THE UNIVERSITY OF MICHIGAN

Department of Pathology

ANNUAL REPORT

1 July 1995 - 30 June 1996

THE UNIVERSITY OF MICHIGAN

DEPARTMENT OF PATHOLOGY

ANNUAL REPORT

1 JULY 1995 - 30 JUNE 1996

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

ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1995 - 30 JUNE 1996

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
   7. Cancer Registery Conference - Occasional

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-investigator, "Analysis of 8P loss in Human Prostate Cancer", Principal Investigator, Jill Macoska, Ph.D. (5% effort).

B. Co-Investigator, "Role of Chromosome 10 Loss in Prostate Cancer Progression", Principal Investigator, Jill Macoska, Ph.D. (SPORE).
C. Co-Investigator, "Role of BRCA-1 in Prostate Cancer Progression", Principal Investigator, Kathy Cooney, M.D. (SPORE).
D. Co-Investigator, "Androgen Related Target Genes in Apoptosis", Principal Investigator, Mark Day, Ph.D. (SPORE).
E. Co-Investigator, "Color Doppler TRUS in the Prediction of Tumor Vascularization", Principal Investigator, Robert Bree, M.D. (SPORE).
F. Principal Investigator, "Tissue and Serum Core for Prostate Cancer", SPORE grant. (30% effort).
G. "Age Specific PSA Ranges in African Americans", Principal Investigator, Joseph Oesterling, M.D. (SPORE).
H. Co-Investigator, "A Phase II Clinical Trial of Dehydroepiandrosterone (DHEA) in Patients with Prostatic Cancer", Principal Investigator, Kenneth J. Pienta, M.D. (20% effort).
I. Co-Investigator, "Emcyt, VP-16 and Taxol for Metastatic Prostate Cancer", Principal Investigator, Kenneth J. Pienta, M.D. (5%).
J. Co-Investigator, "10p and 10q Allelic Loss in Prostate Carcinoma", Principal investigator Jill Macoska, PhD..
K. Principal Investigator, "Tissue Procurement and Histopathology", Core of the Cancer Center (5%).

PROJECTS UNDER STUDY:

A. 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.).
B. Fractal geometric analysis in prostate cancer.
C. Precursor lesions in prostate cancer, PIN, AAH.
D. Role of chromosome 6, 13 and 17 loss in prostate cancer prognosis with Kathleen Cooney, M.D.
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. Effects of "TUNA" on prostate tissue. Sponsored by Vita Med with Drs. Oesterling and Issa.
I. Longitudinal % Free in a Screening Population. Colaboration with the New England Research Institute.
J. Effect of Fenasteride on % Free PSA. Collaboration with Merk, Abbott, Hybritech, Dianon, and Wallac.
K. Organ Specific Apoptosis in the Spawning Chinook Salmon.

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. "Pathological Assessment of the Radical Prostatectomy Specimen: The Prostate, Its Diseases and Associated Conditions", a three day course presented by the Michigan Prostate Institute and the University of Michigan, Dearborn, Michigan, October 20-22, 1995.
2. "Pathologic Staging of Prostate Cancer", Consensus workshop on critical issues in prostate cancer. Mayo Clinic, Rochester Minnesota, November 1-2, 1995.
3. "% Free PSA Increases Sensitivity and Specificity Over Total PSA but Does Not Predict Stage of Disease: Tumor Angiogenesis Alters the Molecular Forms of PSA", PSA II Congress, West Palm Beach, Florida, January 19-21, 1996.
4. "DHEA as a Chemopreventative Agent in Prostate Cancer; A Paradigm for Laboratory Based Chemoprevention Trials", Prostate Cancer Prevention Workshop, Annapolis Maryland, April 1-2, 1996.
5. Consensus Workshop on Prostatic Intraepithelial Neoplasia, Bethesda, Maryland, June30-July2, 1996.
6. "Grading of Prostate Cancer by Fractal Geometric Analysis", Fourth SPORE Investigators Workshop, Rockville Maryland, July 14-16, 1996.
7. "Utility of Percent Free PSA in the Diagnosis and Management of Prostate Cancer", International PSA Workshop, Chicago Illinois, August 1, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Macoska, J.A., Trybus, T.M., Benson, P.D., Saki, W.A., Grignon, D.J., Wojno, K.D. and Powell, I.J.: Evidence for three tumor suppressor gene loci on chromosome 8p in human prostate cancer. Cancer Res. 53:896 1996.
2. Chang, A.K., Michels, V., Poland, G.A., King, B.F., Wojno, K.J. and Oesterling, J.E.: Neurofibromatosis with involvement of the prostate gland. Urology 47:448-51, 1996.

3. Cooney, K.A., Wetzel, J., Merjaver, S.D., Macoska, J.A. and Wojno, K.J.: Loss of heterozygosity involving chromosome 13q14.3 in sporadic prostate cancer. Cancer Res. 56:1142-45, 1996.
4. Sakr, W.A., Wheeler, T.M., Blute, M., Bodo, M., Calle-Rodrigue, R., Henson, D.E., Mostofi, F.K., Seiffert, J. Wojno, K. and Zincke, H.: Staging and reporting of prostate cancer-sampling of the radical prostatectomy specimen. Cancer 78:366-368, 1996.
5. Trybus, T.M., Burgess, A.C., Wojno, K.J., Glover, T.W. and Macoska, J.A.: Distinct areas of allelic loss on chromasomal regions 10p and 10q in human prostate cancer. Cancer Res. 56:2263-2267, 1996.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Gaudin, P, Wojno, KJ, Sesterhan and Epstein, J.I.: The significance of high-grade PIN on TURP without adenocarcinoma. Submitted to Cancer.
2. Strohbehn, K., Quint, L.E., Prince, M.R., Wojno, K.J., Ashton-Miller, J.A. and DeLancey, J.O.L.: MRI anatomy of the urethra: Comparative histology. Submitted to Obstetrics and Gynecology.
3. Cohan, R.H., Wilson, T., Wojno, K.J. and Korobkin, M.: Cystic renal masses: Accuracy of the bosniac classification system revisited. Amer. J. Radiol., In Press.
4. Haggman, M., Macoska, J., Wojno, K.J. and Oesterling JE.: The relationship between PIN and prostate cancer: Critical issues. Submitted J. Urol.
5. Vashi, A.R., Wojno, K. J., England, B.A., Henricks, W.H., Vessella R.L., Lang, P.H., Wright, G.W., Schellhammer, P.F., Weigand, R., Olson, R.M., Dowell B.L. and Oesterling, J.E.: Determination of the "reflex range" and appropriate cutpoints for percent free PSA in 413 men referred for prostatic evaluation using the AxSYM system. Submitted to JAMA.
6. Cooney, K.A., Wetzel, J,C, Consolino, C.M. and Wojno, K.J.: Identification and characterization of proximal 6q deletions in prostate cancer. Submitted to Cancer Research.
7. Thiel, R.P., Oesterling, J.E., Wojno, K.J., Partin, A.W., Chan, D.W., Carter, H.B., Stamey, T.A., Prestigiacomo, A.R., Brawer, M.K., Petteway J.C., Carlson G. and Luderer A.A.: Prostate volume affects the diagnostic efficiency of free PSA. Submitted to NEJM.
8. Richardson, T.D., Wojno, K.J., Liang, L.W., Giacherio, D.A., England, B.G., Henricks, W.H., Schork, A. and Osterling, J.E.: Serum half life determination of free prostate specific antigen. Submitted to Urology.
9. Haggman, M., Wojno, K. and Macoska, J.: Allelic loss of chromosone 8p sequence in prostatic intraepithelial neoplasia (PIN) and invasive prostate cancer. Submitted to Urology.
10. Goh, M., Kleer, C.G., Kielczewski, P.A., Wojno, K.J., Kim, K. and Oesterling, J.E.: Autologous blood transfusion prior to anatomical radical retropubic prostatectomy: Is it necessary? Submitted to J. Urol.

BOOK CHAPTERS:

1. Wojno, K.J.: New pathologic techniques for diagnosing GU malignancies in cancer treatment and research, Kluwer Academic Publishers, 1996.

