15:41-52.
6. Judd WJ. Antibody elution from red blood cells: theoretical and practical considerations. *Trans Med Rev*: Accepted.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999

I. CLINICAL ACTIVITIES:

- A. Director of Molecular Diagnostics.
 - 1. Interpretation and sign-out of Molecular Diagnostics Tests
- B. Director of Clinical Chemistry Section.
 - 1. 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 Block D House Staff.
- D. Lectures to Pathology House Staff and Faculty at Clinical Pathology Rounds.
- E. Research advisor to visiting scholar: Dr. I. Cetin Ozturk.
- F. Thesis Committee Member, and Research Co-advisor to Ph.D. Candidate: Ms. M. Kachman, Dept. of Chemistry, University of Michigan.

III. RESEARCH ACTIVITIES:

FUNDING REQUESTED:

“National Reference Laboratory for Congenital Adrenal Hyperplasia”. UM Venture Capital Fund. \$131,300. Pending decision.

PROJECTS UNDER STUDY:

- A. Molecular Genetics of CYP21 (Congenital Adrenal Hyperplasia).

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, Steering Committee, UM Pathology/Parke-Davis Genomic Pathology Laboratory

- F. Faculty Participant, Genetics Residency Training Program (In Dept. of Human Genetics).

INSTITUTIONAL:

- A. Member GME Program Director's Committee

REGIONAL AND NATIONAL:

- A. Chair, Molecular Pathology Subdivision of American Association for Clinical Chemistry (Jan 1999-Dec 1999).
- B. Member, Chemistry Resource Committee, College of American Pathologists (as of June 1999)
- C. Member, Publications Committee, Association for Molecular Pathology.
- D. Editor of ACLPS Newsletter.
- E. Member, AACC, ASHG, CAP, ACLPS, AMP.
- F. Manuscript Reviewer, Clinical Chemistry, Molecular Diagnosis, and Biotechniques.

V. INVITED LECTURES AND SEMINARS:

- 1. "Molecular and Biochemical Genetics of Congenital Adrenal Hyperplasia". Association for Molecular Pathology Annual Meeting, 1998
- 2. "Genetics of Cardiovascular Disease". William Beaumont Annual Symposium, 1999.
- 3. "Molecular Pathology". Osler Pathology Review Course, Spring, 1999.

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

- 1. 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* 12:1045-1050, 1998.
- 2. Killeen AA, Jiddou R, Sane KS: Characterization of frequent polymorphisms in intron 2 of CYP21. Application to analysis of segregation of CYP21 alleles. *Clinical Chemistry* 42:2140-2145 1998.
- 3. Wei W-L, Killeen AA: Analysis of 4 common salt-wasting mutations in CYP21 (steroid 21-hydroxylase) by cleavage fragment length polymorphism analysis and characterization of a frequent polymorphism in intron 6. *Molecular Diagnosis* 3: 171-178, 1998.
- 4. Jiddou RR, Wei W-L, Sane KS, Killeen AA: Single nucleotide polymorphisms in intron 2 of CYP21P: evidence for a higher rate of mutation at a CpG dinucleotide in the functional steroid 21-hydroxylase gene, and application to segregation analysis in congenital adrenal hyperplasia. (*Clinical Chemistry*, 45:625-629, 1999).
- 5. Zhou M, Sheldon S, Akel N, Killeen AA: Chromosomal aneuploidy in leukemic blast crisis: a potential source of error for interpretation of bone marrow engraftment analysis by VNTR amplification. (*Molecular Diagnosis*, in press, 1999).
- 6. Ozturk IC, Killeen AA: Molecular genetic factors in cardiovascular disease. (*Archives of Pathology and Laboratory Medicine*, In press, 1999).

7. Jone C, Killeen AA: Monitoring of bone marrow engraftment by PCR of D1S80 with capillary electrophoretic separation of amplicons. (Molecular Diagnosis, accepted).

VII. ARTICLES SUBMITTED:

1. Wei W-L, Ozturk IC, Palaniappan L, Rubenfire M, Killeen AA: Analysis of the frequencies of coding polymorphisms in steroid 21-hydroxylase in 3 ethnic populations: further evidence of non-amplifying CYP21 alleles. (Submitted).
2. Bavikatty NR, Killeen AA, Akel, N, Schmaier AH: Association of the prothrombin 20210 (G to A) mutation with factor V Leiden in a Midwestern American population. (submitted).

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

1. Killeen AA: Biochemical and Molecular Genetics of Congenital Adrenal Hyperplasia. *Check Sample*. American Society of Clinical Pathologists, Chicago, IL, 1998.
2. Wei W-L, Killeen AA: Identification of a frequent *RsaI* polymorphism in the CYP21 (steroid 21-hydroxylase) gene. *Clin Chem* 44:A33, 1998.
3. Wei W-L, Killeen AA: Analysis of 4 common salt-wasting mutations in CYP21 by CFLP. *American Journal of Pathology* 153:1651, 1998.
4. Jiddou RR, Wei W-L, Killeen AA: Characterization of single nucleotide polymorphisms in intron 2 of CYP21P. Accepted for poster presentation at 1999 American Association for Clinical Chemistry meeting, New Orleans.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Board Certification, Anatomic Pathology.
- B. Autopsy Pathology (2 days).
- C. Diagnostic Renal Biopsy Service (28 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. M1 Molecular and Cell Biology 501 Lecture - (6 hours)
- F. Curriculum Development - MCB 501(40 hours)
- G. Gross Pathology Conference.
- H. Renal Pathology for Pathology Residents (five hours).
- I. Renal Pathology for Nephrology Fellows (nine hours).
- J. Renal Pathology Fellows - Lois Arend - (40 hours).
- K. Dissertation Committees (one).
- L. Graduate Program Oral Examiner (two examinations)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Director, Molecular/Morphology Core, George M. O'Brien Renal Center, NIH-P50-DK39225, (5% Effort) \$129,949/year, 8/1/98-7/30/03.
- B. Co-Investigator, "IGF-I is an Osmoprotectant in Neuroglial Cells", NIH-R01-DK38304, (5% Effort) \$103,045 direct costs/year, 3/1/98 to 2/28/2003
- 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, 4/1/98-3/31/03.

PENDING SUPPORT:

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

PROJECTS UNDER STUDY:

- A. Regulation of collagen 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, Departments 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:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. 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.

2. 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.
3. Minto AW, Kalluri R, Togawa M, Bergijk EC, Killen PD, Salant DJ: Augmented Expression of Glomerular Basement Membrane Specific Type IV Collagen Isoforms (•3-•5) in Experimental Membranous Nephropathy. *Proc Assoc Amer Phys*, 110:207-217, 1998.
4. Porcellati F. Hlaing T. Togawa M. Stevens MJ. Larkin DD. Hosaka Y. Glover TW. Henry DN. Greene DA. Killen PD: Human Na(+)-myo-inositol cotransporter gene: alternate splicing generates diverse transcripts. *Am J Physiol*, 274:C1215-25, 1998.
5. Lenz O. Striker LJ. Jacot TA. Elliot SJ. Killen PD. Striker GE: Glomerular endothelial cells synthesize collagens but little gelatinase A and B. *J Am Soc Nephrol*, 9:2040-7, 1998
6. 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. *Am J Physiol*, in press 1999.
7. Lu W, Phillips CL, Killen PD, Hlaing T, Harrison WR, Elder FFB, Miner JH, Overbeek PA, Meisler MH: Insertional mutation of the collagen genes Col4a3 and Col4a4 in a mouse model of Alport syndrome. *Genomics*, in press 1999.

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 1999.
2. 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, submitted 1999.
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 1999.

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

1. 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* 9:53a, 1998.
2. 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* 9:55a, 1998.
3. Van Vliet AI, Van Alderwegen IE, Baelde HJ, De Heer E, Killen PD, Kalluri RK, Bruijn JA: Differential expression of collagen IV subchains in experimental renal interstitial fibrosis. *J Amer Soc Nephrol* 9:529a, 1998

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

- A. Host Defense Sequence, First Year Medical School
- B. Lecture in didactic seminar series for Pediatrics
- C. Lecture Pathology 581
- D. Academic Advisor, Immunology graduate program
- E. Member, Molecular Mechanisms of Microbial Pathogenesis training grand program committee
- F. Member, Pathology graduate program committee
- G. Member, Lung Immunopathology Post-doctoral Training Program (Pathology)
- H. Member, Experimental Immunopathology Training Program (Pathology)
- I. Member, Pulmonary Cellular and Molecular Biology Training Program
- J. Member, Pediatric Training Grant "Cellular and Molecular Biology in Pediatrics"
- K. Chair, Pathology Graduate Examination Committee
- L. Member, Graduate Teaching Award Review Committee
- M. Member, Task force for Medical School Graduate Program for Joint recruitment Joint Admissions
- N. Supervised the following postdoctoral fellows, graduate students, medical students and undergraduates:
 - Fellows; Drs., Emma Campbell, Kate Blease, Kim Tekkanat, Akihiro Matsukawa, Sandra Oliveira.
 - Graduate Students (MSTP); Sara Cheng, Cindi Bone-Larsen
 - Medical students: Matt Steinhauser
 - Undergraduate Students: Joe Barber, Craig Assenmacher, Scott Lipinski
- O. Doctoral Thesis Committee Member/Orals Committee for the following graduate students: Brian Lane (CMB), Joyce J. Lai (Public Health), Shimin Hu (Pathology), Wannee Asavaroengchai (Pathology), Sara Cheng (MSTP, CMB), Cindi Bone-Larson (MSTP, Pathology), Deb Battaglia (Physiology).
- P. Oral preliminary examination committee (Daniel J. Becker MSTP (CMB) Jeffrey J. Bednarski (MSTP, Chemistry), Tom Hlaing (Pathology), and J. Zhang (Pathology)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. NIH - Macrophage/Monocyte Signals 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. SCOR Occupational and Immunological Lung Disease, P50HL-46487 Principal Investigator for Project 3
- E. SCOR Acute Lung Injury, P50HL60289, Principal Investigator Project 3.

PATENTS:

- A. "CXC Chemokines as Regulators of Angiogenesis" #5,871,723 issued February 16, 1999
- B. "Method For treating Asthma Using CSF Antibody" #5,911,988 issued June 15, 1999

DISCLOSURES:

The role of stem cell factor (SCF) for the protection and regeneration of liver function. Nicholas W. Lukacs, Kenneth Simpson, Steven Kunkel, Cory Hogaboam, and Robert Strieter. November, 1998.

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/tumorigenesis

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Operating committee Pathology graduate program
- B. Space utilization and research committee
- C. Interview candidates for graduate program
- D. Divisional Co-Director of General Pathology
- E. Chair, Graduate Program's Examination committee
- F. Member, Department of Pathology ACAPT 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. Associate Dean for Interdisciplinary Programs, Rackham Graduate School
- J. Task Force for Medical School's Joint Recruitment/Joint Admissions Committee
- G. The University of Michigan medical school LCME self-study Graduate education in the basic medical sciences committee
- H. Search Committee, Vice President for Research University of Michigan
- I. Co-Chair Immunology Task Force

REGIONAL AND NATIONAL:

- A. Associate Editor, Journal of Clinical Investigation
- B. Senior Associate Editor, American Journal of Pathology
- C. Associate editor, American Journal of Respiratory Cell and Molecular Biology
- D. Associate Editor, Experimental and Molecular Pathology,
- E. Associate Editor, Shock
- F. Editorial board, Mediators of Inflammation
- G. Chair, 2000 Gordon Conference on Chemotactic Cytokines
- H. Co-Chair, 1999 Keystone Conference on Chemokines
- I. Co-Chair, 1999 Keystone Conference on Inflammatory Paradigms and the Vasculature
- J. Co-Chair 2001 Keystone Conference on Biology of Chemokines
- K. member, Advisory Board Xith International vascular Biology Meeting
- 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. Plenary Speaker, Cytokines & Inflammatory Bowel Disease '98, Bath, UK July 1998.
- 2. Session Chair and Invited Speaker, International Society for Heart Research, Ann Arbor, MI, August 1998

3. Platform Speaker, Animal Models of Human Respiratory Diseases, Santa Fe, New Mexico, September , 1998
4. Invited participant, National Institutes of Health Systemic Sarcoidosis Symposium, New Haven, CT October 1998
5. Invited Speaker, American Society of Nephrology, Philadelphia, PA, October 1998
6. Symposium Speaker, Ninth International Conference of the Inflammation Research Association, Inflammatory Processes, Hershey, PA, Nov 1998
7. Invited Speaker, NIAID sponsored conference on allergy, Bethesda, MD, Dec 1998
8. Speaker and Co-organizer, Keystone Chemokine Conference, Keystone CO, Jan 1999
9. Speaker and co-organizer, Keystone Conference on Inflammatory Paradigms and the Vasculature, Santa Fe, NM Feb 1999
10. Invited Speaker, Society of Toxicology, New Orleans, LA, March 1999
11. Invited Speaker, University of Florida, Gainesville, FL, March 1999
12. Invited Speaker, University of California, Riverside CA, April 1999
13. Invited Speaker, Albert Einstein Medical School, New York, NY, June 1999

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Hogaboam, C.M., Smith, R.E., Kunkel, S.L. Dynamic interactions between lung fibroblasts and leukocytes: Implications for fibrotic lung disease. *Proc. Assoc. Amer. Phys.* 1998;110:313-320.
2. Arenberg DA, Keane MK, DiGiovine B, Kunkel SL, Morris SB, Xue Y-Y, Burdick MD, Glass MC, Iannettoni MD, Strieter RM. Epithelial neutrophil activating peptide (ENA-78) is an important angiogenic factor in non-small cell lung cancer. *J. Clin Invest.* 1998; 102:465-472.
3. Lukacs, N.W. Kunkel, S.L. Chemokines and their role in disease. *Int J Clin Lab Res* 1998, 28:91-95.
4. Kunkel, S.L., Kukacs, N.W., Strieter, R.M., Chensue, S.W. Animal models of granulomatous inflammation. *Sem Respir Infect.* 1998; 13:221-228.
5. Yan, X.T., Tumpey, T.M., Kunkel, S.L., Oakes, J.E., Lausch, R.N. Role of macrophage inflammatory protein-2 in neutrophil migration, tissue injury, and virus clearance in the HSV-1 infected cornea. *Invest. Ophthalmol Vis Sci.*; 1998 39:1854-1862.
6. Smith, R.E., Strieter, R.M., phan, S.H., Lukacs, N., S.L. Kunkel. TNF and IL-6 mediate MIP-1 alpha expression in bleomycin-induced lung injury. *J. Leuko. Biol.* 1998; 64: 528-536.
7. Ruth, J.H., Lukacs, N.W., Warmington, K.S., Polak, T.J., Burdick, M., Kunkel, S.L., Strieter, R.M., Chensue, S.W. Expression and participation of eotaxin during mycobacterial (type1) and schistosomal (type 2) antigen-elicited granuloma formation. *J. Immunol.* 1998; 161:4276-4282.
8. Campbell, E.M., Kunkel, S.L., Strieter, R.M., Lukacs, N.W. Temporal role of chemokines in a murine model of cockroach allergen-induced airway hyperreactivity and eosinophilia. *J. Immunol.* 1998;161:7047-7053.
9. Driscoll, KE, Carter, JM, Howard, BW, Burdick, M, Kunkel SL, Strieter, RM. Interleukin-10 regulates quartz-induced pulmonary inflammation in rats. *Am J. Physiol.: Lung Cell Mol. Physiol.* 1998;L887-894.
10. Colletti LM, Cortis A, Lukacs N, Kunkel SL, Green M Strieter RM. Tumor necrosis factor upregulates ICAM-1, which is important in the neutrophil-dependent lung and liver injury associated with hepatic ischemia and reperfusion in the rat. *Shock.* 1998;10:182-191
11. Colletti LM, Green M, Burdick MD, Kunkel SL, Strieter RM. Proliferative effects of CXC chemokines in rat hepatocytes in vitro and in vivo. *Shock.* 1998;10:248-257.

12. Steinhauser, M.L., Kunkel, S.L., Hogaboam, C.M., Evanoff, H., Strieter, R.M., Lukacs, N.W. Macrophage/fibroblast coculture induces macrophage inflammatory protein-1 alpha production mediated by intercellular adhesion molecule-1 and oxygen radicals. *J. Leukoc. Biol.* 1998;64:636-641.
13. Zikus, C., Kunkel, S.L., Simpson, K., Evanoff, H., Glass, M., Strieter, R.M., Lukacs, N.W. Differential regulation of C-C chemokines during fibroblast-monocyte interactions: adhesion vs. inflammatory cytokine pathways. *Mediators Inflamm* 1998;7:269-274.
14. Zisman, D.A., Strieter, R.M., Kunkel, S.L., Tsai, W.C., Wilkowski, J.M., Buckell, K.A., Standiford, T.J. Ethanol feeding impairs innate immunity and alters the expression of Th1- and Th2-phenotype cytokines in murine *Klebsiella pneumoniae*. *Alcohol Clin. Exp. Res.* 1998;22:621-627.
15. Hogaboam, C.M., Steinhauser, M.L., Chensue, S.W., Kunkel, S.L. Novel roles for chemokines and fibroblasts in interstitial fibrosis. *Kid Int* 1998, 54:2152-2159.
16. Szekanecz Z, Strieter RM, Kunkel SL, Koch AE. Chemokines in rheumatoid arthritis. *Springer Sem Immunopathol* 1998; 20:115-132.
17. Morrison, D., Strieter, R.M., Burdick, M.D., Kunkel, S.L., MacNee, W. Neutrophil chemokines in bronchoalveolar lavage fluid and leukocyte-conditioned medium from nonsmokers and smokers. *Eur. Respir. J.* 1998;10:1067-1072.
18. Steinhauser, M.L., Hogaboam, C.M., Kunkel, S.L., Lukacs, N.W., Strieter, R.M., Standiford, T.J. IL-10 is a major mediator of sepsis-induced impairment in lung antibacterial host defense. *J. Immunol.* 1999; 162:392-399.
19. Hogaboam, CM, Simpson, KJ, Chensue, SW, Steinhauser, ML, Lukacs, NW, Gauldie, J, Strieter, RM, Kunkel, SL. Macrophage inflammatory protein-2 gene therapy attenuates adenovirus- and acetaminophen-mediated hepatic injury. *Gene Therapy.* 1999; 6:573-584.
20. Gourley, T, Roys, S, Lukacs, NW, Kunkel, SL, Flavell, RA, Chang, CH. A novel role for the major histocompatibility complex class II transactivator CIITA in the repression of IL-4 production. *Immunity.* 1999; 10:377-386.
21. Keane, M.P., Belperio, J.A., Moore, T.A., Moore, B.B., Arenberg, D.A., Smith, R.E., Burdick, M.D., Kunkel, S.L., Strieter, R.M. Neutralization of the CXC chemokine, macrophage inflammatory protein-2, attenuates bleomycin-induced pulmonary fibrosis. *J. Immunol.* 1999; 162:5511-5518.
22. Steinhauser, M.L., Hogaboam, C.M., Lukacs, N.W., Strieter, R.M., Kunkel, S.L. Multiple roles for IL-12 in a model of acute septic peritonitis. *J. Immunol.* 1999; 162:5437-5443.
23. Hogaboam, C.M., Gallinat, C.S., Taub, D.D., Strieter, R.M., Kunkel, S.L., Lukacs, N.W. Immunomodulatory role of C10 chemokine in a murine model of allergic bronchopulmonary aspergillosis. *J. Immunol.* 1999; 162:6071-6079.
24. Moore, B.B., Arenberg, D.A., Stoy, K., Morgan, T., Addison, C.L., Morris, S.B., Glass, M., Wilke, C., Xue, Y.Y., Sitterding, S., Kunkel, S.L., Burdick, M.D., Strieter, R.M. Distinct CXC chemokines mediate tumorigenicity of prostate cancer cells. *Amer. J. Pathol.* 1999; 154:1503-1512.
25. Chensue, S.W., Warmington, K.S., Allenspach, E.J., Lu, B., Cerard, C., Kunkel, S.L., Lukacs, N.W. Differential expression and cross-regulatory function of RANTES during mycobacterial (type 1) and schistosomal (type 2) antigen-elicited granulomatous inflammation. *J. Immunol.* 1999, 163:165-173.
26. Keane MP, Moore BB, Wilke CA, Smith RE, Burdick MD, Glass MC, Arenberg DA, Kunkel SL, Strieter RM. Neutralization of the CXC chemokine, macrophage inflammatory protein-2

- (MIP-2), attenuates pulmonary fibrosis via inhibition of angiogenesis. *J. Immunol.* 1999; 162:5511-5518.
27. Bian ZM, Elner SG, Strieter RM, Kunkel SL, Lukacs NW, Elner, V. IL-4 potentiates IL-1beta- and TNF-alpha-stimulated IL-8 and MCP-1 protein production in human retinal pigment epithelial cells. *Curr. Eye Res.* 1999; 18:349-357.

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.
2. Lukacs, N.W., C. Hogaboam, E. Campbell, and S.L. Kunkel. 1998. Chemokines: Function, regulation, and alteration of inflammatory responses. *Chemokines.* Ed. Alberto Montavani. Chemical Immunology. Karger.
3. Campbell, E., S.L. Kunkel, and N.W. Lukacs. 1998. Differential regulation of T cell responses by chemokines. Ed. Mark Rothenberg.
4. Kunkel, S.L., N.W. Lukacs, R.M. Strieter, and S.W. Chensue. 1999. The role of chemokines in the immunopathology of pulmonary disease. In: *Forum Trends in Experimental and Clinical Medicine.*
5. Strieter, R.M., Kunkel, S.L., Walz, A. epithelial neutrophil activating protein (ENA-78): A member of the CXC chemokine family. In. Aggarwal BB (ed) *Human cytokines: handbook for basic and Clinical Research Vol III.* Blackwell Science, Inc., Cambridge MA 1998 pp 314-348.

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

1. S.S. Chang, E. Strieter, N.W. Lukacs, and S.L. Kunkel. 1999. Induction of CCR3 expression on human Neutrophils. *Keystone Symposium; chemokine biology.*
2. S.H.P. Oliveira, S.L. Kunkel, R.M. Strieter, and N.W. Lukacs. 1999. Production of chemokines and their receptors by mast cells and eosinophils by stem cell factor stimulation. *Keystone Symposium; chemokine biology.*
3. W.J. Karpus, K.J. Kennedy, B.T. Fife, R.M. Strieter, N.W. Lukacs, and S.L. Kunkel. 1999. Chemokine and chemokine receptor regulation of immune-mediated central nervous system demyelinating disease. *Keystone Symposium; chemokine biology.*
4. E. Campbell, I.F. Charo, S.L. Kunkel, R.M. Strieter, and N.W. Lukacs. 1999. Monocyte chemoattractant protein-1 mediates cockroach allergen-induced bronchial hyperreactivity in normal but not CCR2 ^{-/-} mice: The role of mast cells. *Keystone Symposium; chemokine biology.*
5. R.M. Allen, N.W. Lukacs and S.L. Kunkel. 1999. Downregulation of chemokine production by MAP kinase inhibitors in human neutrophils and mononuclear cells. *Exp. Biology '99 #643.28*
6. C.L. Bone-Larson, C.M. Hogaboam, M.L. Steinhauser, N.W. Lukacs, R.M. Strieter, S.W. Chensue, and S.L. Kunkel. 1999. The multiple roles of SCF in a murine model of fecal peritonitis. *Exp Biology '99, #750.6.*
7. E.M. Campbell, I. Charo, S.L. Kunkel, R.M. Strieter, L. Boring, J. Gosling, and N.W. Lukacs. 1999. Mechanisms of monocyte chemoattractant protein-1-induced bronchial hyperreactivity in normal and allergic mice. *Exp Biol. '99.*
8. S.S. Cheng, E. Strieter, P. Ponath, N.W. Lukacs, and S.L. Kunkel. 1999. Induction of CCR2 and CCR3 expression on human neutrophils. *Exp Biol. '99.*

9. T.S. Gourley, S. Roys, N.W. Lukacs, S.L. Kunkel, R.A. Flavell, and C-H. Chang. 1999. A novel role for the major histocompatibility complex class II transactivator in the repression of IL-4 production. *Exp. Biol.* '99.
10. C.M. Hogaboam, C.L. Bone-Larson, M.S. Steinhauser, N.W. Lukacs, L.M. Colletti, K.J. Simpson, R.M. Strieter, and S.L. Kunkel. 1999. Novel CxCR2-dependent liver regenerative qualities of ELR-containing CxC chemokines. *Exp. Biol.* '99
11. A. Matsukawa, N.W. Lukacs, R.M. Strieter, and S.L. Kunkel. 1999. Neutralization of IL-13 increases lethality in a murine model of acute septic peritonitis. *Exp. Biol.* '99.
12. SHP Oliveira, S.L. Kunkel, R.M. Strieter and N.W. Lukacs. 1999. SCF stimulation of mast cells and eosinophils induces chemokine production. *Exp. Biol.* '99.
13. Belperio JA, Chen B, Xue YY, Burdick MD, Morris S, Keane MP, Kunkel SL, Strieter RM. Lung transplantation allograft rejection is attenuated by in vivo neutralization of RANTES. *Am J. Respir. Crit. Care Med.* 159:A276, 1999.
14. Koch AE, Volin MV, Woods JM, Burdick MD, Harlow LM, Woodruff DC, Kunkel SL, Strieter RM. The CXC chemokines IL-8, ENA-78, and GRO regulate angiogenesis in the rheumatoid joint. *J. Investig. Med.* 47:196A, 1999.
15. Arenberg D, Strom S, Keane M, Kunkel S, Burdick M, Strieter R. Macrophage infiltration in human and experimental lung cancer: the role of CC chemokines. *J. Investig. Med.* 47:181A, 1999.
16. Belperio JA, Chen B, Xue YY, Burdick MD, Morris S, Keane MP, Kunkel SL, Strieter RM. Elevated levels of MCP-1 are associated with acute rat lung transplantation allograft rejection. *FASEB J.* 13:A1130, 1999.

**RICHARD W. LIEBERMAN, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENTS OF PATHOLOGY AND
OBSTETRICS & GYNECOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Gynecologic Pathology Consultation - twelve months.
- B. Gynecologic Oncology Semimonthly Tumor Planning Conference - twelve months.
- C. Autopsy service – twelve months (15 weeks, 6 weekends).
- D. Gynecologic Oncology – Colposcopy Clinic, one half day/week, September – June, 1999.

II. TEACHING ACTIVITIES:

- A. Residents:
 - 1. Review cases and supervise presentation of semimonthly Gynecologic Oncology Tumor Planning Conference – twelve months.
 - 2. Sign-out - Gynecologic Pathology and Autopsy cases. Cover placental pathology sign-out in Dr. Heidelberger's absence.
 - 3. Instruction in the Gross Examination, frozen section diagnosis, and processing of Gynecologic Surgical specimens, August 1998.
 - 4. Instruction and supervision in the performance, presentation and sign-out of autopsy cases.
 - 5. Teaching Conferences- lectures in Gyn Pathology, two weeks, May 1999.
 - 6. Consult Case Conference - two/year.
 - 7. Miscellaneous resident evening conferences in Gyn Path
 - 8. Resident resource web page in Gyn Pathology (<http://gynonc.path.med.umich.edu> – Web access to Gyn Pathology Grossing Manual, lecture slides, and other resources
- B. Medical Students:
 - 1. M2, Obstetrics & Gynecology Sequence: Four hours Gynecologic Pathology lectures; preparation of examination questions.
 - 2. M2, Obstetrics & Gynecology Sequence: Laboratory instruction.
 - 3. M2 resource web page in Gyn Pathology (<http://gynonc.path.med.umich.edu> – Web access to Gyn Pathology laboratory, lecture slides, and other resources
- C. Ob/Gyn Residents and Gynecologic Oncology Fellow:
 - 1. Semimonthly Tumor Planning Conference – twelve months.
 - 2. Colposcopy clinic staff – one-half day per week (September 1998- June 1999)
 - 3. Lectures in Gynecologic Pathology to Gyn Oncology Service – two/year
 - 4. Gyn Pathology Rotation for 3rd year Gyn Oncology Rotation – one month

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Cost effectiveness of vaginal smear screening after total hysterectomy for benign disease". Project Investigator, Dr. Michael D. Fetters, Department of Family Medicine. Sponsored by Blue Cross Blue Shield of Michigan. Salary support – 3%.

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. Medical College Alumni Society (MCAS) Invited Lecturer at the Sesquicentennial Reunion. "Medical Imaging and the Internet". Ann Arbor, Michigan, September 11, 1998.

Web broadcast: archived at: <http://s-umhs-telemed2.mcit.med.umich.edu/conferences/9-11-98.ram> at 1hr 3min into program.

2. "Important New Imaging Formats for Pathology on the Web (Intermediate)" Drs. Lieberman and Lougee" Workshop Presentation, Anatomic Pathology Informatics, Imaging, and the Internet (APIII) Meeting in Pittsburgh, Pennsylvania. November 6, 1998. Web broadcast: archived at: <http://www.pathology.pitt.edu/apiii98/av-98/288/day2/liebermanlougee.ram> or Slide show at: <http://www.pathology.pitt.edu/apiii98/talks/lieber/default.htm>
3. "Image Capture, Manipulation, and Display for a Pathology Web Site Richard W. Lieberman, MD" Information Technology Workshop, presented to the Automated Information Management in the Clinical Laboratory (AIMCL) 17th Annual Symposium at Towsley Center, The University of Michigan. May 28, 1999.

VI. PUBLICATIONS:

ARTICLES ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lieberman RW, Henry MR, Laskin W, Walenga JF, Buckner S, O'Connor DM. "Colposcopy in pregnancy: Directed brush cytology compared with cervical biopsy." Accepted for publication in *Obstetrics & Gynecology*. (~August 1999)
2. Taylor RT, Zeller J, Lieberman RW, O'Connor DM. "An analysis of two versus three grades for endometrial carcinoma." Accepted for publication in *Gynecologic Oncology*. (~July 1999)

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 1998 - 30 JUNE 1999**

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 four postdoctoral fellows (Steven Domino, M.D., Ph.D., Jonathon Homeister, M.D., Ph.D., Moonjae Cho, Ph.D., and Glenda Smithson, Ph.D.).
- B. Supervision of two MSTP students (Daniel Becker and David Kim).
- C. Lecturer - Postdoctoral Research Training Program.
- D. Member of four Ph.D. thesis committees (Stephanie M. Alt, Stacey Arnold, George Pipia, and Vance H. Thomas).
- E. Oral prelim committees; Department of Pathology, Ph.D. Program.
- F. Member, Cell and Molecular Biology 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

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
- C. Member, University of Michigan Health Services Strategic Planning Research Subcommittee.

