THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL

Department of Pathology

ANNUAL REPORT



1 July 1996 - 30 June 1997

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MEDICAL SCHOOL

Department of Pathology

ANNUAL REPORT



1 JULY 1996 - 30 JUNE 1997

LIST OF FACULTY

LIST OF FACULTY

Name	Rank	Institutional Affiliation
Abell, Murray R	Professor Emeritus	The University of Michigan
Abrams, Gerald D.	Professor	The University of Michigan
Annesley, Thomas M.	Associate Professor	The University of Michigan
Appelman, Henry, D.	Professor	The University of Michigan
Baker, James R.	Associate Professor	The University of Michigan
Barr Jr., Mason+	Professor	The University of Michigan
Beals, Theodore F.	Assistant Professor	Veterans Affairs Medical Center
Blaivas, Mila	Clinical Associate Professor	The University of Michigan
Bonadio, Jeffrey	Associate Research Scientist	The University of Michigan
Brawn, Peter	Assistant Professor	Veterans Affairs Medical Center
Caplan, Michael J.	Clinical Assistant Professor	The University of Michigan
Capps, Rodney D.	Assistant Professor	The University of Michigan
Chamberlain, Priscilla	Clinical Instructor	Veterans Affairs Medical Center
Chensue, Stephen W.	Associate Professor	Veterans Affairs Medical Center
Crockett-Torabi, Elahe	Research Investigator	The University of Michigan
D'Amato, Constance J.	Assistant Professor	The University of Michigan
Davenport, Robertson	Assistant Professor	The University of Michigan
de la Iglesia, Felix**	Adjunct Research Scientist	Warner-Lambert; Parke Davis
Devaney, Kenneth O.	Associate Professor	The University of Michigan
Dixit, Vishva M.	Professor	The University of Michigan
Dressler, Gregory R.	Assistant Professor	The University of Michigan
Elner, Victor M.++	Assistant Professor	The University of Michigan
England, Barry G.	Associate Professor	The University of Michigan
Fantone, Joseph C.	Professor and Director, Anatomic Pathology	The University of Michigan
Fearon, Eric R.*	Professor	The University of Michigan
Flint, Andrew	Associate 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
Goldman, Robert T.	Visiting Lecturer	The University of Michigan
Gordon, David	Associate Professor	The University of Michigan
Greenson, Joel	Assistant Professor and Director, Surgical Pathology	The University of Michigan
Headington, John T.	Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Heidelberger, Kathleen P.	Professor	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan
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	The University of Michigan
Lieberman, Richard W.+++	Visiting Lecturer	The University of Michigan
Lowe, Lori	Clinical Assistant Professor	The University of Michigan
Lowe, John B.	Associate Professor	The University of Michigan
Lukacs, Nicholas	Research Investigator	The University of Michigan
McKeever, Paul E.	Associate Professor	The University of Michigan
Michael, Claire W.	Clinical Assistant Professor	The University of Michigan
Midgley, A. Rees	Professor	The University of Michigan
Miller, Richard A.	Professor	The University of Michigan
Mitra, Raj S.	Assistant Research Scientist	The University of Michigan
Mosley, R. Lee	Assistant Research Scientist	The University of Michigan
Murphy, Hedwig S.	Research Investigator	The University of Michigan
Naylor, Bernard	Professor Emeritus	The University of Michigan
Nickoloff, Brian	Visiting Associate Professor	The University of Michigan
Nunez, Gabriel	Associate Professor	The University of Michigan
Oberman, Harold A.	Professor	The University of Michigan
Phan, Sem H.	Professor	The University of Michigan
Pierson, Carl L.	Assistant Professor	The University of Michigan
Polverini, Peter J.**	Professor	The University of Michigan
Rasche, Rodolfo	Clinical Assistant Professor	The University of Michigan
Rekhter, Mark	Assistant Research Scientist	The University of Michigan
Remick, Daniel G.	Associate Professor	The University of Michigan
Ross, Charles W.	Assistant Professor	The University of Michigan
Rowe, Nathaniel H.*	Professor	The University of Michigan
Schmidt, Robert W.	Professor Emeritus	The University of Michigan
Schnitzer, Bertram	Professor	The University of Michigan
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
Sima, Anders A.F.	Visiting Professor	The University of Michigan
Singleton, Timothy P.	Assistant Professor	The University of Michigan
Stoolman, Lloyd M.	Associate Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Sulavik, Denise	Lecturer	The University of Michigan
Till, Gerd O.	Professor	The University of Michigan
Varani, James	Professor	The University of Michigan
Ward, Peter A.	Professor and Chairman	The University of Michigan
Warren, Jeffrey S.	Associate Professor and Director, Clinical Pathology	The University of Michigan
Weiss, Bernard	Professor	The University of Michigan
Weiss, Sharon W.	Professor	The University of Michigan
Wojno, Kirk J.	Assistant Professor	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

In Memorium:

The following faculty members passed away during the 1996/1997 academic year:
Samuel P. Hicks, M.D.
Lee A. Weatherbee, M.D.



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DEPARTMENTAL OVERVIEW

DEPARTMENTAL OVERVIEW
1996/1997

Major institutional changes within the Medical Center have impacted on the Department and have provided us with a number of opportunities. Continuing implementations of the CDS agreement and the Faculty Group Practice (FGP) plan, together with institutional development of revenue "withhold" and incentive plans have caused us to focus on innovative strategies to become more efficient and cost-effective. Implementation of the Cost Efficiency Plan imposed by the institution have caused us to reduce the operating budget for the clinical laboratory services (both Anatomical and Clinical Pathology services) by more than 10%. While these changes have been challenging, operating efficiencies of the services have improved, as has the educational activities as related to House Officers. This is due to the fact that 14 separate clinical laboratory groups have been consolidated into 5 groups. With continuing demands for incremental services, especially by clinical activities such as the bone marrow transplant program, it has become a great challenge to provide sufficient staffing for laboratories such as the Blood Bank, Cytogenetics Laboratory, and the Tissue Typing Laboratory to meet these demands.

Consistent with the unified FGP and encouraged by the institution to have effective financial incentive plans to reward for greater efficiencies and incremental revenue, the Department has forwarded to the Dean's Office a request for Risk II Incentive (or the equivalent), which we have not previously had in place. By setting aside a certain portion of what has been flexible revenue (which in the past had been used for academic enhancement and related activities), the Department should have in place effective 1 September 1997 a new incentive plan that will meet the objectives listed above. It will be especially important to ensure that this program will not undermine the academic foundations of the Department or generate within faculty members an attitude that we are now moving to a private practice setting. It will be the challenge for everyone to see to it that the prevalent attitude of each faculty member is one of dedication to and pride in belonging to a great academic enterprise.

During the past year significant administrative changes occurred, with Dr. Joseph C. Fantone assuming Directorship of the Division of Anatomic Pathology, and Dr. Joel Greenson assuming title of Director of Surgical Pathology. In addition, Dr. Steven L. Kunkel became Co-director of the Division of General Pathology, assuming responsibility with Dr. Ward for this Division.

Teaching activities

Faculty members continue to fill leadership roles as course directors, sequence coordinators, and Director of Component I/II in the Medical School curriculum. Several faculty members are recognized as exceptional teachers. The 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 quarter of the Medical School class each year and receive very high evaluations. The summer program for minority first year medical students enrolled 10 students this year. Three fourth year students who participated in the program entered Pathology residency training. A new course to meet the specific needs of the Medical Illustration students was developed. This course received excellent evaluations by students. The Department continues to present a semester-long Dental Pathology course. This course is being restructured to be focused on the specific needs of dental students and engage them in more active learning activities. The Pathology graduate program was successful in recruiting two new students (including an M.D./Ph.D. woman student) and graduating two students this past year. The Department along with Microbiology and Immunology initiated a joint

effort for a combined Immunobiology graduate program. This is in part supported by an NIH Experimental Immunology training grant. 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 of whom 13 are women and 4 under-represented minority. Last year all graduates of the house officer program found desirable positions, including fellowships at Stanford and University of Alabama Birmingham, as well as positions at Cleveland Clinic, University of Texas Southwestern Medical School (Dallas), Northwestern Medical School, and Indiana University.

Clinical service activities

Despite implementation of the institutionally-mandated cost efficiency program, growth in several major clinical programs, the opening of the new Cancer and Geriatrics Center, and expansion of M-Labs activities, the Clinical Laboratories continued to provide excellent, full-spectrum service. In 1996-97, the Clinical Laboratories performed more than 3 million billable analyses. The maintenance of high quality and the reduction in cost per unit of activity provided by the Clinical laboratories, in the face of increasing complexity of demands, is a testimony to the professionalism of the staff and the management capabilities of the laboratory directors and senior laboratory personnel. The Clinical Laboratories successfully completed the biannual on-site College of American Pathologists (CAP) inspection. The Divisional Quality Assurance Program, as a component of the Departmental Program for Excellence, continues to be at the forefront both within the University of Michigan Medical Center and among clinical laboratories located in tertiary care facilities throughout the United States. Maintenance of the delicate balance among quality service, cost effective testing, utilization control, and the research and development, which characterizes an academic institution, will be a continuing challenge.

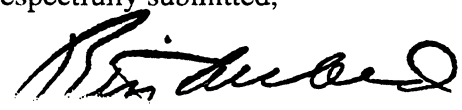
1996-97 was marked by several major initiatives. In response to pressures to reduce our cost/unit of laboratory service and to improve operating efficiency, a comprehensive plan for laboratory reorganization was initiated. Reorganization entailed a nearly 10% reduction in operating budget, consolidation of several laboratories, and reorganization of inpatient phlebotomy services. Major cost efficiencies were gained through agreements with the Southeastern Michigan American Red Cross (blood products) and Johnson and Johnson (chemistry instruments and reagents). The initial phases of this plan have been implemented with the expectation that laboratory reorganization will be completed by late autumn. This reorganization will entail further consolidation of the Immunopathology, Ligand Assay, Toxicology/Therapeutic Drug Monitoring, and Chemistry Laboratories into a single unit, consolidation of the Hematology, Flow Cytometry, and Coagulation Laboratories (formerly Internal Medicine) into a single unit, and streamlining of the administrative structure of these and other laboratories. Second, the Clinical laboratories continued to reallocate resources needed to meet the continuing and marked increase in transplantation activity (especially bone marrow) experienced in 1996-97. Augmentation of the capabilities of the Blood Bank, Tissue Typing and Cytogenetics Laboratories was contributory to this process. Finally, the Clinical laboratories have responded to the institutional initiative to acquire broader primary care capabilities within the region. This activity has been coupled with expansion of on-site primary care capabilities within the region. This activity has been coupled with expansion of on-site point-of-care testing and data handling activities. In preparation for the future, the Clinical Laboratories continue to support the growing M-Labs outreach program, to forge strong collaborative relationships with local and regional reference laboratories and intensify our role in institutional utilization management. The activity in Surgical Pathology and Cytopathology continues to be stable and increasing in selected areas. With the opening of the Cancer Center and

expansion of clinical programs, there has been an increasing demand for fine needle aspiration and dermatopathology support. The extramural clinical consultation service continues to thrive reflecting the national and international reputation of the faculty. Department faculty members play major roles in multidisciplinary clinical programs. The Department maintained an active presence in the local community through its support of the Washtenaw County Medical Examiner's Office.

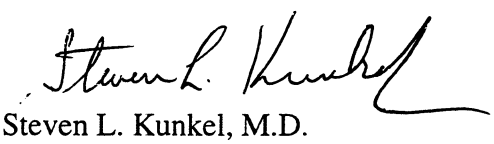
Research activities

The research activities in the Department of Pathology continue to be very vibrant, as indicated by the successful acquisition of extramural research support, the publication record of our faculty, and the number of national and international postdoctoral fellows who seek training in our laboratories. During the past year, expenditures of active grants and contracts credited to research efforts associated with the Department of Pathology totaled nearly $9.5 million. This total includes approximately $6.8 million in direct expenditures and $2.7 in indirect expenditures. Presently, in the Department there are over 57 individual research grants from the National Institutes of Health, which totals over $9.028 million in direct and indirect funds to the Department of Pathology and the University of Michigan. Two faculty members hold MERIT grants from the National Institutes of Health. In addition, the Department's faculty have been successful in competing for research funds from other extramural sources, including grants from NSF, U.S. Army, American Heart Association, American Lung Association, as well as contract grants from industry. The publication record of members of the Department is a notable attribute to the active research efforts in both the experimental and clinical arena. These peer reviewed publications cover diverse research interests, including anatomical pathology, clinical pathology, and basic cellular and molecular mechanisms of disease activity. During this past year, the faculty members in the Department have collectively published hundreds of scholarly articles in numerous scientific journals. Many of these articles are published in journals with a high citation index impact. Our faculty are involved in peer review of submitted scientific articles, 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 post doctoral fellows in the various laboratories. The Department of Pathology has the second largest number of post doctoral fellows in the Medical School. Post doctoral scholars from 11 different countries have actively sought research positions in our Department to enhance their research careers. Our faculty members continue to provide expertise for both internal and external program review processes. These include serving as ad hoc and permanent member 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 chairing/cochairing different clinical and experimental scientific meetings and conferences.

Respectfully submitted,



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



Steven L. Kunkel, M.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 1996 - 30 JUNE 1997

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 - 6 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 - 4 contact hours.
   3. Principles of Medical Ethics - small group seminar - 2 hours
   4. Introductory Histopathology Sequence, Sequence Director, Lecturer, Lab Instructor - 28 contact hours (8 lectures, 20 lab hours).
   5. Pathologic correlation in Gross Anatomy Labs - 6 contact hours.

B. Sophomore Medical Class:
   1. Cardiovascular Sequence - 4 lecture hours.
   2. Cardiovascular Sequence - Pathology Lab Coordinator.
   3. Pathology Lab Instructor - all sequences, 50 contact hours.

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

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

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

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

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

H. Invited Lectures:
   1. Keynote Address, Medical School White Coat Ceremony - August, 1996.

I. Production of Teaching Materials:
   1. Glass slide loan sets with accompanying syllabus for M-1 Histopathology Sequence.

J. Honors:
   1. Elected Class Marshall, Medical Class of 1997.

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. Mycophenolate in prevention of cardiac allograft rejection, with J. Nicklas.
D. Combidex 7227 as MRI agent to evaluate lymph nodes, with J. Brunberg.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member, Pathology House Officer Selection Committee.

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

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

REGIONAL AND NATIONAL:

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

V. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Lee, D.Y., Williams, D.M., and Abrams, G.D.: The Dissected Aorta Part II. Differentiation of the True from the False Lumen. Radiology, 1997; 203:32-36.

BOOKS/CHAPTERS IN BOOKS:

1. Abrams, G.D. in Price, S.A. and Wilson, L. M.(eds) Pathophysiology: Clinical Concepts of Disease Processes, 5th ed. Mosby, 1997
   Chapter 1: General Concepts of Disease, 3-5.
   Chapter 3: Cellular Injury and Death, 28-37.
   Chapter 4: Response of the Body to Injury: Inflammation and Repair, 38-60.
   Chapter 6: Response of the Body to Infectious Agents, 84-91.
   Chapter 7: Disturbances in Circulation, 92-107
   Chapter 8: Disturbances in Growth, Cellular Proliferation, and Differentiation, 108-124.
2. Abrams, G.D. in Ming, S.C. and Goldman, H. (eds) Pathology of the Gastrointestinal Tract, 2nd ed. Williams & Wilkins, 1997 in press.
   Chapter 28: Infectious Disorders of the Intestines.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

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.
C. Graduate Students/Fellow:
   1. Walter Henricks, Clinical Chemistry ACGME Fellowship.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Biochemistry Section, Clinical Pathology Laboratories.
B. M-Labs Technical Group.

REGIONAL AND NATIONAL:

A. Board of Directors, American Board of Clinical Chemistry.
B. Clinical Chemistry Examination Committee, American Board of Clinical Chemistry.

C. Task Force on Postdoctoral Training and Certification, American Board of Clinical Chemistry.
D. Faculty, National Toxicology Review Course, American Association for Clinical Chemistry.
E. Executive Committee/Journal Management Group, Clinical Chemistry Journal.
F. Task Force on Journal Operations, American Association for Clinical Chemistry.
G. Member, Academy of Clinical Laboratory Physicians and Scientists.
H. Member, Clinical Ligand Assay Society.
I. Member, American Association for Advancement of Sciences.
J. Member, Association of Clinical Scientists.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

OTHER:

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

INVITED LECTURES/SEMINARS:

1. "Rationales for Clinical Toxicology Screening", Botsford Hospital, Detroit, Michigan, September, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kugler, A.R., Olson, S.C., Annesley, T.M., Nordblom, G.D., and Koup, J.R.: Cross-reactivity of fosphenytoin in two human plasma phenytoin immunoassays. Clin. Chem., submitted.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

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 - two full class lectures.
   2. Pathology 630 (dental) - one full class lecture.

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

C. Interdepartmental:
   1. G-I Tumor Conference - Every other Wednesday (three hours/month).
   2. Liver Biopsy Conference - one hour per month.
   3. Gastrointestinal Biopsy Conference for fellows and staff, 6 hours.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Hepatic histopathologic changes in methotrexate-treated psoriatics, with Andrew Flint and members of the Gastroenterology Division.
B. National Study of Thymosin Treatment of Chronic Hepatitis B with Milton Mutchnick (Wayne State), and others.
C. Classification of gastric polyps with Priscilla Chamberlain.
D. Genetic changes in hepatoma with Graeme Macdonald, Rick Boland and Joel Greenson.
E. The changing appearance of ulcerative colitis in biopsies with time and treatment, with Celina Kleer
F. Stromal tumors of the abdominal colon and anorectum, with Joe Tworek, Joel Greenson, Sharon Weiss, and John Goldblum (Cleveland Clinic)

G. The effect of diet on recurrence rates of colonic adenomas, with Klaus Lewin (UCLA) and Arthur Schatzkin (NCI)
H. Clinical trial of difluoromethylornithine in Barrett's esophagus, with Dean Brenner of the U of Mich, Gary Stoner of Ohio State Univ, and Stuart Spechler, Donald Antolioli and Anil Rustgi of Harvard.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Coordinator for Pathology, Randomized Therapeutic Trail in Cancer of the Esophagus, International Organization for Statistical Studies of Diseases of the Esophagus, Paris, France.
B. Visiting Pathologist for Regional Workshops on Pathologic Diagnosis in Inflammatory Bowel Disease, sponsored by the Crohn's and Colitis Foundation of America and the University of Chicago.
C. Central Pathologist, Polyp Prevention Trial, National Cancer Institute, Washington, DC
D. Member, Editorial Board, Human Pathology.
E. Member, Editorial Board, Modern Pathology.
F. Member, Editorial Board, American Journal of Surgical Pathology.
G. Reviewer, Archives of Pathology and Laboratory Medicine, Cancer, Gastroenterology, Annals of Internal Medicine, and American Journal of Gastroenterology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Lectures: 1. "A whirlwind tour through esophagogastric inflammations".
2. "Precancers, dysplasias, in situ cancers and intramucosal cancers from esophagus to anus". Pathology Update for Practicing Pathologists: Recent Advances and Selected Topics. American Society of Clinical Pathologists course, Chicago, IL, July, 23, 1996
2. Lectures: 1. "Epidemiologic and histologic distinctions for carcinomas arising around the gastroesophageal junction." 2. "The value of cytology in non-dysplastic Barrett's esophagus." 3. "The morphologic features of achalasia." 4. "The diagnostic criteria for early invasion in esophageal carcinomas." 5th International Polydisciplinary Congress, International Organization for Statistical Studies on Diseases of the Esophagus, September 4-7, 1996, Paris, France.

3. Lectures: 1. "Helicobacter pylori and its gastritis"; 2. "Colitides other than ulcerative colitis". Presented at the Clinical Gastroenterology Symposium. Eastern Maine Medical Center, Bangor, Maine, September 19, 1996
4. Lecture; "The pathologist's role in inflammatory bowel diseases". Maine Society of Pathologists, Bangor, ME, September 16, 1996
5. Visiting Professor Lecture: "Annoying gut biopsies", Department of Pathology and Laboratory Medicine, Albany Medical Center, Albany, NY, Nov 6, 1996
6. Visiting Professor, Departments of Pathology, Cornell University and Memorial-Sloan Kettering Hospital, New York, NY. Microscopic case seminar on GI biopsies, Visiting Professor Lecture: "The role of the pathologist in inflammatory bowel diseases", Dec 16, 1996.
7. Half day course with McKenna BJ: Practical Approaches to Gastrointestinal Biopsy Pathology: How Much Clinical Data is Essential? American Society of Clinical Pathologists Annual Meeting: San Diego, CA , September, 1996. and at an ASCP weekend, Las Vegas, NV, Feb, 1997
8. Visiting Professor, Department of Pathology, Medical College of Virginia, Lecture: Annoying GI Biopsies, Richmond, VA, April 18, 1997
9. Lecture: Weird Colon Cancers; What Do They Do to the Database", Tumor Board presentation, St Joseph Mercy Hospital, Pontiac MI, April 23, 1997
10. Half day course: "Neoplastic Diseases of Intestine", American Society of Clinical Pathologists, St Petersberg, FL, May, 1997.
11. Visiting Professor, Department of Pathology, Loyola University, Maywood, IL, Microscopic case seminar on GI biopsies, May 19, 1997
12. Slide Seminar: It Takes Guts to be a Gastrointestinal Pathologist, Chicago Society of Pathologists, May 19, 1997.
13. Microscopic tutorial in GI biopsy pathology for house staff and faculty, Department of Pathology and Laboratory Medicine, Albany Medical Center, Albany NY, June 18, 1997

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Huang JC, Appelman HD. Another look at the chronic appendicitis resembling Crohn's disease. Mod Pathol. 9:975-981, 1996
2. Goff JS, Barnett JL, Pelke T, Appelman HD. Collagenous colitis: histopathology and clinical course. Am J Gastroenterol. 92:57-60, 1997
3. Tworek JA, Appelman HD, Singleton TP, Greenson JK. Stromal tumors of the jejunum and ileum. Mod Pathol, 10:200-209, 1997
4. Lucey, MR, Carr K, Beresford TP, Fisher LR, Shieck V, Brown KA, Campbell DA, Appelman HD. Alcohol use after liver transplant in alcoholics: a clinical cohort follow-up study. Hepatology. 25:1223-1227, 1997

BOOKS/CHAPTERS IN BOOKS:

1. Lewin KJ, Appelman HD. Tumors of the Esophagus and Stomach Fascicle. Volume 18, Third Series, Atlas of Tumor Pathology, Armed Forces Institute of Pathology, Washington, D.C., 1996.

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

1. Kleer CG, Appelman HD. Ulcerative colitis: patterns of involvement in colorectal biopsies with time. Mod Pathol. 10:58A, 1997.
2. Tworek JA, Goldblum JR, Weiss SW, Greenson JK, Appelman HD. Stromal tumors of the colon. Mod Pathol. 10:66A, 1997.
3. Tworek JA, Goldblum JR, Weiss SW, Greenson JK, Appelman HD. Stromal tumors of the rectum and anus. Mod Pathol. 10:66A, 1997.
4. Schoen RE, Weissfeld J, Burt R, Lance P, Iber F, Corle D, Cranston L, Hasson M, Lewin K, Appelman H, Schatzkin A. When is colonoscopy necessary: - Distal-proximal adenoma relationships in the polyp prevention trial (PPT). American Society of Gastrointestinal Endoscopy, Washington, DC, May 14, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Director, Histocompatibility and Immunogenetics Laboratory

II. TEACHING ACTIVITIES:

A. Director, Basic Immunology Course for Allergy Fellows-In-Training
B. Instructor, Host Defense Course, First-Year Medical School Students
C. Attending, General Internal Medicine Service
D. Instructed Pathology Residents, Renal Fellows and Allergy Fellows in HLA typing
E. Supervised undergraduate students in research:
Jill Knapp
F. Supervisor for:
Allergy Fellows: Drs. Alice Chou, Anna Dobracki
Postdoctoral Fellows: Drs. Ali Motani, James Bretz
G. Director, Allergy Training Program

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIAID - National Institutes of Health, RO1 A I 37141-01, "Immune Responses to Thyroid Peroxidase", J. Baker, Principal Investigator, 01/01/95 - 12/31/97, (budget approximately $653,708)
B. University of Michigan-MAC, National Institutes of Health, D. Fox, Principal Investigator, (2 P0 AR20557-15), "Hybridoma Core", J. Baker, Principal Investigator, 01/01/93 - 12/31/97, (budget approximately $276,765)
C. Michigan Diabetes Research and Training Center, National Institutes of Health, D. Greene, Principal Investigator, (5 P60 DK20572-16), "Hybridoma Core", J. Baker, Principal Investigator, 12/01/92 - 11/30/97, (budget approximately $171,413)
D. Syntex Corporation, (ICM MYC/1880/USA), "Long-Term Effects of Mycophenolate Mofetil in Renal Transplants", J. Baker, Principal Investigator, 07/01/93 - 06/30/97, (budget approximately $53,904)

E. Michigan Molecular Institute, "Development of Starburst Dendrimers as a Gene Transfer Agent", J. Baker, Principal Investigator, 07/01/95-12/31/97, (budget approximately $299,901)
F. Elsa U. Pardee Foundation, "Dendrimer Vector for Antisense Nucleotide Therapy of Cancer", J. Baker, Principal Investigator, 10/01/95-09/30-97, (budget $151,845)
G. DARPA, "Nanomolecular-Based Agents for Pathogen Counter Measure", J. Baker, Principal Investigator, 2/1/97-1/31/01, (budget $8,708,397)
H. NIH/NIAMS, "Gene Thereapy for Rheumatic Disease: Mechanisms of Perifollicular Transfection", B. Roessler, Principal Investigator, 9/30/96-9/29/01, (budget $1,608,982)
I. NIH/NIAID, "Mucosal Gene Transfer Using Dendrimer Polymers", J. Baker, Principal Investigator, 4/1/97-3/31/02, (budget $1,110,590)

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

1. Editor, JAMA Primer

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Gene Transfer Using Starburst™ Dendrimer Polymers." Cambridge Healthtech Institute Conference on Artifical Self-Assembling Systems, Coronado CA, November 1996.
2. "Gene Transfer Using Synthetic Polymers and Lipids." Michigan State University, Neuroscience Program Seminar, East Lansing, MI, March 1997.

SCIENTIFIC ACTIVITIES:

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

J. Reviewer, Journal of Endocrinological Investigation
K. Reviewer, The American Journal of Medicine
L. Regional Accreditation Commissioner, American Society for Histocompatibility and Immunogenetics

WORKSHOPS/PANEL DISCUSSIONS:

The Endocrine Society, Minneapolis, MN, June 1997.

VI. PUBLICATIONS:

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

1. Bielinska AU, Kukowska-Latallo JF, Baker JR Jr. The interation of plasmid DNA with polyamidoamine dendrimers: Mechanism of complex formation and analysis of alterations induced in nuclease sensitivity and transcriptional activity of the complexed DNA. Biochimica et Biophysica Acta, in press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Qin L, Pahud DR, Ding Y, Bielinska AU, Kukowska-Latallo JF, James JR Jr, Bromberg JS. Efficient transfer of genes into murine cardiac grafts by Starburst™ polyamidoamine dendrimers.
2. Arscott PL, Knapp J, Rymaszewski M, Bartron JL, Bretz JD, Thompson ND, Baker JR Jr. Regulation of Fas (APO-1, CD95) mediated apoptosis in thyroid cells.

BOOKS AND CHAPTERS IN BOOKS:

1. Kloos RT, Baker JR Jr: Thyroiditis. In: Robert ER (ed): Conn's Current Therapy (W.B. Saunders Company, 1996,) 634-641.
2. Baker JR Jr, Bielinska A, Johnson J, Yin R, Kukowska-Latallo JF. Efficient transfer of genetic material into mammalian cells using Starburst dendrimer as synthetic vectors. In: Felgner PL, Heller MJ, Lehn P, Behr JP, Szoka JR FC (eds): Artificial Self-Assembling Systems for Gene Delivery (American Chemical Society, Washington, DC, 1996) 129-145.

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

1. Fox RE, Stoll ST, Gin GY, Schall CA, Baker JR Jr. Mid and high resolution typing obtained through a single polymerase chain reaction. 22nd Annual Meeting, American Society for Histocompatibility and Immunogenetics, San Diego, CA, Oct 1996.
2. Schall CA, Baker JR Jr. Kidney transplantation from a blood group A_2 donor to a group O recipient with a 7 HLA antigen match. 22nd Annual Meeting, American Society for Histocompatibility and Immunogenetics, San Diego, CA, Oct 1996.

3. Baker JR Jr. The use of autoantibodies in the diagnosis of autoimmune thyroid disease. The Endocrine Society, Minneapolis, MN, June 1997.
4. Kukowska-Latallo JF, Raczka Wojtowicka E, Chen C, Rymaszewski M, Baker JR Jr. Surfactant provides a major barrier to non-viral gene transfer in the endobronchial tree. Department of Pathology, University of Michigan, Ann Arbor, MI, June 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Diagnostic Electron Microscopy, Veterans Affairs Medical Center, Director of Electron Microscopy Center of Excellence.
B. Cytopathology, Veterans Affairs Medical Center, Director Center of Excellence.
C. Surgical Pathology, Veterans Affairs Medical Center.
D. Fine Needle Aspiration, Veterans Affairs Medical Center.
E. Autopsy Pathology, Veterans Affairs Medical Center.
F. Tumor Board, Veterans Affairs Medical Center.
G. Consultant: Diagnostic Electron Microscopy; Allen Park VAMC, University Hospitals.
H. Chief Pathology and Laboratory Medicine, Ann Arbor and Toledo OPC, Veterans Affairs Medical Center.

II. TEACHING ACTIVITIES:

A. Pathology House Officer elective: Diagnostic Electron Microscopy and Cytopathology
B. Diagnostic Electron Microscopy Case Conferences.
C. Instructor, National Laboratory Practicum Program, Department of Veterans Affairs

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Tumor suppressor gene loci on chromosome 18 and prognosis in squamous cell carcinoma (co-investigator, Thomas E. Carey, Principal Investigator).
B. Head and Neck Oncology Program Project (with 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).
F. Detection of *Pneumocystis carinii* in cytology specimens.

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. Medical School Admissions Committee.
I. Dean's Committee, Veterans Affairs Medical Center.
J. Facility Management Committee, VISN#11, Department of Veteran Affairs

REGIONAL AND NATIONAL:

A. Department of Veterans Affairs, Veterans Health Administration, Patient Care Services, Chief Consultant Officer, Diagnostic Services Strategic Healthcare Group.
B. Department of Veterans Affairs, Veterans Health Administration; Acting 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/DAD/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.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Short Course, Closed Lung Biopsy Interpretation, with Andrew Flint, USCAP, Washington, D.C.
2. Beals TF, Reorganization of VHA and the Pathology Regional commissions. Quality Oversight and Regulations in Pathology and Laboratory Medicine Conference, Chicago, 1996.
3. Beals TF, VHA Management Databases; Laboratory Management Index Program National Satellite Program, VHA, Salt Lake City, 1996.

4. Beals TF, Telemedicine in the Veterans Health Administration, Intercom '97 Conference, Miami 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Milik AM, Buechner-Maxwell VA, Sonstein J, Kim S, Seitzman GD, Beals TF, Curtis JL. Lung lymphocyte elimination by apoptosis in the murine response to intratracheal particulate antigen. J Clin Invest 99:1082-1091,1 997.
2. Su L, Beals T, Bernacki EG, Giordano TJ. Spindle epithelial tumor with thymus-like differentiation: A case report with cytologic, histologic, immunohistologic and ultrastructural findings. Mod Pathol 10:510-514, 1977.
3. Jones JW, Raval JR, Beals TF, Worsham MJ, Van Dyke DL, Esclamado RM, Wolf GT, Bradford CR, Miller T, Carey TE. 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.
4. Bradford CR, Zhu S, Poore J, Beals T, Fisher SG, Wolf GT. p53 mutations in advanced laryngeal carcinoma. Archives of Oto-NHS, 1996.

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 1996 - 30 JUNE 1997

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 referred by other hospitals in- and out-of-state throughout the year.
D. Consultations on brain biopsies, autopsied brains and rheumatology cases.

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

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

F. Primary CNS vasculitis, with J. Trobe and A. Alrawi, Ophthalmology.
G. Evaluation of temporal lobectomy/hippocampectomy cases with epilepsy group.
H. Edited the chapter on brain tumors written by Dr. H.S. Greenberg, neurooncology and prepared illustrations with figure legends for it.
I. Histology and histochemistry of orbicularis muscle, normal and aging.
J. Collaboration with EMG group, Radiology (S. Gebarski, M.D.), pulmonary/internal medicine on various projects.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL:

A. Member of the Admissions Committee.

REGIONAL AND NATIONAL:

A. Lectures on muscle, nerve and brain pathology to pathology residents of St. John Hospital in Detroit.
B. Consulting with outside pathologists, neurologists and family practitioners on muscle and nerve biopsies performance and interpretation.
C. Member, American Association of Neuropathologists, IAP, and AAN.
D. Attended IAP, American Association of Neuropathologists and International Society of Neuropathologists meetings.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Tworek, J., Mikhail, A. and Blaivas, M.: Meningioma: Local recurrence and metastasis diagnosed by fine needle aspiration. Acta Cytol., 41, 3:946-947, 1997.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Robertson, P.L., Pavkovic, I., Donovan, C. and Blaivas, M.: Immature teratoma of the leptomeninges in an 8-year-old child: unusual presentation with recurrent transient oculomotor nerve pulses and rapid progression to diffuse brain ischemia. Pediatric Neurology, accepted to.

2. Wang, J.M., Zheng, H., Blaivas, M. and Kurachi, K.: Long-term, systemic production of human factor IX in mice by non-viral skeletal myoblast-mediated gene transfer: feasibility of repeat cell implantation. Accepted to Blood.
3. Levy, R.A. and Blaivas, M.: Desmoplastic medulloblastoma: magnetic resonance imaging findings. Am. J. Neuroradiol., accepted to.
4. Robertson, P.L., Muraszko, K.M., Blaivas, M. and Brunberg, J.A.: Symptomatic leptomeningeal fibrosis: association with delayed diagnosis of an intracranial PNET. Pediatric Neurology, accepted to.
5. Sorenson, E.J., Sima, A.A.F., Blaivas, M., Sawchuk, K. and Wald, J.J.: Clinical features of perineuritis. Muscle and Nerve, accepted to.
6. Ross DA, Kish P, Muraszko KM, Speed G, Blaivas M, Strawderman M: Chemoprevention of ethylnitrosourea-induced rat gliomas by retinoic acid. To: Neurosurgery.
7. Cemeroglu AP, Blaivas M, Muraszko KM, Robertson PL, Vasquez DM. Lymphocytic hypophysitis presenting with diabetes insipidus in a 14-year old girl. Accepted To: Peds Endocrinol.

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

1. Gebarski, S. and Blaivas, M.: Five germinal matrices, not one. Implications in understanding primary neurodevelopmental brain neoplasm. To be presented in Neuroradiology Fall meeting.
2. Sorenson, E.J., Sima, A.F., Blaivas, M., Sawchuck, K. and Wald, J.J.: Clinical features of perineuritis. Presented at AAN meeting, Fall 1996.
3. Bruch LA, Blaivas M, Parisi JE: Primary cerebral angiitis with selective permeability and serum protein extravasation. J Neuropathol Exp Neurol, 56(6):608, 1997; Platform presentation at the American Association of neuropathologists meeting, June 1997.
4. Gebarski S, Blaivas M: Mucin: an underappreciated cause for high attenuation in CNS lesions. Presented at the Neuroradiology meeting, Fall 1997.
5. Perucchini D, Delancey JOL, Blaivas M: Evidence of major myopathic changes in the striated urethral sphincter muscle in the female. Presented at the ICS International conference in Japan and at the American Neurogynecological Society meeting in Tucson, Arizona.
6. Smith AG, Blaivas M, Russell JW, Urbanits S, Grisold W, Feldman EL: The clinical and pathologic features of focal myositis. For: AAEN meeting, Sept. 1997.

BOOKS AND CHAPTER IN BOOKS:

1. McKeever, P.E., Blaivas, M. and Nelson, J.S.: The diagnosis of brain and spinal tumors by conventional light microscopic methods (Chapter 2), in, Diagnostic Neuropathology, Mosby-Year Book, Inc., Philadelphia, Pennsylvania, 1997.
2. Sima, A.A.F. and Blaivas, M.: Pathology of the peripheral nerve biopsy, Chapter, in, Diagnostic Neuropathology, Mosby-Year Book, Inc., 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Graduate Students:
None.

B. Postdoctoral Fellow:
1. Jianming Fang, M.D.

C. Undergraduate Students:
None.

D. Courses:
1. Anatomy and Cell Biology 525 (Skeletal tissues)
2. M2 Pathology (Laboratory instructor)
3. Molecular Cell Biology 500 (Section head, extracellular matrix)
4. Pathology 581 (Course director)

E. Continuing Medical Education:
None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Direct Osteoinductive Gene Transfer", Sponsored Research Agreement, Matrigen, Inc.

B. Collaborator, "Center for Restoration of Oral Health", National Institutes of Health, AR44043

PENDING:

A. Co-Investigator, "Gene Delivery Systems for Cardiovascular Diseases", National Institutes of Health
B. Co-Investigator, "Anabolic Mechanisms of PTH Action in Bone", National Institutes of Health

PROJECTS UNDER STUDY:

A. Molecular cloning of activins, members of the TGF-b superfamily
B. Direct gene transfer in vivo

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Biomechanics Core Steering Committee, Multipurpose Arthritis and Musculoskeletal Diseases Center

DEPARTMENTAL:

A. Oversight Committee, Graduate Program, 1989 -

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Ad-hoc Reviewer:
Journal of Biological Chemistry
American Journal of Pathology
Orthopedic Research and Education Fund

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

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

INVITED LECTURES/SEMINARS:

1. "Gene transfer and tissue engineering", Invited lecture, Johnson & Johnson Professional, Inc., Raynham, MA, September 10, 1996

2. "Direct gene transfer in vivo using the GAM technology", Invited presentation, Cold Spring Harbor Gene Therapy meeting, Cold Spring Harbor, NY, September 25-29, 1996
3. "Gene transfer and tissue engineering", Invited lecture, Advanced Tissue Sciences, Inc., San Diego, CA, October 30, 1996
4. "Tissue engineering via direct in vivo gene transfer", Invited presentation, alza, Palo Alto, CA, October 31, 1996
5. "Tissue engineering via direct in vivo gene transfer", Invited presentation, Howmedica, Newark, NJ, November 5, 1996
6. "Tissue engineering via direct in vivo gene transfer", Invited presentation, Sprout Group, Menlo Park, CA, November 13, 1996
7. "Tissue engineering via direct in vivo gene transfer", Invited presentation, Norian, Cupertino, CA, November 14, 1996
8. "Tissue engineering via direct in vivo gene transfer", Invited presentation, Alta Partners, San Francisco, CA, November 14, 1996
9. "Tissue engineering via direct in vivo gene transfer", Invited presentation, Sierra Ventures, Menlo Park, CA, November 14, 1996
10. "Tissue engineering via direct in vivo gene transfer", Invited presentation, Robertson Stephens & Company, San Francisco, CA, November 15, 1996
11. "Tissue engineering via direct in vivo gene transfer", Invited presentation, Intermedics Orthopedics/Denver, Inc., Denver, CO,
12. January 6, 1997
13. "Pharmaceutical Delivery of DNA", Invited presentation, Genzyme Corporation, Boston, MA, February 28, 1997
14. "Cytokines and Extracellular Matrix" (Discussion leader / session chair) Elastin and Elastic Tissue Gordon Conference, Meriden, NH, July 20-25, 1997
15. "Pharmaceutical Gene Delivery for Tissue Repair / Regeneration", Invited presentation, Biomaterials: Biocompatibility and Tissue Engineering Gordon Conference, Plymouth, NH, July 20-25, 1997

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ducy, P., Desbois, C., Boyce, B., Pinero, G., Story, B., Dunstan, C., Smith, E., Bonadio, J., Goldstein, S., Gundberg, C., Bradley, A., and Karsenty, G. (1996) Incresed bone formation in osteocalcin-deficient mice. Nature 382, 448-452.
2. Fang, J., Yin, W., Smiley, E., Wang, S.Q., and Bonadio, J. (1996) Molecular cloning of the mouse activin bE subunit gene. Biochem. Biophys. Res. Comm. 228, 669-674.
3. Fang, J., Wang, S.Q., Smiley, E., and Bonadio, J. (1997) Genes coding for mouse activin bC and bE are closely linked and exhibit a liver-specific expression pattern in adult tissues. Biochem. Biophys. Res. Comm. 231, 655-661.
4. Hammnod, R.W., Oana, H., Schwinefus, J.J., Bonadio, J., and Morris, M.D. (1997) Capillary electrophoresis of supercoiled and linear DNA in dilute hydroxyethyl cellulose solution. Anal. Chem. 69, 1192-1196.

5. Yin, W., Fang, J., Smiley, E., and Bonadio, J. TGF-bp structural motifs are the site of covalent binding between LTBP-3 and latent TGF-b1. J. Biol. Chem., in press.
6. Fang, J., Li, X., Smiley, E., Francke, U., Mecham, R.P., and Bonadio, J. Mouse latent TGF-b binding protein-2: molecular cloning and developmental expression. Biochim. Biophys. Acta, in press.

BOOKS/CHAPTERS IN BOOKS:

1. Labhasetwar V, Ciftci K, March K, Chen B, Muller DWM, Bonadio J, Levy RJ. (1997) Gene-based therapies for restenois. Advanced Drug Delivery Reviews 24, 109-120.

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

1. Schwinefus, J.J., Hammond, R.W., Oana, H., Wang, S-C., Bonadio, J., Levy, R.J., and Morris, M.D. Dynamics of supercoiled plasmids during capillary electrophoresis in dilute linear polymers. High Performance Capillary Electrophoresis meeting, Anaheim, CA, January 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Director, Forensic Pathology and Medicolegal Autopsies.
B. Supervision of Medicolegal Autopsies (six months, six days per week).
C. Supervision of Hospital Autopsies (six weeks, plus one weekend).
D. Deputy Medical Examiner, Washtenaw County, Coordinator of Medical Examiner Investigator activities for University Hospitals, Consultant to Medical Examiner Investigators for University and St. Joseph Mercy Hospitals.
E. Courtroom testimony, Washtenaw, Wayne, Livingston, and Jackson Counties (District and Circuit courts).
F. Intradepartmental Consultant, Surgical Pathology (for specimens of medicolegal interest), and to pathology faculty for courtroom testimony regarding medicolegal matters and referral cases which involve medicolegal issues.

II. TEACHING ACTIVITIES:

A. Autopsy supervision, pathology house officers (including gross autopsy and case signout).
B. Twice-weekly gross Autopsy Conference.
C. Advisor, extended Gross Autopsy Conference.
D. Autopsy supervision, M4 (Senior Medical Student) clerkship, and M2 (Sophomore Medical Student) autopsy requirement. .
E. Monthly Forensic Pathology Conference (Pathology House Officer Series), September 1996 - April 1997.
F. Forensic Pathology review for ASCP Pathology Resident In-Service Examination and American Board of Pathology Certifying Examinations to Pathology House Officers (April, 1997).
G. Presentation to University of Michigan Nursing Students, "Introduction/Orientation to the Autopsy Room", September, 1995.
H. "Facing Alcohol Challenges Together (F.A.C.T.)" Program, Biweekly Presentation to Teenage Substance Users.

III. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

INTERDEPARTMENTAL/INTERDISCIPLINARY:

A. Consultant, Office of Clinical Affairs/Risk Management.
B. Participant, Sentinel Events, Mott Hospital.

IV. INVITED LECTURES AND SEMINARS:

1. Presentations to Michigan State Police Officers in training (Recruits), "The Role of the Forensic Pathologist/Medicolegal Autopsy in Death Investigation", Fall, 1996, and Spring, 1997.
2. Guest Lecturer, "Introduction to Forensic Sciences", Undergraduate Course, Michigan State University School of Criminal Justice, "Introduction to Forensic Pathology", April 10, 1996.
3. Presentation: Michigan State University Undergraduate Criminal Justice Association, "Forensic Pathology", November 17, 1996.
4. Presentation: Transplantation Society of Michigan Continuing Education Program, "Organ and Tissue Harvesting in Medical Examinaer's Cases", January 28, 1997.
5. Presentation: Michigan Ontarion Identification Association (M.O.I.A.) 1997 Spring Training Conference, "Lessons from Medicolegal Masquerades", May 17, 1997.

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

ANNUAL DEPARTMENT REPORT
1 JULY 1996 - 30 JUNE 1997

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 greivance procedures.
B. Hematology, daily evaluation of pathologist referred blood smears, bone marrow smears, Veterans Affairs Medical Center.
C. Surgical/Frozen Section Diagnosis and Quality Control, (5 months in 1996, approx. 2200 cases/year).
D. Autopsy Service, rotational basis, on call 13 weeks/year (staffing 15-20 cases/year).
E. Special Chemistry/Immunology, daily interpretation of protein electrophoreses, isoenzyme studies, and problem ligand studies, Veterans Affairs Medical Center.
F. Blood Bank, consults and investigations, full time as needed, Veterans Affairs Medical Center.

II. TEACHING ACTIVITIES:

A. Graduate course, Epidemiology 520.
B. Pathology house officers, Surgical Pathology/Autopsy supervision and instruction, (5 months/year)
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 annually, 1997-2000).

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. Member of graduate student thesis committees.
B. 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, voting member.
C. Clinical Executive Board,Veterans Administration Medical Center, member at large.
D. Personnel employment and annual evaluations.

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. Parisitology
B. Medical Advisory Commitee, American Red Cross, SMBSR

V. OTHER RELEVANT ACTIVITIES:

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chensue, S. W., Warmington, K.S., Ruth, J.H., Sanghi, P.S., Lincoln, P.M., and S.L. Kunkel. Role of monocyte chemotactic protein-1 in Th1 (Mycobacterial) and Th2 (Schistosomal) antigen-induced granuloma formation: Relationship to local inflammation, Th cell expression and IL-12 production. J. Immunol. 1996, 157:4602-08.
2. Luckacs, N.W., Strieter, R.M., Lincoln, P.M., Brownell E., Pullen D.M.. Schock, H.J., Chensue, S.W., Taub, D.D. and S.L. Kunkel. Stem cell factor (c-kit ligand) influences eosinophil recruitment and histamine levels in allergic airway inflammation. J. Immunol. 1996, 156:3945-51.
3. Luckacs, N.W., Standiford, T.J., Chensue, S.W., Kunkel, R.G., Strieter, R.M. and Kunkel, S.L. C-C chemokine-induced eosinophil chemotaxis during allergic airway inflammation. J. Leuk. Biol. 1996, 60:573-578.
4. Kunkel, S. L., Lukacs, N.W., Strieter, R.M., and Chensue, S.W. Th1 and Th2 responses regulate experimental lung granuloma development (Review). Sarcoidosis Vasculitis and Diffuse Lung Diseases. 13:120-128
5. Chensue, S. W., Warmington, K.S., Ruth, J.H., and S.L. Kunkel. Effect of slow release IL-12 and IL-10 on inflammation, local macrophage function and the regional lymphoid response during mycobacterial (Th1) and schistosomal (Th2) antigen-elicited pulmonary granuloma formation. Inflammation Res. 1997, 46:86-92.
6. Luckacs, N.W., Strieter, R.M., Warmington, K.S., Lincoln P., Chensue, S.W., and Kunkel, S.L. Differential recruitment of leukocyte populations and alteration of airway hyperreactivity by C-C family chemokines in allergic inflammation. J. Immunol. 1997, 158:4398-4404.
7. Luckacs, N.W., Addison, C.L., Gauldi, J., Graham, F., Simpson, K., R.G., Strieter, Warmington, K. S., Chensue, S.W., and Kunkel, S.L. Transgene-induced production of IL-4 alter the development and collagen expression of T helper 1-type pulmonary granulomas J. Immunol. 1997, 158:4478-4484.
8. Luckacs, N.W., Chensue, S.W., Karpus, W.J., Lincoln, P., Keefer, C., Strieter, R.M. and Kunkel, S.L. C-C chemokines diferentially alter interleukin-4 production from lymphocytes. Am. J. Pathol., 150:1861-1868.

BOOKS AND CHAPTERS IN BOOKS:

1. Chensue, S. W. Cytokines in granuloma formation. *In,* Cytokines and Infection-Target for Therapy, G.E. Griffin ed., Cambridge Medical Publications, West Sussex, UK., 1997.

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

1. Ruth, J. H., Lukacs, N. W., Warmington, K. S., Polak, T., Burdick, M.,Strieter, R. S, Kunkel, S. L. and Chensue, S. W. Expression and participation of eotaxin during Th1 and Th2 cytokine-mediated granuloma formation. AAAAI/AAI/CIS Joint Meeting, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Cooordinator 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. Executive Committee of the Admissions Committee.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

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

VI. PUBLICATIONS:

ARTICLES ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS, BOOK CHAPTERS:

1. Sima AAF, Defendini R, Keohane C, Path FRC, D'Amato, CJ, Foster NL, Parchi P, Gambetti P, Lynch T, Wilhelmsen KC: The neuropathology of chromosome 17-linked dementia. Annals of Neurology, 39:734-743, 1996.
2. Albin RL, Minoshima S, D'Amato CJ, Frey KA, Kuhl DA, Sima AAF: Fluoro-Deoxyglucose positron emission tomography in diffuse Lewy body disease. Neurology, 47:462-466, 1996.
3. Sima AAF, D'Amato, CJ: Dementias and other neurodegeneration diseases. In: Neuropathology: The Diagnostic Approach, J. Garcia (ed.), Philadelphia, Mosley. (Available July 1997)

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

1. Kluin KJ, Gilman S, Foster NL, Sima AF, D'Amato C, et al. Degeneration of substantia nigra pars compacta contributes to the dysarthria of PSP. Neurology 48:A97, 1997

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Introductory course in Blood Banking/Transfusion Medicine for Pathology House Officers.
B. Daily teaching rounds for Pathology House Officers assigned to the Blood Bank.
C. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
   1. Presented Workshop entitled: "Theraupeutic Activities in the Blood Bank".
   2. Presented talk entitled: "Solvent Detergent Plasma".
   3. Moderated session on New Technologies.
D. Clinical Pathology Grand Rounds: "Clinical Application of Hematopoietic Growth Factors", May 23, 1997.
E. Clinical Pathology M-4 Elective:
   1. Lecture/Discussion: "Blood Component Utilization".
   2. Lecture/Discussion: "Transfusion Reactions".
   3. Lecture/Discussion: "Bone Marrow Transplantation".
   4. Lecture/Discussion: "Apheresis".

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

PROJECTS UNDER STUDY:

A. Cytokine production in hemolytic transfusion reactions.
B. Safety and efficacy of solvent/detergent treated plasma.
C. Mechanisms of immune suppression by blood transfusion.
D. Mechanisms of action of leukoreduction filters.
E. Mechanisms of hypotensive transfusion reactions.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Transfusion Committee.

V. OTHER RELEVANT ACTIVITIES:

A. Reviewer, Chest.
B. Reviewer, Transfusion.
C. Reviewer, American Journal of Clinical Pathology.
D. Executive Committee, Michigan Association of Blood Banks.
E. Program Committee, Michigan Association of Blood Banks.
F. Scientific Section Coordinating Committee, American Association of Blood Banks.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Snyder EL, Mechanic S, Baril E, Davenport R: Removal of soluble biologic response modifiers (complement and chemokines) by a bedside leukoreduction filter. Transfusion 36:707-713, 1996.
2. Davenport RD: Cytokines as intercellular signals in hemolytic transfusion reactions. Biol Signals 5:240-245, 1996.

ABSTRACTS, AND PRESENTED PAPERS:

1. Davenport RD, Giacherio DA: Removal of potassium from red blood cells and whole blood by ion exchange. Transfusion 36:14S, 1996.

BOOKS:

1. Davenport,R.D. and Snyder, E.L.: Cytokines and Biological Response Modifiers. A Transfusion Medicine Primer. AABB Press In Press.

CHAPTERS IN BOOKS:

1. Davenport, R.D.: Hemolytic reactions, in, Popovsky, M.D. (ed), Transfusion Reactions. AABB Press 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 -30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. None

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Editorial Board Member, Drug Metabolism Reviews

INVITED LECTURES/SEMINARS:

1. "Cholecytstokinin Does Not Modulate Gabapentin-Induced Pancreatic Acinar Cell Tumors in Rats." Society of Toxicology, Cincinnati, Ohio, March 1997.
2. "Gabapentin Inhibits Intracellular Calcium, Mobilization in Rat Pancreatic AR42J Tumor Cells." Society of Toxicology, Cincinnati, Ohio, March 1997.
3. "Subchronic Toxicity of the Antidiabetic Troglitazone in B6C3F1 Mice." Society of Toxicology, Cincinnati, Ohio, March 1997.
4. "52-Week Oral Toxicity Study of Troglitazone in Cynomolgus Monkeys." Society of Toxicology, Cincinnati, Ohio, March 1997.
5. "Subchronic Toxicity of the Antidiabetic Troglitazone in Wistar Rats." Society of Toxicology, Cincinnati, Ohio, March 1997.
6. "Differential Effects of Epidermal Growth Factor in Intestinal Mucosa from Non-Human Primates." Society of Toxicology, Cincinnati, Ohio, March 1997.
7. "Cellular Changes in Intestinal Mucosa of Wistar Rats after Epidermal Growth Factor I-48." Society of Toxicology, Cincinnati, Ohio, March 1997.
8. "Localization of Cellular Proliferation in Marmosets Treated with Human Recombinant EGF 1-48," American College of Veterinary Pathologists, Seattle, Washington, December 1996.
9. "Is Mitochondrial Dysfunction the Basis for the Observed Hepatotoxicity of Tacrine?", American Association for the Study of Liver Diseases, Chicago, Illinois, November 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. F. A. de la Iglesia, E. J. McGuire, J. R. Haskins and N. Lalwani. Structural Diversity of Peroxisome Proliferators and Their Effects on Mammalian Cells In Vivo. Ann, N.Y. Acad. Sci. 804: 310-327, 1996.

2. N. D. Lalwani, L. A. Dethloff, J. R. Haskins, D. G. Robertson and F. A. de la Iglesia. Increased Nuclear Ploidy, Not Cell Proliferation is Sustained in the Early Stages of Peroxisome Proliferation in Rat Liver. Toxicol. Pathol. 25(2): 265-175, 1996.
3. J.F. Reindel, G.D. Pilcher, A.W. Gough and F.A. de la Iglesia. Recombinant Human EGF 1-48 Induced Morphologic Changes in the Digestive Tract of Cynomolgus Monkeys. Toxicol. Pathol. 24: 669-680, 1996.
4. E. J. McGuire, J. A. Anderson, A. W. Gough, J. R. Herman, D. G. Pegg, J. C. Theiss and F. A. de la Iglesia. Preclinical Toxicology Studies with the Angiotensin-Converting Enzyme Inhibitor Quinapril Hydrochloride (Accupril). J. Toxicol. Sci. 21: 207-214, 1996.
5. H. Shimazu, K. Yasuda, Y. Katsumata, T. Takamatsu, T. Umemura, T. Ishikura, K. Kaneko, M. Watanabe, J. Anderson and F. de la Iglesia. Reproductive and Developmental Toxicity Studies of Gemfibrozil. Jap. Pharmacol. Therap. 25(3): 745-761, 1997.
6. Y. Nagashima, H. Akai, S. Yamazaki, K. Tamura, K. Kaneko, M. Watanabe, E. McGuire and F. de la Iglesia. 52-Week Repeated Oral Dose Toxicity Study of Gemfibrozil in Dogs. Jap. Pharmacol. Therap. 25(3): 725-744, 1997.
7. Y. Nagashima, H. Akai, K. Tamura, K. Kaneko. M. Watanabe. E. McGuire and F. de la Iglesia. 13-Week Repeated Oral Dose Toxicity Study and 5-Week Recovery Study of Gemfibrozil in Dogs. Jap. Pharmacol. Therap. 25(3): 703-724, 1997.
8. Y. Nagashima, H. Akai, K. Tamura, K. Kaneko. M. Watanabe. E. McGuire and F. de la Iglesia. Single and Intermittent Escalating Dose Toxicity Studies of Gemfibrozil in Dogs. Jap. Pharmacol. Therap. 25(3): 699-702, 1997.
9. S. Okazaki, K. Suwa, S. Yamazaki, K. Tamura, Y. Yamaguchi, K. Kaneko, M. Watanabe, E. McGuire and F. de la Iglesia. 52-Week Repeated Oral Dose Toxicity Study of Gemfibrozil in Rats. Jap. Pharmacol. Therap. 25(3): 673-697, 1997.
10. S. Okazaki, K. Shuzo, S. Yamazaki, K. Tamura, K. Kaneko, M. Watanabe, E. McGuire and F. de la Iglesia. 13-Week Repeated Oral Dose Toxicity Study and 5-Week Recovery Study of Gemfibrozil in Rats. Jap. Pharmacol. Therap. 25(3): 653-671, 1997.
11. S. Okazaki, K. Suwa, K. Tamura, Y. Goto, K. Kaneko, M. Watanabe, E. McGuire and F. de la Iglesia. Single Dose Toxicity Studies of Gemfibrozil and its Main Metabolite (Me) in Rats. Jap. Pharmacol. Therap. 25(3): 645-651, 1997.

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 1996).
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. Archives Toxicol. (submitted 1997).

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. J. Pharm. Exp. Therap. (submitted 1997).
4. J. Sims and F. de la Iglesia. Designing Non-Clinical Safety Evaluation Programmes for Colony Stimulating Forces, Growth Factors and Hormones: Recommendations and the Way Forward. Human Exper. Toxicol. (submitted 1997).

BOOKS/CHAPTERS IN BOOKS:

1. A. L. Metz, A. W. Gough, D. G. Robertson, F. A. de la Iglesia and S. P. Bishop. Agents Associated with the Development of Cardiac-Hypertrophy and/or Cardiac Failure. In: Comprehensive Toxicology, Volume 6: Cardiovascular Toxicology. (in press 1996).
2. F. A. de la Iglesia, D. G. Robertson and J. R. Haskins. Morphofunctional Aspects of the Hepatic Architecture: Functional and Subcellular Correlates. In: Handbook of Drug Metabolism. T. Woolf (Ed.) Marcel Dekker (in press 1997).