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

1. Moyad, M., Oesterling, J. and Wojno, K.J.: Age Migration and prostate cancer detection: A new phenomenon in the era of PSA testing, Presented at the North Central Section of the American Urological Association, Meeting September 14, 1995., and the full session of the American Urologic Association, Orlando Florida, May 1996. J. Urol. 155:814A, 1995.
2. Wojno, K.J., Moyad, M. and Oesterling, J.: Correlation of tumor angiogenesis with serum PSA in stage T2 prostate cancer, presented at the North Central Section of the American Urological Association meeting September 14, 1995.
3. Miyauchi, T., Brown, R.S., Grossman, K., Wojno, K. and and Wahl, R.L.: Correlation between 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, Colorado. J. Nuc. Med.
4. Wojno, K.J., Schwab, E.D., Consolino, C.M. and Oesterling, J.E.: Fractal analysis of the Gleason grading system, presented at USCAP Meeting, Washington D.C., March 1996. Mod. Pathol. 9:175A, 1996.
5. Singleton, T.P., Frank, T.S., Fields, K., Sun, R. and Wojno, K.J.: Immunohistochemistry (IHC) for estrogen receptor (ER) using an automated stainer: Comparison with IHC by hand and with the cytosol assay, presented at USCAP Meeting, Washington, D.C., March 1996. Mod. Pathol. 9:175A, 1996.
6. Wojno, K.J., Reilly, C.R., Stern, R.A. and Oesterling, J.E.: Tryptase positive Mast cell density in benign prostate needle biopsies correlates with serum PSA level, presented at USCAP Meeting, Washington, D.C., March 1996. Mod. Pathol. 9:86A, 1996.
7. Oesterling, J.E., Wojno, K.J., Vashi, A. and England, B.E.: A comparison of free to total PSA (F/T) ratio to total PSA for distinguishing benign prostatic hyperplasia (BPH) from prostate cancer (CaP) using the Abbott AxSYM system, presented at The American Urologic Association Meeting, Orlando, Florida, May 1996. J.Urol. 155:370A, 1196. (Best Poster in Session Award)
8. Henricks, W.H., England, B.G., Giacherio, D.A., Oesterling, J.E. and Wojno, K.J.: Free to total PSA ratio does not predict extraprostatic spread of prostatic adenocarcinoma, presented at The American Urologic Association Meeting, Orlando, Florida, May 1996. J. Urol. 155:369A, 1996.
9. Tchetgen, M-B., Wojno, K.J. and Oesterling, J.E.: The effect of a short course of antibiotics on the serum PSA concentration, presented at The American Urologic Association Meeting, Orlando, Florida, May 1996. J. Urol. 155:425A, 1996.
10. Richardson, T.D., Wojno, K.J., Liang, L.W., Giacherio, D.A., England, B.G., Henricks, W.H., Schork, A. and Osterling, J.E.: Serum half life determination of free prostate

specific antigen, presented at The American Urologic Association Meeting, Orlando, Florida, May, 1996. J. Urol. 155:698A, 1996.

11. Haggman, M., Wojno, K. and Macoska, J.: Allelic loss of chromosone 8p sequence in prostatic intraepithelial neoplasia (PIN) and invasive prostate cancer, presented at The American Urologic Association Meeting, Orlando, Florida, May, 1996. J. Urol. 155:325A, 1996.
12. Goh, M., Kleer, C.G., Kielczewski, D.A., Wojno, K.J, and Oesterling, J.E.: Autologous vs homologous blood transfusing following radical prostatectomy, Presented at Michigan Urology Society, May 1996.
13. Lee, C.T., Wojno, K.J., Oesterling, J.E., Singleton, T., McCauley, L., Lehr, J., Montie, J.E. and Pienta, K.: Expression of parathyroid hormone-like protein in prostate cancer and prostatic intraepithelial neoplasia, Presented at AACR. Cancer Res. (Resident Award Poster).
14. Henricks, W.H., Giacherio, D.A., Oesterling, J.E., Wojno, K.J. and England, B.G.: Performance of free/total PSA as measures by two investigational immunoassays compared in patients with prostate cancer, Presented at CLASS.
15. Henricks, W.H., Giacherio, D.A., Oesterling, J.E., England, B.G. and Wojno, K.J.: Free PSA is stable to freezing and does not predict extraprostatic spread of prostate cancer. Am. J. Clin. Pathol. Annual Meeting of the American Society of Clinical Pathologists, Boston, Massachusetts, April, 1996. Amer. J. Clin. Pathol. 105:494, 1996. (**Residents Award Winner Platform Presentation**).
16. Henricks, W.H., Giacherio, D.A., Oesterling, J.E., Wojno,, K.J. and England, B.G.: Performance of free/total PSA as measured by two investigational immunoassays in predicting the presence of prostatic adenocarcinoma. 22nd Annual Meeting Clinical Ligand Assay Society, Los Angeles, California, May 8 - 11, 1996. J Clin Ligand Assay 19:94, 1996.
17. Henricks, W.H., England, B.G., Giacherio, D.A., Oesterling, J.E. and Wojno,, K.J.: A comparison of serum levels of total prostate specific antigen (PSA) and the free to total PSA ratio in detecting prostatic adenocarcinoma. 22nd Annual Meeting Clinical Ligand Assay Society, Los Angeles, California, May 8 - 11, 1996. Clin. Chem. 42:S263, 1996.
18. Henricks, W.H., Giacherio, D.A., Oesterling, J.E., Wojno, K,J. and England, B.G.: Extraglandular spread of prostatic adenocarcinoma: can it be predicted by free to total prostate specific antigen (PSA) ratio? 22nd Annual Meeting Clinical Ligand Assay Society, Los Angeles, California, May 8 - 11, 1996. J. Clin. Ligand Assay 19:94, 1996.
19. Trybus, T.M., Burgess, A.C., Wojno, K.J., Glover, T.W. and Macoska, J.A. Two distinct regions of allelic loss on chromasome 10 in human prostate cancer. American Association of Cancer Research 87th annual meeting. Proceedings AACR 37:247, 1996
20. Review of Tumors of the Kidney, Bladder, and Related Urinary Structures, AFIP Fasicle Series, Am. J. Surg. Pathol., 1996

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
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	The University of Michigan
Fearon, Eric R.*	Professor	The University of Michigan
Flint, Andrew	Associate Professor	The University of Michigan
Frank, Thomas S.	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	The University of Michigan
Giordano, Thomas J.	Assistant Professor	The University of Michigan
Gordon, David	Associate Professor	The University of Michigan
Greenson, Joel	Assistant Professor	The University of Michigan
Headington, John T.	Professor	The University of Michigan
Heidelberger, Kathleen P.	Professor	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan
Judd, W. John	Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Keren, David F.	Clinical Professor	Warde Medical Laboratories
Killeen, Anthony A.	Assistant Professor	The University of Michigan
Killen, Paul D.	Assistant Professor	The University of Michigan
Kunkel, Steven L.	Professor	The University of Michigan
Lowe, John B.	Professor	The University of Michigan
Lukacs, Nicholas	Research Investigator	The University of Michigan
McClatchey, Kenneth D.	Professor	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	The University of Michigan
Nunez, Gabriel	Assistant Professor	The University of Michigan
Oberman, Harold A.	Professor	The University of Michigan
Phan, Sem H.	Professor	The University of Michigan
Pierson, Carl L.	Assistant Professor	The University of Michigan
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
Selvaggi, Suzanne M.	Associate 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
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

Name	Rank	Institutional Affiliation
Warren, Jeffrey S.	Associate Professor and Director, Clinical Laboratories	The University of Michigan
Weiss, Bernard	Professor	The University of Michigan
Weiss, Sharon W.	Professor and Director, Anatomic Pathology	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.

In Memorium:

The following faculty members passed away during the 1995/1996 academic year:

Robert C. Hendrix
Samuel P. Hicks
Dorin L. Hinerman
Lee A. Weatherbee

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DEPARTMENTAL OVERVIEW

DEPARTMENTAL OVERVIEW
1995/1996

This is a time of great challenge. In the past year, as part of the ongoing institutional Cost Efficiency Program (CEP) and in response to mandates from the Reorganization Coordinating Group (RCG), the operating costs of the Clinical Laboratories (both Anatomic and Clinical Pathology Services, but mainly affecting the latter) were dramatically reduced by nearly 25%. This was achieved largely through reorganizations in the Specimen Procurement (Phlebotomy) area and extensive laboratory consolidations. These changes have resulted in a program that is more cost efficient with maintenance of high quality of service, teaching and academic programs. A central issue for the future is how to reduce further the operating costs of the laboratories while remaining able to respond to institutional service demands. It is anticipated that future efficiencies will be gained through changes in utilization, continued, further reorganizations of the Clinical Laboratories, and possibly by affiliations with other institutions.