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, Editorial Board of Glycobiology
- E. Member, Editorial Board of Archives of Biochemistry and Biophysics
- F. 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. Immune defects in fucosyltransferase mutant mice. St. Mark's Hospital, MRC Glycobiology, UK, July 1998.
2. Immune defects in fucosyltransferase-deficient mice. The 19th International Carbohydrate Symposium. San Diego, CA, August 1998.
3. Immune deficiencies and selectin ligand defects in fucosyltransferase-mutant mice. Advances in inflammatory bowel disease. Bath, England, July 1998.
4. Graded L-selectin ligand activities in fucosyltransferase mutant mice. US-Japan meeting in San Diego on Histochemistry. La Jolla, CA, July 1998.
5. Immune deficiencies and selectin ligand defects in fucosyltransferase-mutant mice. Northwestern University Medical School, Chicago, IL, October 1998.
6. Immune deficiencies and selectin ligand defects in fucosyltransferase-mutant mice. Glycostructures in Biological Systems. Hamburg, Germany, December 1998.
7. Developmental consequences of GDP-fucose deficiency in FX-null mice. 1999 Gordon Conference on Glycobiology. Ventura, CA, February 1999.
8. Selectin ligands and leukocyte traffic. Howard Hughes Medical Institute Scientific Meeting, May 1999.

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

1. Swarte VVR, Joziase 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* 28:3040-3047, 1998.
2. 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* 92:2345-2352, 1998.
3. Knibbs RN, Craig RA, Mály P, Smith PL, Wolber FM, Faulkner NE, Lowe JB, and Stoolman LM. $\alpha(1,3)$ -fucosyltransferase VII-dependent synthesis of P- and E-selectin ligands on cultured T lymphoblasts. *J Immunol* 161:6305-6315, 1998.
4. Wolber FM, Curtis JL, Mály P, Kelly RJ, Smith P, Yednock TA, Lowe JB, and Stoolman LM. Endothelial selectins and α_4 integrins regulate independent pathways of T lymphocyte recruitment in the pulmonary immune response. *J Immunol* 161:4396-4403, 1998.
5. Ellies LG, Tsuboi S, Petryniak B, Lowe JB, Fukuda M, and Marth JD. Core 2 oligosaccharide biosynthesis distinguishes between selectin ligands essential for leukocyte homing and inflammation. *Immunity* 9:881-890, 1998.
6. Mohlke KL, Purkayastha AA, Westrick RJ, Smith PL, Petryniak B, Lowe JB, and Ginsburg D. *Mvwf*, a dominant modifier of von Willebrand factor, results from altered lineage-specific expression of a glycosyltransferase. *Cell* 96:111-120, 1999.
7. Roberts AW, Kim C, Zhen L, Lowe JB, Kapur R, Petryniak B, Spaetti A, Pollock J, Borneo JB, Bradford GB, Atkinson SJ, Dinauer MC, and Williams DA. Deficiency of the hematopoietic cell-specific Rho-family GTPase, *Rac2*, is characterized by multiple abnormalities in neutrophils function and impaired host defense. *Immunity* 10:183-196, 1999.
8. Becker DJ, and Lowe JB. Leukocyte Adhesion Deficiency II. *Biochem Biophys Acta*, 1999, in press.
9. Hiraoka N, Tsuboi S, Suzuki M, Petryniak B, Nakayama J, Izawa D, Tanaka T, Miyasaka M, Lowe JB, and Fukuda M. A novel, high endothelial venule-specific sulfotransferase directs expression of 6-sulfo sialyl Lewis x, an L-selectin ligand displayed by CD34. *Immunity*, 1999, in press.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Thall A, Maly P, Petryniak B, Rogers C, Smith PL, Cheng G, Askari S, Saunders T, von Andrian UH, and Lowe JB. The $\alpha(1,3)$ fucosyltransferase Fuc-TIV/ELFT controls leukocyte trafficking by tuning the affinities of E-, P-, and L-selectin ligands. In preparation.
2. Rabb H, Haq M, Saba SR, Liu Z, and Lowe JB. Fucosyltransferase Fuc-TIV-dependent selectin ligands mediate pathologic leukocyte trafficking in ischemic renal perfusion injury. 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.

4. Ulfman LH, Cheng G, Lowe JB, and von Andrian UH. Leukocyte tethering and rolling in non-inflamed skin venules: constitutive contributions by E-selectin and fucosyltransferase IV. In preparation.
5. Masayoshi Oh-eda M, Tsuboi S, Petryniak B, Lowe JB, and Fukuda M. Reconstitution of E-selectin ligand oligosaccharides on CHO cells by expression of two distinct fucosyltransferases. Oligosaccharide structures synthesized by mouse fucosyltransferase IV and VII. In preparation.
6. Hiraiwa N, Domino S, Saunders T, and Lowe JB. Dominant pre-implantation lethality in mice directed by aberrant expression of an $\alpha(1,2)$ fucosyltransferase cDNA. In preparation.
7. Legault DJ, Kelly RJ, Smith PL, and Lowe JB. Acceptor substrate specificities of the $\alpha(1,3/1,4)$ fucosyltransferases are determined by single amino acid differences. In preparation.
8. Zollner O, Huang M-C, Moll T, Maly P, Thall AD, Lowe JB, and Vestweber D. P-selectin glycoprotein ligand-1 and E-selectin ligand-1 are modified by different fucosyltransferases in mouse neutrophils. In preparation.

BOOKS AND CHAPTERS IN BOOKS:

1. Lowe JB. Red Cell Membrane Antigens. *The Molecular Basis of Blood Diseases*. Stamatoyannopoulos G, Nienhuis AW, Majerus PW, and Varmus H (eds.). W. B. Saunders Company, Orlando, Florida, in press, 1999.
2. Lowe JB and Marth J. Outer sequences common to different glycan classes. In *Essentials of glycobiology*. Varki A., Cummings R, Esko J, Freeze H, Hart G, and Marth J. (eds). Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, in press, 1999.
3. Lowe JB and Varki A. The glycosyltransferases. In *Essentials of glycobiology*. Varki A, Cummings R, Esko J, Freeze H, Hart G, and Marth J. (eds). Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, in press, 1999.
4. Lowe JB and Freeze H. Genetic disorders of glycosylation in intact animals. In *Essentials of glycobiology*. Varki A., Cummings R, Esko J, Freeze H, Hart G, and Marth J. (eds). Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, in press, 1999.
5. Cummings RD and Lowe JB. The selectins. In *Essentials of glycobiology*. Varki A., Cummings R, Esko J, Freeze H, Hart G, and Marth J. (eds). Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, in press, 1999.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999

I. CLINICAL ACTIVITIES:

- A. Dermatopathology Service – 12 months.
- B. Dermatopathology Consultation Service (including MLabs and Veterans Administration Hospital) – 12 months.

II. TEACHING ACTIVITIES:

- A. Medical Students:
 - 1. Lecturer, MS II Dermatology Sequence.
 - 2. Laboratory instructor, MS II Dermatology Sequence
 - 3. Dermatopathology, Pathology Clerkship, MS I and MS IV students (6 students).
- B. House Officers:
 - 1. Dermatopathology sign-out.
 - 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).
- E. Honors: "Teacher of the Year Award," Department of Dermatology, 1998-1999

III. RESEARCH ACTIVITIES:

Projects under Study:

- A. 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.).
- B. Utility of Melan-A (MART 1) antigen expression in evaluation of sentinel lymph nodes for metastatic melanoma (V. Sondak, M.D., A. Yohanda, M.D., A. Chang, M.D., T. Johnson, M.D., and L. Su, M.D.).
- C. Prospective evaluation of incidence of perineural invasion in basal cell carcinomas treated with Mohs surgery (D. Ratner, M.D., T.M. Johnson, M.D., and D.J. Fader, M.D.)
- D. Histologic features of thick non-metastasizing melanomas (cohort study – North American Melanoma Pathology Study Group).
- E. Histologic features of thin metastasizing melanomas (cohort study – North American Melanoma Pathology Study Group).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Dermatopathology Service.
- B. Quality Assurance/Quality Control Program. Cutaneous Surgery Unit.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. Lecturer, "The Pathology of Problematic Pigmented Lesions: The Michigan Experience." Michigan Dermatologic Society Meeting, University of Michigan, Ann Arbor, Michigan, February, 1999.

EDITORIAL BOARDS:

- A. Editorial Board, Archives of Dermatology

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. 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 24:915-919, 1998.
- 2. Johnson, T.M., Hamilton, T.A., Lowe, L.: Multiple primary melanomas. J Am Acad Dermatol 39:422-427, 1998.
- 3. Kalaaji, A.N., Douglass, M.C., Chaffins, M., Lowe, L.: Calciphylaxis: a cause of necrotic ulcers in renal failure. J Cutan Med Surg 2:242-244, 1998.
- 4. Karimipour, D., Lowe, L., Blaivas, M., Sachs, D., Johnson, T.M.: Lafora Disease: diagnosis by skin biopsy. J Am Acad Dermatol (in press).
- 5. Sachs, D.L., Lowe, L., Chang, A.E., Carson, E., Johnson, T.M.: Do primary small intestine melanomas exist?: report of a case. J Am Acad Dermatol (in press).

6. Johnson, T.M., Saluja, A., Fader, D., Blum, D., Cotton, J., Wang, T.S., Lowe, L.: Isolated extragenital bowenoid papulosis of the neck. *J Am Acad Dermatol* (in press).

BOOKS/CHAPTERS IN BOOKS:

1. Fazel, N., Wilczynski, S, Lowe, L., Su, L.: Clinical, histopathologic and molecular aspects of cutaneous human papillomavirus infections. *Dermatologic Clinics* (in press)

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

**ANNUAL DEPARTMENT REPORT
1 JULY 1998-30 JUNE 1999**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

1. "Immunopathologic responses in Disease", Pathology 643, Course Instructor, Winter, 1998.
2. Pathology 585, Lecturer, Inflammation section, Summer, 1999.
3. Pathology 581, Dental School and Pathology Grad. Students. Lectures on Inflammation, cytokines and Immunology
4. Post-doctoral fellows- Emma Campbell, Kim Tekkanat, and Sandra Oliveira
5. Visiting Scientists- Akihiro Matsukawa

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.
- E. Principal Investigator, "SCF and mast cells in allergic airway inflammation", NIH R01. 9/1/99-8/30/04.
- F. 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:

1. Departmental representative- Curriculum Committee for Joint Medical School Graduate program, PIBS.
2. Admissions Committee- Immunology –Pathology Joint Graduate Program in PIBS.
3. Curriculum Committee for Pathology Graduate Program.

REGIONAL AND NATIONAL:

-Associate Editor - Journal of Immunology

-ASIP Program Committee for Experimental Biology 1999 and 2000 meeting

-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

-ADHOC GRANT REVIEW ACTIVITIES:

1. Adhoc on Immunology and Microbiology Study section (IMS) at NIH.
2. Adhoc Reviewer-Special Emphasis Panel for NIH.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Chemokines and cytokines in allergic airway inflammation. World Equine airways symposium. Guelph, Ontario, Canada. August 5, 1998.
2. Chemokines and their receptors in allergic airway inflammation. Schering Plough. August 24, 1998.
3. Chemokines and Inflammation. Diagnosis and treatment of Radiation injury. August 31, 1998. Rotterdam, The Netherlands.
4. The role of chemokines and their receptors in Allergic airway inflammation. Serona Research Institute. September 2, 1998. Geneva, Switzerland.
5. Chemokines: Function, Activation, and role during immune responses. Indiana University Medical School, Dept. of Micro/Immuno. Oct. 22, 1998.
6. The role of chemokines in regulation of immune responses. Society for biological therapy. 13th Annual meeting. Pittsburgh. Oct. 23, 1998.
7. Differential role of Chemokines during allergic airway inflammation. Keystone Symposium: Chemokine biology. Jan. 18-23, 1999.
8. Cytokines, chemokines and the immune response. Central Michigan University, Dept of Biology. Jan. 28th, 1998.
9. Cytokines and chemokines in allergic airway inflammation. Huntington Hospital. Feb. 12th, 1999.
10. Chemokine-dependent regulation of immune responses. Institut Pasteur. Euroconferences. Chemokines and their receptors: from basic research to therapeutic intervention. March 11-13, 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERREED JOURNALS:

1. Campbell, E., S.L. Kunkel, R.M. Strieter, and N.W. Lukacs. 1998. Temporal role of chemokines in a murine model of cockroach allergen-induced airway hyperreactivity and eosinophilia. *J. Immunol.* 161:7047-7053.
2. Gharee-Kermani, M., B. McGarry, N. Lukacs, G. Huffnagle, R.W. Egan, and S.H. Phan. 1998. The role of IL-5 in bleomycin-induced pulmonary fibrosis. *J. Leuk. Biol.* 64:657-665.
3. Hogaboam, CM, C.S. Gallinat, C. Bone-Larson, S.W. Chensue, N.W. Lukacs, R.M. Strieter, and S.L. Kunkel. 1998. Collagen deposition in a non-fibrotic lung granuloma model after nitric oxide inhibition. *Am. J. Pathol* 153:1861-1872.
4. Colletti, L.M., A. Cortis, N. Lukacs, S.L. Kunkel, M. Green, and R.M. Strieter. 1998. Tumor necrosis factor up-regulates intracellular adhesion molecule 1, which is important in the neutrophil-dependent lung and liver injury associated with hepatic ischemia and reperfusion in the rat. *Shock* 10:182-191.

5. Steinhauser, M.L., C.M. Hogaboam, S.L. Kunkel, N.W. Lukacs, R.M. Strieter, and T.J. Standiford. Interleukin 10 is a major mediator of sepsis-induced impairment in lung anti-bacterial host defense. *J. Immunol.* 162:392-399.
6. Hogaboam, C.M., K.J. Simpson, S.W. Chensue, M.L. Steinhauser, N.W. Lukacs, J. Gauldie, R.M. Strieter, and S.L. Kunkel. 1999. Macrophage inflammatory Protein-2 gene therapy attenuates adenovirus and acetaminophen-mediated hepatic injury. *Gene Ther* 6:573-584.
7. Kennedy, K.J., R.M. Strieter, S.L. Kunkel, N.W. Lukacs, and W.J. Karpus. 1998. Acute and relapsing experimental autoimmune encephalomyelitis are regulated by differential expression of the CC chemokine macrophage inflammatory protein-1 α and monocyte chemoattractant protein-1. *J. Neuroimmunol.* 92:98-108.
8. Campbell, E., P. Lincoln, C.M. Hogaboam, and N.W. Lukacs. 1999. Stem cell factor-induced airway hyperreactivity in allergic and normal mice. *Am. J. Pathol.* 154:1259-1265.
9. T. Gourley, S. Hill, N.W. Lukacs, S.L. Kunkel, R.A. Flavell and C.H. Chang. 1999. A novel role for the major histocompatibility complex class II transactivator in the repression of IL-4 production. *Immunity* 10:377-386.
10. C. M. Hogaboam, C. S. Gallinat, D. D. Taub, R. M. Strieter, S. L. Kunkel, and N.W. Lukacs. 1999. Immunomodulatory Role of C10 Chemokine in a Murine Model of Allergic Bronchopulmonary Aspergillosis. *J. Immunol.* 162:6071-6079.
11. Hogaboam, C., S.L. Kunkel, R.M. Strieter, D.D. Taub, P. Lincoln, T.J. Standiford, and N.W. Lukacs. 1998. Novel role of transmembrane SCF for mast cell activation and eotaxin production in mast cell-fibroblast interactions. *J. Immunol.* 160:6166-6171.
12. Chensue, S.W., K. Warmington, E.J. Allenspach, Bao Liu, C. Gerard, S.L. Kunkel, and N.W. Lukacs. 1999. Differential expression and cross-regulatory function of RANTES during mycobacterial (Type 1) and schistosomal (type 2) antigen-elicited granulomatous inflammation. *J. Immunol.* 163:165-173.

ARTICLES ACCEPTED FOR PUBLICATION:

1. Wu, Y., N.W. Lukacs, M. Feldmesser, L.M. Weiss, M.B. Prystowsky, and A. Orlofsky. Expression of the murine chemokine C10 in eosinophils and inflammatory macrophages. *Cytokine* (In Press).
2. Campbell, E., I.F. Charo, S.L. Kunkel, R.M. Strieter, L. Boring, J. Gosling, and N.W. Lukacs. 1999. Monocyte chemoattractant protein-1 mediates cockroach allergen-induced bronchial hyperreactivity in normal but not CCR2^{-/-} mice: The role of mast cells. *J. Immunol.* (In Press).

BOOKS/CHAPTERS IN BOOKS:

1. Lukacs, N.W., C. Hogaboam, E. Campbell, and S.L. Kunkel. 1998. Chemokines: Function, regulation, and alteration of inflammatory responses. *Chemokines*. Ed. Alberto Montavani. Chemical Immunology. Karger.
2. Campbell, E., S.L. Kunkel, and N.W. Lukacs. 1998. Differential regulation of T cell responses by chemokines. Ed. Mark Rothenberg.
3. Kunkel, S.L., N.W. Lukacs, R.M. Strieter, and S.W. Chensue. 1999. The role of chemokines in the immunopathology of pulmonary disease. In: *Forum Trends in Experimental and Clinical Medicine*.

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

1. S.S. Chang, E. Strieter, N.W. Lukacs, and S.L. Kunkel. 1999. Induction of CCR3 expression on human Neutrophils. Keystone Symposium; chemokine biology.
2. S.H.P. Oliveira, S.L. Kunkel, R.M. Strieter, and N.W. Lukacs. 1999. Production of chemokines and their receptors by mast cells and eosinophils by stem cell factor stimulation. Keystone Symposium; chemokine biology.
3. W.J. Karpus, K.J. Kennedy, B.T. Fife, R.M. Strieter, N.W. Lukacs, and S.L. Kunkel. 1999. Chemokine and chemokine receptor regulation of immune-mediated central nervous system demyelinating disease. Keystone Symposium; chemokine biology.
4. E. Campbell, I.F. Charo, S.L. Kunkel, R.M. Strieter, and N.W. Lukacs. 1999. Monocyte chemoattractant protein-1 mediates cockroach allergen-induced bronchial hyperreactivity in normal but not CCR2 $-/-$ mice: The role of mast cells. Keystone Symposium; chemokine biology.
5. R.M. Allen, N.W. Lukacs and S.L. Kunkel. 1999. Downregulation of chemokine production by MAP kinase inhibitors in human neutrophils and mononuclear cells. Exp. Biology '99 #643.28
6. C.L. Bone-Larson, C.M. Hogaboam, M.L. Steinhauser, N.W. Lukacs, R.M. Strieter, S.W. Chensue, and S.L. Kunkel. 1999. The multiple roles of SCF in a murine model of fecal peritonitis. Exp Biology '99, #750.6.
7. E.M. Campbell, I. Charo, S.L. Kunkel, R.M. Strieter, L. Boring, J. Gosling, and N.W. Lukacs. 1999. Mechanisms of monocyte chemoattractant protein-1-induced bronchial hyperreactivity in normal and allergic mice. Exp Biol. '99.
8. S.S. Cheng, E. Strieter, P. Ponath, N.W. Lukacs, and S.L. Kunkel. 1999. Induction of CCR2 and CCR3 expression on human neutrophils. Exp Biol. '99.
9. M.M. Glovsky, N.W. Lukacs, and P.A. Ward. 1999. Complement activation- A pathway to bronchial hyperreactivity in a mouse. Exp. Biol '99.
10. T.S. Gourley, S. Roys, N.W. Lukacs, S.L. Kunkel, R.A. Flavell, and C-H. Chang. 1999. A novel role for the major histocompatibility complex class II transactivator in the repression of IL-4 production. Exp. Biol. '99.
11. C.M. Hogaboam, C.L. Bone-Larson, M.S. Steinhauser, N.W. Lukacs, L.M. Colletti, K.J. Simpson, R.M. Strieter, and S.L. Kunkel. 1999. Novel CxCR2-dependent liver regenerative qualities of ELR-containing CxCR2 chemokines. Exp. Biol. '99
12. A. Matsukawa, N.W. Lukacs, R.M. Strieter, and S.L. Kunkel. 1999. Neutralization of IL-13 increases lethality in a murine model of acute septic peritonitis. Exp. Biol. '99.
13. S.H.P. Oliveira, S.L. Kunkel, R.M. Strieter and N.W. Lukacs. 1999. SCF stimulation of mast cells and eosinophils induces chemokine production. Exp. Biol. '99.

PATENTS AND DISCLOSURES:

1. Methods and Pharmaceuticals for modeling and treating asthma. Case No. 95,180. Inventors: Elise Brownall and Nicholas W. Lukacs. Patent Issued Jan., 1999. Patent # 5,911,988.
2. C-x-CR2 binding chemokines in treatment of acute liver damage. Cory Hogaboam, Steven Kunkel, Robert Strieter, Ken Simpson, Lisa Colletti, and Nicholas Lukacs. October, 1998. Disclosure

3. The role of stem cell factor (SCF) for the protection and regeneration of liver function. Nicholas W. Lukacs, Kenneth Simpson, Steven Kunkel, Cory Hogaboam, and Robert Strieter. November, 1998. Disclosure.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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.
- E. General autopsies.

II. TEACHING ACTIVITIES:

DEPARTMENTAL:

- A. Neuroscience Sequence, Neuropathology for Second Year Medical Students. Prepared two laboratories and two lectures on brain tumors; toxic, metabolic, demyelinating and infectious diseases. Taught four laboratories.
- 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, 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 Assistants Erin Loyer, Anne Tkaczyk, and Mary Cates.
- D. UROP Student Lauren Wallner

REGIONAL AND NATIONAL:

- A. Faculty, "New Methods of Brain Tumor Analysis": 37th Annual AFIP Kenneth M. Earle Memorial. Neuropathology Review, Armed Forces Institutes of Pathology, Rockville, Maryland, February 22-26, 1999.
- B. Instructor, Armed Forces Institutes of Pathology Neuropathology Course, Washington, D.C., March 18-29, 1999.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Nycomed Pharmaceuticals. "Transferin Receptor Gene Therapy" 03/15/99 - 05/31/99 (\$10,000 extension 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. Magnetic resonance diffusion and cross relaxation of brain tumors with Drs. James Brunberg, Thomas Chenevert and Brian Ross.
- C. Characterization of Rosai-Dorfman disease in brain with Drs. Michael Boland and Karin Muraszko.
- D. Viral vectors in glioma therapy with Drs. Julian Hoff, Brian Ross and Donald Ross.
- E. Effects of BCNU on histopathology and MRI signals in experimental rat brain tumors with Drs. Brian Ross and Thomas Chenevert.

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.
- B. Editorial Board, Journal of Histochemistry and Cytochemistry and Cytochemistry.
- C. Editor, Histochemical Society Newsletter.
- D. Primary Review Pathologist, Children's Cancer Study Group CCG 9891 nationwide study of childhood low grade gliomas.
- E. Reviewer for the following journals:
 - 1. Journal of Neuropathology and Experimental Neurology.
 - 2. Journal of Neurosurgery.
 - 3. Journal of Histochemistry and Cytochemistry.
 - 4. Journal of Neuro-oncology.
 - 5. American Journal of Pathology.
 - 6. Archives of Pathology and Laboratory Medicine.
- F. Member, Brain Tumor/EMF Study Scientific Advisory Panel, National Cancer Institute, Jonathan Samet, Chairman.
- G. Member, Review Panel, Program for Treatment of Malignant Brain Tumors, National Cancer Institute, William Jewell, Chairman.
- H. Member, Review Panel, Molecular Markers of Glioma Initiation and Progression, National Cancer Institute, Susan Naylor, Chairwoman.
- I. 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--.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. 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.
2. 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.
3. 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.* 57:931-936, 1998.
4. Bigner SH, McLendon RE, Fuchs H, McKeever PE, Friedman HS. Chromosomal characteristics of childhood brain tumors. *Cancer Genetics & Cytogenetics* 97:125-34.

BOOKS/CHAPTERS IN BOOKS:

1. McKeever PE: The Brain, Spinal Cord, and Meninges. Chapter 10 in: Sternberg SS, Antonioli DA, Carter D, Mills SE, Oberman HA (Eds): *Diagnostic Surgical Pathology, Third Edition.* Lippincott Williams & Wilkins, Philadelphia, 1999.
2. McKeever PE: Glial cell pathology. In: Smith BH and Adelman A, eds.: *Encyclopedia of Neuroscience,* Elsevier Science, 1999, pp 812-818.
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, 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).
5. McKeever PE: Laboratory methods. In: Nelson JS, Parisi J, Schochet S (Eds): *Principles and Practice of Neuropathology,* Oxford, New York (in press).

6. McKeever PE: The nervous system. In: Dabbs DJ (Ed): Comprehensive Diagnostic Immunohistochemistry, Harcourt Brace & Co., Orlando (in press).
7. McKeever PE: The nervous system. In: Kohen E (Ed): Fluorescent Probes in Oncology, Imperial College Press, London (in press).

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

1. Rock J, Mehra S, Ho K, Chandler W, McKeever PE, Pindolia K, Worsham M: Molecular genetics of recurrent pituitary neoplasia. Abstract for VIth International Pituitary Congress, Los Angeles.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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 - four weekends.

II. TEACHING ACTIVITIES:

- A. Medical School Students:
 - 1. 1997-Present: Laboratory Instructor, Component II Sequence, Year II Medical students.
 - 2. 1998-Present: Integration of cytopathology component to the medical student curriculum web site.
 - 3. 1999-Present: Introduction to cytopathology, Histology course, Year I Medical students.
 - 4. 1999-Present: Mentor for medical students' senior clerkship.
- 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 – four/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.
- B. National Institute of Health, Co-Investigator (DRDA#98-1650), New Screening Method for Early Detection of Breast Cancer (5% effort) (pending approval of supplement)
- C. Comparison of liquid based media preparations to the conventional Papanicolaou smear (total estimated cost 32, 446) Primary investigator (submitted to Venture Investment Funds)

PROJECTS UNDER STUDY:

1. Hunter B, Michael CW. Cytologic artifacts and pitfalls in fine needle aspirates processed by the ThinPrep technique: cytologic artifacts and diagnostic pitfalls. (Manuscript near completion)
2. Michael CW, Georgy B, Elhosseiny, Collin B. The cytologic spectrum and diagnostic pitfalls of apocrine lesions of the breast. (Manuscript near completion)
3. Michael CW, Buschmann B: Can true breast papillary neoplasms and their mimics be distinguished cytologically? (Near completion)
4. Michael CW, Abd Al-Karim F. Fine needle aspirates of the female genital tract. In:cytopathology. Edited by Shahla Masood.
5. Merajver SD, Michael CW. Genomic deletions in tumors from families with breast and ovarian cancer
6. Michael CW, Tworek J, Wojno JK. The use of newly marketed antibodies in conjunction with the routine panel in the evaluation of serosal fluids.
7. Michael CW, Collin B, Flint A. Neuroendocrine tumors of the lung: Cytologic features and differential diagnosis.
8. Michael CW, Chang A. The cytologic presentation of failed prosthesis.
9. Michael CW, Weiss S. Deciduioid mesothelioma in a young male: a cytohistologic correlation with electron microscopy and immunohistochemistry.
10. Michael CW, Bedrossian CW. Evaluation of mesothelioma in situ by routine immunohistochemical stains and proliferative markers.
11. Michael CW, Pass HI. Can the presence of SV40 and its receptor have diagnostic utility in separating mesothelia from adenocarcinoma in body fluids.
12. Constantine T, Michael CW. The use of Melan A in conjunction with routine panel in the diagnosis of melanoma on fine needle aspirates.

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.

- F. Chair, American Society of Cytopathology, Committee of New Members and Public Information.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Cytopathology of the Respiratory Tract". Short course, Co-director. Twenty second International Cytopathology short course, Congress of the International Academy of Pathology. Nice, France, October 20 1998.
2. "Pregnancy related changes on pap smears". Invited seminar, Michigan society of Cytology, November 21, 1998.
3. "Cytopathology of the lung. Differential diagnosis and diagnostic pitfalls". Workshop, American Society of clinical Pathology, April 1998.
4. "New Techniques and Automation in Cytopathology". Guest Speaker; M-Labs Symposium, Ann Arbor, MI, May 15, 1999.
5. "Pregnancy-Related Changes on Pap Smears" Teleconference, American Society of Cytopathology, June 22, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Tworek J, Giordano T, Michael CW. Comparison of intraoperative cytology with frozen sections in the diagnosis of thyroid lesions. *Am j Clin Path.* 1998;110:456-461.
2. Rock CL, Michael CW, Reynolds RK, Ruffin MT. Prevention of Cervix cancer. *Oncology/Hematology.* (In Press)
3. Michael CW, Naylor B. Amyloid in cytologic specimens: Differential diagnosis and diagnostic pitfalls. *Acta Cytologica* (In Press)
4. Michael CW. The Pap smear and the obstetric patient: a simple test with great benefits. *Editorial Comments. Diagnostic Cytopathol* 1999;21:1-3.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Kleer CG, Michael CW. Fine needle aspiration of breast carcinomas with prominent lymphocytic infiltrate. Can we distinguish medullary carcinoma from invasive ductal carcinoma? Submitted to *Cancer Cytopathology*
2. Tworek JA, Michael CW. Fine needle aspiration of lymphocyte rich parotid lesions: Can we diagnose marginal Zone B-cell lymphoma of mucosa associated lymphoid tissue by cytology? Submitted to *Cancer Cytopathology*.
3. Kintanar EB, Girodano TJ, Thompson NW, Michael CW. Granular cell tumor of trachea masquerading as hurthle cell neoplasm on fine needle aspirate: a case report. Submitted to *Diagnostic Cytopathology*.
4. Rochesrer AB, Roubidoux MA, Michael CW, Patterson SK. Mammographic localization of small lesions of ductal carcinoma in situ. Submitted to *Journal of Women's Imaging*.

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

1. Claire W. Michael. The use of ThinPrep in fine needle aspirates: the facts. *Focus* 1999;6:17.
2. Tworek J, Giordano T, Michael CW. Authors reply to letter to the editor "Frozen section? Just do it. *Am J Clin Pathol* 1999;112:122-126.
3. Michael CW, McConnell J, Afify A, Al-Khafaji B, Pecott J. Comparison of the ThinPrep and AutoCyte liquid based preparations in nongynecologic specimens. *Mod Pathol* 1999;12:49A.
4. Ruffin MT, Bailey JM, Underwood D, Beniasz M, Gregoire L, Johnston C, Reynolds RK, Normelle D, Reed BD, Michael C, Gornflo DW, Lancaster W, Kmak D, Munkarah AR, Brenner DE. The potential use of HPV copy number and E6/E7 expression as biomarkers in cervical dysplasia. *Proceedings of the American Association for Cancer Research* 1999;40:431.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

CLINICAL RESEARCH-RELATED ACTIVITIES:

- A. Guided the Reproductive Sciences Program (RSP) through follow-up discussions after the University 1997-1998 review of RSP.
- B. Continued to develop groundwork for transition to new leadership. Assisted in establishment of a new RSP Executive Committee. Achieved strong support from RSP membership for moving in new directions marked by emphasis on the impact of environmental change on reproduction and underlying molecular mechanisms. Our training grant is being transitioned to new leadership. Stimulated discussions and plans for responding to non-support of our initial attempt for a U01 center to replace our prior P30 center. Discussions are underway to develop other multi-investigator programmatic grants. Planning to reapply for a new NSF Center in Neuroecology – probably again under a collaborative mechanism with Michigan State University - is being led by Doug Foster, and talks to establish program projects in areas like reproductive toxicology are beginning.
- C. Successfully re-competed and maintained our Central Laboratory in a NIH-funded Study of Women's Health Across the Nation as the premier laboratory doing large-scale analyses of reproductive hormones. Services of the laboratory expanded during the last year to include a battery of assays on nearly 40,000 urine samples each year. Completed and continue to run multiple assays on thousands of serum samples each year.
- D. With assistance of five graphics illustrators (biomedical illustration students), three textual content developers (two undergraduate students and one graduate student), one music/sound developer (undergraduate student), and one technical programming assistant (high school graduate) last summer, completed a CD demonstrating the core idea of the Reproductive Learning Collaboratory. Two of the students were volunteers; the rest were paid by a grant from the OVPR. Discussions with Perry Samson and others convinced us that exclusive focus on developing novel ways to help inner city youth learn what they need and want to know about reproductive health and sexuality regardless of reading ability would have difficulty in implementation: adolescents would not likely want to be seen at a kiosk concerning sexual matters. Recognizing that we could re-position the project, we have developed proposals for use in middle level schools (NSF) and post-secondary education (U.S. Dept of Education). Approaching schools is made possible by a new key idea: providing school systems and teachers with ways to customize content. With this addition, initiated, coordinated (14 investigators) and submitted a grant to NASA involving environmental science learning.