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

1. M. R. Bleavins, K. Johnson and F. A. de la Iglesia. Modulation of Mercuric Chloride-Induced Kidney Injury by Two Forms of Recombinant Human Epidermal Growth Factor. The Toxicologist 30: 305, 1996.
2. J. Reindel, N. Lalwani, J. Haskins, D. Altrogge, A. Gough and F. de la Iglesia. Localization of Cellular proliferation in Marmosets Treated with Human Recombinant EGF 1-48. Vet. Path. 33: 273, 1996.
3. D. G. Robertson, D. K. Monteith, T. K. Braden, N. D. Lalwani and F. A. de la Iglesia. Is Mitochondrial Dysfunction the Basis for the Observed Clinical Hepatotoxicity of Tacrine? Hepatology, 24(4): 465A, 1996.
4. C. E. Rothwell, M. R. Bleavins, E. J. McGuire, F. A. de la Iglesia and H. Masuda. 52-Week Oral Toxicity Study of Troglitazone in Cynomolgus Monkeys. The Toxicologist, 36; 273, 1997.
5. F. A. de la Iglesia, B. Tierney and L. Dethloff. Cholecystokinin does not Modulate Gabapentin-Induced Pancreatic Acinar Cell Tumor Cells. The Toxicologist, 36: 178, 1997.
6. L. Dethloff, L. Bestervelt, B. Tierney and F. A. de la Iglesia. Gabapentin Inhibits Intracellular Calcium Mobilization in Rat Pancreatic AR42J Tumor Cells. The Toxicologist, 36: 91, 1997.
7. E. J. McGuire, L. A. Dethloff, K. M. Walsh, F. A. de la Iglesia and H. Masuda. Subchronic Toxicity of the Antidiabetic Troglitazone in B6C3F1 Mice. The Toxicologist, 36: 273, 1997.

8. J. Herman. A. Metz, E. McGuire, F. de la Iglesia and H. Masuda. Subchronic Toxicity of the Antidiabetic Troglitazone in Wistar Rats. The Toxicologist, 36: 273, 1997.
9. J. Haskins, M. Breider, M. R. Bleavins and F. A. de la Iglesia. Cellular Changes in Intestinal Mucosa of Wistar Rats after Epidermal Growth Factor I-48. The Toxicologist, 36: 233, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Service - 20 weeks.
B. Primary Consultant for Bone and Joint Pathology.
C. Primary Consultant for Head and Neck Pathology.
D. Secondary Consultant for Soft Tissue Pathology.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Sophomore Medical Class:
   1. Pathology 600 - lecture - six contact hours.
   2. Pathology 600- laboratory sessions- 10 contact hours.
B. House Officers:
   1. Training in Surgical Pathology.
   2. Weekly Surgical Pathology Conference- "Pathology School"- 50 Hours.
   3. Lectures - three hours.
   4. Surgical Pathology Consultation Conference - four hours.
C. Interdepartmental:
   1. Sarcoma conference - monthly: 48 hours.
   2. Department of Orthopedic Surgery, Orthopaedic Pathology Lecture Series: two hours lecture.
   3. Department of Orthopedic Surgery, Quarterly Interdisciplinary Musculoskeletal Tumor conference: four hours.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT (PENDING APPROVAL):

A. Wolf, G.T., Bradford, C., Carey, T., Esclamado, R., Terrell, J., Urba, S, Wicha, M., Eisbruch, A., Lawrence, T., Beals, T., Devaney, K., McClatchey, K., Nunez, G., Wahl, R., Mason, H., Strawderman, M.: Concomitant chemotherapy and radiation for organ preservation in patients with advanced (stage III, IV) laryngeal cancer.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

UNIVERSITY:

A. Member, Musculoskeletal Core, Year II Curriculum.

REGIONAL AND NATIONAL:

A. Member, Arthur Purdy Stout Society of Surgical Pathologists.
B. Ad hoc Reviewer, Cancer.
C. Abstract Review Board, United States and Canadian Academy of Pathology (1997 program).
D. Pathology Chair, Sarcoma Committee, Southwest Oncology Group.

V. OTHER RELEVANT ACTIVITIES:

WORKSHOPS:

1. Radiologic-Pathologic Correlation in the Diagnosis of Solitary Skeletal Lesions (Donald E. Sweet, M.D. and Kenneth Devaney, M.D., Course Directors), presented at the 1997 Annual Meeting of the United States and Canadian Academy of Pathology (Orlando, Florida).

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ferlito, A., Devaney, K., Rinaldo, A: The squamous neoplastic component in unconventional squamous carcinomas of the larynx. Ann. Otol. Rhinol. Laryngol. 105:926-932, 1966.

2. Levy, R.A,. Quint, D., Devaney, K.: Unusual tumors of the skull and skull base. Can. J. Neuroradiol. 47:434-443, 1996.
3. Ferlito, A., Devaney, K.O., Rinaldo, A., Milroy, C.M., Wenig, B.M., Iurato, S., McCabe, B.F.: Ear cholesteatoma versus cholesterol granuloma. Ann. Otol. Rhinol. Laryngol. 106:79-85, 1997.
4. Frank, C.J., McClatchey, K.D., Devaney, K.O., Carey, T.E.: Evidence that loss of chromosome 18q is associated with tumor progression. Cancer Res. 57:1-4, 1997.
5. Devaney, K., Ferlito, A.: Yolk sac tumors (endodermal sinus tumors) of the head and neck. Ann. Otol. Rhinol. Laryngol. 106:254-260, 1997.
6. Ferlito, A., Weiss, L.M., Rinaldo, A., Carbone, A., Devaney, K.O., MacMillan, C, Barnes, L.: Lymphoepithelial carcinoma of the larynx, hypopharynx and trachea. Ann. Otol. Rhinol. Laryngol. 106:437-444, 1997.
7. Devaney, K., Putzi, M.J., Ferlito, A., Rinaldo, A.: Head and neck Langerhans cell histiocytosis. Ann. Otol. Rhinol. Laryngol. 106:526-532, 1997.
8. Milroy, C.M., Ferlito, A., Devaney, K.O., Rinaldo, A.: The role of DNA measurements of head and neck tumors. Ann. Otol. Rhinol. Laryngol. (in press).
9. Ferlito, A., Rinaldo, A., Devaney, K.O.: Syndrome of inappropriate antidiuretic hormone secretion associated with head and neck cancers. Ann. Otol. Rhinol. Laryngol. (in press).
10. Devaney, K., Hunter, B.C., Ferlito, A., Rinaldo, A.: Pre-treatment pathologic prognostic factors in squamous carcinomas of the head and neck. Ann. Otol. Rhinol. Laryngol. (in press).
11. Johnson, D.B.S., Breidahl, W., Newman, J.S., Devaney, K., Yahanda, A.: Extraskeletal mesenchymal chondrosarcoma of the rectus sheath. Skeletal Radiol. (in press).
12. Ferlito, A., Devaney, K.O., Rinaldo, A.: Papillary squamous cell carcinoma versus verrucous squamous cell carcinoma of the head and neck. Ann. Otol. Rhinol. Laryngol. (in press).
13. Bradford, C.R., Devaney, K.O., Lee, J.I.: Spindle epithelial tumor with thymus-like differentiation (SETTLE): a case report and review of the literature. Laryngoscope (in press).
14. Hunter, B.C., Devaney, K., Ferlito, A., Rinaldo, A.: Alveolar soft part sarcoma of the head and neck. Ann. Otol. Rhinol. Laryngol. (in press).
15. Devaney, K., Ferlito, A., Rinaldo, A.: True giant cell tumor of the larynx. Ann. Otol. Rhinol. Laryngol. (in press).
16. Reinish, E.I., Feinberg, S.E., Devaney, K.: Primary synovial chondromatosis of the temporomandibular joint with distant extracapsular spread. Int. J. Oral Maxillofac. Surg. (in press).
17. Devaney, K., Ferlito, A., Rinaldo, A.: Head and neck manifestations of Wegener's granulomatosis-a pathologic perspective. Ann. Otol. Rhinol. Laryngol. (in press).
18. Ferlito, A., Rinaldo, A., Devaney, K.O., Hunter, B.C.: Different double primary laryngeal cancer. Ann. Otol. Rhinol. Laryngol. (in press).
19. Ferlito, A., Rinaldo, A., Devaney, K.O., Devaney, S.L., Milroy, C.M.: Impact of phenotype on treatment and prognosis of laryngeal malignancies. Ann. Otol. Rhinol. Laryngol. (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

None

BOOKS/CHAPTERS IN BOOKS:

1. Devaney, K.: Sclerosing lesions of bone, in, Rosenberg, A.E. and Schiller, A.L. (eds.), Orthopaedic Pathology, W. B. Saunders, Philadelphia, In Press.
2. Devaney, K.: Fibromatoses, in, Harper, J.I., Oranke, A.P., Prose, N.S. (eds.), Textbook of Paediatric Dermatology, Blackwell Scientific, London, In Press.
3. Devaney, K.: Benign fibro-osseous lesions of bone, in, Helliwell, T. (ed.), Pathology of Bone and Joint Neoplasms, W. B. Saunders, Philadelphia, In Press.
4. Devaney, K.: Lesions of the neck including soft tissue: pathology, in, Fu, Y.S., Wenig B., Abemayor, E. and Wenig, B. (eds.), Pathology of the Head and Neck- with Clinical Correlations, Churchill Livingstone, New York, In Preparation.
5. Devaney, K.: Pathology of malignant tumors, in Ferlito, A. (ed.), Diseases of the Larynx, Chapman and Hall, London, In Preparation.

ABSTRACTS:

1. Hunter, B.C., Devaney, S.L., Weiss, S.W., Devaney, K.: The relationship of apoptosis to grade in malignant fibrous histiocytomas of soft tissue. Modern Pathol. 10:11A, 1997.
2. Montgomery, E.A., Devaney, K., Weiss, S.W.: Inflammatory myxohyaline tumor of distal extremities with Reed-Sternberg-like cells: a novel entity with features simulating myxoid malignant fibrous histiocytoma, inflammatory conditions, and Hodgkin's disease. Modern Pathol. 10:12A, 1997.
3. Williams, S.T., Parham, D.M., Khare, V.K., Shearer, P., Devaney, K., Weiss, S.W.: Angiosarcomas in children: a clinicopathologic study of ten cases. Modern Pathology 10:159A, 1997.
4. Devaney, K.: book review: Dahlin's Bone Tumors- General Aspects and Data on 11,087 Cases, by K.K. Unni. Am. J. Surg. Pathol. 20:1298, 1996.
5. Devaney, K.O., Ferlito, A.: Cartilaginous tumors of the larynx. In *section seven (Neoplastic and Inflammatory Diseases of the Head and Neck)* of the 1997 Home Study Course of the American Academy of Otolaryngology- Head and Neck Surgery.
6. Devaney, K.: book review: Tumors of the Salivary Glands (Atlas of Tumor Pathology, Series 3, Fascicle 17), by G.L. Ellis and P.L. Auclair. Am. J. Surg. Pathol. 21:361, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Supervised the following graduate students: Arul Chinnaiyan, Hangjun Duan, Shimin Hu.
B. Supervised the following post doctoral fellows: David Beidler, Jim Bretz, Claudius Vincenz, Marta Muzio.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

Funded

A. Principal Investigator, "Novel Zinc Finger Protein that Inhibits TNF Cytotoxicity", NIH-9RO1-CA61348, 20% effort, Budget $163,278 current year, $1,201,474 Total, Period 07/01/93 - 06/31/98.
B. Principal Investigator, "Thrombospondin 2; Structure, Expression and Function", NIH-RO1 - CA58182-06, 20% effort, Budget $143,657 current year, $1,236,526 Total, Period 8/04/92 to 05/31/97.
C. Principal Investigator, "Erb-B2 Expression and Resistance to TNF Killing", NIH-LA-64803. 10% effort, Budget $148,779 current year, $858,304 Total, Period 07/01/94 - 06/31/98.
D. Principal Investigator, "Characterization of Fas associated Death Domain (FADD)", NIH-AG13671, 15% effort, Budget $107,000 current year, $809,499 Total, Period 04/01/96 to 03/31/99
E. Principal Investigator, "CD40 Signal Transduction", NIH RO1-HD33881, 15% effort, Budget $151,953 current year, $925,299 Total, Period 07/01/96 to 06/30/00.
F. Principal Investigator, "Identification of Components of the Cell Death Pathway", NIH-ES08111, 15% effort, Budget $139,377 current year, $1,134,752 Total, Period 08/01/96 to 07/31/00.
G. Principal Investigator, "Signal Transduction by the eck Receptor Tyrosine Kinase", NIH RO1 DK52201, 20% effort, Budget $136,777 current year, $875,077 total, Period 04/01/96 to 03/31/00.

H. Principal Investigator, "Identification of FLICE", DAMD17-96-1-6085, 5% effort, Budget $158,941, current year, $794,707 Total, Period 06/01/96 to 05/31/00.

PROJECTS UNDER STUDY:

Characterization of the components of the cell death pathway.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interview prospective graduate students for a) Molecular and Cell Biology Program, and b) Medical Scientist Training Program.
B. Participated in graduate school pathology program.

MEDICAL SCHOOL/HOSPITAL:

A. Review BMRC grants.
B. Taught in Cell and Molecular Biology course for fellows.
C. Committee on Cell and Molecular Biology.

REGIONAL AND NATIONAL:

A. Editorial Board for the following journals:
   1. Journal of Biological Chemistry.
   2. Journal of Clinical Investigation.
B. Pathology A Study Section (Ad-hoc).

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

Invited Speaker, Tularik, Inc., San Francisco, California, 1996.
Invited Speaker, NIH, Bethesda, Maryland, 1996.
Invited Speaker, University of Texas, Dallas, Texas, 1996.
Invited Speaker, Rush Medical College, Chicago, Illinois, 1996.
Invited Speaker, Sixth International Conference on Lymphocyte Activation and Immune Regulation, Newport Beach, California, 1996.
Invited Speaker, St. Louis University, St. Louis, Missouri, 1996.
Invited Speaker, Washington University, St. Louis, Missouri, 1996.
Invited Speaker, Mayo Clinic, Scottsdale, Arizona, 1996.
Invited Speaker, University of North Carolina, Chapel Hill, 1996.
Invited Speaker, Tufts University, Boston, Massachusetts, 1996.
Invited Speaker, Memorial Sloan-Kettering Cancer Center, New York, NY, 1996.

Invited Speaker, National University of Singapore, 1996.
Invited Speaker, Harvard University, Cambridge, Massachusetts, 1996.
Invited Speaker, Boston University, Boston, Massachusetts, 1996.
Invited Speaker, TNF Congress, Rhodes, Greece, 1996.
Invited Speaker, Duke University, Durham, North Carolina, 1996
Invited Speaker, Mt. Sinai Medical Center, New York, New York, 1996.
Invited Speaker, ASBMB/ASIP Conference, New Orleans, Louisiana, 1996.
Invited Speaker, FASEB Summer Research Conference, Saxtons River, Vermont, 1996.
Invited Speaker, Hans Bloemendal Symposium, Netherlands, 1996.
Invited Speaker, NIAAA Symposium, Washington, DC, 1996.
Invited Speaker, Human Genome Sciences, Rockville, Maryland, 1996.
Invited Speaker, Gordon Conference, Andover, New Hampshire, 1996.
Invited Speaker, SmithKline Beecham, Philadephia, Pennsylvania, 1996.
Invited Speaker, Gordon Conference, New London, New Hampshire, 1996.
Invited Speaker, International Vascular Biology Meeting, Seattle, Washington, 1996.
Invited Speaker, University of Pennsylvania, Philadelphia, Pennsylvania, 1996.
Invited Speaker, Michigan State University, East Lansing, Michigan, 1996.
Invited Speaker, Genentech, Inc., San Francisco, California, 1996.
Invited Speaker, AACR Conference, Lake George, New York, 1996.
Invited Speaker, ASBMB Fall Symposium, Lake Tahoe, California, 1996.
Invited Speaker, Biogen Symposium, Boston, Massachusetts, 1996.
Invited Speaker, ISOBM Symposium, San Diego, California, 1996.
Invited Speaker, Autumn Immunology Conference, Chicago, Illinois, 1996.
Invited Speaker, American Society of Hematology Symposium, Orlando, Florida, 1996.
Invited Speaker, Wistar Institute, Philadelphia, Pennsylvania, 1996.

Invited Speaker, National Institutes of Health, Bethesda, Maryland, 1997.
Invited Speaker, Harvard Medical School, Cambridge, Massachusetts, 1997.
Invited Speaker, Keystone Symposium, Keystone, Colorado, 1997.
Invited Speaker, Genetics Institute, Cambridge, Massachusetts, 1997.
Invited Speaker, New York University Medical Center, New York, NY, 1997.
Invited Speaker, University of Chicago, Chicago, Illinois, 1997.
Invited Speaker, AACR Conference, San Diego, California, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Duan, H., Chinnaiyan, A.M., Hudson, P.L., Wing, J.P., He, W.-W. and V.M. Dixit: ICE-LAP3, a Novel Mammalian Homolog of the Caenorhabditis elegans Cell Death Protein CED-3 is Activated During Fas- and Tumor Necrosis Factor-Induced Apoptosis.. J. Biol. Chem. 271:1621-1625, 1996.

2. Chinnaiyan, A.M., Tepper, C.G., Seldin, M.F., O'Rourke, K., Kischkel, F.C., Hellbardt, S., Krammer, P.H., Peter, M.E., and V.M. Dixit: FADD/MORT1 is a Common Mediator of CD95 (Fas/APO-1)- and TNF-Receptor-Induced Apoptosis. J. Biol. Chem. 271:4961-4965, 1996.
3. Chinnaiyan, A.M., Orth, K., O'Rourke, K., Duan, H., Poirier, G.G., and V.M. Dixit: Molecular Ordering of the Cell Death Pathway: Bcl-2 and Bcl-x_L Function Upstream of the CED-3-like Apoptotic Proteases. J. Biol. Chem. 271:4573-4576, 1996.
4. Pandey, A., Liu, X., Di Fiore, P.P., Dixon, J.E., and V.M. Dixit: Direct Association Between the Ret Receptor Tyrosine Kinase and the SH2-containing Adapter Protein Grb7. J. Biol. Chem. 271:10607-10610, 1996.
5. Muzio, M., Chinnaiyan, A.M., Kischel, F.C., O'Rourke, K., Shevchenko, A., Scaffidi, C., Bretz, J.D., Zhang, M., Ni.J., Gentz, R., Mann, M., Krammer, P.H., Peter, M.E., and V.M. Dixit: FLICE, a Novel FADD-homologous ICE/CED-3-like Protease, is Recruited to the CD95 (Fas/APO-1) Death-Inducing Signaling Complex (DISC). Cell 85:817-828, 1996.
6. Orth, K., Chinnaiyan, A.M., Garg, M., Froelich, C.J., and V.M. Dixit: The CED-3/ICE-like Protease Mch2 is Activated During Apoptosis and Cleaves the Death Substrate Lamin A. J. Biol. Chem. 271:16720-16724, 1996.
7. Chinnaiyan, A.M., Hanna, W.L., Orth, K., Duan, H., Poirier, G.G., Froelich, C.J., and V.M. Dixit: Cytotoxic T-cell-derived Granzyme B Activates the Apoptotic Protease ICE-LAP3. Current Biology 6:897-899, 1996.
8. Vincenz, C., and V.M. Dixit: 14-3-3 Proteins Associate with A20 in an Isoform Specific Manner and Function both as Chaperone and Adapter Molecules for Active Raf. J. Biol. Chem. 271:20029-20034, 1996.
9. Orth, K., O'Rourke, K., Salvesen, G.S., and V.M. Dixit: Molecular Ordering of Apoptotic Mammalian CED-3/ICE-like Proteases. J. Biol. Chem. 271:20977-20980, 1996.
10. Chinnaiyan, A.M., O'Rourke, K., Yu, G.-L., Lyons, R.H., Garg, M., Duan D.R., Xing, L., Gentz, R., Ni, J., and V.M. Dixit: Signal Transduction by DR3: a Death Domain-Containing Receptor Related to TNFR-1 and CD95. Science. 274:990-992, 1996.
11. Robinson Singleton, J., Dixit, V.M. and E. L. Feldman: Type I Insulin-like Growth Factor Receptor Activation Regulates Apoptotic Proteins. J. Biol. Chem. 271:31791-31794, 1996.
12. Duan H. and V.M. Dixit: RAIDD is a New 'Death' Adaptor Molecule. Nature. 385:86-89, 1997.
13. Muzio, M., Salvesen, G.S., and V.M. Dixit: FLICE Induced Apoptosis in a Cell Free System: Cleavage of Caspase Zymogens. J. Biol. Chem. 272:2952-2957, 1997.
14. Vincenz, C. and V.M. Dixit: FLICE2: an ICE/Ced-3 Homologue is Proximally Involved in CD95- and p55-Mediated Death Signaling. J. Biol. Chem. 272:6578-6584, 1997.
15. Chinnaiyan, A.M., O'Rourke, K., Lane, B.R. and V.M. Dixit: Interaction of CED-4 with CED-3 and CED-9: A Molecular Framework for Cell Death. Science. 275:1122-1126, 1997.
16. Chinnaiyan, A.M., Woffendin, C., V.M Dixit and G.J. Nabel: The Inhibition of Pro-Apoptotic ICE-Like Proteases Enhances HIV Replication. Nature Med. 3:333-337, 1997.
17. Orth, K. and V.M. Dixit: Bik and Bak Induce Apoptosis Downstream of CrmA but Upstream of Inhibitor of Apoptosis (IAP). J. Biol. Chem. 272:8841-8845, 1997.
18. Hu, S., Vincenz, C., Buller, M. and V.M. Dixit: A Novel Family of Viral Death Effector Domain-Containing Molecules that Inhibit both CD-95 and TNFR-1 Induced Apoptosis. J. Biol. Chem. 272:9621-9625, 1997.

19. Pan, G., O'Rourke, K. Chinnaiyan, A.M., Ruben S.M., Gentz, R., Ni, J. and V.M. Dixit: The Receptor for the Cytotoxic Ligand TRAIL. Science. 276:111-113, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

1995 - Guest Lecturer, Anatomy & Cell Biology course #580
1995 Guest Lecturer, Biology course #421
1996 Guest Lecturer, Biology course #405
1997 Guest Lecturer, Biology course #405
1997 Lectured - Center for Organogenesis Short Course
"Organogenesis of a Complex Tissue" May 12-23, 1997

MEDICAL SCHOOL/HOSPITALS:
NONE

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, Howard Hughes Medical Institute - 001819, "Analysis of Mammalian Developmental Control Genes", (50%), October 1, 1994-September 30, 1997. Approximately $250,000 current year (including staff salaries, supplies and travel) excluding PI's salary and benefits. The actual budget is negotiated yearly.

B. Principal Investigator, "PAX-2 in Normal and Cystic Epithelium Development", NIH/NIDDK - R01 DK51043-02, (25%), September 30, 1995-August 31, 2000. Direct costs approximately $100,000 requested annually.

C. Sponsor, WELLCOME TRUST, "Regulation of PAX-2 in Normal and Cystic Epithelium", Fellowship recipient: Julie Martin, Awardee, Gregory Dressler, Sponsor, (5%), March 1, 1996-February 28, 1998. Direct costs/year (supplies only)-$5,400.

PROJECTS UNDER STUDY:

A. The identification of co-factors required for Pax protein mediated transcription activation.
B. The development of novel methods for identifying genes regulated by Pax proteins.
C. The role of Pax-2 in the initiation and progression of polycystic kidney disease.

D. The GDNF/RET signaling pathway in the developing kidney.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Center for Organogenesis - International Symposium Organizing Committee, October 3-6, 1996
B. Appointed Interim Co-Chairman of Center for Organogenesis
C. Organized - Center for Organogenesis Short Course "Organogenesis of a Complex Tissue" May 12-23, 1997

REGIONAL AND NATIONAL:

NIH Study Section, General Medicine B Review Meeting, June 24-25, 1997

V. OTHER RELEVANT ACTIVITIES:

Membership in the American Society of Nephrology
Membership in Society for Developmental Biology
Membership in University of Michigan Comprehensive Cancer Center
Membership in the Center for Organogenesis, University of Michigan

INVITED LECTURES/SEMINARS:

1. Symosium at Tubingen, Germany - Sept. 11-16, 1996
2. ASN Basic Science Conference, New Orleans, LA November 7-9, 1996
3. Dept. of Cancer Biology, The Cleveland Clinic, Cleveland, OH, February 25, 1997
4. Pennsylvania Center for Molecular Studies of Kidney Diseases, Univ. of Pennsylvania, Philadelphia, PA, March 17-18, 1997
5 Dept. of Cell Biology, Duke University, Durham, NC, March 26-27, 1997
6. Cancer Biology Research Seminar, University of Michigan, May 14, 1997

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Winyard, P.J.D., Risdon, R.A., Sams, V.R., Dressler, G.R., Woolf, A.S. (1996). The PAX2 transcription factor is expressed in cystic and hyperproliferative dysplastic epithelia in human kidney malformations. J. Clin. Invest. 98:451-459.
2. Lechner, M.S. and Dressler, G.R. (1996) Mapping of PAX-2 transcription activation domains. J. Biol. Chem. 271:21088-21093.

3. Vega, Q.C., Worby, C.D., Lechner, M.S., Dixon, J.E., and Dressler, G.R. (1996). Glial cell line-derived neurotrophic factor activates RET and promotes kidney morphogenesis. Proc. Natl. Acad. Sci. USA 93:10657-10661.
4. Dehbi, M., Ghahremani, M., Lechner, M., Dressler, G., and Pelletier, J. (1996). The paired-box transcription factor, PAX2, positively modulates expression of the Wilms' tumor suppressor gene (WT1). Oncogene 13:447-453.
5. Valentini, R., Brookhiser, W.T., Park, J., Yang, T., Briggs, J., Dressler, G.R. and Holzman, L.B. (1997). Post-translational processing and renal expression of mouse indian hedgehog cDNA. J. Biol. Chem. 272:8466-8473.
6. Lechner, M.S., and Dressler, G.R. (1997). The molecular basis of embryonic kidney development. Mechanisms of Development. 62:105-120.

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Cho, E.-A., Patterson, L.T., Brookhiser, W.T., Mah, S., Kintner, C., and Dressler, G.R. (1997). Differential expression and function of cadherin-6 during renal epithelium development. (Submitted to Development).

BOOK CHAPTERS:

1. Dressler, G.R. (1996) Genetic control of kidney development. In: (J.P. Grunfeld, Bach, J.F., H. Kreis, and M.H. Maxwell eds) Advances in Nephrology, Mosby-Year Book, Inc., Chicago, IL pp. 1-12.

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

1. Dressler, G.R. (1996). Pax-2, kidney development, and oncogenesis. Medical and Pediatric Oncology 27:440-444.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

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. USPHS (NIDDKD) 2P60AM20572-10: Michigan Diabetes Research and Training Center, Director Ligand Assay Core Facility, 1993-1998, $130,000/yr., 17% effort.
B. NIH, U01-AG 12495, A.R. Midgley, Principle Investigator, "Menopause and Aging in Women: Central Laboratory," 10/01/94 - 09/30/99, $1,465,338, 10% effort.

SCIENTIFIC COLLABORATIONS:

A. Reproductive Science Program: Vasantha Padmanabhan, Ph.D., A. Rees Midgley Jr. M.D., & John Randolph, M.D.: Preparation of an NIH U54 grant proposal designed to examine the neuroendocrine and paracrine control mechanisms responsible for cellular proliferation and differentiation during ovarian folliculogenesis. Despite the growing body of knowledge of molecular, biochemical and physiologic aspects of determination of which follicles remain quiescent, which ovulate and which undergo atresia remains an enigma. It is our contention that an increase in intrafollicular availability of activin is a major determinant of the fate of the follicle. This proposal will examine: a) if the preovulatory follicular development is related to increased bioavailability of activin. b) if the paracrine factors determining the bioavailability of activin are, in turn, regulated by LH and/or FSH. c) if follicular fate can be modified by alteration of activin bioavailability. and d) Determine the impact of increased androgen production in disrupting activin.
B. University of Missouri: Mark Flinn, Ph.D.: An examination of biochemical markers of growth, puberty, stress and immunological function in children in a small isolated Carribean village has been ongoing for approximately 8 years. We have examined

several markers in saliva samples obtained from children between the ages of 2 and 21. Daily samples, and a detailed history of relevant physical and emotional events, have been collected annually for a 2 - 3 month period throughout the multiyear study. This study has lead to a variety of new insights into the interaction between stress and normal growth and development. We are currently preparing two new grant proposals that will continue and expand this activity.

C. University of Dayton: P.K. Bajpai, Ph.D. and 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 permiotting increasingly tighter control in the rate and length of "drug" delivery.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Central Ligand Assay Laboratory

MEDICAL SCHOOL/HOSPITAL:

A. Director, Chemistry Core Facility, Diabetes Research and Training Center
B. Co-Director, Standards and Reagents Core Facility, Reproductive Sciences Program
C. Member, Selection Committee, Reproductive Sciences Program
D. Associate Research Investigator of Reproductive Biology, Reproductive Science Program

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Richardson, T.D., Wojno, K.J., Liang, L.W., Giacherio, D.A., England, B.G., Henricks, W.H., Schork, A., and Oesterling, J.E.: Half-life determination of serum free Prostate Specific Antigen following radical retropubic prostatectomy. Journal of Urology 48 (Supplement 6A);40-44, 1996
2. Flinn MV, MT Turner, R Quinlan, SD Decker, & BG England 1996. Male-female differences in effects of parental absence on glucocorticoid stress response. Human Nature 7(2):1125-1162.
3. Flinn, M.V. & England, B.G. (1996) Family Composition And Childhood Stress. Current Anthropology (36(5):854-866).
4. Flinn MV & BG England 1997. Social economics of childhood glucocorticoid stress response and health. American Journal of Physical Anthropology 102(1): 33-53
5. Butler, K., H. Benghuzzi, P.K. Bajpai, A. Puckett, M. Tucci, Z. Cason & B.G. England: One Year Histopathological Evaluation of Fibrous Tissue Surrounding TCPL Implants Using Adult

rats as a Model. Biomed. Sci. Instrument., (Paper #97-039, ISA 1045-0032), Vol. 33, pp 233-239, 1997.

6. Cavet, W., M. Tucci, Z. Cason, L. Lemos, B.G. England, Audrey Tsao & H. Benghuzzi: Cellular Responses to Various Levels of Sustained Delivery of Testosterone in the Ventral Prostrate. . Biomed. Sci. Instrument., (Paper #97-027, ISA 1045-0032), Vol. 33, pp 155-160, 1997.
7. Vashi AR Wojno KJ Henricks W England BG Vessella RL Lange PH Wright GL Jr Schellhammer PF Weigand RA Olson RM Dowell BL Borden KK Oesterling JE. Determination of the "reflex range" and appropriate cutpoints for percent free prostate-specific antigen in 413 men referred for prostatic evaluation using the AxSYM system. Urology (1997 Jan) 49(1):19-27
8. Apple MJ Benghuzzi H Parsell D England BG Interrelationship between buffer systems and parti sizes of TCPL drug delivery system. Biomed Sci Instrum (1996) 32:47-53

ARTICLES SUBMITTED FOR PUBLICATION:

1. Henricks, W.H., England, B.G., Giacherio, D.A., Oesterling, J.E., and Wojno, K.J.: Free PSA is stable after multiple freeze-thaws and serum percent Free PSA does not predict extraprostatic spread of prostate cancer. J. Urol, submitted.
2. Flinn, M.V. & England, B.G. Health Condition And Glucocorticoid Stress Response Among Children In A Rural Dominican Village. . (Submitted to The Proceedings Of The National Academy Of Sciences.)

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

1. Wojno, K., Beduschi, M., Giacherio, D., England, B., Gormley, G., Bach, M., Waldstreicher, J., and Oesterling, J.: Finasteride decreases free and total PSA concentration but does not significantly alter the percent free PSA value. (Presented at the American Urologic Association Meeting, New Orleans, LA, April 1997.)
2. Beduschi, M., Wojno, K., Consolino, C., Giacherio, D., England, B., Mohr, B., Yurgalevitch, S, McKinlay, J., Oesterling, J.: Free PSA and percent free PSA increase over time in a healthy male population followed longitudinally for 9 years. (Presented at the American Urologic Association Meeting, New Orleans, LA, April 1997.)
3. England, B., Wojno, K., Beduschi, M., Giacherio, D., Yurgalevitch, S, Mohr, B., McKinlay, J., Longcope, C., Oesterling, J.: Changes in testosterone, free PSA, and percent free PSA over time in a healthy aging population followed longitudinally for 9 years. (Presented at the American Urologic Association Meeting, New Orleans, LA, April 1997.)
4. England, B.G., Wojno, K.J., Giacherio, D.A., Beduschi, M.C., Consolino, C.M., Oesterling,J.E., Mohr,B.A., Yurgalevitch, S, McKinlay, J.: Changes in free PSA and percent free PSA over time in a healthy male population. Clin Chem 43:S235, 1997
5. Giacherio, D.A., Wojno, K.J., Beduschi, M.C., England, B.G., Oesterling, J.E., Gormley, G.J., Bach, M.A., Walstreicher, J.: Finasteride therapy does not significantly alter the percent free PSA value but decreases free and total serum PSA concentrations by fifty percent. Clin Chem 43:S236, 1997.

6. Flinn, MV & BG England 1996. Family environment, glucocorticoid stress response, and health among children in a rural caribbean village. Abstracts of the American Anthropological Association Meetings.
7. Flinn, MV, MT Turner, & BG England 1996. Family environment, stress response, and health among children in a Caribean village. Evolution and Human Behavior Society Meetings 8th Annual Conference Abstracts 8:47.
8. Flinn, MV & BG England 1997. Stress and immune function among children in a rural Caribbean village. Abstracts of the Medical Anthropology Society 1997.
9. Flinn, MV, MT Turner, & BG England 1996. Stress, immune function, and health among children in a Caribbean village. (abstract). American Journal of Physical Anthropology Supplement 22:105.
10. Vashi, Ar, Wojno, Kj, England, Bg, Vessella, Rl, Lange Ph, Wright, G, Schellhammer, Pf, Weigand, R., Olson, Rm,. Dowell, Bl & Oesterling Je. Determination Of The "Reflex Range" And Appropriate Cutpoints For Percent Free PSA In 413 Men Referred For Prostatic Evaluation Using The Axsym Lsystem. In Preparation.
11. Cavett, W., M. Tucci, Z. Cason, L. Lemos, B.G.England, A. Tsao & H. Benghuzzi: Maintenance of Prostatic Function by means of Exogenous Sustained delivery of Testosterone in Castrated Rats. Abstract, Proceeding of the 16th Southern Biomedical Engineering Conference, Biloxi, MS April 4-6, 1997.
12. Butler, K., Benghuzzi, P.K. Bajpai, A. Puckett, M. Tucci, Z. Cason & B.G. England. One Year Histopathological Evaluation of Fibrous Tissue Surrounding TCPL Implants Using Adult Rats as a Model. Abstract, 34th Annual Rocky Mountain Bioengineering Symposium in conjunction with the 34th International ISA Biomedical Sciences Instrumentation Symposium; Dayton, Ohio, April 11-13, 1997.
13. England, B. G., J. B. Smart, W. H. Henricks & D. A Giacherio. Third Generation TSH Immunoassays, A Comparison Of Five Commercially Available Methods. Annual Meeting of the American Thyroid Association, San Diego, CA, Nov. 12-15, 1996.

CHAPTERS IN BOOKS:

1. England, B. G. Endocrine Assays. *In* Vol. VI of Precis: Published by the American College of Obstetricians and Gynecologists, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Autopsy Service.

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. 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. CD/ACD Education Committee.
B. Component I Committee.
C. Component II Committee.
D. Medical Student Basic Science Academic Review Board.
E. Medical Student Clinical Academic Review Board.
F. Medical School Academic Hearing Committee
G. Medical School Information Technology Advisory Committee

REGIONAL AND NATIONAL:

A. ALA of Michigan, Grant Review Committee
B. USMLE, Pathology Test Group.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Crockett-Torabi E, Fantone JC: L-selectin stimulation of canine neutrophil initiates calcium signal secondary to tyrosine kinase activation. Am J. Physiol 272:1302-8, 1997.
2. Brieland J, McClain M, Heath L, Chrisp C, Huffnagle G, LeGendre M, Hurley M, Fantone J, Engleberg C: Coinoculation with Hartmannella vermiformis enhances replicative Legionella pneumophilia lung infection in a murine model of Legionnaires' disease. Infect Immun 64(7):2449-56, 1996.

3. Heath L, Chrisp C, Huffnagle G, LeGendre M, Osawa Y, Hurley M, Engleberg C, Fantone J, Brieland J: Effector mechanisms responsible for gamma interferon-mediated host resistance to Legionella pneumophila lung infection: the role of endogenous nitric oxide differs in susceptible and resistant murine hosts. Infect Immun 64(12):5151-60, 1996.
4. Brieland JK, Heath LA, Huffnagle GB, Remick DG, McClain MS, Hurley MC, Kunkel RK, Fantone JC, Engleberg C: Humoral immunity and regulation of intrapulmonary growth of Legionella pneumophila in the immunocompetent host. J Immunol 157(11):5002-8, 1996.
5. Robins LS, Gruppen LD, Alexander GL, Fantone JC, Davis WK: A predictive model of student satisfaction with the medical school learning environment. Acad Med 72(2):134-9, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Rotations, July (3/4), August (3/4), October (2/4), November (2/4), February (4/4), May (2/4), June (2/4)
B. Estrogen and progesterone receptor analysis of paraffin embedded breast carcinomas
C. Ophthalmic Pathology Service

II. TEACHING ACTIVITIES:

A. Pathology 600 Lectures:
   1. Obstructive Lung Disease - November, 1996
   2. Pulmonary Neoplasms - November1996
   3. Pathology of ARDS - November1995
   4. Tissue Reactions to Infectious Agents - November 1996
   5. Pathology of the Vagina and Vulva - April, 1997
   6. Pathology of the Cervix and Uterus - April, 1997
   7. Pathology of the Ovary - April, 1997
   8. Pathology of Fallopian Tube and Gestational Trophoblastic Diseases - April, 1997
   9. Pulmonary Pathology Review for Medical Students - November, 1996
   10. Gynecologic Pathology Review for Medical Students - April, 1997
   11. General Pathology Review for Medical Students - June, 1997
   12. Laboratory Instructor, September, 1996 - May, 1997
   13. Medical student question and answer sessions, October, 1996 - May, 1997
B. Pathology 630:
   1. Respiratory Disease I - October, 1996
   2. Respiratory Disease II - November, 1996
C. Residency Training:
   1. Diseases of the Chest I - January, 1997
   2. Diseases of the Chest II - January, 1997
   3. Diseases of the Chest III - January, 1997
   4. Surgical Pathology Consultant's Conference, December, 1996; June, 1997
D. Inteflex 211
   1. The Physician as Scientist - January, 1997
E. Other educational activities:
   1. M4 student elective mentor, July 1996, August 1996, February, 1997

2. Center for Research on Learning and Teaching Workshops Teaching with Style - Enhancing Learning by Understanding Teaching and Learning Styles; Interactive Lecturing; Electronic Presentation Technology; How Well are Students Learning?
3. Member, M-2 Respiratory Sequence Committee, 1996-1997
4. Course Director, M-4 Student Pathology Clerkships
5. Participant, Thoracic Surgery Residents Core Curriculum, 1996 - 1997

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)

PROJECTS UNDER STUDY:

A. Histologic predictors of obliterative bronchiolitis in lung transplant patients
B. Histologic prognostic indicators of survival in ARDS patients treated with ECMO
C. The clinical usefulness of the abnormal nondiagnostic lung biopsy sample
D. A cytopathologic analysis of respiratory tract samples obtained from ARDS patients
E. The pathologic manifestations of ocular involvement by Wegener's granulomatois

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interviewer of Pathology House Officer Candidates 1996-1997)
B. Member, Admissions Committee of the University of Michigan Medical School, 1995 - present

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

1. Reviewer, Human Pathology
2. Reviewer, Annals of Thoracic Surgery
3. Reviewer, Urology
4. Member, Abstract Review Board, USCAP

INVITED LECTURES/SEMINARS:

1. "Interstitial Lung Disease" - Advances in Internal Medicine, Towsley Center, Ann Arbor, MI, May, 1997

VI. PUBLICATIONS:

1. DiGiovine B, Lynch, III JP, Martinez FJ, Flint A, Whyte RI, Iannettoni MD, et al: Bronchoalveolar lavage neutrophilia is associated with obliterative bronchiolitis after lung transplantation: role of interleukin- 8. J Immunology 1996, 157: 4194-4202
2. Brown RS, Leung JY, Zasadny KR, Flint A, Wahl RL: Initial evaluation of the importance of glucose transporters, proliferating cells and macrophages to FDG uptake in human non-small cell lung cancer as assessed by PET. Chest (in press)
3. Kazerooni EA, Martinez FJ, Flint A, Jamadar DA, Bross BH, Spizarny DL, Cascade PN, Whyte Ri, Lynch III JP, Toews: Thin-section CT at 10 mm Increments versus limited 3-slide thin-section CT for idiopathic pulmonary fibosis: Correlation with pathologic scoring. Amer J Raoentgen (accepted)
4. Flint A, Lynch, III JP, Martinez FJ, Whyte RI: Pulmonary smooth muscle proliferation occuring after lung transplantation Chest (accepted)
5. Bruch LA, Flint A, Hirschl RB: Pulmonary pathology of patients treated with partial liquid ventilation. Mod Pathol 1997; 10(5):463-468
6. Keane MP, Meaney JFM, Kazerooni EA, Whyte RI, Flint A, Martinez FJ: Accessory cardiac bronchus presenting with hemoptysis. Thorax 52:490-491, 1997
7. DiGiovine B, Lynch, III JP, Martinez FJ, Flint A, Whyte RI, Iannettoni MI, et al: Neutrophilic alveolitis inobliterative bronchiolitis after lung transplantation: role of interleukin-8. J Clin Invest (in press)
8. Gay SE, Kazerooni EA, Toews GE, Lynch III JP, Gross BH, Cascade PN, Spizarny Dl, Flint A, Schork MA, Whyte RI, Popovich J, Hyzy R, Martinez FJ: Idiopathic pulmonary fibrosis: predicting response to therapy and survival. Amer Rev Resp Med Crit Care (in press)

SUBMITTED PUBLICATIONS:

1. Michael CW, Flint A: Cytologic features of Wegener's granulomatosis: a retrospective review. Am J Clin Path
2. Brown RS, Leung JY, Flint A, Wahl RL: Expression of glucose transporters in human lung cancer. Can Res

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

1. DiGiovine B, Lynch JP, Martinez FJ, Flint A, Whyte RI, Iannetoni M, Arenberg DA, Burdick MD, Glass MC, Morris SB, Kunkel SL, Streiter RM: Neutrophilic alveolitis in obliterative bronchiolitis after lung transplantation - Role of Interleukin-8. FASEB Journal V 10 N6, Apr 30, 1996, p1125
2. Kazerooni EA, Martinez FJ, Flint A, Gross BH, Cascade PN, Toews GB: Correlations of high-resolution CT and pathological scoring systems for idiopathic pulmonary fibrosis. Radiology 197:436-437, 1995
3. Brown RS, Leung JY, Zasadny KR, Flint A, Wahl RL: Relationship between SUV-lean and Glut-1 expression in untreated human lung and breast cancer. J Nuc Med 37:250, 1996

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

DEPARTMENTAL:

A. Co-Director of a laboratory section for Pathology 600.
B. Two-week Pathology Informatics course for five pathology house officers, May 5-16.
C. Teaching and supervision of Walter Henricks, fellow in Chemical Pathology and Informatics.

MEDICAL SCHOOL/HOSPITALS:

A. Program Director of the Fifteenth Annual Symposium on Automated Information Management in the Clinical Laboratory (AIMCL) at the Towsley and Power Center, Ann Arbor, Michigan, May 28-30, 1997. The symposium attracted 265 registrants and 39 exhibitors.
B. Two hours of programming from AIMCL were transmitted on May 28 as a realtime audioconference to 40 pathology training programs in the U.S. and Canada. Two additional hours of programming were transmitted on May 29 as an audioconference to laboratory managers located at 35 sites around the country in collaboration with the Clinical Laboratory Management Association.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. The development of a virtual clinical laboratory and academic pathology department.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Clinical Laboratory Directors Committee.

HOSPITAL:

A. Chief Information Officer Executive Committee (CIOEC).

UNIVERSITY:

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

REGIONAL AND NATIONAL:

A. College of American Pathologists (CAP) Committee on Informatics.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. *The Future of Computer in Healthcare.* A lecture delivered to the medical staff of St. Joseph's Mercy Hospitals and Health Services of Macomb, Clinton, Michigan, September 7, 1996.P
2. *Pathology Information Exchange (PIX): A New Relationship Between Pathology Departments Enabled by Information Technology.* A lecture delivered at the Anatomic Pathology Informatics, Imaging, and the Internet Conference sponsored by the Division of Pathology Informatics, Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, PA, November 9, 1996.
3. *Pathology Informatics: New Solutions for New Challenges.* A lecture delivered to a joint AACC/CLMA symposium on automation in the clinical laboratory at Lutheran General Hospital, Des Plains, Illinois, November 13, 1996.
4. *The Role of Information Technology in Shaping the Laboratory of Tomorrow.* A lecture included in a seminar entitled "Transforming the Laboratory Through New Technology: Financial and Management Implications" and sponsored by the Clinical Laboratory Management Association and the Washington G-2 Reports, Orlando, Florida, February 14, 1997.
5. *Laboratory Information Technology within Integrated Delivery Systems: Organizational Integration.* A lecture delivered at a symposium on "Integrated Health Care Strategies for Health Systems and Hospital Laboratories" sponsored by the American Hospital Association, Las Vegas, Nevada, March 6, 1997.
6. *The Virtual Clinical Laboratory and Pathology Department: Projects Under Construction.* A teleconference with an estimated attendance of 231 sponsored by the American Society of Clinical Pathologists, March 12, 1997.

7. *Automated Information Management: The Pursuit of Organizational and Technical Integration.* A lecture presented at the first Congress of Integrated Systems Management, Dallas, Texas, on March 15, 1997.
8. *Integrating Laboratory Information with Other Healthcare Information: The Organizational Perspective.* A workshop presented at the Spring meeting of the American Society of Clinical Pathologists, Chicago, Illinois, on April 8, 1997.
9. *The Virtual Clinical Laboratory and Pathology Department as a Response to Managed Care.* A lecture presented at the 15th annual symposium on Automated Information Management in the Clinical Laboratories (AIMCL), Ann Arbor, Michigan, May 29, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Friedman, B.A.: The challenge of managing laboratory information in a managed care environment. Pathology Patterns Supplement to the Amer. J. Clin. Pathol. 105:S3-S9, 1996.
2. Friedman, B.A.: Pathology informatics: Ensuring a role as a bit player in laboratory medicine. Pathology Patterns Supplement to the Amer. J. Clin. Pathol. 105:S1-S2, 1996.
3. Gendler, S.M., Friedman, B.A. and Henricks, W.: Using hub technology to facilitate information system integration in a healthcare enterprise. Pathology Patterns Supplement to the Amer. J. Clin. Pathol. 105:S25-S32, 1996.

BOOKS/CHAPTERS IN BOOKS:

1. Friedman, B.A.: Regionalization of laboratory information management. Insights into the present and future stages of evolution, in, Steiner, J.W., Root, J.M. and Watt, D.K. (eds,), Roadmap for Laboratory Restructuring, Practical Approaches and Effective Solutions. (Part 2), 1996, Washington G-2 Reports in Association with the Clinical Laboratory Management Association, pp. 49-59.
2. Friedman, B.A. and Mitchell, W.: Community Health Information Networks (CHINs) and their Relationship to Telemedicine. Book chapter, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

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 Kellog Hospitals.
D. Direct the work group overseeing the quality assurance programs for bedside blood glucose testing in the Medical Center.
E. Planning group for the establishment of alternate site testing programs.
F. Technical Director for laboratories at U-M Health Centers off-site clinics.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Medical School:
    1. Chemistry Laboratory Presentations for the M4 Laboratory Medicine Elective.
B. Pathology House Officers:
    1. Clinical Pathology rounds (1 lecture).
    2. Coordinator, Pathology House Officer rotation through Chemistry Lab.
    3. Review daily sign-out and interpretation of electrophoresis results.
    4. Review of selected topics in Clinical Chemistry.
C. Postgraduate:
    1. Ph.D. Thesis Committees, Michael Ducey (5/95 to present) and Aaron Smith (5/96 to present), Department of Chemistry.
    2. Supervision of activities for Walter Henricks, M.D., Fellow in Clinical Chemistry and Informatics.

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. Evaluation of automated immunoassay for cyclosporine. (Abbott Laboratories)
D. Evaluation of deoxypyridinoline assays as a marker of bone metabolism.
E. Evaluation of the performance and clinical utility of free PSA determinations.
F. Cost analysis of point of care testing versus central laboratory testing.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Quality Assurance Committee.
B. Director, Chemistry Laboratory.
C. Director, Point of Care Testing.

MEDICAL SCHOOL /HOSPITAL:

A. East Medical Campus Laboratory Services Planning Group.
B. Brighton Health Center Expansion Project Planning Group.

REGIONAL AND NATIONAL:

A. Executive Committee, Michigan Section AACC.
B. Chair, Program Committee, Michigan Section AACC.
C. Lipids and Lipoproteins Division Member, AACC.
D. Pediatric Clinical Chemistry Division Member, AACC.
E. Consultant, Parke-Davis.
F. Reviewer, Clinical Chemistry.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Point of Care Testing: Blood Gases and Electrolytes." Michigan Society for Clinical Laboratory Scientists Annual Meeting, Troy, MI, April 10, 1997.
2. "Lipoprotein (a) and Homocysteine as Markers of Cardiac Risk". AACC Michigan Section Meeting, May 21,1997.
3. Symposia Moderator, "Cancer Diagnosis and Monitoring: A Look at Emerging Tumor Markers." AACC Michigan Section Meeting, March 6, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Richardson, T.D., Wojno, K.J., Liang, L.W., Giacherio, D.A., England, B.G., Henricks, W.H., Schork, A., and Oesterling, J.E.: Half-life determination of serum free Prostate Specific Antigen following radical retropubic prostatectomy. Journal of Urology, 48(Supplement 6A);40-44, 1996.
2. Wahr, J.A., Anderson, M.M., Giacherio, D.A., Hallock, L., Gawryl, M.S., and Lansden, C.: The effect of a blood salvaging device on blood containing a hemoglobin based oxygen carrier, HBOC-201. J Cardiothorac Vasc Anesth, 11:10-12, 1997.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Henricks, W.H., England, B.E., Giacherio, D.A., Oesterling, J.E., and Wojno, K.J.: Free PSA is stable after multiple freeze-thaws and serum percent Free PSA does not predict extraprostatic spread of prostate cancer. J. Urol, submitted.
2. Palaniappan, L., Rubenfire, M., Anthony, M.N., Elliott, M., Giacherio, D., and Killeen, A.: Coronary artery disease risk factors in young African American women. Submitted for publication.

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

1. Wojno, K., Beduschi, M., Giacherio, D., England, B., Gormley, G., Bach, M., Waldstreicher, J., and Oesterling, J.: Finasteride decreases free and total PSA concentration but does not significantly alter the percent free PSA value. (Presented at the American Urologic Association Meeting, New Orleans, LA, April 1997.)
2. Beduschi, M., Wojno, K., Consolino, C., Giacherio, D., England, B., Mohr, B., Yurgalevitch, S., McKinlay, J., Oesterling, J.: Free PSA and percent free PSA increase over time I a healthy male population followed longitudinally for 9 years. (Presented at the American Urologic Association Meeting, New Orleans, LA, April 1997.)
3. England, B., Wojno, K., Beduschi, M., Giacherio, D., Yurgalevitch, S., Mohr, B., McKinlay, J., Longcope, C., Oesterling, J.: Changes in testosterone, free PSA, and percent free PSA over time in a healthy aging population followed longitudinally for 9 years. (Presented at the American Urologic Association Meeting, New Orleans, LA, April 1997.)
4. England, B.G., Wojno, K.J., Giacherio, D.A., Beduschi, M.C., Consolino, C.M., Oesterling, J.E., Mohr, B.A., Yurgalevitch, S, McKinlay, J.: Changes in free PSA and percent free PSA over time in a healthy male population. Clin Chem 43:S235, 1997.
5. Giacherio, D.A., Wojno, K.J., Beduschi, M.D., England, B.G., Oesterling, J.E., Gormley, G.J., Bach, M.A., Walstreicher, J.: Finasteride therapy does not significantly alter the percent free PSA value but decreases free and total serum PSA concentrations by fifty percent. Clin Chem 43:S236, 1997.

6. Mosca, L., Jahnige, K., and Giacherio, D.G.: Beneficial effects of combination hormone replacement therapy on lipoprotein (a) levels in postmenopausal women. American Heart Association National Meeting.
7. Davenport, R.D. and Giacherio, D.G.: Removal of potassium from red blood cells and whole blood by ion exchange. Transfusion 36:14S, 1996.
8. England, B. G., J. B. Smart, W. H. Henricks & D. A Giacherio. Third Generation TSH Immunoassays, A Comparison Of Five Commercially Available Methods. Annual Meeting of the American Thyroid Association, San Diego, CA, Nov. 12-15, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. 19 days coverage of Nephropathology service for Drs. K. Johnson and P. Killen.

II. TEACHING ACTIVITIES:

A. Renal Sequence for M-2 students, 4 contact hours, Fall term 1996.
B. Pathology Lab Section for M-1 students, 16 contact hours, Winter term 1997.

III. RESEARCH ACTIVITIES:

None.

PROJECTS UNDER STUDY:

None.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Assistant Dean for Medical School Admissions.

REGIONAL AND NATIONAL:

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

E. Reviewer for the Journal of Urology.
F. College of American Pathologists Inspection Team member, Northwestern University Hospital, Pathology Labs, February 27, 1997.

V. OTHER RELEVANT ACTIVITIES:

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. Component II Endocrine Sequence - 2 lectures on Endocrine Pathology.
   2. Endocrine Pathology Laboratories - preparation of course materials.
   3. Pathology Laboratories - 12 sessions.
B. House Officers:
   1. General Surgical Pathology - 5 months.
   2. Endocrine Surgical Pathology - 12 months as needed.
   3. Consultation Conferences - four months.
C. Dental and Graduate Students:
   1. Lecture on Endocrine Pathology.
D. Interdepartmental:
   1. Endocrine Conference, Department of Surgery - monthly.
   2. Endocrinology and Metabolism Clinical Conference - occasional case presentations.
   3. Adrenal Cancer Conference - monthly.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Investigator with Dr. Liz Petty, "Analysis of Genetics Events in the Progression of Adrenocortical Carcinomas, Tumor Progression", ($23,520), Schembechler Adrenal Cancer Research Program, The University of Michigan Comprehensive Cancer Center.

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

PROJECTS UNDER STUDY:

A. Principal Investigator, "Genetic Analysis of Adrenal Cortical Neoplasms."
B. Principal Investigator, "Differential Gene Expression in Adrenal Cortical Neoplasms."
C. Principal Investigator, "Proliferation Studies of Papillary Thyroid Carcinoma During Pregnancy."
D. Co-Investigator, "Pathology of Multiple Endocrine Neoplasia, Type 1," with Dr. Norman Thompson, Department of Surgery.
E. Co-Investigator, "Preclinical Studies on New Drugs for Adrenal Cancer," with Dr. David E. Schteingart, Department of Internal Medicine.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. House Officer Candidate Interviews.
B. Faculty Candidate Interviews.
C. Director, Anatomic Pathology Molecular Diagnostics Laboratory

REGIONAL AND NATIONAL:

A. Consultant, U.S. Surgical Corporation.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Sisson, J.C., Giordano, T.J., Jamadar, D.A., Karerooni, E.A., Shapiro, B., Gross, M.D., Zemple, R.N., Spaulding, R.T.: Treatment of micronodular pulmonary metastases from papillary thyroid cancer treated with 131-I. Cancer, 78:2184-2192, 1996.
2. Few, J., Thompson, N.W., Angelos, P., Simeone, D., Giordano, T. and Reeve, T.: Riedel's thyroiditis: Treatment with tamoxifen. Surgery 120:993-998, 1996.
3. Su L, Beals T, Bernacki EG, McClatchey K, and Giordano T: Spindle epithelial tumor with thymus-like differentiation: A case report with cytologic, histologic immunohistologic and ultrastructural findings. Mod Pathol 10:510-514, 1997.

4. Angelos P, Thompson NW, and Giordano TJ: Spontaneous vocal cord paresis and return to normocalcemia: An unusual presentation of parathyroid adenoma with concomitant abscess. In press.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Simeone, D.M., Giordano, T.J. and Thompson, N.W.: The "Serendipitous" surgical cure of the Zollinger-Ellison Syndrome in a MEN-1 patient despite an unsuspected diagnosis of either disease.
2. Few J, Thompson NW, Angelos P, Simeone D, Giordano T, and Reeve T. Riedel's thyroiditis: Treatment with tamoxifen.
3. Angelos, P., Thompson, N.W. and Giordano, T.J.: Spontaneous vocal cord paresis and return to normocalcemia: An unusual presentation of parathyroid adenoma with concomitant abscess.
4. Sisson JC, Jamadar DA, Kazerooni EA, Giordano TJ, Carey JE, and Spaulding SA. Treatment of micronodular metastases of primary thyroid cancer: Are the tumors too small for effective irradiation from 131-I? (In press to Thyroid).

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

1. Deavney SL, Svoboda-Newman SM, Giordano TJ. Comaprison of immunohistochemical and molecular methods of detecting p53 mutations in adrenal cortical neoplasms. Presented at the 1997 Spring Meeting of the United States and Canadian Academy of Pathology.
2. Fogt F, Vortmeyer AO, Goldman H, Giordano TJ, Merino MJ, and Zhuang Z. Loss of heterozygosity in the development of dysplasia and carcinoma in ulcerative colitis: A genetic characterization. Presented at the 1997 Spring Meeting of the United States and Canadian Academy of Pathology.
3. Wolintz RJ, Trobe JD, Gebarski SS, and Giordano, TJ: There is more than meets the eye. Presented at the 1997 Annual Meeting of the Frank B. Walsh Society.
4. Al-Kassab AS, Koenig RJ, Giordano TJ. Inappropriate antidiuretic hormone secretion secondary to ethmoid sinus esthesioneuroblastoma - A case report. Presented at the 1997 Meeting of the Association for Clinical Endocrinology.