The financial picture of the Department remains strong, but administrative changes in clinical operations (e.g., consolidated Faculty Group Practice Plan, Clinical Delivery System, Relative Value Units as a basis for reimbursement, etc.) make it very difficult to project clinical revenues in the coming years. The current challenge is to have a stable and predictable clinical operation and, at the same time, to adapt to the changing environment and preserve incentives for clinical activities. The last is essential if clinical activities are to remain robust and healthy. Currently the Faculty Group Practice Plan is deliberating on all of these matters. In addition, the Department is formulating its own initiatives.

Teaching activities continue to be key to our rationale for existence. The Department of Pathology faculty continues to make contributions to the educational programs of the Medical School, University and community. Pathology faculty provide leadership and excellent teaching in the first two years of the medical curriculum and in fourth year elective clerkships. The Department's relatively young doctoral graduate program has been successful in recruiting a number of Medical Scientist Training Program (MSTP) students and continues to develop as a small focused program. Pathology faculty provide service teaching to various schools within the University, research opportunities to undergraduate students, and continuing medical education to the community. The Pathology Residency Training Program continues to attract outstanding house officers and is one of the top eight in the country. There is significant concern that pressures by the CDS to markedly reduce the number of specialty training positions will result in a decrease in pathology residents, to a level below a critical mass required to maintain an academic program that stands among the top ten in the country. However, the larger challenge for the Department and Medical Center is maintenance of the breadth and quality of educational programs during a period of increasing clinical demands reduce the total number of faculty.

Clinical service activities remain stable and healthy. There has been a slight increment in annual volume of anatomic and clinical laboratory functions, showing a modest 3% annual rise with, at least to date, proportional increases in revenues generated. As we move towards contracted and managed care, the key will be to reduce utilization and to continue to make the services more efficient.

This can only be done by close and careful collaborative actions with our clinical colleagues in other academic departments.

Research activities in the Department continue to be strong and relatively stable in terms of funding (most being from the National Institutes of Health). In spite of severe pressures nationally, our faculty have, on balance, held their own in national competition. Reflective of the research strengths of the Departmental are the numerous investigators (from Research Investigators and Assistant Professors to full Professors, and involving all three Divisions of the Department) receiving external funding for research. Special mention should be made of national awards from the American Society for Investigative Pathology to Department of Pathology personnel: Young Investigator Award in Training (Aklish Pandey, M.D.); 1996 Parke/Davis Award (Vishva Dixit, M.D.); 1996 Rous-Whipple Award (Peter Ward, M.D.). Such recognition speaks volumes about the standing of research in this Department and the widespread recognition of our investigators. Success in research also enhances our ability to recruit House Officers and faculty.

The Department remains strong and committed to adapting to the ever changing environment. Ahead are many challenges that will provide us with an opportunity to change and adapt in ways that will strengthen the Department as we approach the twenty-first century.

Respectfully submitted,

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

INDIVIDUAL FACULTY REPORTS

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

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Services - four and one-half months.
B. Necropsy Service - on call for consultation.
C. Pathologist, Cardiac Transplant Team. Transplant biopsies - six 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 - four contact hours.
   3. Introductory Histopathology Sequence, Sequence Director, Lecturer, Lab, Instructor - eighteen contact hours (six lectures, twelve lab hours).
   4. Pathologic correlation in Gross Anatomy Labs - six contact hours.

B. Sophomore Medical Class:
   1. Cardiovascular Sequence - four lecture hours.
   2. Cardiovascular Sequence - Pathology Lab Coordinator.
   3. Pathology Lab Instructor - all sequences, fifty contact hours.
   4 Surgical Pathology, Individual Studies Seminar, twenty contact hours.

C. Senior Medical Class:
   1. Pathology Clerkship Mentor - one month, twenty contact hours.

D. Inteflex:
   1. Philosophy-Ethics - two contact hours (I-3).
   2. Annual Retreat - two contact hours.

E. Undergraduate LS&A:
   1. Biology #224 - two contact hours.
   2. Undergraduate Research Opportunities Program - two contact hours.

F. Hospital Conferences:
   1. Cardiovascular Pathology Conference - monthly.
   2. Internal Medicine CPC's - occasional.
   3. Internal Medicine Necropsy Review - occasional.

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

H. Invited Lectures:
   1. Freshman Orientation, August 1995.

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

J. Honors:
   1. Elizabeth Crosby Award for excellence in teaching basic sciences, June 1996.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Pathologic-Radiologic correlation in aortic disease, with D. Williams.
B. Pathogenesis of venous thrombosis, with T. Wakefield.
C. Mycophenolate in prevention of cardiac allograft rejection, with J. Nicklas.

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).

REGIONAL AND NATIONAL:

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

V. PUBLICATIONS:

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Heidelberger, K.P. and Abrams, G.D.: Predictive value of endomyocardial biopsies in pediatric heart transplant patients.
2. Strickberger, S.A., Seip, R., Bogun, F., Abrams, G.D., Ebbini, E., Morady, F. and Cain, C.: Extracardiac application of high intensity focused ultrasound for ablation of ventricular myocardium.
3. Lee, D.Y., Williams, D.M. and Abrams, G.D.: The dissected aorta: II. IVUS findings which distinguish the true and false lumens.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Director, Drug Analysis and Toxicology Laboratory.
B. Consultant to Veterans Administration Hospital, Ann Arbor, Michigan.
C. Laboratory Director, Chelsea Family Practice, M-Care Facility.
D. Laboratory Director, Briarwood Medical Group, M-Care Facility.
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:
   1. Thesis Committee, Daniel Trepanier, University of Windsor, "Carbamylation of Erythrocyte Membrane Components."

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. None

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Drug Analysis and Toxicology Laboratory.
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 Emeritus Status, American Board of Clinical Chemistry.
D. Board of Directors, National Registry in Clinical Chemistry.
E. Toxicology Examination Committee, National Registry in Clinical Chemistry.
F. Credentials Committee, National Registry in Clinical Chemistry.
G. Faculty, National Toxicology Review Course, American Association for Clinical Chemistry.
H. Executive Committee/Journal Management Group, Clinical Chemistry Journal.
I. Member, Academy of Clinical Laboratory Physicians and Scientists.
J. Member, Clinical Ligand Assay Society.
K. Member, American Association for Advancement of Sciences.
L. Member, Association of Clinical Scientists.
M. Executive Committee, TDM/Clinical Toxicology Division, American Association for Clinical Chemistry.

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. "Quality Assurance and Quality Control in Clinical Toxicology", National Meeting of the American Association for Clinical Chemistry, Anaheim California, July, 1995.
2. "Anticonvulsant/Cardiac Drugs", Professional Practice in Toxicology National Review Course, Cincinnati, Ohio, June, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Annesley, T.M., Hunter, B.C., Fidler, D. and Giacherio, D.A.: Stability of tacrolimus (FK506) and cyclosporin G in whole blood. Ther. Drug Monitor. 17:361-365, 1995.
2. Shaw, L.M., Annesley, T.M., Kaplan, B. and Brayman, K.L.: Analytical requirements for immunosuppressive drugs in clinical trials. Ther. Drug Monitor. 17:577-583, 1995.
3. Oellerich M., Armstrong, V.W., Kahan, B., Shaw, L., Holt, D.W., Yatscoff, R., Lindholm, A., Halloran, P. and Annesley, T.M.: Report of the consensus panel on cyclosporine monitoring in organ transplantation. Ther. Drug Monitor. 17:642-654, 1995.
4. Judd, W.J. and Annesley, T.M.: The Acquired-B phenomenon. Transfusion Med. Rev. 10:111-117, 1996.