II. TEACHING ACTIVITIES:

1. Lectures
Served as a primary instructor for a full semester four hours/week laboratory course for dental and health professional students, Pathology 630/631, Fall 1998
2. Primary supervision of 1 graduate student: William Lemon, Bioengineering - doctoral student (successfully defended, Sept. 1998)
3. Supervision/Mentorship of other students:
Brooke Rossi, undergraduate student
Nir Krakauer, undergraduate student
Sherra Cook, biomedical illustration student
Evelyn Mohalski, biomedical illustration student
Travelle Bibbs, biomedical illustration student
Patricia Ferrer, biomedical illustration student
Matt Wimsatt, biomedical illustration student
Jason Tracer, undergraduate student
Matthew Underwood, high school graduate
Rebecca (Becky) Delancey, UROP student
Rebecca (Becca) Meuninck, UROP student
4. Service on Other Dissertation Committees. Palmiere-Hunt, Diana (Educational Psychology, successfully defended, Sept. 1998) Richard Michael Philson (Ctr for Study of Higher and Postsecondary Education, current, successfully defended, Mar. 1999)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

1. NIH, P30-HD 18258, A. R. Midgley, P.I., Center for the Study of Reproduction, 04/01/94 - 03/31/99, \$3,039,072, 15%.
2. NIH, U01-AG 12495, A.R. Midgley, P.I., Menopause and Aging in Women: Central Laboratory, 10/01/94 - 09/30/99, \$1,465,338, 20%. Competitive renewal application funded for an additional 4 years.
3. NIH, U01-AG 12495 SUPPLEMENT, A.R. Midgley, P.I., Hormonal Predictors of Perimenopausal Morbidity, 05/29/96 - 07/31/99, \$2,894,204.
4. NIH, R01-MH 03204, E. Young, P.I., Stress and Reproductive Hormones in Depressed Women, 08/01/94 - 07/31/99, \$661,569, 5%.
5. NIH, T32-HD 07048, D. Foster, P.I., Training Program in Reproductive Endocrinology, 07/01/95 - 06/30/00, \$1,354,407, 5%, (no salary support).

PROPOSAL WRITING (Not Funded):

On behalf of the Reproductive Learning Collaboratory, letters of inquiry to:
Brush Foundation
Burroughs Wellcome Fund
Cowan Slavin Foundation
Educational Foundation
Frost Foundation
General Service Foundation

Harris Foundation
Johnson & Johnson
Kennedy Fund
Public Welfare Foundation
Revlon Foundation
Steelcase Foundation
Weeden Foundation
Preliminary Proposals to:
NSF: Enhancing science learning in middle level schools: A challenging, motivating, and extensible new paradigm
Full applications to:
Metro Health Foundation
Packard Foundation
Spencer Foundation

PROPOSAL WRITING (Pending):

On behalf of the Reproductive Learning Collaboratory, letters of inquiry to:
Canto Cumulus Corp.
Charles Stewart Mott Foundation
Curtice-Burns Foundation
Curtis Foundation
Delano Foundation
DeVlieg Foundation
FileMaker Corp.
Ford Family Foundation
Grossman Family Foundation
Huber Foundation
Josiah Macy Foundation
Klingenstein Fund
New-Land Foundation
Offield Family Foundation
Patrina Foundation
Shifting Foundation
Slocum Foundation
Stewart R. Mott Trust
Stott Family Foundation
Wardlaw Charitable Trust
Weyerhaeuser Family Foundation
Winslow Foundation
Womens Project Foundation
Full applications to:
Congressional Priorities for Postsecondary Education, Dept of Education
NASA-LTP LEARNERS: NASA-Derived Environmental Science Learning in Middle Schools: A Challenging, Motivating, and Extensible New Paradigm

SCIENTIFIC COLLABORATIONS:

Biostatistics

Morton Brown and Yuedong Wang: development and implementation of a means for automating the collection of immunoassay data and organizing it in a distributed database for clinical hormone studies; modeling the distribution of hormone pulses

Pediatrics

Vasantha Padmanabhan: involvement in multiple research projects

Innovation Associates, Ann Arbor, MI

Judith Erb, Immunoassayist: assisted in development of a funded SBIR concerning the development of novel immunosensors able to evaluate fertility and development of a second funded SBIR

PROJECTS UNDER STUDY:

1. Development of a novel, multi-cognitive level, hyperlinked, reproductive learning environment for persons of all ages from 7 to 70 and available in forms accessible in homes, libraries, schools and clinics.
2. Development and utilization of a computer-controlled perfusion system for on-line analysis of cellular responses to pulsatile and other controlled signaling and use of this system to assist in modeling the LH surge (being continued by colleague Vasantha Padmanabhan and commercialized by recent doctoral student, William Lemon).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

1. Director, Center for the Study of Reproduction (NIH P30)
2. Director, Standards and Reagents Core Facility (NIH P30 Center)
3. Director, Central Laboratory, Study of Women Across the Nation (NIH SWAN)

UNIVERSITY:

1. Director, Reproductive Sciences Program
2. Member, Biomedical Engineering
3. Member, Cellular Biotechnology Training Program
4. Member, Michigan Cancer Center, 1993-
5. Member, RUTH International Advisory Panel, 1997- (Raloxifene Use for the Heart)
6. Member, Steering Committee for Environmental Issues and Research on Campus, 1998-

REGIONAL AND NATIONAL:

1. Member, NIDDK Endocrinology Research Program Advisory Committee, 1986-
2. Member, NIDDK Hormone Distribution Program Subcommittee, 1986-
3. Member, NIH Reviewers Reserve, 1989-

REPRODUCTIVE SCIENCES PROGRAM:

1. Director of Program

V. **OTHER RELEVANT ACTIVITIES:**

INVITED LECTURES/SEMINARS:

1. July 8-9, 1998, SWAN reverse site visit, Bethesda, MD
2. Sept 21, 1998, RSP Seminar: Sex, learning & videotape
3. Oct 15-19, 1998, SWAN Steering Cmt mtg, Bethesda, MD
4. Nov 3, 1998, Talk at UM meeting hosted by Ob-Gyn on Reproductive Research in the Academic Medical Center
5. May 12-14, 1999, SWAN Steering Cmt mtg, Bethesda, MD
6. May 27, 1999, Grand Rounds at Ob-Gyn: The RLC: Helping everyone learn what they need and want to know about reproductive health and sexuality

OTHER ACTIVITIES:

1. Implementing chemiluminescence-based, solid state, two site immunoassays to replace and improve upon radioimmunoassays (and thereby reduction in usage of radioactive isotopes)

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Heinze, K., Keener, R.W. and Midgley, A.R., Jr. A mathematical model of luteinizing hormone (LH) release from ovine pituitary cells in perfusion. Am. J. Physiology, In Press, Dec. 1998.
2. Midgley, A.R., McConnell, D.S., England, B.G., Gonzalez, K., Davis, M., Possley, R., Kitzsteiner, S., Skurnick, J., Crawford, S., Santoro, N., Lasley, B. Ensuring reliability of assay results in a large, longitudinal, multiethnic, multicenter, cooperative study of the menopausal transition. Clinical Chemistry, Under revision after favorable review.

ARTICLES IN PREPARATION:

1. Heinze, K., Keener, R.W. and Midgley, A.R., Jr. On the analysis of hormone release.
2. England, B.G., Midgley, A.R., Jr., McConnell, D.S. A sensitized fully automated chemiluminescent immunoassay for estradiol.
3. McConnell, D.S., England, B.G., Midgley, A.R. Automated immunoassay of human gonadotropins in urine.

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

1. Midgley A.R, Rossi B.V., Reproductive Learning Collaboratory: Learning what you need and want to know about reproductive biology, reproductive health and sexuality. Society for the Study of Reproduction, July 31-Aug 3, 1999.

2. DeLancey, R.M., Rossi, B.V., Midgley, R. Reproductive Health and Sexuality. UROP Symposium, April 1999.

VII. DEVELOPMENTAL OBJECTIVES FOR 1999-2000:

1. After 31 years, turn over directorship of RSP to my successor!
2. Obtain external funding for the concept behind the Reproductive Learning Collaboratory.
3. Bring the Reproductive Learning Collaboratory Web site to a usable (albeit content-limited) state.
4. Complete and submit several manuscripts describing novel methodological approaches developed by the Central Laboratory.
5. Develop assays of urinary hormones needed by the U01 Collaborative Centers on the perimenopause.

VIII. EVALUATION OF GOALS AND OBJECTIVES SET LAST YEAR:

Complete our demonstration CD ROM containing a prototype of the Reproductive Learning Collaboratory hyperlinked, multimedia project intended to help persons at all reading levels learn about sex and sexuality in appropriate, interesting and flexible ways.

•Done.

Obtain external funding for the Reproductive Learning Collaboratory.

•So far no success. Submitted 41 letters of inquiry or preliminary applications and 3 full applications (one invited) to foundations, plus one grant to the NSF (middle level schools re. reproductive health), one to Dept. of Education (post-secondary education re. reproductive health), and one to NASA (environmental science learning in middle schools). Most of the foundations have been small. Most rejects to date have been on the basis of limited interests. NSF says area not sufficiently science-related. Spencer Foundation claims only supporting basic educational research – they may be missing the point, I plan to call when a demonstration site is up. This is a very different approach to education that needs to be assessed. It could have profound, positive effects throughout all education.

Complete a significant initial portion of the Reproductive Learning Collaboratory Web site using approaches established over the last year.

•A Web-specific user interface was implemented and features feasible for the Web but not a CD have been implemented: Separate versions for Netscape and Internet Explorer, highlighting of all “active” words (in IE4), auto-pop-up definitions for all active words, pronunciation on clicking all active words, extensive hyperlinking, inclusion of a find command on every page. Approaches to generalize the development of content were implemented. Some content was added.

Complete and submit several manuscripts describing novel methodological approaches developed by the Central Laboratory.

•Only one overview manuscript was submitted. It was favorably reviewed and will be re-submitted shortly. Work is progressing on others: sensitive estradiol, gonadotropins in urine, and algorithmic estimation of free testosterone from concentrations of total testosterone and SHBG.

Develop assays of urinary hormones needed by the U01 Collaborative Centers on the perimenopause.

- Done. Assays now running for luteinizing hormone, follicle stimulating hormone, estrone conjugates, pregnanediol glucuronide, and creatinine.

**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 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate students:

1. Responsible during the current academic year for teaching activities for the following:
 - a. Eight sessions Pathology 851.
2. Program Director, "Experimental Immunopathology Training Grant."
3. Ph.D. Dissertation Committees, University of Michigan:
 - a. Anne Jackson.
 - b. Meera Nathan.
 - c. Pamela Bennett-Baker.
 - d. Tyler Sisk.
 - e. Wannee Asavaroengchai.
4. Ph.D. Dissertation Advisor:
 - a. Michael Eisenbraun.
 - b. Chris Kirk.
 - c. Anavelys Ortiz-Suarez.
5. Undergraduate students:
 - a. Aaron Freilich, CLSA IV.

B. Postdoctoral Fellows:

1. Ami Tamir, Ph.D.
2. Gonzalo Garcia, Ph.D.

C. Visiting Research Scientist:

1. Igor Dozmorov, Ph.D.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator, "Activation Defects in Aging T Cells", NIH AG-09801 (8%), \$170,741 direct costs/year, 8/1/90 - 7/31/99. 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, "Genetics of Age-Sensitive Traits in Mice", NIH AG-16699 (20%), \$647,937 direct costs/year, 5/1/99 - 4/30/04.
- D. Principal Investigator, "Genetic Control of Longevity in Mice", NIH AG-11687 (8%), \$238,348 direct costs/year, 9/1/93 - 8/31/03.
- E. Principal Investigator, "New T Cell Subsets Defined by P-glycoprotein in Aging Mice", NIH R01-AG03978 (0%), \$158,141 direct costs/year, 12/1/95 - 11/30/99.
- F. Director, "Research Development Core", NIH AG-13283 (10%), \$89,400 direct costs/year, 9/1/98 - 6/30/00. (Component of Nathan Shock Center of Excellence for Basic Biology of Aging, John Faulkner, Program Director).
- G. 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).
- H. 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).
- I. Project Director, "Prevention of Disease by Immunotonic Agents in Mice", NIH AG-08808 (5%), \$51,757 direct costs/year, 9/1/94 - 8/31/99. (Component of Claude Pepper Older Americans Independence Center, J. Halter, Program Director).
- J. Program Director, "Research Training in Experimental Immunopathology", NIH T32-AI-07413 (0%), \$205,149 direct costs/year, 4/1/92 - 8/31/03.
- K. Principal Investigator, "Wild Derived Mouse Stocks: New Models for Aging Research," NIH R01-AG13711 (5%), \$155,728 direct costs/year, 9/1/96 - 8/31/99.
- L. Course Director, "Summer Training Courses in Experimental Aging Research", NIH/NIA R13-AG12917 (0%), \$31,337 direct costs/year, 4/1/95 - 3/31/03.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Graduate Education Committee.
- B. Director, Experimental Immunology Training Program.

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. Member, Cancer Biology Training Program.
- H. Member, Executive Committee, Program in Biomedical Sciences.
- I. Member and Deputy Director, Operating Committee, PhD Program in Immunology.

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. Aging: Clinical and Experimental Research

HONORS AND AWARDS:

- A. Geron Corporation-Samuel Goldstein Distinguished Publication Award.
- B. Esther and Isadore Kesten Memorial Lectureship Award.

INVITED LECTURES/SEMINARS:

1998

1. Planning Conference for High-Throughput Technology in Aging Research, Bethesda, MD. Session co-chair. September 21 – 22.
2. Workshop on T and B Cell Memory, Trudeau Institute, Saranac Lake, NY. “Signal Transduction in T Cell Subsets.” September 24 – 27.
3. Department of Microbiology and Immunology, Medical College of Ohio, Toledo, OH. “Signal Transduction Defects in Aged T Cells.” September 30.
4. American College of Nutrition Annual Meeting, Albuquerque, NM. “Genetics of Aging, Immunity, and Weight Trajectory in Four-Way Cross Mice.” October 1 – 3.
5. University of Michigan Cancer Research Series. “Genetics of Aging and Longevity in Mice.” November 11.
6. Annual Meeting of the Gerontological Society of America, Philadelphia, PA. (1) “Survival and immunity in mice treated daily with DHEA throughout life.” (2) “Genetics and biomarker validation in aging four-way cross mice.” (3) “Distinct T cell subsets delineated by P-glycoprotein in mice” (Geron/Goldstein Distinguished Publication Award Lecture). (4) “Are there genes for aging?” (Kleemeier award lecture). November 20 – 22.
7. Medical Grand Rounds, William Beaumont Hospital, Royal Oak, MI. “Are There Genes for Aging?” December 23.

1999

1. Tumor Immunology Program Workshop, University of Michigan. "Genetics of Aging and Tumorigenesis in Mice." January 11.
2. Master Teacher in Gerontology Workshop, St. Simons Island, Georgia. "Biology of Aging." January 16-17.
3. Department of Pathology, Loyola University, Chicago, IL. "T Cell Aging: Primer and Prospectus." January 25.
4. Geriatric Grand Rounds, Drew University, Los Angeles, CA. "Genetics and Aging." January 27.
5. Keystone Symposium on Aging: Genetic and Environmental Influences on Life Span. Durango, CO. February 2 – 6.
6. The Aging Factor in Health and Disease, International Longevity Center, New York, NY. "Immunosenescence and Aging." February 10 – 11.
7. UCLA Roundtable on Coming Research Milestones in Aging, University of California, Los Angeles, CA. "Future Landmarks in Gerontology." February 19 – 20.
8. NIA Workshop on Caloric Restriction – Clinical Implications. Bethesda, MD. March 8 – 10.
9. Wistar Institute, Philadelphia, PA. "T Cells in Aging Mice: Genetic and Biochemical Analyses." March 31.
10. Ester and Isadore Kesten Memorial Lecture, Andrus Gerontology Center, University of Southern California, Los Angeles, CA. "Are There Genes for Aging?" April 15.
11. Andrus Center Leadership Retreat, Rancho Valencia, San Diego, CA. "Aging – Is it All In the Genes?" April 16.
12. International Summer School on the Pathobiology of Aging, Pisa, Italy. "The Aging Immune System." April 24 – 29.
13. American Society for Transplantation Annual Meeting, Chicago, IL. "Aging and Immunity – Current Status and Future Prospects." May 19.
14. International Symposium on Immunity and Aging, Marcel Merieux Foundation, Annecy, France. "Activation Defects in T Cells from Aged Mice." June 5 – 9.
15. Seventh Annual Summer Training Course in Aging Research, Ann Arbor, MI. (1) "Vertebrate Animal Models for Aging" and (2) "Immunological Aspects of Aging." Course director. June 13 – 17.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Miller, R. A., C. Chrisp, A. U. Jackson, and D. Burke.: Marker loci associated with lifespan in genetically heterogeneous mice. *J. Gerontology: Medical Sciences* 53A:M257-M263, 1998.
2. Garcia, G. G. and R. A. Miller.: Increase in Zap-70 association with CD3 ζ in CD4 T cells from old mice. *Cellular Immunology* 190:91-100, 1998.
3. Kirk, C. J. and R. A. Miller.: Analysis of Raf-1 activation in response to TCR activation and co-stimulation in murine T-lymphocytes: effect of age. *Cellular Immunology* 190:33-42, 1998.

4. Witkowski, J. M. and R. A. Miller.: Calcium signal abnormalities in murine T lymphocytes that express the multidrug transporter P-glycoprotein. *Mechanisms of Ageing and Development* 107:165-180, 1999.
5. Jackson, A. U., A. Fornés, A. Galecki, R. A. Miller, and D. T. Burke.: Multiple trait QTL analysis using a large mouse sibship. *Genetics* 151:785-795, 1999.
6. Telford, W. G. and R. A. Miller.: Aging increases CD8 T cell apoptosis induced by hyperstimulation but decreases apoptosis induced by agonist withdrawal in mice. *Cellular Immunology* 191:131-138, 1999.
7. Dozmorov, I. M., and R. A. Miller.: Age-associated decline in responses of naïve T cells to in vitro immunization reflects shift in glucocorticoid sensitivity. *Life Sciences* 64: 1849 – 1859, 1999.
8. Miller, R. A., R. Dysko, C. Chrisp, R. Seguin, L. Linsalata, G. Buehner, J. M. Harper and S. Austad.: Mouse stocks derived from tropical islands: new models for genetic analysis of life history traits. *J. Zoology*, In Press.
9. Miller, R. A., and C. Chrisp.: Lifelong treatment with oral DHEA sulfate does not preserve immune function, prevent disease, or improve survival in genetically heterogeneous mice. *J. American Geriatrics Society*, In Press.
10. Yang, D. and R. A. Miller.: Cluster formation by protein kinase C θ during murine T cell activation: effect of age. *Cellular Immunology*, In Press.
11. Miller, R. A.: Kleemeier Award Lecture: Are There Genes for Aging? *J. Gerontology: Biological Sciences*, In Press.
12. Miller, R. A.: Genes for Ageing? *Trends in Genetics* 15:175-176, 1999.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Kirk, C. J., A. M. Freilich, and R. A. Miller.: Age-related decline in activation of JNK by TCR and CD28-mediated signals in murine T lymphocytes. Submitted for publication.
2. Kirk, C. J., and R. A. Miller.: Age-sensitive and insensitive pathways leading to JNK activation in mouse CD4 T cells. Submitted for publication.
3. Eisenbraun, M. D. and R. A. Miller.: *mdr 1a*-encoded P-glycoprotein is not required for peripheral T cell proliferation, cytokine release, or cytotoxic effector function in mice. *J. Immunol.* In Press.
4. Eisenbraun, M. D., D. H. Teitelbaum, R. L. Mosley, and R. A. Miller.: Altered development of intestinal intraepithelial lymphocytes in P-glycoprotein-deficient mice. Submitted.
5. Miller, R. A., C. Chrisp, and W. Atchley.: Differential longevity in mouse stocks selected for early life growth trajectory. Submitted for publication.
6. Miller, R. A., S. Austad, D. Burke, C. Chrisp, R. Dysko, A. Galecki, A. Jackson, and V. Monnier.: Exotic mice as models for aging research: polemic and prospectus. *Neurobiology of Aging*, submitted for publication.
7. Miller, R. A., D. Burke, and N. Nadon.: Announcement: four-way cross mouse stocks: a new, genetically heterogeneous resource for aging research. Submitted for publication.
8. Miller, R. A. and N. Nadon.: Principles of animal use for gerontological research. Submitted for publication.

BOOKS/CHAPTERS IN BOOKS:

1. E. L. Schneider and R. A. Miller.: Anti-Aging Interventions. In: Brocklehurst's Textbook of Geriatric Medicine, Fifth Edition, R. Tallis, H. Fillit, and J. C. Brocklehurst, eds., Churchill Livingstone, New York. Chapter 13, pp 193 – 199, 1998.
2. 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, Chapter 1, pp 3 – 19, 1999.
3. Miller, R. A.: Aging and Immune Function. In: Fundamental Immunology, Fourth Edition, W. E. Paul, Editor, Lippincott-Raven, Philadelphia. Chapter 28, pages 947 – 966, 1999.
4. Kirk, C. J., and R. A. Miller. 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.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology and Frozen Section Diagnosis (5 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.
- F. Coordinator, "Topics in Pathology", CME accredited lecture series.

II. TEACHING ACTIVITIES:

- 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, (5 months/year)
 - 3. Lecture and Case presentations at weekly Urologic Pathology Conferences
- C. Graduate students:
 - 1. Course Director, Pathology 585, Lecture and Laboratory course for Medical Illustration Graduate students
 - 2. Laboratory Instructor, pathology 600 (M2 pathology course)
- D. Undergraduate students:
 - 1. Human Pathology, Cranbrook-Kingswood (High School Biology Classes).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator "Gender-specific T cell homing and autoimmunity"
(B. Richardson, Internal Medicine, PI) NIH 12/98 - 11/03 (\$1,760,000)
- B. Co-Investigator, "Host Defense of the Lung" Research Enhancement Award Program
(REAP) Veteran's Administration 11/98-10/03 (\$1,350,000)
- C. Collaborator. Lung Injury by Oxygen Metabolites NIH/NIGMS R37 GM29507. National
Institute of Health (Peter A. Ward, Principal Investigator).7/97-6/01. (\$1,123,824)
- D. Co -mentor, Matthew Adams, M.D., Arthritis Foundation, Michigan Chapter. 1/98-12/99
(\$20,000/ year)

PENDING:

- A. Principal investigator, "Source and Function of Vascular Endothelial Cell Oxidants" VA Merit 04/00-03/03 (\$591,300)
- B. Principal Investigator "Endothelial Cell Matrix Metalloproteinases in Human Prostate Cancer" VERAM (\$15,000)
- C. Co-investigator, "Metabolic imaging of Renal and Prostate Cancer using C11 Acetate" VA Merit 04/01/00-03/31/03 (\$359,200)
- D. Collaborator Matthew Adams, M.D., "Gender-specific T cell homing and autoimmunity" NIH-NRSA Award, 09/01/99-08/31/01 (\$85,028)

PROJECTS UNDER STUDY:

- A. Endothelial cell responses in inflammation
 - 1. The enzyme source of endothelial cell oxidants
 - 2. The role of endothelial cell derived oxidants in signaling and cell injury
 - 3. Repertoire of endothelial cell derived cytokines and their role in inflammation
- B. Gender-specific effects of hormones on T cells and endothelial cells in autoimmunity
 - 1. Effect of estrogen on endothelial cell estrogen receptor expression
 - 2. The role of estrogen in endothelial cell adhesion molecule expression and lymphocyte homing

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Autopsy Quality Assurance Review

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Admissions committee of the University of Michigan Medical School, 1999-
- B. Member, Research and Development Committee, Veterans Affairs Medical Center, 1999-

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 Society for Investigative Pathology
 - American Society of Clinical Pathologists
 - The A. James French Society of Pathologists
 - American Association for the Advancement of Science

New York Academy of Science
American Association of University Women

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 evaluation for clinical researchers.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Murphy, H.S., N. Bakopolous, M. Dame, J Varani, P.A. Ward Heterogeneity of inflammatory responses of vascular endothelial cells. *Microvasc Res.* 56:203-211,1998.
2. Murphy, H.S., R. Warner, N, Bakopolous, M, Dame, J Varani, P.A. Ward. Endothelial cell determinants of susceptibility to neutrophil-mediated killing. *Shock* (in press).

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

Chapters in Books

1. Ward, P.A. H.S. Murphy Role of Complement in Endothelial Cell Activation. Molecular and Cellular Basis of Inflammation. C. Serhan, P.A. Ward, eds.1998.

Abstracts

1. Varani, J, Hattori, Y, Murphy, H, Johnson, KJ. Matrix metalloproteinase expression in non-malignant and malignant human prostate tissue. University of Michigan Cancer Center Research Conference. 1999.

SUBMITTED PUBLICATIONS:

1. Robey, T.C., Eiselt, P.M., Murphy, H.S., Mooney, D.J., Weatherly, R.A. Biodegradable external tracheal stents and their use in a rabbit tracheal reconstruction model. *Arch. Otolaryngology.*
2. Robey, T.C., Valimaa, T., Murphy, H.S., Mooney, D.J., Weatherly, R.A The use of internal bioabsorbable LGA "finger-type" stents in a rabbit tracheal reconstruction model. *Arch. Otolaryngology.*

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

- A. Cytopathology.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Advisory Committee on Appointments and Promotions.

REGIONAL AND NATIONAL:

- A. Cytopathology, Editorial Advisory Board.
B. Acta Cytologica, Editorial Advisory Board.
Associate Editor, North American Review Board.
C. Diagnostic Cytopathology, Consulting Editor.
D. International Academy of Cytology:
International Board of Cytopathology, 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. Nashville, Tennessee, November, 1999.

2. Naylor, B.: a). Mesothelioma, b). Transthoracic fine needle aspiration cytology, c) Histology of cytopathology. Lectures, Cytotechnology Training Program, Henry Ford Hospital, Detroit, Michigan, 1999.
3. Naylor, B.: Cytodiagnosis of serous fluids: The unusual, the difficult, and the exotic. Lecture, Greater New York Association of Cytotechnologists, New York, New York, May, 1999.

HONORS AND AWARDS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Naylor B.: Cytologic diagnosis of two rarities: Granulocytic sarcoma and microsporidiosis. Acta Cytol 1999;43:95-97.

BOOKS/CHAPTERS IN BOOKS:

None.

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

None

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Supervised Luis Del Peso, Adalberto Benito, Daryoush Ecketerae, Victor Gonzalez-Muñoz, Yuanming Hu, Naohiro Inohara, Takeyoshi Koseki, Rebecca Liu, Postdoctoral Fellows.
- B. Supervised Mary Benedict, Laura Mancino, and Christine Yee, 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.
- E. Instructor, Microbiology and Immunology 553, Cancer Biology Training Program, University of Michigan, (1 lecture).
- F. Instructor, Cell Biology Course for Graduate Students, University of Michigan (1 lecture).

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

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, Nature Cell Biology.

INVITED LECTURES AND SEMINARS:

University Of Michigan:

- 1. Invited Speaker, "Regulation of Programmed Cell Death," Hematology/Oncology Teaching Conference, University of Michigan Medical Center, February 11, 1999.

2. Invited Speaker, "Regulation of Programmed Cell Death," Michigan Gut Peptide Research Center, University of Michigan Medical School, April 15, 1999.

National and International:

1. Invited Speaker, "Chemotherapy of Experimental and Clinical Cancer," Colby-Sawyer College, New London, NH, July 30.
2. Invited Speaker, "Regulation of Programmed Cell Death," Abbott Laboratories, Abbott Park, IL, August 14.
3. Invited Speaker, "Regulation of Programmed Cell Death," Haddow Laboratories, Academic Haematology and Cytogenetics, Institute of Cancer Research, Sutton, Surrey, England, August 24.
4. Invited Speaker, "Regulation of Programmed Cell Death," Microbiology and Immunology Department, Medical College of Ohio, Toledo, September 8.
5. Invited Speaker, "Molecular Regulation of Apoptosis," 12th International Symposium on Regulatory Peptide, Mackinac Island, Michigan, September 19.
6. Invited Speaker, "Regulation of Programmed Cell Death," Basic Science Seminar Series, Loyola University Medical Center, Chicago, IL, October 7.
7. Invited Speaker, "Regulation of Programmed Cell Death," Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, October 19.
8. Invited Speaker, "Regulation of Programmed Cell Death," Wyeth Ayerst, Princeton, NJ, October 20.
9. Invited Speaker, "Regulation of Programmed Cell Death," Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, December 10.
10. Invited Speaker, "Molecular Regulation of Apoptotic Cell Death," International Conference on *In Vitro* Cytotoxicity Mechanisms, Rome, Italy, January 25-27.
11. Invited Speaker, Regulation of Apoptosis," University of Rome, Italy, January 27.
12. Invited Speaker, "Apoptosis," Oncology Meeting, Spanish Association for Research, March 25.
13. Invited Speaker, "Bcl-2 Family and Caspase Activation," Apoptosis and Programmed Cell Death Keystone Symposium, Breckenridge, Colorado, April 9.
14. Invited Speaker, "Regulation of Programmed Cell Death," Distinguished Visitor Seminar Series, University of Kentucky Chandler Medical Center, Lucille P. Markey Cancer Center, Lexington, Kentucky, May 6.
15. Invited Speaker, "Mecanismos Moleculares que Regulan la Muerte Celular Programada o Apoptosis," Societat Catalana de Biologia Seminari Especial, University of Barcelona, Barcelona, Spain, June 11.
16. Invited Speaker, "Regulation of Apoptosis by Bcl-2 Family," European Society of Hematology, Barcelona, Spain, June 9-12.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNAL:

1. Packham G, White EL, Eischen CM, Yang H, Parganas E, Ihle JN, Grillot DAM, Zambetti GP, Nuñez G, Cleveland JL. Selective regulation of Bcl-x_L by a Jak kinase-dependent pathway is bypassed in murine hematopoietic malignancies. *Genes Dev.* 12(16):2475-2487 (1998).