ROBERT T. GOLDMAN, M.D.
VISITING LECTURER
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Dermatopathology slide reading - 20% of the time

II. TEACHING ACTIVITIES:

Responsible during the current academic year for teaching activities for the following:

a. Pathology residents
b. Dermatology residents

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.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Lecturer, Biomedical Summer Research Program for Minority Students.
B. Laboratory Instructor for Pathology Laboratories for M2 curriculum.
C. Atherosclerosis lecture: Cardiovascular Sequence (M2).
D. Lecturer, M4 Pharmacology course (Lucchesi: "Senior Therapeutics")

III. RESEARCH ACTIVITIES:

A. Patterns of growth factor/cytokine gene expression and cell proliferation in human atherosclerosis and transplant arteriosclerosis.
B. Patterns of collagen type gene expression in human atherosclerosis and transplant arteriosclerosis; relationships to growth factor/cytokine gene expression.
C. Evaluation of the effects of specific genes transferred into the artery wall (collaborative research with Gary and Elizabeth Nabel, Department of Internal Medicine).
D. The pathologic determinants of human and animal model atherosclerotic plaque rupture (collaborative effort with Parke-Davis, Inc.).
E. The pathologic determinants of human and animal model arterial aneurysm formation and enlargement (collaborative effort with Charles Shanley and the Jobst Vascular Research Laboratory in the Division of Vascular Surgery).
F. Pathology support for ongoing melanoma gene transfer studies (Gary Nabel, Principal Investigator).
G. Organizer of the Vascular Biology Forum Journal Club.
H. Member, Cardiovascular Research Center (Cardiology).

SPONSORED SUPPORT:

A. Principal Investigator, "Cell Growth and Collagen Synthesis in Atherosclerosis", National Institutes of Health, HL42119, $677,258 (direct), 1995-1998.
B. Principal Investigator, "Vascular Biology Patterns of Collagen Gene Expression in Human Atherosclerosis", American Heart Association 93013780, three years, $120,000, 1993-1996.
C. Principal Investigator, "A Gene Therapy Approach to Transplant Arteriosclerosis", American Heart Association of Michigan, two years, 1995-1997, $56,000 (direct).
D. Principal Investigator, "The Fibrogenic Intimal Cell of Arteriosclerosis", Taisho Pharmaceuticals Co., 1995-1998, $210,000 (direct).
E. Collaborating Investigator, 10% effort (Principal Investigator, Elizabeth G. Nabel, Cardiology), "Expression and Function of Recombinant TGF-β in Arteries", NIH DK42706, 1993-1998.

F. Collaborating Investigator, 10% effort on morphology core (Principal Investigator, Gary J. Nabel, Internal Medicine), "Molecular Genetic Interventions for Pediatric AIDS", NIH-NIAID AI36606.
G. Collaborating Investigator, 10% effort (Principal Investigator, Elizabeth G. Nabel, Cardiology), "Gene transfer into the pulmonary vasculature", NIH, NHLBI RO1 HL53466.
H. Collaborating Investigator in training grant: "Training in Molecular and Cellular Cardiology (Principal Investigator, Elizabeth G. Nabel, Cardiology) NIH T32 HL07853.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Assistant Dean for Faculty Affairs (30% effort).
B. Cardiovascular Research Center, Executive Committee.
C. Chair: Medical School's Diversity and Career Development Committee
D. Dean's Faculty Affairs Advisory Group.

REGIONAL AND NATIONAL:

A. American Heart Association of Michigan Research Day Program Committee.
B. ASIP Program Committee.
C. Editorial Board, Cardiovascular Pathology

INVITED LECTURES/SEMINARS:

1. "Cell proliferation and collagen synthesis in human atherosclerosis." Talk given to Genentech Inc. (San Francisco, CA) Sept. 4, 1996
2. "Restenosis-- The pathologist's perspective." Talk given at the Cleveland Clinic Foundation's 1997 Restenosis Summit IX (Cleveland, Ohio)
3. "Men's health issues." Workshop conducted at the Towsley Center for the June 21, 1997 African American Health Day. Ann Arbor, MI.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nabel GJ, Gordon D, Bishop DK, Nickoloff BJ, Yang ZY, Aruga A, Cameron MJ, Nabel EG, Chang AE. Immune response in human melanoma after transfer of an allogeneic class I major histocompatibility complex gene with DNA-liposome complexes. Proc Natl Acad Sci USA 1996; 93:15388-15393.
2. Welling TH, Davidson BL, Zelenock JA, Stanley JC, Gordon D, Rossler BJ, Messina LM. Systemic delivery of the interleukin-1 receptor antoagonist protein using a new strategy of direct adenoviral-mediated gene transfer to skeletal muscle capillary endothelium in the isolated rat hindlimb. Human Gene Therapy 1997;7:1795-1802.

3. Sarkar R, Gordon D, Stanley JC, Webb RC. Cell cycle effects of nitric oxide on vascular smooth muscle cells. Am. J. Physiol. 1997; 272:H1810-H1818.
4. Sarkar R, Gordon D, Stanley JC, Webb RC. Dual cell cycle-specific intracellular mechanisms mediate the antimitogenic effects of nitric oxide in vascular smooth muscle cells. J. Hypertension 1997, 15:275-283.
5. Gordon D, Rekhter MD. The growth of human atherosclerosis: Cell proliferation and collagen synthesis. Cardiovasc. Pathol. 1997; 6:103-116.

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:
(others in preparation)

1. Shah NL, Rekhter MD, Andreeva ER, Orekhov AN, Gordon D: "Fibrin is associated with cell proliferation in human atherosclerotic plaques." (Submitted).
2. Rekhter MD, Simari RD, Work C, Nabel GJ, Nabel EG, Gordon D: "Gene transfer into normal and atherosclerotic human blood vessels." (Submitted)
3. Orekhov AN, Andreeva ER, Mikhailova IA, Gordon D: "Cell proliferation in normal and atherosclerotic human aorta. III. Proliferative splash in lipid-rich lesions." (submitted)
4. Ryan MJ, Emig LL, Hicks GW, Ramharack R, Brammer DW, Gordon D, Keiser JA: "Influence of lipoprotein(a) plasma concentration on neointimal growth in a monkey model of vascular injury." (Submitted).
5. Rekhter MD, Shah NL, Simari RD, Work C, Kim J, Nabel GJ, Nabel EG, Gordon D: "Arterial smooth muscle as a target for gene therapy of transplant arteriosclerosis." (Submitted)

BOOKS AND CHAPTERS IN BOOKS:

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

1. Filippov SV, Rekhter MD, Phan SH, Gordon D. Human atherosclerotic plaques are enriched with cells simultaneously expressing TGF-β ant type one procollagen. FASEB J. 1997, 11:897.
2. Rekhter MD, Shah N, Simari RD, Work C, Kim J-S, Nabel GJ, Nabel EG, Gordon D. Gene therapy for transplant arteriosclerosis. FASEB J. 1997, 11:1839.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

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 (1/2 hour new this year).
   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, 1997.
   3. Gastrointestinal and hepatic pathology tutoring - six months.
   4. Four consultation conferences.

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

PROJECTS UNDER STUDY:

A. Study of COX-2 expression in H. pylori gastritis with Division of Rheumatology.
B. Study of liver transplant rejection with Keith Henley, Division of Gastroenterology.
C. Study of MALT lymphomas arising in Helicobacter pylori gastritis with Eric Hsi and Charlie Ross.
D. Study of LOH of the DCC gene in Dukes B colon cancers with Richard Boland and John Carruthers, Division of Gastroenterology, UC San Diego.
E. Study of ischemic colitis with Caroline Dignan.
F. Study of colonic stromal tumors with Joseph Tworek and Henry Appelman.
G. Study of PET scans in detecting metastases in breast cancer with Richard Wahl, Division of Nuclear Medicine.
H. Study of etiology of pancreas cancer with David Garabrandt, School of Public Health.
I. Study of graft vs. host disease with Caroline Dignan.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

A. Reviewer, Cancer.
B. Reviewer, Archives of Pathology and Laboratory Medicine.
C. Reviewer, Gastroenterology.
D. Reviewer, Digestive Diseases and Sciences.
E. Reviewer, American Journal of Surgical Pathology.
F. Reviewer, Liver Transplantation and Surgery.
G. Resident in Training Award Committee, Hans Popper Hepatopathology society resident .
H. Webmaster, Hans Popper Hepatopathology Society.
I. Abstract reviewer, GI section of USCAP meeting.
J. Chairperson, Education Committee of the Gastrointestinal Pathology Society.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1997	Co-director of USCAP course entitled "Infectious Diseases of the GI Tract", March, 1997.
1997	Chairperson of Proferred Papers, Gastrointestinal Pathology section, USCAP Meeting, March 1997.

1997	Invited Speaker, Inflammatory Lesions of the Liver, Greater Detroit Pathology Society, April 1997.
1997	Faculty Member, ASCP Workshop - Surgical Pathology of the Gastrointestinal Tract, St. Petersburg, Florida, April 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Greenson JK: Macrophage Aggregates in Cytomegalovirus Esophagitis. Human Pathology 28:375-378, 1997.
2. Svoboda SM, Greenson JK, Singleton, Sun R, Frank TS: Detection of Hepatitis C in Paraffin Sections of Formalin Fixed Liver Using RT-PCR. (In Press, Diagnostic Molecular Pathology)
3. Greenson JK: Collagenous Colitis and Lymphocytic Colitis, (In Press, Pathology Case Reviews.)
4. Tworek JA, Appelman HD, Singleton TP, Greenson JK: Stromal Tumors of the Jejunum and Ileum. Modern Pathology 10:200-209, 1997.
5. Greenson JK, Stern RA, Carpenter SL, Barnett JL: The Clinical Significance of Focal Active Colitis. Human Pathology 28:729-733, 1997.
6. Scheiman JM, Meise KS, Greenson JK, Coffey RJ: Transforming Growth Factor Alpha (TGFa) Levels in the Human Proximal Gastrointestinal Epithelium: Effect of Mucosal Injury and Acid Inhibition. Digestive Diseases and Sciences 42(2):333-341, 1997.
7. Dignan CR, Greenson JK: Can Ischemic Colitis be Differentiated from Clostridium Diffficile Colitis in Biopsy Specimens? Am J Surg Path 21:706-710, 1997.
8. MacDonald GA, Greenson JK, DelBuono EA, Grady W, Frank TS, Lucy MR, Appelman HD: "Mini"-microabscess Syndrome in Liver Transplant Recipients. (Accepted to Hepatology).
9. Taniuchi T, Mortensen ER, Ferguson A, Greenson JK, Merchant JL. Overexpression of ZBP-89, a zinc finger DNA binding protein, in Gastric Cancer. Biochem Biophys Res Comm 233:154-160, 1997.
10. Fryzek JP, Garabrant DH, Greenson JK, Schottenfield D. A Review of the Epidemiology and Pathology of Pancreas Cancer. GI Cancer 2:99-110, 1997.
11. Hsi ED, Greenson JK, Singleton TP, Eisbruch A, Ross CW, Schnitzer B: Classification of Primary Gastric Lymphomas According to Histologic Features (Accepted, American Journal of Surgical Pathology)
12. Greenson JK. The use of the Polymerase Chain Reaction and In-Situ Hybridization in Detecting Infections of the Gastrointestinal Tract. Acta Endoscopica (In Press).

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Macdonald GA, Greenson JK, Saito K. Appelman HD, Boland CR: Loss of the DNA Mismatch Repair Genes hMSH2 and/or hMLH1 is an early event in hepatic carcinogenesis (Submitted to Hepatology).
2. Carethers JM, Hawn MT, Greenson JK, Hitchcock CL, Boland CR. Prognostic Significance of Allelic Loss of Chromosome 18q for Stage II Colorectal Cancer. (Submitted to Nature - Medicine)

BOOKS/CHAPTERS IN BOOKS:

None

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

1. Dignan CR, Levine J, Ratanatharathorn V, Greenson JK. Evaluating Gastrointestinal Graft vs. Host Disease (GVHD): Where should we biopsy? Poster, USCAP Meeting, 1997, Modern Pathol 10:54A, 1997.
2. Tworek JA, Goldblum JR, Weiss SW, Greenson JK, Appelman HD. Stromal Tumors of the Colon. Poster Presentation at USCAP Meeting, 1997, Modern Pathol 10:66A, 1997.
3. Tworek JA, Goldblum JR, Weiss SW, Greenson JK, Appelman HD. Stromal Tumors of the Rectum and the Anus. Platform Presentation, USCAP Meeting, 1997, Modern Pathol 10:66A, 1997.
4. Carethers JM, Hawn MT, Greenson JK, Hitchcock CL, Boland CR. Loss of Heterozygosity (LOH) at Chromosome 18q is not Associated with Disadvantaged Survival for Stage II Colorectal Tumors. Platform Presentation, AGA Digestive Disease Week, 1997. Gastroenterology 112:A544, 1997.
5. Friis-Hansen L, Li Y, Sundler F, Gillespie PJ, Sonders TL, Greenson JK, Owyang C, Rehfeld JF, Samuelson LC. Reduced Maturation and Function of Parietal and ECL Cells in Gastrin-Deficient Mice. Platform Presentation at AGA Digestive Disease Week, Gastroenterology 112:A1148, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Pediatric Necropsies, daily, twelve months.
B. Pediatric Surgical Consultation Cases, daily, twelve months.
C. Adult Necropsy Service, staff, fourteen weeks.
D. Continued to organize and maintain the Michigan Cardiac Registry, twelve months.
E. Teratology Unit, histology, as necessary, approximately 40 cases per year.
F. 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 of new curriculum.
B. M4: Pathology clerkship mentor, five students.
C. House Officers in Pathology, daily consultation on Pediatric cases in surgical reading rooms, twelve months.
D. House Officers in Pathology, gross and microscopic supervision of most pediatric necropsies, twelve months, and adult cases, fourteen weeks plus on-call weekends.
E. Lecture on Pediatric Necropsy Pathology in Orientation for new House Officers in Pathology.
F. Gross Necropsy Conference, one hour/week, twelve months.
G. Supervised Pediatric Hematology Fellows (one) for Pediatric Pathology elective period.
H. Coordinate two core curriculum lectures in placenta: Pathology and OB/GYN residents.
I. Consult conference (1), pediatric cases for pathology residents.
J. Conferences: Faculty, house staff and students:
    1. Pediatric Cardiology Death Conference, monthly, twelve months.
    2. Pediatric Tumor Conference, twice monthly, twelve months.
    3. Pediatrics CPC/General Death Conference, quarterly.
    4. Pediatric Liver-GI Conference, twice monthly, twelve months.
    5. Pediatric General Surgery Conference monthly, twelve months.

III. RESEARCH ACTIVITIES:

A. Ongoing review of effects of various congenital heart defects on the pulmonary vasculature.
B. Histopathological component of lung changes associated with various cardiopulmonary therapeutic support mechanisms.
C. Study with pediatric cardiologists and thoracic surgeons on the effects of manipulation of various stents in different stenotic vessels (see publications).
D. 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.

PROJECTS UNDER STUDY:

A. Review of the predictive value of pre-ECMO lung biopsy in determining survival and recovery of pulmonary function (Group study, pathologists, surgeons, pediatricians).
B. Continuing correlation of histopathologic classification of neuroblastoma cell/tumor maturity with different tissue gene expressions. (Valerie Castle, M.D., PI.)
C. Review of predictive value of heart biopsies for death in pediatric transplant patients. (Manuscript submitted.)
D. 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.
E. 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.
F. Continuing study/evaluation of normal pediatric heart measurements of Triangle of Koch with Caren Goldberg, M.D. and M. Dick, M.D. for use in electrophysiology therapy of infants and children.

ONGOING RESEARCH:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Departmental ACAPT.
B. Autopsy Protocol Committee (Dan Remick, M.D., chair).
C. Autopsy Infection Control Committee (Dan Remick, M.D., chair).

MEDICAL SCHOOL/HOSPITAL:

A. Executive Committee for Mott/Women's/Holden/Psychiatric Hospitals.
B. Interviewing Pediatric Cardiology fellowship candidates.

REGIONAL AND NATIONAL:

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

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Mendelsohn AM, Dorostkar PC, Moorehead C, Lupinetti FM, Reynolds PI, Ludomirsky A, Lloyd TM, Heidelberger KP and Beekman RH: Stent Redilation in Canine Models of Congenital Heart Disease: Pulmonary Artery Stenosis and Coarctation of the Aorta. Catheterization and Cardiovascular Diagnosis, 38:430-440, 1996.
2. Bove KE and The Autopsy Committee of the College of American Pathologists (Kathleen Heidelberger, member) Practice Guidelines for Autopsy Pathology: The Perinatal and Pediatric Autopsy. Arch Pathol Lab Med, 121:368-376, 1997.

3. Barr M, Sedman AB, and Heidelberger KP: Renal Tubular Dysgenesis Among Twins. (Revised manuscript submitted.)

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

1. Goldberg CS, Heidelberger KP, Caplan MJ, and Dick M: Dimensions of the Triangle of Koch in Children. Abstract: International Society of Electrocardiology, Cleveland, Ohio, July, 1996. Platform presentation.
2. Heidelberger KP, Book review: Keeling JW: Fetal Pathology. Am J of Surg Pathol, 20:1157-58, 1996.
3. Barr M, Sedman AB, Heidelberger KP: Renal Tubular Dysgenesis Among Twins. The DW Smith Workshop on Malformations and Morphogenesis. Lake Arrowhead, CA.; Sept. 1996.
4. Goldberg CS, Heidelberger KP, Caplan MJ, and Dick M: Dimensions of the Triangle of Koch in Children. North American Society for Pacing and Electrophysiology, May 1997. Poster presentation of enlarged study. (Manuscript in preparation.)

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

PENDING SUPPORT:

A. Principal Investigator, "Solid Phase Assay for Transaminases" NIH. SBIR.
B. Principal Investigator, "Adhesion Molecules and Cytokines in Glomerulonephritis", with J. Varani. NIH.
C. Co-Investigator, "Amino Acids and Cell Injury", with Joel Weinberg, Nephrology and James Varani, Pathology. NIH.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

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

V. INVITED LECTURES AND SEMINARS:

1. Visiting Professor, SUNY Buffalo, NY, Department of Anesthesiology, Buffalo, New York, 1996.
2. Invited Speaker, "Mechanisms of Pulmonary and Renal Inflammation", Emory University, Atlanta, Georgia, 1996.
3. Visiting Professor, Metro Health Center, Cleveland, Ohio, 1997.
4. Visiting Professor, SUNY Buffalo, NY, Department of Anesthesiology, Buffalo, New York, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Huber, A.R., Ellis, S., Johnson, K.J., Dixit, V.M. and Varani, J.: Monocyte diapodesis through an in vitro vessel wall construct: inhibition with monoclonal antibodies to thrombospondin. J. Leuk. Biol., In Press.
2. Johnson, K.J., Sulavik, C. and Rehan, A.: Role of oxygen radicals in autologous anti-GBM nephritis. Inflammation, In Press.
3. Mulligan, M.S., Sulavik, C., Ward, P.A., Kunkel, R.G. and Johnson, K.J.: The delayed phase of anti-GBM nephritis is deferoxamine sensative but catalase insensitive. Inflammation, In Press.
4. Knight, P.R., Rutter, T., Tait, A., Coleman, E. and Johnson, K.J.: Pathogenesis of gastric particulate lung injury: A comparison and interaction with acidic pneumonitis. Anest. Analg., In Press.
5. Gregory, M.J., Smoyer, W.E., Kershaw, D.B., Valenti, R.P., Johnson, K., Sedman, A. and Bunchman, T.E.: Long term cyclosporine therapy for pediatric nephrotic syndrome: A clinical and histologic analysis. J.A.S.N. 7:543-549, 1996.
6. Swanson, P.C., Yung, R.L., Blatt, N.B., Eagan, M.A., Norris, J.M., Richardson, B.C., Johnson, K.J. and Glick, G.D.: Ligand recognition by murine anti-DNA autoantibodies II. Genetic analysis and pathogenicity. J. Clin. Invest. 97:1748-1760, 1996.
7. Lowe, N.J., Wieder, J.M., Rosenbach, A., Johnson, K.J., Kunkel, R., Bainbridge, C., Baurget, T., Demovy, I., Simpson, K., Glass, E., Grabie, M.T.: Chronic low dose cyclosporin therapy for severe psoriasis: Effects on renal function and structure. J. Invest. Derm., 1996;35:710-719.
8. Richardson, B.C., Yung, R.L., Rowse, P.E., Johnson, K.J., and Laiwani, N.D.: Monocyte apoptosis in patients with active lupus. Arthritis-Rheumatism. 1996;39:1432-1434.
9. Mulligan, M.S., Schmid, E., Schimmer, B., Till, G.O., Friedl, H.P., Brauer, R.B., Hugli, T.E., Miyasaka, M., Warner, R.L., Johnson, K.J. and Ward, P.A.: Requirement and role of C5a in acute lung inflammatory injury in rats. J. Clin. Invest. 1996;98:503-512.
10. Varani, J., Burmeister, W., Bleavins, M.R. and Johnson, K.J.: All-trans retinoic acid reduces membrane fluidity of human dermal fibroblasts. Assessment by fluorescence redistribution after photobleaching. Am. J. Path. 148:1307-1312, 1996.
11. Vogt, B.A., Shanley, T.P., Croatt, A., Alam, J., Johnson, K.J., and Nath, K.A.: Glomerular inflammation induces resistance to tubular injury in the rat: a novel form of acquired, hemeoxygenase-dependent resistance to renal injury. J. Clin. Invest. 1996;98(9)2139-45.
12. Richardson, B.C., Yung, R.L., Rowse, P.E., Johnson, K.J., and Laiwani, N.D.: Monocyte apoptosis in patients with active lupus. Arthritis-Rheumatism, 1996;39:1432-1434.
13. Varani, J., Hirschl, R.B., Dame, M., and Johnson, K.J.: Perfluorocarbon protects lung epithelial cells from neutrophil-mediated injury in an in vitro model of liquid ventilation therapy. Shock, 1996;6:339-344.
14. Yung, R., Powers, D., Johnson, K., Amento, E., Carr, D., Laing, T., Yang, J., Chang, S., Hemati, N., and Richardson, B.: Mechanisms of drug-induced lupus. II. T-cells overexpressing lymphocyte function-associated antigen 1 become autoreactive and cause a lupus-like disease in syngeneic mice. J. Clin. Invest., 1996;97:2866-2871.

15. Yung, R., Chang, S., Hemati, N., Johnson, K. and Richardson, B.: Mechanisms of drug-induced lupus. IV. Comparison of procainamide and hydralazine with analogs in vitro and in vivo. Arthritis and Rheumatism. 40, 1997.
16. Yung, R., Williams, R., Johnson, K.J., Stoolman, L., Change, S. and Richardson, B.: Mechanisms of drug-induced lupus. III. Sex-specific differences in splenic T cell homing may explain increased severity in female mice. Arthritis and Rheumatism. 40, 1997.
17. Nader-Djalal, N., Knight, P.R., Davidson, B.A., Johnson, K.J.: Hyperoxia exacerbates microvascular lung injury following acid aspiration. Chest. (In Press), 1997.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Ward, P.A., Till, G.O., Kunkel, R.G. and Johnson, K.J.: Protection against neutrophil-mediated lung injury by platelet depletion. Submitted for publication.
2. Hirschl, R.B., Tooley, R., Parent, A., Johnson, K.J. and Bartlett, R.H.: Evaluation of gas exchange, pulmonary function and lung injury during total and partial liquid ventilation in the setting of severe respiratory failure. Submitted for publication.
3. Lebedovych, L.M., Johnson, K.J., McMorris, M.S., Gilardy, A.K., Hirschl, R.B., Ward, P.A. and Baker, J.R.: Characteristics of the late allergic responses in rats previously sensitized with monoclonal IgE antibodies. Submitted for publication.
4. Varani, J., Hirschl, R., Dame, M. and Johnson, K.J.: Neutrophil infiltration is reduced during liquid ventilation: II. In Vitro analysis. Amer. J. Respir. & Crit. Care Med., Submitted.
5. Colton, D.M., Hirschl, R.B. Till, G.O., Johnson, K.J, Dean, S.B., Patel, S. and Bartlett, R.H.: Neutrophil infiltration is reduced during liquid ventilation: 1. In vivo analysis. Amer. J. Respir. & Crit. Care Med., Submitted.
6. Hirschl, R.B., Tooley, R., Parent, A., Johnson, K.J. and Bartlett, R.H.: Evaluation of gas exchange, pulmonary compliance, and lung injury during total and partial liquid ventilation in the acute respiratory distress syndrome. J. Crit. Care Med., Submitted.
7. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K.J, Ichiba, S. and Bartlett, R.H.: Liquid ventilation decreases pulmonary hemorrhage and vascular permeability. Submitted for publication.
8. Annis, K., Sigler, C. Johnson, K.J., Berman, S., Haber, H, Bonalsky, J., Luscombe, F. and Van de Carr, S.: Predictors of angioedema associated with angiotensin converting enzyme inhibitor. Submitted for publication.
9. Hirschl, R.B., Tooley, R., Parent, A., Johnson, K. and Bartlett, R.H.: Evaluation of gas exchange, pulmonary compliance, and lung injury during total and partial liquid ventilation in the acute respiratory distress syndrome. Journal of Critical Care Medicine, Submitted.
10. Sonda, P., Ellis, J.H., Kunkel, R., Platt, J.F., Faerber, G.J., Rubin, J.M. and Johnson, K.J.: Chronic partial renal obstruction in dogs: resistive indices and ratios by duplex doppler sonography. Submitted for publication.
11. Nader-Djala, N., Knight, P.R., Davidson, B.A., Helinski, J. and Johnson, K.J.: Hyperoxia exacerbates microvascular lung injury following acid aspiration. Submitted for publication.
12. Colton, D.M., Till, G.O., Johnson, K.J., Dean, S.B. and Hirschl, R.B.: Neutrophil accumulation is reduced during partial liquid ventilation. Submitted to Critical Care Med.

13. Gipson, T.S., Shanley, T.P., Gibbs, D.F., Jones, M.L., Bleavins, M.R., McConnell, P., Mueller, W., Johnson, K.J., and Ward, P.A.: Role of endogenous rat tissue inhibitor of metalloproteinase-2 in acute lung inflammatory injury. Submitted to Am J of Pathology
14. Nader-Dajal, N., Knight, P.R., Thusu, K., Davidson, B.A., Aljada, A., Holm, B.A., Johnson, K.J., Dandona, P.: The role of reactive oxygen species in oxygen-related lung injury following acid aspiration. Submitted to Chest.
15. Nader-Djalal, N., Knight, P.R., Tait, A.R., Kennedy, T.P. and Johnson, K.J.: Alterations in the course of acid-induced lung injury in rats following general anesthesia: Volatile anesthetics vs ketamine. Submitted to Anesthesia and Analgesia.

BOOKS AND CHAPTERS IN BOOKS:

1. Warren, J.S., Johnson, K.J. and Ward, P.A.: Phagocytes and reactive oxygen substances as mediators of acute lung injury, in, Hyers, T. (ed), Diffuse Alveolar Damage and Respiratory Failure, Futura Press, New York, In Press.
2. Till, G.O., Johnson, K.J. and Ward, P.A.: Oxygen free radicals in inflammation, in, Messmer, K. and Hammersen, F. (eds), Prog. Appl. Microcirc., Volume 9, Karger, Basel, In Press.
3. Ward, P.A., Warren, J.S. and Johnson, K.J.: Oxygen radicals, inflammation and tissue injury, in, Pryor, W. and Godber, S.L. (eds), Free Radical Biology and Medicine, In Press.
4. Varani, J. and Johnson, K.J.: Modulation of endothelial cell injury by all-trans retinoic acid: Role of the anti-inflammatory effects of RA, in, Jesaitis, A. (ed), Molecular basis of oxidative damage by leukocytes. CRC Press, In Press.
5. Ward, P.A., Warren, J.S., Remick, D., Varani, J., Gannon, D. and Johnson, K.J.: Cytokines and oxygen radical mediated tissue injury, in Shoemaker, W.C. (ed), New Horizons III, Critical Care Medicine, 1997.

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

1. Colton, D.M., Johnson, K.J. and Hirschl, R.B.: Partial liquid ventilation with perflurocarbon improves oxygenation and reduces intraalveolar hemorrhage in the setting of acute lung injury. Submitted to: Soc. Univ. Surgeons, 1996.
2. Gibbs, D.F., Varani, J. and Johnson, K.J.: Matrix metalloproteinases of the rat alveolar macrophage: Role in acute lung inflammation. Submitted to: Amer. Assoc. for Cancer Research, 1996.
3. Sonda, P., Ellis, J.H., Kunkel, R., Platt, J.F., Faerber, G.J., Rubin, J.M. and Johnson, K.J.: Chronic partial renal obstruction in dogs: resistive indices and ratios by duplex doppler sonography. Submitted to American Society Urology, 1996
4. Bleavins, M., Johnson, K.J. and de la Iglesia, F.A.: Modulation of mercuric chloride induced kidney injury by two recombinanat human epidermal growth factors. Society of Toxicology, 1996.
5. Smoyer, W.E., Gregory, M.J., Bajwa, R.S., Johnson, K.J. and Bunchman, T.E.: Predictive value of renal biopsies for the subsequent response to cyclosporine in childhood nephrotic syndrome. Submitted to American Society of Nephrology, 1996.

6. Yung, R., Johnson, K. and Richardson, B.: DNA methylation inhibitors cause lupus by inducing T cell LFA-1 overexpression. FASEB J. 10:A1307, 1996.
7. Gipson, T.S., Shanley, T.P., Jones, M.L., Johnson, K.J. and Ward, P.A.: Molecular cloning and regulation of rat tissue inhibitor of metalloproteinase-2 in acute lung injury in rats. FASEB J. 10:A1007. 1996.
8. Crouch, L.D., Shanley, T.P., Johnson, K.J. and Ward, P.A.: IL-13 is transcriptionally expressed in IgG-immune complex-induced lung injury. FASEB J. 10:A1008, 1996.
9. O'Shea, S., Johnson, K.J.J., Moore, M., and Erickson, S.: Heregulin, ErbB2, and ErbB3 heterozygous mice: histological analysis and response to heregulin challenge. Submitted to AACE, 1997.
10. Crouch, L.D., Lentsch, A.B., Warner, R.L., Johnson, K.J., and Ward, P.A.: Regulatory effects of adrenal gland products in IgG immune complex acute lung injury. Submitted to FASEB, 1997.
11. Gipson, T.S., Shanley, T.P., Bleavins, M.R., Tefera, W., Johnson, K.J., and Ward, P.A.: Molecular cloning and in vivo transcriptional expression of rat SLPI in lung inflammation. Submitted to FASEB, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Director, Blood Bank Reference Laboratory.
   1. Generated data to support a procedural change (elimination of the 37 C reading) that will significantly reduce (200+ samples annually; 20% of current reference laboratory workload) the number of unwanted positive pretransfusion antibody detection tests. Procedural change implemented in August, 1997.
   2. Generated data to support a procedural change (omit repeat antibody identification studies except when there is serological or clinical evidence of a new antibody). This change, if implemented, has the potential to reduce current reference laboratory workload by 40% with minimal risk to patient care.

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

II. TEACHING ACTIVITIES:

A. Clinical Pathology Grand Rounds:
   1. Program Director.

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. Hematology/Oncology Fellows:
   1. Provided instruction in immunohematology to Dr. Prasannda (10 contact hours).

F. Pathology Residents:
   1. Residency Training Review Committee.
   2. Coordinated Blood Bank/Immunology/Coagulation and HLA block rotations for house-officer training in clinical pathology.
   3. Provided instruction in immunohematology to house-officers during their Blood Bank Rotation (100 contact hours).
   4. Presented Pizza Seminar on Antibody Identification (2 contact hours).

G. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
   1. Program Director - Planned and coordinated the June, 1997 Current Topics in Blood Banking Symposium and Preconference Workshops.
   2. Presented Workshop entitled: "What's My Type?"
   3. Presented talk entitled: "Eliminating the 37 C Reading."
   4. Moderated morning session on Transfusion Management.

H. Clinical Pathology M-4 Elective:
   1. Member, Coordinating Committee.
   2. Organized Elective in Transfusion Medicine.
   3. Presented talks on pretransfusion testing, immune hemolysis and prenatal/perinatal testing.

III. RESEARCH ACTIVITIES:

A. Judd WJ, Steiner EA, Fullen DR, Knafl PC. Omitting the 37 C reading. Submitted for presentation at the 1997 Annual Meeting of the American Association of Blood Banks, Denver, CO.
B. Judd WJ. Two or three reagent red cells for antibody detection. Submitted for presentation at the 1997 Annual Meeting of the American Association of Blood Banks, Denver, CO.
C. WJ Judd and SH Butch. Repeat antibody identification tests. Submitted for presentation at the 1997 Annual Meeting of the American Association of Blood Banks, Denver, CO.
D. EA Steiner and WJ Judd. Detection of ABO incompatibility in Gel. Submitted for presentation at the 1997 Annual Meeting of the American Association of Blood Banks, Denver, CO.
E. Evaluated new technology (Gamma React) for pretransfusion antibody detection.

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. Chairman, Special Lecture Series Committee - coordinated a series of 60 lectures, two full-day workshops and a two-day review session for medical technologists seeking Certification as a Specialist in Blood Banking
   2. Presented lectures on Rh and MN systems, drugs, lectins and polyagglutination (10.5 contact hours) as part of Special Lecture Series.
   3. Presented lectures on carbohydrate antigens of the RBC membrane, Rh system lectins, polyagglutination and serological artifacts as part of Specialist in Blood Banking Review Program, March, 1997.
   4. Member, Annual Meeting Program Committee.
B. American Association of Blood Banks:
   1. Member, Awards Committee.
   2. Member, Scientific Abstract Review Committee
C. Member, Editorial Board, Transfusion.
D. Reviewer of articles submitted for publication in Transfusion, Immunohematology, and Transfusion Medicine.
E. International Society of Blood Transfusion
   1. WHO Committee on Blood Group Nomenclature

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

1. Why Do You Do What You Do? Sacramento Medical Foundation Blood Bank, Sacramento, CA, September, 1996
2. Why You Must Do What You Do Right. Sacramento Medical Foundation Blood Bank, Sacramento, CA, September, 1996
3. Why Do You Do What You Do? Laguna Hills Medical Center, Laguna Hills, CA, September, 1996.
4. Why You Must Do What You Do Right. Laguna Hills Medical Center, Laguna Hills, CA, September, 1996.
5. Session Moderator - Red Cells and Serological Methods. American Association of Blood Banks Annual Meeting, Orlando, FL, October, 1996.
6. The Perfect Crossmatch. AABB Annual Meeting, Orlando, FL, October, 1996. *Speaker*
7. New Strategies for Pretransfusion Testing. University of Texas Teleconference Center, November, 1996.
8. How to write a scientific paper. American Red Cross, Washington DC, December, 1996.
9. You Do Know Why You Do What You Do Don't You? Baptist Hospital, Jacksonville, FL, March, 1997.
10. Why You Must Do What You Do Right. Baptist Hospital, Jacksonville, FL, March, 1997.
11. The Perfect Crossmatch. Tennessee Association of Blood Banks, Memphis, TN, May, 1997.

VI. PUBLICATIONS:

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

1. Daniels G, Anstee DJ, Cartron JP, Dahr W, Henry S, Jorgenson J, Judd WJ, et al. Terminology for red cell surface antigens: Makuhari report. Vox Sang 1996;71:246-8.
2. Judd WJ. Two or three "screening" cells for antibody detection? Immunohematology 1997: In Press.
3. Judd WJ, Steiner EA, Knafl P. The gel test: sensitivity and specificity for unexpected antibodies to blood group antigens. Immunohematology 1997: In Press.
4. Judd WJ, Davenport RD. On the high probability that a perceived lack of value in obtaining a p value will be detrimental to patient care! Transfusion 1997: In Press.

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

1. Judd, E.A. Steiner, R.D. Davenport. Time of sample receipt and ability to batch tests. Ortho Diagnostic Systems Inc. Raritan, NJ.
2. Judd WJ, Steiner EA, Knafl P. Validation of the gel test. Transfusion 1996;36(S):56.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Lectures to Medical Students in M4 Laboratory Medicine Elective.
B. Lectures to House Staff on Block B, Clinical Pathology, and to Chemical Pathology Fellow
C. Protein Sign-Out in Immunology Laboratory with 1-2 residents for 4-6 hours biweekly
D. Molecular Diagnostics Sign-Out with Fellow, weekly
E. Lectures to Pathology House Staff and Faculty at Clinical Pathology Rounds.
F. Research advisor to undergraduate: Ms. Renee Jiddou, UROP.
G. Research co-advisor to post-doctoral fellow: Dr. J. Srinivasan, Dept. of Chemistry, University of Michigan.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Molcular Diagnostics Laboratory.
B. Director, Clinical Chemistry Section.
C. Member, Pathology Resident Selection Committee.
D. Director, Fellowship Program in Chemical Pathology.

REGIONAL AND NATIONAL:

A. Program Chair, Association for Molecular Pathology Annual Meeting, 1996.
Editor of ACLPS Newsletter
Chair, ACLPS Taskforce on Networking.
B. Member, AACC, ASHG, CAP, ACLPS, AMP
C. Manuscript Reviewer, Clinical Chemistry, Molecular Diagnosis, and Biotechniques
D. Organized Michigan Molecular Diagnostics Forum, June 1997, Ann Arbor, MI.

V. INVITED LECTURES AND SEMINARS:

1. "Diagnostic Molecular Pathology". Midwest Clinical Ligand Assay Society, June, 1996.
2. "Genetics of Breast Cancer". Sectional Meeting of American Association for Clinical Chemistry, March, 1997.
3. "The Michigan Genetic Privacy Bill". Michigan Molecular Diagnostics Forum, June, 1997.

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

1. Killeen AA: Quantification of Nucleic Acids. Clinics in Laboratory Medicine, 17:1-19, 1997.
2. Killeen AA: An overview of current internet resources for pathology. Journal of Clinical Laboratory Analysis, 10:375-379, 1996.
3. Passmore LJ, Killeen AA: Toluidine blue dye-binding method for measurement of genomic DNA extracted from peripheral blood leukocytes. (Molecular Diagnosis, 1:329-334, 1996.
4. Petty EM, Killeen AA: BRCA1 testing: controversies and challenges. Clinical Chemistry 43:6-8, 1997.
5. Srinivasan JR, Liu Y, Venta PJ Siemieniak D, Killeen AA, Zhu Y, Lubman DM: MALDI TOF-MS as a rapid screening method to detect mutations causing Tay-Sachs disease. (In Press)

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Palaniappan L, Rubenfire M, Anthony M-N, Elliott M, Giacherio D, Killeen AA: Coronary artery disease risk factors in young African-American women. (submitted)
2. Killeen AA, Jiddou R, Sane KS: Identification of frequent polymorphisms in the CYP21 (steroid 21-hydroxylase) gene. (submitted)

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

1. Jone C, Killeen AA: Monitoring of bone marrow engraftment by PCR with product detection and quantitation by capillary electrophoresis. Clinical Chemistry 42(6) S201, 1996.
2. Killeen AA: A visible spectrophotometric dye binding method for measurement of genomic DNA. Clinical Chemistry 42(6) S201 1996.

3. Noorhdoek GT, van Embden JDA, Kolk AHJ: Reliability of nucleic acid amplification for detection of M. tuberculosis: an international collaborative study among 30 laboratories. [Participant in this multicenter study] Journal of Clinical Microbiology, 34:2522-2525, 1996.
4. Killeen AA: Review of "Nucleic Acid Analysis", edited by Charles A. Dangler, Wiley-Liss, 1996. Clinical Chemistry 43:197, 1997 (Invited Book Review).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. M2 Pathology Lecture - Renal Sequence (3 hours).
B. M2 Pathology Laboratory- Renal Sequence (20 hours).
C. Co-Coordinator - Renal Sequence (40 hours).
D. Curriculum Development -Renal Sequence (80 hours).
E. Gross Pathology Conference.
F. Renal Pathology for Pathology Residents (four hours).
G. Renal Pathology for Nephrology Fellows (nine hours).
H. Renal Pathology Fellows - Carrie Phillips, Lois Arend - (150 hours).
I. Autopsy Pathology (3 hours).
J. Dissertation Committees (one).
K. Post Doctoral Fellows (one).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Collagen IV Gene Transcription in cpk/cpk Mice", NIH-RO1-DK44848, (25% Effort) $143,000/first year, 9/30/91-9/29/96.
B. Principal Investigator, Project VI, "TGF-β Induced Collagen IV Gene Transcription", NIH-P50-DK39225, (10% Effort) $49,822/year, 8/1/92-7/30/97.
C. Co-Investigator, "Renal Fibrosis", NIH-RO1, (5% Effort) $198,213/ year, 4/1/93-3/30/98.
D. Co-Investigator, "Role of EDRF in the Juxtaglomerular Apparatus", NIH-RO1-DK40042, (5% Effort) $164,666/year, 12/1/93-11/30/98.
E. Core Consultant, Molecular Biology Core, "Michigan Diabetes Research and Training Center", NIH-P60-DK20572, (5% Effort) $100,000 direct costs/year, 4/1/93-3/31/98.

PENDING SUPPORT:

A. Co-Investigator, "Altered Neural Myo-Inositol Metabolism in Diabetes", NIH-R01-DK38304, (20% Effort) $225,547 direct costs/year.
B. Co-Investigator, "IGF-I is an Osmoprotectant in Neuroglial Cells", NIH-R01-DK38304, (5% Effort) $103,045 direct costs/year,.
C. Co-Investigator, "SCOR in Osteoarthritis and Systemic Lupus Erythematosus: Project 5. Predicting Progression in Lupus Nephritis", NIH P50, (20% effort) $142,819 direct costs/year.
D. Director, Morphology Core B, George M. O'Brien Renal Center, NIH-P50-DK39225, (5% Effort) $55,603 direct costs/year.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Planning Committee, Genetic Basis of Renal Disease. NIDDK, NIH.
B. Ad hoc reviewer, Division of Extramural Activities, NIDDK, NIH.
C. Ad hoc Reviewer, Juvenile Diabetes Foundation.
D. Reviewer:
    1. Laboratory Investigation.
    2. American Journal of Pathology.
    3. American Journal of Physiology.
    4. Journal of Clinical Investigation.
    5. Journal of Biological Chemistry.
    6. Journal of American Society of Nephrology.

E. Program Committee, Annual Meeting of the American Society of Nephrology.

V. INVITED LECTURES AND SEMINARS:

1. Invited Speaker, "RT-PCR Quantitation of Collagen I mRNA Predicts Disease Progression", International Congress of Nephrology, Sydney Australia, May 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kuncio, G.S., Alvarez, R., Li, S., Killen, P.D. and Neilson, E.G.: Transforming growth factor beta (TGFβ) modulation of the α1(IV) collagen gene in murine proximal tubular cells. Amer. J. Physiol., 271:F120-F125, 1996.
2. Bergijk, E.C., Baelde, J.J., Kootstra, C.J., de Heer, E., Killen, P.D. and Bruijn, J.A. : Cloning of the mouse fibronectin V-region and alteration of its splicing pattern in experimental immune complex glomerulonephritis. J Pathol 178:462-8 1996.
3. Todd-Turla KM, Zhu XL, Shu X, Chen M, Yu T, Smart A, Killen PD, Fejes-Toth G, Briggs JP, Schnermann JB.:Synthesis and secretion of endothelin in a cortical collecting duct cell line. Amer J Physiol 271:F330-F339, 1996.
4. Bergijk EC, Baelde JJ, Kootstra CJ, de Heer E, Killen PD, Bruijn JA: Cloning of the mouse fibronectin V-region and alteration of its splicing pattern in experimental immune complex glomerulonephritis. J Pathol 178:462-8 1996.
5. Singh I, Grams M, Wang WH, Yang T, Killen PD, Smart A, Schnermann J, and Briggs JP.: Coordinate regulation of the renin angiotensin system and nitric oxide synthase by dietary salt. Amer J Physiol 270:F1027-F1037, 1996.
6. Lee SK, Goyal M, de Miguel M, Thomas P, Wharram B, Dysko R, Phan S, Killen PD, Wiggins RC,: Renal biopsy collagen I mRNA predicts scarring in rabbit anti-GBM disease: Comparison with conventional measures of function and histology. Kidney Int (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Porcellati F, Hlaing T, Togawa M, Stevens M, Larkin D, Glover TW, Henry DN, Greene DA, Killen PD: The human Na^+-*myo*-inositol cotransporter gene: Alternate splicing generates diverse transcripts. Submitted 1997.
2. Minto AW, Kalluri R, Togawa M, Bergijk EC, Killen PD, Salant DJ: Augmented Expression of Glomerular Basement Membrane Specific Type IV Collagen Isoforms (α3-α5) in Experimental Membranous Nephropathy. Submitted 1997.
3. Bergijk EC, Van Alderwegen IE, Baelde HJ, de Heer E, Funabiki K, Miyai H, Killen PD, Kalluri RK, Bruijn JA: Differential expression of collagen IV chains in experimental glomerulosclerosis. Submitted 1997.
4. 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-specfic regulation of *myo*-inositol transport and metabolism. Submitted 1997.

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

1. Feldman, E.L., Greene, D.A., Stevens, M. and Killen, P.D.: IGF-I prevents gloctoxicity in neuroglial cells. EASD, Submitted, 1996.
2. Porcellati, F., Hlaing, T., Togawa, M., Greene, D.A. and Killen, P.D.: Alternate exon utilization results in diverse sodium-dependent *myo*inositol (MI) cotransporter (SMIT) transcripts. Amer. Soc. Nephrol., Submitted, 1996.
3. Phillips, C.L., Arend, L.J., Miyai, H., Briggs, J.P. and Killen, P.D.: Collagen IV gene expression in cultured embryonic kidney rudiments. Amer. Soc. Nephrol., Submitted, 1996.
4. van Griensven, M., Baelde, H., Killen, P.D., de Heer, E. and Bruijn, J.A.: Sex steroid hormones alter collagen gene expression in murine lupus nephritis. Amer. Soc. Nephrol. Submitted, 1996.
5. Maeda, S., Togawa, M., Togawa, M., Hlaing, T., Greene, D.A. and Killen, P.D.: Phosphorylation-dependent binding of an inducible nuclear protein to the aldose reductase (AR) tonicity element (TonE). Amer. Soc. Nephrol., Submitted, 1996.
6. Hosaka, Y., Porcellati, F., Larkin, D., Stevens, M., Killen, P.D. and Greene, D.A.: Alternate splicing of sodium-dependent *myo*inositol (MI) cotransporter (SMIT) mRNA predicts three distinct SMIT isoforms. Amer. Soc. Nephrol., Submitted, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Cytopathology - twelve months
B. Necropsy service - six week-ends
C. Dermatopathology - Back-up, summer.
D. Room C Surgical Service - Back-up.

II. TEACHING ACTIVITIES:

A. Residents and Cytopathology Fellow:
   1. Sign-out - Gynecologic and non-Gynecologic cases.
   2. Instruction in the performance and interpretation of fine needle aspirates.
   3. Instruction and supervision in the performance, presentation and sign-out of autopsy cases.
   4. Monthly Cytopathology Conference - glass slide sessions, comprehensive organ systems review.
   5. Consult Case Conference - two/year.

B. Other Education Activities:
   1. Cytotechnologists - Cytopathology Conference - three/year.
   2. Current concepts update in the practice of Cytology - ongoing process; fellow, residents and cytotechnicians.
   3. Cyto-histologic correlation - ongoing process; fellow, residents and cytotechnicians.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None

PROJECTS UNDER STUDY:

A. Significance of atypia in the urine: Ten-year review with histologic correlate and clinical follow-up, with Dr. Kirk Wojno and Dr. Mahual B. Amin, Henry Ford Hospital.
B. Nuclear matrix proteins in transitional cells: A more sensitive and specific method for detecting transitional cell carcinoma by immunoperoxidase technique, with Dr. Kirk Wojno and Dr. David Smith, Department of Oncology.
C. Prospective review of bladder biopsies: Muscularis mucosa versus muscularis propria invasion - what is the prognostic significance?, with Dr. Kirk Wojno.
D. Cytologic features of Taxol-induced changes in transitional cells, with Dr. Kirk Wojno and Dr. David Smith, Department of Oncology.
E. Nephrogenic metaplastic cells in urine: Potential pitfall mimicking transitional cell carcinoma, with Dr. Kirk Wojno and Dr. Brian Hunter.

F. Comprehensive review of normal and non-neoplastic cytologic findings in the CSF with histologic correlate, with Dr. Mila Blaivas.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None.

MEDICAL SCHOOL/HOSPITAL:

None.

UNIVERSITY OF MICHIGAN:

None.

REGIONAL AND NATIONAL:

None

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Differential Diagnosis of Thyroid Follicular and Papillary Lesions". Guest speaker; M-Labs Symposium, Ann Arbor, Michigan, April 11, 1997.
2. Glass Slide Session, Comprehensive Review of Thyroid Nodule Fine Needle Aspirates. Guest Speaker; Division of Endocrinology and Metabolism, University of Michigan, April 25, 1997.

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:

1. Kintanar EB, Michael CW. Diagnostic pitfalls and mimics of HGSIL. Accepted for platform presentation, American Society of Cytopathology National Meeting, November, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

None

II. TEACHING ACTIVITIES:

A. Epidemiology 570
B. Host Defense Sequence, First Year Medical School
C. Lecture in didactic seminar series in Dermatology
D. Member, Pathology graduate program committee
E. Member, Lung Immunopathology Post-doctoral Training Program (Pathology)
F. Member, Operating committee, Systems and Intergrative Biology Training Program (Physiology)
G. Member, Experimental Immunopathology Training Program (Pathology)
H. Member and Co-Director, Pulmonary Cellular and Molecular Biology Training Program
I. Member, Graduate Teaching Award Review Committee
J. Supervised the following postdoctoral fellows and graduate students: fellows, Drs. Betsy Parks, Ken Simpson, Cory Hogaboam, Cary Caldwell, Bruno DiGiovine
K. Undergraduate students: Kolby Keefer, Matt Steinhouse, Eric Strieter, Scott Lipinski, Carrie Zickus, Harold Schock
L. High school students: Jamal Bufford
M. Doctoral Thesis Committee Member/Orals Committee for the following graduate students: Andrew Merry (Pathology), Jami Foreback (Pathology), Arul Chinnaiyan (Pathology), Hangjun Duan(Pathology), Fran Wolber(Pathology), Jim Parks (Pharmacology), Jeffrey Ruth (Public Health), Mei-Chen Kuo (Public Health), Joyce J. Lai (Public Health), Yaozhong Ding (Microbiology and Immunology), Shimin Hu (Pathology)
N. Sabbatical supervisor for Dr. Keith Walley, University of British Columbia.

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. NIH - The role of TNF and ICAM-1 in Lung Allograft Rejection, Co-Investigator HL-50057
E. NIH-RO1, The role of C-X-C chemokines in lung cancer, Co-Investigator
F. SCOR Occupational and Immunological Lung Disease, Principal Investigator Project P50HL-46487
G. Effect of Alcohol on cytokine mediated lung host defense, Co-Investigator AA-10571

PATENTS:

"Therapeutic Treatment for Inhibiting Vascular Restenosis" #5,571,713 issued November 5, 1996

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Operating committee Pathology graduate program
B. Space utilization and research committee
C. Interview candidates for residency/graduate program
D. Divisional Director of General Pathology

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

A. Member, Committee on medical student research
B. Member, search committee for the Robinson and Huetwell Professor of Rheumatology
C. Medical school admission interview committee
D. Medical scientist training program interviewer
E. Member, Research Council of the Office of the Vice President for Research
F. Member, Michigan cancer center
G. Grant reviewer, Biomedical Research Council
H. Member, Advisory Committee Cancer Center Animal Core
I. Member, Panel of Inquiry into Federally-Sponsored Human Radiation Research at the University of Michigan in the Post-World War II Era

J. Associate Dean, Rackham Graduate School
K. Medical school LCME self-study task force
L. The University of Michigan medical school LCME self-study Graduate education in the basic medical sciences committee

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, Pathobiology
E. Associate Editor, Shock
F. Editorial board, Mediators of Inflammation
G. Vice-chair, 1998 Gordon Conference on Chemokines
H. 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
I. Grant Reviewer, The Arthritis Society
J. Grant Reviewer, Veterans Administration
K. Scientific Advisory Council, American Lung Association
L. Vice-chair, 1998 Gordon Conference on Chemokines
M. National Institute of Health Study Section, Immunological Sciences, Ad Hoc, 1996
N. National Institutes of Health Study Section, Lung Biology and Pathology,

V. OTHER RELEVANT ACTIVITIES:

AWARDS:

1. Endowed Professor in Pathology Research
2. Distinguished Faculty Achievement Award

INVITED LECTURES AND SEMINARS:

1. Invited Speaker, Society for the Study of Reproduction -Macrophage Activation Symposium, London, Ontario, July 1996
2. Invited Speaker, Distinguished Scientist Seminar Program, University of South AB, Oct 1996
3. Invited Speaker, Immunology Section, American College of Rheumatology, Orlando, FL Oct 1996
4. Invited Speaker, Third International Symposium on Surgical Infections, Madrid, Spain, Oct 1996
5. Visiting Professor, Department of Immunology, Brown University, Nov, 1996
6. Invited Speaker, Department of Pathology, Brown University, Nov, 1996
7. Invited Speaker, New England Immunology Conference, Woods Hole, MA, Nov 1996
8. Invited Speaker, Abbott Laboratory, Chicago, IL, Nov 1996

9. Invited Speaker, American Association of Immunologists, "Chemokines and Their Receptors", San Francisco, CA, Feb 1997
10. Invited Speaker, 4th International Congress on the Immune Consequence of Trauma, Shock, and Sepsis, Munich, Germany, March 1997
11. Keynote Address, Keystone Symposium, "The role of chemokines in leukocyte trafficking and disease" Copper Mountain, CO, April 1997
12. Workshop Chair, Genetics Institute Research Retreat "Immune Modulation: Pathway to Disease or Therapy, Ogunquit, ME, May 1997
13. Invited Speaker, The Role of Cytokines in Disease, Medicine in the 21st Century. UMDNJ-New Jersey Medical School, Newark, NJ. June, 1997
14. Chair and Invited Speaker, Gordon Conference on wound Repair. Colby Sawyer Academy, New London, NH, June 1997
15. Invited Speaker, Biotechnology'97 International, "Animal Modeling", Houston, TX, June 1997

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Standiford, T.J., Strieter, R.M., Greenberger, M.J., Kunkel, S.L. Expression and regulation of chemokines in acute pneumonia Bio. Signals. 1996;203-208.
2. Goldstein, L.A., Strieter, R.M., Evanoff, H.L., Kunkel, S.L., Lukacs, N.W. TNF-induced IL-8 and MCP-1 production in eosinophilic line, EOL-1. Med.Inflammation.1996; 5:218-223.
3. Greenberger, M.J., Kunkel, S.L., Strieter, R.M., Lukacs, N.W., Bramson, J., Gauldie, J., Graham, F.L., Hitt, M., Danforth, J.M., Standiford, T.J. IL-12 gene therapy protects mice in lethal Klebsiella pneumonia, J. Immunol. 1996; 157: 3006-3012.
4. Lukacs, N.W., Standiford, T.J., Chensue, S.W., Kunkel, R.G., Strieter, R.M., Kunkel, S.L. C-C chemokines-induced eosinophil chemotaxis during allergic airway inflammation. J. Leukoc, Biol. 1996; 60:573-578.
5. Arenberg DA, Kunkel SL, Polverini PJ, Morris SB, Burdick MD, Glass MC, Taub DT, Iannettoni MD, Whyte RI, Strieter RM. Interferon-g-inducible protein (IP-10) is an angiostatic factor that inhibits human non-small cell lung cancer (NSCLC) tumorigenesis and spontaneous metastases. J. Exp. Med. 1996; 184: 981-992.
6. Lukacs, N.W., Strieter, R.M., Standiford, T.J., Kunkel, S.L. Characterization of chemokine function in animal models of disease. Methods in Enzymol. 1996; 10:158-165.
7. Goodman, R.B., Strieter, R.M., Martin, D.P., Steinberg, K.P., Milberg, J.A., Maunder, R.J., Kunkel, S.L., Walz, A., Hudson, L.D., Martin, T.R. Inflammatory cytokines in patients with persistence of the acute respiratory distress syndrome. Am. J. Respir. and Crit. Care Med.1996; 154: 602-611.
8. Donnelly SC, Strieter RM, Kunkel SL, Burdick MD, O'Riordain M, de Beaux AC, Fearon KCH, Haslett C, Carter DC, Ross JA. Circulating IL-1 receptor antagonist (IL-1ra) as a prognostic marker in acute pancreatitis. Ann Intern. Med. 1996; 125: 191-196.
9. Walley, K.R., Lukacs, N.W., Standiford, T.J., Strieter, R.M., Kunkel, S.L. Balance of inflammatory cytokines related to severity and mortality of murine sepsis. Infect. Immun. 1996; 64:4733-4738.