5. Annesley, T.M.: Quality assurance and quality control in clinical toxicology. QA Issues in Clinical Toxicology, Sterling Press, S. Welch Ed., 39-64, 1996.
6. Annesley, T.M.: Anticonvulsants, cardiac drugs, nicotine and atropine. Professional Practice in Toxicology: A Review, A. Warner Ed., 113-156, 1996.
7. Annesley, T.M.: The Origin, design, and meaning of the division logo. Ther. Drug Monitor. Clin. Toxicol. New. 11:5, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

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

II.. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. Pathology 600 - five full class lectures.
   2. Pathology 630 (dental) - one full class lectures.
   3. Senior medical student, elective rotation in pathology, supervisor one month.
B. House Officers:
   1. Surgical pathology diagnosing room instruction for assigned house officer - 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.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Hepatic histopathologic changes in methotrexate-treated psoriatics, with Andrew Flint and members of the Gastroenterology Division.
B. Helicobacter-associated gastritis and non-ulcer dyspepsia with Grace Elta.
C. The fate of the transplanted liver in chronic alcoholic patients with Michael Lucey and Kyle Carr.
D. National Study of Thymosin Treatment of Chronic Hepatitis B with Milton Mutchnick.
E. Crohn's disease of the appendix with Jane Huang.
F. Recurrent autoimmune hepatitis in the transplanted liver with Michael Lucey and Kyle Carr.
G. Classification of gastric polyps with Priscilla Chamberlain.
H. Genetic changes in hepatoma with Graeme Macdonald and Joel Greenson.

I. Stromal tumors of small intestine with Joe Tworek and Joel Greenson.
J. Carcinoma of ampulla, distal common bile duct and pancreatic head with Margaret Anderson and Joel Greenson.

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. Chairman, Publications Committee and Member, Executive Committee, Gastrointestinal Pathology Society.
B. Coordinator for Pathology, Randomized Therapeutic Trail in Cancer of the Esophagus, International Organization for Statistical Studies of Diseases of the Esophagus, Paris, France.
C. 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.
D. Member, Education Committee, United States-Canadian Academy of Pathology.
E. Member, Editorial Board, Human Pathology.
F. Member, Editorial Board, Modern Pathology.
G. Member, Editorial Board, American Journal of Surgical Pathology.
H. Reviewer, Archives of Pathology and Laboratory Medicine, Cancer, Gastroenterology, and American Journal of Gastroenterology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Lecturer, "The Role of the Pathologist in the Diagnosis and Management of IBD", presented at the Inflammatory Bowel Disease: Memphis Update, Memphis, Tennessee, September 24, 1994.
2. Lecture, "Gastrointestinal Lymphomas: A Gastrointestinal Pathologist's Anti-Intellectual Approach". In Symposium on Gastrointestinal Lymphoproliferative Disorders--the Surgical Pathologist's Approach. XX International Congress of The International Academy of Pathology, Hong Kong, October 12, 1994.
3. Lecture: "It's a Shame to Waste a Liver Biopsy, so Let's Milk It for All It's Worth". Eleventh Annual Eisenstein Memorial Hospital, Mercy Hospital, Port Huron, Michigan, October 21, 1994.

4. Lecturer, "The Adenoma Carcinoma Sequence in the Colon", presented at A Day in Gastrointestinal Pathology and Cytopathology, The University of Western Ontario, London, Ontario, November 4, 1994.
5. Lecturer, Update in Gastrointestinal Pathology and Slide Seminar with Dr. Owen, The First Annual Practical Pathology at Whistler, Whistler, B.C., Canada, February 12-15, 1995.
6. Lecturer, "The Role of the Pathologist in IBD", presented at Inflammatory Bowel Disease (IBD). A Multidisciplinary Discussion, Detroit-Macomb Hospital, February 25, 1995.
7. Short Course, "Inflammatory Conditions of Esophagus, Stomach and Duodenum", with Donald Antonioli, United States and Canadian Academy of Pathology Annual Meeting, Toronto, Ontario, March, 1995.
8. Lecturer, GI Pathology, Second Annual Seminar in Pathology, Pittsburgh, Pennsylvania, May 4-7, 1995. Sponsored by the United Hospital Center, Clarksburg, West Virginia.
9. Lecturer, "Annoying Gut Biopsies", presented at the Suffolk County Society of Pathologists, Great Neck, New York, May 25, 1995.
10. Visiting Professor, Department of Pathology, Stony Brook University Hospital, Stony Brook, New York, May 26, 1995. Lecture on: "Differential Diagnosis of the Acutely Presenting Colitides".
11. Visiting Professor, Department of Pathology, Albany Medical College. Lectures and Seminars in GI Pathology, Albany, New York, June 6-8, 1995.
12. Seminar, "Neoplastic Diseases of Intestine", American Society of Clinical Pathologists, Chicago, Illinois, June, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Appelman, H.D.: Gastritis: Terminology, etiology, and clinicopathological correlations: Another biased view. Hum. Pathol. 25:1006-1019, 1994.
2. Goldblum, J.R. and Appelman, H.D.: Stromal tumors of the duodenum. A histologic and immunohistochemical study of 20 cases. Am. J. Surg. Pathol. 19:71-80, 1995.
3. Henley, K.S., Lucey, M.R., Normolle, D.P., Merion, R.M., McLaren, I.D., Crider, B.A., Mackie, D.S., Shieck, V.L., Nostrant, T.T., Brown, K.A., Campbell, D.A., Ham, J.M., Appelman, H.D. and Turcotte, J.G.: A double-blind, randomized, placebo-controlled trial of prostaglandin E_1 in liver transplantation. Hepatology 21:366-372, 1995.
4. DelBuono, E.A., Appelman, H.D. and Frank, T.S.: Role of polymerase chain reaction in the diagnosis of cytomegalovirus infection in liver transplant patients. Int. J. Surg. Pathol. 2:221-226, 1995.
5. Chey, W.D., Kochman, M.L., Traber, P.G., Appelman, H.D. and Gumucio, J.J.: Possible nizatidine-induced subfulminant hepatic failure. J. Clin. Gastroenterol. 20:164-167, 1995.
6. Silverman, E.M., Sapala, J.A. and Appelman, H.D.: Regression of hepatic steatosis in morbidly obese persons after gastric bypass. Am. J. Clin. Pathol., In Press.

CHAPTERS IN BOOKS:

1. Lewin, K.J. and Appelman, H.D.: Tumor of the Esophagus and Stomach, Fascicle, In Press.

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

1. Greenson, J.K., Appelman, H.D. and Boland, C.R.: Genomic defects in hepatocellular carcinoma: The role of DNA mismatch repair genes. Gastroenterol. 108:A500, 1995.
2. Goff, J.S., Barnett, J.L., Pelke, T. and Appelman, H.D. Collagenous colitis: Natural history and clinical remission rates. Gastroenterol. 108:A824, 1995.
3. Macdonald, G.A., Greenson, J.K., DelBuono, E.A., Grady, W.G, Frank, T.F., Lucey, M.R. and Appelman, H.D.: "Mini"-microabcess syndrome in liver transplant recipients. Gastroenterol. 108:A1114, 1995.
4. Mutchnick, M.G., Lindsay, K.L., Schiff, E.R., Cummings, G.D. and Appelman, H.D. Thymosin α_1 treatment of chronic hepatitis B: A multicenter, randomized, placebo-controlled double blind study. Gastroenterol. 108:A1127, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Director, Histocompability 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:
   1. Isaac Yue, Jill Knapp, Grishma Joshi, Kiran Khanuja
F. Supervisor for:
   1. Allergy Fellows: Drs. Alice Chou, Joseph Lee, Katherine Liddle.
   2. Postdoctral Fellow: Dr. Ali Motani.
   3. Medical Student: Jennifer Johnson.
   4. Internal Medicine Resident: Dr. Sunil Reddy.
G. Director, Allergy Training Program.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Immune Responses to Thyroid Peroxidse", NIAID, National Institutes of Health, RO1 A I 37141-01, 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. Syntex Corporation, (Study IID 2176), "Randomized, Controlled, Dose Ranging Study of Mycophenolate Mofetil", J. Baker, Principal Investigator, 08/12/93 - 08/11/96, (budget approximately $227,296).