2. Han J, Wallen H, Nuñez G, White E. E1B 19K interacts with and inhibits CED-4-dependent, FLICE-mediated apoptosis. *Mol Cell Biol.* 18(10):6052-6062 (1998).
3. Tamatani M, Ogawa S, Nuñez G, Tohyama M. Growth factors prevent changes in Bcl-2 and Bax expression and neuronal apoptosis induced by nitric oxide. *Cell Death Diff.* 5:911-918 (1998).
4. Liu JR, Fletcher B, Page C, Hu C, Nunez G, Baker V. Bcl-x_L is expressed in ovarian carcinoma and modulates chemotherapy-induced apoptosis. *Gynecol Oncol.* 70(3):398-403 (1998).
5. Inohara N, Gourley TS, Carrio R, Muniz M, Merino J, Garcia I, Koseki T, Hu Y, Chen S, Nuñez G. Diva, a Bcl-2 homologue that directly binds to Apaf-1 and induces BH-3-independent cell death. *J Biol Chem.* 273(49):32479-32486 (1998).
6. Hu Y, Ding L, Spencer DM, Nuñez G. WD-40 repeat region regulates Apaf-1 self-association and procaspase-9 activation. *J Biol Chem.* 273(50):33489-33494 (1998).
7. del Peso L, Gonzalez VM, Nunez G. *Caenorhabditis elegans* EGL-1 disrupts the interaction of CED-9 with CED-4 and promotes CED-3 activation. *J Biol Chem.* 273(50):33495-334500 (1998).
8. Lucas R, Garcia I, Donati YR, Hribar M, Mandriota SJ, Giroud C, Buurman WA, Franssen L, Suter PM, Nuñez G, Pepper MS, Grau GE. Both TNF receptors are required for direct TNF-mediated cytotoxicity in microvascular endothelial cells. *Eur J Immunol.* 28(11):3577-3586 (1998).
9. Inohara N, Koseki T, Chen S, Benedict MA, Nuñez G. Identification of regulatory and catalytic domains in the apoptosis nuclease DFF40/CAD. *J Biol Chem.* 274(1):270-274 (1999).
10. Wu D, Hu Y, Chen P-J, Chen S, Nuñez G*, Ellis RE*. *C. elegans* MAC-1, and essential member of the AAA family of ATPases, can bind CED-4 and prevent cell death. *Development.* 126(9):2021-2031 (1999). *joint senior authors
11. Koseki T, Inohara N, Chen S, Carrio R, Merino J, Hottinger MO, Nabel GJ, Nuñez G. CIPER: A novel NF-kappaB-activating protein containing a caspase-recruitment domain with homology to herpes virus-2 protein E10. *J Biol Chem.* 274(15):9955-9961 (1999).
12. Inohara N, Koseki N, del Peso L, Hu Y, Yee C, Chen S, Carrio R, Merino J, Liu D, Ni J, Nuñez G. Nod1, an Apaf-1-like activator of caspase-9 and nuclear factor kappaB. *J Biol Chem.* 274(21):14560-14567 (1999).
13. Tang ED, Nuñez G, Barr FG, Guan KL. Negative regulation of the forkhead transcription factor FKHR by Akt. *J Biol Chem.* 274(24):16741-16746 (1999).
14. Catlett-Falcone R, Landowski TH, Oshiro MM, Turkson J, Levitzki A, Savino R, Ciliberto G, Mocinski L, Nuñez G, Dalton WS, Jove R. Interleukin 6-dependent stat3 signaling induces *bcl-x* gene expression and confers resistance to apoptosis in human myeloma tumor cells. *Immunity.* 10:105-115 (1999).
15. NicAmhloaibh R, Heenan K, Cleary O, Touhey S, O'Loughlin C, Nuñez G, Clynes M. Altered expression of Bcl-2 family mRNAs affect chemoresistance in a low-level multi-drug resistant variant of a human lung carcinoma cell line overexpressing *mdr-1*mRNA. *Int J Cancer.* (In press).
16. Hu Y, Benedict MA, Ding L, Nuñez G. Role of cytochrome c and dATP/ATP hydrolysis in Apaf-1-mediated caspase-9 activation and apoptosis. *EMBO J.* 18 (13):3586-3595 (1999).
17. Liu R, Page C, Beidler DR, Wicha MS, Nuñez G. Overexpression of Bcl-x_L promotes chemotherapy resistance of mammary tumors in a syngeneic mouse model. (Submitted).
18. Ekhterae D, Lin Z, Brosius FC, Nuñez G. ARC inhibits cytochrome c release from mitochondria and protects against hypoxia-induced apoptosis in heart myogenic cells. (Submitted).
19. Nuñez G, del Peso L. Linking extracellular survival signals and the apoptotic machinery. *Curr Opin Neurobiol.* 8:613-618 (1998).

20. Nuñez G, Benedict MA, Hu Y, Inohara N. Caspases: the proteases of the apoptotic pathway. *Oncogene*. 17(25):3237-3246 (1998).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998- 30 JUNE 1999**

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. Chair, Transfusion Committee, Medical Staff
- G. Member of Executive Committee, 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 Diagnostic Radiology sequence for M-4 students (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. Presentation of consultation slide conferences (4) on pathology of the breast to pathology house officers.
- J. Presentation of Grand Rounds, Current Issues in Transfusion Medicine, to Department of Obstetrics and Gynecology. April 29, 1999.

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 of histopathology and molecular pathology with prognosis of cystosarcoma phyllodes (with C. Kleeer).
- F. Inter-institutional study of ductal carcinoma in situ (with L. Pierce).
- G. Phase II evaluation of primary chemotherapy with doxorubicin/doectaxel 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 medicine research strategies committee
 - 2. Liaison to College of American Pathologists
 - 3. Associate editor, TRANSFUSION
- 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

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. Haematology sequence advisory committee, M-2 year

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Associate Editor, TRANSFUSION
- B. Editorial Board, American Journal of Surgical Pathology
- C. Editorial Board, American Journal of Clinical Pathology
- D. Editorial Board, 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.: Ductal carcinoma in situ of the breast. Jaffar Oncology Conference. Detroit, MI September 18, 1998.
2. Oberman HA.: Interesting cases in breast pathology. Course presented at annual meeting of American Society of Clinical Pathologists. Washington, D.C. October 19, 1998
3. Problem solving in the blood bank. Workshop-Problem cases in Transfusion Medicine. Current Topics in Blood Banking. 26th annual symposium. University of Michigan. June 2, 1999.
4. Oberman HA, Goldman EB. Legal aspects of transfusion medicine. Current Topics in Blood Banking. 26th annual University of Michigan. June 3, 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Salas AP, Helvie MA, Wilkins EG, Oberman HA, Possert P, 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.* 1998;5:456-463.
2. Carlson KL, Helvie MA, Roubidoux MA, Kler CG, Oberman HA, Wilson TE, Pollak EW, Rochester AB. Relationship between mammographic screening intervals and size and histology of ductal carcinoma in situ. *American Journal of Radiology.* 1999; 172, 313-317.

TEXTBOOKS, CHAPTERS IN TEXTBOOKS:

1. Associate Editor, *Diagnostic Surgical Pathology*, Ed. 3. Lippincott Raven Williams & Wilkins. Philadelphia, PA 2 volumes. 1999.
2. *The Breast*. (Chapter 9). *Diagnostic Surgical Pathology*, Ed. 3. Lippincott Raven Williams & Wilkins. Philadelphia, PA 1999.
3. Fibroadenomas, adenomas, cystosarcomas and hamartomas (Chapter 4). *Atlas of Pathology of the Female Breast*. Current Medicine. Philadelphia, PA. (in press)
4. *NICER Encyclopedia of Medical Imaging: diseases of the breast*. With Andersson I. Stockholm. (in press)

BOOK REVIEWS, LETTERS TO THE EDITOR:

1. Oberman HA. Ductal Carcinoma in situ of the Breast. *Am J Surg Pathol* 22:902, 1998.

**AUGUSTO FELIX G. PAULINO, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. General Surgical Pathology – five months.
- B. Head and Neck Surgical Pathology, Departmental and Outside Consultation Services – 12 months.
- C. Bone and Soft Tissue Surgical Pathology, Departmental and Outside Consultation Services – 12 months.
- D. M-Labs Surgical Pathology Consultation – 12 months

II. TEACHING ACTIVITIES:

- A. Medical Students:
 - 1. M2: Musculoskeletal Sequence – 2 Lectures.
 - 2. M4: Radiology-Pathology Correlation (with Dr. Martel).
- B. House Officers:
 - 1. General Surgical Pathology – 5 months.
 - 2. Head and Neck Surgical Pathology – 12 months as needed.
 - 3. Bone and Soft Tissue Surgical Pathology – 12 months as needed.
 - 4. Consultation Conferences – four.
 - 5. Salivary Gland Pathology Lecture.
 - 6. Bone Pathology Lecture.
- C. Interdepartmental:
 - 1. Pathology Conference for Oral Surgery Residents – monthly.
 - 2. Sarcoma Tumor Board – weekly.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Co-Investigator “Molecular and Biological Studies of Head and Neck Tumors”, TE Carey (Principal Investigator).
- B. Co-Investigator “Phase I trial of gene therapy (using modified Fas ligand with a smooth muscle promoter in an adenoviral vector) in patients with locally-advanced or metastatic leiomyosarcoma or gastrointestinal stromal tumors”, LH Baker (Principal Investigator).
- C. Co-Investigator “Phase II evaluation of 6 G/m² of ifosfamide plus doxorubicin and G-CSF in the treatment of poor prognosis soft tissue sarcomas”, LH Baker (Principal Investigator).

PROJECTS UNDER STUDY:

- A. Oncoprotein expression in malignant salivary gland tumors (with O Arosarena and G Wolf).
- B. Patterns of local regional failure following parotid sparing conformal and multisegmental intensity modulated radiotherapy for head and neck cancer (with LA Dawson, Y Anzai, L Marsh, and A Eisbruch).
- C. Histologic grading of giant cell tumor of bone (with JS Biermann and CW Hayes).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. House Officer Candidate Interviews.

UNIVERSITY OF MICHIGAN:

- A. None.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS: None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Paulino AFG, Huvos AG. Epithelial tumors of the lacrimal glands: A clinicopathologic study. Ann Diagn Pathol (in press).
- 2. Snyder ML, Paulino AFG. Hybrid carcinoma of the salivary gland – salivary duct adenocarcinoma and adenoid cystic carcinoma. Histopathol (in press).
- 3. Spiro RH, Guillaumondegui O, Paulino AFG, Huvos AG. Margin assessment after resection of tongue cancer. Head Neck Surg (in press).
- 4. Paulino AFG, Huvos AG. Oncocytic and oncocytoid tumors of the salivary glands. Semin Diagn Pathol (in press).
- 5. Paulino AFG, Spiro RH, O'Malley G, Huvos AG. Giant cell tumour of the retropharynx. Histopathol 1998;33:344-348.

BOOKS/CHAPTERS IN BOOKS:

- 1. Huvos AG, Paulino AFG. Salivary Glands. In: Sternberg SS (ed): Diagnostic Surgical Pathology, 3rd Ed, Philadelphia, Pa, Lippincott Williams & Wilkins, pp. 853-884.

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

1. Paulino AFG. Color atlas/text of salivary gland tumor pathology (book review) in Am J Surg Pathol 1998;22:1429.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Autopsy Service.

II. TEACHING ACTIVITIES:

- A. Lecturer, Pathology 580/630 and Pathology 581
- B. Training of postdoctoral fellows
- C. Member, Pathology Graduate Program thesis committees
- E. House officer training in autopsy service
- F. Pathology graduate program student counseling

III. RESEARCH ACTIVITIES:

- 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. 1998-2003 (years 06-10), (Total direct costs: \$906,614).
- C. Project Leader, Project III, "Macrophage function in lung injury and fibrosis," (P.A. Ward, Principal Investigator), NIH, PO-1, HL 31963, (25% effort), 1999-2004, (Total direct costs: \$512,859), Project III only.
- D. Co-investigator, Project 1, "Cytokine networks regulating inflammation of pulmonary fibrosis," (G.B. Toews, Principal Investigator), SCOR NIH, P-50 HL 56402, SCOR in Human idiopathic pulmonary fibrosis, Projects I & III (10% effort), 1996-2001, (Total direct costs \$828,155).

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. Cytokine regulation of myofibroblast apoptosis.
- F. Induction of telomerase expression in lung fibrosis.
- 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.
- D. Member, Pathology House Officer Selection Committee.

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Medical Scientist Training Program Operating Committee.
- B. Member, Immunology Program Planning Committee
- C. Member, Program in Biomedical Sciences Admissions 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/site visitor for NIH Program Project and VA grant proposals.

INVITED LECTURES/SEMINARS:

- 1. Invited Speaker, National Heart, Lung and Blood Institute sponsored workshop on "Airway Remodeling and Repair", Rockville, MD, 1998
- 2. Co-Chair, session on "Interstitial Lung Diseases," at the 1999 International Conference of the American Thoracic Society, San Diego, CA, 1999.
- 3. Invited Speaker, Symposium on "Recent advances in molecular mechanisms and pharmacological interventions of lung fibrosis", Experimental Biology 1999 Annual Meeting, Washington, DC, 1999..
- 4. Co-Chair, Symposium on "Recent advances in molecular mechanisms and pharmacological interventions of lung fibrosis", Experimental Biology 1999 Annual Meeting, Washington, DC, 1999.
- 5. Invited Speaker, "Effects of chondroitinase B on pulmonary fibrosis", Ibex Technologies, Inc., Montreal, Canada, 1999

V. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Smith, R.E., Strieter, R.M., Phan, S.H., Lukacs, N.W., and Kunkel, S.L.: TNF and IL-6 mediate MIP-1 α in bleomycin-induced lung injury. *J. Leukocyte Biol.* 1998; 64:528-536.
2. Gharaee-Kermani, M., McGarry, B., Lukacs, N., Huffnagle, G., Egan, R.W., and Phan, S.H.: The role of IL-5 in bleomycin-induced pulmonary fibrosis. *J. Leukocyte Biol.* 1998; 64:657-666.
3. Zhang, H., and Phan, S.H.: Inhibition of myofibroblast apoptosis by transforming growth factor β_1 . *Am. J. Resp. Cell Molec. Biol.* 1999; in press.

BOOKS/CHAPTERS IN BOOKS:

1. Phan SH.: The myofibroblast as an inflammatory cell. In: *Tissue repair and fibrosis: role of the myofibroblast.* Ed. Desmouliere A.. Springer Verlag, Berlin, 1999, in press.

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

1. Nozaki Y, **Phan SH**: Rat Lung myofibroblast differentiation results in reduced telomerase activity. *Am. J. Resp. Crit. Care Med.* 1999;159:A
2. Gharaee-Kermani M, **Phan SH**: Lung Interleukin-4 expression in bleomycin-induced pulmonary fibrosis. *Am. J. Resp. Crit. Care Med.* 1999;159:A

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999

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"

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. "Trends in Antimicrobial Resistance for Clinical Isolates of *Bacteroides sp.*", Principal Investigator: D. R. Snyderman, New England Medical Center, Boston, Massachusetts.
- B. "The incidence of sexually transmitted diseases among sex workers 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. Assessment of quinolone activity against clinical isolates of *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis*. Medical Reference Laboratories., Reston, VA.
- E. Evaluation of NASBA to detect CMV pp67 mRNA in whole blood. Organon Teknika Corp., Durham, NC.

PROJECTS UNDER STUDY:

- A. Detection of the *mecA* resistance gene in staphylococci growing in blood culture bottles.
- B. Evaluation of Roche HIV PCR to replace the p24 assay.

- C. Quantitative and qualitative measurement of HCV RNA in plasma using the Roche Cobas System.
- D. Evaluation of the automated Cobas System for the detection of *Chlamydia* and *Neisseria gonorrhoeae* in urine.
- E. Assessment of the efficiency of LE/Nitrate urine screening to reduce urine culture.
- F. Development of a PCR procedure to detect *Mycoplasma* spp. in tissue cultures.
- G. Evaluation of microtiter and gradient strip methods for yeast antimicrobial susceptibility.
- H. PFGE methods for the epidemiologic study of vancomycin-resistant *Enterococcus* spp.
- I. Assessment of the accuracy of calculated MICs using the BioMIC system.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Clinical Pathology Laboratory Directors Committee.
- B. Chair, Clinical Microbiology/Virology Senior Staff committee.
- 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.

REGIONAL/NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

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

INVITED LECTURES/ SEMINARS:

- 1. "Clinical value of the *in vitro* susceptibility tests for yeasts." U of Mich. Dermatology Dept.

2. "Germ Warfare-A brief history and current status". CME for the UMHS Clinical Laboratory Staff.

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*, 92 92(2):258-61.
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. *J. Clinical Microbiol.*, 36 (11): 3273-7.
3. Perzigian, RW, Adams, JT, Weiner, GM, DiPietro, MA, Blythe, LK, Pierson, CL, Faix, RG: *Ureaplasma urealyticum* and chronic lung disease in very low birth weight infants during he exogenous surfactant era. 1998. *Pediatric Infectious Disease J*, 17(7):620-5.
4. Snyderman DR, Jacobus, NV, McDermont, LA, Supran, S, Cuchural, GJ, Gorbach, SL, Hecht, DW, Harrell, H, Pierson, CL, Jenkins, S, Iannini, P, Rihs, J, and Finegold, S: A multicenter study of the in vitro susceptibility of the *Bacteroides fragilis* group, 1995-1996 with comparison of resistance trends from 1990-1996. 1999. *Antimicrob. Agents Chemotherapy*, *in press*.

BOOKS/ CHAPTERS IN BOOKS:

1. "Antimicrobial susceptibility testing". In *Clinical Laboratory Medicine*, K.D. McClatchey, ed., Lippincott Williams & Wilkins, 2nd Ed, *in press*

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

1. Young, C, and Pierson, CL: Retrospective comparison of BacT/Alert FAN aerobic media to Isolator for the detection of yeast from blood. Abstract No.C146, 99th General Meeting, American Society for Microbiology, 1999, Chicago, IL, pg. 134.
2. Young, C, Snyder, D, and Pierson, CL: Clinical utility of *mecA* PCR to rapidly detect oxacillin-resistant staphylococci. Abstract No. C225, 99th General Meeting, American Society for Microbiology, 1999, Chicago, IL, pg. 150.
3. Cullen K, Young, C and Pierson, C: Comparison of *Burkholderia cepacia* selective agar to *Pseudomonas cepacia* agar for use on cystic fibrosis patient cultures. Abstract No. C451, 99th General Meeting, American Society for Microbiology, 1999, Chicago, IL, pg. 198.
4. Grossman, S, Young, C, and Pierson, CL: Use of the BacT/Alert for bone marrow product sterility testing. Abstract No. C498, 99th General Meeting, American Society for Microbiology, 1999, Chicago, IL ,pg. 207.
5. Pierson, CL, Wiedbrauk, DL, and Burd, EM: Detection of HCMV viremia in organ transplant patients using the Nuclisens CMV pp67 assay: comparison to PCR and pp65 antigenemia assays. Abstracts, Pan American Society for Clinical Virology, 1999. Clearwater Beach, FL , pg. 82.

Articles for the *SPECTRUM*

1. Hankerd R, and Pierson, CL: New test for *Helicobacter pylori*; 12(3):2-3, 1998.
2. Pierson, CL: *Chlamydia trachomatis* DNA probe replaced by PCR assay; 13(2):1-2, 1999.

**STEPHEN RAMSBURGH, M.D.
CLINICAL INSTRUCTOR II
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

A. General Surgical Pathology – 24 weeks

II. TEACHING ACTIVITIES:

A. Graduate students:

1. M2 Pathology Lab – 70 hours

B. House Officers:

1. General Surgical Pathology – 24 weeks

2. Resident Teaching Conference – 45 hours

3. Consultation Conferences – 4 hours

4. Intraoperative consultation – 70 hours

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None

PENDING:

None

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None

MEDICAL SCHOOL/HOSPITAL:

None

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

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Surgical Pathology coverage of M-Labs cases, including most from the following hospitals/clinical practices:
 - 1. Trillium Community Hospital, Albion, MI;
 - 2. Addison Hospital, Addison, MI;
 - 3. University of Michigan Health Service;
 - 4. Livonia SurgiCenter and other University of Michigan Clinics and satellite sites;
 - 5. Other clients such as clinics outside of Washtenaw County.
- B. Outside consults to a growing list of pathologists. These are stat consults and we provide fast turn around times. Most of these cases are shown in consultation to other faculty.
- C. Autopsy coverage at the University Hospitals, for weekdays and weekends. Autopsy coverage is also provided to Trillium Hospital, in Albion and Addison Hospital, Addison, MI.
- D. Perform bone marrow aspiration and biopsies at Trillium Hospital, Albion, MI.
- E. Review peripheral smears at Trillium Hospital, Addison Community Hospital and University of Michigan Health System.
- F. Clinical Pathology consults for M-Labs client hospitals.
- G. Cytopathology: perform FNA services (performance of aspirate/interpretation) at U of M Hospitals and at Trillium Hospital.
Cover PAP smear interpretation and nongyn cytology read-out, one day a week.
Provide coverage for the Cytopathology Service when needed.
- H. Frozen sections at Trillium Hospital and the Livonia Surgical Center (U of M Facility).

II. TEACHING ACTIVITIES:

- A. Sign out M-Labs and University of Michigan autopsies with residents.
- B. Organize and lecture at the M-labs Symposium (13th Symposium in April 1999), a one day-long event with lectures and case presentations for pathologists (most are M-Labs clients). CME credits are provided. Held twice a year (October/April).
- C. Sign-out in cytopathology one day a week, with residents, fellow and, occasionally with medical students.
- D. In-service teaching to laboratory staff at Albion Community Hospital and the University of Michigan Health Service (UHS).
- E. Monthly colposcopy meetings with the Gyn medical staff at UHS.
- F. Gross Autopsy Conference, 6 hours.

III. RESEARCH ACTIVITIES:

None.

IV. ADMINISTRATIVE ACTIVITIES:

- A. Associate Director, M-Labs: (for more details, see M-Labs' Annual Report). Participate in planning, marketing and implementation of M-Labs programs.
 - a. Marketing activities with potential new clients;
 - b. Contacts with pathologists from client hospitals and others, as part of our support to pathologists; this includes providing occasional coverage;
 - c. Laboratory network activity:
 - Joint Venture Hospital Laboratory – (JVHL) QA committee, which meets approximately once every three months.
 - Great Lakes Network – (GLN) Medical Affairs Committee, which meets monthly.
 - d. Coordinating M-Labs QA activities with D. Moss; monthly review of occurrence reports;
 - e. Problem solving of M-Labs related issues
- B. Medical Director of the University of Michigan Health Service Laboratory.
- C. Active medical staff member at Trillium Hospital and Addison Community Hospital. Conduct Tissue Review and Transfusion Review meetings. Attend their medical staff meetings.
- D. Intra-departmental meetings (e.g., Cytopathology)

V. OTHER:

- A. Mentorship Program at the University of Michigan – Mentor
- B. Referee for the Hematology Survey, College of American Pathologists (CAP)
- C. Inspector, for the CAP Accreditation Program. Performed two inspections.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Director, Autopsy Service.
- B. Director, Electron Microscopy Service.
- C. Supervision of Autopsies-12 weeks, signed out 65 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 Washtenaw County.

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. Lecturer, Pathology 580 course (Dental School), 1 contact hour.
- E. Pathology 600, Provided written critiques of student autopsy write-ups (167).
- F. Laboratory Instructor, Histopathology Laboratory for M1 students, 20 contact hours.
- G. Laboratory Instructor Pathology 585, (Medical Illustrators course). 12 contact hours.
- H. Laboratory Instructor, Pathology 600 (M2 pathology course), year long.
- I. Thesis Committee - Andrew Merry
- J. 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. Jiyoun Kim, Ph.D.
- K. Medical Students – Azadeh Shahshahani
- L. Graduate Students – Andrew Merry
- M. Undergraduate Students - David Newcomb, Rob Cohen, Emily Beers
- N. Travel to Malawi and South Africa. Under a grant from the Fogarty Foundation we are establishing a training program to bring physicians from Malawi to the University of Michigan to train in pathology. I traveled to Malawi and South Africa to set up the proposed curriculum and determine the training needs.

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. Chemokines in the pathogenesis of murine asthma.
- 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. Co-ordinator of call schedule, both weekend and weekday, autopsy service.
- E. Coordinator, medical examiner investigator call schedule, University of Michigan.

MEDICAL SCHOOL/HOSPITAL:

- A. Member, Medical School Admissions Committee.
- B. Member, Biomedical Research Council Undergraduate Research Council.
- C. Academic Credentials, Appointments and Promotions and Tenure, Instructional Tract, 1997 – 2001.
- D. Chair, Academic Credentials, Appointments, Promotions and Tenure, Instructional Tract, 1999 – 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. Member, Strategic Planning Committee, including executive group, 1999 – present.
- I. Pathology representative to Medical Device Explant Committee.
- J. Program in Biomedical Sciences (PIBS) Admissions Committee, 1999.
- K. Pathology Graduate Program Curriculum Revision Committee, 1999.

REGIONAL AND NATIONAL:

- A. Chair, Michigan Association of Medical Examiners.
- B. Deputy Medical Examiner for Washtenaw County.
- C. Regular member National Institutes of Health, Surgery, Anesthesiology and Trauma Study Section Oct 1999 to June 2003.
- D. Member, Michigan Coalition on Donation.
- E. Publications Committee, International Cytokine Society.
- F. Awards Committee, Shock Society.
- G. Member, Michigan Association of Medical Examiners, Shock Society, American Association of Immunologists, A. James French Society, American Society of Investigative Pathologists, United States-Canadian Academy of Pathology.

V. OTHER RELEVANT ACTIVITIES:

- A. Editorial Board: Shock, Journal of Immunology.
- B. Symposium Chair, Experimental Biology 1999, Mediators of Inflammation.
- C. Symposium Chair, Experimental Biology 1999, Poster Discussion Session, Mediators of Inflammation.
- D. 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 Investigation.
 - 7. Infection and Immunity.
 - 8. Blood.
 - 9. Shock.

10. American Journal of Physiology.
11. Journal of Gerontology.
12. Clinical Immunology
13. Cytokine
14. American Journal of Respiratory Cell and Molecular Biology
15. Grant Reviewer, Swiss Government

INVITED LECTURES/SEMINARS:

1. Visiting Professor, Norwegian University of Science and Technology, Trondheim, Cytokines and Sepsis, the Evolving Story, 1998.
2. Keynote Speaker, Michigan Dementia Postmortem Network Conference, Michigan State University, The Value of Autopsy in Modern Society, 1998.
3. Invited Speaker, Children's environmental Health and Disease Prevention Research Centers, Research Triangle Park, North Carolina, Murine Chemokines in Asthma, 1998.
4. Visiting Professor, Michigan State University Department of Surgery, Lansing Michigan Sepsis – Nothing Works, 1999.
5. Visiting Professor, Michigan State University Department of Surgery, Lansing Michigan, Role of Reactive Oxygen Intermediates and Reactive Nitrogen Intermediates in Chemokine Gene Expression, 1999.
6. Visiting Professor, Beijing Medical University, Institute of Vascular Medicine, Beijing, China, Reactive oxygen and the regulation of chemokines, 1999.
7. Invited Speaker, Shanghai Institute of Materia Medica, Shanghai, China Regulation of Cytokine Gene Expression, 1999.
8. Visiting Professor, University of Natal, Durban South Africa, Department of Pathology, Cytokine regulation by reactive oxygen and reactive nitrogen intermediates, 1999.
9. Invited presentation, Pioneer High School Health Occupations Class, Ann Arbor, Michigan, Value of Autopsies in Modern Society, 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Brieland JK, Remick, DG, LeGendre, ML, Engleberg, NC and Fantone, JC: In vivo regulation of replicative *Legionella pneumophila* lung infection by endogenous interleukin-12. *Infection & Immunity* 66: 65-69, 1998.
2. Call DR and Remick, DG: Low molecular weight heparin is associated with greater cytokine production in a stimulated whole blood model. *Shock* 10: 192-197, 1998.
3. Evans CA, Garcia, HH, Hartnell, A, Gilman, RH, Jose, PJ, Martinez, M, Remick, DG, Williams, TJ and Friedland, JS: Elevated concentrations of eotaxin and interleukin-5 in human neurocysticercosis. *Infection & Immunity* 66: 4522-4525, 1998.
4. Evans CA, Jellis, J, Hughes, SP, Remick, DG and Friedland, JS: 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: 1582-1587, 1998.

5. Foreback JL, Sarma, V, Yeager, NR, Younkin, EM, Remick, DG and Ward, PA: Blood mononuclear cell production of TNF-alpha and IL-8: engagement of different signal transduction pathways including the p42 MAP kinase pathway. *Journal of Leukocyte Biology* 64: 124-133, 1998.
6. Hunter B, French, D, Warner, J and Remick, D: Correlation of body mass index with thoracic and abdominal panniculus. *Journal of Forensic Sciences* 43: 427-430, 1998.
7. Newcomb D, Bolgos, G, Green, L and Remick, DG: Antibiotic treatment influences outcome in murine sepsis: mediators of increased morbidity. *Shock* 10: 110-117, 1998.
8. Remick DG, Garg, SJ, Newcomb, DE, Wollenberg, G, Huie, TK and Bolgos, GL: Exogenous interleukin-10 fails to decrease the mortality or morbidity of sepsis [see comments]. *Critical Care Medicine* 26: 895-904, 1998.
9. Wang SC, Klein, RD, Wahl, WL, Alarcon, WH, Garg, RJ, Remick, DG and Su, GL: Tissue coexpression of LBP and CD14 mRNA in a mouse model of sepsis. *Journal of Surgical Research* 76: 67-73, 1998.
10. Cooper PJ, Awadzi, K, Ottesen, EA, Remick, D and Nutman, TB: Eosinophil sequestration and activation are associated with the onset and severity of systemic adverse reactions following the treatment of onchocerciasis with ivermectin. *Journal of Infectious Diseases* 179: 738-742, 1999.
11. Hennein HA, Kiziltepe, U, Barst, S, Bocchieri, KA, Hossain, A, Call, DR, Remick, DG and Gold, JP: Venovenous modified ultrafiltration after cardiopulmonary bypass in children: a prospective randomized study. *Journal of Thoracic & Cardiovascular Surgery* 117: 496-505, 1999.
12. Ebong SJ, Call, DR, Bolgos, GL, Newcomb, DE, Granger, JI, O'Reilly, M and Remick, DG: Immunopathologic responses to non-lethal sepsis. *Shock*, In press.