10. DiGiovine B, Lynch, III JP, Martinez FJ, Flint A, Whyte RI, Iannettoni MI, Arenberg DA, Burdick MD, Glass MC, Wilke, C.A., Morris SB, Kunkel SL, Strieter RM. Bronchoalveolar lavage neutrophilia is associated with obliterative bronchiolitis after lung transplantation: Role of interleukin-8. J. Immunol. 1996; 157: 4194-4202.
11. Chensue, S.W., Warmington, K.S., Ruth, J.H, Sanghi, P.S., Lincoln, P. Kunkel, S.L. Role of monocyte chemoattractant protein-1 (MCP-1) in Th1 (Mycobacterial) and Th2 (Schistosomal) antigen-induced granuloma formation: Relationship to local inflammation, Th cell expression, and IL-12 production J. Immunol. 1996; 157:4602-4608.
12. Huffnagle, G.B., Toews, G.B., Burdick, M.D., Boyd, M.B., McAllister, K.S., McDonald, R.A., Kunkel, S.L., Strieter, R.M. Afferent phase production of TNF-alpha is required for the development of protective T cell immunity to Crytococuss neoformans. J. Immunol. 1996; 157: 4529-4536.
13. Driscoll, K.E., Howard, B.W., Carter, J.M., Asquith, T. Johnston, C., Detilleux, P., Kunkel, S.L., Isfort, R.J. Alpha-quartz-induced chemokine expression by rat lung epithelial cells. Effects of in vivo and in vitro particle exposure. Am. J. Pathol. 1996; 149:1627-1637.
14. Smith, R.E., Strieter, R.M., Phan, S.H., Kunkel, S.L. C-C chemokines: Novel mediators of the pro-fibrotic inflammatory response to bleomycin challenge. Am. J. Respir. Cell. Mol. Biol. 1996; 15:693-702.
15. Colletti, L.M., Kunkel, S.L., Green M., Burdick, M., Strieter, R.M. Hepatic inflammation following 70% hepatectomy may be related to up-regulation of epithelial neutrophil activating protein-78. Shock. 1996; 6:397-402.
16. Kunkel, S.L., Lukacs, N., Strieter, R.M., Chensue, S.W. Th-1 and Th-2 responses regulate experimental lung granuloma development. Sarcoidosis Vasculitis and Diffuse Lung Dis. 1996; 13:120-128.
17. Lukacs NW, Kunkel SL, Strieter RM, Evanoff H, Kunkel RG, Key ML, Taub DD. The role of stem cell factor (C-Kit ligand) and inflammatory cytokines in pulmonary mast cell activation. Blood. 1996; 87:2262-2268.
18. Redl H, Schlag G, Paul E, Bahrami S, Buurman WA, Strieter RM, Kunkel SL, Davies J., and Foulker, R. Endogenous modulators of TNF and IL-1 response are under partial control of TNF in baboon bacteremia. Am J. Physiol. 1996; 271:R1193-R1198.
19. Elner VM, Elner SG, Standiford TJ, Lukacs NW, Strieter RM, Kunkel SL. Interleukin-7 (IL-7) induces retinal pigment epithelial cell MCP-1 and IL-8. Experimental Eye Research 1996; 63:297-303.
20. Bian, Z.M., Elner,S.G.,Strieter, R.M., Glass, M.B., Lukacs, N.W., Kunkel, S.L., Elner, V.M. Glycated serum albumin induces cytokine gene expression in human retinal pigmented epithelial cells. J. Leukoc. Biol. 1996; 60:405-414.
21. Laichalk LL, Kunkel SL, Strieter RM, Danforth JM, Standiford TJ. TNF mediates lung antibacterial host defense in murine *Klebsiella* pneumonia. Infect. Immun. 1996; 64:5211-5218.
22. Bell, M.D., Taub, D.D., Kunkel, S.L., Strieter, R.M., Foley, R., Gauldie, J., Perry, V.H. Recombinant human adenovirus with rat MIP-2 gene insertion causes prolonged PMN recruitment to the brain. Eur. J. Neurosci. 1996; 8:1803-1811.
23. Lukacs NW, Chensue SW, Karpus WJ, Lincoln P, Keefer C, Strieter RM, Kunkel SL. C-C chemokines differentially alter IL-4 production from lymphocytes. Am. J. Pathol. 1997;150:1861-1868.

24. Lukacs, N.W., Strieter, R.M., Warmington, K., Lincoln, P., Chensue, S.W., Kunkel, S.L. Differential recruitment of leukocyte populations and alteration of airway hyperreactivity by C-C family chemokines in allergic airway inflammation. J. Immunol. 1997;158:4398-4404.
25. Kurtz RM, Elner VM, Bian ZM, Strieter RM, Kunkel SL, Elner SG. Dexamethasone and Cyclosporin A modulation of human retinal pigment epithelial cell MCP-1 and IL-8. Invest. Ophth. Vis. Science. 1997; 38:436-445.
26. Lukacs, N.W., Addison, C., Gauldie, J., Graham, F., Simpson, F., Strieter, R.M., Warmington, K., Chensue, S.W., Kunkel, S.L. Transgene-induced production of IL-4 alters the development and collagen expression of Th1 type pulmonary granulomas. J. Immunol. 1997;158:4478-4484.
27. Elner SG, Elner VM, Bian ZM, Lukacs, N.W., Kurtz, R.M., Strieter RM, Kunkel SL. Human retinal epithelial cell interleukin-8 and monocyte chemotactic protein-1 modulation by T-lymphocyte products. Invest. Ophth. Vis. Science, 1997; 38:446-455.
28. Hay, R.V., Skinner, R.S., Newman, C., Kunkel, S.L., Lyle, L.R., Shapiro, B. M. Gross, M.D. Scintigraphy of acute inflammatory lesions in rats with radiolabeled recombinant human interleukin-8. Nuc. Med. Comm. 1997;18:367-378.
29. Broug-Holub E, Toews GB, van Iwaarden JF, Strieter RM, Kunkel SL, Paine R, Standiford TJ. Alveolar macrophages are required for protective pulmonary defenses in murine *Klebsiella* pneumonia: elimination of alveolar macrophages increases neutrophil recruitment but decreases bacterial clearance and survival. Infect Immun 65:1139-1146, 1997.

BOOKS AND CHAPTERS IN BOOKS:

1. Strieter, R.M., Kunkel, S.L., Walz, A. Epithelial neutrophil activating protein (ENA78): A member of the CXC chemokine family. in Human Cytokines. Handbook for basic and clinical research. Volume III. Edited by Aggarwal B.B., Blackwell Science Inc., Cambridge, MA.
2. Arenberg, D.A., Polverini, P.J., Kunkel, S.L., Shanafelt, A., Strieter, R.M. In vitro and in vivo systems to assess the role of CXC chemokines in the regulation of angiogenesis. in: Chemokines and chemokine receptors. Methods in Enzymology. Edited by Abelson, J.N.and Simon M.I. Academic Press Inc. Orlando, FL.
3. Kunkel, S.L., Lukacs, N., Strieter, R.M., Standiford, T.J. Cytokine networks dictate inflammatory events at the alveolar interface. in: Update in Intensive Care and Emergency Medicine. Edited by J.L. Vincent. Springer-Verlag. Berlin, Germany
4. Kunkel, S.L., Lukacs, N., Hogaboam, C., Strieter, R.M., Standiford, T.J. Advanced forms of pharmacological interventions on pulmonary host defenses. in: Update in Intensive Care and Emergency Medicine. Edited by J.L. Vincent. Springer-Verlag. Berlin, Germany
5. Gauldie, J., Kunkel, S.L. Acute Phase Response. in: Encyclopedia of human biology. Second Edition, Academic Press, New York, NY 1997

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

1. DiGiovine B, Whyte RI, Iannettoni MD, Arenberg DA, Burdick MD, Glass MC, Morris SB, Kunkel SL, Strieter RM. CXC chemokine composition of stage I and stage II adenocarcinomas of the lung correlates with clinical outcome. J. Invest. Med. 44:345A, 1996.

2. DiGiovine B, Lynch III JP, Martinez FJ, Flint A, Whyte RI, Iannettoni MD, Florn R, Arenberg DA, Burdick MD, Glass MC, Morris SB, Kunkel SL, Strieter RM. Interleukin-1 receptor antagonist is elevated in lung transplant recipients with obliterative bronchiolitis. Chest 110:37S, 1996.
3. DiGiovine B, Lynch III JP, Martinez FJ, Whyte RI, Iannettoni MD, Hariharan K, Arenberg DA, Burdick MD, Glass MC, Morris SB, Kunkel SL, Strieter RM. The presence of pro-fibrotic cytokines correlate with outcome in patients with idiopathic pulmonary fibrosis. Chest 110:24S, 1996
4. Arenberg D, Kunkel S, Polverini P, Whyte R, Iannettoni M, Burdick M, Glass M, Morris S, DiGiovine B, Strieter R. Interferon-g-inducible protein 10 (IP-10) regulates tumor growth, angiogenesis, and metastasis in non-small cell lung cancer (NSCLC). J. Invest. Med. 44:371A, 1996.
5. Parks E, Lukacs NW, Gauldie J, Strieter RM, Kunkel SL. Transient IL-10 and IL-12 overexpression modifies disease in murine collagen induced arthritis. Arth Rheumat 39(9):578, 1996.
6. Keane MP, Arenberg DA, Lynch JP, Whyte RI, Iannettoni MD, Burdick MD, Wilke CA, Morris SB, Glass MC, DiGiovine B, Kunkel SL, Strieter RM. CXC chemokines are important regulators of angiogenic activity in idiopathic pulmonary fibrosis. Presented at The Sixth Annual Lung Cell Biology Symposium at Woods Hole, Cape Cod, MA, October 20-23, 1996.
7. Strieter RM, DiGiovine B, Lukacs NW, Rolfe MW, DeMeester SR, Whyte RI, Iannettoni MD, Kunkel SL. Early response cytokines and chemokines in lung transplantation. Presented at the Bilateral Workshop USA-Italy on lung transplantation, Washington University Medical Center, St. Louis, MO, October 31-November 1, 1996.
8. Arenberg D, Kunkel SL, Burdick MD, Glass M, Morris S, Strieter RM. Interferon-g-inducible protein 10 (IP-10) prolongs survival in a mouse model of non-small cell lung cancer (NSCLC). Presented at the American Cancer Society, Michigan Division, The University of Michigan, Ann Arbor, MI, November 22, 1996.
9. DiGiovine B, Whyte RI, Iannettoni MD, Arenberg DA, Burdick MD, Glass MC, Morris SB, Kunkel SL, Strieter RM. CXC chemokine composition of Stage I adenocarcinoma of the lung correlates with clinical outcome. Presented at the Fifth Annual Department of Internal Medicine Research Day, Ann Arbor, MI, February 1, 1997.
10. Keane MP, Arenberg DA, Burdick MD, Wilke CA, Morris SB, Glass MC, Kunkel SL, Strieter RM. The angiostatic CXC chemokines, IP-10 and MIG are reduced during the pathogenesis of bleomycin-induced pulmonary fibrosis. Presented at the Fifth Annual Department of Internal Medicine Research Day, Ann Arbor, MI, February 1, 1997.
11. Ruth JH, Lukacs NW, Warmington KS, Pollack T, Burdick M, Strieter RM, Kunkel SL, Chensue SW. Expression and participation of eotaxin during TH_1 and TH_2 cytokine-mediated granuloma formation. Presented at the first AAAAI/AAI/CIS Joint Meeting, San Francisco, CA, February 21-26, 1997.
12. DiPietro LA, Rahbe SM, Burdick M, Kunkel SL, Strieter RM. MIP-1a is an essential macrophage chemoattractant in wound repair. J. Allergy Clin. Immunol. 99:S247, 1997.
13. Lukacs NW, Strieter RM, Glass M, Taub DD, Kunkel SL. Mast cell-fibroblast interaction induces histamine release and C-C chemokine production. J. Allergy Clin. Immunol. 99:S387, 1997.

14. Strieter RM, Arenberg DA, Polverini PJ, Kunkel SL. The role of CXC chemokines in the regulation of angiogenesis in association with lung cancer. Presented at the Keystone Symposia on "The role of chemokines in leukocyte trafficking and disease", Copper Mountain, CO, March 31-April 5, 1997.
15. Parks E, Gauldie J, Lukacs NW, Strieter RM, Kunkel SL. Transient gene transfer of IL-12 and TGF-b regulates chemokine expression and disease severity in experimental arthritis. To be presented at the Keystone Symposia on "The role of chemokines in leukocyte trafficking and disease", Copper Mountain, CO, March 31-April 5, 1997.
16. Hogaboam CM, Lukacs NW, Strieter RM, Chensue SW, Kunkel SL. Inhibition of nitric oxide alters TH1-type lung ganuloma formation and chemokine generation. Presented at the Keystone Symposia on "The role of chemokines in leukocyte trafficking and disease", Copper Mountain, CO, March 31-April 5, 1997.
17. Lukacs NW, Kunkel SL, Chensue SW, Strieter RM. Role of chemokines in allergic airway inflammation and airway reactivity. Presented at the Keystone Symposia on "The role of chemokines in leukocyte trafficking and disease", Copper Mountain, CO, March 31-April 5, 1997.
18. Hogaboam CM, Lukacs NW, Strieter RM, Chensue SW, Kunkel SL. Nitric oxide contributes to TH1-type lung ganuloma formation and chemokine generation. FASEB J. 11:A125, 1997.
19. Keane MP, Arenberg DA, Burdick MD, Wilke CA, Morris SB, Glass MC, Kunkel SL, Strieter RM. The angiostatic CXC chemokines, IP-10 and MIG, are reduced during the pathogenesis of bleomycin-induced pulmonary fibrosis. FASEB J. 11:A228, 1997.
20. Lukacs NW, Addison C, Gauldie J, Simpson K, Strieter RM, Chensue SW, Kunkel SL. Transgene-induced production of IL-4 alters the development and collagen expression of TH1-type pulmonary granulomas. FASEB J. 11:A229, 1997.
21. Arenberg D, DiGiovine B, Morris S, Burdick M, Kunkel S, Polverini P, Strieter RM. Angiogenesis mediated by ENA-78 promotes growth of human non-small lung cancer (NSCLC). FASEB J. 11:A544, 1997.
22. DiGiovine B, Whyte RI, Iannettoni MD, Arenberg DA, Burdick MD, Glass MC, Morris SB, Kunkel SL, Strieter RM. CXC chemokine composition of stage I adenocarcinoma of the lung correlates with clinical outcome. Am. J. Respir. Crit. Care Med.155:A37, 1997.
23. Keane MP, Arenberg DA, Lynch JP, Whyte RI, Iannettoni MD, Burdick MD, Wilke CA, Morris SB, Glass MC, DiGiovine B, Kunkel SL, Strieter RM. CXC chemokines are important regulators of angiogenic activity in IPF. Am. J. Respir. Crit. Care Med.155:A315, 1997.
24. Zisman DA, Kunkel SL, Strieter RM, Tsai WC, Wilkowski JM, Bucknell KA, Standiford TJ. The role of interleukin-12 in sepsis. Am. J. Respir. Crit. Care Med.155:A467, 1997.
25. Arenberg D, Kunkel SL, Polverini PJ, Burdick MD, Glass M, Morris S, Strieter RM. Interferon-g-inducible protein 10 (IP-10) prolongs survival in a mouse model of non-small cell lung cancer (NSCLC). Am. J. Respir. Crit. Care Med.155:A500, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

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 seven postdoctoral fellows (E. Paul Scheidegger, M.D., Daniel Legault, M.D., Steven Domino, M.D., Ph.D., Jonathon Homeister, M.D., Ph.D., Somi K. Cho, Ph.D., Moonjae Cho, Ph.D., and Hedwig Murphy, M.D., Ph.D.)
B. Lecturer - Postdoctoral Research Training Program.
C. Member of five Ph.D. thesis committees (Stephanie M. Alt, Arul Chinnaiyan, Hangjun Duan, George Pipia, and Vance H. Thomas).
D. Oral prelim committees; Department of Pathology, Ph.D. Program.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Oligosaccharide function during murine embryogenesis". Source of award: Howard Hughes Medical Institute
B. Principle Investigator, "Molecular biology of human α1,3fucosyltransferase genes". NIH GM47455 (25% effort), $286,925/five years direct cost, 5/1/92 - 4/30/97
C. Principle Investigator, "Molecular biology of the human H and Se blood group genes", NIH HL48859 (25% effort), $276,554/five years direct cost, 08/01/92 - 12/31/97
D. 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
E. 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
F. Sponsor, Physician Scientist Award, "Structure-function relationships of fucosyltransferases", Daniel J. Legault, M.D., 07/01/94 - 06/30/99
G. 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
H. Sponsor, Physician Scientist Award, "Structure and function of recombinant selectin ligands", Hedwig Murphy, M.D., Ph.D., 09/01/94-08/31/99

PROJECTS UNDER STUDY:

A. Structure and regulation of mammalian oligosaccharide genes. Efforts are focused on the isolation and analysis of gene(s) for human and murine glycosyltransferases, using mammalian gene transfer techniques, and on characterization of immune defects in glycosyltransferase knock-out mice.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

A. Deputy Editor, The Journal of Clinical Investigation.
B. Member, Pathobiochemistry Study Section, Division of Research Grants, National Institutes of Health.
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. Impaired selectin ligand expression, and defective leukocyte trafficking, in fucosyltransferase-deficient mice. International Symposium on Molecular and Cell Biology of Glycoconjugate Expression, Rigi Kaltbad, Switzerland, August, 1996.
2. Selectin-Carbohydrate Interactions. Symposium on Cytokines and Adhesion Molecules, Snowbird, Utah, September, 1996.
3. Selectin-ligand defects in fucosyltransferase mutant mice. Society for Glycobiology, Boston, MA, November, 1996.
4. Selectin ligand defects in fucosyltransferase mutant mice. 1996 Pluto Club Meeting, Cabo San Lucas, Mexico, December, 1996.

5. Selectin ligand defects in fucosyltransferase deficient mice. Glycobiology of Cell Communication, University of Helsinki, Finland, December, 1996.
6. Fucosyltransferase-mutant mice disclose collaborative roles for Fuc-TIV and Fuc- TVII in selectin ligand synthesis. Glycobiology Gordon Research Conference, Ventura, CA, February, 1997.
7. Defective selectin ligand synthesis in fucosyltransferase-deficient mice. International Symposium on Glycosyltransferases and Cellular Communications. Osaka, Japan, March 26-28, 1997.
8. Selectin-dependent immune deficiencies in fucosyltransferase deficient mice. 2nd Carbohydrate Bioengineering Meeting, La Rochelle, France, April, 1997.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wagers AJ, Lowe JB, and Kansas GS. An important role for the α1,3fucosyltransferase Fuc-TVII in leukocyte adhesion to E-selectin. Blood 88:2125-2132, 1996.
2. Maly P, Thall AD, Petryniak B, Rogers CE, Smith PL, Marks RM, Kelly RJ, Gersten KM, Cheng G, Saunders TL, Camper SA, Camphausen RT, Sullivan FX, Isogai Y, Hindsgaul O, von Adrian UH, and Lowe JB. The α(1,3)fucosyltransferase Fuc-TVII controls leukocyte trafficking through an essential role in L-, E-, and P-selectin ligand expression. Cell 86:643-653, 1996.
3. Dohi T, Yuyama Y, Natori Y, Smith PL, Lowe JB, and Oshima M. Detection of N-acetylgalactosaminyltransferase mRNA which determines expression of Sda blood group carbohydrate structure in human gastrointestinal mucosa and cancer. Int J Cancer 67:626-631, 1996.
4. Prieto PA, Larsen RD, Cho M, Rivera HN, Shilatifard A, Lowe JB, Cummings RD, and Smith DF. Expression of human H-type α1,2-fucosyltransferase encoding for blood group H (O) antigen in Chinese hamster ovary cells. Evidence for preferential fucosylation and truncation of polylactosamine sequences. J Biol Chem 272:2089-2097, 1997.
5. Lee KP, Carlson LM, Woodcock JB, Ramachandra N, Schultz TL, Davis TA, Lowe JB, Thompson CB, and Larsen RD. Molecular cloning and characterization of CFT1, a developmentally regulated avian α(1,3)fucosyltransferase gene. J Biol Chem 271:32960-32967, 1996.
6. Fuhlbrigge RC, Alon R, Puri KD, Lowe JB, and Springer TA. Sialylated, fucosylated ligands for L-selectin expressed on leukocytes mediate tethering and rolling adhesions in physiologic flow conditions. J Cell Biol 135:837-848, 1996.
7. Lowe JB and Ward PA. Therapeutic inhibition of carbohydrate-protein interactions in vivo. J Clin Invest 99:822-826, 1997.
8. Lowe JB. Selectin ligands, leukocyte trafficking, and fucosyltransferase genes. Kidney Int 51:1418-1426, 1997.
9. Domino S, Hiraiwa N, and Lowe JB. Structure and tissue-specific expression of a murine α(1,2) fucosyltransferase gene. Biochem. J., 1997 (in press).

ARTICLES SUBMITTED OR IN PREPARATION:

1. Swarte VVR, Joziasse DH, Van den Eijnden DH, Petryniak B, Lowe JB, Kraal G, and Mebius RE. Regulation of fucosyltransferase-VII expression in peripheral lymph node high endothelial venules. Submitted.
2. Niemela R, Natunen J, Majuri M-L, Maaheimo H, Helin J, Lowe JB, Renkonen O, and Renkonen R. Complementary acceptor- and site-specificities of Fuc-TIV and Fuc-TVII allow effective biosynthesis of sialyl-triLex and related polylactosamines present on glycoprotein counterreceptors of selectins. Submitted.
3. Thall AD, Lu Y, Murphy HS, Homeister J, Awwad M, Lowe JB, and Lussow A. Anti-gal-mediated mouse heart graft rejection in α1,3galactosyltransferase deficient mice. Submitted.
4. Thall A, von Adrian UH, Cheng G, Petryniak B, Camper S, Saunders T, and Lowe JB. Robust leukocyte E- and P-selectin ligand expression, but subtle defects in leukocyte rolling, in mice deficient in the ELAM Ligand Fucosyltransferase (ELFT, Fuc-TIV). In preparation.
5. Masayoshi O, Shigeru Tsuboi S, Bronia Petryniak B, Lowe JB, and Fukuda M. Reconstitution of E-selectin ligand oligosaccharides on CHO cells by expression of two distinct fucosyltransferases. Oligosaccharide structures directed by mouse fucosyltransferase IV and VII. In preparation.
6. Frenette PS, Moyna C, Daqing W, Hartwell DW, Lowe JB, Hynes RO and Wagner DD. Platelet-endothelial interactions in inflamed mesenteric venules. In preparation.
7. Hiraiwa N, Domino S, Saunders T, and Lowe JB. Dominant pre-implantation lethality in mice directed by aberrant expression of an α(1,2)fucosyltransferase cDNA. In preparation.
8. Smith PL, Phillips ML, Ketchum K, Paulson JC, and Lowe JB. A biochemical lesion in a cytosolic GDP-D-mannose 4,6-dehydratase activity is responsible for the leukocyte adhesion defect in the human leukocyte adhesion deficiency II syndrome. In preparation.

BOOKS AND CHAPTERS IN BOOKS:

None

LORI LOWE, M.D.
CLINICAL ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Dermatopathology
B. Dermatopathology Consultation Cases (including MLabs and Veterans Administration Hospital)

II. TEACHING ACTIVITIES:

A. Medical Students:
   1. Lecturer, MS II Dermatology Sequence
   2. Instructor, dermatopathology portion of clinical pathology rotation, MS IV clerkship in general pathology
B. House Officers:
   1. Dermatopathology signout
   2. Review of dermatopathology consultation material
   3. Dermatopathology teaching conference/weekly
   4. Anatomic Pathology Conference, dermatopathology/2 per year
C. Dermatology Diagnostic Conference/weekly
D. Multidisciplinary Melanoma Conference/bi-monthly
E. Cutaneous Lymphoma Conference/monthly

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

PENDING:

A. Principal Investigator: Barbara Reed, OB-GYN, "Multifactor assessment of vulvodynia" (NIH Grant)

PROJECTS UNDER STUDY:

A. Scarring alopecia of black women: A histologic study (Vera Price, M.D., University of California at San Francisco, and John T. Headington, M.D.)
B. Melanoma occurring in the second decade: A histologic analysis.
C. Histologic effects of cutaneous application of hydrogen peroxide (Sewan Kang, M.D., Department of Dermatology)

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interim Director, Dermatopathology Service

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "Self-Assessment in Dermatopathology," Faculty, American Society of Dermatopathology Annual Meeting, San Francisco, CA, March, 1997.
2. Invited Lecturer, "Basic Dermatopathology Self-Assessment," Faculty, American Academy of Dermatology Annual Meeting, San Francisco, CA, March, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lowe, L.: Grover's disease: Accurate diagnosis through clinical correlation. Pathol Case Reviews 1:141-144, 1996.
2. Karimpour, D.J., Johnson, T.M., Kang, S., Wang, T.S., Lowe, L.: Mucinous carcinoma of the skin. J Am Acad Dermatol 36:323-326, 1997.
3. Shwayder, T.A., Conn, S., Lowe, L.: Acral peeling skin syndrome. Arch Dermatol 133:535-536, 1997.
4. Burns, R.L., Lowe, L.: Xanthomonas maltophilia infection presenting as erythematous nodules. J Am Acad Dermatol (in press).
5. Saluja, A., Peters, N.T., Lowe, L., Johnson, T.M.: A surgical wound infection due to Mycobacterium chelonae successfully treated with clarithromycin. J Dermatol Surg Oncol (in press).
6. Johnson, T.M., Headington, J.T., Baker, S., Lowe, L.: Utility of the staged excision for lentigo maligna and lentigo maligna melanoma: The "Square" procedure. J Am Acad Dermatol (in press).
7. Wittenberg, G.P., Douglass, M.C., Azam, M., Lee, M.W., al-Vjayli, B., Lowe, L.: Cutaneous malacoplakia presenting in a patient with the acquired immune deficiency syndrome. Arch Dermatol (in press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Wang, T.S., Lowe, L., Smith, J.W., Francis, I.R., Sondak, V.K., Dworzanian, L., Finkelstein, S., Slingluff, C.L., Johnson, T.M.: Complete spontaneous regression of pulmonary metastatic melanoma: A case report. Cancer.
2. Johnson, T.M., Dolan, O.M., Hamilton, T.A., Lu, M.C., Swanson, N.A., Lowe, L.: Trends in clinical and histologic features of melanoma from 1984-1995. Arch Dermatol.

3. Dolan, O.M., Lowe, L., Orringer, M.B., Rinck, M., Johnson, T.M.: Basal cell carcinoma arising in a sternotomy scar: Report of 3 cases. Ann Thoracic Surg.

BOOKS/CHAPTERS IN BOOKS:

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

POSTER EXHIBITS AT SCIENTIFIC MEETINGS

1. Bogomilsky, J., Shwayder, T., Lowe, L.: Congential self-healing reticulohistiocytosis presenting as a solitary lesion. American Academy of Dermatology Summer Meeting, Orlando, FL, July, 1996.
2. Fabian, B., Florentino, F., Lowe, L.: Necrolytic migratory erythema without systemic manifestations. American Academy of Dermatology Summer Meeting, Orlando, FL, July, 1996.
3. Burn, R., Balle, M.R., Lowe, L.: Lymphoepithelioma-like carcinoma of the skin. Michigan Dermatologic Society Meeting, December 4, 1996.
4. Burns, R., Lowe, L.: Xanthomonas maltophilia cellulitis: Clinical presentation as erythema nodosum-like nodules. Michigan Dermatologic Society Meeting, December 4, 1996.
5. Johnson, T.M., Headington, J.T., Lowe, L.: Lentigo maligna excised by the "Square" technique. Michigan Dermatologic Society Meeting, March 5, 1997.
6. Bogomilsky, J., Merkle, S., Lowe, L.: Connective tissue nevus in a patient with multiple endocrine neoplasia type 1. American Academy of Dermatology Annual Meeting, San Francisco, CA, March, 1997.
7. Wittenberg, G., Douglass, M., Krull, E.A., Lowe, L., Lee, M.: Cutaneous malacoplakia presenting in a patient with the acquired immune deficiency syndrome. American Academy of Dermatology Annual Meeting, San Francisco, CA, March, 1997.

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

ANNUAL DEPARTMENT REPORT
1 JULY 1996-30 JUNE 1997

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. "Immune mechanisms of Disease", Epidemiology 570, Course Instructor, Fall, 1996.
B. Supervised Undergraduate students, Matt Steinhauser, Scott Lipinski, Carrie Zickus, and MSTP Students, Sara Chang and Cindi Bone-Larson.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Role of C-C chemokines in eosinophil airway inflammation", R-29 FIRST Award, National Institutes of Health. 5-1-96 to 4-30-01.
B. Principal Investigator, "Leukocyte recruitment in eosinophilic inflammation", American Lung Association Research Grant, 7-1-95 to 6-30-97.
C. Co-Investigator, "The role of chemokines in autoimmune encephalomyelitis", NIH RO1 NS34510-01, with William J. Karpus, Ph.D. Microbiology/Immunology, Northwestern University, Chicago, Ill. Sept., 1995 to Aug., 1999.
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. 12-1-96 to 11-30-01

PENDING SUPPORT:

A. Principal Investigator, "The role of SCF in allergic airway inflammation", RO1 12/1/97-11/30/02, National Institutes of Health.

PROJECTS UNDER STUDY:

A. Rgulation 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:

None

REGIONAL AND NATIONAL:

-Reviewer for the following Journals:

1. American Journal of Pathology
2. Journal of Immunology
3. American Journal of Respiratory Cell and Molecular Biology
4. Infection and Immunity
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. The Israel Science Foundation Grants
2. The Veterans Administration MERIT Grants
3. The Canadian Medical Research Council
4. Welcome Trust Fund Grants (United Kingdom)
5. Onterio Lung Grants
6. Special Emphasis Panel-RFA AI-96-005: Asthma, Allergy, and Immunological Disseases Cooperative Centers

-Task Force recommendation on NIH Funding 1996

Immediate hypersensitivity and Allergy with K. Frank Austen

-Section on Animal models

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Role of C-C chemokines in allergic airway inflammation. University of Michigan Medical School, Rheumatology Division. Sept. 17th, 1996.
2. Chemokines in allergic airway inflammation. University of Toledo, Department of Pharmacology. October 17th, 1996.

3. Role of Chemokines in disease regulation. Japanese Society of Immunology. 25th annual Conference. Yokohama, Japan. November 26th, 1996.
4. Cytokines and chemokines in allergic airway inflammation. Mason Laboratories, Worchester, MA. Febuary 6, 1997.
5. Role of chemokine in allergic airway inflammation and airway reactivity. Keystone Symposium on Chemokines. Copper Mt, CO. April 3, 1997.
6. The role of endothelium in vascular inflammation. ILAR Congress of Rheumatology. Molecular basis of Inflammation-Adhesion molecules and Endothelial responses. Singapore. June 9th, 1997.
7. The role of chemokines in inflammation. . ILAR Congress of Rheumatology. Molecular basis of Inflammation II. Singapore. June 9th, 1997.
8. Tolerance and Immunity. ILAR Congress of Rheumatology. Congress Symposium Chair. Singapore. June 9th, 1997.
9. Leukocyte-Endothelial interaction in Vasculitis. ILAR Congress of Rheumatology. Systemic Vasculitis. Singapore. June 9th, 1997.
10. Role of Immune system and cytokines in Asthma. UpJohn-Pharmacia. June 15th, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERREED JOURNALS:

1. Walley, K.R., N.W. Lukacs, T.J. Standiford, R.M. Strieter, and S.L. Kunkel. 1996. Balance of inflammatory cytokines is related to severity and mortality of murine sepsis. Infect Immun 64:4733-4738.
2. Lukacs, N.W., T.J. Standiford, R.M. Strieter, S.W. Chensue, R.G. Kunkel, and S.L. Kunkel. 1996. C-C chemokine-induced eosinophil chemotaxis during allergic airway inflammation. J. Leuk Biol. 60:573-578.
3. Elner, V.M., S.G. Elner, TJ Standiford, N.W. Lukacs, RM Strieter, and S.L. Kunkel. 1996. Interleukin 7 (IL-7) induces retinal pigment epithelial cell MCP-1 and IL-8. Exp Eye Res 63:297-303.
4. Elner, V.M., S.G. Elner, ZM Bian, N.W. Lukacs, RM Kurtz, RM Strieter, and S.L. Kunkel. 1997. Human retinal pigment epithelial cell interleuki-8 and monocyte chemotactic protein-1 modulation by T lymphocyte products. Invest Opthalmol Vis Sci. 38:446-455.
5. Bian, ZM, S.G Elner, RM Strieter, MB Glass, NW Lukacs, SL Kunkel, and VM Elmer. 1996. Glycated serum albumin induces chemokine gene expression in human retinal pigment epithelial cells. J. Leukoc Biol 60:405-414.
6. Kunkel, S.L., N.W. Lukacs, T. Kasama, and R.M. Strieter. 1996. The role of chemokines in inflammatory joint disease. J Leukoc Biol 59:6-12.
7. Lukacs, N.W., C. Addison, J. Gauldie, F. Graham, K. Simpson, R.M. Strieter, K. Warmington, S.W. Chensue, and S.L. Kunkel. 1997. Transgene-induced production of IL-4 alters the development and collagen expression of Th1 type pulmonary granulomas. J. Immunol 158:4485-4492.

8. Lukacs, N.W., R.M. Strieter, K. Warmington, P. Lincoln, S.W. Chensue, and S.L. Kunkel. 1997. Differential recruitment of leukocyte populations and alteration of airway hyperreactivity by C-C family chemokines in murine allergic airway inflammation. J. Immunol 158:4398-4404.
9. Karpus, W.J., N.W. Lukacs, K.J. Kennedy, W.S. Smith, S.D. Hurst, and T.A. Barrett.1997. Differential CC Chemokine-induced potentiation of Th cell cytokine production. J. Immunol 158:4129-4136.
10. Lukacs, N.W., W. Lamm, R.M. Strieter, and R. Albert. 1997. Airway hyperreactivity is associated with specific leukocyte subset infiltration in a mouse model of allergic airway inflammation. Pathobiology 64:308-313.
11. Lukacs, N.W., S.W. Chensue, C. Keefer, W.J. Karpus, R.M. Strieter, and S.L. Kunkel. 1997. C-C chemokines differentially alter IL-4 production from lymphocytes. Am J. Pathol. 150:1861-1868.
12. Karpus, W.J. and N.W. Lukacs. 1996. The role of chemokines in oral tolerance. Abrogation of nonresponsiveness by treatment with anti-monocyte chemotactic protein-1. Ann N Y Acad Sci 778:133-144.
13. Walley, K.R., N.W. Lukacs, T.J. Standiford, R.M. Strieter, and S.L. Kunkel. Elevated macrophage inflammatory protein-2 in severe murine peritonitis increases neutrophil recruitment and mortality. Infect. Immun. In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Lukacs, N.W. and P.A. Ward. Pro-inflammatory and anti-inflammatory cytokines in the inflammatory response. IN: Pro-inflammatory and anti-inflammatory peptides. ED: Claude Lenfant. Marcel Dekker, Inc. New York,N.Y.
2. Lukacs, N.W. and P.A. Ward. Early response cytokines in pulmonary inflammation. IN: News and Perspectives. 10:581-586.
3. Kunkel, S.L., N.W. Lukacs, R.M. Strieter, T.J. Standiford, and S.W. Chensue. The function of chemokines in health and disease. IN: Chemokines and Cancer, Ed. Barret J. Rollins, M.D., Ph.D., Humana Press, Totowa, NJ.

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

1. Lukacs, N.W., R.M. Strieter, M. Glass, D.D. Taub, and S.L. Kunkel. 1997. Mast cell-fibroblast interaction induces histamine release and C-C chemokine production. J. Allergy Clin. Immunol. S387.
2. Karpus, W.J., K.J. Kennedy, and N.W. Lukacs. 1997. CC-chemokine regulation of T cell differentiation and autoimmune disease. J Allergy Clin. Immunol. S488.
3. Hogaboam, C.M., N.W. Lukacs, R.M. Strieter, S.W. Chensue, and S.L. Kunkel. 1997. Inhibition of nitric oxide alters TH1-type lung granuloma formation and chemokine generation. Keystone Symposium on Chemokines.
4. N.W. Lukacs, S.L. Kunkel, S.W. Chensue, and R.M. Strieter. 1997. Role of chemokine in allergic airway inflammation and airway reactivity. Keystone Symposium on Chemokines.

5. Parks, E., J. Gauldie, N.W. Lukacs, R. M. Strieter, and S.L. Kunkel. 1997. Transient gene transfer of IL-12 and TGF-b regulates chemokine expression and disease severity in experimental arthritis. Keystone Symposium on Chemokines.
6. C.M. Hoga boam, N.W. Lukacs, R.M. Strieter, S.W. Chensue, and S.L. Kunkel. 1997. Nitric oxide contributes to the TH1-type lung granuloma formation and chemokine generation. FASEB J. p. A125.
7. Lukacs, N.W., C. Addison, J. Gauldie, K. Simpson, R.M. Strieter, S.W. Chensue, and S.L. Kunkel. 1997. Transgene-induced production of IL-4 alters the development and collagen expression of Th1 type pulmonary granulomas. FASEB J. p. A229.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

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 ADRC: brain cutting, sampling, microscopic examination, and special stains.

II. TEACHING ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

A. Faculty, "New Methods of Brain Tumor Analysis: 35th Annual AFIP". Neuropathology Review, Armed Forces Institutes of Pathology, Rockville, Maryland, February 22, 1997.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Investigator, "Antimetabolite Selectivity: Regional Treatment and Modulation," National Institutes of Health Program Project, NIH CA-42761-04, 1 August 1993-31 July 1996.

B. Nycomed Pharmaceuticals
"Transferin Receptor Gene Therapy" 07/01/96 - 06/30/97 ($35,000 for project).
C. 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, submitted to J. Neuro-oncology.
B. Extracellular matrix products and plasminogen activators of gliomas with Drs. James Varani, Robert Sitrin, Dario Caccamo and Suzanne Fligiel.
C. Magnetic resonance diffusion and cross relaxation of brain tumors with Drs. James Brunberg, Thomas Chenevert and Brian Ross.
D. Characterization of Rosai-Dorfman disease in brain with Drs. Michael Boland and Karin Muraszko.
E. Viral vectors in glioma therapy with Drs. Julian Hoff, Brian Ross and Donald Ross.
F. Effects of BCNU on histopathology and MRI signals in experimental rat brain tumors with Drs. Brian Ross and Thomas Chenevert.
G. Artemesinin toxicity with Dr. Steven Meshnick.

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 scheduled twice monthly QA/QC meetings and various ad hoc reviews requested by faculty.

REGIONAL AND NATIONAL:

A. Editorial Board, Journal of Neuro-Oncology, Primarily reviewed, found referees for and reviewed decisions on approximately 15 manuscripts.
B. Primary Review Pathologist, Children's Cancer Study Group CCG 9891 nationwide study of childhood low grade gliomas.
C. Reviewer for various pathology, neuroscience and neuro-oncology journals.
D. M-Labs Neuropathology Services.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

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

INVITED LECTURES/SEMINARS:

1. Faculty, "New Methods of Brain Tumor Analysis: 34th Annual AFIP Neuropathology Review, Armed Forces Institutes of Pathology, Rockville, Maryland, 1996.
2. Speaker, "Assessment of Grade of Malignancy and Transferrin Receptor Staining of Astrocytomas," Nycomed Research Conference, Philadelphia, Pennsylvania, 1996.
3. Lecturer, "Immunocytochemical Assessment of Proliferative Capacity," Tenth International Congress of Histochemistry and Cytochemistry, Kyoto, Japan, 1996.
4. Speaker, The Histochemical Society Presidential Symposium, "Insights about Brain Tumors Gained through Immunohistochemistry and In Situ Hybridization of Nuclear and Phenotypic Markers", Microscopy and Microanalysis '97, Cleveland, Ohio, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. McKeever PE, Varani J, Papadopoulous SM, Wang M, McCoy JP: Products of cells from gliomas: IX. Evidence that two fundamentally different mechanisms change extracellular matrix expression by gliomas. J Neuro-Oncol 24:267-280, 1995.
2. Suarez GA, Giannini C, Bosch EP, Barohn RJ, Wodak J, Ebeling P, Anderson R, McKeever PE, Bromberg MB, Dyck PJ: Immune brachial plexus neuropathy: Suggestive evidence for an inflammatory-immune pathogenesis. Neurol 46:559-561, 1996.

3. McKeever PE, Dennis TR, Burgess AC, Meltzer PS, Marchuk DA, Trent JM: Chromosome Breakpoint at 17q11.2 and insertion of DNA from three different chromosomes in a glioblastoma with exceptional glial fibrillary acidic protein expression. Cancer Genet Cytogenet 87:41-47, 1996.
4. Levy RA, Allen R, McKeever PE: Pleomorphic xanthoastrocytoma presenting with massive intracranial hemorrhage. AJNR 17:154-156, 1996.
5. McKeever PE, Ross DA, Strawderman MS, Brunberg JA, Greenberg HS, Junck L: A comparison of the predictive power for survival in gliomas provided by MIB-1, bromodeoxyuridine and proliferating cell nuclear antigen with histopathologic and clinical parameters. J Neuropathol Exp Neurol 7:798-805, 1997.
6. Kamchonwongpaisan S, McKeever P, Hossler P, Ziffer H, Meshnick SR. Artemisinin neurotoxicity: Neuropathology in rats and mechanistic studies in vitro. Am J Trop Med Hyg 56(1)7-12, 1997.
7. Roberson PL, Ten Haken RK, McKeever PE, Ensminger WD: Nonuniform liver dose for yttrium-90-microsphere therapy in a rabbit model. J Nucl Med, (in press).
8. Chenevert TL, Ross BD, McKeever PE: Monitoring early response of experimental brain tumors to therapy using diffusion MRI.

BOOKS/CHAPTERS IN BOOKS:

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

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

1. Junck L, Strawderman M, Ross DA, Betley AT, Brunberg JA, Greenberg HS, and McKeever PE: Prognostic value of PET-FDG scans in untreated gliomas. 1995 American Academy of Neurology Scientific Meeting.
2. McKeever PE, Wang M: Internal standardization of archival tissue sections enables evaluation of chromosomal abnormalities by *in situ* hybridization. Lab. Invest. 72:136A, 1995.

3. Junck L, Stawderman M, Ross DA, Betley AT, Brunberg JA, Greenberg HS, McKeever PE: Prognostic value of PET-FDG scans in untreated gliomas. Neurol. 45 (Suppl. 4): A387, 1995.
4. Mikhail AA, Yamini B, McKeever PE, Blaivas M: MIB-1 proliferation index predicts survival among patients with low grade astrocytoma. Lab. Invest. 74:141A, 1996. Subsequent invited re-presentation at the 47th Annual Meeting of the Histochemical Society, August 2, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

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 - one week and six weekends.

II. TEACHING ACTIVITIES:

A. 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 - two/year.
B. Other Education Activities:
    1. Cytotechnologists - Cytopathology Conferences - three/year.
    2. Visiting Cytopathologist - two weeks.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

PROJECTS UNDER STUDY:

A. The cytologic spectrum of mesothelioma in situ, with Dr. C.Bedrossian, C.W.M., Wayne State University.
B. Can true papillary neoplasms and their mimickers be distinguished cytologically?, with Buschmann, B., University of South Alabama.
C. The differential diagnosis of Psammoma bodies on cervical smears.
D. Mammographic identification of microinvasive carcinoma (in conjunction with Roubidoux, M., Department of Radiology).

E. Fine needle aspirates prepared by thin prep technique: Artifacts and diagnostic pitfalls, with Dr. B. Hunter.
F. Fine needle aspirates of malignant melanoma, with Dr. D. Fullen.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interim Director, Cytopathology Laboratory.
B. Interim General Laboratory Supervisor (January 14 - March 1, 1997).
C. Interim 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.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Pregnancy Related Changes on Cervical Smears," invited seminar, Department of Pathology, Wayne State University, August 16, 1996.
2. "Fine Needle Aspiration of the Breast: A Pattern Recognition". Guest speaker; M-Labs symposium, Ann Arbor Michigan,April 11, 1997.
3. "Non Neoplastic Entities". Guest speaker, Michigan Society of Cytology. Mackinac Island, Michigan, May 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Michael CW, Lawrence WD, Bedrossian CWM: Intraoperative consultation in ovarian lesions: A comparison between cytology and frozen sections. Diagn Cytopathol 1996; 15:387-394.
2. Michael CW, King J, Hester R: Confocal laser scanning microscopy (CLSM) and three-dimensional reconstruction of serous fluids. Diagn Cytopathol (in press).

3. Michael CW and Esfahani FM: Pregnancy related changes: A retrospective review of 278 patients. Diagn Cytopathol (in press).
4. Gomez DM, Roubidoux M, Michael CW: Mammographic demonstration of transient microcalcifications in postpartum state: A case report. J. of Woman's Radiology (in press).

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Rochester A, Roubidoux M, Michael CW, Helvie MA: Mammographic location of small ductal carcinomas in situ. Radiology.
2. Stastny FJ, Geisinger KR, Michael CW, Raab SS, Powers CN, Davila MR. Another quality assurance issue. Amended reports: What do we really know about them. Diagn Cytopathol.
3. Michael CW, Flint A: Cytologic features of Wegeners Granulomatosis: A retrospective review. Am J Clin Path.
4. Tworek J, Giordano T, Michael CW. Comparison of intraoperative cytology with frozen sections in the diagnosis of thyroid lesions. Am J Clin Path.

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

1. King J, Elkhalifa M, Michael CW. Malignant lymphoma identified on a cervical cytologic smear with immunophenotypic analysis. (Letter to the Editor) Acta Cytol (in press).
2. Michael C, Flint A: Cytologic features of Wegeners Granulomatosis: A retrospective review. Platform presentation, American Society of Cytopathology, Denver, Colorado, Nov. 1996. Acta Cytol.40:1028, 1996.
3. Bedrossian C, Dawamneh MF, Nelson J, Michael CW. Morphologic and immunocytochemical study of serous fluids in cell blocks and thin preps. Acta Cytol 40: 1058, 1996.
4. Attal H, Michael CW, Davila C, Dawamneh MF, Nelson J, Bedrossian C. Malignant serous effusions in women, is there a role for immunocytochemistry in predicting the primary site? Mod Pathol: 10, 97A, 1997.
5. Attal H, Davila R, Michael CW, Hughes J, Bedrossian C. Effect of cytopathology methods in the immunocytochemistry of serous fluids: A comparison between cell blocks and thin preps. Am J Clin Path: 107, 482-83, 1997.
6. Attal H, Michael CW, Davila R, Bedrossian C. Differentiation antigens in malignant effusions processed as cell blocks and thin preps. Am J Clin Path: 107. 480, 1997.
7. Tworek J, Giordano T, Michael CW. Comparison of intraoperative cytology with frozen sections in the diagnosis of thyroid lesions. Am J Clin Path: 107, 480, 1997.
8. Kintanar EB, Michael CW. Diagnostic pitfalls and mimics of HGSIL. Accepted, American Society of Cytopathology National Meeting, Nov.1997.
9. Michael C, Naylor B. Amyloid in cytologic specimens: Differential diagnosis and diagnostic pitfalls. Accepted, American Society of Cytopathology National Meeting, Nov. 1997.
10. Michael CW, Georgy B, Elhosseiny, A: The cytologic spectrum and diagnostic pitfalls of apocrine lesions of the breast. Accepted, American Society of Cytopathology National Meeting, Nov. 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

CLINICAL RESEARCH-RELATED ACTIVITIES:

A. Continued to develop groundwork for transition to new leadership in the Reproductive Sciences Program involving discussions and planning with its Executive Committee and Membership. The membership has now demonstrated its ability to move ahead vigorously with planning for our internal review and for submission of two major, new center grants: one to replace our existing NIH P30 Center and the other to establish a new NSF Center in Neuroscience under a collaborative mechanism with Michigan State University.

B. Responded to suggestions of a site team, achieved all designated milestones, and received approval to initiate running a battery of assays on thousands of serum samples collected as a key component of our involvement as the Central Laboratory in an NIH-funded Study of Women's Health Across the Nation. The laboratory now operates smoothly in its expanded quarters on Green Road, involves a high degree of automation, implements QC and reagent control systems good for multi-year studies; implements GLP-type practices; and utilizes new, state-of-the art custom methods

C. Devoted my sabbatical to acquiring information, assembling an outstanding, dedicated team of participants and beginning development of a hypermedia-based learning system re. human sex, sexuality and reproduction with an aim to be of value to persons at a wide range of ages and from middle school years through residency training. An initial skeleton Web site has been developed that demonstrates our idea of a way to present sex and sexuality to persons of disparate cognitive levels. The site now provides for four levels to meet the needs of persons with cognitive abilities typical of a 2nd grader, 7th grader, 12th grader and health professional.

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 1996
   Lectured to Bioengineering 500, Dynamics of cellular response.

2. Primary supervision of 2 graduate students:
   Karen Heinze, Bioengineering - Successfully defended on June 5, 1997.
   William Lemon, Bioengineering - doctoral student (to defend this summer)
3. Supervision/Mentorship of other students:
   Jasmin Ghuznavi, pre-medical student
   Chris Liu, pre-medical student
   Mona Prasad, pre-medical student
4. Service on Other Dissertation Committees.
   Palmiere-Hunt, Diana (Educational Psychology, current)
   Guo, Wensheng (Biostatistics, current)
   Michael Poplawski (Electrical Engineering & Computer Science, current)
5. Worked with Visiting Scientist:
   Bent G. Boving, Ph.D. Extramural Associate, Dept. of Embryology, Carnegie Institute of Washington

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%.
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 - 07/31/97, $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).
6. SBIR, R43-HD 33776, S. Pincus, P.I., Does FSH secrete more irregularly than LH in humans?, 03/15/96 - 09/14/96, $99,918 ($29,840 subcontract to U of M).

PROPOSAL WRITING (Not Funded):

1. NIH, U54-HD 29184-04, N. Reame, P.I., National Center for Infertility Research at Michigan, Project I, Dynamic Mechanisms of Neuroendocrine Feedback in PCO, 09/01/96 - 08/31/01, $5,496,007 ($1,050,776, Project I), 28% (Project I and administrative) - (requested)

2. NIH, R01-HD 34732-01, R. Midgley, P.I., Dynamic Mechanisms of Neuroendocrine Feedback in PCOS, 12/01/96 - 11/30/01, $1,204,357, 20%, (requested).
3. NIH, R01, A.R. Midgley, Mechanisms Responsible for the LH Surge, 04/1/97 - 03/31/02, $1,247,332 (requested direct), 20%
4. Univ of Michigan, President's Initiative Fund, Reproductive Learning Collaboratory, $250,721 (requested)

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

Institute of Gerontology
Matthew Witten: Developing a mathematically based model of the sheep reproductive system (with Robert Keener (Statistics), Yuedong Wang (Biostatistics), Fred Karsch (Physiology), Vasantha Padmanabhan (Pediatrics) and Doug Foster (Obstetrics & Gynecology)

Obstetrics and Gynecology
John Randolph and Greg Christman: Analysis of hormonal time series profiles in control women and women with polycystic ovarian syndrome

Pediatrics
Vasantha Padmanabhan: co-investigator of a project in the NCIR grant and development of a new RO1 grant - concerning the regulation of pituitary gonadotropin secretion

Innovation Associates, Ann Arbor, MI
Judith Erb, Immunoassayist: assisted in development of a funded SBIR concerning the development of simplified immunoassays able to evaluate fertility and development of a second funded SBIR.

Massachusetts General Hospital
Pat Sluss, Reproductive Biologist: development of assays for inhibin, follistatin and activin

Yale University
Steve Pincus, mathematician-entrepreneur associated with Yale, is collaborating with our laboratory to explore ways in which application of his measure of approximate entropy to reproductive hormones will be useful.

PROJECTS UNDER STUDY:

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 perifusion 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
3. Neuroendocrine causation of polycystic ovarian syndrome; mechanisms controlling pituitary gonadotropin secretion.
4. Development of novel biosensors and immunoassays

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

1. Director, Center for the Study of Reproduction (NIH P30)
2. Associate Director, National Center for Infertility Research at Michigan (NIH NCIR) (terminated Fall, 1996)
3. Director, Standards and Reagents Core Facility (NIH P30 Center)
4. Director, Assay Development Core (NIH U01 NCIR; terminated Fall, 1996)
5. Director, Central Laboratory, Study of Women Across the Nation (NIH SWAN)

UNIVERSITY:

1. Director, Reproductive Sciences Program.
2. Member, Ob-Gyn Search Committee
3. Member, Biomedical Engineering
4. Member, Cellular Biotechnology Training Program
5. Member, Michigan Cancer Center, 1993-

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. June 9-11, 1996, SWAN Steering Cmt meeting, San Francisco
2. June 11-14, 1996, Endocrine Society Meeting, San Francisco
3. July 11, 1996, Site Visitor for NIH to Ogden/McKesson laboratory
4. Oct 9-12, 1996, U01 Perimenopause meeting, Washington, D.C.
5. Oct 24-25, 1996, Seminar at Univ. of Wisconsin, Madison
6. Nov 1, 1996, RSP Poster Day
7. Nov 20-21, 1996, Apple HotSauce (Project X) conference, Cupertino, CA
8. Mar 5-7, 1997, U01 Perimenopause meeting, Washington, D.C.
9. May 20, 1997, Symantec Conference on Java, Chicago, IL

OTHER ACTIVITIES:

1. Sabbatical, Jan 1-June 30, 1997: Focused on development of a means to help all persons understand reproduction, sex and sexuality, British Virgin Islands and Ann Arbor.
2. Interviewed over 40 faculty throughout the University and assembled a dedicated team of experts in diverse areas to implement the above project. The current status of this project can be reviewed at http://141.214.50.93/rlc but doing so requires authorization and a password (each of which I would be delighted to provide).
3. Developing an immunoassay analysis system with potential to assist many investigators
4. Implementing ELISA and chemiluminescence-based, solid state, two site immunoassays in Standards and Reagents Core as a partial replacement for radioimmunoassays (and thereby reduction in usage of radioactive isotopes).

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wang, Q.F., Khoury, R.H., Smith, P.C., McConnell, D.S., Padmanabhan, V., Midgley, A.R., Jr., Schneyer, A.L., Crowley, W.F., Jr. and Sluss, P.M. A two-site monoclonal antibody immunoradiometric assay for human follistatin: Secretion by a human ovarian teratocarcinoma-derived cell line (PA-1). J. Clin. Endo. Metab., 81:1434-1441, 1996.
2. Cantor, H.C., Padmanabhan, V., Favreau, P.A. and Midgley, A.R., Jr. Use of a newly designed microperifusion system with amperometric sensors for near continuous on-line monitoring of hormone secretion. I. Details of LH secretory response characteristics to GnRH. Endocrinology, 137:2782-2790, 1996.
3. McConnell, D.S., Padmanabhan, V., Pollak, T.B., Groome, N.P., Ireland, J.J., Midgley, A.R., Jr. Development of a two-site solid phase immunochemiluminescent assay for measurement of dimeric inhibin in human serum and other biological fluids. Clinical chemistry, 42:1159-1167, 1996.
4. Midgley, A.R., Jr., McFadden, K., Ghazzi, M.*, Karsch, F.J., Brown, M.B., Mauger, D.T. and Padmanabhan, V. Nonclassical secretory dynamics of LH revealed by hypothalamo-hypophyseal portal sampling of sheep. Endocrine 6:133-144, 1997.
5. Padmanabhan, V., McFadden, K., Mauger, D.T., Karsch, F.J. and Midgley, A.R., Jr. Neuroendocrine control of FSH secretion: I. Direct evidence for separate episodic and basal components of FSH secretion. Endocrinology, In Press, 1997.
6. Plant, T.M., Padmanabhan, V., Ramaswamy, S., McConnell, D.S., Winters, S.J., Groome, N., Midgley, A.R., Jr. and McNeilly, A.S. J Clin Endo Metab In Press, 1977.

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

1. Padmanabhan, V., McConnell, D.S., Sluss, P.M., Bolf, N., Wang, Q., Khoury, R.H., Schneyer, A.L. and Midgley, A.R., Jr. Characterization of a sensitive specific two-site chemiluminescent assay to detect free follistatin suggests all of circulating follistatin is in an activin-bound state in both men and cycling women. International Inhibin Meeting, Tokashima, Japan, Nov 9 and 10, 1996.
2. Lemon, W.J., Boving, B.G., Padmanabhan, V., Favreau, P.A. and Midgley, A.R., An enhanced perifusion system capable of delivering complex patterns with high fidelity including the GnRH surge *in vitro*. 79th Annual Meeting of the Endocrine Society, Minneapolis, June 11-14, 1997.
3. Padmanabhan, V, Battaglia, D, Karsch, F.J., Lee, J.S., Midgley, A.R., Mucci, N.R., Van Cleef, J. Bioavailable activin is a major determinant of circulating FSH. 79th Annual Meeting of the Endocrine Society, Minneapolis, June 11-14, 1997.

4. Padmanabhan, V., Evans, L.W., Wyman, T., McConnell, D.S., Midgley, A.R., Groome, N.P. Hypophyseal portal blood contains follistatin as revealed by a new, chemiluminescent assay. 79th Annual Meeting of the Endocrine Society, Minneapolis, June 11-14, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Thirteen sessions Pathology 850.
   2. Program Director, "Experimental Immunopathology Training Grant."
   3. Ph.D. Dissertation Committees, University of Michigan:
      a. Anne Jackson.
      b. Alex Greenwood.
      c. Pamela Bennett-Baker.
      d. Frances Wolber.
   4. Ph.D. Dissertation Advisor:
      a. Michael Eisenbraun.
      b. Chris Kirk.
   5. Undergraduate students:
      a. Jennifer Knapp, CLA III.

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

C. Assistant Research Scientist:
   1. R. Lee Mosley, Ph.D.
   2. Jacek Witkowski, M.D., Ph.D.

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Activation Defects in Aging T Cells", NIH AG-09801 (15%), $170,741 direct costs/year, 8/1/90 - 7/31/98. MERIT award.
B. Principal Investigator, "Immune and Muscle Function Assays as Biomarkers of Aging", NIH AG-11067 (8%), $162,629 direct costs/year, 4/1/93 - 3/31/98.
C. Principal Investigator, "Genetic Control of Longevity in Mice", NIH AG-11687 (8%), $211,266 direct costs/year, 9/1/93 - 8/31/98.
D. Principal Investigator, "New T Cell Subsets Defined by P-glycoprotein in Aging Mice", NIH R01-AG03978 (15%), $96,288 direct costs year, 12/1/95 - 11/30/98.
E. Principal Investigator, "New T Cell Subsets in Aging Mice", AlliedSignal Award for Research on Aging, $50,000 direct costs year, 1/1/95 - 12/31/96.
F. 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).
G. 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).
H. Project Director, "Prevention of Disease by Immunotonic Agents in Mice", NIH AG-08808 (5%), $50,235 direct costs/year, 9/1/94 - 8/31/99. (Component of Claude Pepper Older Americans Independence Center, J. Halter, Program Director).
I. Program Director, "Research Training in Experimental Immunopathology", NIH T32-AI-07413 (5%), $243,644 direct costs/year, 4/1/92 - 3/31/97.
J. Co-Director, "Breast Cancer in Elderly Women", (M. Wicha, PI), NIH/NCI P20-AG13094 (5%), $25,000 direct costs/year, 9/30/94 - 8/31/98.
K. Course Director, "Summer Training Courses in Experimental Aging Research", NIH/NIA R13-AG12917 (0%), $29,358 direct costs/year, 4/1/95 - 3/31/98.
L. Principal Investigator, "Wild Derived Mouse Stocks: New Models for Aging Research," NIH R01-AG13711 (5%), $187,826 direct costs/year, 9/1/96 - 8/31/99.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Graduate Education Committee.
B. Qualifying Examination Committee.
C. Research Colloquia, Course Coordinator.
D. Director, Experimental Immunopathology 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. Co-director, Breast Cancer in Elderly Women Project, UM Cancer Center.
H. Member, Cancer Biology Training Program.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

INVITED LECTURES/SEMINARS:

1. FASEB Summer Conference on "Clonal Senescence and Differentiation." Snowmass, CO. "Defective Signal Transduction in Lymphocytes from Old Mice." August 17 - 22.
2. Stanford University Immunology Program. "Aging T Cells: Subsets, Signals, and Survival." October 16.
3. Gerontological Society of America Annual Meeting. Washington, DC. Session Chair. "The First Ten Minutes: Protein Kinase Defects in T Cells from Old Mice." November 17 - 20.
4. University of Michigan Comparative Medicine Research Colloquium. "Genetically Heterogeneous Mice for Studies of Aging, Disease, and Longevity." November 22.
5. University of California, Los Angeles. "T Cells in Old Mice: Subsets, Signals, and Survival." December 18.
6. Gordon Research Conference on the Biology of Aging, Ventura, CA. "Genetic Analysis of Longevity and Disease in Mice." January 5 - 11.
7. Medical College of Pennsylvania. "Aging and Immune Function." January 16.
8. University of Iowa. "T Cells in Old Mice: Subsets, Signals, and Survival." January 22.
9. Department of Internal Medicine, University of Michigan. "Aging T Cells: Subsets, Signals, and Survival." January 31.
10. Department of Physiology, University of Michigan. "Aging T Cells: Subsets, Signals, and Survival." March 12.
11. 5th EUCAMBIS Conference on the Molecular Basis of Immunosenescence, Cordoba, Spain. "T Cells in Old Mice: Subsets, Signals, and Survival." (Keynote Lecture). May 15.
12. James J. O'Leary Memorial Symposium, University of Minnesota. "Aging and T Cell Immunity." Keynote speaker. June 2.