F. Michigan Molecular Institute, "Development of Starburst Dendrimers as a Gene Transfer Agent", J. Baker, Principal Investigator, 07/01/95-12/31/96, (budget approximately $299,901).

G. ImmuLogic Pharmaceutical Corporation, "Clinical Trial of Allervax Ragweed", J. Baker, Principal Investigator, 06/01/95-05/31/96, (budget approximately $132,845).

H. NIH, National Cancer Institute, R43 CA 68820 (Phase I SBIR), "Development of Targeted Gene Transfer Vectors for Treating Colon Cancer", J. Baker, Principal Investigator on Subcontract, 08/01/95-01/31/96, (budget approximately $91,964).

I. Armour Pharmaceutical Co., "Clinical Trial of RPR 109413v and Gamimune N", J. Baker, Principal Investigator, 07/01/95-06/30/96, (budget approximately $51,023).

J. 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).

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:

A. Chair, Awards Committee, American Thyroid Association.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Allergic Inflammation in Sinuisitis: New Concepts," Los Angeles Allergy Society, Los Angeles, California, September, 1995.
2. "Dendrimers as Gene Transfer Vectors," National Conference on Artificial Self-Assembling Systems for Gene Transfer, Cambridge Heathcare Institute, Wakefield, Massachusetts, September, 1995.
3. "Dermal Transfection Using Dendrimers," Unilever Research, Edgewater, New Jersey, October, 1995.
4. "Transfection Using Dendrimers," Pfizer - Central Research Division, Groton, Connecticut, November, 1995.
5. "Transfection Using Dendrimers," Alza Corporation, Palo Alto, California, December, 1995.
6. Lecturer, "Endoscopic Sinus Surgery Course," University of Michigan, Department of Postgraduate Medicine and Health Professions Education, Ann Arbor, Michigan, April, 1996.

7. "New Advances in Transplantation and the Prevention of Allograft Reaction," New Jersey Medical School, Newark, New Jersey, May, 1996.

SCIENTIFIC ACTIVITIES:

A. Reviewer, Journal of Clinical Endocrinology and Metabolism.
B. Reviewer, Annals of Internal Medicine.
C. Reviewer, Journal of Clinical Investigation.
D. Reviewer, Endocrinology.
E. Reviewer, Journal of Leukocyte Biology.
F. Reviewer, Autoimmunity.
G. Reviewer, Thyroid.
H. Reviewer, Journal of Biological Chemistry.
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.
M. Editor, JAMA Primer.

WORKSHOPS/PANEL DISCUSSIONS:

1. "Animal Models of Allergic Diseases," American Academy of Allergy Asthma and Immunology, New Orleans, Louisiana, March, 1996.
2. "Training Program Directors Committee on Research," American Academy of Allergy Asthma and Immunology, New Orleans, Louisiana, March, 1996.
3. "Gene Transfer Using Starburst™ Dendrimer Polymers," Genetic Therapeutics, Advances, Challenges and Applications for Self-Assembling Systems, Boston, Massachusetts, June 1996.

VI. PUBLICATIONS:

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

1. Hitomi, Y., McDonnell, W.M., Baker, J.R. Jr. and Askari, F.K.: High efficiency prokaryotic expression and purification of a portion of the hepatitis C core protein and analysis of the immune response to recombinant protein in BALB/c mice. Viral Immunol. 8:109-118, 1995.
2. Arscott, P.L., Koenig, R.L., Kaplan, M.M., Glick, G.D. and Baker, J.R. Jr.: Unique autoantibody epitopes in an imunodominant region of thyroid peroxidase. J. Biol. Chem. 271:4966-4973, 1996.
3. Boyd, C.M. and Baker, J.R. Jr.: The immunology of thyroid cancer. Endocrinology and Metabolism Clinics of North America 25:159-179, 1996.
4. Kukowska-Latallo, J.F., Bielinska, A.U., Johnson, J., Spindler, R., Tomalia, D.A. and Baker, J.R. Jr.: Efficient transfer of genetic material into mammalian cells using Starburst polyamidoamine dendrimers. Proc. Natl. Acad. Sci. U.S.A. 93:4897-4902, 1996.

5. Baker, J.R. Jr: Allergy and immunology. JAMA 275:1794-1795, 1996.
6. Belinska, A., Kukowska-Latallo, J., Johnson, J., Tomalia, D. and Baker, J.R. Jr.: Regulation of *in vitro* gene expression using antisense oligonucleotides or antisense expression plasmids transfected using Starburst™ PAMAM dendrimers. Nucleic Acids Research 24:2176-2182, 1996.
7. The Mycophenolate Mofetil Renal Refractory Rejection Study Group. Mycophenolate mofetil for the treatment of refractory, acute, cellular renal transplant rejection. Transplantation 61:722-729, 1996.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Motani, A.S., Arscott, P.L., Hennessey, L.R., McInerney, M.F. and Baker, J.R. Jr.: Thyroid peroxidase (TPO) in an autoantigen in non-obese diabetic (NOD) mice which develop autoimmune thyroiditis.

BOOKS AND CHAPTERS IN BOOKS:

1. Baker, J.R. Jr.: Immunologic aspects of thyroid follicular neoplasms, in, Wartofsky, L. (ed), Thyroid Cancer, Clinical Management, Humana Press, Totowa, New Jerseu, In Press.

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

1. Shanley, T.P., Johnson, K.J., Lebedovych, L., O'Connor, C., Jones, M.L., Ward, P.A. and Baker, J.R., Jr: Expression of chemokines, cytokines and adhesion molecules in late-phase allergic (LAR) lung inflammation in rats passively sensitized with monoclonal IgE antibody, Presented, American Thoracic Society, AAA/ATS Conference on Asthma, July 1995.
2. Motani, A.S. and Baker, J.R. Jr.: Proliferation of splenic mononuclear cells from NOD mice in response to staphylococcal superantigens, Poster Presentation, 9th International Congress of Immunology, San Francisco, California, July, 1995.
3. Motani, A.S., Arscott, P., Shen. M.R., Hennessey, L., McInerny, M. and Baker, J.R. Jr.: Thyroid peroxidase is an autoantigen in non-obese diabetic mice with thyroiditis, Poster Symposium, The American Thyroid Association, 11th International Thyroid Congress, Toronto, Canada, September, 1995.
4. Kukowska-Latallo. J., Rymaszewski, M., Bielinska, A., Tomalia, D. and Baker, J,R., Jr.: Efficient transfer and expression of genetic material *in vivo* in rat lung using Starburst™ dendrimer synthetic vectors, Annual Meeting, American Academy of Allergy, Asthma, and Immunology, New Orleans, Louisiana, March, 1996.
5. Bielinska, A., Kukowska-Latallo, J.F., Johnson, J., Tomalia, D.A. and Baker, J.R. Jr.: Modulation of gene expression by antisense oligonucleotides and expression plasmids transfected with Starburst™ PAMAM dendrimers, Joint Meeting, ASBMB, ASIP, AAI, New Orleans, Louisiana, June, 1996.
6. Kukowska-Latallo, J.F., Bielinska, A., Johnson, J., Tomalia, D.A. and Baker, J.R. Jr.: Cells specific transfer of genetic material into eukaryotic cells using synthetic polymer, Joint Meeting, ASBMB, ASIP, AAI, New Orleans, Louisiana, June, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Diagnostic Electron Microscopy, Veterans Affairs Medical Center, Director of Electron Microscopy Center ofxcellence.
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. Deputy Washtenaw County Medical Examiner.
H. Consultant: Diagnostic Electron Microscopy; Allen Park VAMC, University Hospitals.
I. 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. Medical Records Committee, Veterans Affairs Medical Center.
F. Cancer Committee, Veterans Affairs Medical Center.
G. Automated Data Processing Committee, Veterans Affairs Medical Center.
H. Coordinator of Data Processing Committee for Pathology and Laboratory Medicine Service, Veterans Affairs Medical Center.
I. Medical School Admissions Committee.
J. Dean's Committee, Veterans Affairs Medical Center.