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

1. Immunopathology Of A "2-Hit" Model Of Lung Injury. J. Nemzek, D. Call, S. Ebong, G. Bolgos, D. newcomb, & D. Remick, Experimental Biology, Washington D.C., April 1999.
2. Two Models Of Septic Shock, Similarities And Differences. G. Bolgos, D. Call, D. Newcomb, & D. Remick, Experimental Biology, Washington D.C., April 1999.
3. Immunopathologic Alterations In Murine Sepsis Models Of Increasing Lethality. S. Ebong, D. Call, G. Bolgos, J. Nemcek, D. Newcomb, & D. Remick, Experimental Biology, Washington D.C., April 1999.
4. Immunocomplexes Stimulate Progression To A Proinflammatory State Which Is Blunted By Sulfazalaine. P. Nybom and D. Remick, Experimental Biology, Washington D.C., April 1999.
5. Modulation Of Inflammatory State In An Ex Vivo System. D. Newcomb and D. Remick, Experimental Biology, Washington D.C., April 1999.
6. Regulation Of Chemokines By Reactive Oxygen And Nitrogen Intermediates. D. Remick, International Symposium on Advances of Neuroimmunology, Shanghai, China, May, 1999.
7. Chemokine Redundancy Ensures An Appropriate Biologic Response D. Remick, L. Green, D. Newcomb, S. Garg, G. Bolgos, & D. Call, Fourth International Shock Congress, Philadelphia, Pennsylvania, June, 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998- 30 JUNE 1999**

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 I¹³¹ anti-B1 radioimmunotherapy for B-cell lymphoma, Coulter Pharmaceutical.
- B. Inspector, CAP Laboratory Accreditation Program, University of Alabama at Birmingham, February 1999.
- C. Ad hoc manuscript reviewer, Human Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

- 1. Lecturer, "Hematologic Coups: A practical approach to challenging cases in hematology diagnosis", American Society of Clinical Pathologists National Meeting, April, 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Singleton TP, Anderson MM, Ross CW, Schnitzer B. Leukemic phase of mantle cell lymphoma, blastoid variant. Am J Clin Pathol 111:495-500, 1999.

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. *J Nucl Med* 39:21S-27S, 1998.
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. *Am J Clin Pathol* 110:327-333, 1998.
4. Kroft SH, Hsi ED, Ross CW, Schnitzer B, Singleton TP. Evaluation of CD23 expression in paraffin-embedded gastric lymphomas of mucosa-associated lymphoid tissue. *Mod Pathol* 11:967-70, 1998.
5. McCarthy CJ, Sheldon S, Ross CW, McCune WJ. Cytogenetic abnormalities and therapy-related myelodysplastic syndromes in rheumatic disease. *Arthritis Rheum* 41: 1493-1496, 1998.
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* 110:95-99, 1998.
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. *Am J Clin Pathol* 110:582-589, 1998.
8. Iravani S, Singleton TP, Ross CW, Schnitzer B. Precursor B lymphoblastic lymphoma presenting as lytic bone lesions (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Terhune M, Parry E, Strawderman M, Ross CW, Neckel S, Mostow E, Stevens S, Cooper K. A simple clinical scoring system to improve the sensitivity and standardization of the diagnosis of mycosis fungoides type cutaneous T-cell lymphoma: logistic regression of clinical and laboratory data.
2. Yang F, Tran T-A, Carlson A, Hsi ED, Ross CW, Arber DA. Paraffin section immunophenotype of cutaneous and extracutaneous mast cell disease: comparison to other hematopoietic neoplasms.
3. Skacel M, Ross CW, Hsi ED. Primary malignant lymphoma of the thyroid gland.
4. Kroft SH, Finn WG, Schnitzer B, Dawson DB, Singleton TP, Ross CW. Precursor B-lymphoblastic transformation of grade I follicle center lymphoma.

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

1. Padmore RF, Finn WG, Singleton TP, Ross CW and Schnitzer B. Fascin expression in immunophenotypic variants of classical Hodgkin's disease. *Mod Pathol* 12(1):144A, 1999.
2. Skacel M, Ross CW, Hsi ED. Primary malignant lymphoma of the thyroid gland. *Mod Pathol* 12(1):146A, 1999.
3. Valdez R, Kroft SH, Schnitzer B, Ross CW, Singleton TP, Peterson LC, Finn WG. Cerebrospinal fluid (CSF) involvement by mantle cell lymphoma. *Mod Pathol* 12(1):147A, 1999.

4. Yang F, Tran TA, Carlson JA, Ross CW and Arber DA. Paraffin section immunophenotype of cutaneous and extracutaneous mast cell disease: comparison to other hematopoietic neoplasms. *Mod Pathol* 12(1):149A, 1999.
5. Alereidi F, Terebelo H, Erba H, Ross C. Transformation of chronic lymphocytic leukemia (CLL) to Hodgkin's disease (HD) – a treatable entity. *Blood* 92(10), supplement 1: 88a, 1999.

**MARK A. RUBIN, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Room #1 and 2 support, several weeks annually.
- B. Bladder, prostate and urinary surgical consultation cases, intra and extra mural, daily, twelve months.
- C. Prostate Pathology, daily, twelve months.
- D. GU fellow training, daily, twelve months
- E. Continued to organize and maintain research lab, twelve months.
- F. Supervise research projects
- G. Continually seek out funding for various projects.

II. TEACHING ACTIVITIES:

- A. 1996-present Anatomic Pathology Journal Club
- B. 1995-present Second Year Medical School Pathology Labs
- C. 1999-present Urology resident pathology lectures

III. RESEARCH ACTIVITIES:

- A. Prostate Cancer Research
- B. Genitourinary Research

SPONSORED SUPPORT:

- A. Co-Investigator - P50 CA69568 - 09/30/95-07/31/00 - NIH \$82,054, section - 30% Tissue and Serum Core Resource for Prostate Cancer (SPORE grant).
- B. Co-Investigator - 5P30 CA46952 - 06/92-05/01 - NIH \$64,850 - 10% Tissue Procurement and Histopathology Core.
- C. Project Director - (Macoska - Co-investigator) - 8/01/99-02/28/200 - MUNN Idea Award \$10,000 - 0% Molecular Profiling to Distinguish Flat Urothelial Carcinoma in situ from Reactive changes following BCG Therapy.
- D. Principal Investigator - 99-3397 - 6/01/99-5/31/01 - NIH/NCI - \$815,520 - 20% Enhancement of Prostate SPORE related tissue acquisition, processing, and sharing.

PENDING SUPPORT:

- A. Principal Investigator 99-2696 - 11/1/99-10/31/02 - Dept of Defense - \$539,762 - 20%. Identifying Biomarkers for Prostate Cancer using High Through-Put Tissue Microarray Technology.

ONGOING RESEARCH:

- A. Molecular alterations associated with flat carcinoma in-situ and atypia of the bladder following BCG treatment. (Funded – Munn Award).
- B. Development and validation of tissue microarray for use in evaluating biomarkers: Inter-S.P.O.R.E. collaboration with Johns Hopkins and Baylor (Funded- S.P.O.R.E. supplement).
- C. Identification of HPV in men with penile carcinoma: collaborative study with Dr. W. Quint (Delft Holland), Dr. A. Cubillia (Paraguay) and G. Ayalla (Baylor). (Funded through private sources.)

IV. ADMINISTRATIVE ACTIVITIES:

- A. Director of experimental immunohistochemistry/histology laboratory.

MEMBERSHIPS AND OFFICES IN PROFESSIONAL SOCIETIES:

- A. 1996-present University of Michigan Comprehensive Cancer Center.
- B. 1996-present United States and Canadian Academy of Pathology.
- C. 1996-present New York Pathological Society.
- D. 1991-present International Urologic Pathology Society Arztekammer Berlin (Germany).

DEPARTMENTAL:

Director of Urologic Pathology
Coordinates and oversees GU Pathology Fellows
Faculty advisor for AP Journal club

MEDICAL SCHOOL/HOSPITAL:

- A. G.U. module for second year pathology course.
- B. Clinical Pathologic correlation course with Radiology (4th year).

REGIONAL AND NATIONAL:

EXTRAMURAL INVITED PRESENTATIONS

- 1. “WHO/ISUP Urothelial Lesions, 1999” Veterans Administration Hospital – Ann Arbor, MI on 4/12/99.

2. "Classification of Bladder Tumors" Thirteenth MLabs Symposium – Ann Arbor, MI on 5/15/99.
3. "Review of Gleason's Grading for Prostate Cancer" Thirteenth MLabs Symposium – Ann Arbor, MI on 5/15/99.

V. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Han EK, Rubin MA, Lim, T., Arber N, Xing WQ, Weinstein IB. Cyclin D1 Expression in Human Prostate Carcinoma Cell Lines and Primary Tumors. *Prostate* 1998, 35(2): 95-101.
2. Rubin M.A., Parry JP, Singh B. Kaposi's Sarcoma-Associated Herpesvirus DNA Sequences: Lack of Expression in Prostatic Tissue of HIV-Negative Immunocompetent Men. *J Urology* 1998 (1): 146-148.
3. Ennis RD, Bozena KM, Rescigno J, Whitman AE, Heitjan DF, O'Toole KM, Rubin MA, Schiff PB Biologic Classification as an alternative to Anatomic Staging for Clinically Localized Prostate Cancer: A Proposal based on Patients Treated with External Beam Radiotherapy. *Urology* 1998, 51:265-270.
4. Ennis RD, Bozena KM, Heitjan DF, Rubin MA, O'Toole KM, Schiff PB Changes in Biochemical Disease-Free Survival Rates as a Result of Adoption of the Consensus Conference Definition in Patients with Clinically Localized Prostate Cancer Treated with External-Beam Radiotherapy. *Int J Radiation Oncology Biol Phys* 1998, 41: 511-517.
5. Rubin MA, de La Taille A, Bagiella E, Olsson CA, O'Toole KM. Cribriform Carcinoma of the Prostate and Cribriform Prostatic Intraepithelial Neoplasia: Incidence and Clinical Implications. *Am. J Surg. Pathol* 1998, 22 (7): 840-848.
6. Liu QY, Rubin MA, Omene C, Llederman S, Stein CA: Fas Ligand is Constitutively Secreted by Prostate Cancer Cells in Vitro. *Clin Cancer Res* 1998, Jul; 4 (7) :1803-1811
7. de la Taille A, Rubin MA, Bagiella E, Olsson CA, Buttyan RE, Burchardt T.O'Toole KM, Katz A: Can Perineural Invasion on Prostate Predict PSA Recurrence?. *J of Urology* (1999).
8. Tickoo SK, Reuter VE, Amin MB, Srigley JR, Epstein JI, Min KW, Rubin MA, Ro JY: Renal Oncocytosis: A Morphologic Study of 14 cases. In press. *AJSP* 1999, (in press).
9. Nastiuk KL, Mansukhani M, Kularatne,P, Rubin MA, Melamed J, Ittmann M, Krolewski JJ Common Mutations in BRCA1 and BRCA2 Do Not Increase The Relative Risk of Prostate Cancer in Young Jewish Men. In press. *Prostate*.
10. de la Taille A, Katz A, Bagiella E, Olsson CA, O'Toole KM, Rubin MA: Perineural Invasion on Prostate Needle Biopsy: An Independent Predictor of Final Pathologic State. In press. *Urology* (1999).
11. Rubin Mark, Ann Arbor, MI. Atypical small acinar proliferation: a clinically significant diagnostic category. 1999, *J of Urologic Path.*
12. Rubin MA, Gerstein A, Reid K, Bostwick DG, Cheng L, Parsons R, Papadopoulos N: 10q23.3 Loss of Heterozygosity is Higher in Lymph Node-Positive Prostate Cancer (pT2-3, N+). Submitted for publication 1999.
13. Bassily N, Vallorosi CJ, Akdas G, Montie JE, Rubin MA: Coordinate Expression of Cytokeratins 7 and 20 in Prostate Adenocarcinoma and Bladder Urothelial Carcinoma. Submitted for publication (1999).

14. Rubin MA, Bassily N, Sanda M, Montie J, Strawderman MS, Wojno K.: Relationship and Significance of Greatest Percentage of tumor and Perineural Invasion on Needle Biopsy in Prostatic Adenocarcinoma. Submitted for publication.
15. Marcovish R, Wojno K, Wei JT, Rubin MA, Montie JE, Sanda MG: Bladder Neck Sparing Modification of Radical Prostatectomy Adversely Affects Surgical Margins in Pathologic T3a Prostate Cancer. Submitted for publication.
16. Rubin MA, Dunn R, Kambham N, Misick CP, O'Toole KM: Should a Gleason score be assigned to a minute focus of carcinoma on prostate biopsy? Submitted for publication.

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

1. Rubin MA, Buyyounouski M, Katz AE, Olsson CA and Ennis RD. Microvessel density in prostate cancer: lack of correlation with tumor grade, pathologic stage, and clinical outcome. *Modern Pathol* 11:A540, 1998.
2. Rubin MA, Reid KA, Wang SI, Lequesne E, Olsson CA and Parsons R. *PTEN*, a putative prostate tumor suppressor gene: loss of heterozygosity in localized prostate cancer. *Modern Pathol* 11:A539, 1998.
3. Kambham N, Taylor JA and Rubin MA. Atypical small acinar proliferation: cop-out or clinically significant diagnostic category. *Modern Pathol* 11:A496, 1998.
4. Tickoo SK, Reuter VE, Amin MB, Srigley JR, Epstein JE, Min KW, Rubin MA. Renal Oncocytosis: Morphologic spectrum and morphogenetic considerations. *Modern Pathol* 11:A558,1998.
5. Rubin MA, Reid K, Gerstein A, and Papadopoulos N. Laser Capture Microdissection of Archival Prostatic: Adenocarcinoma for PCR Analysis. US&C Academy of Path. Mar.20-26, 1999:Pg. 105A.
6. Vallorosi CJ, Bassily NH, Akdas G, Montie JE, & Rubin M, Ann Arbor, MI. Coordinate expression of cytokeratins 7 & 20 in Prostate adenocarcinoma and bladder urothelial carcinoma. AUA meeting Dallas (1999).
7. Rubin MA, Reid KA, Gerstein A, Bostwick, L Cheng and Papadopoulos N. *PTEN*, A putative Prostate Tumor Suppressor Gene. US&C Academy of Path. Mar.20-26,1999:Pg. 106A.
8. Rubin Mark, Ann Arbor, MI. Atypical small acinar proliferation: a clinically significant diagnostic category. *J of Urologic Pathology* MS JUP-304 (1999).
9. Rashid Michael, Wojno Kirk J., Marcovich Robert, Rubin Mark, Montie James E., & Sanda Martin G, Ann Arbor, MI. Maximum Tumor Dimension Provides a Clinically useful and independently significant measure for predicting PSA-Free Survival Following Radical Prostatectomy. *J of Urology* (1999).
10. Rubin MA, Strawderman M, Bassily N, Williams JF, Sanda M, & Montie JE, Ann Arbor, MI. Prostate Cancer Staging: Evaluation of nomogram predicting unfavorable pathology. *J of Urology* (1999).
11. Bassily NH, Montie JE, Pienta KJ, & Rubin MA, Ann Arbor, MI. Significance of Gleason pattern 4 as an independent prognostic indicator of postoperative PSA failure in prostatic adenocarcinoma. *J of Urology* (1999).
12. Ennis RD, Putzi M, & Rubin MA, Ann Arbor, MI. Treatment of the peripheral zone only in clinically localized early stage prostate cancer: is it a reasonable alternative? *J of Urology* (1999)

13. Rubin M, de La Taille A, Olsson CA, Bagiella E, Sharir S, Burchardt T, Cao Y, & Katz AE, New York, NY. Microvessel Density as a predictor of PSA recurrence after radical prostatectomy: Comparison of CD-31 or CD-34 staining. J of Urology (1999).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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.
- B. Director of Graduate Medical Education (Hematopathology)

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. Schnitzer, B: Videomicroscopy Workshop, "Interesting Lymphoid Lesions," ASCP Workshop, Washington, DC, October, 1998.
- 2. Schnitzer, B: Microscopy Tutorial Workshop, "Lymph Node Pathology," ASCP Workshop, Washington, DC, October, 1998.
- 3. Schnitzer, B: Hodgkin's Disease: A Practical Approach to Diagnosis and Differential Diagnosis, ASCP Workshop, Washington, DC, October, 1998.
- 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, New Orleans, LA, November, 1998.
- 5. "Reactive Lymphadenopathies," Tutorial on Neoplastic Hematopathology, Department of Laboratory Medicine and Pathology, Cornell University, Miami, Florida, February, 1999.
- 6. Schnitzer, B., Ross, CW and Singleton, T: "Hematologic Coups," ASCP Workshop, Orlando, FL, April, 1999.

7. Schnitzer, B.: Videomicroscopy Workshop, "Interesting Lymphoid Lesions," ASCP Workshop, Orlando, FL, April, 1999.
8. Schnitzer, B.: Microscopy Tutorial Workshop, "Lymph Node Pathology," ASCP Workshop, Orlando, FL, April, 1999.
9. Schnitzer, B.: "A Practical Approach to the Diagnosis and Differential Diagnosis of Extranodal Lymphomas," ASCP Workshop, Orlando, FL, April, 1999.
10. Schnitzer, B.: Precursor B-lymphoblastic lymphoma. Specialty Conference, Hematopathology. USCAP Meeting, San Francisco, CA, March, 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. 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* 110:95-99, 1998.
2. 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. *Am J Clin Pathol* 110:582-589, 1998.
3. Kroft SH, Hsi ED, Ross CW, Schnitzer B, Singleton TP: CD23 expression in paraffin embedded gastric lymphomas of mucosa-associated lymphoid tissue. *Mod Pathol* 11:967-970, 1998.
4. Hussong JW, Perkins S, Schnitzer B, Hargreaves H, Frizzera G: Extramedullary plasmacytoma, a form of marginal zone lymphoma. *Am J Clin Pathol* 111:111-116, 1999.
5. Hsi Ed, Singleton TP, Svoboda SM, Schnitzer B, Ross CW: Characterization of the lymphoid infiltrate in Hashimoto thyroiditis by immunohistochemistry and polymerase chain reaction for immunoglobulin heavy chain gene rearrangement. *Am J Clin Pathol* 110:327-333, 1998.
6. Singleton TP, Anderson MM, Ross CW, Schnitzer B: Leukemic phase of mantle cell lymphoma, blastoid variant. *Am J Clin Pathol* 111:495-500, 1999.
7. Izban F, Wrone-Smith T, Hsi Ed, Schnitzer B, Quevedo ME, Alkan S: Characterization of the interleukin-1 β -converting enzyme/Ced-3-family protease, capsase-3-CPP32, in Hodgkin's disease. Lack of capsase-3 expression in nodular lymphocyte predominance Hodgkin's disease. *Am J Pathol* 154:1439-1447, 1999.
8. Irvani S, Singleton TP, Ross CW, Schnitzer B: Precursor-B lymphoblastic lymphoma presenting as lytic bone lesions. *Am J Clin Pathol* (accepted for publication).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Grogan TM, Unger J, Miller TP, Kjeldsberg C, Tubbs R, LeBlanc M, Braziel R, Foucar K, Leith C, Spier C, Slovak ML, Nelson MA, Arber DA, Gulley M, Nathwani B, Schnitzer B, Fisher RI: The Hodgkin's-like and classic variants of anaplastic large cell lymphoma: A Southwest Oncology Group analysis: *Blood*.

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. Valdez R, Kroft SH, Schnitzer B, Ross CW, Singleton TP, Peterson LC, Finn WG: Cerebrospinal fluid involvement by mantle cell lymphoma. Mod Pathol 12:147A, 1999.
2. Padmore RF, Finn WG, Singleton TP, Ross CW, Schnitzer B: Fascin expression in immunophenotypic variants of classical Hodgkin's disease. Mod Pathol 12:144A, 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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, Department of Pathology, University of Michigan "Hemostasis", April 9, 1999.
- D. Eight lectures on Hemostasis and Thrombosis, School of Allied Health, Eastern Michigan University, April 1999.
- E. Lecture, "Principles of Hemostasis". Junior and Senior Students, Central High School, Grand Rapids, MI., May 11, 1999.

III. RESEARCH ACTIVITIES:

None.

IV. PUBLICATIONS:

- 1. Shanberge JN: Transfusion Medicine in Philately, *Transfusion*, 39:534-536, 1999.
- 2. Monthly prints of pertinent stamps to accompany articles in *Journal of Infectious Diseases*.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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 residents, fellows and medical students:
1. Instruction in cytogenetics as it relates to both genetic and acquired disease.
2. Laboratory rotation for genetics residents.
- C. Hematology/Oncology fellows:
1. Instruction in cytogenetics as it relates to adult hematologic disease.
2. Instruction in cytogenetics relating to pediatric hematologic disorders and solid tumors.
- D. Clinical Pathology Grand Rounds, two lectures.
- E. Pediatric Genetics Rounds, weekly participant, one lecture.
- F. Leukemia Conference, biweekly.
- G. Genetic Counseling graduate students:
1. Two lectures.
2. Individual tutorials.
- H. Maternal fetal medicine fellow – Laboratory rotation and lectures

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Role of the use of growth factors and mitogens for cytogenetic examination of hematologic malignancies in a clinical laboratory.
- B. Use of growth factors to elaborate expression of a Philadelphia chromosome.
- C. Use of intercalating agents to enhance resolution of chromosome bands.
- D. Correlation of ploidy with expression of differential function.
- E. Role of chromosome abnormalities in eosinophilia.
- F. Fluorescence in situ hybridization for identification of marker chromosomes.
- G. Fluorescence in situ hybridization as "interphase cytogenetics".
- 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", San Francisco, March, 1999.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. McCarthy, C, Sheldon, S, Ross, C, and McCune, J.: Myelodysplastic syndromes in rheumatic diseases after immunosuppressive therapy: a cytogenetic study; *Arthritis & Rheumatism* 41(8):1493-1496, 1998.
2. Zhou, M, Sheldon, S, Akel, and Kileen, A.: Chromosomal aneuploidy in leukemic blast crisis; *Molecular Diagnosis* 4:153-157, 1999.

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

1. Finn WG, Sheldon S, Ross CW, Singleton TP, Schnitzer B: Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) arising in the setting of pre-existing B-CLL.
2. Schnitzer B, Singleton TP, Ross CW, Sheldon S, Finn WG: Extramedullary myeloid cell tumor of differentiated monocytic cells followed by development of acute myelogenous leukemia, FAB M5b.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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. Growth. In FY 1999, MLabs added 39 new physician offices and specialty service practices to our client list. The majority of these were related to our contract to provide coverage to M-Care patients. Some were for specialty services (dermatopathology, flow cytometry, muscle and nerve biopsy), and a few were UMHS acquired practices. There were also 3 new full reference laboratory accounts, one hospital, one correctional institution, and one intensive care facility. No contracts for services were terminated.
Net billings for clinical pathology services increased by 7% while net billing for anatomic pathology services decreased by 13%.
Net billings for combined AP and CP services were almost flat (reduced by 0.6%).
MLabs submitted 8 proposals to prospective major clients during FY99. Of these, 3 were rejected, 3 were accepted, and 2 are pending.
3. Managed Care Activities
MLabs has expanded our agreement with M-Care to supply outpatient laboratory services to include the majority of their provider groups (IDNs) for the HMO, POS, and Medicaid products. We have begun discussions with M-Care to develop a full-risk outpatient lab agreement for all groups and products to become effective 1/1/2000 (current target date).
MLabs continues to manage the M-Care/MLabs agreement for Medicare HMO Program (Senior Plan). Five subcontracts are in place. We developed and implemented a system for reimbursement for testing done by other labs within network (Cross System Testing). We have finalized and facilitated most M-Care HMO, POS, and Medicaid Contracts and Subcontracts. The other subcontracts are in progress.
We prepare quarterly QA reports on lab services for M-Care's QA department and have conducted a Physician Satisfaction Survey for MLabs subcontracted providers and reported the results to M-Care. We assist M-Care with resolution of laboratory service issues.
4. Networks. MLabs is a member of 2 laboratory networks, Great Lakes Laboratory Network (GLN) which consists of 28 hospital laboratories, predominantly in the western and northern parts of Michigan, and Joint Venture Hospital Laboratories (JVHL) which has 13 member laboratories located in southeastern Michigan. GLN has no contracts yet. JVHL has contracts for laboratory services with 10 managed care organizations, including Select Care, and a subcontract with MLabs for M-Care work.
I serve on JVHL's Executive committee and its "elabs" committee.
We are working towards a cooperative effort of the 2 networks to bid in the next fiscal year for the provision of laboratory services to Blue Care Network.
Mlabs is preparing a proposal to provide reference lab services to JVHL's new "elab" internal esoteric testing initiative.

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 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Director, Clinical Immunohistochemistry for Hematopathology
- B. Diagnostic Hematopathology
- C. Diagnostic Flow Cytometry
- D. 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 (four contact hours)
- B. Dental Students
 - 1. Lecturer, Second Year Dental Students (one contact hour)
- C. Residents and Fellows
 - 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. Hematopathology journal review, monthly
 - 4. Hematopathology unknown conference (one contact hour)
- D. Clinical Pathology Grand Rounds (one contact hour)
- E. Interdepartmental Conferences
 - 1. Lymphoma conference (weekly)
 - 2. Leukemia conference (biweekly)
 - 3. Hematology conference (biweekly)

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. ALK+ B-cell lymphomas
- B. Splenic lymphomas
- C. Follicular Hodgkin's disease
- D. Monoclonal gammopathies in malignant lymphoma
- E. Myelodysplasia in Fanconi's anemia
- F. Apoptosis in myelodysplastic syndrome

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Director, Clinical Immunohistochemistry for Hematopathology

REGIONAL AND NATIONAL:

- A. Ad hoc reviewer, American Journal of Pathology

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

- A. Hematological Coups: A practical approach to challenging cases in hematology diagnosis. (Four contact hours, American Society for Clinical Pathology, with Drs. Ross and Schnitzer, Orlando, FL)

VI. PUBLICATIONS:

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

1. Iravani S, Singleton TP, Ross CW and Schnitzer B. Precursor B lymphoblastic lymphoma presenting as lytic bone lesions (*American Journal of Clinical Pathology*, in press)
2. Hsi ED, Singleton TP, Swinnen L, Greenson JK and Alkan S. Lymphomas of mucosa-associated lymphoid tissue (MALT) occurring after transplantation: A form of posttransplant lymphoproliferative disorder (PTLD)? (*American Journal of Surgical Pathology*, in press)
3. Klee CG, Wojno KJ, Fields K, and Singleton TP. Detection of Estrogen Receptor in Carcinomas of the Breast: Comparison of Monoclonal Antibodies, Automated and Hand Immunohistochemistry and the Cytosol Assay. (*Practical Immunohistochemistry and Molecular Morphology*, in press)
4. Singleton TP, Anderson MM, Ross CW and Schnitzer B. Leukemic phase of mantle cell lymphoma, blastoid variant. *American Journal of Clinical Pathology* 111:495-500, 1999.
5. Kroft SH, Hsi ED, Ross CW, Schnitzer B and Singleton TP. Evaluation of CD23 expression in paraffin-embedded gastric lymphomas of mucosa-associated lymphoid tissue. *Modern Pathology* 11:967-70, 1998.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Izban KF, Singleton TP, Alkan S, Hsi ED. Multiparameter immunohistochemical analysis of the cell cycle proteins cyclin D1, Ki-67, p21WAF1, p27KIP1 and p53 in mantle cell lymphoma.

ABSTRACTS, PUBLICATIONS IN UNREFEREED JOURNALS:

1. Bavikatty NR, Ross CW, Finn WG, Schnitzer B and Singleton TP. CD10 detection in acute leukemia by immunohistochemistry in paraffin sections. (American Society for Clinical Pathology, September 1999)
2. Bavikatty NR, Finn WG, Schnitzer B, Ross CW and Singleton TP. Expression of CD99 and terminal deoxynucleotidyl transferase in acute myeloid leukemia (American Society for Clinical Pathology, September 1999)
3. Padmore RF, Finn WG, Singleton TP, Ross CW and Schnitzer B. Fascin expression in immunophenotypic variants of classical Hodgkin's disease. Mod Pathol 12(1): 144A, 1999.
4. Valdez R, Kroft SH, Schnitzer B, Ross CW, Singleton TP, Peterson LC and Finn WG. Cerebrospinal fluid (CSF) involvement by mantle cell lymphoma. Mod Pathol 12(1): 147A, 1999.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999

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. **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. Dr. Tanigawa's research shows that T-cells in lymph nodes draining experimental murine sarcomas are restricted to a small population of T-cells synthesizing binding sites for the selectin family of adhesion receptors. T-lymphoblasts derived from this population suppressed the growth of pulmonary metastases more efficiently than T-lymphoblasts generated using current state-of-the-art techniques. Two manuscripts are currently in preparation entitled: "Tumor-reactive T1-precursors in lymph nodes draining murine sarcomas synthesize P-selectin ligands: impact on adoptive cellular immunotherapy" and "Tumor-reactive T1-precursors in lymph nodes draining murine sarcomas are found in the minor subset of L-selectin^{low} cells that synthesize ligands for P-selectin".
 - 2. **Randall Knibbs, Ph.D., Research Scientist (January, 1994-present)** - Dr. Knibbs continued his investigation of selectin-ligand synthesis with publication of a manuscript entitled " $\alpha(1,3)$ Fucosyltransferase-VII dependent synthesis of P- and E-selectin ligands on cultured T- lymphoblasts" in **Journal of Immunology (1998. 161: 6305)**. Dr. Knibbs also developed a high-capacity transient transfection system using novel microcarriers that increases both the output and duration of protein production. The system currently supports NIH-funded investigations in the laboratory and incremental funding is being sought for commercial development. Dr. Knibbs will continue characterization of selectin ligand synthesis *in vivo* and attempt sequence analysis of the carbohydrate groups responsible for selectin binding activity of human T-lymphoblasts.
 - 3. **Katie Phillips, senior undergraduate (Nov 1995-present):** Ms. Phillips worked ~10 hours/week during the academic year and full-time during the Summer, 1998 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 and presentation of an abstract at Experimental Biology 1999 entitled: "**P-selectin ligands identify tumor-reactive T1-precursors in lymph nodes**"; **K. Phillips, R. Craig, K. Tanigawa, R. Knibbs, A. Chang and L. Stoolman**. Ms. Phillips will attend Duke University Medical School beginning Fall, 1999.

- B. Computerworld-Smithsonian Program Laureate and Award Finalist for development of Internet-based courseware entitled: The Virtual Microscope-Interactive Laboratory Syllabii for Medical and Dental Pathology Courses.** This Award Program is jointly sponsored by the Smithsonian Institution and Computerworld Magazine. It solicits Case Studies from companies and individuals that illustrate the benefits of information technology to society as a whole. Thousands of Case Studies are submitted each year for consideration. This year ~400 Case Studies were selected for inclusion in the American History Museum's Information Age Exhibit and added to the Smithsonian's Permanent Research Collection. In addition, **The Virtual Microscope** was selected as one of five finalists for the Computerworld-Smithsonian Award from the 75 Laureates in the Education and Academia Category. Judging criteria included the application's "benefit to society, difficulty, originality and the primacy of information technology in the definition or resolution of the task addressed". It was one of 15 Laureates in the category from the University of Michigan and the first from any unit of the institution to be selected as a Finalist in the Program.
- C. Director, General Pathology Laboratory Course for Dental Students (Pathology 631) and co-director, General Pathology Lecture Course (Pathology 630):** The second generation Virtual Microscope Pathology Laboratory Interactive Syllabus was developed and deployed for the course (<http://141.214.6.12/cyberscope631/>). 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 the user 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.
- D. 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). The second generation of The Virtual Microscope-Hematopathology Interactive Syllabus was developed and deployed for the course (<http://141.214.6.12/virtualheme98/>). This site utilizes the image server and the general approach outlined above for the Dental Pathology Laboratory Website. The sequence, particularly the laboratory component, is one of the highest rated sequences in Component II.
- E. 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.