13. 10th Annual Grantee Conference, American Federation for Aging Research. Airlee, VA. "T Cells in Old Mice: Subsets, Signals, and Survival." June 7
14. 5th Annual Summer Training Course in Aging Research, Buck Center for Research on Aging, San Rafael, CA. "Animal Models for Aging" and "Aging and Immune Function." Course director. June 8 - 12.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chrisp, C. E., Turke, P., Luciano, A., Swalwell, S., Peterson, J. and Miller, R.A.: Lifespan and pathology in genetically heterogeneous (four-way cross) mice: a new model for aging research. Veterinary Pathology 33:735-743, 1996.
2. Dozmorov, I.M. and Miller, R.A.: Regulatory interactions between virgin and memory CD4 T lymphocytes. Cellular Immunology 172:141-148, 1996.
3. Bining, N. and Miller, R.A.: Cytokine production by subsets of CD4 memory T cells differing in P-glycoprotein expression: effects of aging. J. Gerontol. Biol. Sci., In Press.
4. Miller, R.A., Bookstein, F., van der Meulen, J.H., Engle, S., Kim, J., Mullins, L. and Faulkner, J. Candidate biomarkers of aging: age-sensitive indices of immune and muscle function co-vary in genetically heterogeneous mice. J. Gerontol. Biol. Sci. 52A:B39-B47, 1997.
5. Garcia, G. G. and Miller, R.A.: Differential tyrosine phosphorylation of zeta chain dimers in mouse CD4 T lymphocytes: effect of age. Cell. Immunol. 175:51-57, 1997.
6. Gorgas, G., Butch, E.R., Guan, K. and Miller, R.A.: Diminished activation of the MAP kinase (MEK/ERK) pathway in CD3-Stimulated T lymphocytes from old mice. Mechanisms of Ageing and Development, In Press.
7. Miller, R.A.: Age-related changes in T cell surface markers: a longitudinal analysis in genetically heterogeneous mice. Mechanisms of Ageing and Development, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Telford, W.G., Nam, S.Y., Podack, E.R. and Miller, R.A. CD30-mediated apoptosis in murine CD8 T cells after cessation of TCR signals. Submitted for publication.
2. Dozmorov, I.M. and Miller, R.A.: In vitro production of antigen-specific T cells from unprimed mice: role of dexamethasone and anti-IL-10 antibodies. Submitted for publication.
3. Bining, N. and Miller, R.A.: In vitro responses to recall antigens: age-associated decline in IL-10 production attributable to accumulation of cells expressing P-glycoprotein. Submitted for publication.
4. Dozmorov, I. M. and Miller, R.A.: Generation of antigen-specific Th2 cells from unprimed mice in vitro: effects of dexamethasone and anti-IL-10 antibody. Submitted for publication.
5. Mosley, R.L., Koker, M.M. and Miller, R.A.: Idiosyncratic alterations of TCR size distributions affecting both CD4 and CD8 T cell subsets in aging mice. Submitted for publication.
6. Miller, R.A., Chrisp, C. and Galecki, A.: CD4 memory T cell levels predict lifespan in genetically heterogeneous mice. Submitted for publication.

BOOKS/CHAPTERS IN BOOKS:

1. Miller, R.A.: Invecchiamento e tumori: un'unica faccia della stessa medaglia. (Mini-review: Aging and cancer - one side of the same coin.) (In Italian and English; translation by E. Bergamini). Giornale di Gerontologia 44: 39-46, 1996.

2. Miller, R.A.: The biology and genetics of aging and longevity, in Kelley, W.N. (ed), Textbook of Internal Medicine. 3rd Edition, Lippincott-Raven, New York. Chapter 18, pp 102-110, 1997.
3. Miller, R.A.: Aging and Immune Function, in, Paul, W.E. (ed), : Fundamental Immunology, Fourth Edition, Lippincott-Raven, New York, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

Students: Jennifer Knapp, (Undergraduate student, Department of Biology)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, Biased T Cell Receptor Utilization by Peripheral T Lymphocytes in Aged Mice. University of Michigan Geriatrics Center Pilot Feasibility Grant, Nathan Shock Center for Basic Biology of Aging, and Claude Pepper Older Americans Independence Center. $20,000. July 1, 1996-June 30, 1997.
B. Principal Investigator, Skewed T Cell Repertoires in Aged Mice. RO3AG14178-01. Pilot Project Research Grant Program for the NIA. $74,755 total costs. September 1, 1996-August 31, 1997.
C. Consultant, (John M. Hilfinger, PI), Dipeptide Transporter Expression In Vitro. National Institute of Health, Institute of General Medical Sciences. R43GM53850-01. $100,000 annual costs.

PENDING:

A. Principal Investigator, T Cell Repertoire Skewing in Aged Mice. FIRST (R29) Application and PA-97-003, Immunobiological Consequences of Aging. $530,789 total costs, April 1, 1998 - March 31, 2003.
B. Principal Investigator, T Cell Repertoire of Tumor Infiltrating Lymphocytes From Prostatic Hyperplasia and Cancer. Comprehensive Cancer Center, Prostate SPORE Faculty Developmental Research Project. $49,766. August 1, 1997 - July 31, 1998.

PROJECTS UNDER STUDY:

A. Enumeration and Identification of Postthymic T Stem Cells.
B. Frequency and Expansionary Potential of Postthymic T Stem Cells from Aged Mice.

C. Age-Related Effects of Mucosal T Lymphocytes.
D. Effects of Aging on T Cell Repertoire.
E. T Cell Repertoire in Tissues from Prostatic Hyperplasia and Adenocarcinoma.

IV. ADMINISTRATIVE ACTIVITIES:

None.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. D. H. Teitelbaum, J. Del Valle, B. Reyes, A. Gupta, R. L. Mosley, and R. M. Merion. 1996. Intestinal intraepithelial lymphocytes (IEL) influence the production of somatostatin. Surgery 120:227-223.
2. M. Hamad, R. L. Mosley, J. Wang, and John R. Klein. 1996. Stimulation via the CD43 coreceptor augments T cell proliferation during the early phase of antigen-induced activation. Dev. Comp. Immunol. 20:77-82.
3. R. L. Mosley. 1997. Aging, immunity and neuroendocrine hormones. Adv. Neuroimmunol. 6:419-432.

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

1. M. M. Koker, R. L. Mosley, and R. A. Miller. 1997. Age-associated skewing of murine T cell repertoires in $CD4^+$ and $CD8^+$ T lymphocyte subsets. Annual Meeting of the American Geriatrics Society and American Federation for Aging Research.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITITES:

1. Pathology, Laboratory Course for Dental students, Medical Illustration students, 1996.

III. RESEARCH ACTVITIES:

SPONSORED SUPPORT:

A. Principle Investigator, NHLBI Clinical investigator Development Award K08 HL03181-01: Structure and Function of Recombinant Selectin Ligands. 09/01/94-08/31/99. $402,916.
B. Principal Investigator, Biological Responses of Vascular Endothelial Cells. American Heart Association, Michigan Affiliate (MHA#03GB978 (7/97-6/98) $30,000.00).
C. Collaborator. Lung Injury by Oxygen Metabolites NIH/NIGMS R37 GM29507. National Institute of Health (Peter A. Ward, Principal Investigator).

PROJECTS UNDER STUDY:

A. Endothelial cells and inflammatory injury
B. Effects of hormones on T cell and endothelial cell function in autoimmunity
C. Structure and function of recombinant glycoproteins and endothelial cell expression of selectin ligands

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None.

MEDICAL SCHOOL/HOSPITAL:

None.

REGIONAL AND NATIONAL:

A. Reviewer, Clinical Immunology and Immunopathology
B. Reviewer, Biochemical pharmacology
C. Reviewer, Shock
D. Scientific Consultant, Warner Lambert/Parke Davis Pharmaceutical Research, Ann Arbor, Michigan

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

None.

HONORS AND AWARDS:

None.

PATENTS:

None.

INVITED LECTURES/SEMINARS:

1. Invited Speaker: "Vascular Endothelial Cells in Inflammatory Injury". Warner Lambert/Parke Davis Pharmaceutical Research, Ann Arbor, Michigan
2. Invited participant: Conference on Angiogenesis, Warner Lambert/Parke Davis Pharmaceutical Research, Ann Arbor, Michigan

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. AD Thall, Y Lu, HS Murphy, J Homeister, M Awwad, JB Lowe, A . Lussow. Anti-Gal mediated mouse heart graft rejection in α1,3-galatosyltransferase deficient mice. Transplantation.

BOOKS/CHPATERS IN BOOKS:

None.

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

1. RL Warner,S Kang, HS Murphy, MK, Dame, J Varani.Expression of Nitric Oxide from Cultured Human Skin Cells and Punch Biopsies in Response to Retinoic Acid and Cytokines. Microcirculation 4 (1):1997.
2. HS Murphy, R Warner, N Bakopoulos, MK Dame, J Varani: Vascular endothelial cells differ in susceptibility to neutrophil-mediated killing and in nitric oxide generation depending on their site of origin.. FASEB J, 11:A121, 1997.
3. AD Thall, HS Murphy, J Homeister, M Awwad, JB Lowe, L Gao, R Buelow, AR Lussow: Hyperacute Rejection of Cardiac Grafts in α1,3-Galactosyltransferase "Knock-out" Mice is Analogous to Human Rejection of Xenografts. Am Soc of Transplant Phy. May 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Pathology residents - Lecture and seminar.
B. Sophomore medical students: Instructor (Pulmonary and Endocrine Sequence), Pathology 600 laboratory.
C. Dental and graduate students - Lectures (Dermatopathology).

III. RESEARCH ACTIVITIES:

A. Cytopathology, with particular reference to serous fluids.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Advisory Committee on Appointments and Promotions.

REGIONAL AND NATIONAL:

A. American Society of Cytopathology:
Chairman, Awards Committee.
Long Range Planning Committee.
Inspector, Cytotechnology Training Program, University of Puerto Rico.
B. Cytopathology, Editorial Advisory Board.
C. Acta Cytologica, Editorial Advisory Board.
Associate Editor, North American Review Board.
D. Diagnostic Cytopathology, Consulting Editor.

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, Denver, Colorado, November, 1996.
2. Naylor, B.: a). Mesothelioma, b). Transthoracic fine needle aspiration cytology. Lectures, Cytotechnology Training Program, Henry Ford Hospital, Detroit, Michigan, February and April, 1997.
3. Naylor, B.: Moderator, Diagnostic Panel, Michigan Society of Cytology, Mackinac Island, May 1997.

HONORS AND AWARDS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Helvie, M.A., Bude, R.O., Joynt, L., Naylor, B., Rubin, J.M.: *In vitro* sonographic evaluation of aspirated hypoechoic and anechoic breast cyst fluid. Breast Dis 1996; 9, 15-22.

BOOKS/CHAPTERS IN BOOKS:

1. Naylor, B.: Pleural, Peritoneal and Pericardial Fluids. In: Comprehensive Cytopathology, M. Bibbo ed, Second Edition, Philadelphia, WB Saunders, 1996, 551-621.

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 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Supervised Luis Del Peso, Daryoush Ecketerae, Maribel Gonzalez-Garcia, Didier Grillot, Yuanmin Hu, Naohiro Inohara, Takeyoshi Koseki, Rebecca Liu, Philip Simonian, Dayang Wu, Postdoctoral Fellows.
B. Supervised Mary Benedict and Herschel Wallen, graduate students.
C. Laboratory Instructor, Pathology 630/631. Full semester, two hours/week.
D. Department of Pathology, Graduate Program Course 581, University of Michigan, Ann Arbor, Michigan.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Genetic Regulation of Apoptotic Cell Death," National Institutes of Health, $813,000 (total direct costs).
B. Principal Investigator, Research Career Development Award, "Genetic Regulation of Apoptotic Cell Death," National Institutes of Health, $315,000 (total direct costs).
C. Principal Investigator, "Bcl-x_s Mediated Apoptosis of Kaposi's sarcoma Cells," National Institutes of Health, $1.292.048 (total direct costs).
D. Principal Investigator, "Molecular analysis of Bcl-x_s induced apoptosis in breast cancer," U.S. Army Medical Research and Material Command, Fort Detrick, Frederick, MD $801,917 (total).
E. Principal Investigator, "Regulation of Apoptosis in Hematopoietic Progenitors" Fellowship for Daryoush Ekhterae, Research Fellow. National Institutes of Health, $29,500.00.
F. Principal Investigator, "Molecular Interactions of Bcl-2 Family Members, U. S. 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, Cultural Diversity Assessment Steering Committee, University of Michigan, Ann Arbor, MI.
F. Member, Hybridoma Core Committee, Multipurpose Arthritis Center, University of Michigan, Ann Arbor, MI.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Molecular and Cellular Biology Program.
B. Member, University of Michigan Cancer Center.
C. Member, Transgenic Core Facility Committee, Multipurpose
D. Member, Faculty Search Committee, Rheumatology Division, and Department of Microbiology/Immunology.
E. Reviewer, Departmental Grants.
F. Committee Member, Culture Diversity Assessment Steering Committee, University of Michigan Medical School, Ann Arbor, MI.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

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

INVITED LECTURES AND SEMINARS:

UNIVERSITY OF MICHIGAN:

1. Invited Speaker, "Control of cell death by the Bcl-2 gene family," Cancer Biology Research Seminar Comprehensive Cancer Center, University of Michigan Meical Center, June 12, 1996.
2. Invited Speaker, "Regulationof Apoptotic Cell Death," Nephrology Division Basic Science, University of Michigan Medical Center, May 27, 1997.

NATIONAL AND INTERNATIONAL:

1. Invited Speaker, Symposium on Oncogenes, "Regulation of Cell Death by Bcl-2 Gene Family," San Sebastian, Spain, October 2-5, 1996.
2. Invited Speaker, Mechanism of Cell Death: A Symposium presented by the Cell Death Society, Queens College, City University of New York, Music Building, LeFrak Concert Hall, Flushing, New York, October 12, 1996.
3. Invited Speaker, "Regulation of Cell Death by the Bcl-2 gene family." Parke-Davis, Warner-Lambert, Ann Arbor, MI, October 14, 1996.
4. Invited Speaker and Session Chairman, "Programmed Cell Death." Keystone Symposium, February 3, 1997.
5. Invited Speaker, Symposium on Apoptosis, Keystone, CO, April 17, 1997.
6. Invited Speaker, "Regulation of Apoptosis by Bcl-2 Family Proteins," Programmed Cell Death, Immune Regulatory Pathways in Autoimmune and neuroimmunological Diseases, Tucson, AZ, March, 20, 1997.
7. Invited Speaker, "Genetic regulation of cell death," McMaster University, Hamilton, Ontario, April 30, 1997.
8. Invited Speaker," "Genetic regulation of cell death," The Hospital for Sick Children, Toronto, Ontario, Canada, May 1, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNAL

1. Benito A, Silva M, Grillot D, Nuñez, G, Fernadez-Luna JL: Apoptosis-induced by erythroid differentiation of human erythroleukemia cell lines is inhibited by Bcl-x_L. Blood 1996;11:3837-3843.
2. Grillot DAM, Merino R, Pena JC, Fanslow WC, Finkelman FD, Thompson CB, Nuñez, G: Bcl-x exhibits regulated expression during B cell development and activation and modulates lymphocyte survival in transgenic mice. J. Exp. Med. 1996;183:381-391.
3. Middleton G, Nuñez G, and Davies A: Bax promotes neuronal survival and antagonizes the survival effects of neurotrophic factors. Development 1996; 122:695-701.
4. Gibson LF, Piktel BS, Narayanan R, Nuñez G, Landreth KS: Stromal cells regulate Bcl-2 and expression in pro-B cells. Experimental Haematology, 1996;24:628-637.

5. Lopez-Hoyos M, Carrio R, Merino R, Buelta L, Izui S, Nuñez, G., Merino J: Constitutive expression of Bcl-2 in B cells causes a lethal form of lupus-like autoimmune disease after induction of neonatal tolerance of $H\text{-}2^b$ alloantigens. J. Exp. Med. 1996;183:2523-2531.
6. Simonian, PL, Grillot DAM, Merino R, Nuñez G: Bax can antagonize Bcl-x_L during etoposide and cisplatin-induced cell death independently of its heterodimerization with Bcl-x_L. J. Biol Chem. 1996, 149:795-803.
7. Foreman KE, Clarke MF, Wrone-Smith T, Boise LH, Thompson CB, Polverini PJ, Apel IJ, Simonian PL, Nuñez G, Nickoloff BJ: Kaposi's sarcoma tumor cells preferentially express Bcl-x_L and undergo apoptosis when induced to overexpress the Bcl-x_L-inhibitor Bcl-x_S. Am. J. Path. 1996; 149:795-803.
8. Carrio R, Lopez-Hoyos M, Jimeno J, Benedict MA, Merino R, Benito A, Fernandez-Luna JL, Nuñez G, Garcia-Perrero JA, Merino J: *A1* demonstrates restricted tissue distribution during embryonic development and functions to protect against cell death. Am. J. Path. 1996;149:2133-2142.
9. Heermeier K, Benedict M, Li M, Further P, Nuñez G, Henninghauser L: BAX and Bcl-x_S are induced at the onset of apoptosis in involuting mammary epithelial cells. Mech. Dev. 1996;56:197-207.
10. Dole MG, Clarke MF, Holman P, Benedict M, Lu J, Jasty R, Eipers P, Thompson CB, Rode C, Block C, Nuñez G, Castle VP: Bcl-x_S enhances adenoviral vector-induced apoptosis in neuroblastoma cells. Cancer Research, 1996; 56:5743-5740.
11. Ray S, Bullock G, Nuñez G, Tang C, Ibrao AM, Huang Y, Bhalla K: Enforced expression of Bcl-x_S induces differentiation and sensitizes chronic myelogenous leukemia-blast crisis K562 cells to 1-β-D-arabinofuranosyleytosine-mediated differentiation and apoptosis. Cell Growth & Differentiation. 1996;7:1617-1623.
12. Simonian PL, Grillot DAM, Nuñez G: Bax homodimerization is not required for Bax to accelerate chemotherapy-induced cell death. J. Biol Chem. 1996;271:32073-32077.
13. Wu D, Wallen HD, Nuñez G: Interaction and regulation of subcellular localization of CED-4 by CED-9. Science, 1997:275:1126-1128.
14. Mitra RS, Wrong-Smith T, Simonian P, Foreman KE, Nuñez G, Nickoloff BJ: Apoptosis in keratinocytes is not dependent on induction of differentiation. Lab. Invest. 1997;76:99-107.
15. Inohara N, Ding D, Chen S, and Nunez G: *harakiri*, a novel regulator of cell death, encodes a protein that activates apoptosis and interacts selectively with survival-promoting proteins Bcl-2 and Bcl-x_L. The EMBO Journal, 1997;16:1686-1694.
16. Grillot DAM, Gonzalez-Garcia, Ekhterae D, Duan L, Inohara N, Ohta S, Seldin MF, and Nuñez G. Genomic organization, promoter region analysis and chromosome localization of the mouse *bcl-x* gene. J. Immunol. 1997;158:4750-4757.
17. Wu D, Wallen HD, Inohara N, Nuñez, G: Interaction and regulation of the *C. Elegans* death protease CED-3 by CED-4 and CED-9. J. Biol Chemistry (In press).
18. Simonian PL, Grillot DAM, Nuñez G: Bcl-2 and Bcl-x_L can differentially block chemotherapy-induced cell death. Blood (in press).
19. Simonian PL, Grillot DAM, Nuñez G: Bak can accelerate chemotherapy-induced cell death independently of its heterodimerization with Bcl-x_L and Bcl-2. Oncogene (In press).
20. Schneider TJ, Grillot D, Foote LC, Nuñez G, and Rothstein TL: Bcl-x_L protects primary B cells against Fas-mediated apoptosis. (Submitted).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Director, Blood Bank and Transfusion Service, University Hospitals.
B. Diagnosis of surgical specimens from University Hospital patients.
C. Diagnosis of surgical specimens from M-Labs.
D. Diagnosis of consultation breast cases from pathologists elsewhere in the U.S.
E. Medical direction of Transfusion Service.
F. Member, University of Michigan Breast Care Center.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Lectures on breast pathology and transfusion medicine to sophomore class. (five contact hours)
B. Laboratory course for sophomore medical students (Pathology 600)
C. Daily case review with pathology house officer assigned to blood bank.
D. Weekly lecture/discussion on Transfusion Medicine for Pathology, Hematology and Pediatric hematology house officers
E. Lecture-Discussion (2) on Transfusion Medicine to senior student elective course in Laboratory Medicine
F. Postgraduate course, "Current Topics in Blood Banking", Planning Committee.
G. Lectures on Transfusion Medicine presented to Pathology and Hematology/Oncology House Officers.
H. Seminars and lectures on Pathology of Breast to Pathology House Officers.
I. Lectures on Transfusion Medicine to Pharmacology and Therapeutics senior student elective course. February 9, 1997.
J. Planning committee for curriculum in hematology for sophomore medical students
K. Presentation of consultation slide conferences (4) on pathology of the breast to pathology house officers.
L. Lecture, The Evolution of Carcinoma. Graduate course in Microbiology and Biologic Sciences. September 5, 1996.
M. Presentation of grand rounds on transfusion medicine. University of Michigan Department of Surgery. April 3, 1997.

UNIVERSITY:

A. Doctoral Committee for Stephanie E. Macksood, candidate for Ph.D. in School of Public Health.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Rapid 4D MRI of Gad-DTPA enhancement for breast lesion characterization (Grant DAMD 17-94-J-4381 from US Army medical reseach acquisition activity ($605,849./4 years) (with members of Department of Radiology, T. Chenevert, P.I.)
B. New Ultrasound Methods for Cancer Diagnosis and Treatment (3-5 years at 5 % effort)
C. Microvascular and Structural Imaging of Breast Cancer (3-5 years at 3 % effort)
D. Adenoid cystic carcinoma of the breast. (with C. Kleer)
E. Microinvsive carcinoma of the breast (with L Pierce)
F. Evaluation of diseases of the breast and premalignant significance. Tecumseh project (with D. Schottenfeld)

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

A. American Association of Blood Banks
    1. Transfusion Practices Committee
    2. Transfusion medicine research strategies committee
B. American Society of Clinical Pathologists
C. College of American Pathologists
    1. Task Force on Breast Cancer, Chairman
    2. Task Force to develop clinical practice guidelines for transfusion reactions
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 Task Force, Michigan Department of Public Health
H. Referee, Canadian Red Cross Society Research and Development Proposal Evaluations, 1996-7.

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL/UNIVERSITY:

A. Transfusion Committee, Chairman
B. Breast Care Center
C. Bone marrow homotransplantation task force
D. Executive Committee on Clinical Affairs of University Hospital
E. Hospital Program for Excellence advisory committee
F. Haematology sequence advisory committee, M-2 year
G. University of MIchigan Senate Assembly
H. Ad hoc committee on intravenous access initiation

V. OTHER RELEVANT ACTIVITIES:

HONORS:

A. Distinguished Alumnus Award, University of Nebraska College of Medicine

EDITORIAL BOARDS:

A. Associate Editor, TRANSFUSION.
B. Editorial Board, American Journal of Surgical Pathology.
C. Editorial Board, American Journal of Clinical Pathology.
D. Editorial Board, Archives of Pathology and Laboratory Medicine.
E. Editorial Board, Modern Pathology
F. Reviewer, AMA Archives of Surgery
G. Reviewer, Journal of the American Medical Association.
H. Reviewer, Blood.
I. Reviewer, Cancer.
J. Reviewer, Human Pathology

INVITED LECTURES/PAPERS/SEMINARS:

1. Legal aspects of Transfusion Medicine. Chicagoland Blood Bank Society. Chicago, Ill. September 19, 1996.
2. Predicting the clinical course of carcinoma of the breast: Useful and less than useful information in the era of cost containment. H. E. MacMahon Memorial Lecture. Mount Auburn Hospital. Boston, MA October 29, 1996.
3. History of Transfusion Medicine. Victor Vaughan Society lecture. December 9, 1996.
4. Kleer CG, Oberman HA. Adenoid cystic carcinoma of the breast: value of histologic grading and proliferative activity. Annual meeting, United States and Canadian Academy of Pathology. Orlando, FL March 1, 1997.
5. Problem solving in the blood bank. Workshop. Current Topics in Blood Banking. 22nd annual symposium. University of Michigan. June 4, 1997.

6. Oberman HA, Goldman EB. Legal aspects of transfusion medicine. Current Topics in Blood Banking. 22nd annual University of Michigan. June 5, 1997.
7. Transfusion transgressions-Issues in Blood Banking. University of Michigan Medical School Northern Michigan Summer Conference. June 16, 1997.
8. Prognostic assessment of invasive versus non-invasive breast cancer. University of Michigan Medical School Northern Michigan Summer Conference. June 16, 1997.
9. Clinicopathologic conferences. University of Michigan Medical School Northern Michigan Summer Conference. June 16 and 20, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hume H, Popovsky M, Benson K, Glassman AB, Oberman HA, Pisciotto PT, Anderson K. Hypotensive reactions: a previously uncharacterized complication of platelet transfusion? Transfusion. 36:904-909, 1996.
2. Henson DE, Oberman HA, Hutter RVP. Practice protocol for the examination of specimens removed from patients with cancer of the breast. AMA Arch Pathol Lab Med 121:27-33, 1997.
3. Oberman HA. Transfusion: the first decade, volume 4. Transfusion. 37:442-443, 1997.
4. Oberman HA. Transfusion: the first decade, volume 5. Transfusion. 37:531-532, 1997.
5. Oberman HA. Transfusion: the first decade, volume 6. Transfusion. 37:668-669, 1997.
6 Benson K, Popovsky MA, Hines D, Hume H, Oberman HA, Glassman AB, Pisciotto PT, Thurer RL, Stehling L, Anderson KC. Nationwide survey of home transfusion practices. Transfusion.(in press)
7. Butch SH, Oberman HA. The computer, or electronic, crossmatch. Transfusion Medicine Reviews. (in press)

BOOK REVIEWS, LETTERS TO THE EDITOR:

1. Book Review Editor, American Journal of Surgical Pathology
2. Oberman HA. Review of Hermanek P, et al.: Prognostic Factors in Cancer. Am J Surg Pathol. 20: 905, 1996.
3. Oberman HA. Irradiated blood components. Am J Clin Pathol 107:251, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Autopsy Service

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITES:

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

PROJECTS UNDER STUDY:

A. Lung macrophage/monocyte, recruitment and activation during lung injury and fibrosis.
B. Cytokine regulation of fibroblast function.
C. Regulation of α-smooth muscle actin expression and myofibroblast phenotype.
D. Regulation of production of fibrogenic mediators and cytokines by fibroblasts and eosinophils.

E. Production of monocyte chemotactic factors by alveolar macrophage, eosinophils, and fibroblasts, and its regulation by bleomycin and cytokines.
F. Regulation of cytokine gene expression in fibrotic tissues.
G. Mechanisms of eosinophil recruitment.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Member, Medical Scientist Training Program Operating Committee.

REGIONAL AND NATIONAL:

A. Ad hoc member, NCI Program Project Site Visit Team.
B. Ad hoc member, Lung Biology and Pathology Study Section, National Institutes of Health.
C. Associate Editor, American Journal of Pathology.
D. 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.

INVITED LECTURES/SEMINARS:

1. Invited speaker, 6th International Inhalation Symposium, Hannover, Germany, February 1997.
2. Co-Chair, session on "Cellular mechanisms of pulmonary fibrosis," at the 1997 International Conference of the American Thoracic Society, San Francisco, CA, May 1997.
3. Invited Speaker, 1997 International Conference of the American Thoracic Society, San Francisco, CA, May 1997.
4. Invited speaker and session chair at the NATO Advanced Study Institute on ARDS, Corfu, Greece, June 1997.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Gharaee-Kermani M, Denholm EM, and Phan SH: Co-stimulation of fibroblast collagen and transforming growth factor β_1 gene expression by monocyte chemoattractant protein-1 via specific receptors. J. Biol. Chem. 1996;271:17779-17784.
2. Zhang K, Gharaee-Kermani M, McGarry B, Remick D, and Phan SH: TNF-α mediated lung cytokine networking and eosinophil recruitment in pulmonary fibrosis. J. Immunol. 1997;158:954-959.
3. Zhang H, Gharaee-Kermani M, and Phan SH: Regulation of lung fibroblast α-smooth muscle actin expression, contractile phenotype and apoptosis by IL-1β. J. Immunol. 1997;158:1392-1399.
4. Gharaee-Kermani M, and Phan SH: Lung interleukin-5 expression in murine bleomycin-induced pulmonary fibrosis. Am. J. Resp. Cell Molec. Biol. 1997;16-438-447.
5. Shanley CJ, Gharaee-Kermani M, Sarkar R, Welling TH, Kriegel A, Ford J, Stanley JC, and Phan SH: Transforming growth factor-β_1 increases lysyl oxidase enzyme activity and mRNA in rat aortic smooth muscles cells. J. Vasc. Surg. 1997;25:446-452.
6. Lee S-K, Wiggins RC, de Miguel M, Goyal M, Wharram B, Thomas P, Dysko R, Phan SH, Killen PD: Renal biopsy collagen I mRNA predicts scarring in rabbit anti-GBM disease: Comparison with conventional measures of function and histology. Kidney International, 1997, in press.

BOOKS/CHAPTERS IN BOOKS:

1. Zhang K, and Phan SH: Cytokines and pulmonary fibrosis. J. Biol. Signals, 1996; 5:232-239.
2. Smith RE, Strieter RM, Phan SH, Kunkel SL: C-C chemokines: Novel mediators of the profibrotic inflammatory response to bleomycin challenge. Am. J. Resp. Cell Mol. Biol. 1996;15:693-702.

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

1. Filippov S, Rekhter MD, Phan SH, Gordon D: Human atherosclerotic plaques are enriched with cells simultaneously expressing TGF-β and type one procollagen. FASEB J. 1997;11:A154.
2. Gharaee-Kermani M, McGarry B, Huffnagle G and Phan SH: Anti-interleukin-5 antibody I inhibits bleomycin-induced pulmonary fibrosis and lung eosinophilia. FASEB J. 1997;11:A228.
3. Walley KR, Lukacs NW, Phan SH, Kunkel SL: Cytokine and chemokine expression in a murine lung injury model of fibrotic ARDS. Am. J. Resp. Crit. Care Med. 1996; 155:A89.
4. Zhang H, Gharaee-Kermani M, Phan SH: Interleukin-1β induced lung myofibroblast apoptosis. Am. J. Resp. Crit. Care Med. 1996;155:A448.

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

ANNUAL DEPARTMENTAL REPORT
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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. Director, UMHC -Medsport Clinical Laboratory.
E. Coordinator, Infectious Disease Microbiology Laboratory Rounds.
F. Technical Consultant - M-Labs.
G. New clinical test development, validation and implementation.

II. TEACHING ACTIVITIES:

A. Instructor, Pathology House Officer Microbiology/Virology Program.
B. Lecturer, Clinical Pathology Grand Rounds.
C. Lecturer, Pathology PHT CLNL - 101 (M-4 elective).
D. Coordinator, Clinical Microbiology/Virology In-service Program.
E. Instructor, Infectious Disease Laboratory Rounds.
F. 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. Snydman, New England Medical Center, Boston, Massachusetts.
B. "The incidence of sexually transmitted diseases among women in Bali", Principal Investigator: Barbara Reed, School of Public Health, University of Michigan..
C. "Evaluation of novasomes and dendrimers as barrier molecules for the prevention and treatment of infectious disease", Principal Investigator: James Baker, Jr., Dept. of Pathology, University of Michigan..
D. Study of amoxicillin administration protocols for the optimal treatment of acute otitis media", Principal Investigator: Richard Linsk, Dept. of Pediatrics, University of Michigan.

PROJECTS UNDER STUDY:

A. PCR for detection of HPV in endocervial biopsies/scrapings.
B. Detection of the mecA resistance gene in staphylococci growing in blood culture bottles.
C. Rapid detection of group B *Streptococcus* in urogential specimens.
D. Epidemiologic studies of *Pseudomonas aeruginosa* comparing pulse-field gel electrophoresis and Cleavase.
E. Activity of LY333328, a new glycopeptide, against vanA-expressing *Enterococcus*
F. Effectiveness of bacitracin instilled in hemodialysis shunts in preventing line-associated infections.
G. Detection of *Escherichia coli* SLT I & II in fecal specimens by EIA.
H. Evaluation of DFA methods to detect CMV pp65 antigen in blood leukocytes.
I. Susceptibility of respiratory bacterial pathogens using the E-test strips.
J. Quantitation of HIV in patients receiving antiviral therapy.
K. Quantitative changes in antibody titer in patients infected with *Helicobacter pylori* presenting with gastrointestinal bleeding, with William Chey, GI Medicine.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL/NATIONAL:

A. Executive Board, South Central Association for Clinical Microbiology.
B. Co-Chair, Michigan Microbiology Laboratory Directors Association.
C. Co-Chair, TriCounty Clinical Microbiology Association.
D. CAP Inspection Team-Northwestern Memorial Hospital, Feb. 27, 1997.

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. Association for Molecular Pathology.
E. Michigan Infectious Disease Society.
F. South Central Association for Clinical Microbiology.
G. TriCounty Clinical Microbiology Association.

INVITED LECTURES/ SEMINARS:

1. "The diagnosis of *Helicobacter pylori*: the organism, the diseases, the tests for detection" Michigan Society for Clinical Laboratory Science Annual Meeting, Troy, MI, April 9,1997.
2. "Infections caused by *Mycoplasma* and *Ureaplasma",* West Virginia University Hospitals Morgantown, WV, May 14, 1997.
3. "The recovery and identification of enteropathogenic bacteria" (Workshop), Fall Meeting, Michigan Branch of the American Society for Microbiology, Dearborn, MI, October 11, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Blackwood, R.A., Rode, C.K., Pierson, C.L. and Block, C.A.: Pulse-field gel electrophoresis genomic fingerprinting of hospital *E. coli* bacteria isolates. 1997. J. Med. Microbiol. 46: 506-510.
2. Jacobson, PA, West, NJ, Spadoni, V, Maksym, CJ, and Pierson, CL: Sterility of Filgrastim (G-CSF) in syringes. 1996. Pediatrics, 30: 1238-1241.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Carver, P.L., Welage, L., Pierson, C.L., and Kauffman, C.: Alterations in gastric acidity in HIV-infected patients. Clinical Infectious Diseases
2. Marinella, M.A., Pierson, C.L. and Chenoweth, C.: The stethoscope: a potential source of nosocomial infection.
3. Faix, RG, Perzigian, RW, Adams,JT, Weiner, GM, DiPietro, MA, Blythe, LK and Pierson, CL: *Ureaplasma urealyticum* and chronic lung disease in very low birth weight infants during he exogenous surfactant era.

BOOKS/ CHAPTERS IN BOOKS:

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

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

1. 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. Abstracts of the General Meeting, American Society for Microbiology, 1996; page 277.
2. Pearlman, M., Pierson, C., and Faix, R.: *Streptococcus agalactiae* (Group B Strep) resistance to clinidamycin and erythromycin. Abstracts, Infectious Diseases in Obstetrics and Gynecology , 1997; in press.
3. Faix, R., Pierson, C., and Pearlman, M.: Interpartum chemoprophylaxis for Group B Streptococcus: high frequency of resistance to recommended penicillin alternatives in clinical isolates. Abstracts, The American Pediatric Society / The Society for Pediatric Research, 1997; in press.
4. Young, C., and Pierson, C., and Burkett, J: Case report: recovery of vancomycin-dependent *Enterococcus* from blood culture. Abstracts, South Central Association for Clinical Microbiology Spring Meeting, 1997; page 15.

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

ANNUAL DEPARTMENTAL REPORT
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OVERVIEW:

Most of my efforts continued to be devoted to the M-Labs program . In addition , I also continued my commitments to help the Cytopathology Lab with Pap-smear interpretation once-a-week and the Autopsy Service with coverage . Surgical pathology sign-out for M-Labs cases (including outside consults from client hospitals) constituted another significant portion of my activity.

Last year we continued to see a significant change in the hospital market . Because of excess bed capacity and the need to become more cost-competitive, consolidations and networking between hospitals seemed to get most of our attention. As a result, we had to re-direct our marketing strategies. Instead of targetting individual hospitals , we became involved in several developing hospital networks, such as the Great Lakes Network , the Central Michigan Network , the Joint-Venture Hospital Laboratory Network (which includes W.Beaumont , Oakwood , St.John , Mt. Clemens General and others) , HealthLink [Foote Hospital, Bronson , Lakeland and Hackley Hospital (Muskegon)] and the Lake Erie Regional Alliance (15 hospitals in Ohio). More details of these activities can be found in M-Labs' Annual Report .

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

The group of client pathologists continues to increase as more hospitals send us reference lab work and so does my involvement in our support to them. The M-Labs Symposium for pathologists continues to be successful. The nineth was held in April, 1997. The volume in surgical pathology cases continues at the same level , with the cases from the satellite clinics or acquired physician offices in addition to the cases from Albion and Addison Hospitals.

I. CLINICAL ACTIVITIES:

A. Reading surgicals for M-Labs' clients (Albion and Addison Hospitals and selected offices). This activity is predominantly performed by E.M. Silverman, M.D. Reporting on consultation cases from our clients.
B. Stat outside surgical pathology consults for M-Labs client hospitals.These stat-consults rely on our courier service and provide fast turnaround times. Most of these cases are shown in consultation to other faculty.
C. Cytopathology: reviewing and verifying Pap smears one day-a-week with the Cytopathology fellow and residents .
D. Autopsy coverage at the University Hospitals approximately five weeks a year and six week-ends a year.
E. Pathologist, on site coverage for Albion and Addison Community Hospitals.
F. Frozen sections at Livonia SurgiCenter, Livonia (frequency: up to 6 cases / year)

II. TEACHING ACTIVITIES:

A. Read out autopsies with house officers.
B. Organize and lecture at the M-Labs Symposium, a one day-long event with lectures and case presentations for pathologists . Discussions also include Managed Care and Utilization. Held twice a year (October/April).

C. In-service teaching to laboratory staffs at Albion Community Hospital and the University of Michigan Health Service.
D. Colposcopy meetings held once-a-month with the Gyn medical staff at the University of Michigan Health Service .

III. RESEARCH ACTIVITIES:

Utilization of urine cultures- with the medical and laboratory staff at the University Health System. Criteria for ordering urine cultures were developed and are currently in use.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

OTHER:

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

V. OTHER RELEVANT ACTIVITIES:

A. Continued enhancement of the M-Labs version of the Spectrum, a newsletter sent to our clients and their medical staff.
B. Inspector for College of American Pathologists Inspection and Accreditation Program.
C. Fellow, College of American Pathologists.
D. Quality Assurance program in Surgical Pathology , for M-Labs client pathologists .
E. CAP-sponsored meeting on Outcomes Research , held in St. Petersburg, FL , Jan 1997
F. Member, QA committee , Joint Venture Hospital Laboratory Network , beginning June 1997

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

ANNUAL DEPARTMENTAL REPORT
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I. CLINICAL ACTIVITIES:

A. Director, Autopsy Service.
B. Director, Electron Microscopy Service
C. Supervision of Autopsies-8 weeks, signed out 51 autopsies.
D. Coordinator of Senior Staff Autopsy Call Schedule.
E. Deputy Medical Examiner for University Hospitals.

II. TEACHING ACTIVITIES:

A. Coordinator, Biweekly Pathology Gross Conference.
B. Lectures to Pathology House Officers in Anatomic and Clinical Pathology.
C. Lecturer, Pathology 600 Course.
D. Pathology 600, Provided written critiques of student autopsy write-ups (200).
E. Laboratory Instructor, Histopathology Laboratory for M1 students.
F. Laboratory Instructor, Pathology 600 (M2 pathology course)
G. High Student Science Rotation: Hosted 30 Honors Science Students in the laboratory for an afternoon on 3 separate occasions to provide a research experience.
H. Mentor, Michael Shillingford, U of Michigan Post-baccalaureate student, now admitted to medical school
I. Thesis Committee - Andrew Merry, Jami Foreback
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. Graduate Students - Jami Foreback, Medical Students - Liza Green, Hilliary Cohen, Undergraduate Students - David Newcomb, Rob Cohen.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Regulation of gene expression of soluble mediators of inflammation using the following models:
   1. Endotoxin-stimulated human whole blood.
   2. Endotoxin injection in mice.
   3. Cecal ligation and puncture.

B. Toxic effects of immunomodulators.
C. Pathophysiology of septic shock.
D. Quantitation of mediators in septic shock.
E. Cloning, sequencing, and expressing cytokines including mTNF, hTNF, mIL-6, hIL-8, MCP, JE, IL-1ra.
F. Oxident regulation of IL-8 gene expression.
G. Mechanisms of nosocomial pneumonia, and association with IL-8.
H. Immunopathology of inflammatory bowel disease.
I. Body wall fat as predictor of morbid obesity.
J. 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, "The Effects of IL-10", $31,500, 1994-97.
C. Pricipal Investigator, "Regulation of IL-8 gene expression: four years, GM50401 $870,822, 1995-1999.
D. Amgen Inc. "Keratinocyte Growth Factor Regulation of Acid Induced Lung Injury" 1997-1998 $25,000
E. Novaset "PMX modulation of cytokine production" 1996 - 1997, $7,000

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, autopsy service.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Faculty Senate
B. Member, Medical School Admissions Committee
C. Member, Biomedical Research Council Undergraduate Research council

REGIONAL AND NATIONAL:

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

D. Deputy Medical Examiner for Washtenaw County.
E. Member, Executive Committee, Michigan Association of Medical Examiners.
F. Secretary, Michigan Association of Medical Examiners.
G. Member, Michigan Association of Medical Examiners, Shock Society, American Association of Immunologists, A. James French Society, American Society of Investigative Pathologists, United States-Canadian Academy of Pathology.

V. OTHER RELEVANT ACTIVITIES:

A. Ad hoc reviewer, NIH Study Section - Surgery, Anesthesiology and Trauma, Jun 1997
B. Editorial Board: Shock
C. Reviewer:
1. Laboratory Investigation.
2. Journal of Immunology.
3. Journal Leukocyte Biology.
4. American Journal of Pathology.
5. Immunology and Infectious Diseases.
6. Journal of Clinical Investigations.
7. Infection and Immunity.
8. Blood.
9. Shock.
10. American Journal of Physiology.
11. Journal of Gerontology.

INVITED LECTURES/SEMINARS:

1. Visiting Professor, Case Western Reserve University, Cleveland Ohio, The role of cytokines in inflammatory bowel disease, Nov 18 - 19, 1996.
2. Invited lecture, University Laboratory Animal Medicine, Ann Arbor, MI The role of cytokines in the pathogenesis of sepsis, Jan 10, 1997.
3. Invited participant, Michigan Medical Examiner Database Project, Michigan Public Health Research Institute, Lansing, Michigan, Jun 9, 1997
4. Invited participant, Upjohn-Pharmacia sponsored seminar, Autoimmune Research Advances, Ann Arbor, Michigan, Jun 2, 1997
5. Invited lecture, University Laboratory Animal Medicine, The pathogenesis of sepsis, Ann Arbor, MI Jan 10, 1997

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wang, H., X. Tan, H. Chang, F. Gonzalez-Crussi, D. G. Remick, and W. Hsueh. 1997. Regulation of platelet-activating factor receptor gene expression in vivo by endotoxin, platelet-activating factor and endogenous tumour necrosis factor. Biochem.J. 322 (Pt 2):603.

2. Villarete, L. H., and D. G. Remick. 1997. Nitric oxide regulation of interleukin-8 gene expression. Shock 7:29.
3. Zhang, K., M. Gharaee-Kermani, B. McGarry, D. Remick, and S. H. Phan. 1997. TNF-alpha-mediated lung cytokine networking and eosinophil recruitment in pulmonary fibrosis. J.Immunol. 158:954.
4. Balazovich, K. J., S. J. Suchard, D. G. Remick, and L. A. Boxer. 1996. Tumor necrosis factor-alpha and FMLP receptors are functionally linked during FMLP-stimulated activation of adherent human neutrophils. Blood 88:690.
5. Gilmont, R. R., A. Dardano, J. S. Engle, B. S. Adamson, M. J. Welsh, T. Li, D. G. Remick, D. J. Smith, Jr., and R. S. Rees. 1996. TNF-alpha potentiates oxidant and reperfusion-induced endothelial cell injury. J.Surg.Res. 61:175.
6. Yi, E. S., D. G. Remick, Y. Lim, W. Tang, C. E. Nadzienko, A. Bedoya, S. Yin, and T. R. Ulich. 1996. The intratracheal administration of endotoxin: X. Dexamethasone downregulates neutrophil emigration and cytokine expression in vivo. Inflammation 20:165.
7. Yi, E. S., A. Bedoya, H. Lee, E. Chin, W. Saunders, S. J. Kim, D. Danielpour, D. G. Remick, S. Yin, and T. R. Ulich. 1996. Radiation-induced lung injury in vivo: expression of transforming growth factor-beta precedes fibrosis. Inflammation 20:339.
8. Friedland, J. S., J. C. Porter, S. Daryanani, J. M. Bland, N. J. Screaton, M. J. Vesely, G. E. Griffin, E. D. Bennett, and D. G. Remick. 1996. Plasma proinflammatory cytokine concentrations, Acute Physiology and Chronic Health Evaluation (APACHE) III scores and survival in patients in an intensive care unit [see comments]. Crit.Care Med. 24:1775.
9. Yi, E. S., H. Lee, Y. K. Suh, W. Tang, M. Qi, S. Yin, D. G. Remick, and T. R. Ulich. 1996. Experimental extrinsic allergic alveolitis and pulmonary angiitis induced by intratracheal or intravenous challenge with Corynebacterium parvum in sensitized rats. Am.J.Pathol. 149:1303.
10. Villarete, L. H., and D. G. Remick. 1996. Transcriptional and post-transcriptional regulation of interleukin-8. Am.J.Pathol. 149:1685.
11. Cooper, P. J., R. H. Guderian, D. Prakash, D. G. Remick, I. Espinel, T. B. Nutman, D. W. Taylor, and G. E. Griffin. 1996. RANTES in onchocerciasis: changes with ivermectin treatment. Clin.Exp.Immunol. 106:462.
12. Remick, D. G., Y. Negussie, D. Fekade, and G. Griffin. 1996. Pentoxifylline fails to prevent the Jarisch-Herxheimer reaction or associated cytokine release. J.Infect.Dis. 174:627.
13. Remick, D. G., and L. Villarete. 1996. Regulation of cytokine gene expression by reactive oxygen and reactive nitrogen intermediates. J.Leukoc.Biol. 59:471.

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

1. High Systemic IL-8 Does Not Prevent Local Inflammation. G. Bolgos, D. Newcomb, L.Green, S.Garg & D.Remick, U of Michigan, Ann Arbor MI 48109 Experimental Biology, 1997
2. IL-10 Fails to Decrease the Mortality or Morbidity of Sepsis. Daniel G. Remick*, Sunir J. Garg, David E. Newcomb, Paul Taheri, Thomas K. Huie and Gerald L. Bolgos, Experimental Biology, 1997, New Orleans, LA
3. Comparative Glucocorticoid Inhibition of Cytokine Production in Human Whole Blood. Daniel Remick, Rob Cohen, and Gerald Bolgos, University of Michigan, Ann Arbor, Shock Conference, June, 1997, Indian Wells CA

4. The Integrity of Different Housekeeping Genes. Ebong, G. Bolgos, D. Newcomb, R. Cohen, and D. Remick. Experimental Biology, 1997, New Orleans LA
5. Cytokine and LPS Levels are not Associated with the Morbidity of Antibiotic Treatment. D. Newcomb, G. Bolgos, L. Green, and D.Remick, Experimental Biology, 1997, New Orleans LA
6. Correlation of Body Mass Index with Thoracic and Abdominal Panniculus. Brian Hunter, M.D. Diana French, John Warner, Daniel Remick, Am. Acad. Forensic Sciences, 1997, New York, NY

BOOKS AND CHAPTERS IN BOOKS:

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

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996- 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

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

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

D. Clinical Pathology Grand Rounds (one lecture).
E. Clinical Pathology Case Conference/weekly.

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.
E. Role of Epstein-Barr virus in lymphoid neoplasia and reactive immune states.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL/NATIONAL:

A. Pathology reviewer, multicenter phase II dosimetry study of I^{131} anti-B1 radioimmunotherapy for B-cell lymphoma, Coulter Pharmaceutical.
B. Ad hoc manuscript reviewer, Cancer.
C. Ad hoc manuscript reviewer, Blood.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Lecturer, "Hematologic Coups: A practical approach to challenging cases in hematolymphoid diagnosis", American Society of Clinical Pathologists National Meeting, April, 1997.
2. Lecturer, "Clinical Flow Cytometry", M-Labs CME for clinical laboratory staff and medical technology students, Hurley Hospital, Flint, MI, May 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kaminski MS, Zasadny KR, Francis IR, Fenner MC, Ross CW, Milik AW, Estes J, Tuck M, Regan D, Fisher S, Glenn S, Wahl RL. 131-I-Anti-B1 Radioimmunotherapy for B-Cell Lymphoma. J Clin Oncol 14:1974-1981, 1996.
2. Hsi ED, Siddiqui J, Schnitzer B, Alkan S, Ross CW. Analysis of immunoglobulin heavy chain gene rearrangement in myoepithelial sialadenitis by polymerase chain reaction. Am J Clin Pathol 106:498-503, 1996.
3. Anderson MM, Ross CW, Singleton TP, Sheldon S, Schnitzer B. Ki-1 anaplastic large cell lymphoma with a prominent leukemic phase. Hum Pathol 27:1093-1095, 1996.

ARTICLES SUBMITTED FOR PUBLICATION:

1. McCarthy CJ, Sheldon S, Ross CW, McCune WJ. Cytogenetic abnormalities and therapy-related myelodysplastic syndromes in rheumatic disease.
2. Hsi ED, Eisbruch A, Greenson JK, Singleton TP, Ross CW, Schnitzer B. Classification of primary gastric lymphomas according to histologic features.
3. Singleton TP, Anderson MM, Ross CW, Sheldon S, Schnitzer B. Leukemic phase of mantle cell lymphoma, blastoid variant.
4. Su LD, Schnitzer B, Ross CW, Vasef M, Mori S, Shiota M, Mason DY, et. al. The t(2;5)-associated P80 NPM/ALK fusion protein in nodal and cutaneous CD30+ lymphoproliferative disorders.
5. Kroft SH, Singleton TP, Dahiya M, Ross CW, Schnitzer B, Hsi ED. Absence of occult B-cell clones within traumatically ruptured spleens with expanded marginal zones.
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.

BOOKS AND CHAPTERS IN BOOKS:

1. Ross, CW, Sadler, DA and Keren, DF: Flow cytometric evaluation of immunodeficiency diseases in Bauer KD, Duque, RE and Shankey TV (eds), Flow Cytometry: Principles and Clinical Applications, Williams and Wilkins, In Press.

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

1. Hsi ED, Singleton TP, Svoboda S, Frank TS, 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. Mod Pathol 10:127A, 1997.
2. Kroft SH, Singleton TP, Dahiya M, Ross CW, Schnitzer B, Hsi ED. Absence of occult B-cell clones within traumatically ruptured spleens with expanded marginal zones. Mod Path 10:128A, 1997.
3. Pearsall CP, Kroft S, Ross C, Schnitzer B, Singleton TP. Apoptosis in myelodysplastic syndromes. Mod Path 10:132A, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

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

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. University of Michigan Health Service Laboratories.

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.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

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

INVITED LECTURES/SEMINARS:

1. "A Practical Approach to the Diagnosis of Extranodal Lymphomas", ASCP Workshop, New Orleans, Louisiana, September, 1995.
2. "Reactive Lymphadenopathies",Tutorial on Neoplastic Hematopathology, Department of Laboratory Medicine and Pathology, University of Minnesota, San Diego, California, January, 1997.
3. Schnitzer, B., Ross, C.W. and Singleton, T.: "Hematologic Coups", ASCP Workshop, Chicago, Illinois, April, 1997.
4. Schnitzer, B.: Videomicroscopy Workshop, "Interesting Lymphoid Lesion", ASCP Workshop, Chicago, Illinois, April, 1997.
5. "Acute Lymphoproliferative Disorders", ASCP Workshop, Chicago, Illinois, April, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hsi, E.D., Siddiqui, J., Schnitzer, B., Alkan, S. and Ross, C.W.: Analysis of immunoglobulin heavy chain gene rearrangement in myoepithelial sialadenitis by polymerase chain reaction. Am J Clin Pathol 106:498-503, 1996.
2. Anderson, M.M., Ross, C.W., Singleton T.P., Sheldon S. and Schnitzer, B.: Ki-1 anaplastic large cell lymphoma with prominent leukemic phase. Human Pathol 27:1093-1095, 1996.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Alkan, S., Ross, C.W., Siddiqui, J., Hanson, C.A. and Schnitzer, B.: Whipple's disease in lymph nodes: Quick confirmation by polymerase chain reaction amplification.

2. Hsi, E.D., Eishbruch, A., Greenson, J.K., Singleton, T.P., Ross, C.W.and Schnitzer, B.: Classification of primary gastric lymphomas according to histologic features.
3. Singleton, T.P., Anderson, M.D., Ross, C.W., Sheldon S. and Schnitzer, B.: Leukemic phase of mantle cell lymphoma, blastoid variant.
4. Su, L.D., Schnitzer, B., Ross, C.W., et al: The t(2;5)-associated P80 NPM/ACK fusion protein in nodal and cutaneous CD30+ lymphoproliferative disorders. J Cutaneous Pathol

BOOKS AND CHAPTERS IN BOOKS:

None

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

1. Pearsall, C.P., Krofts, S., Ross, C., Schnitzer, B., and Singleton, T.P.: Apoptosis in myelodysplastic syndromes. Lab Invest 76:132a, 1997; Mod Pathol 10:132a, 1997.
2. Hsi, E., Singleton, T.P., Svoboda, S., Frank, T.S., Schnitzer, B., and Ross, C.W.: Characterization of the lymphoid infiltrate in Hashimoto's thyroiditis by immunohistochemistry and polymerase chain reaction fro immunoglobulin heavy chain gene rearrangement. Lab Invest 76:127a, 1997; Mod Pathol 10:127a, 1997.
3. Su, L., Singleton, T.P., Schnitzer, B., Mori, S., Shiota, M., and Headington, J.T.: The t(2;5) translocation-associated p80 NPM/ALK fusion protein is expressed in some nodal ki-1 anaplastic large cell lymphomas but not in primary cutaneous ki-1 lymphomas or lymphomatoid papulosis. Lab Invest 76:47a, 1997; Mod Pathol 10:47a, 1997.
4. Kroft, S.H., Singleton T.P., Dahiya, M., Ross, C.W., Schnitzer, B., and Hsi, E.: Absence of occult B-cell clones within traumatically ruptured spleens with expanded marginal zones. Lab Invest 76:128a, 1997; Mod Pathol. 10:128a, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Clinical Cytogenetics Laboratory.

II. TEACHING ACTIVITIES:

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

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

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

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

H. Clinical Pathology M4 elective: eight hour lecture/laboratory.
I. Minority Medical Students, five hour lecture/laboratory.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Role of the use of growth factors and mitogens for cytogenetic examination of hematologic malignancies in a clinical laboratory.
B. Use of growth factors to elaborate expression of a Philadelphia chromosome.
C. Use of intercalating agents to enhance resolution of chromosome bands.
D. Correlation of ploidy with expression of differential function.
E. Role of 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", Orlando, March, 1997.
2. Blue Cross Blue Shield of Michigan Genetics Symposium, "State of the Art Cytogenetics for Patient Care".

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Innis, JW, Asher, JH, and Sheldon S: Autosomal dominant microcephaly without mental retardation, short palpebral fissures, and digital anomalies. Am. J. Med. Genet., in press.
2. Innis, JW, Asher, J, Liang, Y, Wike, C, Dietick, H, Kazen-Gillespie, K, Sheldon, S, Glover, T, and Friedman, T: Exclusion of BMP6 as a candidate gene for cleidocranial dysplasia. Am. J. Med. Gen, in press.

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

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

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

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 a growing list of pathologists at M-Labs client hospitals (Dr. Rasche does most of these).

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.

D. Gave commencement address at Hurley Hospital's 1996 Graduation of Medical Technologist class.

III. RESEARCH ACTIVITIES:

A. Investigation of malacoplakia of the endometrium and vasitis nodosa.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

B. Director, M-Labs:
   1. Provide leadership for and participate in planning, marketing, and implementation of M-Labs programs.
   2. Expansion of M-Labs.
      a. The additional personnel hired beginning 2 years ago have added to the effectiveness of our highly motivated and talented M-Labs team. We are now better able to deal with support of existing clients as well as

marketing. We have now improved our Quality Assurance activities and monitor errors and problems in a systematic way with a more organized effort to resolve problems.

b. Through the efforts of PDS, we have our second fully operational interface between the University of Michigan laboratory computer system and a client hospital's computer system. One other is under development and two more are planned.