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. American Society of Clinical Pathologists, Quality Management, Cytology Committee.
G. National Veterans Affairs Cytopathology Committee, Chair.
H. National Veterans Affairs Surgical Pathology Committee, Chair.
I. National Veterans Affairs Diagnostic Electron Microscopy Ad Hoc Advisory Group.
J. Clinical Information Council.
K. Laboratory Medicine Committee, Veterans Health Administration/Department of Defense/National Institutes of Health/Indian Health Service.
L. Interagency Coordinating Committee for Minority Health Care Careers, VHA/DAD/HHS/Commerce/DOE/NASA.
M. Department of Veterans Affairs, Veterans Health, Administration, Office of Information Technology, Clinical Applications Requirement Group.
N. Department of Veterans Affairs, Veterans Health Administration, Office of Information Technology, Laboratory Expert Panel.
O. 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. Steering Committee, Iron Mountain/Milwaukee VA HOST Telepathology Project.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Wideroff, L., Schottenfeld, D., Carey, T.E., Beals, T., Fu, G., Sakr, W., Sarkar, F., Schork, A., Grossman, H.B. and Shaw, M.W.: Human papillomavirus DNA in malignant and hyperplastic prostate tissue from black and white males. The Prostate 28:117-123, 1996.
2. Jones, J., Raval, J., Beals, T.F., Worsham, M.J., Van Dyke, D.L., Bradford, D.L. and Carey, T.E.: Loss of heterozygosity on chromosome 18q in squamous cancers confirms high frequency of 18q loss identified by karyotyping of head and neck tumor cell lines and indicates a new locus of loss at 18q12.3. Proc. Am. Assoc. Cancer Res. 36:A863, 1995.
3. Varani, J., Fligiel, S.E., Inman, D.R., Beals, T.F. and Hillegas, W.J.: Modulation of adhesive properties of DEAE-dextran with laminin. J. Biomed. Mater. Res. 29:993-997, 1995.
4. Bradford, C.R., Zhu, S., Wolf, G.T., Poore, J., Fisher, S.G., Beals, T., McClatchey, K.D. and Carey, T.E.: Overexpression of p53 predicts organ preservation using induction chemotherapy and radiation in patients with advanced larygeal cancer. Department of Veterans Affairs Laryngeal Cancer Study Group. Otolaryngol. Head Neck Surg. 113:408-412, 1995.

BOOKS AND CHAPTERS IN BOOKS:

None.

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

1. Beals, T.F., Bundy, M.A., Fowler, W.B., Higbee, J.W., Johnson, D. and Markin, R.S.: Key trends in cost containment. Roundtable discussion. MLO Med. Lab. Obs. 27:30-33, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Nine and one-half months of Neuropathology Service.
B. Three weeks of Autopsy Service and six 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 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.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Histochemistry and morphometry of skeletal muscle in patients with hypertension and diabetes. with Hypertension Clinic at the University of Michigan and Sweden.
B. 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.
C. Urethral musculature in aging and incontinence, with John DeLancey group, Obstetrics/Gynecology.
D. Rat model in brain tumors growth and treatment, with Donald Ross, Neurosurgery and Philip Kish.
E. Genetic treatment of hemophilia in mice model, with Kotoku Kurachi's group in the Department of Genetics.G.

F. Evaluated 83 cases of temporal lobectomy/hippocampectomy with Lori Shuh of epilepsy group.
G. Edited the chapter on brain tumors written by Dr. H.S. Greenberg and in the process of collecting illustrations for it.
H. Provided illustrations of nerve/muscle pathology for John Wald's chapter on neuromuscular diseases in the Textbook of Neuroanesthesia, ed. Maurice S. Albin.
I. Histology and histochemistry of orbicularis muscle, normal and aging.
J. Histochemistry, morphometry and EM of levator palatini muscle in children with cleft palate.

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. Coverage of muscle and nerve biopsy service for MSU during Dr. M. Z. Jone's vacation.
D. Member, American Association of Neuropathologists, IAP, and AAN.
E. Attended IAP, American Association of Neuropathologists and International Society of Neuropathologists meetings.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN PEER REVIEWED JOURNALS:

1. Eldevik, D.P., Blaivas, M., Gabrielsen, T.O., Hald, J.K. and Chandler, W.E.: Craniophyringioma: Radiologic and histologic findings and recurrence. Am. J. Neuroradiol. 17:1-13, 1996.
2. Tworek, J., Mikhail, A. and Blaivas, M.: Meningioma: Local recurrence and metastasis diagnosed by fine needle aspiration. Acta Cytol., Accepted.

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, Submitted.
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. Proceedings of American Academy of Science, Submitted.
3. Levy, R.A. and Blaivas, M.: Desmoplastic medulloblastoma: magnetic resonance imaging findings. Am. J. Neuroradiol., Submitted.
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, Submitted.
5. Sorenson, E.J., Sima, A.A.F., Blaivas, M., Sawchuk, K. and Wlad, J.J.: Clinical features of perineuritis. Muscle and Nerve, Submitted.

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

1. McKeever, P.E. and Blaivas, M. for: Gy, L.. Midroni, and Bilbao, J.M.: Biopsy dignosis of peripheral neuropathy, Newton, M.A. (ed), Butterworth. In: Am. J. Surg. Path. 20:904-105, 1996.
2. McKeever, P.E. and Blaivas, M. for: Richardson, E.P. and DeGerolami, U.: Pathology of the periphral nerve, W.B. Sanders, Co. In: Am. J. Surg. Path., 1996.
3. Blaivas, M., Mikhail, A., Perry, A., McKeever, P.E., Singleton, T., Scheithauer BW: Macrophages in glioblastomas with or without associated infarct. Neuropathol Exp Neurol 55:656, 1996. Presented at the American Association of Neuropathologists meeting, June, 1996.
4. Rodas, R.A., Mikhail, A., McKeever, P.E., Blaivas, M., Dickinson, L.D., Ross, D.A., Papadopoulos, S.M., Greenberg, H.S. and Junck L: Correlation of pathologic findings of intraluminal vascular thrombosis with development of perioperative deep vein thrombosis in brain tumor patients. Presented at the 48th Annual Meeting of American Association of Neurologists, March, 1996.
5. Mikhail, A.A., Yamini, B., McKeever PE, Blaivas M: MIB-1 Proliferation index predicts survival among patients with low grade astrocytoma. Presented at the United States and Canadian Academy of Pathology Meeting in March, 1996.
6. Gebarski, S. and Blaivas, M.: Five germinal matrices, not one. Implications in understanding primary neurodevelopmental brain neoplasm. To be presented in Neuroradiology Fall meeting.
7. Sorenson, E.J., Sima, A.F., Blaivas, M., Sawchuck, K. and Wald, J.J.: Clinical features of perineuritis. To be presented at AAN meeting, Fall 1996.

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, Submitted.

2. Sima, A.A.F. and Blaivas, M.: Pathology of the peripheral nerve biopsy, Chapter, in, Diagnostic Neuropathology, Mosby-Year Book, Inc., Submitted.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Graduate Students:
   1. Jeffrey Rouleau (Bioengineering).
   2. Robert Guldberg (Bioengineering).

B. Postdoctoral Fellows:
   1. Wushan Yin, M.D.
   2. Jianming Fang, M.D.

C. Undergraduate Students:
   1. None.

D. Courses:
   1. Pathology 600: Laboratory Instructor.
   2. Molecular Cell Biology: Section Head, Extracellular Matrix.
   3. Pathology 581: Course Director.

E. Continuing Medical Education:
   1. None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

B. Principal Investigator, "LTBP Genes and Proteins: Regulators of TGF-b Activity," National Institutes of Health, AR44043 (pending)

PROJECTS UNDER STUDY:

A. Molecular cloning of microfibril constituents and members of the TGF-b superfamily.

B. Direct gene transfer *in vivo*.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Member, Pre-Clinical Advisory Program, 1988 - present.
B. Biomechanics Core Steering Committee, Multipurpose Arthritis and Musculoskeletal Diseases Center, 1991 - present.
C. Member, University of Michigan Multipurpose Arthritis Center.
D. Member, University of Michigan Cancer Center.
E. Member, University of Michigan Program Bioengineering Program.
F. Patents:
   1. "Composition and Method for Production of Transformed Cells." (08/390,700).
   2. "Gene Transfer into Bone Cells and Tissues." (08/199,780).
   3. "Methods and composition for Stimulating Bone Cells." (08/316,650).
   4. "Methods and Composition for Stimulating Bone Cells." (PCT/US95/02251).
   5. "Latent TGF-Beta Binding Protein Genes, Composition and Methods." (Submitted).
   6. "Compositions and Methods for Coating Medical Devices." (Submitted).
   7. "*In Vivo* Methods for Wound Healing." (Submitted).

DEPARTMENTAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Ad-hoc Reviewer:
   1. Journal of Biological Chemistry.
   2. Connective Tissue Research.
   3. American Journal of Human Genetics.
   4. Pediatric Pathology and Laboratory Medicine.
   5. Developmental Dynamics.
B. Consultant Editor:
   1. European Journal of Experimental Musculoskeletal Research, 1991-present.
C. Study Sections:
   1. NIH, NIAMSD, Ad Hoc Program Project Review Meeting, July 10, 1995.

INVITED LECTURES/SEMINARS:

1. "LTBP Structure and Expression" and "Stimulation of New Bone Formation by Direct Transfer of Osteoinductive Transgenes", Invited lectures (2), Shriners' Hospital for Crippled Children, Portland Oregon, November 6, 1995.
2. "Gene Therapy for Wound Healing: DNA as a Pharmaceutical", Invited Lecture, Scios Nova, Mountain View, California, January 8, 1996.
3. "Gene Therapy for Bone Repair", Invited Lecture, Genetics Institute, Andover, Massachusetts, March 28, 1996.
4. "Gene Therapy for Fracture Repair", Invited Lecture, The Third Annual Symposium of the UCSD Institute for Biomedical Engineers: The Cellular and Molecular Basis of Skeletal Tissue Engineering, University of California, San Diego, San Diego, California, May 11, 1996.
5 "Gene Therapy for Fracture Repair", Invited Lecture, Symposium on Bone Biology and Bone Disease, U-M Multipurpose Arthritis and Musculoskeletal Diseases Center, Ann Arbor, Michigan, May 15, 1996.
6. "Gene Transfer and Tissue Engineering", Invited Lecture, Bioengineering and Orthopedic Science, Gordon Conference, Proctor Academy, Andover, New Hampshire, July 28-August 2, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Fang, J., Zhu, Y-Y., Smiley, E., Bonadio, J., Rouleau, J.A., Goldstein, S.A. MacCauley, L.K., Davidson, B. and Roessler, B.: Stimulation of new bone formation by direct transfer of osteoinductive plasmid genes. Proc.Natl. Acad. Sci., U.S.A. 93:5753-5758, 1996.
2. Ducy, P., Desbois, C., Boyce, B., Pinero, C., Story, B., Dunstan, C., Smith, E., Bonadio, J., Goldstein, S., Gundberg, C., Bradley, A. and Karsenty, G.: Increased bone formation in ostocalcin-deficient mice. Nature, In Press.
3. Jepsen, K.J., Goldstein, S.A., Kuhn, J.L., Schaffler, M.B. and Bonadio, J.: Type I collagen mutation compromises hierarchical toughening of long bone: Implications for the pathogenesis of skeletal fragility. J. Orthop. Res., In Press.
4. Tseng, K-F., Bonadio, J., Stewart, T.A. and Goldstein, S.A.: The effects of local overexpression of human growth hormone by osteblasts on murine cortical bone. J. Orthop. Res., In Press.
5. Fang, J., Li, X., Smiley, E., Yin, W., Francke, U., Mecham, R.P. and Bonadio, J.: Isolation and characterization of the mouse latent TGF-b binding protein-1 gene (Ltbp-2). J. Biol. Chem., In Press.
6. 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.

BOOKS/CHAPTERS IN BOOKS:

1. Labhasetwar, V., Ciftci, K., March, K., Chen, B., Muller, D.W.M., Bonadio, J. and Levy, R.J., in, Gene-Based Therapies for Restinosis. Advanced Drug Delivery Revieews. Special Issue on Restinosis, Submitted, 1996.

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

1. Bonadio, J.: Calcified tissue pathology and therapeutics: State of the Art. Fifth International Conference on the Chemistry of Biology of Mineralized Tissues, Kohler, Wisconsin, October 22-27, 1995.
2. Ciftci, C., Smiley, E., Labhasetwar, V., Bonadio, J. and Levy, R.J.: Effect of lysosomotropic agents on gene expression *in vitro* American Association of Pharmaceutical Scientists, Tenth Annual Meeting.
3. Bonadio, J.: Tissue engineering and gene transfer.
4. Bonadio, J., Smiley, E., Goldstein, S.A., Ciftci, K., Labhasetwar, V. and Levy, R.J.: Direct gene transfer *in vivo* using the GAM technology. Cold Harbor Gene Therapy Meeting, Cold Spring Harbor, New York, September 25-29, 1996.

PETER BRAWN, M.D.
ASSISTANT PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. AP/CP Pathology, Veterans Administration Hospital.

II. TEACHING ACTIVITIES:

A. Pathology House Officers, Surgical Pathology/Autopsy, Department of Veterans Affairs Medical Center.

III. RESEARCH ACTIVITIES:

None.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Member, Research and Development Committee, Department of Veterans Affairs Medical Center.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

A. Member, International Society of Urological Pathology.
B. Editorial Board, Oncology Reports.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Brawn, P.N., Kuhl, D., Johnson, C.F., Speights, V.O. and Lind, M.: The incidence of unsuspected metastases from clinically benign prostate glands with latent prostate carcinoma. Arch. Pathol. Lab. Med. 119:731-733, 1995.
2. Brawn, P.N., Speights, V.O., Riggs, M., Kuhl, D., Bell, N., Lind, M. and Weaver, B.: How many prognostically significant grades of prostate cancer are there? Oncology Reports 3:323-328, 1996.
3. Brawn, P.N., Jay, D.W., Foster, D.M., Kuhl, D., Speights, V.O., Johnson, E.M., Riggs, M., Lind, M., Coffield, K.S. and Weaver, B.: Prostatic acid phosphotase levels (enzymatic method) from completeley sectioned, clinically benign, whole prostates. The Prostate 28:295-299, 1996.
4. Speights, V.O. and Brawn, P.N.: Serum prostate specific antigen levels in non-specific granulomatous prostatitis. Brit. J. Urology 77:408-410, 1996.

5. Studies done jointly with the Pathology Departments of Case Western University School of Medicine, Mayo Clinic, Texas A&M University School of Medicine, University of Liverpool and University of Colorado. Studies done jointly with Urology Departments of Texas A&M University School of Medicine, Hammersmith Hospital and University of Colorado. Status unknown.

CHAPTERS IN BOOKS:

1. Brawn, P.N.: Histologic features of metastatic prostate carcinoma, in, Foster, C. and Bostwick, D. (eds), Pathology of the Prostate, Major Problems in Pathology Series, W. B. Saunders, Co., In Press.
2. Brawn, P.N.: Adenocarcinoma of prostate - grading of prostate carcinoma, in, Ro, J., Ayela, A., Amen, M. and Grignon, D. (eds), Surgical Pathology of the Prostate Gland, W. B. Saunders, Co., Status Unknown.

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

1. Abstracts of several published articles reprinted in Yearbook of Pathology and Clinical Pathology, The International Monitor in Oncology.

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

ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Director, Forensic Pathology and Medicolegal Autopsies.
B. Supervision of Medicolegal Autopsies (ten months, six days per week).
C. Supervision of Hospital autopsies (six weeks, plus 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. Bi-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. M4 (Senior Medical Student) individual elective in Forensic Pathology, May, 1996.
F. Monthly Forensic Pathology Conference (Pathology House Officer Series), September 1995 - April 1996.
G. Forensic Pathology review for ASCP Pathology Resident In-Service Examination and American Board of Pathology Certifying Examinations to Pathology House Officers (May, 1996).
H. Presentation to University of Michigan Nursing Students, "Introduction/Orientation to the Autopsy Room", September, 1995.
I. Anatomical Pathology Conference, "Medicolegal Aspects of Molecular Pathology", February 27, 1996.
J. Emergency Medicine Residency lecture series, "Forensic Pathology and its Application to Emergency Medicine", January 19, 1996, and February 7, 1996.
K. In-Service on Forensic Pathology, to University and Mott Hospital Operating Room Nurses and Technologists, January 25, 1996, and March 7, 1996.