- F. **Section leader, Hematopathology Section of Component II-** several sequences use specialists to cover pertinent laboratories. This is in addition to serving as co-director for the sequence and as an instructor in the general pathology laboratories of Component II.
- G. **Lecturer, Host Defense Sequence of Component I.**
- H. **Lecturer, Advanced Topics in Immunology, Department of Microbiology/Immunology.**

III. RESEARCH ACTIVITIES:

ACTIVE SUPPORT (70% funded effort):

- A. Principal Investigator- T Cell Trafficking in Adoptive Cellular Immunotherapy; NIH, R01CA73059, 30% effort, \$180,000 (annual, direct); Apr 1998-Mar 2001.
- B. Principal Investigator, project 3- "Structure of selectin-ligands synthesized by human T-lymphoblasts", NIH, P01AI33189 (Oligosaccharides as Anti-inflammatory Agents; PA Ward, Program Director), 15% effort, \$90,000 (annual, direct for the sub-project); Sept 1996-Aug 2000.
- C. Co-investigator (with B. Richardson, Rheumatology Division, University of Michigan)- "Gender specific T-cell homing and autoimmunity"; NIH, R01AI42753, 15% effort, \$187,000 (annual, direct); Apr 1998-Mar 2003 (NEW).
- D. Co-investigator (with A. E. Chang, Surgical Oncology Division, University of Michigan)- "T-cell Activation for Cancer Immunotherapy"; NIH R01CA82529, \$211,282 (annual, direct); 5% effort, Jul 1999-June 2004 (NEW).
- E. Co-investigator (with G. Kansas, Department of Microbiology/Immunology, Northwestern University)- "Leukocyte Recognition of P-selectin", American Cancer Society, \$120,000 (annual, direct), 5% effort, Jul 1999-June 2001 (NEW).

PENDING APPLICATIONS:

- A. Co-investigator and coordinator for Pathology Department section- "Rational Design of Adhesion Blocking Anti-Inflammatories" (Jon O. Nagy, PI, Ligocyte Pharmaceuticals, Inc.); NIH, SBIR R43AI/GM43789, \$988,598 (annual, direct), 10% effort, Dec 99-Nov 2003 (priority score – 137).
- B. Principal Investigator, "Microcarrier Enhanced Production of Recombinant Proteins"; NIH, STTR, \$100,000 (annual, direct), 10% effort, Jan 2000-Dec 2002 (review pending).

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 Millenium). 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 Sequence II Content
- 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).

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED IN PEER REVIEWED PUBLICATIONS:

1. R.N. Knibbs, R.A. Craig, P., Mály, P.L. Smith, F.M. Wolber, N.E. Faulkner, J.B. Lowe and L.M. Stoolman. 1998. $\alpha(1,3)$ Fucosyltransferase-VII dependent synthesis of P- and E-selectin ligands on cultured T- lymphoblasts. . J. Immunol. 161: 6305.
2. Snapp,K.R., Craig,R., Herron,M., Nelson,R.D., Stoolman,L.M., Kansas,G.S. 1998. Dimerization of P-selectin glycoprotein ligand-1 (PSGL-1) required for optimal recognition of P-selectin. J. Cell Biol. 142(1): 263.
3. Wagers,A.J., Stoolman,L.M., Craig,R., Knibbs,R.N., Kansas,G.S. 1998. An sLe^x-deficient variant of HL60 cells exhibits high levels of adhesion to vascular selectins: further evidence that HECA-452 and CSLEX1 monoclonal antibody epitopes are not essential for high avidity binding to vascular selectins. J. Immunol. 160 (10): 5122.
4. Wagers,A.J., Waters,C.M., Stoolman,L.M., Kansas,G.S. 1998. Interleukin 12 and interleukin 4 control T cell adhesion to endothelial selectins through opposite effects on $\alpha 1$, 3-fucosyltransferase VII gene expression. J. Exp. Med. 188 (12): 2225.
5. Stoolman, L.M., Lougee, M., Gibbs, D., Peterson, T., Abrams, G., Phillips, K., Anastasia, D., White, C. "Case Study: The Virtual Microscope-Interactive Online Syllabii for Dental and Medical Student Pathology Laboratories". Computerworld-Smithsonian Program Laureate and Finalist, 1999. Selected as one of five finalists in the Education and Academia Category (from a field of 75, first University of Michigan submission from any Unit to be selected as a finalist), installed in the Permanent Research Collection of the Smithsonian Institution, displayed in the

Information Technology Exhibit in the Smithsonian American History Museum (1999-2000).
URL for the online collection of Case Studies: <http://198.49.220.47/tehis/si/sc/innovate/>.

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

1. K. Phillips, R. Craig, K. Tanigawa, R. Knibbs, A. Chang and **L. Stoolman**. P-selectin ligands identify tumor-reactive T1-precursors in lymph nodes. *Experimental Biology*, 1999 (Washington, DC).
2. R. Knibbs, R. Craig, G.S. Kansas, A. Wagers and **L. Stoolman**. Regulation of selectin ligand synthesis in human peripheral blood lymphocytes. *Experimental Biology*, 1999 (Washington, DC).
3. **Stoolman, L.M.** The Virtual Microscope-Interactive Hematopathology Syllabus (Hematopathology Laboratory Syllabus for Medical Students). URL=<http://141.214.6.12/virtualheme98/>.
4. **Stoolman, L.M.** The Virtual Microscope-Interactive Pathology 631 Syllabus (General and Organ Systems Pathology for Dental Students). URL= <http://141.214.6.12/cyberscope631/>

**LYNDON SU, M.D.
CLINICAL ASSISTANT PROFESSOR
DEPARTMENT OF PATHOLOGY**

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. Dermatopathology Service – (University Hospital and Transfer cases) – 12 months
- B. Dermatopathology Consultation Service (including personal, M-Labs, and Veterans Administration Hospital consultations) – 12 months

II. TEACHING ACTIVITIES:

- A. Medical Students:
 - 1. Nasim Fazel, 4th year medical student – (2 month elective rotation in dermatopathology)
- B. House Officers:
 - 1. Dermatopathology sign-out (dermatology and pathology residents and medical students)
 - 2. Review of dermatopathology consultation material
 - 3. Dermatopathology Teaching conference – (dermatology residents-weekly)
 - 4. Dermatopathology Teaching conference – (pathology residents-monthly)
 - 5. Anatomic Pathology Core Conference – (2 per year)
 - 6. Anatomic Pathology Consultation Conference – (2 per year)
- C. Diagnostic Conference, Department of Dermatology – (weekly)
- D. Hospital Conferences:
 - 1. Multidisciplinary Cutaneous Lymphoma Conference (twice monthly)
 - 2. Veterans Administration Hospital, Selected Topics in Dermatopathology (1-2 per year)

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

- A. Expression of matrix metalloproteinases in Merkel cell carcinoma (Yukari Hatori, M.D., Ph.D., and Guliz Akdas, M.D.)
- B. Utility of melan-A immunostain in melanoma sentinel lymph nodes (Araba Afenyi-Annan, M.D.)
- C. Histologic and immunophenotypic features that distinguish cutaneous graft versus host disease from drug reactions (Christine Martin, M.D.)
- D. Papular acantholytic dyskeratosis of the genitocrural region (Nasim Fazel, 4th year medical student and Hope Haefner, M.D.)

- E. Interstitial mycosis fungoides: a variant of mycosis fungoides resembling inflammatory morphea and granuloma annulare (Youn Kim, M.D., Susan Swetter, M.D., Philip LeBoit, M.D., and Sabine Kohler, M.D.)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

- A. Co-director, Dermatopathology Service

VI. PUBLICATIONS:

ARTICLES PUBLISHED, ACCEPTED OR SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Su, L., Duncan, L.: Lymphoma- and leukemia-associated atypical CD30+ reactive cutaneous T-cell infiltrates. (Submitted to Journal of Cutaneous Pathology)
2. Romero, J.B., Rasmussen, J.E., Su, L.: Multiple light yellow papules: pseudoxanthoma elasticum-like papillary dermal elastolysis. A case report. Archives of Dermatology (in press)
3. Sachs, D., Su, L., Dlugosz, A.: Annular ulcerated hip plaques: superficial granulomatous pyoderma. A case report. (Submitted to Archives of Dermatology)
4. Woo, J., Su, L., Kohler, S., Bowen, G.M.: Pseudolymphoma developing at the sites of subcutaneous vitamin K injections. A case report. (Submitted to Archives of Dermatology)
5. Bowen, G.L., Peters, N.T., Fivenson, D.P., Su, L., Nousari, H.C., Anhalt, G.J., Cooper, K.D., Stevens, S.R.: Lichenoid dermatitis in paraneoplastic pemphigus: a pathogenic trigger of epitope spreading? (Submitted to Journal of the American Academy of Dermatology).

BOOKS/CHAPTERS IN BOOKS:

1. Fazel, N., Wilczynski, S., Lowe, L., Su, L.: Clinical, histopathologic and molecular aspects of human papillomavirus infections. Dermatologic Clinics (in press).

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

- A. None

II. TEACHING ACTIVITIES:

- A. General Pathology for Dental Students and Graduate Students (Pathology 630/580)
B. Graduate student - Lai Ming Lee
C. Faculty, NIH Training Grant, Burn and Trauma Surgery

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

- A. Principal Investigator , "Role of Cytokines and Adhesion Molecules in Thermal Injury", (NIH GM-48477).
B. Principal Investigator, "Effect of Polynitroxyl Albumin (PNA) on Protein Extravasation Following Thermal Burn Trauma" (SynZyme Technologies, LLC).
C. Co-Investigator, "Liquid Ventilation in ARDS" (NIH HL-54224)
D. Co-Investigator, "Lung Injury Produced by Oxygen Metabolites", (NIH GM-29507).

PENDING SUPPORT:

- A. Co-Investigator, "Mechanisms and Prevention of Lung Injury Caused by Mustard Gas," (USAMRMC)

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. Pathophysiological 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. Member Doctoral Thesis Committee
- D. Interviewed candidates for faculty positions
- E. Consultant for clinical research programs
- F. Reviewer of intra-departmental grant proposals

REGIONAL AND NATIONAL:

None

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

- A. Member Editorial Board Immunopharmacology, 1998-present
- B. Reviewer for the following scientific journals:
 - 1. American Journal of Pathology.
 - 2. American Journal of Physiology: Gastrointestinal and Liver Physiology
 - 3. Immunopharmacology
 - 4. Journal of Applied Physiology
 - 5. Journal of Clinical Investigation.
 - 6. Journal of Leukocyte Biology.
 - 7. Shock

INVITED LECTURES/SEMINARS:

- 1. Visiting Professor at the Department of Trauma Surgery, University of Freiburg, Germany, January 20-22, 1999

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ravage, Z.B., Gomez, H.F., Czermak, B.J., Watkins, S.A., Till, G.O.: Mediators of microvascular injury in dermal burn wounds. *Inflammation*. 22:619-629, 1998
2. Colton, D.M., Till, G.O., Johnson, K.J., Gater, J.J., Hirschl, R.B. Partial liquid ventilation decreases albumin leak in the setting of acute lung injury. *J. Crit. Care*. 13:136-139, 1998
3. Colton, D.M., Till, G.O., Johnson, K.J., Dean, S.B., Bartlett, R.H., Hirschl, R.B. Neutrophil accumulation is reduced during partial liquid ventilation. *Crit. Care Med*. 26:1716-1724, 1998
4. 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 air space injury following acute blood loss. *Acad. Emerg. Med.*. 5:659-665, 1998
5. Ward, P.A., Mulligan, M.S., Friedl, H.P., Huber-Lang, M., Till, G.O., Hugli, T., Czermak, B. The numerous proinflammatory functions of C5a. *Molec. Immunol*. 35:324-327, 1998
6. Mulligan, M.S., Warner, R.L., Rittershaus, C.W., Thomas, L.J., Ryan, U.S., Foreman, K.E., Crouch, L.D., Till, G.O., Ward, P.A. Endothelial targeting and enhanced antiinflammatory effects of complement inhibitors possessing sialyl Lewis^x moieties. (in press)
7. Piccolo, M.T.S., Wang, Y., Verbrugge, S., Warner, R.L., Sannomiya, P., Piccolo, N.S., Piccolo, M.S., Hugli, T.E., Ward, P.A., Till, G.O. Role of chemotactic factors in neutrophil activation after thermal injury in rats. *Inflammation* (in press)
8. Seekamp, A., Hultquist, D.E., Till, G.O. Protection by vitamin B₂ against oxidant-mediated acute lung injury. *Inflammation* (in press)
9. Piccolo, M.T.S., Wang, Y., Sannomiya, P., Piccolo, N.S., Piccolo, M.S., Hugli, T.E., Ward, P.A., Till, G.O. Chemotactic mediator requirements in lung injury following skin burns in rats. *Exp. Molec. Pathol.* (in press)
10. Schlag, G., Redl, H., Till, G.O., Davies, J. Anti-L-selectin antibodies treatment of traumatic shock in baboons. *Crit. Care Med.* (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. Younger, J., Saleh, E., Sasaki, N., Ravage, Z. Ward, P.A. Till, G.O. Complement activation in hemorrhagic shock. *Shock(Suppl.)* 11:A79, 1999

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

- A. Post-doctoral fellows (1998-99):
1. Boris Czermak, M.D.
 2. Kathleen Diehl, M.D.
 3. Ren-Fang Guo, M.D.
 4. Rosemary Hernandez, M.D.
 5. Markus Huber-Lang, M.D.
 6. Jacqueline Jordan, Ph.D.
 7. J. Eric McDuffie, Ph.D.
- B. UROP Undergraduate Students:
1. Hillary Cohen, Senior.
 2. Karen Rosner, Sophomore.
 3. Richard Carter, Freshman.
 4. Morgan Althoen, Medical Student.
- C. Supervision of two Research Scientists (Drs. Younger and Vincenz)
- D. Gross Autopsy Conference, 25 hours
- E. Clinical Pathology Grand rounds Lecture, Reflections on the Pathology Board Examination
- F. 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), 07/01/98 -03/01/04.

- D. Principal, Investigator, "Oligosaccharides as Inflammatory Agents", PO1-AI-33189 (10%), \$93,443/year (Proj. II) \$26,853/year (Core A), 09/01/98-08/31/00.

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.
Technology Transfer Committee
- C. Dean's Advisory Council.
- D. Geriatric Center Executive Committee.
- E. Howard Hughes Medical Institute Dean's Advisory Committee.
- F. Internal Medicine Advisory Committee for the University of Michigan George M. O'Brien Renal and Urologic Center.
- G. Michigan Eye Bank Research Review Committee.
- H. Undergraduate Research Opportunity Program, University of Michigan.
- I. 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 Society for Clinical Investigation.
- C. Association of American Physicians.
- D. American Thoracic Society.
- E. Association of Pathology Chairmen
- F. A. James French Society of Pathologists, 1988-present.
- G. Health Policy Agenda for the American People, Advisory Committee.
- H. Institute of Medicine, National Academy of Sciences, July, 1990-present.
- I. Michigan Society of Pathologists.
- J. Michigan Thoracic Society, 1988-present.
- K. National Research Council.
 - 1. Chair, Institute of Laboratory Animal Research.

- L. 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, 1977-1998.
- 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:

- A. Fellow, American Association for the Advancement of Science, Anaheim, California, January 23, 1999
- B. American Board of Pathology, Life Trustee (Chicago, Illinois; May 23, 1999)

INVITED LECTURES/SEMINARS:

1. Invited Speaker, "Macrophage Activation and Inflammation", NIAAA/Alcohol and Inflammation Workshop, NIH, Bethesda, Maryland, August 24, 1998.
2. Invited Lecturer, "Destruction by Phagocytic Cells", 1998 IFCC/Beckman European Conference, University of Regensburg, Regensburg, Germany, September 17, 1998.
3. Invited Lecturer, "How the Inflammatory Response is Regulated", Heart-Lung Institute Seminar, Ohio State University, Columbus, Ohio, October 7, 1998.
4. Invited Lecturer, "How the Inflammatory Response is Regulated", 8th Annual Robert E. Stowell Lecture, American Registry of Pathology, Armed Forces Institute of Pathology, Washington, DC, October 8, 1998.
5. Invited Lecturer, "The Numerous Proinflammatory Functions of C5a", XVIIth International Complement Workshop, Rodos Palace Congress Center, Rhodes, Greece, October 16, 1998.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. 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, 1998;153(4):1113-1122.

2. 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*, 1998;47(7):308-315.
3. Lentsch, A.B. and **Ward, P.A.**: NF- κ B activation and lung inflammatory injury. *Curr Trends Immunol*, 1998;1:199-207.
4. 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*, 1998;22(6):583-598.
5. 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- κ B. *Am J Respir Cell Mol Biol*, 1999;20(4):692-698.
6. **Ward, P.A.** and Lentsch, A.B.: The acute inflammatory response and its regulation. *Arch Surg*, 1999;134:666-669.
7. Murphy, H.S., Bakopoulos, N., Dame, M.K., Varani, J., and **Ward, P.A.**: Heterogeneity of vascular endothelial cells: Differences in susceptibility to neutrophil-mediated injury. *Microvascular Res*, 1998, 56:203-211.
8. Lentsch, A.B., Jordan, J.A., Czermak, B.J., Diehl, K.M., Younkin, E.M., Sarma, V., and **Ward, P.A.**: Inhibition of NF κ B activation and augmentation of I κ B β by secretory leukocyte protease inhibitor during lung inflammation. *Am J Pathol*, 1999, 154:239-247.
9. Lentsch, A.B., Czermak, B.J., Jordan, J.A., and **Ward, P.A.**: Regulation of acute lung inflammatory injury by endogenous interleukin-13. *J Immuno* 1999, 162:1071-1076.
10. Bless, N. M., Warner, R.L., Padgaonkar, V., Lentsch, A.B., Czermak, B.J., Schmal, H., Friedl, H. P., and **Ward, P.A.**: Roles for CXC chemokines and C5a in lung injury following hind limb ischemia/reperfusion. *Am J Physiol, (Lung Cell. Mol. Physiol.)* 1999, 276(1pt1):L57-63.
11. Czermak, B.J., Sarma, V., Bless, N.M., Schmal, H., Friedl, H.P., and **Ward, P.A.**: In vitro and in vivo dependency of chemokine generation on C5a and TNF α . *J Immuno* 1999, 162(4):2321-2325.
12. Czermak, B.J., Breckwoldt, M., Ravage, Z.B., Huber-Lang, M., Schmal, H., Bless, N.M., Friedl, H.P., and **Ward, P.A.**: Mechanisms of enhanced lung injury during sepsis. *Am J. Pathol* 1999, 154: 1057-1065.
13. Mulligan, M.S., Warner, R.L., Rittershaus, C.W., Thomas, L.J., Ryan, U.S., Foreman, K.E., Crouch, L.D., Till, G.O. and **Ward, P.A.**: Endothelial targeting and enhanced anti-inflammatory effects of complement inhibitors possessing sialyl Lewis^x moieties. *J Immuno*, 1999, 162:4952-4959.
14. Mulligan, M.S., Warner, R.L., Bolling, S.F., and **Ward, P.A.**: Regulatory roles of chemokines in delayed cardiac xenograft rejection. *J Heart and Lung Transplantation*, 1999, 18(1):59.
15. Gipson, T.S., Bless, N.M., Shanley, T.P., Crouch, L.D., Bleavins, M.R., Younkin, E.M., Sarma, V., Gibbs, D.F., Wongelawit, T., McConnell, P.C., Mueller, W.T., Johnson, K.J., and **Ward, P.A.**: Regulatory effects of endogenous protease inhibitors in acute lung inflammatory injury. *J Immuno*, 1999, 162:3653-3662.
16. Czermak, B.J., Lentsch, A.B., Bless, N.M., Schmal, H., Friedl, H.P., and **Ward, P.A.**: Synergistic enhancement of chemokine generation and lung injury by C5a or the membrane attack complex of complement. *Am J Pathol.*, 1999, 154:1513-1524.
17. **Ward, P.A.**, and Lentsch, A.B.: The acute inflammatory response and its regulation. *Arch Surg* 1999;134(6):666-669.

18. Guo, R.F., **Ward, P.A.**, Hu, S.M., McDuffie, J.E., Huber-Lang, M., and Shi, M.M.: Molecular cloning and characterization of a novel human CC chemokine, SCYA26. *Genomics* 1999;58(3):313-317.
19. Lentsch, A.B., and **Ward, P.A.**: Activation and regulation of NF κ B during acute inflammation. *Clin. Chem. Lab Med* 1999;37(3):205-208.
20. Glovsky, M.M., Lukacs, N., and **Ward, P.A.**: Is complement activation a factor in bronchial asthma? *Int Arch Allergy Immunol* 1999;118(2-4)330-332.
21. Lentsch, A.B., Crouch, L.D., Jordan, J.A., Czermak, B.J., Yun, E.C., Guo R., Sarma, V., Diehl, K.M., and **Ward, P.A.**: Regulatory effects of interleukin-11 during acute lung inflammatory injury. *J Leukoc Biol* 1999;66(1)151-157.
22. Czermak, B.J., Sarma, V., Pierson, C.L., Warner, R.L., Huber-Lang, M., Bless, N.M., Schmal, H., Friedl, H.P., and **Ward, P.A.**: Protective effects of C5a blockade in sepsis. *Nature Med* 1999;5(7):788-792.
23. Lentsch, A.B., Yoshidome, H., Warner, R.L., **Ward, P.A.**, and Edwards, M.J.: Secretory leukocyte protease inhibitor regulates local and remote organ inflammatory injury induced by hepatic ischemia/reperfusion. Accepted in *Gastroenterology*, 1999.

BOOKS/CHAPTERS IN BOOKS:

None

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

1. Shanley, T.P., Warner, R.L., Crouch, L., Dietsch, G.N., Gallatin, W.M., and **Ward, P.A.**: Identification and functional role of a novel integrin, α D in an *in vivo* model of pulmonary inflammation. *Critical Care Med*, 26(1S):75A, 1998.
2. Glovsky, M.M., Lukacs, N., and **Ward, P.A.**: Complement activation – a pathway to bronchial hyperreactivity in the mouse. *Experimental Biology* 259.22:A337, 1999.
3. Lentsch, A.B., Yoshidome, H., **Ward, P.A.**, and Edwards, M.J.: Secretory leukocyte protease inhibitor (SLPI) regulates hepatic ischemia/reperfusion injury. *Experimental Biology* 412.13:A507, 1999.
4. Huber-Lang, M., Czermak, B.J., Friedl, H.P. and **Ward, P.A.**: Blockade of C5a protects from enhanced lung injury in experimental sepsis. *Experimental Biology* 634.1:A817, 1999.
5. Jordan, J.A., Yun, E.C., Sarma, V.J., Czermak, B.J., Huber-Lang, M.S., McDuffie, J.E., and **Ward, P.A.**: Pro-inflammatory effects of interleukin-18 in acute lung injury. *Experimental Biology* 634.4:A818, 1999.
6. Guo, R.F., Hu, S.M., McDuffie, J.E., Sarma, V., **Ward, P.A.**, and Shi, M.M.: Molecular cloning and functional characterization of a novel human CC chemokine. *Experimental Biology* 643.27:A844, 1999.
7. Guo, R.F., Jordan, J.A., Czermak, B.J., Huber-Lang, M., **Ward, P.A.**, and Shi, M.M.: Eotaxin expression in Sephadex-induced pulmonary inflammation. *Experimental Biology* 643.30:A845, 1999.
8. Diehl, J.M., Warner, R.L., and **Ward, P.A.**: Adhesion molecule blockade decreases inflammatory mediator production from macrophages. *Experimental Biology* 750.1:A1017, 1999.

9. Jordan, J.A., Yun, E.C., Sarma, V.J., Czermak, B.J., Warner, R.L. and **Ward, P.A.**: The role of interleukin-17 in LPS-induced inflammatory lung injury. *Experimental Biology* 750.4:A1017, 1999.
10. Lentsch, A.B. and **Ward, P.A.**: Regulatory functions of secretory leukocyte protease inhibitor. *Recent Research Developments in Immunology, Research Signpost*, 1999. In Press.
11. Czermak, B.J., Friedl, H.P., and **Ward, P.A.**: Role and regulation of chemokines in rodent models of lung inflammation. Accepted in *ILAR Journal*, 1999.

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

**ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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 peripheral blood parasite 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; (40 contact hours).
- B. Clinical Pathology Grand Rounds:
 - 1. "Cases and images in immunopathology" (12/18/98).
 - 2. "Serology of autoimmune liver disease" (1/8/99).
 - 3. "ANA testing and interpretation" (01/15/99).
- C. Immunopathology signout: pathology residents, M-4 medical students, EMU medical technology students (three times/week; 26 weeks/year).
- D. Immunopathology component of Block B (Clinical Pathology); ad hoc topical reviews: pathology residents (28 contact hours).
- F. M-1 Histopathology sequence; 1st year medical students; (15 contact hours).
- G. M-1 Host Defense sequence; "Immunologic testing and diagnosis" (4/26/99); (1 contact hour).
- H. Supervision of Research activities for:
 - 1. Karen Powers (Undergraduate, 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); (8/15/96-10/31/98).
 - 5. 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).
 - 6. Nicole Chisolm (Student, Huron High School, Ann Arbor, MI, Youth Mentoring Program) (sponsored by University of Michigan Medical School) (8/1/98-10/30/98).
- I. Ph.D. Thesis Committees:
 - 1. Jennifer Bowen, Department of Physiology and the Reproductive Biology Program, University of Michigan Medical School (2/5/97-4/10/99).

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 and smooth muscle cell functions by the membrane attack complex (MAC) of complement, reactive oxygen intermediates, and reactive nitrogen intermediates.
- 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. 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. Member-elect, Executive Committee, University of Michigan Medical School, 1999-present.
- B. Finance Subcommittee, advisory to Faculty Group Practice (FGP) Executive Committee, 1997-present.
- C. Member, Task Force on Faculty Administrative Services, advisory to FGP Executive Committee and Chief Executive Officer, University of Michigan Health System, 1998-present.
- D. Dean's Advisory Committee (ad hoc substitute for Dr. Peter Ward), 1994-present.
- E. Clinical Council (ad hoc substitute for Dr. Peter 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, Department of Pathology Quality Assurance Committee, 1993-present.
- E. Clinical Associate and Advisory Committee for Medical Technology Program, Eastern Michigan University, 1993-present.
- F. 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, 1990-1998.
- C. Member, Test Committee for Clinical Pathology, American Board of Pathology, 1999-present.
- D. Vice-Chair, Area Committee on Clinical Immunology and Ligand Assays, National Committee for Clinical Laboratory Standards, 1999-present.

- E. Member, Council for Diagnostic Immunology and Molecular Pathology, American Society of Clinical Pathologists, 1998-present.
- F. Team Leader, College of American Pathologists Inspection, University of Alabama Hospitals, Birmingham, AL, Feb. 17-18, 1999.

V. **INVITED LECTURES/SEMINARS:**

- 1. Warren JS: Diagnostic immunology and molecular pathology update. New (or not fully appreciated) assays in the immunology laboratory. ASCP National Meeting, Washington, D.C., October 19, 1998.
- 2. Warren JS: Induction of chemokine expression by the distal complement components C8 and C9 requires GPI-linked surface molecules. Experimental Biology, Washington, D.C., April 19, 1999.

VI. **PUBLICATIONS:**

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

- 1. Kilgore KS, Imlay MM, Malani A, Allen DI, Beyer JT, Anderson MB, Warren JS: The carbohydrate sialyl Lewis^X glycomimetic GM2941 attenuates glucan-induced pulmonary granulomatous vasculitis in the rat. *J Pharmacol and Exper Therapeutics* 286:439-446, 1998.
- 2. Szaflarski J, Ivacko J, Liu XH, Warren JS, Silverstein FS: Excitotoxic injury induces monocyte chemoattractant protein-1 expression in neonatal rat brain. *Molec Brain Res* 55:306-314, 1998.
- 3. Schimmer RC, Schrier DJ, Flory CM, Laemont KD, Tung D, Metz AL, Friedl HP, Conroy MC, Warren JS, Beck B, Ward PA: Streptococcal cell wall-induced arthritis: requirements for IL-4, IL-10, IFN- γ , and MCP-1. *J Immunol* 160:1466-1471, 1998.
- 4. 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* 22:583-598, 1998.
- 5. Gomez HF, Miller MJ, Desai A, Warren JS: *Loxosceles* spider venom induces the production of α and β chemokines; Implications for the pathogenesis of dermonecrotic arachnidism. *Inflammation* 23:207-215, 1999.
- 6. 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* 60:740-746, 1999.
- 7. Desai A, Miller MJ, Gomez HF, Warren JS: *Loxosceles deserta* spider venom induces NF- κ B-dependent chemokine production by endothelial cells. *J Toxicol Clin Toxicol* (in press).
- 8. Desai A, Huang X, Warren JS: Intracellular glutathione redox status modulate MCP-1 expression in pulmonary granulomatous vasculitis. *Lab Invest* (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. 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).
3. Galasso JM, Miller MJ, Harrison JK, Warren JS, Silverstein FS: Monocyte chemoattractant protein-1 is a mediator of NMDA-induced neurotoxicity in neonatal rat brain. *J Neuroscience* (submitted).
4. Townson DH, Bowen JM, Remick DG, Warren JS, Keyes PL: The effect of dexamethasone on prolactin-induced luteolysis and macrophage infiltration in corpora lutea of the rat. *Biol Reproduction* (submitted).
5. Miller MJ, Desai A, Warren JS: Nitric oxide suppresses cytokine-induced MCP-1 expression in endothelial cells. *J Immunol* (submitted).
6. Gomez HF, Miller MJ, Trachy JW, Marks RM, Warren JS: Intradermal anti-Loxosceles Fab fragments attenuate dermonecrotic arachnidism. *Acad Emerg Med* (submitted).
7. Desai A, Lankford HA, Warren JS: Loxosceles deserta spider venom induces the expression of vascular endothelial growth factor (VEGF) in keratinocytes. *Inflammation* (submitted).
8. Whetstone WD, Gomez HF, Ernsting KS, Miller MJ, Marks RM, Warren JS: Inhibition of dermonecrotic arachnidism with interleukin-8 monoclonal antibody. *Acad Emerg Med* (submitted).

BOOKS/CHAPTERS IN BOOKS:

1. Warren JS, Ward PA: The inflammatory response, in Beutler E, Lichtman MA, Collier BS, Kipps TJ and Seligsohn U (eds.) *Williams' Hematology*, 6th Edition, McGraw-Hill, New York, NY, (in press).
2. Warren JS: Leukocyte functional assays by flow cytometry, in Keren DF, McCoy JP, Carey JL, and Hanson CA (eds.) *Flow Cytometry and Clinical Diagnostics*, 3rd Edition, ASCP Press, Chicago, IL, (in press).
3. Warren JS: Immunodeficiency disease, in McClatchey KD (ed.) *Clinical Laboratory Medicine*, 2nd Edition, Lippincott Williams and Wilkins, Philadelphia, PA, (in press).