3. Growth. This year, M-Labs has experienced a 37.7% increase in net billings for clinical pathology activities. This increase was due to a 31% increase in net revenues from billings to clients for clinical pathology services and a 51% increase in net billings to patients for clinical pathology services. Billing for AP surgical pathology cases has increased by 6%.
   a. In this fiscal year we added the reference laboratory work of two 300 bed hospitals, a 41 bed hospital, and several large group practices and individual physicians' offices.
   b. We lost one small hospital because we were not permitted to bid because of State of Michigan regulations.
   c. We have submitted 3 proposals, one to a hospital and 2 to networks of hospitals.
4. Managed Care Activities. M-Labs has implemented our agreement with M-Care to supply outpatient laboratory services for that portion of the enrollees in its new Medicare (Senior Plan) subscribed to 4 of M-Care's hospital group providers. (The work from the remaining 3 hospitals will go to an independent Laboratory). In order to accomplish this task, M-labs developed and implemented processes for claims transfer from and means of distribution of capitated revenue among the subcontracted laboratory providers, and developed and implemented a Quality Assurance plan to meet with M-Care's and HCFA's requirements for this product. M-Labs responded to a RFP from M-Care for provision of outpatient laboratory services for its HMO, POS, and Medicaid products. We proposed to subcontract these services to M-Care's provider hospital laboratories. We will be allowed to subcontract to six hospital systems' laboratories (the four in the Medicare product and two more.) Final terms of the arrangement are still being developed.
5. Networks. We are still working with a group of Michigan hospital laboratories to form GreatLakes Laboratory Network, which will have the capability to negotiate for statewide and, eventually, regional managed care contracts for laboratory services. M-Labs personnel now work in key committees of this group.
   a. We have joined JVHL, a network of major hospital laboratories in the Detroit area. I have been appointed as one of 2 representatives of the Michigan Health Corporation to JVHL.

B. Director, Laboratory at Trillium Hospital, Albion, Michigan.
C. Director of Laboratories, Addison Community Hospital, Addison, Michigan.
D. Chair, Tissue/Transfusion and Infection Control Committees, Trillium Hospital, and Addison Community Hospital.
E. Member, Surgical and Medicine/Family Practice Committees, Trillium Hospital.
F. Member, Executive Committee and Peer Review Committee, Addison Community Hospital.
G. Plan and review Laboratory QA and CQI at Trillium and Addison Community Hospitals.
H. 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 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Review of lymph node and bone marrow biopsies, peripheral blood smears and body fluids.
B. Review of immunophenotyping by flow cytometry
C. Quality control and antibody development for clinical immunohistochemistry.
D. Review of biopsies for interdepartmental conferences.
   1. Weekly lymphoma conference.
   2. Biweekly leukemia conference
   3. Biweekly hematology conference

II. TEACHING ACTIVITIES:

A. Lecturer, second year medical students, Lymphoproliferative Disorders
B. Laboratory Instructor, second year medical students, Hematology
C. Lecturer, fourth year medical students, Red Cell Disorders.
D. Laboratory Instructor, fourth year medical students, Hematology
E. Lecturer, second year dental students, Leukocyte Disorders
F. Informal teaching conferences, pathology residents, bimonthly hematopathology unknown conference
G. Informal teaching conferences, pathology residents, bimonthly immunohistochemistry conference
H. Informal teaching, pathology residents, sign-out of hematopathology and flow cytometry
I. Grand Rounds, Clinical Pathology, Introduction to lymphoproliferative disorders

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Classification of lymphomas in ocular adnexa
B. Expression of cyclin D1 in small B-cell lymphoproliferative disorders
C. Lymphoproliferative disorders of MALT-type occuring after transplantation
D. Lymphoblastic lymphomas presenting as lytic bone lesions

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Assistant Director, Cancer Center Core Facility for Tissue Procurement, Research Immunohistochemistry and Histology

UNIVERSITY OF MICHIGAN:

None.

REGIONAL AND NATIONAL:

None.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

1. Lecturer, Hematological Coups: A practical approach to challenging cases in hematolymphoid diagnosis. Course at the American Society for Clinical Pathology, April 1997.

VI. PUBLICATIONS:

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

1. Su L, Schnitzer B, Ross CW, Vasef, M, Mori S, Shiota M, Mason DY, Pulford K, Headington JT, Singleton TP. The t(2;5) translocation-associated p80 NPM/ALK fusion protein is expressed in some nodal Ki-1 anaplastic large cell lymphomas, but not in primary cutaneous Ki-1 lymphomas or lymphomatoid papulosis. (in press, J Cutaneous Pathol)
2. Khalidi HS, Singleton TP and Weiss SW. Do Leukocyte Markers Distinguish Inflammatory Malignant Fibrous Histiocytoma from Hodgkin's and non-Hodgkin's Lymphoma? (in press, Mod Pathol)
3. Hsi ED, Greenson JK, Singleton TP, Eisbruch A, Ross CW and Schnitzer B. Classification of primary gastric lymphomas according to histologic features. (in press, Am J Surg Pathol)
4. Anderson MM, Ross CW, Singleton TP, Sheldon S and Schnitzer B: Ki-1 anaplastic large cell lymphoma with a prominent leukemic phase. Hum Pathol 27:1093-5, 1996

5. Tworek JA, Appelman HD, Singleton TP and Greenson JK. Stromal tumors of the jejunum and ileum. Mod Pathol 10(3):200, 1997
6. Svoboda-Newman SM Greenson JK Singleton TP Sun R Frank TS. Detection of hepatitis C by RT-PCR in formalin-fixed paraffin- embedded tissue from liver transplant patients. Diagn Mol Pathol (1997 Apr) 6(2):123-9

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Singleton TP, Anderson MM, , Ross CW, Sheldon S, Schnitzer B: Leukemic phase of mantle cell lymphoma, blastic variant.
2. Kroft SH, Singleton TP, Dahiya M, Ross CW, Schnitzer B and Hsi ED. Absence of occult B-cell clones within traumatically ruptured spleens with expanded marginal zones.
3. Kroft SH, Finn WG, Singleton TP, Ross CW, Sheldon S and 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.

ABSTRACTS IN UNREFEREED JOURNALS:

1. Pearsall CP, Kroft S, Ross C, Schnitzer and Singleton TP. Apoptosis in myelodysplastic syndromes. (United States and Canadian Academy of Pathology, 1997, Mod Pathol)
2. Hsi ED, Singleton TP, Svoboda S, Frank TS, Schnitzer B and Ross CW. Characterization of the lymphoid infiltrate in Hashimoto's thyroiditis by immunohistochemistry and polymerase chain reaction for immunoglobulin heavy chain gene rearrangement. (United States and Canadian Academy of Pathology, 1997, Mod Pathol)
3. Su L, Singleton TP, Schnitzer B, Mori S, Shiota M, Headington JT. The t(2;5) translocation-associated p80 NPM/ALK fusion protein is expressed in some nodal Ki-1 anaplastic large cell lymphomas, but not in primary cutaneous Ki-1 lymphomas or lymphomatoid papulosis. (United States and Canadian Academy of Pathology, 1997, Mod Pathol)
4. Kroft SH, Singleton TP, Dahiya M, Ross CW, Schnitzer B and Hsi ED. Absence of occult B-cell clones within traumatically ruptured spleens with expanded marginal zones. (United States and Canadian Academy of Pathology, 1997, Mod Pathol)
5. Lee CT Wojno K Oesterling JE Singleton T McCauley L Lehr J Montie JE Pienta K. Expression of parathyroid hormone-like protein in prostate cancer and prostatic intraepithelial neoplasia (Meeting abstract).Proc Annu Meet Am Assoc Cancer Res (1996) 37:A1676

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Flow Cytometry Diagnostic Service - interpretation of cell surface marker studies and cellular DNA analyses in the evaluation of hematologic disorders, primary and secondary immune deficiencies and autoimmune processes.

B. Autopsy service.

II. TEACHING ACTIVITIES:

A. Research supervisor for undergraduate, graduate and research-track investigators:

1. Francis Wolber, Ph.D. candidate in Experimental Pathology (July, 1992-present) - Ms. Wolber completed her project on the role of adhesion receptors in the recruitment of mononuclear leukocytes during the pulmonary immune response. Her study is based on *in vitro* modeling from this laboratory showing that T-lymphoblasts use P-selectin, E-selectin and the β1-integrin VLA-4 to initiate contact with activated endothelium at physiologic levels of linear-shear stress. Ms. Wolber demonstrated that the selectins and the VLA-4 account for 90% of the T-lymphoblast recruitment into the lung during the immune response to particulate antigens. This constitutes the first direct evidence that both selectins and the β1-integrin VLA-4 contribute to T-cell recruitment in hypersensitivity pneumonitis.
2. Randall Knibbs, Ph.D., Research Scientist (January, 1994-present) - Dr. Knibbs published the first evidence that regulation of a single fucosyltransferase, FucT-VII, controls the synthesis of ligands for E-selectin on T-cells. These ligands are essential for the entry of T-cells into both normal and pathologic immune lesions in the skin. A second manuscript shows that the same enzyme regulates the synthesis of P-selectin ligands on T-cells as well. These discoveries provide the first specific target for development of agents which suppress selectin-mediated T-cell recruitment in immune mediated diseases. Dr. Knibbs efforts now focus on the structure of the carbohydrate portion of the selectin ligands on T-cells and on the signalling pathways controlling FucT-VII activity.

B. 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). Developed new lectures series covering the growth, differentiation and normal physiology of leukocytes. The sequence, particularly the laboratory component, continues to enjoy one of the highest ratings (both student and faculty) for any sequence in Component II.

C. 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.

D. Section leader, Hematopathology Section of Component II- several sequences use specialists to cover pertinent laboratories. This is in addition to serving as an instructor in the general pathology laboratories of Component II.
E. Co-director and lecturer, General Pathology Course for Dental and Graduate Students (Pathology 580/630): assumed co-directorship with special emphasis on the use of computer-based learning in laboratories. Completely revamped the slide material, kodachromes and syllabus used in the General and Organ Systems Pathology portion of the course. Developed new lecture series on the growth, differentiation and normal physiology of leukocytes and autoimmune diseases. Initiated development of computer-based learning tools that include high-resolution, digitalized images of all slide materials used in the course.
F. Lecturer, Host Defense Sequence of Component I
G. Attending, Flow Cytometry Service.
H. Attending, Autopsy Service.

III. RESEARCH ACTIVITIES:

ACTIVE SUPPORT:

A. Principal Investigator, project 3- "Structure of selectin-ligands synthesized by human T-lymphoblasts", NIH, PO1AI33189 (Oligosaccharides as Anti-inflammatory Agents; PA Ward, Program Director), 15% effort, $347,950; 9 September 1996- 31 August 2001.
B. Principal Investigator, project 5- "Mononuclear Leukocyte Adhesion and Recruitment in Chronic Inflammatory Lung Disease" - NIH, P01, HL31963 (Inflammatory Cells and Lung Injury; PA Ward, M.D., Program Director), 20% effort, $500,000; 1 Mar 1994 - 28 February 1999.
C. Co-investigator, (J. Curtis, Principal Investigator), project 4- "Mechanisms of Lymphocyte Recruitment to the Lungs", NIH, P50HL46487 (SCOR in Pulmonary Fibrosis; G. Toews, M.D., Program Director), 15% effort, $650,000; 1 December 1991 - 31 November 1996.

PENDING APPLICATIONS:

A. Principal Investigator- "T-cell Trafficking in Adoptive Cellular Immunotherapy", NIH, RO1CA73059, 30% effort, submitted 7/1/97: This project builds on the discovery that the entry of tumor-reactive T-lymphoblasts into sites of metastatic disease can be increased by stimulating the synthesis of adhesion receptors. Furthermore, the adhesion receptors on the tumor-reactive T-lymphoblasts can be used to separate effector cells (those that inhibit malignancies in vivo) from suppressor cells (those that prevent the immune-response against the malignancy in vivo). The proposed studies will use these discoveries to improve the clinical outcome in adoptive immunotherapy.
B. Co-investigator (B. Richardson, Principal Investigator)- "Gender specific T-cell homing and autoimmunity", NIH, RO1 (new), 15% effort, submitted 6/1/97: This project builds on the observation that female gonadal steroids markedly increase the trafficking or auto-reactive T-lymphoblasts to the spleen. This increased recruitment is associated with development of a lupus-like syndrome in genetically susceptible mice. Autoimmune diseases generally occur with greater frequency in females. Consequently, gender-specific differences in trafficking/accumulation of auto-reactive T-cells may be a contributing factor. This project will determine whether differential regulation of vascular/lymphocytic adhesion receptors by gonadal steroids explains the observed differences in T-cell trafficking to the spleen. Furthermore, it will determine whether trafficking and the development of the lupus-like syndrome are causally related.

PROJECTS UNDER STUDY:

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

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

IV. ADMINISTRATIVE ACTIVITIES:

A. **Director of Research Flow Cytometry Laboratory and Co-Director of Clinical Flow Cytometry Laboratory**- manage the development and maintenance of the analytic systems for clinical laboratory. Lead the evaluation of new instrumentation for both the clinical and research laboratories. Participate in the consolidation of Clinical Flow Cytometry and Hematology Laboratories. Manage the operation of the research instruments (provide access for departmental investigators (currently 8-10) with grant support for flow cytometry). After lengthy negotiations, a new contract was signed with the Coulter Co. to replace Becton-Dickinson FACScan Flow Cytometers with new EPICS XL-MCL 4-color instruments. This contract replaces aging equipment, pays for development of an interface with General Laboratory Computer System, provides no-cost upgrades to the next generation of analysis software and substantially reduces (~30%) the operating costs for the clinical laboratory.

B. **Co-Director, Hematology Sequence in Component II and Pathology 580/630**- responsible for design and implementation of the laboratory components of these sequences. A major effort was launched this year to develop computer-based learning tools for Pathology sequences. Ideally, these courses need high-resolution images that can be panned and zoomed. The hardware and software needed to accomplish this goal has been indentified and brought online in the Department of Pathology. Digitalization of the image-library and construction of Websites for both courses will begin this summer.

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 JOURNALS:

1. Varani, J., Dame, M.K., Diaz, M. and Stoolman, L.M. 1996. Deferoxamine interferes with adhesive functions of activated human neutrophils. Shock. 5(6): 395-401.
2. Knibbs, R.N., Craig, R.A., Natsuka, S., Chang, A., Cameron, M., Lowe, J.B. and Stoolman, L.M. 1996. The Fucosyltransferase FucT-VII Regulates E-selectin Ligand Synthesis in Human T-Cells. J. Cell Biol. 133(4): 911-920.
3. Gerszten, R.E., Luscinskas, F.W., Ding, H.T., Dichek, D.A., Stoolman, L.M., Gimbrone, M.A.,Jr., and Rosenzweig, A. 1996. Adhesion of memory lymphocytes to vascular cell adhesion molecule-1- transduced human vascular endothelial cells under simulated physiological flow conditions in vitro [see comments]. Circ.Res. 79(6):1205.
4. Snapp KR, Wagers AJ, Craig R, Stoolman L.M., Kansas GS. 1997. P-selectin glycoprotein ligand-1 (PSGL-1) is essential for adhesion to P-selectin but not E-selectin in stably transfected hematopoietic cell lines. Blood: 89, 896.
5. A.J. Wagers, L.M. Stoolman, R. Craig, R. Kannagi and G.S. Kansas. 1997. Expression of leukocyte fucosyltransferases regulates binding to E-selectin: relationship to previously implicated carbohydrate epitopes. J. Immunol. (in press)
6. R. Yung, R. Williams, K. Johnson, L. Stoolman, S. Chang and B. Richardson. 1997. Mechanisms of drug-induced lupus. III. Gender-specific differences in splenic T-cell homing explain increased disease severity in female mice. Arthritis and Rheumatism (in press)

MANUSCRIPTS SUBMITTED/IN PREPARATION FOR PUBLICATION:

1. Knibbs, R.N., Craig, R.A., Thall, A., Maly, P., Smith, P., Lowe, J.B. and Stoolman, L.M. Fucosyltransferase-VII dependent synthesis of P-selectin ligands on human and murine lymphoblasts.
2. F.M. Wolber, J.L. Curtis, A.M. Milik, K.L. Fields, S. Kim, J. Sonstein and L.M. Stoolman. Lymphocyte recruitment and the kinetics of adhesion receptor expression during the pulmonary immune response to particulate antigen.
3. L.M. Stoolman, Craig, R.A., Wolber, F., Abbassi, O., Smith, C.W., McIntire, L.V. and JR Ballew. α4-integrin mediated T-cell tethering to endothelium: activation requirements and efficiency relative to the selectins.
4. LM Stoolman, RA Craig, MJ Cameron and AE Chang. Ex-vivo expansion of human T-lymphocytes for adoptive immunotherapy: optimal growth conditions for expression of selectin-ligands and attachment to vascular endothelium under shear.
5. F.M. Wolber, J.L. Curtis, J. Lowe, P. Maly, P. Smith, R.J. Kelly and L.M. Stoolman. Endothelial selectins and α4 integrins regulate independent pathways of T-lymphocyte recruitment in pulmonary inflammation.
6. F.M. Wolber, J.L. Curtis, J. Lowe and L.M. Stoolman. Roles of selectins and α4 integrin in mediating neutrophil and lymphocyte recruitment during the pulmonary immune response.
7. A.J. Wagers, L.M. Stoolman, R. Craig and G.S. Kansas. HECA-452 and CSLEX1 epitopes are not essential for high avidity binding to vascular selectins.

DENISE SULAVIK, M.D.
LECTURER
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Diagnostic Surgical Pathology, Hematopathology.
B. Clinical Hematology Laboratory.
C. Clinical Flow Cytometry Laboratory.
D. Hematopathology Consultation Cases (including M-Labs).

II. TEACHING ACTIVITIES:

A. House Officers:
   1. Sign-out of bone marrow biopsies, aspirates, blood smears and body fluids in Hematology Laboratory.
   2. Sign-out of lymph node biopsies and review of hematopathology consultation material.
   3. Flow Cytometry sign-out.

B. Medical Students:
   1. Laboratory instructor, M4 Clerkship in Clinical Pathology.

C. Hematopathology Teaching:
   1. Lymphoma conference/weekly.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Histomorphologic, flow cytometric and cytogenetic variances of blasts in a treated acute lymphoblastic leukemia.

IV. ADMINISTRATIVE ACTIVITIES:

None.

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Lecturer in General Pathology for Dental Students and Graduate Students (Pathology 630/580)
B. Research supervisor for postdoctoral investigators
   1. Maria-Thereza S. Piccolo, M.D.
   2. Elisabeth Schmid, M.D

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

PENDING SUPPORT:

A. None.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Chair, Honors and Awards Committee of the American Shock Society, 1996/97

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Member Editorial Advisory Board Immunobiology.
B. Reviewer for the following scientific journals:
    1. American Journal of Pathology.
    2. Circulation.
    3. Free Radical Biology and Medicine.
    4. Journal of Clinical Investigation.
    5. Journal of Leukocyte Biology.
    6. Redox Report
    7. Shock.

INVITED LECTURES/SEMINARS:

1. Invited speaker on "Pathophysiological Relevance of Complement in Trauma, Shock and Sepsis." The 4th International Congress on The Immune Consequences of Trauma, Shock and Sepsis in Munich, March 4 - 8, 1997.
2. Moderator of a symposium on "Controlling the Complement System in Inflammation." The 4th International Congress on The Immune Consequences of Trauma, Shock and Sepsis in Munich, March 4 - 8, 1997.
3. Invited speaker on "Inflammatory Mediators in Burns and Trauma". at Michigan State University, Kalamazoo Center for Medical Studies, April 17, 1997.
4. Moderator of session on Young Investigator Award paper presentations at the 20th Annual Meeting of the Shock Society. Indian Wells, California, June 15-18, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Mulligan, M.S., Schmid, E., Schimmer, B., Till, G.O., Friedl, H.P., Brauer, R. B., Hugli, T. E., Miyasaka, M., Warner, R. L., Johnson, K.J. Ward, P.A. Requirement and role of C5a in acute lung inflammatory injury in rats. J. Clin. Invest. 98: 503-12, 1996.
2. Mulligan, M.S., Schmid, E., Till, G.O., Hugli, T.E., Friedl, H.P., Roth, R.A., Ward, P.A. C5a-dependent up-regulation in vivo of lung vascular P-selectin. J. Immunol. 158: 1857-1861, 1997.
3. Schmid, E., Warner, R.L., Crouch, L.D., Friedl, H.P., Till, G.O., Hugli, T.E., Ward, P.A. Neutrophil chemotactic activity and C5a following systemic activation of complement in rats. Inflammation (in press).
4. Schmid, E., Piccolo, M.-T.S., Friedl, H.P., Warner, R.L., Mulligan, M.S., Hugli, T.E., Till, G.O., Ward, P.A. Requirement for C5a in lung vascular injury following thermal trauma to rat skin. Shock (in press).
5. Piccolo, M.-T.S., Wang, Y., Verbrugge, S., Warner, R.L., Sannomiya, P., Piccolo, N.S., Piccolo, M.S., Hugli, T.E., Till, G.O., Ward, P.A. Role of chemotactic mediators in blood neutrophil activation, the development of dermal burn wound edema, and the occurrence of secondary lung injury in rats. Am. J. Pathol. (in press).
6. Lai, J.C., Johnson, M.W., Martonyi, C.L., Till, G.O. Complement-induced retinal arteriolar occlusions in the cat: a transient forme fruste of Purtscher's Retinopathy. Invest. Ophthalmol. Vis. Sci. (in press).
7. Colton, D.M., Till, G.O., Johnson, K.J., Gater, J.J., Hirschl, R.B., Partial liquid ventilation (PLV) decreases pulmonary hemorrhage and albumin leak in the setting of acute lung injury. Chest (in press).
8. Colton, D.M. Till, G.O., Johnson, K.J., Dean, B.S., Bartlett, R.H., Hirschl, R.B. Neutrophil accumulation is reduced during partial liquid ventilation. Crit. Care.Med. (in press).
9. Rodriguez, J.L., Kelty, L., Miller, C.G., Garner, W.L., Smith, D.J., Till, G.O., Remick, D.G.: Interleukin-8 (IL-8) and acute burn injury. Surgery. (in press).
10. Winn, W.C., Davis, G.S., Durda, J.P., Till, G.O.: The effect of neutropenia on experimental Legionella pneumonia. Infec. Immun. (in press).
11. Seekamp, A. Schmal, H. Friedl, H.P., Hultquist, D.E. Ward, P.A. Till, G.O.: Protection by vitamin B2 against oxidant-mediated acute lung injury. Free Radic. Biol. Med. (in press).
12. Schlag, G. Redl, H., Till, G.O., Davies, J. Anti-L-selectin antibodies treatment of traumatic shock in baboons. Shock (in press)
13. Younger, J.G., Taqi, A.S., Till, G.O., Hirschl, R.B. Partial liquid ventilation protects the lung during resuscitation from shock. J. Appl. Physiol. (in press).

BOOKS AND CHAPTERS IN BOOKS:

1. Till, G.O.: Chemotactic Peptides. In: The Complement System; Rother K. O., Till G. O., Hänsch G. M. eds. Springer-Verlag Berlin Heidelberg (in press)
2. Rother, K.O., Till, G.O. Haensch, G.M. The Complement System. Springer-Verlag Berlin Heidelberg, (in press)

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

1. Till, G.O. Pathophysiological relevance of complement in trauma, shock and sepsis. Shock (Suppl.) 7:71, 1997.
2. Schmid, E., Friedl, H.,P., Ward, P.A., Till, G.O. Anti-C5a prevents upregulation of lung vascular ICAM-1 after thermal injury in rats. Shock (Suppl.)7:73, 1997.
3. Younger, J., Saleh, E., Till, G.O., Remick, D., Hirschl, R. Partial liquid ventilation increases lung TNF after shock. Shock (Suppl.) 7:58, 1997
4. Piccolo, M.-T.S., Wang, Y. Warner, R.L., Till, G.O., Ward, P.A. Role of chemotactic mediators in blood neutrophil asctivation, the development of dermal burn wound edema and the occurrence of secondary lung injury in the rat. J. Burn Care Rehab.18:S157, 1997
5. Younger, J., Saleh, E., Till, G.O., Remick, D., Hirschl, R. Partial liquid ventilation increases bronchoalveolar TNF and IL-6 following hemorrhagic shock. Proceedings SAEM Annual Meeting, May 19-22, 1997.
6. Schlag, G., Redl, H. Davies, J., Till, G.O., Martin, U. Protective effects of anti-L-selectin antibody treatment in a subchronic baboon model of hermorrhagic-traumatic shock. Proceedings 26th Educational and Scientific Symposium "Critical Care: The Beacon of Excellence", San Diego, CA, February 6-10, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Peptide-Coated Microcarriers for Enhanced Adhesion," NIH, CA58154, 3/1/95-2/28/97.
B Principal Investigator, "Squamous Epithelial Invasion in Organ Culture," NIH CA60958, 3/1/95-2/28/98.
C. Principal Investigator, "High Density Cell Growth in Microcarrier Aggregate," NIH. CA 61616, 7/1/96-6/30/98.
D. Principal Investigator on Project 10, "Retinoic Acid and Cells of the Skin," Johnson and Johnson Corporation, 7/1/91- 6/30/2006.
E. Co-Investigator, "Erb-b-2 Expression and Resistance to TNF Killing," NIH CA 64803, 9/01/94-8/30/98.
F. Co-Investigator, "Protease-Oxidant Interactions in Lung Inflammation," NIH HL42607, 7/1/94-6/30/98.
G. Principal Investigator, "Trimethylamine as a substrate for high-density cell growth under serum-free conditions," HIH CA 74595, 7/1/97-12/31/97.

PROJECTS UNDER STUDY;

A. The development of substrates for optimum growth of cells in large-scale culture.
B. The biology of human squamous carcinoma cell invasion.
C. Biological basis of photoaging and natural aging in skin.
D. Mechanisms of vascular cell injury in lung inflammation.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member, Department of Pathology Advisory Committee on Appointments, Promotions and Tenure.
B. Member, Department of Pathology Space and Research Committee.
C. Member, Department of Pathology Graduate Program Committee.
D. Member, Department of Pathology Human Resource Committee.
E. Member, Department of Pathology Graduate Program Comprehensive Exam Committee.
F. Director, Pathology Research Seminar Series.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Medical School Committee on Summer Research Opportunities.
B. Program Director, University of Michigan Cancer Center Program on Tumor Cell Metastasis and the Extracellular Matrix.
C. Member, University of Michigan Cancer Center Basic Research Committee.
D. Member, Cancer Biology Research Training Grant Scientific Steering Committee.
E. Member, Department of Dermatology Research Training Grant Steering Committee.
F. Member, University Committee on Use and Care of Animals (UCUCA).

UNIVERSITY:

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

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/PRESENTATIONS

1. Johnson & Johnson Consumer Products. Skillman, NJ. November 10, 1996.
2. Department of Medicinal Chemistry. University of Tenn., Memphis, TN, March 20, 1997.
3. Society for Investigative Dermatology, Washington DC, April 26, 1997.
4. Johnson & Johnson Retinoid Symposium, Short Hills, New Jersey, May 15,16, 1997.
5. 46th Symposium on Biology of the Skin, Aspen, Colorado, July 26, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS.

1. Varani, J., Trinh, D., Liebert, M., Wheelock, M.J. and Carey, T.E.: Human squamous epithelial cell invasion in organ culture and expression of cell surface adhesion molecules. Invasion and Metastasis, 15:189-196, 1996.
2. Fisher, G.J., Wang, Z.Q., Datta, S.C., Talwar, H.S., Kang, S., Varani, J. and Voorhees, J.J.: Upregulation of collagen- and elastin-degrading matrix metalloproteinases by doses of ultraviolet B light (UVB) too low to cause sunburn. Nature 379:335-339, 1996.
3. Ginsburg, I., Gibbs, D.F., Tarapchak, S.J. and Varani, J.: A novel approach to the assessment of toxicity of hexachlorcyclohexane (lindane) and of selected organic solvents. In Vitro Toxicology, 9:305-313, 1996.
4. Ginsburg, I., Yedgar, S. and Varani, J.: Diethylcarbamate and nitric oxide synergize with oxidants and with membrane-damaging agents to injure mammalian cells. Free Rad. Toxicol. (In Press).
5. Varani, J., Burmeister, W., Bleavins, M.R. and Johnson, J.K.: All-trans retinoic acid reduces membrane fluidity of dermal fibroblasts: Assessment by fluorescence redistribution after photobleaching. Amer. J. Pathol. 148:1307-1312, 1996.
6. Varani, J., Josephs, S. and Hillegas, W.J.: Human diploid fibroblast growth on polystyrene microcarriers in aggregates. Cytotechnology 22:111-117, 1996.
7. Varani, J., Dame, M.K., Diaz, M. and Stoolman, L.: Deferoxamine interferes with adhesive functions of activated human neutrophils. Shock 5:395-401, 1996.
8. Varani, J., Hirschl, R.B., Dame, M. and Johnson, K.: Perfluorocarbon protects lung epithelial cells from neutrophil-mediated injury in an in vitro model of liquid ventilation therapy. 6:339-344, 1996.
9. Zeigler, M.E., Krause, S., Karmiol, S. and Varani, J.: Growth factor-induced epidermal invasion of the dermis in human skin organ culture: Dermal invasion correlated with epithelial cell motility. Invasion & Metastasis, 16:3-10, 1996.
10. Zeigler, M.E., Dutcheshen, N.T., Gibbs, D.F. and Varani, J.: Growth factor-induced epidermal invasion of the dermis in human skin organ culture: Expression and role of matrix metalloproteinases. Invasion & Metastasis, 16:11-18, 1996.

11. Varani, J., Zeigler, M.E., Perone, P., Carey, T.E. and Datta, S.C.: Human squamous carcinoma cell invasion in organ-cultured skin. Cancer Lett., 11:51-57, 1997.
12. Varani, J.: Human skin in organ culture: A model for the study of normal and pathological responses of skin. Histology and Histopathology (In Press).
13. Varani, J.: Mechanisms of skin aging and retinoid reveral. J. Invest. Dermatol. (In Press).
14. Varani, J., Chi, Y., Walker, J., Datta, S.C., Johnson, T. and Zeigler, M.E., Elaboration of matrix metalloproteinases (MMPs) and MMP inhibitors by human skin in organ culture during invasion. Int. J. Cancer (In Press).
15. Fisher, G.J., Wang, Z-Q,., Datta, S.C., Varani, J., Kang, S. and Voorhees, J.J. Pathophysiology and retinoic acid prevention of sun-induced premature skin aging. New Eng. J. Med. (In Press).
16. Varani, J., Kang, S., Warner, R., Wang, Z-Q,., Datta, S.C., Fisher G.J. and Voorhees, J.J. Molecular mechansims of intrinsic skin aging and retinoid-induced repair and reversal. Nature Medicine (In Press).

BOOKS AND CHAPTERS IN BOOKS:

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

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

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

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Nicolas Bless, M.D., Postdoctoral Fellow.
      b. Larry Crouch, Ph.D., Postdoctoral Fellow.
      c. Boris Czermak, M.D., Postdoctoral Fellow.
      d. Jami Foreback, Pathology Graduate Program Student (MSTP student) (mentor).
      e. Alex Lentsch, Ph.D., Postdoctoral Fellow.
      f. Hagen Schmal, M.D., Postdoctoral Fellow.
      g. David Tung, Ph.D., Postdoctoral Fellow.
      h. Roscoe Warner, Ph.D., Postdoctoral Fellow.
      i. UROP Undergraduate Students:
         - Hillary Cohen, Senior.
         - Karen Rosner, Sophomore.
         - Richard Carter, Freshman.
      j. Morgan Althoen, Medical Student.
   2. Supervision of four Research Scientists.
   3. Gross Autopsy Conference, 25 hours.
   4. Clinical Pathology Grand Rounds Lecture, Reflections on the Pathology Board Examination.
B. Undergraduate students:
   1. Lecture, College Honors Seminar 250 (LS&A), three hours.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Lung Immunopathology" (Training Grant), NHLBI-NIH-HL-07517 (5%), $218,805/year, 6/1/86-5/31/01.
B. Principal Investigator, "Lung Injury by Oxygen Metabolites", NIGMS-NIH-GM-29507 (20%), $272,284/year ($1,123,824/four years), 7/1/97-6/30/01.
C. Principal Investigator, "Inflammatory Cells and Lung Injury", NHLBI-PO1-HL-31963 (25%), $189,794/year (Proj. I) $630,840 (all projects), 3/1/84-2/28/99.
D. Co-Investigator, "Mechanisms of Glomerular and Tubular Injury", NIADDK-NIH-DK-39255 (5%), $49,597/year (Project 7), 8/1/92-7/31/97.

E. Principal, Investigator, "Oligosaccharides as Inflammatory Agents", PO1-AI-33189 (10%), $93,443/year (Proj. II) $26,853/year (Core A), 9/30/96-08/31/99.
F. Co-Investigator, "The Role of Cytokines and Adhesion Molecules in Thermal Injury", GM48477 (5%), $178,772/year ($1,384,651/five years), with G.O. Till, Principal Investigator.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Division of General Pathology.

MEDICAL SCHOOL/HOSPITAL:

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

UNIVERSITY OF MICHIGAN:

A. Senate Assembly Committee on University Affairs, September, 1995-present.
    1. Chair, Medical Affairs Advisory Committee, Chair, September, 1996-present.

REGIONAL AND NATIONAL:

A. American Association of Immunologists.
B. American Board of Pathology, effective January 1, 1988:
    1. Immediate Past President, 1997.
    2. President, 1996.
    3 Vice-President, 1995.
    4. Trustee, 1980-present.
    5. Immunopathology Test Committee, 1980-present.
    6. Anatomic Pathology Examination Committee, 1988-present.
    7. By-Laws Committee, 1988-present.
    8. Examination Evaluation Committee, 1988-present.
    9. Professional Qualification/Competence Committee, 1988-present.
    10. ABP/ABPRF Research Committee, 1989-present.
    11. Residency Review Committee for Pathology.
    12. Building Committee, 1992-present.
    13. Planning and Development Committee, 1992-present.
    14. Test Committee for Molecular Pathology, 1993-present.
C. American Society for Clinical Investigation.
D. Association of American Physicians.
E. American Society of Investigative Pathologists, President 1979-80, member since 1967.
F. American Pathology Foundation.
G. American Thoracic Society.

H. Association of Pathology Chairmen.
I. A. James French Society of Pathologists, 1988-present.
J. Health Policy Agenda for the American People, Advisory Committee.
K. Institute of Medicine, National Academy of Sciences, July, 1990-present.
L. Michigan Society of Pathologists.
M. Michigan Thoracic Society, 1988-present.
N. National Research Council.
   1. Institute of Laboratory Animal Resources.
   2. Committee on Human Rights, Correspondent.
O. The Oxygen Society, 1988-present.
P. United States and Canadian Academy of Pathology, Inc.
   1. Council Member, April, 1986-1989.
   2. Member, Finance Committee, April, 1986-1990.
   3. Vice-President, 1990.
   4. President-Elect, 1991.
   5. President, 1992.
   6. Past-President, 1993.
Q. Universities Associated for Research and Education in Pathology, Inc., Board of Directors.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. American Journal of Pathology, Editorial Board, 1982-present.
B. American Review of Respiratory Diseases, Consulting Editor, 1977-present.
C. Biological Signals, Consulting Editor.
D. Cellular Immunology, Editorial Board, 1994-1997.
E. Clinical Immunology and Immunopathology, Consulting Editor, 1977-present.
F. CRC Critical Reviews in Free Radical Research, Advisory Board, 1986-present.
G. CRC Critical Reviews in Toxicology, Advisory Board, 1986-present.
H. Free Radical Biology & Medicine, Editorial Board, 1995-present.
I. Journal of Clinical Investigation, Consulting Editor.
J. Toxicologic Pathology, Editorial Board, 1988-present.

HONORS AND AWARDS

None

PATENTS:

None

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "Adhesion Molecules, Cytokines and Lymphocyte Recruitment into the Lung", Central Society for Clinical Research, Drake Hotel, Chicago, Illinois, September 20, 1996.
2. Invited Lecturer, "Complement Requirement for *In Vitro* and *In Vivo* Expression of Endothelial Adhesion Molecules", IBC Conference, San Diego, California, October 4, 1996.
3. Invited Lecturer, "Complement, Cytokines and Adhesion Molecules in Inflammation", University of Shizuoka School of Pharmaceutical Science, Shizuoka, Japan, December 10, 1996.
4. Invited Lecturer, "Role of Complement and Cytokines in Lung Inflammatory Injury", Sanwa Kagaku Kenkyusho Co., Ltd., Nagoya, Japan, December 11, 1996.

5. Invited Lecturer, "Regulation of Lung Expression of P-selectin and ICAM-1", Osaka University, Osaka, Japan, December 12, 1996.
6. Invited Lecturer, "Complement, Cytokines and Adhesion Molecules in Inflammation", Kanebo Co. Ltd., Osaka, Japan, December 13, 1996.
7. Invited Lecturer, "Role of Selectins in Inflammatory Injury", Okayama University Medical School, Okayama, Japan, December 13, 1996.
8. Invited Lecturer, "Role of Selectins in Inflammatory Injury", Keio University School of Medicine, Tokyo, Japan, December 14, 1996.
9. Invited Lecturer, "Endogenous Regulation of the Inflammatory Response", The Immune Consequences of Trauma, Shock and Sepsis: Mechanisms and Therapeutic Approaches, Munich, Germany, March 5, 1997.
10. Invited Lecturer, "Lung", The Immune Consequences of Trauma, Shock and Sepsis: Mechanisms and Therapeutic Approaches, Munich, Germany, March 6, 1997.
11. Invited Lecturer, "Alpha-d as an Inflammatory Mediator", ICOS Corporation, Seattle, Washington, March 25, 1997.
12. Invited Lecturer, "Endogenous Regulation of Inflammation", State University New York at Buffalo, Buffalo, New York, April 3, 1997.
13. Invited Lecturer, "Complement, Chemokines and Inflammation", University of Medicine and Dentistry of New Jersey, Stratford, New Jersey, April 14, 1997.
14. Invited Lecturer, "Cytokines, Inflammation and Autoimmune Disease", University of Nebraska Medical Center, Omaha, Nebraska, April 18, 1997.
15. Invited Lecturer, "Regulation of the Inflammatory Response in Lung", Pathology Research Conference, University of Louisville Dental School, Louisville, Kentucky, April 22, 1997.
16. Invited Lecturer, "Cytokines and Chemokines as Therapeutic Targets", Pediatric Academic Societies' Symposium "New Therapies for Diseases of the Newborn Infant", Washington, DC, May 6, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Ward, P.A.: Commentary: Role of complement in lung inflammatory injury. Rous-Whipple Lecture, ASIP Meetings, New Orleans, June, 1996. Amer. J. Pathol. 149(4):1081-1086, 1996.
2. Doerschuk, C.M., Quinlan, W.M., Doyle, N.A., Bullard, D.C., Vestweber, D., Jones, M.L., Takei, F., Ward, P.A. and Beaudet, A.L.: The role of P-selectin and ICAM-1 in acute lung injury as determined using blocking antibodies and mutant mice. J. Immunol. 157:4609-4614, 1996.
3. Eppinger, M.J., Ward, P.A., Bolling, S.F. and Deeb, G.M.: Regulatory effects of interleukin-10 on lung ischemia-reperfusion injury. J. Thor. Cardiovasc. Surg. 112:1301-1305, 1996.
4. Ward, P.A.: Editorial Review: Neutrophils and adjuvant arthritis. Clin. Exp. Immunol. 107(2):225, 1997.
5. Lowe, J.B. and Ward, P.A.: Therapeutic inhibition of carbohydrate-protein interactions *in vivo*. J. Clin. Invest. 99(5):822-826, 1997.
6. Shanley, T.P., Schmal, H., Warner, R.L., Schmid, L., Friedl, H.P. and Ward, P.A.: Requirement for C-X-C chemokines (macrophage inflammatory protein-2 and cytokine-induced neutrophil chemoattractant) in IgG immune complex-induced lung injury. J. Immunol. 158:3439-3448, 1997.
7. Beck-Schimmer, B., Schimmer, R.C., Warner, R.L., Schmal, G., Nordblom, G., Flory, C.M., Lesch, M.E., Friedl, H.P., Schrier, D.J., and Ward, P.A.: Expression of lung vascular and airway ICAM-1 after exposure to bacterial lipopolysaccharide. Am. J. Resp. Cell & Mol. Bio. 16:1-9, 1997.

8. Mulligan, M.S., Schmid, E., Till, G.O., Hugli, T.E., Friedl, H.P., Roth, R.A. and Ward, .PA.: C5a-dependent upregulation in vivo of lung vascular P-selectin. J. Immunol. 158(4):1857-1861, 1997.
9. Eppinger, M.J., Deeb, G.M., Bolling, S.F. and Ward, P.A.: Mediators of ischemia-reperfusion injury in rat lung. Am. J. Path. 150:1773-1784, 1997.
10. Kilgore, K.S., Schmid, E., Shanley, T.P., Flory, C.M., Maheswari, V., Tramontini, N.L., Cohen, H., Ward, P.A., Friedl, H.P. and Warren, J.S: Sublytic concentrations of the membrane attack complex (MAC) of complement induced endothelial interleukin 8 (IL-8) and monocyte protein 1 (MCP-1) through nuclear factor kappa-B (NF-kB) activation. Am. J. Path. 150(6):2019-2031, 1997.
11. Ward, P.A.: Recruitment of inflammatory cells into lung: Roles of cytokines, adhesion molecules, and complement. J. Lab. Clin. Med. 4:400-404, 1997.
12. Shanley, T.P., Foreback, J.L., Remick, D.G., Ulich, T.R., Kunkel, S.L. and Ward, P.A.: Regulatory effects of IL-6 in IgG immune complex-induced lung injury. Am. J. Path. 1997;151(1):193-203.
13. Schmid, E., Warner, R.L., Crouch, L.D., Friedl, H.P., Till, G.O., Hugli, T.E., and Ward, P.A.: Neutrophil chemotactic activity and C5a following systemic activation of complement in rats. Inflammation. In Press.
14. Schmid, E., Piccolo, T.S., Friedl, H.P., Warner, R.L., Mulligan, M.S., Hugli, T.E., Till, G.O. and Ward, P.A.: Requirement for C5a in lung vascular injury following thermal trauma to rat skin. Shock. In press.

BOOKS/CHAPTERS IN BOOKS:

1. Ward, P.A.: Role of complement, chemokines, and regulatory cytokines in acute lung injury, New York, pp. 104-112, 1996.
2. Warren, J.S. and Ward, P.A.: Consequences of oxidant injury, Chapter 175, in, Crystal, R.G., West, J.B., Weibel, E.R. and Barnes, P.J. (eds), The Lung: Scientific Foundations, Second Edition, Lippincott-Raven Press, New York, pp. 2279-2288, 1996.
3. Warren, J.S. and Ward, P.A.: Immunoglobulin and complement mediated immune injury, Chapter 185, in, Crystal, R.G., West, J.B., Weibel, E.R. and Barnes, P.J. (eds), The Lung: Scientific Foundations, Second Edition, Lippencott-Raven Press, New York, pp. 2411-2419, 1996.
4. Ward, P.A. and Mulligan, M.S.: Adhesion molecules in inflammatory lung injury, Chapter 20, in, Issekutz, T.B. (ed), Targeting Cell Adhesion Molecules for Theraputic Application, Marcel Dekker, Inc., New York, pp. 523-537, 1996.
5. Ward, P.A.: Chemokines and regulatory cytokines in acute lung injury, in, Chignard, M., Pretolani, M, Renesto, P., Vargaftig, B.B. (eds), Cytokines and Adhesion Molecules in Lung Inflammation, Annals of the New York Academy of Sciences, New York, pp. 104-112, 1996.
6. Ward, P.A.: Cytokines and adhesion molecules in the lung inflammatory response, in, D. Johnstone (ed), William Harvey Research Conference Proceedings, New Targets in Inflammation: Inhibitors of COX-2 or Adhesion Molecules, New Orleans, April 15-16, 1996, Kluwer Academic Publishers, Lancaster, United Kingdom, 1996.
7. Ward, P.A.: Selectins in animal models of acute inflammatory lung injury, in, Vestweber, D. (ed), The Selectins: Initiators of Leukocyte Endothelial Adhesion, Harwood Academic Publishers, The Netherlands, pp. 125-132, 1997.
8. Lukacs, N.W. and Ward, P.A.: Chemotactic molecules and cellular activation, in, Kaplan, A.P. (ed.), Allergy, Second Edition, W.B. Saunders Co., Orlando, pp.276-286, 1997.
9. Ward, P.A.: Inflammation: Basic concepts, in Asthma, Barnes, P.J., Grunstein, M.M., Leff, A. and Woolcock, A.J. (eds), Lippincott-Raven Publishers, Philadelphia, pp. 241-248, 1997.

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

1. Crouch, L.D., Lentsch, A.B., Warner, R.L., Johnson, K.J. and Ward, P.A.: Regulatory effects of adrenal gland products in IgG immune complex acute lung injury. Submitted to FASEB, 1997.
2. Gipson, T.S., Shanley, T.P., Bleavins, M.R., Wongelawit, T., Johnson, K.J. and Ward, P.A.: Molecular cloning and *in vivo* transcriptional expression of rat SLPI in lung inflammation. Submitted to FASEB, 1997.
3. Schmal, H., Bless, N., Czermak, BJ., Friedl, H.P. and Ward, P.A.: Regulation of macrophage inflammatory protein 1 β (MIP-1 β) in a rat model of acute lung injury. Submitted for the 4th International Congress on the Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches, 1997.
4. Bless, N., Czermak, B.J., Schmal, H., Friedl, H.P. and Ward, P.A.: Upregulation of Airway ICAM-1 in Acute Lung Injury and Its Role for the Expression of Chemokines. Submitted for the 4th International Congress on the Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches, 1997.
5. Czermak, B.J., Bless, N., Schmal, H., Friedl, H.P. and Ward, P.A.: *In vivo* regulation of chemokine expression in acute lung injury in rats. Submitted for the 4th International Congress on the Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches, 1997.
6. Ward, P.A.: Effects of prolonged exposure to low doses of nitric oxide or nitrogen dioxide on alveolar septa of the adult rat lung, by Mercer, R. et al. (Editorial). J. Lab. Invest. In Press.
7. Stockley, R.A., Bice, D. and Ward, P.A.: An overview of immunology of the lung, in, Stockley, R.A. and Hill, S.L. (eds), Issues in Infection: The Interaction Between Lung Defences and Bacteria - Time for a Reappraisal, Cambridge Medical Publications, West Sussex, England, pp. 10-12, 1996.
8. Ward, P.A.: Inflammation, in, 1997 Yearbook of Science & Technology, McGraw-Hill Publisher, New York.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Director, Division of Clinical Pathology/Clinical Laboratories, May 1993-present.
B. Director, Clinical Immunopathology Service; September 1989-present.
C. Microbiology Laboratory; review of malaria smears; July 1996-present.

II. TEACHING ACTIVITIES:

A. "Current Topics in Immunopathology" series: pathology residents, M4 students; (25 contact hours).
B. Clinical Pathology Grand Rounds:
   1. "Scleroderma and Its Relatives" (1/24/97).
C. Immunopathology journal club: EMU medical technology students, medical technologists (6 contact hours).
D. Immunopathology signout: pathology residents, M-4 medical students, EMU medical technology students (three times/week; 26 weeks/year).
E. Immunopathology component of Block C (Clinical Pathology); ad hoc topical reviews: pathology residents (48 contact hours).
F. M-4 Laboratory Medicine Elective; 4th year medical students, four week block; (8 contact hours).
G. M-1 Histopathology sequence; 1st year medical students; (16 contact hours).
H. Supervision of Research activities for:
   1. Valary Evans (Undergraduate, University of Michigan); (9/1/94-present), (sponsored in Howard Hughes Medical Institute Student Fellowship Program; sponsored in Student Biomedical Research Program).
   2. Vipul Maheswari (Undergraduate, University of Michigan); (6/15/95-12/10/96); (sponsored by American Heart Association of Michigan Fellowship).
   3. Karen Powers (Undergradate, University of Michigan); (9/1/95-present), (sponsored in Student Biomedical Research Program).
   4. Leah Thurm (Undergraduate, University of Michigan); (4/15/96-4/30/97); (sponsored in UROP).
   5. Paul Khawam (Undergraduate, University of Michigan); (4/15/96-4/30/97); (sponsored in UROP).
   6. Anjali Desai, Ph.D. (Postdoctoral Fellow); (6/15/96-present).
   7. Hernan Gomez, M.D. (Assistant Professor; Emergency Medicine, University of Michigan); (6/1/96-present).
   8. Mark Miller, Ph.D. (Postdoctoral Fellow); (8/15/96-present).
I. Ph.D. Thesis Committees:
   1. James Park, Department of Pharmacology, University of Michigan Medical School (6/2/95-present).
   2. Jennifer Bowen, Department of Physiology and the Reproductive Biology Program, University of Michigan Medical School (2/5/97-present).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Oxidant-Induced Beta Chemokines in Granuloma Formation", NIH (RO1-HL48287), (40% effort), $877,511; direct costs, 7/1/96-6/30/01.
B. Co-Investigator, "Monocyte Chemoattractant Protein 1 in Corpus Luteum", NIH (RO1-HD33478), (10% effort), $651,215; direct costs, 5/1/96-4/30/00 (Landis Keyes, Ph.D., Department of Physiology, University of Michigan, Principal Investigator).
C. Principal Investigator, "Monocyte Chemoattractant Protein-1 Receptor Antagonist Studies" 1/1/96-12/31/96 Roche Bioscience (Syntex) ($15,000).
D. Principal Investigator, "Carbohydrate P-Selectin Antagonist Studies In Vivo and In Vitro" 1/1/96-12/31/96 Glycomed ($9,300).

PROJECTS UNDER STUDY:

A. Role of neutrophil-derived mediators in MCP-1-mediated pulmonary granulomatous vasculitis.
B. Modulation of proinflammatory endothelial cell functions by C5a and the membrane attack complex (MAC) of complement.
C. Role of MCP-1 in luteolysis (collaboration with Landis Keyes, Ph.D., Department of Physiology, University of Michigan Medical School).
D. Ischemia-reperfusion injury in perinatal rat brain (collaboration with Faye Silverstein, M.D., Departments of Pediatrics and Neurology, University of Michigan Medical School).
E. MCP-1 in arterialized vein grafts (collaboration with John Hoch, M.D., Department of Surgery, University of Wisconsin, Madison, Wisconsin).
F. P-selectin antagonists in glucan-induced granulomatous vasculitis (collaboration with Mark Anderson, Ph.D., GlycoMed Corp., Alameda, California).
G. MCP-1 antagonists in granulomatous vasculitis (collaboration with Kurt Jarnagin, Ph.D, Roche Bioscience, Palo Alto, California).
H. Role of MAC in tissue factor production by endothelial cells (collaboration with James Park, Benedict Lucchesi, M.D., Ph.D., Department of Pharmacology, University of Michigan, Ann Arbor, Michigan, and Rob Davenport, M.D., Department of Pathology, University of Michigan, Ann Arbor, Michigan).
I. Pathogenesis of Loxosceles reclusa venon-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. Clinical Contracting Strategic Advisory Group, University of Michigan Medical Center, 1994-present.
B. Dean's Advisory Committee (ad hoc substitute for Dr. Ward), 1994-present.
C. Finance Subcommittee, advisory to Faculty Group Practice Executive Committee, 1997-present.
D. Medical Leadership Council, University of Michigan Medical Center, 1996-present.
E. Cancer Center Clinical Leadership Committee, 1996-present.

F. Member, Standardization and Product Evaluation Committee, 1996-present.
G. Clinical Council (ad hoc substitute for Dr. Ward), 1996-present.
H. Senate Assembly, Alternate, 1996-present.

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

A. Ad hoc referee for:
   1. American Journal of Pathology.
   2. Laboratory Investigation.
   3. Human Pathology.
   4. Journal of Applied Physiology.
   5. Lung.
   6. Blood.
   7. Journal of Laboratory and Clinical Medicine.
   8. Pediatric Research.
   9. Journal of Leukocyte Biology.
   10. American Review of Respiratory Disease.
   11. Chest.
   12. Journal of Pharmacology and Experimental Therapeutics.
   13. Circulation.
   14. Ophthalmology.
   15. American Journal of Respiratory Cell and Molecular Biology.
   16. Clinical Immunology and Immunopathology.
   17. Circulation Research.
   18. Journal of Immunology.
   19. Surgery.
   20. Reviews of Infectious Diseases.
   21. Infection and Immunity.
   22. Experimental Lung Research.
   23. Journal of Rheumatology.
   24. Clinical Infectious Diseases.
   25. Journal of Clinical Investigation.
   26. Cytometry.
   27. Biological Signals.
   28. Metabolism.
   29. Molecular Medicine Today.
   30. American Journal of Respiratory and Critical Care Medicine.
   31. The Cancer Journal
B. Preparation of Immunopathology Subspecialty Board Exam Questions, 1990-present.
C. Preparation of Clinical Pathology Board Exam Questions, 1991-present.

D. Ad hoc reviewer:SCOR Program in Acute Lung Injury; National Institutes of Health (NHBLI); Bethesda, MD; October 31, 1996.
E. Representative, National Committee for Clinical Laboratory Standards, 1996-present.

V. INVITED LECTURES/SEMINARS:

1. "Update in immunopathology: Antinuclear antibody testing and autoimmune disease", ASCP Workshops, San Diego, CA, October 2, 1996.
2. "Membrane attack complex triggers nuclear factor kappa B-dependent interleukin-8 and monocyte chemoattractant protein-1 secretion from endothelial cells", American Association of Immunologists/Clinical Immunology Society Joint Meeting, San Francisco, CA, February 24, 1997.
3. "Clinical immunopathology laboratory assays", Rheumatology Division, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, March 7, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Townson, D.H., Warren, J.S., Flory, C.M., Naftalin, D.M. and Keyes, P.L.: Expression of monocyte chemoattractant protein-1 (MCP-1) in the corpus luteum of the rat. Biol. Reproduction 54:513-520, 1996.
2. Eddy, A. and Warren, J.S.: Expression and function of monocyte chemoattractant protein-1 in experimental nephrotic syndrome. Clin. Immunol. and Immunopathol. 78:140-151, 1996.
3. Rand, M.L., Warren, J.S., Mansaur, M.K., Newman, W. and Ringler, D.J.: Inhibition of T cell recruitment and cutaneous delayed-type hypersensitivity-induced inflammation with antibodies to monocyte chemoattractant protein. Am. J. Pathol. 148:855-864, 1996.
4. Bowen, J.M., Keyes, P.L., Warren, J.S. and Townson, D.H.: Prolactin-induced regression of the rat corpus luteum: expression of monocyte chemoattractant protein-1 and invasion of macrophages. Biol. Reprod. 54:1120-1127, 1996.
5. Berman, J.W., Guida, M.P., Warren, J.S., Amat, J. and Brosnan, C.F.: Localization of monocyte chemoattractant peptide-1 expression in the central nervous system in experimental autoimmune encephalomyelitis and trauma in the rat. J. Immunol. 156:3017-3023, 1996.
6. Kilgore, K.S., Miller, B.F., Flory, C.M., Evans, V. and Warren, J.S.: The membrane attack complex of complement selectively induces monocyte chemoattractant protein-1 and interleukin-8 secretion from human umbilical vein endothelial cells. Am. J. Pathol. 149:953-961, 1996.
7. Tang, W.W., Qi Meiying and Warren, J.S.: Monocyte chemoattractant protein 1 mediates glomerular macrophage infiltration in α-GBM Ab GN. Kidney Int. 50:665-671, 1996.
8. Barton, P.A., Imlay, M.M., Flory, C.M. and Warren, J.S.: Role of intercellular adhesion molecular-1 (ICAM-1) in glucan-induced pulmonary granulomatosis in the rat. J. Lab. Clin. Med. 128:181-193, 1996.
9. Kilgore, K.S., Imlay, M.M., Szaflarski, J.P., Silverstein, F.S., Malani, A.N., Evans, V.M. and Warren, J.S.: Neutrophil and reactive oxygen intermediates mediate glucan-induced pulmonary granuloma formation through the local induction of MCP-1. Lab. Invest. 76:191-202, 1997.
10. Kilgore, K.S., Schmid, E., Shanley, T.P., Flory, C.M., Maheswari, V., Tramontini, N.L., Cohen, H., Ward, P.A., Friedl, H.P. and Warren, J.S.: Sublytic concentrations of membrane attack complex (MAC) of complement induce endothelial interleukin 8 (IL-8) and monocyte

chemoattractant protein 1 (MCP-1) through nuclear factor kappa-B (NF-κB) activation. Am J Pathol, (In Press).

11. Ivacko, J., Szaflarski, J., Malinak, C., Flory, C.M., Warren, J.S. and Silverstein, F.S.: Hypoxic-ischemic injury induces monocyte chemoattractant protein-1 expression in neonatal rat brain. J. Cerebral Blood Flow Metabolism, (In Press).

ARTICLES SUBMITTED FOR PUBLICATION:

1. Pearson, J.P. and Warren, J.S.: Mechanisms of neutrophil-dependent anti-neutrophil cytoplasmic antibody-mediated endothelial cell injury. An in vitro analysis. Submitted to Lab. Invest.
2. Szaflarski, J., Liu, X-H, Warren, J.S. and Silverstein, F.S.: Treatment with antibody to monocyte chemoattractant protein-1 attenuates excitotoxic brain injury in perinatal rats. Submitted to J. Neuroscience.
3. Kilgore, K.S., Imlay, M.M., Malani, A., Allen, D.I., Beyer, J.T., Anderson, M.B. and Warren, J.S.: The carbohydrate sialyl Lewis glycomimetic GM2941 attenuates glucan-induced pulmonary granulomatous vasculitis in the rat. Submitted to Immunopharmacol.
4. Schimmer, R.C., Schrier, D.J., Beck, B., Flory, C.M., Laemont, K.D., Metz, A.L., Friedl, H.P., Conroy, M.C., Warren, J.S. and Ward, P.A.: Streptococcal cell wall-induced arthritis: requirements for VLA-4/VCAM-1, IL-4, IL-10, and MCP-1. Submitted.