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

1. Powers KL, Kilgore KS, Anderson MB and Warren JS. Structural analysis of glycomimetic inhibitors of P-selectin-mediated neutrophil adhesion. *International Society for Heart Research*, Ann Arbor, MI, August 9-12, 1998. *J Molec Cell Card* A233, 1998.
2. Bavikatty NR, Warren JS. Frequency and significance of antinuclear antibody-negative, anti-extractable nuclear antigen-positive serologic test results in a referral-based population. *Am J Clin Pathol* 110(4): 544, 1998 (abstract).
3. Warren JS. Sublytic concentrations of the membrane attack complex of complement induce endothelial chemokine expression through nuclear factor- κ B activation. *Symposium on Complement in Human Disease*, New Delhi, India, October 29-31, 1998.
4. Silverstein FS, Galasso JM, Harrison JK, Miller MJ, and Warren JS. Acute excitotoxic injury induces expression of the monocyte chemoattractant protein-1 (MCP-1) receptor, CCR2 in neonatal rat brain. *Society for Neuroscience*, Los Angeles, CA, (abstracts), (in press), 1998.

5. Warren JS, Miller MJ. Induction of chemokine expression by the distal complement components C8 and C9 requires GPI-linked surface molecules. American Society of Investigative Pathology, Washington, D.C., April 18-21, 1999.
6. Miller M, Desai A, Huang C, Warren JS. Nitric oxide (NO) suppresses cytokine-induced monocyte chemoattractant protein-1 (MCP-1) expression in endothelial cells: Implications for the pathogenesis of granulomatous vasculitis. American Society of Investigative Pathology, Washington, D.C., April 18-21, 1999.

SECTION REPORTS

ANATOMIC PATHOLOGY

DIVISION OF ANATOMIC PATHOLOGY

ANNUAL REPORT

1 JULY 1998 - 30 JUNE 1999

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 Health System, Medical School, and University. This past year can best be characterized as exciting with seven new faculty joining the division; Dr. Alaa Affify (Barnes Hospital, St. Louis, Missouri) and Dr. Basim Al-Khafaji (M.D. Anderson Hospital, Houston, Texas), Dr. Kathleen Cho (Johns Hopkins Hospitals, Baltimore, Maryland) Dr. Augusto Paulino (Memorial Sloan Kettering Cancer Center, N.Y., N.Y.), Dr. Mark Rubin (Columbia University, N.Y., N.Y.), Dr. Stephen Ramsburgh (Univ. of Michigan) and Dr. Lyndon Su (Stanford University, Palo Alto, Calif.). In addition Dr. Celina Kleer (University of Michigan) is joining the department beginning July 1, 1999. 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.

Faculty research programs and extramural support continues to increase especially in programmatic areas associated with the Cancer Center, GI pathology and SPORE in Urologic Disease. There continues to be expansion of core research facilities directed by faculty in the division including; tissue microarrays, laser capture microdissection, histology/immunoperoxidase/FISH, and tissue procurement. Several faculty have expanded collaborations with biomedical research companies including Genetech (Calif.) and Parke-Davis (Mich.).

Three senior residents completed surgical pathology fellowships. Four additional house officers completed fellowship training in informatics, cytopathology, urologic pathology, and hematopathology. All found excellent positions in sub-specialty (2) and research (2) fellowships, private practice (1), and academic faculty positions (2).

Overall, the in-house clinical activity in surgical pathology and cytopathology increased by approximately 6% and 8%, respectively. The dermatopathology service realized a 12% increase in cases. While the Medical Center Cost Efficiency Program (CEP) resulted in consolidation of laboratory functions and enhanced productivity in several areas over the past several years, any significant additional reductions in laboratory support in the context of increasing service volumes will negatively impact our ability to provide high quality service. Limitations in laboratory and faculty office space also hinder our ability to maximize productivity and accommodate the increased volumes and requests for expanded diagnostic services. However, re-design with expansion of the frozen section area is underway and will allow the department to support increased activity of the surgery service. New renovations to the autopsy suite were completed and have enhanced productivity, service to families, and increased safety. 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 maintaining the high quality of our Anatomic Pathology laboratory services.

With continued expansion of clinical services and academic programs as well as future faculty retirements, it will be necessary in the next three years to recruit additional faculty especially in areas of dermatopathology, pediatrics pathology, general surgical pathology and cytopathology. These are clearly exciting times of opportunity for the division, department and medical school and we are well positioned to continue as one of the pre-eminent academic divisions and departments in the country.

AUTOPSY SERVICE

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1998 - 30 JUNE 1999

I. Timely Completion of Autopsy Reports:

We have made substantial progress in proving the timely completion of our autopsies. All cases were completed in 90 days and virtually all were finished within 60 days for the 1998-99 year. While this is a significant improvement, we need to ensure that all of our work is completed and available to our clinical colleagues within 60 days.

Time Interval	% completed in 60 days	% completed in 90 days	# of Autopsies
1995-96	40	58	541
1996- 97	64	89	565
1997- 98	64	85	424
1998-June 1, 1999	96	100	378

II. **Labeling of blocks**

In response to a citation by the College of American Pathologists, we have begun to identify by block all tissue submitted for microscopic examination. We previously had not done this since the guidelines called for labeling of blocks only when appropriate. Labeling of blocks will make retrieval of tissue easier when blocks are requested by outside agencies.

III. **Autopsy percentage**

We have begun to determine the autopsy rate by clinical service in the hospital. This is prepared every month by Paulette Dozier's staff. This information is provided to the departmental chairs on a regular basis. The autopsy percentage is for the 1998-99 year is listed below.

Medicine	27%
Surgery	25%
Pediatrics	41%
Other services	37%

IV. **Conferences**

The autopsy service has begun to actively participate in the weekly surgery death and complications conference. We provide important the feedback to the surgery department concerning our findings at autopsy. This helps to reinforce the importance of our work and gives the first year residents experience at making short presentations.

V. **Medical Examiner Cases**

The Department of Pathology continues to have a presence in Medical Examiner issues in the State of Michigan and Washtenaw County. Locally, the hospital has provided medical examiner investigators for the University Hospital who are available on a 24 hour basis. Several house

officers participate in this activity. On a state-wide basis, the Director of the Autopsy Service has been elected Chair of the Michigan Association of Medical Examiners. Drs. Remick and Hunter has worked to help develop a state-wide course to train lay investigators. This course has been offered in several different counties in the state of Michigan and funding has been secured to upgrade the training. Additionally, the Director has served as for the development of a database of medical examiner cases for the entire state.

VI. Statistics:

This covers the time period July 1, 1997 to June 30, 1998.

Total number of autopsies performed	378
Total hospital autopsies	247
Total number of medical examiner cases	75

Daniel G. Remick, M.D.

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL REPORT 1 JULY 1998 – 30 JUNE 1999

This year has been very eventful to the laboratory with the addition of Dr. Alaa Afify and Dr. Basim Al-Khafaji as the two new Cytopathology faculty. In addition, Mr. Brian Smola and Mrs. Binita Naylor joined our laboratory as the two new cytotechnologists.

Total gynecologic specimens for the year were 42,473, representing a 11.7% increase over the previous year. Non-gynecologic specimens numbered 5,581; a 1.9% decrease from last year. Fine needle aspirations performed by cytopathologists (an indicator of fine needle aspiration clinic usage in the cancer center) totaled 282 for the current year, a 16% increase over the previous fiscal year. In addition, the number of deep-seated fine needle aspirates performed in the Radiology Department or the endoscopy directed totaled 328 this year, representing a 12.3% increase over last year. With the additional personnel and the stability of the Department, the laboratory achieved the turnaround time for non-gynecologic specimens within 24 to 28 hours and the Papanicolaou smears within 5 to 7 working days, despite the increase in number of accessioned specimens.

Mr. James Pecott was appointed President, Miss Jenise Gyurnek, Vice President, and Mr. Brian Smola, Membership Chairman for the Michigan Society of Cytology. Our Department also hosted the annual meeting for the Michigan Society of Cytology in June of 1999 at the University of Michigan.

Our fellowship program continued to be highly successful, Dr. Jim McConnell completed his training with distinction. Several changes in the fellowship structure and schedule were addressed this year in order to streamline the fellow's experience in cytopathology in light of the increased number of specimens and fine needle aspirations.

The Department continued its active role in assessing the new cytologic mono-layer techniques (ThinPrep and AutoCyte). Dr. Michael in collaboration with Jim Pecott and the remaining Cytology faculty presented their preliminary findings in comparison of the two techniques in non-gynecologic specimens at the USCAP meeting.

The Cytopathology Section had excellent representation at national and international meetings. At this year's national meetings, our faculty presented five abstracts and three platforms. Dr. Michael also directed a workshop at the ASCP meeting (with the assistance of Miss Jenise Gyurnek) and co-directed a short course at the IAP meeting. Dr. Michael also presented a national teleconference sponsored by the American Society of Cytology. Dr. Naylor directed a workshop at the ASC. Mr. Smola had a case study published in the MSC newsletter.

Mr. James Pecott continued his involvement with the V500 Program. At this stage we are testing the working module and addressing problems.

The Section of Cytology successfully passed the CAP inspection. We are currently involved in the Q-Track Program (quality control) through the M-Labs.

Claire W. Michael, M.D.
Director, Cytopathology Laboratory

DERMATOPATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 – 30 JUNE 1999

The Dermatopathology Service receives diagnostic case material from six different sources: (1) UMMC (ID) cases; (2) outside contractual (MD) cases; (3) personal consultation 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).

The clinical service volume is as follows:

	1996-1997	1997-1998	1998-1999
ID	4,491	5,225	5,865
MD	3,832	4,138	4,401
TD	815	919	1,228
Consultation service (LO, SU, HE)	681	473	595

The Dermatopathology Service has continued to expand with an ever-increasing workload. Dermatopathology cases represented 35% of total surgical pathology accessions, and represented 50% of all M-Labs accessions. Overall, there has been a 12% increase in ID cases, a 6% increase in MD cases, a 26% increase in consult cases and a 33% increase in TD cases. This growth in TD and consult cases represents a substantial volume of difficult pigmented lesions. The total number of cases for 1998-1999 was 12,089, a 12% increase, and was seen by 1.6 FTE.

Dermatopathology teaching in the Department of Dermatology remains an integral part of residency education. Teaching includes 1-1/2 hour formal didactic sessions weekly, as well as informal teaching at the microscope during signout.

Correlative activities include active participation in the University of Michigan Multidisciplinary Melanoma Clinic Tumor Board (bi-weekly), the busiest service in the Cancer Center, as well as Cutaneous Lymphoma Conference (bi-weekly) and Diagnostic Conference in the Department of Dermatology (weekly).

Lori Lowe, M.D.
 Director
 Dermatopathology Service

NEUROPATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999

Dr. Mila Blaivas, Ms. Constance J. D'Amato, and Dr. Paul E. McKeever contributed to the Neuropathology Service.

I. CLINICAL ACTIVITIES:

1. There were over 800 neurosurgical cases examined this year. There were over 100 personal consult cases.
2. The Diagnostic Unit of the Neuropathology Core Laboratory of the MADRC processed 46 dementia brain cases. Of these 46 brains, 31 were MADRC hospital cases, 9 were neurology hospital patients, and 6 were from the Michigan Dementia Network Program.
3. There were 307 muscle biopsies, 38 with electron microscopy. There were 77 peripheral nerve biopsies. There were 7 teased fiber preparations and 71 with electron microscopy.
4. There were over 300 University Hospital brains examined.
5. 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.
6. There are two neuropathology quality assurance meetings scheduled each month, and attended as necessary.

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 CME accredited conferences where Neurology, monthly CME accredited Rheumatology Pathology Grand Rounds and occasional CPC conferences, twice monthly Continuing Medical Education (CME) accredited conferences where 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 858, an 8-hour laboratory course; bimonthly conferences with Neuroradiology, Neurosurgery and Neuroradiology House Staff and every third month a microscopic conference for dementia brain cases. Weekly seminars are provided to neurological and neurosurgical house staff on clinico-pathological correlations.
4. Electives: Pathology, Neurosurgery, Neurology Residents and a UROP student chose elective rotations in the Neuropathology Section.

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. Blaiwas is working on the histology of animal models of rheumatoid arthritis with the 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); 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. Skeletal muscle in hypertensive diabetics with the hypertension group of Internal Medicine.
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 predictive value of markers 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, the latter as study pathologist for the Children's Cancer Group.
4. 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
(CLINICAL IMMUNOHISTOCHEMISTRY, IMMUNOFLUORESCENCE AND NEURAL AND
MUSCULAR STUDIES)**

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 -- 30 JUNE 1999**

INTRODUCTION

Dr. Alaa Afify is the new Director of Clinical Immunohistochemistry for Anatomic Pathology (beginning January 1, 1999), and Dr. Singleton continues as Director of Clinical Immunohistochemistry for Hematopathology. During the past year 19 new antibodies and new protocols have been added to the current menu for immunohistochemistry. There has been a 276% increase in Clinical Immunohistochemistry since last year. New high intensity detection kits have been introduced to our lab which improve the quality and turn around time of certain antibodies.

The FDA has issued guidelines for regulating many antibody stains as Analyte Specific Reagents (ASR). The new classification recognizes that it is the responsibility of the individual laboratories to validate the protocols and clinical utility of antibody stains.

Under the direction of Dr. Paul Killen, the Ventana automated immunostainer is now performing immunofluorescence on frozen tissues, replacing the prior manual method. This has helped with the increased case load for skin, heart and renal biopsies

Under the direction of Dr. Blaivas, the volume of cases for neural and muscular studies has also been increasing.

CLINICAL IMMUNOHISTOCHEMISTRY

The year end figures show 28,920 total slides stained including 19,416 patient slides and negative controls and 9504 positive control slides. The figures for last year were 10,368 total slides stained including 8016 patient slides and negative controls and 2352 positive control slides. This represents a 276% increase over last year. The laboratory performed on average 108 immunohistochemical stains per day which includes 72 antibody stains on patient tissues and negative controls on patient tissues and 36 positive controls tissues. The highest volume to date was 202 slides in one day (equivalent to 6 Ventana runs). The current number of 4 FTE's in the lab is working at full capacity to keep up with the ever increasing work load in Clinical Immunoperoxidase as well as the other 2 areas of the lab. 1999 has shown a substantial increase in specimens in all 3 work areas.

Over the last year, the laboratory has added 19 antibodies to the routine menu. These include CD23, Fascin, CD5, CD10, Her2/neu, MIB1, CD1a, CD56, CD44, ALK Protein, Cytokeratin 7, Cytokeratin 20, Inhibin, p53, EBV-LMP, AE1, AE3, p27, SV40, Bclx, Bax, E-Cadherin, Cyclin D1, and Melan A.

As always, other new antibodies are in developmental stages and currently available antibodies are being optimized for best results.

There have been two major improvements that have increased the quality and turn around time of the immunohistochemical stains over the last year. The current turn around time for an unstained slide is now 6-8 hours from time of receipt.

- (1) Ventana has introduced a high intensity detection kit that can be used on the automated stainer. This kit has much better sensitivity for the colorimetric reporting of bound antibody. Several antibodies including BCL-2, BERH2, CD23, CD5, CD10, Cyclin D1, CD56, and NSE now use this technique. This has enabled the lab to decrease the incubation time and subsequently, turn around time of some of these antibodies.
- (2) Microwave pretreatment in Tris-EDTA buffer has improved the quality of stains for several antibodies. The traditional microwave pretreatment has been in citrate buffer. Tris has enabled us to expand our menu for some difficult antibodies.

The laboratory is currently using DAKO's FDA-approved test for analysis of HER-2/neu. Although the test is currently performed manually, DAKO has offered to give the laboratory a DAKO stainer to automate the test if bench space can be made available.

The highly complex nature of Clinical Immunoperoxidase necessitates our participation in biannual CAP Proficiency testing. Our lab continues to perform well on all of the required stains. It remains an important task to keep up with new methodology and new antibodies for patient care as well as to remain proficient for the CAP testing.

Similarly we have passed the 1999 CAP inspection with no deficiencies. The visiting inspectors were very impressed with our Access database for antibody information.

ANALYTE SPECIFIC REAGENTS (ASR)

Almost all antibodies utilized in clinical immunohistochemistry have package inserts stating that these antibodies are for research only, even though it would be medicolegal malpractice not to use them for clinical purposes. In recognition of this dilemma, the FDA created a new classification (ASR) that formally makes it the responsibility of the individual laboratories to validate the protocols and clinical utility of antibody stains. The manufacturers are to re-label their reagents as ASR's, and if an ASR is used in a test, the FDA requires a precisely worded disclaimer.

This disclaimer has been implemented, currently, at the University of Michigan as comment "FDA2" by the transcriptionists, to distinguish it from "FDA1" which is utilized by the Molecular Diagnostics laboratory. This disclaimer will be needed for almost all of the tests offered by the immunohistochemistry laboratory. Some kits (such as for immunofluorescence) might be labeled as In Vitro Diagnostic (IVD) and not need a disclaimer, and other kits (such as HER-2/neu) will be FDA-approved and not need a disclaimer.

IN SITU HYBRIDIZATION

There is a clinical need for in situ hybridization for several analyses on paraffin-embedded tissues. The laboratory is considering automated instrumentation for in situ hybridization. Ventana has an instrument that is scheduled to become available in the fall of 1999. Ventana's prior automated instrument for in situ hybridization was thought to be unreliable, according to several initial testers but the new model has been extensively redesigned. We will also look at a manual method from Fisher

called the Microprobe Manual Staining System. This will enable us to compare cost and reliability of the two methods.

IMMUNOFLUORESCENCE

Under Dr. Paul Killen's direction, immunofluorescence for cutaneous and renal biopsies is now being performed on the Ventana automated immunostainer, replacing the prior manual method. This has improved the efficiency of the laboratory. Utilization of the Ventana instrument for 2 distinct tests is cost effective however as the patient load for each test continues to rise we will have to address acquisition of another instrument and space to put it in. There were 335 renal cases for the period 6/97-5/98 and 405 cases for 6/98-5/99 (17% increase). Similarly, there were 125 skin and heart cases for the period 6/97-5/98 and this increased to 162 cases for 5/98-6/99 (23% increase). More details about immunofluorescence on renal biopsies can be found under the renal report.

NEURAL AND MUSCULAR STUDIES

Under Dr. Blaiwas' direction the volume of stains in this laboratory has been continuing to increase. The muscle biopsy load for 6/97-5/98 was 237 and the nerve biopsy load for the same period was 66. The muscle biopsy load for 6/98-5/99 was 258 (8% increase). The nerve biopsy load for the same period was 70 cases (5% increase). More details can be found in the neuropathology report.

CONCLUSION and FUTURE PLANS

Clinical Immunohistochemistry is in the midst of a rapidly evolving renaissance. New tests, new protocols and new FDA requirements have all been added without increasing the number of laboratory personnel, by improving efficiency. There is extensive cross training of personnel in this laboratory for the performance of several specialized tests. However, the demands on the laboratory will continue to increase. Our future goals include further reducing turn around time by automating some of the remaining manual staining procedures as well as streamlining current procedures to increase efficiency.

We will begin the process of establishing in situ hybridization in the laboratory by examining two in situ systems. One is an automated method from Ventana Medical Systems and the other is a manual method from Fisher called the Microprobe Manual Staining System.

Timothy Singleton, M.D., Director of Clinical Immunohistochemistry for Hematopathology

Alaa Afify, M.D., Director of Clinical Immunohistochemistry for Anatomic Pathology

Kristina Fields B.S. Senior Clinical Technologist Special Studies Laboratory

SURGICAL PATHOLOGY SERVICE
DEPARTMENT OF PATHOLOGY
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1 JULY 1998 - 30 JUNE 1999

The Surgical Pathology Division continues to grow, having experienced a 6.7% increase in volume compared to last year. This year, the Division saw 34,449 in-house surgical specimens, 3,256 personal consults, and 8661 M-Lab cases. This year saw the arrival of Augusto Paulino, M.D. as our new head and neck, bone, and soft tissue pathologist as well as Mark Rubin, M.D. as our new GU pathologist and Kathleen Cho, M.D. as our new OB/GYN pathologist. Steven R. Ramsburgh, M.D. also joined the faculty as a lecturer in pathology, rounding out an impressive group of new faculty recruitments.

Our ever-increasing volume has provided many new challenges to the histology laboratory, however; the laboratory continues to find new ways to become more efficient under the guidance and leadership of Ms. Kathy Smieszny. We are eagerly planning for a new and enlarged gross room/frozen section area in the upcoming year. The scheduled increase in the number of operating rooms coupled with the increase in operating room hours and the increased demand for tissue procurement make the enlargement of this area of critical importance.

Our surgical pathology fellowship program continues to be highly successful. All of this year's graduates are staying in academic pathology. Celina Kleer, M.D. will remain here at Michigan as an assistant professor of pathology. She will join the surgical pathology service with a focus on breast pathology. Carolyn Misick, M.D. will be joining the surgical pathology faculty at Ohio State University as an assistant professor of pathology. Peter Lucas, M.D., Ph.D. will be doing a post-doc in Dr. Gabriel Nunez's lab.

Despite our increasing service commitments, the Surgical Pathology Division has maintained its productivity at national meetings and international meetings. At this year's USCAP meeting, our faculty presented nine abstracts, directed a short course, and moderated or spoke at numerous companion meetings/subspecialty conferences. Three faculty members also presented at this year's IAP meeting in France, two of whom taught a long course. Our faculty also taught several courses at the annual ASCP meeting.

As always, it is an honor to work with such outstanding colleagues.

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 (more than 800 different laboratory analyses) as the UMHS has expanded both its volume and scope in ambulatory care activities, experienced growth in several major clinical programs, and promoted the expansion of M-Labs activities. Particular effort has been directed towards the improvement of test ordering, laboratory logistics, achievement of compliance with HCFA-mandated rules on documentation of test-ordering indications, and achievement of compliance with federal rules related to FDA approval of testing methods. Superimposed upon these efforts has been further development of computer links with M-Labs clients and software conversion to a Y2K-compliant clinical laboratory information system. In 1998-99 the Clinical Laboratories again performed more than 3 million billable analyses, supported a wide array of clinical and research programs, and added new testing methods. The maintenance of high quality provided by the Clinical Laboratories, in the face of increasing complexity of demands, is 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 triannual JCAHO inspection in October, 1998 and the biannual on-site College of American Pathologists inspection in May, 1999. 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.

1998-99 was marked by several major initiatives. The first initiative was to add new clinical laboratory testing capability and to increase support of new and/or expanding clinical programs. Among a wide variety of developments in this area were the addition of several new assays (e.g. homocysteine, FISH analyses in cytogenetics, DNA-based tissue typing, and others, new instrumentation in the Hematology and Chemistry Laboratories, and expanded support of clinical programs (therapeutic apheresis, lipoprotein apheresis, etc.).

The second initiative was achievement of UMHS-wide compliance with new HCFA-mandated rules related to documentation of justification for laboratory test ordering. In conjunction with the UMHS Compliance Committee, a system-wide requirement for the entry of ICD-9 diagnosis codes on all ambulatory test requests was implemented. (Ambulatory patients account for approximately 50% of all clinical laboratory test volume). In conjunction with institutional enforcement of this mandate, the Division has endeavored to improve test ordering through redesign and control of requisition content, direct cooperation with ambulatory care management, improvement of collection of demographic information at the point of test ordering, and the provision of periodic audit data for use by the Division, the Compliance Committee, and the Clinical Departments.

The third initiative was a renewed effort to more tightly regulate esoteric test utilization and sendouts. We expect this effort to result in substantial additional direct cost savings.

Finally, the Clinical Laboratories have continued to respond to the change in scope and organization of UMHS patient care activities. In contrast to the early 1990s when 70% of laboratory testing volume came from inpatient services and 30% from ambulatory patients, the split is now approximately 50% each. The laboratories currently support more than 30 UMHS-owned regional satellite facilities as well as many more patients who are M-Care subscribers. These shifts have substantially increased our focus on informatics, logistics, and cost-containment.

Faculty and laboratory staff participated in a wide variety of intramural and extramural educational programs during 1998-99. For instance, the 26th annual Blood Bank/Transfusion Medicine course and the 17th Laboratory Information Systems (LIS) course were again well attended, making them among the most visible courses of their kinds in the United States. These programs, coupled with a strong 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 informatics initiatives, promise to further enhance the Department's leadership role in this important area. The May LIS course was again linked to a highly successful Executive Briefing which brought together leaders from a variety of institutions and laboratory information technology fields to discuss the future of clinical pathology practice. These programs, 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", was updated in 1998-99. In keeping with a thematic approach, the 1998-99 update entailed the establishment of four rotation blocks and places 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 will continue to face new challenges. 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 its attention to informatics, the clinical molecular diagnostics program and, in cooperation with the M-Labs program, will 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**

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PATIENT CARE:

Use of blood component continued to mount during this year, related to increased numbers of surgical procedures requiring extensive transfusion support, and increased activity on the hematology program. Moreover, the transfusion service was engaged in study of new program additions and modifications related to posttransfusion infectious disease and variations in component provision.

There was increased reliance on peripheral blood progenitor cells, rather than bone marrow, for transplantation purposes, and this had a pronounced impact on both the transfusion and apheresis area and on the main laboratory of the blood bank. The inadequate space for both functions is currently being reviewed, as solutions to the problem must be defined to adequately support the BMT program.

The transfusion and apheresis area continues to require more space for additional cell separators as well as for patient accommodation. Not only is space needed for support of BMT stem cell procurement, but also for therapeutic apheresis and immunoadsorption procedures. In addition, without additional space the laboratory is unable to implement liposorber apheresis for lowering of LDL cholesterol in patients with homozygous familial hypercholesterolemia. 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 latter area has tripled and the number of liquid nitrogen storage tanks has increased in relation to the number of harvesting procedures.

Plasma treated with the solvent/detergent technique was introduced for selected patients during this past year. This treatment of the plasma is intended to eliminate lipid-encapsulated viruses, such as HIV, HBV, and HCV from the plasma. The laboratory is studying two other initiatives. First, prestorage leukocyte reduction of all blood components will have several benefits for our patients, including reduction of febrile nonhemolytic transfusion reactions, reduce alloimmunization to platelet transfusions and enhance platelet survival, reduce the possibility of transfusion-related cytomegalovirus infection, and prevention of transfusion-related immunomodulation which is claimed to increase the risk of postoperative sepsis and the possibility of metastasis in patients transfused intraoperatively.

The laboratory staff participated in providing a Revised Version of the pamphlet, "Blood Transfusion – Your Options." This is to be given to patients prior to hospitalization for transfusion and is a part of the informed consent program.

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 occasional PUBS procedures. Ms. Butch led the Quality Management program of the clinical laboratories of the Department of Pathology and Mrs. Stoe chaired the Department's Laboratory Safety Committee

EDUCATIONAL ACTIVITIES:

As in previous years, the medical, technical and nursing staffs of the Blood Bank/Transfusion Service were 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 segment, and a presentation on Transfusion Medicine was provided for the medical student senior elective course in Pharmacology and Therapeutics. Hematology fellows in internal medicine rotated through the laboratory. In addition, the laboratory supported the medical technology training program of Eastern Michigan University and Ferris State College.

The 26th annual postgraduate course, "Current Topics in Blood Banking", was held on June 2-4, 1999. The course, under the direction of Mr. Judd, attracted over 150 technologists and physicians from throughout the United States and Canada. 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 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. Dake, Mr. Meade and Ms. Butch were active in educational programs of the University of Michigan Health Center and 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. Her efforts were recognized on a National level, as she received the John Elliott award from the American Association of Blood Banks.

PROFESSIONAL ACTIVITIES:

Members of the Blood Bank and Transfusion Service medical and technical staffs were active at the regional and national levels. Dr. Oberman served as Associate Editor of TRANSFUSION and was a member of the Research Initiatives 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 past year was marked by larger than expected increases in laboratory workload. The Chemistry Section experienced an approximate 10 % increase in overall test volume this year. Included in this was a 18% increase in the more manual testing areas of Special Chemistry, Immunology, and Ligand Assay. This workload was absorbed without the addition of incremental personnel.

The focus of the Chemistry Section this past year was on selecting new immunoassay analyzers and special chemistry analyzers that would allow for further consolidation of workstations in the laboratory and achieve savings on reagent pricing. Considerable time and effort was spent on visits to view different analyzers in operation and gather performance data. The committee involved in the process finally selected the Vitros ECi analyzer from Ortho-Clinical Diagnostics. Plans are currently underway for the implementation of these new analyzers.

Several new assays were set up in the laboratory. In the toxicology area, a gas chromatography assay for detection of gamma hydroxybutyrate (GHB) in urine was developed and validated. The special chemistry section evaluated and implemented the RIBA assay for confirmation of Hepatitis C virus infection.

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. Testing for Hemoglobin A1c in diabetics and prothrombin time in patients on coumadin has increased in scope and volume. An evaluation of tests for antibody to *H. pylori* in patients with GI symptoms is underway, with likely implementation of a testing protocol at multiple health care centers in the fall of 1999. The lab staff participated in a recently completed evaluation of new activated clotting time (ACT) analyzers to be used by the operating room perfusion teams.

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 worked with nursing personnel to standardize training and record keeping in preparation for the JCAHO inspection of the institution. Several new glucose meters are currently being evaluated by the Point-of-Care Testing group and nursing units, and the Chemistry Lab continues to actively pursue options for the computerized collection and analysis of both quality control and patient data from these meters.

The laboratory staff contributed a significant amount of time and effort during the past year to the evaluation of new laboratory information system software for the department. Finally, credit should be given to all laboratory personnel who help with preparation for the CAP accreditation inspection. No major deficiencies were found in the Chemistry Section during the inspection.

Donald Giacherio, Ph.D.

CLINICAL CYTOGENETICS LABORATORY

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After a delay of almost 7 years, the Clinical Cytogenetics Laboratory moved to a larger space on July 14, 1998. A month earlier, four technologists, or 40% of the staff left to pursue educational or other opportunities. Two of these positions have been refilled, none with experienced technologists, so our efforts have been further diluted by training issues. The volume has remained approximately constant in most areas, some more than others. In the area of prenatal diagnosis, 650 amniotic fluid specimens, a decrease of 200 from last year, approximately 85 (vs 85 in 1996) chorionic villus biopsy, and 85 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 85 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 four years ago, to 707 in the last year to 1100 in the current fiscal year. Over half of these require analysis of extra cells to exclude possible mosaicism. Increasingly, these require "FISH" (fluorescence in situ hybridization) to characterize some of the abnormalities, or may require some other specialized modality, such as a "core wash" to obtain cells. All 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, 511 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. I have received a request to perform "FISH" for n-MYC amplification on the in house specimens, and not just those received from MLabs clients.

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. Now that the AMA has approved CPT codes for molecular cytogenetics, these assays are considered clinical and can be handled accordingly. In the last year we have done over 120 unique sequence probes, several dozen for malignancies, characterized a

variety of markers and apparently unbalanced translocations. We participated in the so-called "FISH III" project with the Great Lakes Regional Genetics Group, characterizing the BCR-ABL probe.

I would comment that while our volume had increased dramatically in some areas, staffing has decreased. 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. At this juncture, I hope that the Laboratory staffing remains stable, so that we can regroup and take advantage of the increased space.