BOOKS/CHAPTERS IN BOOKS:

1. Warren, J.S. and Ward, P.A.: Immunoglobulin and complement mediated immune injury, in Crystal, R.G., West, J.B., Weibel, E.R. and Barnes, P.J. (eds.) The Lung: Scientific Foundations, Second Edition, Lippincott-Raven Publishers, Philadelphia, PA 2411-2419, 1997.
2. Warren, J.S. and Ward, P.A.: Consequences of oxidant injury, in Crystal, R.G., West, J.B., Weibel, E.R. and Barnes, P.J. (eds.) The Lung: Scientific Foundations, Second Edition, Lippincott-Raven Publishers, Philadelphia, PA 2279-2288, 1997.
3. Keren, D.F. and Warren, J.S.: Immunodeficiency disorders and their effects on the gastrointestinal tract, in Ming, S-C and Goldman, H. (eds.) Pathology of the Gastrointestinal Tract, Second Edition, Williams and Wilkins, Baltimore, MD, (In press).
4. Warren, J.S.: Role of cytokines in lung injury, in Remick, D.G. and Friedman, J. (eds.) Cytokines in Health and Disease, Second Edition, Marcel Dekker, Inc., New York, NY (In press).
5. Warren, J.S.: Cytokines in autoimmune disease, in Keren, D.F. and Nakemura, R.M. (eds.) Progress and Controversies in Autoimmune Disease Testing, First Edition, Saunders, Inc., Philadelphia, PA (In Press).

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

1. Townson, D.H., Remick, D.G., Warren, J.S. and Keyes, P.L.: The effect of dexamethasone on prolactin-induced monocyte chemoattractant protein-1 (MCP-1) expression and macrophage infiltration in regressing corpora lutea of the rat. Society for Study of Reproduction, Western Ontario, CN, July 10, 1996 (abstract).

2. Kilgore, K.S., Flory, C.M., Maheswari, V., Evans, V.M. and Warren, J.S.: The membrane attack complex of complement induces IL-8 and MCP-1 secretion from human endothelial cells. American Heart Association of Michigan, East Lansing, MI, September 6, 1996 (abstract).
3. Anderson, M.B., Warren, J.S., Kilgore, K.S. and Powers, K.: From the pharaoh's tomb to the pharmacy: glycomimetics as inhibitors of the selectins. International Medicinal Chemistry Society, The Hague, The Netherlands, September 17, 1996 (abstract).
4. Kline-Rogers, E., McCrumb, L., Hayden, K., Warren, J., Giacherio, D., Schmaier, A., Johnson, S., Dowling, M., Birchard, G., Erber, M.L. and Moscucci, M.: Transporting coagulation samples via a pneumatic tube system yields reliable results and time savings. American Heart Association (abstract).
5. McCune, W.J., Li, T., Warren, J.S., Friedman, A. and Reichlin, M.: Treatment of severe systemic lupus (SLE) with monthly intravenous cyclophosphamide plus prednisome (IVCTX) for 6 months reduced antibodies to Sm and RNP but not immunoglobulin G levels. American College of Rheumatology (abstract).
6. Evans, V.M., Park, J.L., Kilgore, K.S., Davenport, R.D. and Warren, J.S.: The membrane attack complex (MAC) of complement induces tissue factor production by human endothelial cells. University of Michigan Student Biomedical Research Forum, Ann Arbor, MI, November 12, 1996 (abstract).
7. Powers, K.L., Kilgore, K.S. and Warren, J.S.: An intact complement system and the anaphylatoxin C5a are necessary for glucan-induced pulmonary granuloma formation. University of Michigan Student Biomedical Research Forum, Ann Arbor, MI, November 12, 1996 (abstract).
8. Maheswari, V., Kilgore, K.S. and Warren, J.S.: The membrane attack complex of complement induces interleukin-8 (IL-8) and monocyte chemoattractant protein (MCP-1) production through activation of the NF-κB transcription factor. University of Michigan Student Biomedical Research Forum, Ann Arbor, MI, November 12, 1996 (abstract).
9. Anderson, M., Warren, J.S., Kilgore, K.S., Powers, K.L., Imlay, M.M., Allen, D.I. and Beyer, J.T.: Glycomimetics as inhibitors of cell adhesion. 1996 Pacific Conference. 32nd American Chemical Society Western Regional Meeting. San Francisco, CA, October 29-November 2, 1996 (abstract).
10. Warren, J.S., Kilgore, K.S., Schmid, E., Shanley, T.P., Flory, C.M., Maheswari, V., Tramontini, N.L., Cohen, H., Ward, P.A. and Friedl, H.P.: Sublytic concentrations of the membrane attack complex (MAC) of complement induce endothelial IL-8 and MCP-1 through NF-κB activation. Autoimmune Research Advances: New Therapeutic Approaches and Unintended Consequences. Ann Arbor, MI, June 2, 1997 (abstract).
11. Silverstein, F.S., Galasso, J.M. and Warren, J.S.: Monocyte chemoattractant protein-1 exacerbates NMDA-induced striatal neurotoxicity in neonatal rats. Society for Neuroscience. New Orleans, LA, October 25-30, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Organizer and discussion leader of seminar course on Ethics in Science -Cellular and Molecular Biology Training Program.
B. Supervision of three postdoctoral fellows.
C. Program Committee, Graduate Program in Pathology.
D Chairman, Examination Committee, Graduate Program in Pathology.
E. Member, dissertation committee for one graduate student.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Prevention and Repair of DNA Damage in Bacteria", National Science Foundation, DMB-8922562.
B. Principal Investigator, "Endonuclease V of *Escherichia coli*", National Institutes of Health, NIEHS, RO1 ES06047.

PROJECTS UNDER STUDY:

A. A superoxide response regulon of *Escherichia coli.*
B. A DNA repair endonuclease of *Escherichia coli.*

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Co-director, Graduate Training Program in Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited lecturer, Center for Biotechnology, University of Nebraska-Lincoln, February 5, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Gaudu, P. and Weiss, B.: Sox R, a [2Fe-2S] transcription factor, is active only in its oxidized form. Proc. Natl. Acad. Sci, U.S.A. 1996;93:10094-10098.
2. Guo, G., Ding, Y. and Weiss, B.: *nfi*, the gene for endonuclease V in *Escherichia coli* K-12. J. Bacteriol. 1997;179:310-316.
3. Gaudu., P., Moon, N., and Weiss, B.: Regulation of the *soxRS* oxidative stress regulon: reversible oxidation of the Fe-S clusters of SoxR *in vivo.* J. Biol. Chem. 1997;272:5082-5086.

BOOKS AND CHAPTERS IN BOOKS:

1. Weiss, B.: Regulation of endonuclease IV as part of an oxidative stress response in *Escherichia coli*, in Nickoloff, J.A. and Hoekstra, M. (eds.)., DNA Damage and Repair: Biochemistry, Genetics, and Cell Biology. Humana Press (In Press).

SHARON W. WEISS, M.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Service - three and one-half months.
B. Consultant for Bone and Soft Tissue - twelve months.

II. TEACHING ACTIVITIES

A. Sophomore Medical Class:
   1. Pathology 600 - lecture - two contact hours.
   2. Pathology 600 - laboratory section - thirteen hours
B. House Officers:
   1. Training in Surgical Pathology.
   2. Lectures - five hours.
   3. Surgical Pathology Consultation Conference - six hours.
C. Hospital Conferences:
   1. Sarcoma Conference - twice monthly.
D. Post-Doctoral Fellow:
   1. Responsible for training of Dr. Gelareh Farshid, June 1996-July 1997.
E. Visiting Scientists:
   1. Andrew Folpe, M.D. - University of Washington (Seattle).
   2. Susan Williams, M.D. - University of Tennessee.
   3. Sigrid Regauer, M.D. - University of Graz, Austria.
F. Medical Students:
   1. Araba Arfenzi-Annan - Surgical Pathology Clerkship - July, 1996.

III. RESEARCH ACTIVITIES

PROJECTS UNDER STUDY:

A. Second opinions in pathology: Cost effectiveness.
B. Liposarcoma.
C. Typical and atypical giant cell tumors.
D. Needle biopsy in the diagnosis of soft tissue tumors.
E. Fibromatosis and well-differentiated fibrosarcoma.
F. Angiosarcoma in children.

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL:

A. Director, Division of Anatomic Pathology (7/96 - 1/15/97).
B. Chief, Surgical Pathology (7/96 - 1/15/97).
C. Member, Division Directors' Committee.
D. Member, Photography Committee.
E. Member, Program Committee, Residency Training Program.
F. Co-Director, Surgical Pathology Fellowship Program.

UNIVERSITY:

A. Member, Neurofibromatosis Center.
B. Member, University of Michigan Cancer Center.
C. Member, Tissue and Invasive Procedures Committee.
D. Member, Musculoskeletal Core, Year II Curriculum.
E. Member, Operating Room Committee.
F. Dean's Task Force for Restructuring Salaries.
G. LCME Self Study Task Force Committee.
H. Chair, Academic Appointments, Promotions, and Tenure Committee.

REGIONAL AND NATIONAL:

A. Chairman, WHO Committee for Classification of Soft Tissue Tumors.
B. President, U.S.-Canadian Academy of Pathology.
C. Anatomic Pathology Test Writing Committee, American Board of Pathology.
D. Association of Directors of Anatomic Pathology.
E. Consultant in Pathology, National Institutes of Health.
F. Member, Michigan Society of Pathologists.
G. Member, Arthur Purdy Stout Society of Surgical Pathologists.
H. Ad hoc reviewer, Laboratory Investigation.
I. Ad hoc reviewer, American Journal of Pathology.
J. Editorial consultant, Human Pathology.

V. OTHER RELEVANT ACTIVITIES

EDITORIAL BOARDS:

A. Editorial Board, American Journal of Surgical Pathology.
B. Editorial Board, American Journal of Clinical Pathology.
C. Editorial Board, Seminars in Diagnostic Pathology.
D. Editorial Board, International Surgical Pathology.
E. Editorial Board, AFIP Fascicles (3rd Series).
F. Editorial Board, Modern Pathology.

INVITED LECTURES:

1. Slide Seminar, Arthur Purdy Stout Society Program, International Academy of Pathology Meeting, Budapest, Hungary, October, 1996.
2. Chairperson, "An Approach to the Diagnosis of Soft Tissue Tumors," International Academy of Pathology Meeting, Budapest, Hungary, October, 1996.
3. Speaker, "Liposarcoma: An Update," University of British Columbia, Whistler, British Columbia, February, 1997.
4. Speaker, "Vascular Tumors: Problematic Areas," University of British Columbia, Whistler, British Columbia, February, 1997.
5. Slide Seminar, North and South Carolina Society of Pathologists, Charlotte, North Carolina, February 1, 1997.
6. William Myles Shelly Memorial Lecture, North and South Carolina Society of Pathologists, Charlotte, North Carolina, February, 1997.
7. Lecture, Florida Society of Pathologists, March, 1997.
8. Rosalie Saffos Memorial Lecture, University of Florida at Gainesville, March, 1997.
9. Speaker, "Liposarcoma: Current Concepts," Portuguese Society of Pathologists, Tomaz, Portugal, April, 1997.
10. Slide Seminar, Portuguese Society of Pathologists, Tomaz, Portugal, April, 1997.
11. William Shelly Memorial Lecture, Johns Hopkins University School of Medicine, May, 1997.
12. Resident Slide Seminar, Pathology Department, Johns Hopkins University School of Medicine, May, 1997.
13. Speaker, "Second Opinions and Frozen Sections are Cool," 25th Reunion Class Academic Program, Johns Hopkins Medical Alumni Biennial Meeting, June, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Perkins, P. and Weiss, S.W.: Spindle cell hemangioendothelioma: An analysis of 78 cases with re-evaluation of pathogenesis and biologic behavior. Am. J. Surg. Pathol., 20:196-204, 1996.
2. Henricks, W.H., Goldblum, J.R. and Weiss, S.W.: Dedifferentiated liposarcoma: An assessment of 155 cases with a proposal of an expanded definition of dedifferentiation. Am. J. Surg. Pathol., 21:271-281, 1997.
3. Weiss, S.W.: P53 alterations in benign and malignant nerve sheath tumors. Am. J. Clin. Pathol., 106:271-272, 1996.
4. Weiss, S.W.: Lipomatous tumors. Monogr. Pathol. 38:207-239, 1996.
5. Khalidi, H.S., Singleton, T. P. and Weiss, S.W.: Inflammatory malignant fibrous histiocytoma: Distinction from Hodgkin's disease and non-Hodgkin's lymphoma by a panel of leukocyte markers. Mod. Pathol, June, 1997.
6. Gnepp, D.R. and Weiss, S.W.: Fibromatosis of the nasal and paranasal sinuses. Cancer, In Press.

7. Lane, K., Shannon, R. and Weiss, S.W.: Hyalinizing spindle cell tumor with giant rosettes: A distinctive lesion confused with fibromatosis and low grade fibromyxoid sarcoma. Am. J. Surg. Pathol., In Press.

SUBMITTED FOR PUBLICATION:

1. Farshid, G., Weiss, S.W.: Massive localized lymphedema in the morbidly obese simulating liposarcoma. Submitted to Am. J. Surg. Pathol.
2. Montgomery, E.A., Devaney, K.O., Weiss, S.W.: Low grade fibroblastic sarcomas and their distinction from deep fibromatosis. Submitted to Am. J. Surg. Pathol.
3. Montgomery, E.A., Devaney, K.O., Weiss, S.W.: Inflammatory myxohyaline tumor of distal extremities with Reed-Sternberg-like cells. Submitted to Mod. Pathol.
4. Quezado, M.M., Middleton, L.P., Zhuang, Z., Bryant, B., Wang, C., Lane, K., Weiss, S.W., Merino, M.J.: Allelic loss on chromosome 229 in epithelioid sarcomas. Submitted to Hum. Pathol.

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

1. Hunter, D.C., Devaney, S.L., Weiss, S.W., Devaney, K.O.: The relationship of apoptoses to grade in malignant fibrous histiocytomas of soft tissue. Mod. Pathol. 10:11A, 1997.
2. Montgomery, L.A., Devaney, K.O., Weiss, S.W.: Inflammatory myxohyaline tumor of distal extremities with Reed-Sternberg-like cells: A novel entity with features simulating myxoid malignant fibrous histiocytoma, inflammatory conditions and Hodgkin's disease. Mod. Pathol. 10:12A, 1997.
3. Farshid, G., Weiss, S.W.: Massive localized lymphedema in the morbidly obese simulating liposarcoma. Mod. Pathol. 10:9A, 1997.
4. Tworek, J.A., Goldblum, J.R., Weiss, S.W., Greenson, J.K., Appelman, H.D.: Stromal tumors of the colon. Mod. Pathol. 10:66A, 1997.
5. Tworek, J.A., Goldblum, J.R., Weiss, S.W., Greenson, J.K., Appelman, H.D.: Stromal tumors of the rectum and anus. Mod. Pathol. 10:66A, 1997.
6. Williams, S.T., Parham, D.M., Khane, V.K., Shearer, P., Devaney, K.O., Weiss, S.W.: Angiosarcomas in children: A clinical pathology study of ten cases. Mod. Pathol. 10:159A, 1997.

KIRK J. WOJNO, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
AND UROLOGY
DEPARTMENTS OF PATHOLOGY AND SURGERY

ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1996 - 30 JUNE 1997

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Services-four months.
B. Surgical Pathology On-call-six weeks.
C. Immunoperoxidase Service-six months.
D. Consultant for Genitourinary Pathology.
E. Back-up Consultant for Endocrine Pathology.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Sophomore Medical Class:
   1. Reproductive sequence - one lecture hour.
   2. Renal/Genitourinary Sequence - three lecture hours, one laboratory.
B. House Officers:
   1. Pathology Consult Conference - Occasional.
   2. Pathology Resident Series - Occasional.
   3. Immunoperoxidase conference - Occasional.
C. Interdepartmental:
   1. GU Grand Rounds - Weekly.
   2. GU Pathology Conference - Monthly.
   3. Peds Urologic Pathology/Radiology - Occasional.
   4. GU Oncology Conference - Weekly.
   5. GU Journal Club - Weekly.
   6. Prostate SPORE Research Conference - Monthly
D. Elective Courses and Mentor Programs
   1. Elective in Urologic Pathology (J.C. Cerny, 1995; J. Brown, 1996)
   2. UROP Program (E. Keilhorn; S. Jesweak, 1996)
   3. PhD. Advisor (M. Moyad, 1995-1996; A. Maskulick, 1996)

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, Tissue and Serum Core for Prostate Cancer (SPORE grant). (30% effort)
B. Principal Investigator, Tissue Procurement, Histopathology and Immunoperoxidase Core of the Cancer Center. (5% effort)
C. Co-Investigator, Analysis of 8P Loss in Human Prostate Cancer. Principal Investigator, Jill Macoska, Ph.D. (10% effort)
D. Co-Investigator, A Phase II Clinical Trial of Selenium in Patients with Prostatic Cancer. Principal Investigator, David Smith, M.D. (11.5% effort)
E. Co-Investigator, Emcyt, VP-16 and Taxol for Metastatic Prostate Cancer. Principal Investigator, Kenneth J. Pienta, M.D. (5% effort)
F. Co-Investigator, Role of Chromosome 10 Loss in Prostate Cancer Progression. Principal Investigator, Jill Macoska, Ph.D. (SPORE)
G. Co-Investigator, Role of BRCA-1 in Prostate Cancer Progression. Principal Investigator, Kathy Cooney, M.D. (SPORE)
H. Co-Investigator, Androgen Related Target Genes in Apoptosis. Principal Investigator, Mark Day, Ph.D. (SPORE)
I. Co-Investigator, Color Doppler TRUS in the Prediction of Tumor Vascularization. Principal Investigator, Robert Bree, M.D. (SPORE)
J. Co-Investigator, Assessment of % Free PSA and Age Specific Reference Ranges in African American Men. Principal Investigator, David Schottenfeld, M.D. (SPORE)
K. Consultant, A Phase I/II Study of Oral Tetrathiomolybdate (TM)as a Decoppering and Anti-agiogenesis for Metastatic Cancer. Principal Investigator, Sofia Merajver, M.D.

PROJECTS UNDER STUDY:

A. Angiogenesis: Genetech and Prostate SPORE.
B. Evaluation of surrogate and point biomarkers as prognostic indicators in prostate and bladder cancer . (Bcl2, Bclx-l, Bax, Her2nu, P53, Angiogenesis. PP32, Ki67, PC-1, Pth-LP, Tib-166, Gp78, etc.).
C. Fractal geometric analysis in prostate cancer.
D. Precursor lesions in prostate cancer, PIN, AAH.
E. Role of Chromosome 8 and 10 loss in prostate cancer progression with Jill Macoska, Ph.D.
F. Hereditary prostate cancer, sib-pair analysis with K. Cooney.
G. Significance of free PSA measurements with Drs. England, Giacherio, and Oesterling.
H. Longitudinal % Free in a Screening Population. Collaboration with the New England Research Institute.

I. Effect of Fenasteride on % Free PSA. Collaboration with Merk, Abbott, Hybritech, Dianon, and Wallac.
J. Organ Specific Apoptosis in the Spawning Chinook Salmon.
K. Significance of atypia in the urine: Then-year review with histologic correlate and clinical follow-up, with Drs. Amin and Kintanar, Henry Ford Hospital.
L. Nuclear matrix proteins in transitional cells: A more sensitive and specific method for detecting transitional cell carcinoma by immunoperoxidase technique, with Drs. Smith and Kintanar, Department of Oncology
M. Prospective review of bladder biopsies: Muscularis mucosa versus muscularis propria invasion - what is the prognostic significance?, With Dr. Kintanar.
N. Cytologic features of Taxol-induced changes in transitional cells, with Drs. Smith and Kintanar, Department of Oncology.
O. Nephrogenic metaplastic cells in urine: Potential pitfall mimicking transitional cell carcinoma, with Drs. Hunter and Kintanar.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Special Function Laboratory; Immunoperoxidase & Special Histochemistry & Histology.

INTERDEPARTMENTAL

A. Director, Tissue Procurement Core and Histopathology Core of the Cancer Center.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Consensus Workshop on Prostatic Intraepithelial Neoplasia, Bethesda, Maryland, June30-July2, 1996.
2. "Grading of Prostate Cancer by Fractal Geometric Analysis", Fourth SPORE Investigators Workshop, Rockville Maryland, July 14-16, 1996.
3. "Utility of Percent Free PSA in the Diagnosis and Management of Prostate Cancer", International PSA Workshop, Chicago Illinois, August 1, 1996.
4. Fractal Geometric Analysis as an Alternative to the Gleason Grading System for Prostate Cancer Prognostication. Reed M. Nesbit Urological Society, Biennial Meeting, Ann Arbor, Michigan, September 27-28, 1996.
5. The Prostate: A Pathologists Perspective. Prostate Controversies: Diagnosis and Management. Second Annual Conference, University of Michigan, Ann Arbor, Michigan, October 18-20, 1996.
6. Percent Free PSA: Controversies and Clinical Utility. Cancer Diagnosis and Monitoring: A Look at Emerging Tumor Marker. The Michigan Section of the AACC. University of Michigan Hospital, Ann Arbor, Michigan, January 9, 1997.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Rozansky T, Wojno K, Bloom D: The Remnant Orchiectomy. The Journal of Urology, 155: 712-714, 1996
2. Richardson T, Wojno K, Liang L, Giacherio D, England B, Henricks W, Schork A, Oesterling J: Half-life Determination of Serum Free Prostate-Specific Antigen Following Radical Retropubic Prostatectomy. Urology, 48:40-44, 1996.
3. Thiel R, Oesterling J, Wojno K, Partin A, Chan D, Carter H, StameyT, Prestigiacomo A, Brawer M, Petteway J, Carlson G, Luderer A: Multi-center Comparison of the Diagnostic Performance of Free Prostate-Specific Antigen. Urology, 48:45-50, 1996.
4. Vashi A, Wojno K, Henricks W, England B, Wessella R, Lange P, Wright Jr. G, Shcellhamer P, Weigand R, Olson R, Dowell B, Borden K, Oesterling J: Determination of the "Reflex Range" and Appropriate Cutpoints for Percent Free Prostate-Specific Antigen in 413 Men Referred for Prostatic Evaluation Using the AxSys System. Urology, 49:19-27, 1997.
5. Wilson T, Doelle E, Cohan R, Wojno K, Korobkin M: Cystic Renal Masses: A Reevaluation of the Usefulness of the Bosniak Classification System: Academic Radiology, 3:564-570, 1996.
6. Cooney K, Wetzel J, Consolino C, Wojno K: Identification and Characterization of Proximal 6q Deletions in Prostate Cancer. Cancer Research, 56(18):4150-4153, 1996.
7. Strohbehn K, Quint L, Price M, Wojno K, Delancey J: Magnetic Resonance Imaging Anatomy of the Female Urethra: A Direct Histologic Comparison. Obstetrics and Gynecology, 88(5):750-756, 1996.
8. Gaudin P, Sesterhenn I, Wojno K, Mostofi F, Epstein J: Incidence and Clinical Significance of High-Grade Prostatic Intraepithelial Neoplasia in TURP Specimens. Urology, 49(4), 1997.
9. Goh M, Kleer C, Kielczewski P, Wojno K, Kim K, Oesterling J: Autologous Blood Donation Prior to Anatomical Radical Retropubic Prostatectomy: Is It Necessary? Urology, 49(4),569-574, 1997.
10. Partin A, Subong E, Walsh P, Wojno K, Oesterling J, Kattan M, Scardino P, Pearson J: Combination of PSA, Clinical Stage and Gleason Score to Predict Pathological Stage in Men with Localized Prostate Cancer: A Multi-Institutional Update 1996. JAMA, 277(18):1445-1460, 1997.
11. Haggman M, Macoska J, Wojno K, Oesterling J: The Relationship Between PIN and Prostate Cancer: Critical Issues. Urology, 158 (1):12-22, 1997.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Montie J, Wojno K, Klein E, Pearsall C, Levin H: Transitional Cell Carcinoma in Situ of the Seminal Vesicles: Eight Cases with Discussion of Pathogenesis, Clinical, and Biologic Implications. (Accepted to The Journal of Urology.)
2. Bitton R, Braine HG, Enger C, Fuller A, Jones J, Shabooti M, Swan V, Wojni K: Acute Bleeding Post BMT - Incidence and Effect on Survival. A Quantitative Analysis in 1402 Patients. (Submitted to BLOOD.)
3. Visualization of Primary Renal Cancer by FDG-PET and Histopathological Findings. (Presented at the 1996 Society of Nuclear Medicine 43rd Annual Meeting June 3-6, 1996, Denver, CO.) Accepted to J Nuc Med.

4. Trybus T, Burgess A, Wojno K, Glover T, Macoska J: Two Distinct Regions of Allelic Loss on Chromosome 10 in Human Prostate Cancer. (Presented at the 87th Annual Meeting of the American Association of Cancer Research.) Proceedings AACR 37:247, 1996.
5. Vashi A, Wojno K, Gillespie B, Oesterling J: Patient Age and Prostate Gland Size Determine the Appropriate Number of Cores Per Prostate Biopsy. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.) The Journal of Urology 157(4):1428, 1997.
6. Washbum J, Wojno K, Macoska J: Deletion of Loci Mapping to 3p23-pter in Human Prostate Cancers. (Presented at the 88th Annual Meeting of the American Association of Cancer Research.) Proceedings AACR 38:A3456, 1997.

BOOK CHAPTERS

1. The Prostate and Seminal Vesicle (manuscript in preparation). Diagnostic Surgical Pathology, 2nd ed. Edited by Sternberg, Antonioli, Crater, Mills, and Oberman.

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

1. Trybus T, Burgess A, Wojno K, Glover T, Macoska J: Two Distinct Regions of Allelic Loss on Chromosome 10 in Human Prostate Cancer. (Presented at the 87th Annual Meeting of the American Association of Cancer Research.) Proceedings AACR 37:247, 1996.
2. Sanda M, Pearsall C, Derrow S, Charles L, Monite J, Clarke M, Wojno K: Transitional Cell Carcinoma is Characterized by Overexpression of bclx-1 and is Susceptible to Apoptosis Induction by Adenovirus-mediated bclx-s Gene Transfer. (Presented at the 1996 SBUR meeting.)
3. Yurgalevitch S, Beduschi M, Mohr BM, Wojno K, Longcope C, Oesterling J, McKinlay: Changes in Dihydrotestosterone (DHT) and Prostate-Specific Antigen (PSA) in a Random Sample of Healthy Aging Men. (Presented at the 79th Annual Meeting of the Endocrine Society.)
4. Pearsall C, Sanda M, Montie J, Wojno K: Regulators of Programmed Cell Death are Overexpressed in Invasive Transitional Cell Carcinoma. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.)
5. Wojno K, Beduschi M, Giacherio D, England B, Gormley G, Bach M, Waldstreicher J, Oesterling J: Finasteride Decreases Free and Total Serum PSA Concentration but does not Significantly Alter the Percent Free PSA Value. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.)
6. Becker C, Piironen T, Pettersson K, Bjork T, Wojno K, Oesterling J, Lilja H: Clinical Utility of a Novel, Highly Sensitive and Specific Assay for Human Prostatic Glandular Kallikrein (hK2) in Serum. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.)
7. Partin A, Chang E, Walsh P, Wojno K, Oesterling J, Kattan M, Scardino P, Pearson J: Combination of PSA, Clinical Stage and Gleason Score to Predict Pathological Stage: A Multi-institutional Update 1996. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.)
8. Lee C, Wojno K, Montie J, Oesterling J: Critical Pathoways for Radical Retropubic Prostatecomy: Improving Efficiency of Patient Care Without Compromising Cancer Control. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.)

9. Lee C, Wojno K, Oesterling J, Singleton T, McCauley L, Lehr J, Montie J, Pienta K: Expression of Parathyroid Hormone-like Protein in Prostate Cancer and Prostatic Intraepithelial Neoplasia. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.)
10. Beduschi M, Wojno K, Consolino C, Giacherio D, England B, Mohr B, Yurgalevitch S, McKinlay J, Oesterling J: Free PSA and Percent Free PSA Increase Over Time in a Health Male Population Followed Longitudinally for 9 Years. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.)
11. England B, Wojno K, Beduschi M, Giacherio D, Yurgalevitch S, Mohr B, McKinlay J, Longcope C, Oesterling J: Changes in Serum Testosterone (T), Free PSA, and Percent Free PSA Over Time in a Healthy Aging Population Followed Longitudinally for 9 Years. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.)
12. Vashi A, Wojno K, Gillespie B, Oesterling J: Patient Age and Prostate Gland size Determine the Appropriate Number of Cores per Prostate Biopsy. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.)
13. Wojno K, Brown J, Consolino C, Schwab E, Oesterling J: Fractal Geometric Analysis as an Alternative to the Gleason Grading System for Prostate Cancer. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.)
14. Cooney K, Huang L, Wetzel J, Macoska J, Wojno K: Deletion Analysis of Chromosome 17 Loci in Prostate Cancer. (Presented at the 1997 Annual Meeting of the American Association for Cancer Research.)
15. Vashi A, Wojno K, Vessella R, Lange P, Wright G Jr., Schellhammer P, Oesterling J: Percent Free PSA Correlates Directly with Patient Age. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.) The Journal of Urology 157(4):432, 1997.
16. Sanda M, Wojno K, Consolino C, Oesterling J: Free PSA Total PSA, and % Free PSA as Predictors of Prostate Cancer Volume. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.) The Journal of Urology 157(4):443, 1997.
17. Moyad M, Sakr W, Pontes E, Singleton T, Henricks W, Oesterling J, Wojno K, Civantos F, Soloway M, Fay R, Snow R: The Relationship of Tumor Angiogenesis and Race to Serum PSA Levels in Carcinoma of the Prostate. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.) The Journal of Urology 157(4):890, 1997.
18. Derrow S, Wojno K, Pearsall C, Charles L, Montie J, Clarke M, Sanda M: Apoptosis Induction by Adenovirus-BCLX-S: A Rational Strategy for Bladder Cancer Gene Therapy. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.) The Journal of Urology 157(4):1207, 1997.
19. Vashi A, Wojno K, Gillespie B, Oesterling J: Patient Age and Prostate Gland Size Determine the Appropriate Number of Cores Per Prostate Biopsy. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.) The Journal of Urology 157(4):1428, 1997.
20. Barnhill S, Zhang Z, Madyastha K, Zhang H, Beduschi M, Wojno K, Oesterling J: The ProstAsure™ Index is Useful in the Diagnosis of Early Prostate Cancer But Does Not Predict Pathologic Stages in Men with a Serum PSA Level Less Than 4.0 ng/ml. (Presented at The American Urologic Association Meeting, New Orleans, LA, April 1997.) The Journal of Urology 157(4):1809, 1997.
21. Cooney K, Huang L, Wetzel J, Macoska J, Wojno K: Deletion Analysis of Chromosome 17 Loci in Prostate Cancer. (Presented at the 88th Annual Meeting of the American Association of Cancer Research.) Proceedings AACR 38:A3455, 1997.
22. Washbum J, Wojno K, Macoska J: Deletion of Loci Mapping to 3p23-pter in Human Prostate Cancers. (Presented at the 88th Annual Meeting of the American Association of Cancer Research.) Proceedings AACR 38:A3456, 1997.

23. Macoska J, Prasad M, Trybus T, Wojno K: 8p22 Cosmid and 8cen Dual FISH Analysis of Prostate Tissues: Association of Genetic Alterations with Recurrent Disease. (Presented at the 88th Annual Meeting of the American Association of Cancer Research.) Proceedings AACR 38:A3465, 1997.
24. Darrow S, Wojno K, Pearsall C, Charles L, Montie J, Clarke M, Sanda M: Apoptosis Induction by Adenovirus-bclx-s. A Rational strategy for Bladder Cancer Gene Therapy. (Presented at the 88th Annual Meeting of the American Association of Cancer Research.) Proceedings AACR 38:A69, 1997.

SECTION REPORTS

ANATOMIC PATHOLOGY

DIVISION OF ANATOMIC PATHOLOGY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

The Division of Anatomic Pathology continues to enjoy a strong national and international academic reputation while providing a breadth of expertise in support of the clinical and educational programs of the University of Michigan Medical Center, Medical School, and University. During the past year, faculty continued a strong presence in major national academic programs including the United States and Canada Association of Pathologists (USCAP), American Society of Cytology, and American Society of Clinical Pathologists. Dr. Sharon Weiss served as Vice-President of USCAP and will serve as President in the upcoming academic year. Extramural support for faculty academic programs continues to increase especially in programmatic areas associated with the newly opened Cancer Center and SPORE in Urologic Disease.

In addition to graduating 6 residents, 3 house officers completed fellowship training in the division including 2 in renal pathology and 1 in soft tissue pathology. Extramural support for a new fellowship in urologic pathology was identified beginning in 1997-98.

During the past year there have been several changes in the administrative leadership of the division and the departure of two faculty. Dr. Joseph Fantone was appointed Director of Anatomic Pathology and Dr. Joel Greenson Director of Surgical Pathology. Dr. Suzanne Selvaggi, after spending five years in the Department, left to assume the Directorship of Cytology and subsequently Anatomic Pathology at Loyola Medical Center in Chicago, Illinois. Dr. Terry Headington retired after more than 25 years as a faculty member. Dr. Headington is an internationally recognized dermatopathologist who has been a beloved teacher of Pathology and Dermatology residents. We look forward to his continued participation in our resident educational programs as an active emeritus professor. Drs. Claire Michael and Lori Lowe serve as Directors of Cytology and Dermatopathology, respectively, as searches to replace Drs. Selvaggi and Headington continue.

Overall, the clinical activity in surgical pathology and cytology remains stable. In fact there continues to be increases in the intramural fine needle aspiration and extramural surgical pathology consultation services. Further, with the integration of the Washtenaw County Forensic Pathology Program there has been a significant increase in the volume of necropsies performed. While implementation of the Medical Center Cost Efficiency Program (CEP) has resulted in consolidation of laboratory functions and enhanced productivity in several areas, significant additional reductions in laboratory support in the absence of decreased utilization will result in limitation of service. Constraints on space for the laboratories, clinical service (frozen section area) and faculty significantly limit enhancement in productivity and program expansions when required. The efforts of Kathy Smiezney (Anatomic Pathology Laboratory Supervisor), Jim Pecott (Cytology Laboratory Supervisor) and all laboratory staff have been instrumental in successfully implementing the CEP and the completion of the Anatomic Pathology laboratory CAP inspection.

The Division is well positioned to continue as one of the pre-eminent academic divisions in the country provided the Medical Center clinical programs continue to thrive. There is currently an excellent balance of senior and junior faculty with expanding academic programs. It will be critical that the current junior faculty are supported and retained and the recruitment for academically oriented faculty successful.

AUTOPSY SERVICE

DEPARTMENT OF PATHOLOGY
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I. Timely Completion of Autopsy Reports:

This past year has seen a major effort to ensure that all autopsies are completed within 60 days. Substantial progress has been made towards this goal, but we are still not achieving 100% completion. This has been identified as a program for excellence within the hospital and we are continuing to make progress towards our goal of 100% completion of cases within 60 days.

Time interval	# autopsies	Average days to completion	% completed in 60 days	% completed in 90 days
1995/96	541	96	40	58
1996/97	538	53	59	83

II. Trauma/Burn Conference:

We have begun a joint meeting with the trauma/burn service which takes place once a month in Ford Auditorium. These are working conferences which closely evaluate 2 - 3 patients each month. The conference is composed of radiologists, first responders (EMTs), trauma surgeons, emergency room physicians, and pathologists. For selected motor vehicle accidents, the engineers from the University of Michigan Transportation Research Institute present their findings about the condition of the automobile that was involved in the crash. The first year residents are expected present their autopsy findings. This conference has been well received by both the house officers and the attending staff.

III. Medical Examiner Contract:

We are in the process of renegotiating our contract for Forensic Autopsies with the Washtenaw County Medical Examiners Office. There have been several problems with the contract including difficulties with reimbursement and timely completion of reports. The present contract has been extended through September 30, 1997.

IV. Cause of Death Included on Necropsy Protocol:

Starting May 1, 1997, the cause of death has been included on all necropsy reports. This has been done in order to have a more complete report. The Department of Pathology completes the death certificate on all deaths at the University and maintains these on file. We have access to the signed death certificate that is filed with the State of Michigan. Our autopsy reports now include the cause of death and the name of the physician who signed the death certificate.

V. Statistics:

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

Total number of autopsies performed	538
Total number of medical examiner cases	238

Daniel G. Remick, M.D.

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
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This year has brought several substantial changes to the laboratory with the precipitous departure of Dr. Selvaggi and Mrs. B. Davis. Dr. C. Michael is currently serving as the interim director, while the recruitment search for a director and a junior cytopathologist continues. Dr. Kintanar joined our department in December of 1996, Mr. J. Pecott was appointed the chief clinical cytotechnologist in March, 1997, and Ms. J. Gyurnek, the new cytotechnologist, started May, 1997.

Total gynecologic specimens for the year were 35,015. Non-gynecologic specimens numbered 5396; a 4% decrease that continues a gradual declining trend that started back in 1991 when 7592 specimens were processed. Pressure on clinicians and surgeons to eliminate superfluous testing will continue to drive this trend. However, fine needle aspirations remains constant due to the rapid turnaround time which helps the clinicians in cost containment and avoiding hospital admissions for more prolonged workup.

It was a difficult year due to being short staffed one cytotechnologist and/or one specimen-prep technician for six months. The lab continued to thrive to maintain the turnaround time for the non-gynecologic specimens within 24 to 48 hours, while gynecologic turnaround time was prolonged.

The following steps were taken to address the cost containment and turnaround time issues:

- The physical plan designs for the consolidation of cytology and histology were finalized; and will allow a more efficient utilization of personnel through cross training and staffing into the early evening.

- Cytotechnologists no longer assist with fine needle aspirations, allowing more time for screening.

- Evaluated a new stainer and coverslipper to reduce the labor intensity of specimen preparation and reduce the turnaround times.

- Started plans for Cerner's V500 implementation. We are optimistic that the QA/QC module can replace the approximate four days per month of manual counting and record keeping that is currently necessary to meet CAP standards (CLIA 88). This time can be better utilized by the cytotechnologists for screening.

This year also brought us another CAP inspection by a team from the University of Pittsburgh. The department had only two phase 2 violations for insufficient personnel and insufficient space. We are attempting to address both issues with the steps taken above.

Preparations for the fine needle aspiration clinic at the Cancer Geriatric Center in collaboration with Dr. Baker and Mrs. Waldingar were finalized, and the clinic began operation on May 9, 1997. Recruitment of an additional cytopathologist will ensure continuous staffing.

Work began on a grant to study the morphologic changes that occur with the new thin prep technology. Dr. Brian Hunter is assisting Dr. Michael with this study. This study is designed to evaluate the most efficient and appropriate methods to utilize this technique in fine needle aspirations.

In the 11th year of our Cytopathology Fellowship Program, Dr. Vonda Douglas and Dr. Lyndon Su completed their training with distinction.

The cytotechnologists have been actively involved in the Regional Cytology Society. Dr. Michael and Dr. Naylor have presented papers and workshops at national meetings, cytologic societies and cytotechnology schools.

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

DERMATOPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1996- 30 JUNE 1997

The Dermatopathology Service receives diagnostic case material from six different sources: (1) UMMC (ID) cases; (2) outside contractual (MD) cases; (3) personal consultations (HE and LO) cases; (4) outside slides reviewed for referred patients (TD) cases; (5) miscellaneous intramural referrals (IE, IF, IS, ME, SC, TS) cases; (6) and informal consultations (intramural, VAH and MU).

Work load volume is as follows:

	1992-1993	1993-1994	1994-1995	1995-1996	1996-1997
HE	981	694	569	639	1555
ID	4255	4791	4759	4787	4491
MD	1347	1663	2240	2560	3832
TD	550	709	553	578	815
Misc		71	218	300	75
Informal	225	254	106	125	9
LO					124

A significant change in personnel occurred in 1996-1997 with the retirement of the Director of the service (John T. Headington, M.D.). This role has been filled on an interim basis by Dr. Lori Lowe and supported with the assistance of Dr. Robert Goldman. Recruitment efforts to fill the full-time faculty slot for this service have been successful with our selected candidate scheduled to join the faculty in July 1998.

There was again an increase in the number of personal consultations and a significant increase in the number of cases coming from M-Labs. TD cases increased in parallel with an increased number of melanoma patients.

Dermatopathology teaching in the Department of Dermatology remains unchanged with formal presentations made to both the medical and dental students.

Correlative activities include participation in the Multidisciplinary Melanoma Conference (bi-weekly) Cutaneous Lymphoma Conference (monthly), and Dermatology Grand Rounds (weekly).

Joseph C. Fantone, M.D.,
Director, Division of Anatomic Pathology
for the Dermatopathology Service

NEUROPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

Neuropathology continues to have three interrelated functions: Diagnostic service, teaching, and research. Dr. Mila Blaivas, Ms. Constance J. D'Amato, and Dr. Paul E. McKeever contributed to the Neuropathology Service.

I. CLINICAL ACTIVITIES:

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

1. There were 563 neurosurgical cases examined this year, with 97 of these cases coming from outside hospitals in consultation.
2. The Diagnostic Unit of the Neuropathology Core Laboratory of the MADRC processed 52 hospital dementia brain cases. Nine additional brain cases were processed by the Core Laboratory from the Michigan Dementia Network Program.
3. There were 305 muscle biopsies with 15% with electron microscopy. There were 101 peripheral nerve biopsies. There were 30% teased fiber preparations, 30% with electron microscopy and all except 13 cases were processed in plastic.
4. The Brain Tumor Board of the University of Michigan Cancer Center and Hospitals, supported weekly by a neuropathologist, reviewed neuropathology and clinical aspects of more than 130 difficult neuro-oncology cases.
5. There are two neuropathology quality assurance meetings scheduled each month, and attended as necessary. Attendees include neuropathologists from nearby institutions in Michigan and Ohio.

II. TEACHING ACTIVITIES:

1. Medical Students: This year the neuropathology faculty taught in the eight week Neuroscience Sequence for our second year medical school curriculum. There were fourteen hours of neuropathology taught: six hours of lecture and eight hours in the laboratory.
2. Dental Students: 2 lectures
3. House Officers, Graduate Students, Postgraduate and other students and faculty. :These include periodic conferences with Neurology, monthly CME accredited Rheumatology Pathology Grand Rounds and occasional CPC conferences, twice monthly Continuing Medical Education (CME) accredited conferences with all biopsies are presented and interpreted; a weekly conference where abnormal brains are examined (including one week for dementia cases) with all clinicians invited; monthly nerve and muscle biopsy conference accredited for CME; individual instruction on autopsies and biopsy material; Neuropathology 868, an 8-hour laboratory course; bimonthly conferences with Neuroradiology, Neurosurgery and Neuroradiology House Staff and every third

month microscopic conference for dementia brain cases. Weekly seminars are provided to neurological and neurosurgical house staff on clinico-pathological correlations.

4. Electives: Two Pathology Residents, one Neurosurgery, four Neurology Residents and one M-4 student chose elective rotations on the Neuropathology Service.

III. RESEARCH ACTIVITIES:

1. Dr. Sima and Ms. D'Amato provided neuropathology support for MADRA. Ms. D'Amato is Core Coordinator of the Diagnostic Neuropathology Unit of the Neuropathology Core of MADRC. Ms. D'Amato is also Co-Investigator with Dr. Anders Sima on the MADRC Project: The Pathology of Diffuse Lewy Body Disease.
2. Dr. Blaivas is working on the histology of animal models of rheumatoid arthritis with Arthritis and Rheumatology Section for possible grant "Molecular synovectomy by in vivo gene transfer," with Blake Roessler and Timothy Laing; Urethral musculature in aging and incontinence, with John DeLancey group, Obstetrics/Gynecology; Rat model in brain tumors growth and treatment, with Donald Ross, Neurosurgery and Philip Kish. (Grant application submitted); Genetic treatment of hemophilia in mice model, with Kotoku Kurachi's group in the Department of Genetics; Neurochemical anatomy of human temporal lobe in epilepsy, with D. Ross and N. Selden, Neurosurgery; Primary CNS vasculitis, with J. Trobe and A. Alrawi, Ophthalmology; Evaluation of temporal lobectomy/hippocampectomy cases with epilepsy group; Edited the chapter on brain tumors written by Dr. H.S. Greenberg, neurooncology and prepared illustrations with figure legends for it; Histology and histochemistry of orbicularis muscle, normal and aging; Collaboration with EMG group, Radiology (S. Gebarski, M.D.), pulmonary/internal medicine on various projects.
3. Dr. McKeever and associates are determining the extent and cause of differences in gene product expression in brain tumors. These differences may result from a separate population of cells within brain tumors or from genetic instability in neoplastic cells. They are assessing the prognostic value of DNA content, specific chromosomal markers by in situ hybridization and Ki-67, PCNA and BUDR labeling indices in brain tumor specimens. He is principal investigator on an NIH funded project studying the prognostic potential of MIB-1 proliferation marker on brain tumors. He is the study pathologist for a multi-institutional transferrin receptor targeted glioma treatment protocol, and for a multi-institutional study of treatments of low grade astrocytoma. He is studying treatments of low grade astrocytomas as study pathologist for the Children's Cancer Group.
4. Groups in the University of Michigan Cancer Center faculty and staff with clinical research interests in brain tumors, met and generated a number of project considerations from Pathology, Neurosurgery, Nuclear Medicine, Neuropathology, Neurology and Neuroradiology collaborations.
5. Collaboration with Neurology, Michigan State University, The Alzheimer's Association, Henry Ford Hospital, Butterworth and Blodgett Hospitals, and Wayne State University has established a registry for Alzheimer's disease and other dementias and degenerative diseases.

Paul E. McKeever, M.D., Ph.D.
Chief, Section of Neuropathology

SPECIAL FUNCTIONS LABORATORY (IMMUNOPEROXIDASE, IMMUNOFLORESCENCE, NEURAL MUSCULAR STUDIES, AND ELECTRON MICROSCOPY)

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1996 - 30 JUNE 1997

The immunohistology laboratory has continued to offer over 75 different immunohistochemical stains for paraffin and frozen tissues and perform approximately 650 tests each month or over 7500 tests per year. This level has been steady over the past two years since we decreased utilization of redundant antibodies on individual cases as part of the cost efficiency program. During this time period there has not been a single documented incidence where the reduced ordering of redundant antibodies has impacted patient care in any way. We will continue to make inroads into the most cost effective use of immunoperoxidase staining in anatomic pathology.

Over the past year the laboratory successfully passed its CAP inspection without any deficiencies or recommendations.

Over the past year we have made substantial progress in cross training laboratory personnel in immunohistochemistry, immunoflorescence, and neuromuscular studies. Due to the highly specialized nature of electron microscopy and the spatial separation, we have not implemented cross training in this area. With the renovations in the main hospital due to be completed in the Fall, we anticipate moving the special function laboratory except for electron microscopy into the current histology laboratory which is supervised by Kathy Smieszny. Kathy's expertise in immunohistochemistry will facilitate further optimization of this laboratory as well as maximize productivity due to cross training.

Anatomic Pathology research efforts as well as preparation of slides for conferences, national meetings, and SWOG protocols are continued to be performed in the two research histology laboratories (Cancer Center, Pathology Department). This removal of research work from the clinical laboratory has greatly facilitated our ability to meet the cost efficiency program goals. In conclusion we have made significant inroads into optimizing the efficient use of these laboratories and we will continue these efforts over the upcoming year while maintaining excellent quality of work.

Kirk J. Wojno, M.D.
Director

Timothy P. Singleton, M.D.
Assistant Director

SURGICAL PATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

The Surgical Pathology Division remains an active University Hospital service despite changes in personnel and leadership. This year, the Division saw nearly 30,000 in-house surgical specimens, 5,000 personal consults, and 7,800 M-Lab cases. We continue to work to improve our turnaround time to better assist our clinical colleagues and the cost-efficiency program. We have initiated a one-day turn-around time for all in-patient biopsy specimens.

The Surgical Pathology Service would like to acknowledge the hard work and dedication of Tom Frank, who left the Division July 1 to work for Myriad Genetics Incorporated. The Division will also sadly miss Dr. Terry Headington, who retired this spring. Drs. Henry Appelman, Kenneth Devaney and Esperanza Kintanar, are to be commended for helping out the Dermatopathology Service while we search for a replacement for Dr. Headington. The Surgical Pathology Service would also like to welcome Dr. Robert Goldman as a new addition to our Dermatopathology faculty. We would also like to welcome Dr. Richard Lieberman as a consultant in OB-GYN pathology.

The Histopathology Laboratory has also undergone many changes over the last year. We are preparing for the full integration of Cytology and Immunohistochemistry into the laboratory this Fall. The consolidation of these three units will allow better cross-training of individuals to maximize our use of laboratory personnel. We have been fortunate to recruit Ms. Kathy Smieszny as the new supervisor of the histology laboratories. Ms. Smieszny has done an excellent job in reorganizing the laboratory in the aftermath of cost-efficiency downsizing. We continue to work closely with Pathology Data Systems to computerize as many tasks as possible in Surgical Pathology. We are preparing for a new version of our LIS software as well as the addition of barcoding of surgical pathology specimens.

Our fellowship programs have also felt the weight of cost-efficiency downsizing. This year Surgical Pathology and Cytopathology fellows were all internal candidates. Drs. Lyndon Su, Steve Ramsburgh, and Joseph Tworek all completed their surgical pathology fellowships this year. All three are continuing fellowship training next year. Dr. Gelareh Farshid completed her soft tissue fellowship with Dr. Sharon Weiss. This coming year we look forward to the continued training of Steve Ramsburgh and Joseph Tworek as surgical pathology and cytopathology fellows. In addition, we welcome Dr. Stephanie Dillard from the University of Alabama - Birmingham and Dr. Tamara Smith from the Cleveland Clinic as new surgical pathology and soft tissue pathology fellows.

Although the Surgical Pathology Division has endured more than its share of hardship this year, its productivity has remained superb. At this year's USCAP meeting, our faculty presented 14 abstracts and directed 2 short courses. In addition, Dr. Sharon Weiss was installed as the President of the USCAP. It is an honor to work with such outstanding faculty members.

Joel K. Greenson, M.D.
Director, Surgical Pathology

CLINICAL PATHOLOGY

DIVISION OF CLINICAL PATHOLOGY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

Despite implementation of the institutionally-mandated cost efficiency program, growth in several major clinical programs, the opening of the new Cancer and Geriatrics Center, and expansion of M-Labs activities, the Clinical Laboratories continued to provide excellent, full-spectrum service. In 1996-97 the Clinical Laboratories performed more than 3 million billable analyses. The maintenance of high quality and the reduction in cost per unit of activity provided by the Clinical Laboratories, in the face of increasing complexity of demands, is a testimony to the professionalism of the staff and the management capabilities of the laboratory directors and senior laboratory personnel. The Clinical Laboratories successfully completed the biannual on-site College of American Pathologists (CAP) inspection. The Divisional Quality Assurance Program, as a component of the Departmental Program for Excellence, continues to be at the forefront both within the University of Michigan Medical Center and among clinical laboratories located in tertiary care facilities throughout the United States. Maintenance of the delicate balance among quality service, cost effective testing, utilization control, and the research and development which characterizes an academic institution, will be a continuing challenge.

1996-97 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 initiated. Reorganization entailed a nearly 10% reduction in operating budget, consolidation of several laboratories, and reorganization of inpatient phlebotomy services. Major cost efficiencies were gained through agreements with the Southeastern Michigan American Red Cross (blood products) and Johnson and Johnson (chemistry instruments and reagents). The initial phases of this plan have been implemented with the expectation that laboratory reorganization will be completed by late autumn. This reorganization will entail further consolidation of the Immunopathology, Ligand Assay, Toxicology/Therapeutic Drug Monitoring, and Chemistry Laboratories into a single unit, consolidation of the Hematology, Flow Cytometry, and Coagulation Laboratories (formerly Internal Medicine) into a single unit, and streamlining of the administrative structure of these and other laboratories. Second, the Clinical Laboratories continued to reallocate resources needed to meet the continuing and marked increase in transplantation activity (especially bone marrow) experienced in 1996-97. Augmentation of the capabilities of the Blood Bank, Tissue Typing, and Cytogenetics Laboratories was contributory to this process. Finally, the Clinical Laboratories have responded to the institutional initiative to acquire broader primary care capabilities within the region. This activity has been coupled with expansion of on-site point-of-care testing and data handling activities. In preparation for the future, the Clinical Laboratories continue to support the growing M-Labs outreach program, to forge strong collaborative relationships with local and regional reference laboratories, and intensify our role in institutional utilization management.

Faculty and laboratory staff participated in a wide variety of intramural and extramural educational programs during 1996-97. For instance, the 28th annual Blood Bank/Transfusion Medicine course and the Laboratory Information Systems course were each well attended, making them among the most visible courses of their kind in the United States. Twenty pathology residents from around the nation received scholarships to attend the June LIS course. This program, coupled with a burgeoning collaborative relationship with the Informatics Program in the Department of Pathology at the University of Pittsburgh, an exceptionally strong presence by information technology-savvy senior pathology house officers, an informatics focus in the Chemistry Fellowship (see below), and establishment of a house officers website on the Internet, along with several pending Departmental and Institutional initiatives promise to further enhance the Department's leadership role in this growing and important area. These courses, along with the M-Labs educational programs, are prominent examples of educational outreach activities. Evaluations from senior medical students enrolled in the fourth M4 Laboratory Medicine course were again highly laudatory. The revised clinical pathology residency training format (July, 1993), which organizes pathology residents into teams that rotate through three blocks of clinical laboratories that are grouped according to "relatedness of discipline", continues to meet with critical success. The continued high quality of trainees in the Hematopathology Fellowship program has enhanced the service, educational, and academic missions of the Hematopathology group and the Department. Certification of a Clinical Chemistry Fellowship was received from the ACGME. This fellowship has further enhanced the service, academic, and educational missions of the Division and Department.

The academic achievements of faculty members within the Clinical Pathology Division have been outstanding. As a group, the CP faculty had approximately 100 articles published in peer reviewed journals. Most faculty members played highly visible leadership roles in national organizations, courses, symposia, as well as on editorial boards, examining committees, and research review study sections; an illustration of their high levels of recognition throughout the United States (see individual reports). Numerous faculty members received extramural funding that supported a variety of scholarly activities (see individual reports).

The Clinical Pathology Division is faced with numerous challenges in the future. In addition to its ongoing academic enterprises, educational issues, faculty diversity initiatives, leadership and development in quality assurance, and laboratory resource utilization in the context of the hospital cost efficiency program, the Division plans to continue to expand its attention to informatics and other new technology (e.g. automation), its clinical molecular diagnostics program and, in cooperation with the M-Labs program, to optimize its position in the regional clinical laboratory market. Achievement of these objectives will require the continued commitment, professionalism, and hard work of the faculty, laboratory staff, administration, and house officers.

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

UNIVERSITY HOSPITALS BLOOD BANK AND TRANSFUSION SERVICE

DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1996 - 30 JUNE 1997

PATIENT CARE:

Blood component utilization approximated 100,000 units. This was related to further expansion of the liver and bone marrow transplantation programs and the need to provide support for these patients prior to, and following, the actual procedure, as well as to growth in areas such as trauma care, and extracorporeal membrane oxygenation. A major impact on the laboratory was the large blood component requirements of the hypothermic circulatory arrest procedures for treatment of aneurysms of the aortic arch. Efforts to contain blood utilization in University Hospital were thwarted by this clinical growth, and the reduced staffing of the laboratory, related to cost containment, was a further problem.

Component utilization increased particularly in the areas of platelet and plasma transfusion. The requests for platelet transfusions were monitored by laboratory technical and medical staff to ensure their appropriateness. A new initiative was the interdepartmental efforts to designate appropriate blood component use during operative procedures. This was an interdisciplinary effort by the blood bank, anesthesiology and general surgery.

The Transfusion and Apheresis area, was further compromised by the increased demands for therapeutic plasma exchange and for stem cell harvesting. The latter resulted in scheduling an average of 3 procedures daily, and this, in turn, posed increased demands on technologists performing technical processing of the stem cells. An additional blood cell separator and increased technical support likely will be needed within the next year because of the institution of allogeneic BMT for pediatric patients and also because of the initiation of the breast and ovarian cancer BMT program. Moreover, it will be necessary to transfer transfusional and infusional activities on cancer patients to the cancer center or to an area elsewhere in the hospital to make room for the expansion of apheresis services.

Members of the staff played an integral role in support of specialized clinical activities. Mrs. Hoffman worked closely with the Bone Marrow Transplantation Program and also coordinated orders for HLA-matched Single Donor Platelets from our blood suppliers. The reference laboratory section supported the Department of Obstetrics and Gynecology, attending their weekly high-risk pregnancy conference, and playing a vital role in PUBS procedures. Ms. Butch led the Quality Management program of the clinical laboratories of the Department of Pathology and Mrs. Stoe chaired the Department's Laboratory Safety Committee.

EDUCATIONAL ACTIVITIES:

As in previous years, the medical, technical and nursing staffs of the Blood Bank/Transfusion Service were active in providing educational programs within the institution and at regional and national meetings. The long-standing two-week Blood Bank orientation program for House Officers at University Hospital was presented on two occasions during the year so that this information would be provided in proximity to the lab rotation. The Blood Bank portion of the Laboratory Medicine elective

course for senior medical students was well received. Three hours of lecture were provided for the sophomore medical class in the context of the hematology portion of the Department of Pathology course, and a presentation on Transfusion Medicine was provided for the medical student senior elective course in Pharmacology and Therapeutics. Finally, senior medical students partaking of a month-long pathology elective, spent three to five days in the laboratory.

The 24th annual postgraduate course, "Current Topics in Blood Banking", was held on June 4-6, 1997. The course, under the direction of Mr. Judd, attracted approximately 200 technologists and physicians from throughout the United States. It continues to be one of the most popular postgraduate courses in the country devoted to blood bank topics. Members of the Blood Bank and Transfusion Service staff presented Workshops on a variety of topics, and Ms. Butch, Mr. Judd, Mr. Meade and Drs. Oberman and Davenport participated in the plenary sessions of the symposium.

Members of the Blood Bank and Transfusion Service faculty and staff participated in the annual meeting of the American Association of Blood Banks, providing poster presentations, courses and lectures covering a variety of topics. In addition, members of the laboratory, including Mr. Judd, Ms. Butch, Mrs. Stoe, Ms. Steiner and Drs. Davenport and Oberman, presented invited lectures to a variety of regional and national blood banking organizations and state societies.

Aside from the lectures and presentations noted in the individual faculty reports of Mr. Judd and Drs. Davenport and Oberman, Mrs. Stoe, Mrs. Hoffman and Ms. Butch were active in educational programs of the Michigan Association of Blood Banks. Ms. Butch was particularly active on the national scene, lecturing on computer utilization in the blood bank, quality management and the use of the electronic crossmatch. She co-edited a guide for use of blood irradiators. Mrs. Hoffman provided a presentation on stem cell processing at the MABB spring meeting.

PROFESSIONAL ACTIVITIES:

Members of the Blood Bank and Transfusion Service medical and technical staffs were active at the regional and national levels. Dr. Oberman served as Associate Editor of TRANSFUSION and was a member of the Transfusion Practices Committee of the American Association of Blood Banks. Ms. Butch also served on the Information Systems Committee and on the Chief Technologist's Forum of the American Association of Blood Banks. 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 Mr. Judd record their publications and investigative efforts related to blood banking and Transfusion Medicine. In addition, Mr. Judd and Ms. Steiner continued their study of the use of a gel-based system for pretransfusion blood testing.

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

CHEMISTRY SECTION LABORATORIES
(DRUG ANALYSIS AND TOXICOLOGY, LIGAND ASSAY AND CHEMISTRY)

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The Chemistry Section focused on reorganization and continued automation of manual assays in order to meet personnel reduction goals. A great deal of planning time was spent on a renovation project that will allow the consolidation of the Drug Analysis and Toxicology Laboratory (DATL) into Chemistry. The implementation of this consolidation, along with restructuring of automated chemistry and special chemistry/ligand assay/immunology areas and subsequent cross-training of personnel in the coming year should allow for greater flexibility and potential further budget reductions. The Chemistry Section experienced an approximate 10.0 % decrease in test volume, performing nearly 3.3 million tests this past fiscal year. Much of this decrease can be attributed to decreases in inpatient length of stay, with a corresponding decrease in automated chemistry profiles.

The Chemistry Section made a series of changes aimed at increasing the number of tests performed on automated, random access analyzers. All high volume therapeutic drug monitoring assays were switched to the Abbott AxSYM. This allowed the closing of the midnight shift in DATL, with Chemistry techs trained to perform the remaining low volume Toxicology assays. Tacrolimus determinations were transferred from Chemistry to DATL, and lithium analysis was moved from DATL to the automated chemistry area. The lab evaluated and switched to improved assays for LH and free T4 on the Chiron ACS-180. In special chemistry, angiotensin converting enzyme (ACE) was switched to a more automated assay on the Cobas FARA, and the ceruloplasmin determination was moved to the Beckman Array in Immunology. Troponin I was evaluated and introduced as a marker of myocardial injury, with subsequent modification of the Emergency Department Chest Pain Evaluation protocol to include this new, specific cardiac marker. The staff of Chemistry, DATL, Ligand Assay, and Immunology should be congratulated for their efforts in making these changes successful.

The laboratory directors, chemistry fellow, pathology house officers, and laboratory staff participated in a significant number of evaluations and research studies. These included:

1. Evaluation of methods for measuring the free fraction of PSA and the use of percent free PSA as an improved marker of prostate cancer.
2. Evaluation of the performance of phenobarbital and carbamazepine determinations by the Johnson and Johnson Vitros 950 immunorate dry slide technology.
3. Evaluation of Troponin I as a marker of myocardial injury following cardiac catheterization.
4. Interference of a polymerized hemoglobin based blood substitute on laboratory testing.
5. Evaluation of CA-125 assay on the Abbott AxSYM.
6. Comparison of HPLC versus immunoassay for the determination of whole blood cyclosporine concentration.
7. Evaluation of Carbamazepine and Tobramycin assays on the Chiron ACS-180.

8. Evaluation of deoxypyridinoline (Dpd) as a marker of bone turnover.
9. Evaluation of an immunoassay for the direct measurement of LDL cholesterol.
10. Evaluation of the Beckman Image analyzer for specific protein determinations.

The Chemistry Laboratory continued its active role in Point of Care testing both within the hospitals and at the off-site health care centers. East Ann Arbor Medical Center opened this past fall with a laboratory staffed and supervised by Chemistry section personnel. Laboratory staff have participated in the planning of new health care facilities in Brighton and Livonia. As the University has acquired more physician office practices, Chemistry point-of-care coordinators have played an active role in setting up laboratories and managing specimen and data flow back to University Hospital from these locations. All off site centers have successfully passed COLA accreditation with no deficiencies.

The lab has continued its active role in the supervision of bedside blood glucose monitoring programs at University Hospitals. The lab maintains quality control, linearity, and proficiency testing records on 75 whole blood glucose meters stationed throughout the institution. Several new glucose meters are being evaluated by the Point of Care Testing group, and the Chemistry Lab continues to actively pursue options for the computerized collection and analysis of quality control data from these meters.

The Point of Care group in Chemistry has implemented a number of other smaller projects. An i-STAT analyzer was placed at Livonia Surgery Center, and Hemoglobin A_{1c} is being performed in the Pediatric Diabetes Clinic in Taubman Center. The large NOVA blood gas electrolyte analyzer at Kellogg Surgery Center was replaced by a small point-of-care device, the Diametrics IRMA. In all of these programs, clinic personnel perform the tests, and Chemistry Lab staff are reponsible for training, quality assurance, and proficiency testing.

New NOVA Stat Profile Ultra analyzers were evaluated and placed in the operating rooms of Main and Mott Hospitals, as well as in the Emergency Department. Chemistry section personnel maintain these instruments and interfaces for them to the laboratory information system. Data entry for a Coumadin monitoring project was successfully taken on by the distribution area of the Chemistry Section.

The laboratory recently successfully passed a CAP accreditation inspection. Credit should be given to the chief technologist, section supervisors, and all laboratory staff for their efforts in preparing for this inspection. Finally, this past year was highlighted by the successful completion of the first Fellowship in Chemical Pathology and Informatics by Walter Henricks III, M.D. It was a pleasure to have worked with Wally in the laboratory.

Donald Giacherio, Ph.D.

CLINICAL CYTOGENETICS LABORATORY

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The Clinical Cytogenetics Laboratory has seen an increase in volume in most areas, some more than others. In the area of prenatal diagnosis, 850 amniotic fluid specimens, an increase from 760 last year, 110 (vs 85 in 1996) chorionic villus biopsy, and 70 tissues were analyzed. Of interest is the increase in the number of cases that are seen solely for the purpose of growing fibroblasts with the ultimate aim of DNA or biochemical diagnosis; these cases are in addition to the 50 enumerated above. Approximately 50 tissues were rejected as inappropriate specimens ie. blood clots instead of placenta, of little use clinically, or already fixed in formalin.

The bone marrow specimens continue to skyrocket, from under 400 four years ago, to 707 in the last year to 914 in the current fiscal year. These requests are scrutinized more carefully due to staffing problems and our active program of utilization review. The increased volume does not include the approximately 250 requests which were declined for one or more reasons. In addition, 498 peripheral blood specimens were analyzed. Approximately 50 of these tests were for high resolution karyotypes. Much of the increase was accounted for by repeat analyses requested by physicians whose patients had had studies performed at commercial laboratories.

Cytogenetic analysis of solid tumors has remained steady. Pediatric sarcomas and "small round, blue cell tumors" remain the specimens most commonly submitted. Although there are descriptions of various other tumors with specific cytogenetic abnormalities, often the clinical significance is unclear.

The demand for molecular Cytogenetic analysis has increased from one request a month to 2 or more per week. The Laboratory is currently offering a number of specific gene probes for fluorescence in situ hybridization on a research basis including those for Prader-Willi, Angelman's, Williams, and DiGeorge syndromes. Marker chromosomes are characterized. A probe for the so-called minor breakpoint cluster region in the bcr/abl gene rearrangement in CML and ALL are being developed as a potential supplement to cytogenetic analysis, as has nMYC amplification for neuroblastoma. In situ hybridization is performed on at least a weekly basis.

I would comment that while our volume increased dramatically in some areas, increased staffing has not been allotted to the laboratory. Despite this, we were able to decrease the turn around time for prenatal specimens by a concerted effort on the part of the group. We maintained our improved turn around times until we were forced to deal with a dramatic turnover in personnel in the latter part of this year, often working with 20-30% fewer technologists than has been approved for this laboratory. This, of course, impacts turn around time in a negative fashion.

Again, the Laboratory is faced with space constraints, and the consequent staffing constraints. This is particularly worrisome as other Clinical Services are being encouraged to expand by the institution of a Clinical Delivery System. Cytogenetics technologists still require a minimum of one year to train, and several years to properly evaluate the more complex specimens which are being received at an increasingly frequent rate.

Susan Sheldon, Ph.D.
Director, Clinical Cytogenetics

CLINICAL FLOW CYTOMETRY LABORATORY

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I. LABORATORY SERVICE ACTIVITIES

A. Increased volume of work

1. The Clinical Flow Cytometry Laboratory processed approximately 4150 specimens, a volume increase of 22% from the previous year. The percentage change in volume (relative to 1995-96) is listed below for each of the major test categories:

Test Category	Change from 1995-96
Immunodeficiency monitoring	+ 31%
CD34 stem cell counts	+ 79%
Chronic leukemia/lymphoma phenotyping	+ 43%
Acute leukemia phenotyping	+ 26%
T-cell subset monitoring in organ transplant recipients	- 51%
Antiplatelet and antineutrophil antibody testing	+ 7%

2. M-Labs referrals continue to comprise a substantial part of the work volume, including 36% of all acute leukemia immunophenotyping panels, 45% of all chronic leukemia/lymphoma panels, and 43% of all immunodeficiency monitoring.

B. Cost efficiency measures

1. Reduction in technologists by 0.5 FTE. In addition, one FTE resigned and has been replaced by a cross-training technologist transferred from the main Hematology Laboratory.
2. Negotiated contract with Coulter for instrumentation and reagents that will result in reduced cost per test.
3. Collaboration with Pathology Data Systems and Coulter to write software for new Coulter instruments to provide more efficient data archiving and result reporting.
4. Validated more efficient sample prep technique for leukemia/lymphoma profiles.
5. Titering of all new antibodies from Coulter/Immunotech (new reagent supplier) and validation of a single-tube, 4-color immunodeficiency profile in anticipation of implementation during 1997-98.
6. Changed to technologist verification of acquired immunodeficiency reports to improve turnaround time and reduce cost.

7. Effected program of close communication and cooperation with Apheresis Service in Blood Bank to enhance turnaround of CD34 stem cell result reporting. This has resulted in a reduction of unnecessary repeat stem cell harvests by apheresis.
8. Continued monitoring of all requests for leukemia/lymphoma immunophenotyping, with cancellation of unwarranted requests. Of the 950 specimens submitted for leukemia/lymphoma immunophenotyping, pathologist review lead to cancellation of 314 of these requests.
9. Discontinuing microfiche archives of all reports except for leukemia/lymphoma panels.

C. Other changes

1. Collaborated with Pathology Data Systems to streamline report formats.
2. Validating methodology for cytoplasmic detection of myeloperoxidase, CD22 and CD3 in acute leukemia.

II. TEACHING AND RESEARCH ACTIVITIES

1. The hematopathology fellow, pathology house officers, and fellows from Pediatric and Adult Hematology/Oncology participated in flow cytometry case sign-out and teaching conferences.
2. Increased service demands on the laboratory in the face of personnel reductions has substantially curtailed continuing education opportunities for the technologists.
3. Increased service demands with fewer personnel has forced a discontinuation of all intramural and extramural research collaborations.

III. GOALS FOR 1997-98

1. Complete transition to new instrumentation/reagents, with collaborative assistance of Pathology Data Systems to achieve improved results reporting.
2. Continue integration of flow cytometry service with hematology and coagulation to promote more effective allocation of personnel, equipment, and space.

Charles W. Ross, M.D.
Director

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

CLINICAL HEMATOLOGY LABORATORY

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I. LABORATORY ACTIVITIES:

A. Improved cost efficiency
   1. Reduction in technologists by 3 FTEs.
   2. Opened additional Cancer Geriatric Center laboratory with no increase in FTEs, while keeping open Taubman and Main Hematology laboratories.
   3. Added coverage of Microbiology on the midnight shift, including blood cultures, Gram stains on cerebrospinal fluids and respiratory syncytial virus and streptococcal screens.
   4. Added coverage of the Death Registry on afternoons, weekends and holidays
   5. Elimination of all overtime, except holidays
   6. Added coverage of outpatient phlebotomy, 15 hours per week, until May 5, 1997

B. Increased volume of work
   1. The number of bone marrows increased by 23% over the last year, from 2200 in 1995-1996 to 2700 in 1996-1997.
   2. The number of in-house cases signed out by the hematopathologists (excluding flow cytometry, peripheral blood smears and body fluids) increased by 41% over the last year and by 122% over the last four years. Over the last four years, the number of hematopathologists signing out these cases has increased from 3 to 3.5 FTEs, with the addition of a part-time pathologist.
   3. The number of transfer cases signed out by the hematopathologists has increased 5% over the last year and 116% over the last four years.
   4. The number of other laboratory tests in the hematology laboratory has remained similar to the prior year (% change).

a.	Complete blood counts	253,000	(-3%)
b.	Differential counts on blood	46,000	(+2%)
c.	Fluids	6,100	(-8%)
d.	Urines	51,200	(-9%)

C. Changes implemented
   1. Changed the administrative structure of the laboratory to include flow cytometry and coagulation, with institution of one Chief Technologist. Some cross-training of personnel has begun.
   2. Added new generation of Coulter's hematology analyzer, the Gen-S, for the Cancer Geriatric Center laboratory, on a uni-directional interface.

II. TEACHING ACTIVITIES:

A. Pathology House Officers and Hematopathology Fellows, Fellows from Pediatric 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, extranodal lymphoid proliferations, and splenectomies.
   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. Monthly review of cases for Cutaneous Lymphoma Conference.

B. Accredited Hematopathology Fellowship Program.
C. Continuing medical education for medical technologists.
D. Formal lectures and laboratories for freshman and sophomore medical students.
E. Formal lectures and laboratories for elective by fourth year medical students.

III. FISCAL YEAR 1997/1998 GOALS:

A. Continue to integrate flow cytometry, hematology and coagulation
   1. The laboratories are being redesigned to facilitate more efficient utilization of personnel.
   2. Cross-training will proceed for routine tests.
   3. Move flow cytometry from Medical Science I to the main hospital.
B. Utilize two new generation Coulter instruments, the Gen-S, in the Main Hematology laboratory after receiving new software for a bi-directional computer interface. The bi-directional interface will be added to the third Gen-S in the Cancer Geriatric Center laboratory.
C. Schedule bone marrow biopsies.
D. Discontinue routine support for bone marrow biopsies on Saturday morning. Staff approval will be needed.

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

Timothy P. Singleton, M.D.
Assistant Director, Clinical Hematology Laboratory

HISTOCOMPATIBILITY AND IMMUNOGENETICS LABORATORY

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The HLA Laboratory has had a very successful year. The laboratory has made a number of changes that have increased both the efficiency and the function of the facility.

CLINICAL ACTIVITIES:

Clinical activity of the Histocompatibility Laboratory doubled over the prior year. Essentially the Laboratory has shown a four-fold increase in activity over the past two years. This tremendous increase in activity has been painful for the Laboratory to absorb and has been primarily the result of increased activity in the Bone Marrow Transplant Program and Solid Organ Kidney Program. The Laboratory has had to expand to seventeen individuals to accommodate this increased activity and has had to streamline all areas of its function. Average numbers of tissue typings per month are in the 200 range for Class I and Class II typings whereas cross matches are in the 500 per month range. This activity is remarkable and makes the Laboratory one of the ten busiest in the country.

More importantly, the Bone Marrow Transplant Unit has required the development of entirely new procedures for histocompatibility testing. High resolution Class II DNA typing has been initiated and achieved with excellent results. In conjunction with the DNA Sequencing Core for the University, essentially any polymorphism in Class II HLA DRß can now be identified by the Laboratory within 72 hours. This capability was initiated with minimal equipment and without any additional requirement for laboratory space. This is a truly remarkable achievement that has made the Laboratory the envy of any other in the country.

TEACHING ACTIVITIES:

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

NEW GOALS:

The goal for the Laboratory is to continue to deal with the increasing activity from the transplant programs. Starting August 1 the Laboratory will assume all of the non-living related bone marrow evaluations. This will increase the typings by approximately fifty per week and save the Hospital Clinical Delivery System approximately $500,000.00 a year in send-out costs. It is hope that the

transplant programs will be more active in clinical and basic research although currently it appears that their heavy clinical load precludes this. The transplantation laboratory, however, is interested in supporting a research role for the clinical transplant programs.

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

CLINICAL IMMUNOPATHOLOGY LABORATORY

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I. OVERVIEW:

The Immunopathology Laboratory performed more than 50,000 analyses in 1996-97. 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. continued to signout tissue immunofluorescence studies under the auspices of the Anatomic Pathology Division. Drs. Johnson and Killeen, and Paul Killen, M.D., Ph.D. also provided coverage of anti-neutrophil cytoplasmic antibody (ANCA) and anti-GBM studies.

II. CLINICAL SERVICES:

There was the continued growth in several specialized assays; most notably the ANCA test and the anti-GBM indirect immunofluorescence test. Neutrophil cytoplasmic antibody determinations increased from approximately 125/month to more than 150/month. More than 200 indirect immunofluorescence assays for anti-glomerular basement membrane antibodies were interpreted in 1996-97. New procedures were also implemented in the protein electrophoresis area; in hemolytic complement assays, and in the measurement of antibodies to extractable nuclear antigens. We have recently evaluated and initiated a series of new utilization control measures in the laboratory. Finally, laboratory personnel continued cross-training programs with the Chemistry Laboratory. This was one of the chief goals of the Chemistry Section consolidation.

III. RESEARCH AND DEVELOPMENT:

The laboratory participated in an ongoing methods comparison study of microalbuminuria assays. This study is being conducted by Dr. Patricia Mueller at the Centers for Disease Control and Prevention in Atlanta. Involvement in this study was an outgrowth of our support of clinical studies of ambulatory diabetic patients that were carried out by Dr. William Herman (Department of Medicine, University of Michigan) and Dr. Mindy Smith (Department of Family Practice, University of Michigan). We continued laboratory support of clinical studies of the effects of cytotoxic/immunosuppressive drugs on IgG, IgA and IgM as well as IgG subclass concentrations in lupus patients in conjunction with Dr. Joseph McCune (Department of Medicine, University of Michigan). Several commercially-financed methods and instrument evaluations were also carried out. These studies involved anti-streptolysin O, anti-cardiolipin antibody measurements, and several nephelometric assays.

IV. QUALITY ASSURANCE:

The laboratory participated in the development of a department-wide utilization management database and activity plan.

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 6 times during the academic year. Clinical Pathology Grand Rounds included immunopathology presentations by Dr. John Carey (Henry Ford Hospital, Detroit), Dr. Glen Bowen (Department of Dermatology, University of Michigan), Dr. David Keren (Warde Medical Laboratory, Ann Arbor), and Dr. Warren (see individual faculty report. Drs. Warren and Keren continued the weekly series of didactic sessions entitled "Current Topics in Immunopathology". Other professional activities of faculty and staff in the laboratory are summarized under individual reports.

Jeffrey S. Warren, M.D.
Director, Clinical Immunopathology Laboratory

CLINICAL MICROBIOLOGY/VIROLOGY LABORATORIES

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I. CLINICAL ACTIVITIES:

The total annual test volume remained about the same as was reported last year with M-Labs specimens now contributing about 10% of our overall volume. The specimen sources and type of testing changed considerably during the year in response to changing clinical needs. We implemented four new tests to decrease our sendout volume and provide more rapid and meaningful reports to our clinicians: HIV quantitation in plasma by RT-PCR, HSV in spinal fluid by PCR, a semi-quantitative whole-blood CMV antigenemia test by IFA for our transplant population, and Parvovirus B19 antibody testing. Nucleic acid detection methods are currently being evaluated for clinical use for the direct detection of *Bordetella pertusis* and *Mycoplasma pneumoniae* in pulmonary specimens and HPV in endocervial biopsies. In addition to adding test methods, we have initiated several discussions with various clinical services to review the specimens being submitted from their services for clinical utility and, as a result, altered the types and number of several tests being sent.

We continue to work with Infection Control Services to assist them in controlling antimicrobial usage within the medical center and to monitor for developing resistance. We implemented a tiered antimicrobic reporting system to encourage the use of effective, less expensive antimicrobics. We added a broad screening program to detect vancomycin-resistant *Enterococcus* spp. from multiple body sites and assumed the responsibility for initiating a fan-out reporting system to control nosocomial spread of this organism to other susceptible patients. We are in the final stages of evaluating a new susceptibility plate reading system which should assist us in the early detection of isolates becoming more resistant to antimicrobics currently in use.

As a result of discontinuing our midnight shift, we temporarily discontinued direct testing of respiratory specimens for RSV and *Streptococcus pyogenes*. In response to a request by our Emergency Services, we worked with Clinical Hematology personnel to provide both tests during the midnight shift thus providing 24-hour testing as requested.

II. RESEARCH ACTIVITIES:

Clindamycin and erythromycin are considered effective alternatives to penicillin for the treatment of pregnant women at risk for developing intrapartum *Streptococcus agalactiae* (group B Streptococcus) fetal infection. We documented that there is a significant percent of isolates that are resistant to both of these alternative antibiotics and that such isolates must be tested for resistance to avoid treatment failure. This data was reported at several national conferences by faculty members of our departments of Pediatrics and Ob/Gyn.

We completed the evaluation of a new commercial formulation of blood culture media which showed increased recovery of selected bacteria, primarily staphylococci. This media is now in commercial production.

It is gratifying to see several new antimicrobial agents completing clinical testing and receiving FDA approval. Several of these new drugs have been or are now being tested in our laboratory for *in*

vitro efficacy against our clinical isolates. This data is being utilized by our Pharmaceutical and Therapeutic Committee to assess the value of such agents for patient care in our center.

III. ABSTRACTS PRESENTED:

1. Boubeau, P., Reily, J., Heiter, B., Master, R., Young, C., and Pierson, C.: Use of the BacT/Alert for culture of sterile body fluids other than blood. Abstracts of the General Meeting, American Society for Microbiology, 1996; page 277.
2. Pearlman, M., Pierson, C., and Faix, R.: *Streptococcus agalactiae* (Group B Strep) resistance to clindamycin and erythromycin. Abstracts, Infectious Diseases in Obstetrics and Gynecology, 1997; in press.
3. Faix, R., Pierson, C., and Pearlman, M.: Interpartum chemoprophylaxis for Group B Streptococcus: high frequency of resistance to recommended penicillin alternatives in clinical isolates, Abstracts, The American Pediatric Society / the Society for Pediatric Research, 1997; in press.
4. Young, C., Pierson, C, and Burkett, J.: Case report: recovery of vancomycin-dependent *Enterococcus* from blood culture. Abstracts, South Central Association for Clinical Microbiology Spring Meeting, 1997; page 15.

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

MOLECULAR DIAGNOSTICS LABORATORY

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Clinical Activities

The volume of testing in the Molecular Diagnostics Laboratory continued to increase in 1996/97 to over 2,000 cases annually. Growth has been due to the addition of new tests for hereditary hemochromatosis, and the monitoring of bone marrow engraftment in patients in the bone marrow transplant program. The latter has been an important component of the monitoring of patients undergoing this procedure in conjunction with cytogenetics and morphology.

We obtained a new gel imaging system which has improved the detection of PCR products. This has been particularly useful for monitoring engraftment of bone marrow transplant patients. We have switched several detection schemes from radioisotopes to chemiluminescence. This has enabled us to reduce the amount of radioisotope used in the laboratory. Eventually we would like to eliminate the use of radioisotopes.

The laboratory staff underwent turnover in the spring. Two technologists left to pursue advanced degrees. We were fortunate to recruit outstanding medical technologists from within the institution and from the area. The molecular diagnostics field is still extremely dependent on non-automated technologies, and the work of the technologists at the bench is critical for the generation of accurate and timely reports.

Our growth has brought us to fill the capacity of the existing laboratory space, and we need to expand into better equipped physical space in the near future. We also need more office space for administrative functions. This issues need to be addressed in the coming year.

Teaching

Residents are now regularly involved in the sign-out of cases in molecular diagnostics. This provides them with an important educational opportunity to see the application of these technologies applied to the management of individual patients. During the past year, Dr. Walter Henricks, the Chemical Pathology Fellow spent a considerable amount of time working in the Molecular Diagnostics Laboratory. We have had several inquiries during the year from prospective applicants for training in molecular diagnostics. As an institution, we somehow need to identify sources of funding for such applicants. We do have formal accreditation to run a molecular genetics training program.

Anthony A. Killeen, M.D., Ph.D.
Assistant Professor
Director, Clinical Chemistry/Molecular Diagnostics

PHLEBOTOMY SERVICES AND CENTRAL DISTRIBUTION

DEPARTMENT OF PATHOLOGY
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The following are the major achievements for Phlebotomy and Central Distribution during 1996-1997:

- Extensive reengineering was done in the spring of 1996 for the June 1996 downsizing of 35.7 FTE's as follows:

Inpatient Phlebotomy	21.45 FTE's
Outpatient Phlebotomy	6.75 FTE's
Central Distribution	8.50 FTE's

  At the completion of the Reengineering process, we were still able to offer the same services.

- Drawing of Clozaril patients in the Psych ER and remotely at designated sites. Delivery of service was changed from one phlebotomist to 1.5 phlebotomists by June, 1997. The workload increased 25 % over the last year and 90 plus patients are drawn per day. Help from a nurse at one site is no longer available.

- Entering of point of care results performed at the bedside into the PathNet database includes these tests as part of the patient's electronic record, and in addition captures revenue of the hospital. For the Fiscal year 1997, 145,808 tests were entered creating a revenue of $2.3 million.

- An average of ten patients were drawn from children/adolescents at the Hawthorn Center in Northville Township two days per week, was started July, 1995. Stat service was provided 24 hours/day, seven days/week. This service ended, June 1997.

- A new blood drawing station opened in the Cancer Geriatric Center May 5, 1997. The patient load is increasing each month. In May, 1,832 patients were drawn, and in June 2,598. Indwelling catheters are being accessed as a new service to this population.

- The average monthly MCare specimens has remained approximately the same as for the 1995-1996 year with an average of 10,567 for 1996-1997.

- Handling a significant increase in the number of specimens that are sent to other reference labs, due in largely to specimens coming from Mlab clients and in-house downsizing of number of tests offered. Billable tests for the 1997 fiscal year was approximately to 39,849, up from 1996 fiscal year of 29,438.

Suzanne Johnson

GENERAL PATHOLOGY

ELECTRON MICROSCOPY SERVICE

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

The EM service has continued its strong growth which began in the past year. There has been a substantial increase in the number of cases submitted and processed into the lab. This has stretched the capacity of the laboratory such that turnaround times have begun to increase to an unacceptable level. Several options were explored to deal with the problem. A temporary employee has been hired to assist with the workload. We also anticipate securing funds to upgrade the electron microscope to a newer, more efficient model with an integrated digital imaging system.

	1995	1996	1997	Increase # of cases from 1995
Neuro	252	275	308	56 (22%)
Renal	256	276	333	77 (30%)
Other, including research	23	43	20	
Total Cases	531	594	661	130 (24%)

The following table indicates the activity of the EM Service. The column "submitted" indicates the number of specimens submitted, to the lab, the column "hold" indicates the number of specimens that were processed only as far as placing them in buffer. The column "thick" indicates the number of cases embedded, semi-thin sectioned, and examined by the pathologist, and the column "thin/scope" indicates the number examined under the electron microscope.

	Submitted	Hold	Thick	Thin/Scope
Nerve	87	2	48	37
Muscle	200	154	9	37
Renal	333	39	45	249
Other	39	7	6	26
Total Cases	659	202	108	349

The following table is a breakdown of how the cases were submitted, i.e. from inside the institution or outside of the institution.

	Submitted	Inside	Outside
Nerve	87	43	44
Muscle	200	134	66
Renal	333	117	216
Other	39	34	5
Research	2	2	0
Total Cases	661	330	331

Daniel G. Remick, M.D.

M-LABS

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I. GOALS:

1. To generate increased revenue and decreased unit operating cost of the University of Michigan Hospitals Clinical Laboratory System by outreach testing for:

   - Reference laboratory services to hospitals.
   - Group Practices.
   - Physicians offices.
   - Managed care organizations.
   - Specific esoteric services such as renal biopsies, molecular diagnostics, cytogenetics, and flow cytometry, and other "centers of excellence".
   - Clinical trials for clinical research organizations and pharmaceutical firms.

2. Develop and participate in hospital laboratory networks to:

   - Compete effectively for managed care laboratory testing.
   - Reduce costs through test sharing and consolidation.

3. Through our outreach efforts, to build bridges to other institutions that will facilitate working arrangements between these institutions and other branches of the University of Michigan Clinical Delivery System.

4. To replace independent laboratories as the provider of outpatient laboratory services to M-Care and to arrange that these services be provided by a network or networks of hospital laboratories which will be potential M-Labs clients.

II. M-LABS EXPANSION:

The additional personnel hired 2 years ago are now trained and performing in their positions and have added to the effectiveness of our highly motivated and talented MLabs team. We are now better able to deal with the support of existing clients as well as marketing to new clients, especially the previously neglected area of physician's office practices. Operations functions are now being addressed in a more coordinated fashion. The operations manager has developed and implemented a Quality Assurance Plan for systematically identifying and rectifying problems in accessioning, testing, and reporting results.

III. GROWTH:

- CP test volume increased 27.5% over FY96.
- Total CP net billing increased 37.7% over FY96.
- CP client net billing increased 31% over FY 96.
- CP third party payor billing increased 51% over FY 96.
- Billing for AP surgical pathology cases increased by 6% over FY96.

New MLabs accounts during FY 96 include:

- Botsford Hospital - a 300 bed hospital, located in Farmington Hills, MI.
- Flower Hospital - a 300 bed hospital located in Toledo, Ohio.
- Eaton Rapids Community Hospital a 41 bed hospital, Eaton Rapids, MI.
- Several large group practices and individual physician's offices.
- Lost account in FY96: Hawthorn Psychiatric Hospital in Northville, Michigan due to State of Michigan regulation prohibiting M-Labs from bidding on contracts with State of Michigan organizations.

IV. INTERFACES:

Interfaces have now become requisite to obtaining contracts for reference laboratory services for all large hospitals and even for hospitals of 100 beds (or less).

Through the efforts of PDS, we now have interfaces between the University of Michigan laboratory computer system and two hospital laboratories (Mount Clemens General Hospital and Botsford Hospital). One interface is under development (Hurley Hospital) but that interface has gone slowly and is not yet completed.

Interfaces are also planned for 3 more client hospitals.

V. MANAGED CARE ACTIVITIES:

M-Labs has implemented our agreement with M-Care to supply outpatient laboratory services for that portion of the enrollees in its new Medicare (Senior Plan) subscribed to 4 of M-Care's hospital providers. (The work from the remaining 3 hospitals will go to an independent Laboratory).

In order to accomplish this task, M-labs developed and implemented processes for claims transfer from and means of distribution of capitated revenue among the subcontracted laboratory providers, and developed and implemented a Quality Assurance plan to meet with M-Care's and HCFA's requirements for this product.

M-Labs responded to a RFP from M-Care for provision of outpatient laboratory services for its HMO, POS, and Medicaid products. We proposed to subcontract these services to M-Care's provider hospital laboratories. We will be allowed to subcontract to six hospital systems' laboratories (the four in the Medicare product and two more.) Final terms of the arrangement are still being developed.

VI. NETWORKS:

In order to provide geographic coverage for managed care products, and to compete with the large national laboratories which are now dominant in that arena, hospital laboratories are now increasingly banding together in networks. M-Labs has joined JVHL, a network of major hospital laboratories in the Detroit area formed to do laboratory work for Select Care and other managed care organizations.

We are still working with a group of Michigan hospital laboratories to form GreatLakes Laboratory Network which will have the capacity to negotiate for statewide managed care contracts for laboratory services.

We have submitted responses to RFPs for reference laboratory work to 2 hospital laboratory networks. One of these is composed of 17 hospitals based in Ohio and Michigan; the other consists of 4 Michigan hospitals.

VII. PROSPECTS:

The developing shifts from indemnity insurance to managed care as well as the trend to reduced reimbursement by payors for each unit of laboratory testing can be expected to lead to reduced revenue from current clients.

In addition alliances, purchases, and consolidation of health care delivery systems which do not include the University of Michigan will put some of our current clients at risk and put potential new clients into other camps and out of M-Labs' reach.

We propose to maintain our market share and continue growing by the following means:

1. Participate in developing hospital laboratory networks to contact for managed care laboratory work and position our labs to benefit from possible future rationalization of laboratory testing among network members.
2. Assist in the identification of potential "centers of excellence" in our laboratories and marketing of these to networks, managed care entities, and other potential clients.
3. Continue our efforts to contract with M-Care for all of its outpatient laboratory testing which would be subcontracted to its provider hospital laboratories and who would become potential clients of M-Labs.
4. Work with Pathology Data Systems to implement the most efficient information transfer of data to our clients. Information system support has become the single most important concern to many of our potential and current clients.
5. Explore and develop non-core activities such as clinical trials laboratory testing.

VIII. CLINICAL TRIALS LABORATORY TESTING:

Clinical trials laboratory testing represents a very small part of the M-Labs operation but billing of this service to a large local pharmaceutical firm increased by 5% in FY97.

IX. IMPEDIMENTS TO GROWTH:

- **External:**

- Revenues can be expected to decrease from:
  - Increased penetration of managed care.
  - Continued erosion of pricing.
  - Outpatient DRGs.
  - Alliances, consolidations, and purchases of hospitals not involving the University of Michigan put existing clients at risk and other potential clients out of reach.

- **Internal:**

- Maintaining a broad test menu and rapid turnaround times in spite of internal demands for cost reduction.
- Accessioned tests have increased by 27.% over FY 96 but the accessioning staff has been reduced. There are no plans as yet, to address the increased testing due to arrive soon from newly added physician practices, and from other clients should our proposals to the LERC or HealthLink network be accepted. We are concerned that error rates will increase and cause concern to our clients and their patients.
- Commitment to the M-Labs outreach among Department of Pathology faculty and hospital laboratory staff is spotty.
- Indecision about the direction of affiliation of the University Health Systems with other institutions.
- Lack of coordination of our efforts with those of M-Care.
- Two of our large clients have not been chosen by M-Care to participate as subcontractors in M-Care's contract to provide outpatient laboratory services to their own patients. Instead the work has been contacted to an independent laboratory. This puts our relationship with these clients at risk.

Eugene M. Silverman, M.D.

PATHOLOGY DATA SYSTEMS

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The following is a bulleted list of some of the major accomplishments of Pathology Data Systems during the past academic year, July 1996 through June 1997:

Improvements in daily operational support for the clinical laboratories and the faculty

- Installed and operationalized help-desk software (LanDesk) that documents requests for service into Pathology Data Systems. Since the software was installed in October 1996, a total of 1,211 "tickets" have been documented, permitting analysis of the extent to which problems are resolved within the unit.
- Multiple interfaces have been installed between PathNet and analytical instruments in the clinical laboratories, including the GenS in hematology and the Kirby-Bauer reader in microbiology.
- Conversion of the departmental network backbone to fiberoptic cable, resulting in greater stability and speed.
- Continuation of minimal total downtime performance for PathNet at 0.8%, measured on a 7/24 hour basis.
- Server and network operating system upgrade to Novel V. 4.11 in preparation for the conversion to GroupWise 4.0 installation, which itself will result in a more robust email system for the department.
- Installation of three NT servers, with two more to be installed in the very near future, in preparation for the conversion to the PathNet Millennium project in early 1998.

Interface engine (hub) enhancements and deployment of new interfaces to "foreign" systems

- Brought up interface to Mayo Labs such that test results generated by Mayo can be written directly to the PathNet database, resulting in large manpower savings for departmental personnel.
- Installed two HL-7 interfaces to the hub for two MLabs clients – Hurley and Bottsford Hospitals. This automated information exchange between these two important clients.

PathNet enhancements, upgrades, and preparation for V. 500 of the software

- Continuing major efforts to prepare for the installation of the PathNet V. 500 (Millennium client-server product) in the Spring of 1998.

MLabs-related activities

- Multiple new MLabs clients sites brought up, involving such activities as creating computer links with ClientLink and support of billing applications.
- Recent test installation of a Cerner PC-based client workstation product , PathLink, that will eventually be installed at all MLabs sites and will allow test ordering, results viewing, and local storage of test results.

Web-based initiatives

- Local development of a prototype web-based test results viewer, which will be used by Cerner to design their own web viewer which will be integrated into the Millennium release of PathNet.
- On the basis of discussions with Cerner, the company will now proceed to co-develop with PDS a web-based ordering application, which will eventually be used for test and product ordering across all ancillaries at the University of Michigan Medical Center.

Enterprise-wide information technology activities

- Helped to coordinate, at the request of the COO, the elimination of "green" and "gold" interim hardcopy results for inpatients. This was an interim, but important step, in the movement of the enterprise toward the electronic medical record.
- Coordinated with the Bone Marrow Transplant Team the direct ordering of laboratory tests into PathNet. This is the first instance of non-pathology personnel placing electronic orders directly into the LIS.
- Worked with Enterprise Information System (EIS) personnel to validate laboratory information that is copied from PathNet to the Clinical Data Repository (CDR) which is early in its development cycle. Allied with this effort has been the assistance of PDS personnel in the development of the CDR database model.
- Worked with the SEC Company, the vendor of the information system in Trauma-Burn to "push" lab results directly to that system rather than to have it query PathNet periodically.
- As a preparatory step to facilitate the elimination of "green" and "gold" interim hardcopy reports for inpatients, PDS personnel installed new drives to accommodate two years of test results data on-line. It is extremely unusual for hospitals to store this amount of laboratory data on-line.

Educational and committee activities

- The fifteenth annual Symposium on Automated Information Management in The Clinical Laboratory (AIMCL) was presented at the Chrysler Center and Media Union on the North Campus May 28-30. There were 39 vendors in attendance at the meeting and 265 paid registrants. Two two-hour sessions were broadcast as audioconferences to 40 training programs in pathology and 35 CLMA chapters on the first two afternoons of the plenary conference.
- Steve Gendler has acted as chairman of two extremely important committees operating at the enterprise level: the Workstation Management Software Committee, which selected a product for remote control and monitoring of workstations and E-net, which is technical advisory committee for enterprise networking.
- Bruce Friedman continued as a member of the CIO Executive Committee which is composed of all of the information technology directors for the enterprise. He also provided a two-week pathology informatics course for five house officers in May.

Developmental efforts

- Deployment wireless workstations on a pilot basis in chemical pathology that were connected to a server running Citrix software. The latter software permits a less powerful front-end device like the Symbol Technologies wireless terminals to run complex software like Windows 95 or NT.
- Planning for an imaged-based document management system to be deployed in the HLA laboratory.

Bruce A. Friedman, M.D.
Laboratory Director

PATHOLOGY EDUCATION OFFICE

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The Department of Pathology continues to offer a number of diverse programs within the Medical School, Dental School, School of Public Health, College of Literature, Science and the Arts, and the Rackham School of Graduate Studies. These include: courses requiring formal lecture and laboratory exercises, senior medical and undergraduate student Pathology clerkships, and research training for undergraduate, graduate, and medical students, as well as postdoctoral fellows. Within the Medical Center, Departmental teaching activities extend not only to medical students, but also house officers and the staff of many clinical departments in the form of regularly scheduled clinical conferences. Departmental teaching also extends to practitioners in the region and nation through courses given through Continuing Medical Education Programs of The University of Michigan and the United States and Canada Association of Pathologists (USCAP). The major challenge facing the Department faculty is to maintain the breadth and quality of educational programs offered in the face of increasing clinical demands and efforts to down-size the total faculty.

Medical Student Education:
Pathology faculty provide leadership (e.g. course directors, sequence coordinators, Director Component I/II) and excellent teaching in the first two years of the medical student curriculum. A significant new effort to increase student active learning experiences in a web-based teaching format has begun. The elective fourth year clerkships in General Pathology and Laboratory Medicine continue to be highly evaluated by students and meet important curriculum educational goals. The special topics clinical elective rotation has been successful meeting specific student career needs especially those with a subspecialty orientation. The summer program for M-1 students is popular and has resulted in a significant increase in the number of these students entering pathology.

Residency Training:
The Department offers combined residency training in Anatomic and Clinical Pathology as well as fellowships in Cytopathology, Hematopathology, Surgical Pathology, Urologic Pathology, Soft Tissue Pathology and Medical Informatics. Approximately 27 residents and fellows receive training annually. Six house officers and four fellows completed training this past year. Graduates found desirable employment and fellowships including institutions such as Stanford, Northwestern, and the Cleveland Clinic. Acute pressures to reduce the number of training positions has subsided.

Graduate Program:
The Department's doctoral graduate program is a small program (approx. 10 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. An

effort to develop a joint Immunobiology graduate program with Microbiology and Immunology was begun.

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 Dental student pathology course is under new faculty leadership and undergoing significant restructuring both in content and learning process. A new course in general pathology designed to meet the specific needs of Medical Illustration students was developed this past year to be implemented in the summer of 1997. The Pathology Informatics CME course continues to expand and has gained national recognition.

Joseph C. Fantone, M.D.

DEPARTMENT OF VETERANS AFFAIRS MEDICAL CENTER
PATHOLOGY AND LABORATORY MEDICINE SERVICE

DEPARTMENT OF PATHOLOGY
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I. INTRODUCTION:

The Department of Veterans Affairs Medical Center (VAMC) is a tertiary health care provider for veterans, affiliated with the University of Michigan. It is one of three tertiary medical centers in Veterans Integrated Service Network (VISM) #11 which covers the veteran population of Michigan, and portions of Ohio, Indiana and Illinois. The VAMC Pathology and Laboratory Medicine Service maintains a close relationship with the University Department of Pathology at every level. All pathologists in the VAMC have academic appointments and participate in university activities in a manner similar to other departmental sections. Recruitment efforts for pathologists are combined and candidates are selected on the basis of academic performance and potential as well as professional competence similar to any departmental candidate. There are four full-time pathology staff positions. Three resident training positions in the Department's program are supported with funds from the VAMC. 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 and Cytopathology. The Chief, Pathology and Laboratory Medicine Service at the VAMC is a voting member of the Dean's Committee. The VAMC laboratory is fully accredited by the College of American Pathologists. The VA Medical Center is inspected by the JCAHO and is currently accredited. The medical center's Decentralized Hospital Commuter System is considered the state of the art integrated medical information system. This combines all of the clinical management of the patient. Date storage for all components of pathology and the clinical laboratories contains full patient information for more than a decade.

Two major reorganization thrusts are underway at the VAMC. 1) The facility is refocusing its mode of healthcare delivery, down sizing inpatient care and greatly expanding its ambulatory care. In keeping with this change, a substantial building program is currently in progress. Two additional parking structures have been built. A clinical addition is in mid-progress. This 34,000 sq. ft provides ambulatory care, new surgical suites, vascular cath facilities, intensive care units and a floor for diagnostic services (Pathology, Clinical Labs, Radiology and Nuclear Medicine). This includes 23000 sq. ft for complete relocation of Pathology and Laboratory Medicine). 2) The VISN is moving toward an integrated health delivery system. Diagnostic Services will be a target for networking among the current 8 independent hospitals. This will probably result in additional sharing of service responsibilities, decrease in fee basis testing to non-VA clinical labs and increase in workload in anatomic pathology and the VAMC's clinical labs.

II. ANATOMIC PATHOLOGY:

A. **Surgical Pathology:** 4914 surgical cases have been accessioned and reported during this period of time. This represents an 8% increase over the prior reporting period. The resident assigned to surgical pathology, usually a first year resident, acts as coordinator of the section and in that capacity has the opportunity to examine all of the specimens grossly and microscopically under close one-to-one supervision 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 Institutes of Pathology, University of Michigan, and other outside consultations. 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:** 32 autopsies were performed during this year that is a rate of approximately 23% of in-patient deaths. Assigned residents perform the autopsies, prepare the pathologic diagnosis, and present the case in conference to the staff pathologists and other residents. The resident cuts and otherwise prepares the tissue for the preparation of slides and then reviews them and makes a microscopic diagnosis. These steps are supervised by staff pathologists who permit a gradual increase in independence for the resident with increased experience. Several autopsies performed at the VAMC were also presented at the extended Gross Conference at the University.

C. **Cytology:** 2532 cases were examined and diagnosed during this period. This is an increase of 207 over the last reporting year. Nearly all of the cytology specimens are of a diagnostic type, with very few screening cytologies. Although there is not a formal rotation in cytology within the VAMC the cytological material is readily available and is used as correlatinve information for surgical and autopsy pathology. This laboratory is a "Center for Excellence" in cytology.

D. **Electron Microscopy:** 266 electron microscopy cases were reported. An elective rotation is available for pathology residents in electron microscopy. In other rotations the electron microscope findings are used to complement surgical or cytopathology diagnoses. During the academic year Dr. Beals presents electron microscopy seminars at the University of Michigan. This VAMC is a "Center of Excellence" in electron microscopy and serves as consultant to other VA Medical Centers, to the University of Michigan Medical Center and to other hospitals by contact.

III. CLINICAL PATHOLOGY:

During the period of this report $918,086 clinical pathology procedures were done in the laboratory. In Chemistry, there were 755,267 in Hematology113,173; in Microbiology 28,776 and in Blood Bank 20,880. This represents productivity (billable) rather than weighted test numbers. There is not a formal clinical pathology rotation available for pathology residents at this time although the residents may participate or observe clinical pathology procedures when this activity is appropriate in relation to their rotations. Dr. Chensue is director of clinical pathology and makes available interesting and pertinent clinical laboratory available to residents as desired. Clinical Pathology data is available to residents via computer for their information in surgical pathology, autopsy pathology, and elective rotations.

IV. EDUCATION AND TEACHING:

In surgical pathology the staff pathologists provide one-to-one teaching during the surgical sign out time. In addition, there is a surgical pathology conference approximately every other week and an autopsy conference with the entire staff following each autopsy. Residents join in continuing educational activities in histopathology and cytopathology from the AFIP, CAP , and ASCP. Because of the closeness of various sections of the laboratory there is frequent consultation among the pathologists and the residents are involved throughout. Since the VAMC is physically close to the University, the residents are expected to attend the appropriate teaching conferences at the University as well. The staff contribute to the laboratory and lecture portions of the second year medical students at the University of Michigan. The VA staff also participate in other ad hoc lectures and in a moderate number of seminars for the resident staff, most often given at the University of Michigan. Both Dr. Beals and Dr. Chensue have made presentations at international pathology conferences.

V. RESEARCH:

The specific efforts of the pathology staff are included on individual reports. Dr. Stephen Chensue has a strong funded research program that was renewed during this reporting period. He also participates in cooperative studies with other investigators at the University of Michigan. Dr. Beals maintains a strong role in the University/VAMC cooperative studies in head and neck cancer with the Department of Otolaryngology. Staff participates in various clinical studies and collaborate with a variety of investigators. The laboratory in general serves the VAMC research program by providing considerable technical support for clinical research and in some cases for more basic research in both anatomic and clinical pathology. The staff also serves as consultants and advisors for a number of research programs. Dr. Peter Brawn continues his research in carcinoma of the prostate gland and has been a member of the VA Research and Development Committee since 1 July 1993.

VI. ADMINISTRATION:

During this reporting period Dr. Beals served as acting, then full 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. 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 continues his appointment as Acting Director of Pathology for the VA nationally. He has been designated as 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' administration oversight of: Pathology, Clinical Laboratories, Radiology and Nuclear Medicine throughout the VA system.

The VA's National Cytopathology Proficiency Program's administrative offices are located in the VAMC. 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 third year with more than 430 circulating glass cytology smears and 400+ pathologist enrolls.

VII. SUMMARY:

The Department of Veterans Affairs Medical Center Pathology and Laboratory Medicine Service considers the practice of high quality medicine and the appropriate care of patients as its first and highest responsibility. There is close supervision of resident activities as they are involved with patient care. All staff members are privileged and evaluated in accordance with their training, experience, continuing education and participation in quality improvement activities. Within the service there is an extensive quality improvement program that integrates with that of the hospital as a whole. The Pathology and Laboratory Medicine Service has been accredited by the College of American Pathologists since the early 1960's. The Blood Bank is certified by the American Association of Blood Banks and is approved by the Federal Drug Administration. The association with the University of Michigan serves to strengthen and improve the quality of patient care. The teaching effort involving both residents and medical students is of benefit to the two institutions. The physical plant of the VAMC Pathology and Laboratory Medicine Service is short of space. Correction of this deficiency is currently underway with the building of a Clinical Addition that will house: Ambulatory Care, Surgical Suites, the Intensive Care Units, Nuclear Medicine, Radiology and the full Clinical and Anatomic Pathology laboratories. Move to the new structure is scheduled for the end of 1997.

Theodore F. Beals, M.D.
Acting Chief, Pathology and Laboratory Medicine Service
Ann Arbor VA Medical Center

WARNER-LAMBERT/PARKE-DAVIS
UNIVERSITY OF MICHIGAN JOINT PROGRAM

DEPARTMENT OF PATHOLOGY
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The Department of Pathology for several years has enjoyed a close professional relationship with the Department of Toxicology/Pathology at the Parke-Davis Pharmaceutical Research Division of Warner-Lambert Company which is located in Ann Arbor. This Department at Parke-Davis is headed by Dr. Felix De la Iglesia who also has a faculty appointment in the Department. Dr. De la Iglesia is a world expert on hepatic injury as well as morphometric analysis of cellular injury. For several years we have collaborated scientifically with Dr. De la Iglesia and his colleagues which has resulted in several publications.

In the past few years these collaborative interactions have been greatly expanded in the context of increased collaborations between the University and Parke-Davis. Parke-Davis and the University of Michigan, Department of Pathology have entered into an agreement with Dr. De la Iglesia and colleagues to enhance joint research interests. This includes combining positions for postdoctoral fellowship programs as well as providing research opportunities for individuals at both institutions. Currently, there is one Parke-Davis postdoctoral fellow in the Department and several fellows from the Department who collaborate with colleagues at Parke-Davis including working at the Parke-Davis Faculty. In terms of faculty interactions there are collaborations with faculty from Parke-Davis and the Pathology Department dealing with models of inflammation and the regulation of the inflammatory response. There are also collaborations dealing with the mechanisms of apoptosis and DNA alteration in diseases such as SLE as well as morphometric evaluation of tissue injury. These interactions are mutually beneficial and have provided both groups with expertise that is not otherwise available at only one of the two institutions. These collaborations have been mutually reinforcing as demonstrated by joint seminars between the two institutions and joint efforts in recruitment of postdoctoral fellows.

These interactions are expected to continue to increase in the future. This industrial-academic partnership represents an important model for collaborative experiment research that will be jointly beneficial. It also provides an important exposure for our fellows to needs of the pharmaceutical industry.

Felix de la Iglesia

Peter Nard

FINANCE AND ADMINISTRATION

DIVISION OF FINANCE AND ADMINISTRATION

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1996 - 30 JUNE 1997

INTRODUCTION:

The Division of Finance and Administration, which is under the auspices of the Office of the Chairman and directed by Mr. Eugene J. Napolitan, Department Administrator is comprised of four units as follows:

A. ADMINISTRATIVE SUPPORT CENTER - PATHOLOGY LABORATORIES

Nancy A. Coray, Financial Analyst and Billing Coordinator
Deborah Day Jansen, Administrative Coordinator for Pathology Laboratories
Thomas D. Morrow, Assistant Administrator for Finance and Administration
Beverly J. Smith, Administrative Assistant, personnel and payroll functions

Clinical Faculty Offices & Surgical Pathology Transcription, University Hospitals:

Deborah Day Jansen, Administrative Coordinator
Paulette Dozier, Office Manager, Surgical Pathology Transcription
Janice Kitley, Office Manager, Clinical Faculty Offices

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

David R. Golden, Clinical Department Associate
Joseph L. DeJohn, Student Services Assistant
John E. Harris, Administrative Assistant
Susan M. Hunter, Administrative Assistant

C. OFFICE OF THE CHAIRMAN

Laura D. Blythe, Staff Assistant
Carol N. Galofaro Executive Secretary

D. PATHOLOGY PHOTOGRAPHY AND IMAGING CENTER:

Mark V. Deming, Photographer

This Division is responsible for the business, operational and fiscal affairs of the Department of Pathology as mandated by the policies of the Chairman, Clinical Delivery System (CDS), Medical School and University. In addition to directing this division, Mr. Napolitan serves on various

departmental, CDS, Medical School and University Committees, several professional society committees and as a board director for non-profit organizations.

A major reorganization of this division was accomplished in Fiscal Year 1997. With the departure of Mrs. Maydis Caldwell Skeete, Research and Education Administrator, the Education and Research Administration Office was consolidated into the Finance Unit under the direction of Mr. David R. Golden. This new unit, the Office of Academic and Business Affairs - Medical School, has resulted in cost savings in personnel, space and commodities. Administrative support staff formerly located on the fourth level of the Pathology Building have been relocated to the fifth level sharing space with staff from the former Finance Unit. This reorganization also allowed us to vacate space that is vital to the academic programs of the Department.

In addition to the management of daily activities, each of the units has completed major projects which are summarized as follows:

ADMINISTRATIVE SUPPORT CENTER/PATHOLOGY LABORATORIES:

This unit is directed by Mr. Thomas Morrow, Assistant Administrator and is responsible for the business, operational and fiscal affairs of the Anatomic and Clinical Pathology Laboratories. This includes preparation and monitoring of all Hospitals laboratories revenue, expense and capital budgets, and personnel and payroll systems. Mr. Morrow assisted with the planning, development and implementation of the Cost Efficiency Program for the Pathology Laboratories as mandated by CDS Administration and the Redesign Coordinating Group (RCG). For Fiscal Year 1996/1997, the fifth year of the University Hospitals Cost Efficiency Plan, our RCG mandated staff reduction, based upon MECON data, was 20FTEs - equal to $622,359. The majority of the staff reductions, as targeted by the CDS, were in the Blood Drawing and Central Distribution Unit. Mr. Morrow was responsible for analyzing the MECON data for comparison of our laboratory productivity with similar academic institutions. A reorganization of these units including re-definition of phlebotomy services provided to the Hospitals is being proposed. Key administrative support in addition to the Assistant Administrator include:

Administrative Coordinator: This individual, Mrs. Deborah Day Jansen, assists with the coordination of intra and inter laboratory activities for the anatomic and clinical pathology laboratories which include coordination of required proficiency tests; coordination of inspections required for continuing certification or licensure by the JCAH, CAP and MDPH; serving as departmental representative on the Safety Committee, Disaster Committee and as United Way Chairperson. In addition, the Administrative Coordinator acts as the liaison with the Hospital for renovation projects and coordinates the publication of the Pathology Laboratories Handbook (including on-line version) and the SPECTRUM Newsletter; and is responsible for all requisition modifications. This individual also manages the Surgical Transcription Unit and has assumed responsibility for the Faculty Office Suite in the Hospitals. With the opening of the Cancer and Geriatrics Center in April 1997, Mrs. Jansen was responsible for coordinating the move of the Hematology and Phlebotomy services to this facility. Additionally, expansion of our Autopsy Suite including planning and design of a multipurpose room for viewing of bodies, chaplain and police services, etc., and the installation of a new refrigeration unit was completed. Renovation to

the Pathology Laboratories as outlined in last year's CEP has been initiated and is targeted for completion in Spring 1998.

Billing Coordinator: This individual, Ms. Nancy Coray, is responsible for processing and auditing all laboratory charges (gross charges of approximately $142,000,000), ensuring the accuracy of the daily billing files, correction of all errors with the appropriate Hospital department and responding to all questions regarding interdepartmental, MLabs or Hospital patient billings (technical portion). This position is also responsible for our billing system related to the MLabs Program.

Administrative Assistant: This individual, Mrs. Beverly Smith, oversees the clerical support staff assigned to the Administrative Support Center and coordinates personnel and payroll paperwork for all Pathology Laboratories staff (approximately 370 FTE staff). The Administrative Assistant is responsible for the compilation of the Pathology Telephone Directory (on-line and hard copy) and serves as lead for the Departmental Orientation Program. Responsibility for the implementation of the new Paid Time Off system and the development of Department of Pathology guidelines were coordinated by Mrs. Smith.

OFFICE OF ACADEMIC AND BUSINESS AFFAIRS - MEDICAL SCHOOL:

This unit, which is managed by Mr. David Golden, is responsible for the Medical School all funds budget preparation and variance reporting; tracking of all Medical School expenditures, professional fee billing operations; general funds and teaching and administration funds; departmental renovation and remodeling; and management of the Word Processing Center. In addition, the responsibilities formerly administered in the Office of Research and Education Administration were assumed by this unit in March 1997.

All business and administrative functions associated with our sponsored research and education programs including coordination of the application process, receipt of grant awards, establishment of budgets, monitoring of expenditures and acting as liaison between the Principal Investigators, research sponsors and other University departments are now performed by staff in this unit. In addition, personnel and payroll paperwork associated with non-instructional staff (Medical School paid), house officers and post-doctoral fellows is coordinated in this office.

This unit also assists the Coordinator of the Pathology Education Programs with Medical School courses, the Pathology Graduate Program and the House Officer Training Program.

Mr. John Harris has assumed responsibility for oversight of the staff supporting our Research Programs and Mrs. Susan Hunter is responsible for the payroll and personnel issues for staff in the Medical School (approximately 150 FTEs) and our House Officer Program (24 FTEs).

OFFICE OF THE CHAIRMAN:

In addition to providing support to the Chairman, Mrs.Carol Galofaro is responsible for processing faculty appointments and promotions through our ACAPT, the Medical School and University. She also assists the Division Directors with coordinating schedules for faculty recruits.

Mrs. Laura Blythe provides staff support to the Administrator, Mr. Eugene J. Napolitan. In addition, she is responsible for the supervision of faculty support staff, the Chairman's Office Receptionist and temporary office staff. Additional responsibilities include payroll and personnel issues, and travel and dues reimbursements for faculty.

PATHOLOGY PHOTOGRAPHY AND IMAGING UNIT:

Mr. Mark Deming is the photographer assigned to this service. He is responsible for a variety of photography and imaging services including those requested by our clinical and research faculty and house officer staff.

SUMMARY OF FINANCIAL DATA:

1. Grants and Contracts:

225 active grants, contracts and other accounts

Total Direct Expenditures:	$ 6,981,980
Indirect Research Expenditures:	$ 2,693,743
Total Sponsored Projects:	$ 9,674,722

2. Faculty Group Practice Plan - Pathology:

Number of charge entries:	107,452
Gross Billings - Anatomic and Clinical Pathology:	$ 15,166,943
CDS Payment	$ 4,050,000
Part A Payment:	$ 2,572,000
M-Labs Net Transfer:	$ 786,000

3. Pathology Laboratories:

Number of billed tests reported to MECON:	2,499,487
Total Gross Revenue - Pathology Laboratories:	$142,026,778
Total Direct Expenses Pathology Laboratories:	$ 29,171,811

Respectfully submitted,

Eugene J. Napolitan
Administrator