Susan Sheldon, Ph.D.
Director, Clinical Cytogenetics

**COMBINED HEMATOLOGY LABORATORY
(HEMATOLOGY, BONE MARROW, FLOW CYTOMETRY, COAGULATION)**

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I. HEMATOLOGY AND BONE MARROW:

- A. Automated slidemaker implementation:
1. Completed beta-testing of automated slidemaker module for Beckman-Coulter Gen S instrument.
 2. Implemented automated slidemaker for full-time use in the Cancer and Geriatrics Center
 3. Began phasing-in automated slidemakers in the main Hematology Laboratory.
- B. Moved the Taubman Center Hematology Laboratory to a new location, and expanded hours of operation to accommodate needs of the nephrology service.
- C. Began accommodating extended weekend operations of the Cancer and Geriatrics Center infusion service.
- D. Improved turn-around times for cytochemical studies on bone marrow specimens by increasing frequency of service.
- E. Passed the College of American Pathologists inspection with no deficiencies.
- F. Quality Improvement Program:
1. Instituted a bi-weekly conference with Beckman-Coulter focusing on quality improvement of automated instruments.
 2. Established a regional Beckman-Coulter Gen S users' group.
- G. Increasing Volume of Work.

Volumes continued to increase in the general hematology and bone marrow areas:

Test	Volume Fiscal 1999	Change from previous year
Complete blood counts	298,259	+8.8%
Manual differential counts	51,548	+8.5%
Body fluid samples	5,913	-1.4%
Urine samples	48,234	+8.1%
Bone marrow aspirate samples	1,569	+8.6%
Bone marrow biopsy samples	1,676	+4.4%

II. FLOW CYTOMETRY

The Clinical Flow Cytometry section processed about 5300 specimens, a volume increase of 18% from the previous year. The percentage change in volume (relative to 1997-98) is listed below for each of the major test categories:

<u>Test Category</u>	<u>Change from 1997-98</u>
Immunodeficiency monitoring	+11%
CD34 stem cell counts	+17%
Chronic leukemia/lymphoma phenotyping	+33%
Acute leukemia phenotyping	+26%
T-cell subset monitoring in organ transplant recipients	+69%
Antiplatelet antibody testing	+50%

M-Labs referrals continue to comprise a substantial part of the work volume, including 31% of all acute leukemia immunophenotyping panels, 41% of all chronic leukemia/lymphoma panels, and 40% of all immunodeficiency monitoring.

Attending staff continue to triage all requests for leukemia/lymphoma immunophenotyping, with cancellation of unwarranted requests. Of the 1647 specimens submitted for leukemia/lymphoma immunophenotyping, pathologist review lead to cancellation of 566 of these requests.

Over the past year, the section validated and implemented new four-color test profiles for immunodeficiency disorders and acute leukemias. Three- and four-color testing procedures for chronic leukemias/lymphomas were also validated and implemented. Three new test panels were developed for monitoring lymphocyte subsets in transplant recipients receiving novel immunosuppressant drugs.

The flow cytometry section passed the College of American Pathologists inspection with no deficiencies.

III. COAGULATION

A. Laboratory Consolidation and Staffing:

1. The laboratory has been fully integrated with the staff of the main hematology laboratory.
2. 3 FTEs perform coagulation laboratory studies. One individual is full-time; 4 individuals are part-time.
3. As result of perceived staffing needs, a new half-time individual has been trained to perform specialized coagulation studies. Having this individual has improved coverage of the laboratory. At present, there are two individuals performing specialized coagulation testing daily in the laboratory.
4. Coagulation laboratory did not receive any negative citations on the recent (5/99) CAP inspection.

B. New Programs in the Laboratory:

1. All goals outlined in July, 1998 for fiscal year 1999 have been met at the time of this writing.

2. A second new Amelung Coagulation instrument was set-up to perform thrombin times, fibrinogen assays in the routine coagulation laboratory area.
3. The training and implementation of anti-factor Xa assays for heparin and any low molecular weight heparin (enoxaparin, dalteparin, danaparoid sodium) has been implemented on a routine basis, 24 h/day for patients that need the assay. These assays provide a great service to patient care in the hospital.
4. An improved factor VIII:C coagulant assay for patients with severe Hemophilia A has been established in the laboratory for physicians who deal with these patients.
5. A factor Xa chromogenic assay to measure factor X levels has been established for patients on warfarin who also have Lupus Anticoagulants.
6. New aminolytic assays procedures had to be established for plasminogen were established this year as result of a previous vendor discontinuing their assay kits.
7. A plasma fibrin split products assay was established. This assay procedure obviates the need to collect blood in a special tube to perform fibrin split assays. It thus decreases the need to have a special tube to collect samples for FDPs.

C. Laboratory Growth:

1. University of Michigan Hospitals System.

Overall, there was a 21.7% increase in U of M Hospital Activity in the Coagulation Laboratory from fiscal year '98 to an annualized fiscal year '99. Total gross revenues increased from \$4,244,062 to \$5,165,061. There was an across-the-board increase in all categories of tests measured.

2. M-Labs Activity:

There was 27.5% increase in net M-Labs activity in specialized coagulation testing from fiscal year '97 to '98. In fiscal year '97, combined net patient and client incomes were \$129,013. In fiscal year '98, combined net patient and client incomes were \$164,614. The revenue distribution was equalized over the breath of assays performed in the laboratory.

IV. TEACHING AND RESEARCH ACTIVITIES: Hematology/Flow Cytometry

- A. Developed orientation program for new residents on CP-A rotation
- B. 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.
- C. Accredited Hematopathology Fellowship
- D. Training and continuing education for medical technologists

- E. Formal lectures and laboratories for freshman and sophomore medical students

TEACHING AND RESEARCH ACTIVITIES: Coagulation Laboratory

- A. Pathology House Officers: Residents participated in a twice weekly sign out rounds of specialized coagulation testing with the laboratory director. Each resident became an active participant in this activity by actually dictating the report. Pathology residents have been assigned first call for questions and problems related to the Coagulation Laboratory.
- B. Two in-services were prepared for the Hematology Laboratory personnel.

V. GOALS FOR 1999-00: Hematology/Flow Cytometry

- A. Cross-train technologists in Flow Cytometry and Bone Marrows, while maintaining specialized expertise.
- B. Continue phasing-in the automated slide spreader for routine hematology with the new generation Coulter Gen-S, for those blood smears which need manual review.
- C. Continue collaboration with Coulter and Pathology Data Systems to enhance reporting and databasing of flow cytometry results.

GOALS FOR 1999-00: Coagulation Laboratory

- A. Establish new reagents lots and possible new equipment for the next five years for routine and specialized coagulation testing in the laboratory.
- B. Assay development.
 - 1. Adapt new chromogenic assays (antithrombin III, protein C) to existing equipment or new equipment and reagents.
 - 2. Develop a new collagen-induced von Willebrand factor agglutination assay.
 - 3. Consider ELISA-based D-Dimer assay.
- C. Teaching.
 - 1. Continue to integrate Pathology Residents more into the operation of the Coagulation Laboratory.
 - 2. Provide Pathology Residents with Hemostasis/Thrombosis synopsis as a teaching tool for this field.
 - 3. Consider developing a fellowship in Clinical Pathology for hemostasis testing.

Bertram Schnitzer, M.D.
Director, Hematopathology

Lloyd M. Stoolman, M.D.
Co-Director, Flow Cytometry

William G. Finn, M.D.
Director, Hematology Laboratory

Alvin Schmaier, M.D.
Director, Coagulation Laboratory

Charles W. Ross, M.D.
Director, Flow Cytometry

CLINICAL IMMUNOPATHOLOGY LABORATORY

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I. OVERVIEW:

The Immunopathology Laboratory performed more than 54,000 analyses in 1998-99. 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:

Integration of clinical immunopathology testing into the Chemistry Section continued to progress. New procedures were implemented in the protein electrophoresis area, in complement assays, and in the measurement of antibodies to extractable nuclear antigens. We recently evaluated and initiated a series of new utilization control measures in the laboratory.

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 3 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 a 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**DEPARTMENT OF PATHOLOGY
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Both Laboratories continue to concentrate on identifying those tests that impact patient care and to work with medical services to eliminate or change ordering practices for tests shown to have little clinical benefit. A major success was the drastic reduction in the number of fungus blood cultures being submitted and the virtual elimination of the bacterial direct antigen test. In response to clinical demand, *mecA* gene testing and *Clostridium difficile* fecal toxin testing was expanded to include weekends. Due to the recent success of "highly active antiretroviral therapy (HAART), the ultrasensitive HIV quantitation assay was introduced to monitor for the development of low-level drug resistance. At the request of Ambulatory Care, the Laboratory cooperated with their investigative team to evaluate a point-of-care test for *Helicobacter pylori* antibody. A test for *Helicobacter pylori* fecal antigen was also added to the test menu which should essentially eliminate the need to perform the more expensive and inconvenient Urea Breath test. Discussions were held with physicians responsible for the care of patients with cystic fibrosis to design and implement a more efficient selective growth medium for *Burkholderia cepacia* and an appropriate antimicrobial testing battery. Dermatology requested that the Microbiology Laboratory assume responsibility for all dermatophyte cultures and this has occurred. Many personnel hours were devoted to computer issues, especially to the Millennium (V 500) project.

II. RESEARCH ACTIVITIES:

Several clinical investigations were completed during the fiscal year, five of which resulted in poster presentations at national meetings. We documented that the use of the blood Isolator tube in addition to the standard blood culture set for the isolation of yeast was unnecessary. The accuracy of detecting oxacillin resistance in staphylococci using PCR for detecting the *mecA* genetic sequence was demonstrated. Parallel testing of selective media to efficiently isolate *Burkholderia cepacia* from respiratory specimens obtained from cystic fibrosis patients showed that the *Burkholderia cepacia* Selective Agar was superior to the older *Pseudomonas cepacia* Agar. We documented that our current blood culture medium and system was excellent for performing bone marrow product sterility testing which reduces personnel handling time. Virology personnel participated in a multicenter study to assess the clinical utility of a molecular method (NASBA) to detect mRNA in whole blood samples submitted for CMV antigenemia assays. We continue to cooperate with School of Public Health investigators to assess the incidence of sexually transmitted diseases present in a select patient population in Indonesia by performing molecular diagnostic tests on collected specimens. Cooperation was also extended to both the pulmonary research team and to various infectious disease section investigators to collect, test and ship isolates for new antimicrobial clinical investigations.

III. TEACHING ACTIVITIES:

All laboratory personnel continue to provide periodic instruction to Pathology House Officers and Infectious Disease Fellows and residents on diagnostic procedures used in the Microbiology/Virology Laboratories. Infectious Disease Laboratory rounds are held each weekday during which staff members and assigned Pathology House Officers interact with ID team members to answer questions, demonstrate laboratory diagnostic procedures and discuss interesting findings. Laboratory personnel also provided expert instruction to students enrolled in the Medical Technology program at Eastern Michigan University. Numerous in-service education programs were held during the course of the year with individual technologists and Pathology House Officers giving presentations to staff members.

IV. PROFESSIONAL DEVELOPMENT:

Both supervisors and most Sr. Technologists attended one or more regional and national scientific meetings during the year and presented their posters at these meetings. Several other staff members attended regional meetings of interest. In addition, the Laboratory subscribed to two audioconference programs which provided a total of 15 conferences during the year that were available to all staff members as part of our ongoing CME program.

Carl L. Pierson, Ph.D., Director
Clinical Microbiology/Virology Laboratories

MOLECULAR DIAGNOSTICS LABORATORY

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1998 - 30 JUNE 1999

Overview

The Laboratory had a 20% increase in volume during the year. Charles Ross, M.D., and William Finn, M.D. both participated actively in the work-up of cases in molecular hematology. Jeffrey Warren, M.D. provided invaluable cross-coverage for Dr. Killeen during the year.

Clinical Services

The move of the Laboratory to larger space in Medical Science I resulted in more space being available for bench work and for clerical functions. This eased the congestion and overcrowding that was noticeable in the older laboratory. Plans to develop a new gel analysis room were drawn up, and work on this began at the end of the academic year.

For much of the year the Laboratory had to function at a reduced staffing level due to medical absences. Despite these, the turnaround times and overall levels of service were not adversely affected. This was accounted for by the extra effort made by the remaining technologists who are to be thanked for their work during the year.

The Laboratory again saw an increase in annual volume to approximately 3500 tests during the 1998-9 academic year. The growth in test volume was mostly accounted for by the Bone Marrow Transplant program, for which the Laboratory provides engraftment studies. In addition there were significant increases in the number of requests for genetic tests of inherited thrombophilia risks. As the laboratory grows, there is a need to obtain equipment to undertake more advanced genetic studies, including sequencing apparatus.

Education

Dr. I. Cetin Ozturk, a visiting physician from Turkey, spent 8 months in the laboratory. His activities included service work and research with Dr. Killeen. He also gave a number of talks during his time in the Laboratory. In addition, Dept. of Pathology Residents rotated through the Laboratory periodically and participated in sign-out activities. With the implementation of a formal Genetics Residency Program, it is expected that Residents from other clinical departments will rotate through the Laboratory in the future.

Future Plans

There continues to a demand for services related to the Bone Marrow Transplantation Programs. These include the need for additional markers of malignancy. There is also a need for the provision of

genotyping services for certain viruses (e.g., Hepatitis C). It is planned to consolidate the molecular detection and quantification of Hepatitis C and HIV in the Microbiology Laboratory and to develop genotyping capability in the Molecular Diagnostics Laboratory.

Anthony A. Killeen, M.D., Ph.D.

Assistant Professor

Director, Clinical Chemistry/Molecular Diagnostics

GENERAL PATHOLOGY

ELECTRON MICROSCOPY SERVICE

DEPARTMENT OF PATHOLOGY ANNUAL REPORT 1 JULY 1998 - 30 JUNE 1999

This previous year has seen the start of installation of a new electron microscope in the Department of Pathology. The new TEM is an Hitachi 7500. This scope offers several advanced features compared to the previous Zeiss, which has been donated to a local college. The new electron microscope has substantially increased power which offers greater resolution and the possibility of higher magnification.

Another important feature of the new electron microscope is the attached digital camera. Since its installation, virtually all of our cases have been done with the digital camera. The principal users of the electron microscopy service have been very pleased with the quality of the images. The images are virtually always diagnostic. These digital camera has eliminated the darkroom time, although this is partially offset by increased time spent manipulating the digital image.

The renovations of electron microscopy suite have an ongoing for more than a year. The third phase of the construction project has not yet begun, and the lab is not able to operate at optimal efficiency. With the completion of the third and final phase, we anticipate a decrease in the turn around time required for generating the diagnostic images. Additionally, it is anticipated there will be the network support for the digital images so that the long time report to print the images will no longer be necessary.

This table lists the clinical activity over the past 5 years. The % increase is relative to the 1994-95 year. A portion of the increase in the other is due to immotile cilia syndrome and platelet cases. We anticipate that these numbers will continue to increase over the next year.

	94-95	95-96	96-97	97-98	98-99	% increase
Nerve/Muscle	252	275	308	258	275	9%
Renal	256	276	333	320	349	36%
Other	23	43	20	55	100	334%
Total	531	594	661	669	724	36%

This is a breakdown of how cases are processed. Inside cases are from University Hospital patients while outside cases are from outside the hospital. Prints indicate that the specimen was processed completely, all the way to generating the prints.

	Inside	Outside	Submitted	Prints	% processed
Renal	177	172	349	247	71%
Nerve/Muscle	130	145	275	100	36%

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

M-LABS

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1998 - 30 JUNE 1999

I. MISSION:

MLabs is the University of Michigan Health System's reference laboratory program, established in 1985. MLabs offers the high quality reference laboratory services and other resources of the Department of Pathology laboratories to hospitals, clinics, other institutions, and physician offices. MLabs mission is to ensure that the Department of Pathology laboratories: (1) remain financially strong, (2) receive sufficient laboratory specimens for teaching, training and research programs, and (3) to encourage increased productivity of the laboratory staff.

II. CURRENT STATUS:

Since its origin, the MLabs program has experienced continuous growth, most notably since 1994 at which time the University Hospital chose to increase resources devoted to it. Gross billings have increased fourfold in the last four years.

MLabs currently provides full anatomic pathology coverage and esoteric clinical laboratory services to two hospitals and to the University of Michigan Health Service. MLabs is the primary reference laboratory and provides full esoteric laboratory testing to another ten hospitals in Michigan and northern Ohio and to another local University Health Service. MLabs receives large volumes of esoteric testing from a regional medical laboratory and from a local pharmaceutical firm. MLabs also now provides daily courier service and receives laboratory testing from 23 Integrated Health Associates' practices, 40 MCare physician offices/clinics, 7 UMHS physician office acquisitions, and a nearby correctional facility.

III. 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.

IV. GROWTH:

- In FY99, MLabs added 39 new physician offices and specialty service practices to our client list. The majority of these were related to our contract to provide coverage to M-Care patients. Some were for specialty services (dermatopathology, flow cytometry, muscle and nerve biopsy), and a few were UMHS acquired practices.
- 3 new full reference laboratory accounts including one new hospital, one correctional institution, and one intensive care practice.
- No contracts for services were terminated.
- MLabs submitted 8 proposals to prospective major clients during FY99. Of these, 3 were rejected, 3 were accepted, and 2 are pending.

IV. BILLING ACTIVITY:

- In spite of the new clients, total net billing was relatively flat (decreased by 0.6%) based on increased billings for clinical pathology services of 7% and decreased billings for anatomic pathology services of 13%

V. MANAGED CARE ACTIVITIES:

In the last two years, MLabs has contracted with M-Care for provision of outpatient lab services, first to its Medicare members, and later for members enrolled in M-Care's commercial and Medicaid products. MLabs subcontracted much of the work to M-Care's provider hospital labs with benefits to hospitals and patients. These contracts are capitated, which will result in considerable savings to M-Care over its previous fee for service contracts for these lab services.

In FY99, MLabs has expanded our agreement with M-Care to supply outpatient laboratory services to include the majority of their provider groups (IDNs) for the HMO, POS, and Medicaid products. We have begun discussions with M-Care to develop a full-risk outpatient lab agreement for all groups and products to become effective 1/1/2000 (current target date).

MLabs continues to manage the M-Care/MLabs agreement for Medicare HMO Program (Senior Plan). Five subcontracts are in place. We developed and implemented a system for reimbursement for

testing done by other labs within network (Cross System Testing). We have finalized and facilitated most MCare HMO, POS, and Medicaid Contracts and Subcontracts. The other subcontracts are in progress.

We prepare quarterly QA reports on lab services for MCare's QA department and have conducted a Physician Satisfaction Survey for MLabs subcontracted providers and reported the results to MCare. We assist MCare with resolution of laboratory service issues.

VI. NETWORK ACTIVITY:

In the past several years, hospitals throughout the country have been forming networks in order to cope with the evolving demands of a changing health care system including intense cost cutting by third party payors, reduction in inpatient laboratory testing, competition from commercial laboratories, and carve out of outpatient laboratory services (to large independent labs) from managed care contracts. The formation of laboratory networks gives hospital labs the geographic coverage which allows them to successfully compete in a managed care environment as well as to decrease unit costs and increase revenue streams through outreach activities.

MLabs has been positioning itself to deal with an increase in managed care testing by playing a key role in two laboratory networks. Great Lakes Laboratory Network (GLN) consists of 28 hospital laboratories, predominantly in the western and northern parts of Michigan; Joint Venture Hospital Laboratories (JVHL) has 13 member laboratories located in southeastern Michigan. GLN has no contracts yet. JVHL has contracts for laboratory services with 10 managed care organizations, including Select Care, and a subcontract with MLabs for MCare work.

MLabs is represented on JVHL's Executive committee and its "elab's" committee, and on the GLN steering committee as well as on the marketing, operations, and medical staff committees of these 2 networks. We are working towards a cooperative effort of the 2 networks to bid in the next fiscal year for the provision of laboratory services to Blue Care Network. MLabs is preparing a proposal to provide reference lab services to JVHL's new "elab" internal esoteric testing initiative.

VII. PROSPECTS:

Looking ahead, we foresee an increasingly competitive market for outreach and esoteric laboratory testing. We are already experiencing fierce competition in the hospital reference laboratory market from increasingly consolidated large independent laboratories with a national presence who offer a broad range of esoteric testing at extremely competitive prices. Purchasing agreements among groups of hospitals and affiliations/consolidations among groups of hospitals may also dictate their use of reference laboratories other than MLabs.

In the next few years, MLabs will focus its efforts on maintaining and increasing its existing hospital client base. This will require some reduction in our pricing, some broadening of our test menu, and continued efforts to interface the Department of Pathology's information system with client hospital information systems. We may also enter into arrangements with client hospitals where we would provide some management of their outreach programs.

Our recently much increased physician office client base will require efforts to make our services run smoothly, particularly in the area of phlebotomy. In addition to the managed care work contracted to MLabs, we will focus our efforts on obtaining the discretionary (pull-through) laboratory work from these physician clients.

MLabs plans to increase our efforts significantly in marketing specialty (niche) areas such as dermatopathology, renal pathology, cytogenetics, molecular diagnostics, neuropathology, hematopathology, and flow cytometry. We will continue our efforts to try to obtain esoteric laboratory testing from the two hospital laboratory networks (JVHL and GLM) to which we belong. Other areas of potential growth are laboratory work from nursing homes and from clinical trials.

IX. IMPEDIMENTS:

Serving the burgeoning physician office market has reduced the ability of MLabs marketing personnel to provide services to our hospital clients and markedly reduced our ability to investigate and solicit business from prospective new markets. Additional personnel will be required to reestablish growth of revenue-producing markets.

Prepared by Eugene M. Silverman, M.D.

EDUCATIONAL PROGRAMS

DEPARTMENT OF PATHOLOGY ANNUAL REPORT 1 JULY 1998 - 30 JUNE 1999

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 continues to be recognized as recipients of student teaching awards. Efforts to increase student active learning experiences in a web-based teaching format continue with the development of the "Virtual Microscope" (Smithsonian Award recipient, Dr. L. Stoolman) and interactive laboratory exercises (Dr. A. Flint). Elective fourth year clerkships in General Pathology and specialty experiences continue to be highly evaluated by students and meet important curriculum educational goals..

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. This year new fellowships in Molecular Pathology and Transfusion Medicine were initiated. 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 two fellows completed training this past year. Graduates found desirable employment including fellowships at Johns Hopkins Hospitals and University of Minnesota as well as faculty positions at Ohio State University Hospitals and the University of Michigan Hospitals.

Graduate Program:

The Department's doctoral graduate program is a small program (approx. 6 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. 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 an active participant with other basic science departments in the Program in Biomedical Science (PIBS). This program involves a joint recruitment effort of biomedical graduate programs to recruit the very best students to the University of Michigan and allow them to delay selection of specific departments until they have completed their first year of study. Several faculty serve on both the curriculum and admissions committees for the program. Results from the past year indicate a positive response to the recruitment effort and increased academic quality of students indicating an interest in pathology.

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. Faculty continues to develop internet based educational modules that can be linked established and future CME programs. The fall A.J. French Society meeting continues to be a focal point for CME especially for graduates of our resident training programs.

**ANN ARBOR VA HEALTH SYSTEM
PATHOLOGY AND LABORATORY MEDICINE SERVICE**

**DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

INTRODUCTION:

The VA Ann Arbor Healthcare System (VAAAHS) 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 VAAAHS Pathology and Laboratory Medicine Service maintains a close relationship with the University Department of Pathology at every level. All pathologists in the VAAAHS have medical school appointments and participate in university activities in a manner similar to other departmental sections. Recruitment for VAAAHS 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 VAAAHS is a voting member of the Dean's Committee. The VAAAHS laboratory was inspected in 1998 and retains full accredited by the College of American Pathologists. The VAAAHS 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 1 ½ decades. 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 VAAAHS. 1) The facility is refocusing its mode of healthcare delivery, downsizing inpatient care and greatly expanding its ambulatory care. In keeping with this change, a substantial capital improvement program was completed this year. Included are Research Building, two additional parking structures and a 340,000 sq. ft. Clinical Addition. This building is attached to the existing hospital and provides space for ambulatory care, new surgical suites, post surgical recovered unit, vascular cath facilities, four 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 was accomplished in three working days without interruption in clinical services. 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 an increase in the workload in Ann Arbor VAAHS's anatomic pathology and the clinical labs.

ANATOMICAL PATHOLOGY:

- A. **Surgical Pathology:** 5,138 surgical cases have been accessioned and reported during this period of time. This continues a steady increase over the prior reporting periods. 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:** 38 autopsies were performed during this year that is a rate of approximately 27% 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. Staff pathologists who permit a gradual increase in independence for the resident with increased experience supervise these steps. Several autopsies performed at the VAAHS are also presented at the extended Gross Conference at the University. The Department of Veterans Affairs has issued a new policy to recognize the value of the autopsy and to encourage increased utilization. There is an expectation that all facilities will obtain permission to perform autopsies on at least 30% of their in-house deaths. The VAAHS has participated in the last national VA Autopsy Conference and is planning to attend this year's conference, to learn mechanisms to more fully realize the values from autopsies and increase the number of next of kin who grant permissions for autopsy.
- C. **Cytology:** 2,641 cases were examined and diagnosed during this period. This is a slight decrease 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 VAAHS the cytological material is readily available and is used as correlative information for surgical and autopsy pathology. This laboratory is a VA "Center of Excellence" in cytology. They process and report all of the cytology specimens from one neighboring VA and the GYN cases from another.

- D. **Electron Microscopy:** 206 electron microscopy cases were processed. Ultrastructural diagnosis is provided through sharing agreements with several Michigan hospitals. The unit also serves several VAAHS 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 VAAHS 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 940,047 clinical pathology procedures were performed in the laboratory. In Chemistry there were 722,788; in Hematology 94,218; in Urinalysis 12,135, in Microbiology 29,818, and in Blood Bank 25,109. These figures represent productivity (billable) rather than weighted test numbers. Each of these numbers has increased slightly during this year, with the exception of the hematology procedures. 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 VAAHS is physically close to the University, the residents are expected to attend the appropriate teaching conferences at the University as well. The staff contributes to the laboratory and lecture portions of the second year medical students at the University of Michigan. The VA staff also participates 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. 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 VAAHS. All staff participate in various clinical studies and collaborate with a variety of investigators. The laboratory in general

serves the VAAAHS research program by providing considerable technical support for clinical research and in some cases for more basic research in both anatomic and clinical pathology.

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 school 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 is 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 VAAAHS. 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 fifth 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 maintains approval 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 now houses: Ambulatory Care, Surgical Suites, the Intensive Care Units, Nuclear Medicine, Radiology and the full Clinical and Anatomic Pathology laboratories.

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
ANNUAL DEPARTMENTAL REPORT
1 JULY 1998 - 30 JUNE 1999**

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
Yolande Salwoski, Office Manager, Clinical Faculty Offices

B. OFFICE OF ACADEMIC AND BUSINESS AFFAIRS - MEDICAL SCHOOL:

David R. Golden, Clinical Department Associate
Michael Hulbert-Shearon, Student Services Assistant
John E. Harris, Financial Analyst
Catherine A. Niemiec, Administrative Assistant

C. OFFICE OF THE CHAIRMAN

Laura D. Blythe, Staff Assistant
Janice M. Kitley, Executive Secretary

D. PATHOLOGY PHOTOGRAPHY AND IMAGING CENTER:

Mark V. Deming, Photographer
Lynne Smith, 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, University of Michigan Health System (Medical

School and Hospitals) and the University. In addition to directing this division, Mr. Napolitan serves on various departmental, Health Systems and University Committees, several professional society committees and as a board director for non-profit organizations.

Significant staff turnover in this division occurred in Fiscal Year 1999. The Education Office is staffed with new employees including Michael Hulbert-Shearon (Student Services Assistant), Gail DesMarais and Lisa Blackman. Ms. Jeannie Slater and Ms. Kim Biery have replaced Mrs. Camille Young and Mrs. Vicki Fredette in the grant and contract administrative support area and Ms. Catherine Niemiec has replaced Mrs. Susan Hunter in the Finance Unit's administrative area. The services provided by this unit continue to be outstanding and the addition of these new staff members has provided additional expertise to the individual units with this office.

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 Operation Improvement Program (expense reduction) for the Pathology Laboratories as mandated by Hospital and Health Centers Administration and the Operation Improvement Group. For Fiscal Year 1999, we were required to develop reductions in the amount of \$1,300,000. A new manager for Central Distribution and Phlebotomy Services was hired in May 1999. This staff member is working closely with Mr. Morrow and his staff on retention and staffing issues for these two units. 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. In May 1999, the College of American Pathologists completed an on-site laboratory inspection. In addition, the University of Michigan Hospitals, including the Pathology Laboratories, were inspected by the Joint Commission for the accreditation of Hospitals (JCAHO). Two new faculty offices were completed in the AGH Faculty Office Suite. This renovation converted this space from an existing office and clerical support space. Mrs. Jansen also participated in the development of the "Pathology Idea Program" designed to provide staff members with alternatives for introducing new ideas and to handle complaints regarding work space, assignments, etc. For FY 2000 Mrs. Jansen has agreed to lead the Hospital and

Health Services Blood Drawer Program which was assigned to Pathology by Hospital Administration. This program was previously directed by the Emergency Group.

Billing Coordinator: This individual, Ms. Nancy Coray, is responsible for processing and auditing all laboratory charges (gross charges of approximately \$152,030,285), 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. To assist with the increased workload, an additional staff member, Mrs. Edie Trobaugh was assigned to this unit.

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 413 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.

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 Ms. Catherine Niemiec is responsible for the payroll and personnel issues for staff in the Medical School (approximately 138 FTEs) including our House Officer Program (24 FTEs), Post Doctoral Fellows (39 FTEs) as well as supervising the staff in the Pathology Education Office.

OFFICE OF THE CHAIRMAN:

In addition to providing support to the Chairman, Mrs. Janice Kitley is responsible for processing faculty appointments and promotions through our departmental 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 faculty appointments, payroll, and personnel issues, and travel and dues reimbursements.

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. To provide additional support with the increased work, an additional photographer, Ms. Lynne Smith was hired for this unit. A major renovation including installation of a fire door and card swipe security system is currently underway. Our photography laboratory has been temporarily relocated to a research laboratory during the completion of this project.

SUMMARY OF FINANCIAL DATA:

1. Grants and Contracts and Other Accounts:

240 active grants, contracts and other accounts

Total Direct Expenditures:	\$7,182,654
Indirect Research Expenditures:	<u>\$3,220,353</u>
Total Sponsored Projects:	\$10,403,007

2. Faculty Group Practice Plan - Pathology:

Number of charge entries:	124,914
Gross Billings - Anatomic and Clinical Pathology:	\$16,924,317
CDS Payment	\$ 5,968,559
Part A Payment:	\$ 2,572,000
M-Labs Net Transfer:	\$ 892,000

3. Pathology Laboratories:

Number of billed tests reported to MECON:	\$ 2,949,284
Total Gross Revenue - Pathology Laboratories:	\$152,030,285
Total Direct Expenses Pathology Laboratories:	\$ 40,641,909

Eugene J. Napolitan
Administrator