L. In-Service, "Guidelines for Reporting Deaths to the Medical Examiner", Department of Surgery Saturday Conference, Spring, 1996.
M. Presentation: St. Joseph Mercy Hospital Monthly Trauma Conference, Fall, 1995, and March 5, 1996.
N. Presentation: St. Joseph Mercy Hospital Pulmonary Medicine Conference, December 20, 1995.

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, 1995, and Spring, 1996.
2. Presentation, "The Utility of Post-Mortem Radiology in Forensic Pathology", Michigan Society of Radiologic Technologists, Educational Conference, Foote Hospital, Jackson, Michigan, November 4, 1995.
3. Presentation: Ann Arbor Lions Club, "The Role of the Forensic Pathologist in Law Enforcement", Webers Inn, Ann Arbor, Michigan, January 9, 1996.
4. Presentation: University of Michigan Undergraduate Research Opportunities Program, (UROP), January 31, 1996.
5. Guest Lecturer, "Introduction to Forensic Sciences", Undergraduate Course, Michigan State University School of Criminal Justice, "Introduction to Forensic Pathology", April 10, 1996.
6. Presentation: "An Anatomy Tutorial for the Phlebotomist", University of Michigan Hospital, Towsely Center, April 20, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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 counseling and grievance procedures.
B. Hematology, daily evaluation of pathologist referred blood smears, bone marrow smears, Veterans Affairs Medical Center.
C. Surgical/Frozen Section Diagnosis and Quality Control, (five months/year, approximately 2,200 cases/year).
D. Autopsy Service, rotational basis, on call 17 weeks/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, four lecture hours.
B. Pathology House Officers, Surgical Pathology/Autopsy supervision and instruction, (five months/year).
C. Technologists, technicians and hospital staff, ongoing continuing medical education instruction on clinical laboratory topics.
D. Graduate students, research training toward doctoral degrees.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

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

PROJECTS UNDER STUDY:

A. Cytokine manipulation of mycobacterial (TH1) and schistosomal (TH2) Ag mediated forms of hypersensitivity granuloma formation.
B. Production and regulation of interleukin-1 receptor antagonist during immune/inflammatory responses.
C. Role of chemotactic cytokines, MCP, MIP and RANTES, in granulomatous inflammation.
D. Regulation of chemotactic cytokine production by leukocytes and stromal cells.
E. Analysis of eosinophil recruitment factors in *Schistosoma mansoni* egg-induced granulomatous inflammation.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member of graduate student thesis committees.
B. Interviewing and evaluation of resident and faculty applicants.

MEDICAL SCHOOL/HOSPITAL:

A. Blood Utilization Review Committee, Veterans Administration Medical Center, Chairman.
B. Ambulatory Care Committee, Veterans Administration Medical Center, voting member.
C. Ancillary Testing Committee, Veterans Administration Medical Center, Chairman.
D. Hospital Quality Assurance Investigations, ad hoc committees.
E. Personnel employment and annual evaluations.
F. Editor, "VALABS Interface Laboratory News", Laboratory Newsletter.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited faculty lecturer, Symposium on Cytokines in Infectious Diseases, International Congress of Infectious Diseases, Annual Meeting, Hong Kong, June 10-13, 1996.
2. Case presentations at Tumor Board and Morbidity and Mortality Conferences.
3. Tissue evaluation for clinical researchers.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chensue, S.W., Ruth, J. Warmington, K., Lincoln, P. and Kunkel, S.L.: In vivo regulation of macrophage IL-12 production during type 1 and type 2 cytokine-mediated granuloma formation. J. Immunol. 155:3546-3551, 1995.
2. Lukacs, N.W., Strieter, R.M., Chensue, S.W. and Kunkel, S.L.: Activation and regulation of chemokines in allergic airway inflammation. J. Leukocyte Biol. 59:13-17, 1996.
3. McDonnell, W.M., Chensue, S.W., Askari, F.K. and Moseley, R.H.: Hepatic fibrosis in Ahr-/- mice. (Technical Comment) Science 271:223-224, 1996.
4. Shanley, T.P., Peters, J.L., Jones, M.L., Chensue, S.W., Kunkel, S.L. and Ward, P.A.: Regulatory effects of endogenous interleukin-1 receptor antagbonist protein in immunoglobulin G immune complex-induced lung injury. J. Clin. Invest. 97:963-970, 1996.

5. Ruth, J.H., Bienkowski, M., Warmington, K.S., Lincoln, P.M., Kunkel, S.L. and Chenuse, S.W.: IL-1 receptor antagonist (IL-1ra) expression, function, and cytokine-mediated regulation during mycobacterial and shistosomal antigen-elicited granuloma formation. J. Immunol. 156:2503-2509, 1996.

BOOKS/CHAPTERS IN BOOKS:

1. Kunkel, S.L., Chensue, S.W., Lukacs, N.W. and Strieter, R.M.: Macrophage derived cytokines in lung infection, in, Lipscomb, M. and Russel, S. (eds), Lung Macrophages and Dendritic Cells, Marcel Dekker, Inc., New York, New York.

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

1. Caldwell, C.A., Scales, W.E., Lukacs, N.W., Colletti, L.M., Chensue, S.W., Strieter, R.M. and Kunkel, S.L.: Hepatic interleukin 10 levels following bile duct ligation. American Association for the Study of Liver Diseases, Chicago, Illinois, November 3-7, 1995.
2. Beck, J.M., Preston, A.M., Warmington, K.S. and Chensue, S.W.: Cytokine production during *Pneumocystis carinii* pneumonia in intact and immunodeficient mouse models. American Thoracic Society 1996 International Conference, New Orleans, Louisiana.
3. Waldhauser, L., Guan, J., Dupre', J., Addison, C., Kunkel, S., Chensue, S. and Gauldie, J.: Gene therapy directed to selected organs by adenovirus-mediated expression of immunomodulatory cytokines. Canadian Society for Immunology, Sainte-Adele, Quebec, March, 1996.
4. Beck, J.M., Preston, A.M., Warmington, K.S. and Chensue, S.W.: Th1 and Th2 cytokine responses during experimental *Pneumocystis carinii* pneumonia in mice. American Society of Parisitologists and Society of Protozoologists Joint Meeting, Tucson, Arizona, June 11-15, 1996.
5. Warmington, K.S., Ruth, J.H., Sanghi, P.S., Kunkel, S.L. and Chensue, S.W.: Differential expression of monocyte chemoattractant protein-1 (MCP-1) in Th1 and Th2 cytokine-mediated granuloma formation. FASEB J. 10:A1006, 1996.
6. Chensue, S.W.: Cytokines in granuloma formation. 7th International Congress for Infectious Diseases, Hong, Kong, Abstract 79.004, June 10-13, 1996.
7. Lukacs, N.W., Kunkel, S.L., Strieter, R.M., Karpus, W.J., Keefer, C., Lincoln, P. and Chensue, S.W.: C-C chemokines differentially alter IL-4 production from lymphocytes. FASEB J. 10:A1036, 1996.
8. Strieter, R.M., Kunkel, S.L., Chensue, S.W., Burdick, M.D., Evanoff, H.L. and Lukacs, N.W.: Mast cell-derived ENA-78 functions as a potent neutrophil chemoattractant during allergic airway inflammation. FASEB J. 10:A1212, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Training and supervision of premedical/medical students in research.

III. RESEARCH ACTIVITIES:

A. Signal transduction pathways of neutrophil activation through Mac-1 molecule.
B. Mechanisms of L-selectin-induced neutrophil activation.
C. Signal transduction pathways of neutrophil activation through FcγR.
D. Mechanisms of immune complex-induced human neutrophil activation.

SPONSORED SUPPORT:

A. Principal Investigator, "Mechanisms of Fc Dependent Neutrophil Activation", NIH-1R29 AI/GM 31436 (85%), $556,500/total costs, July 1, 1991 - July 1, 1996.
B. Principal Investigator, "Mechanisms of L-Selectin Dependent Human Neutrophil Activation", American Heart Association of Michigan Grant-in-Aid, 63GB956 (15%), $28,000 total direct costs/year, July 1, 1995 - June 30, 1996.

IV. ADMINISTRATIVE ACTIVITIES:

None.

V. OTHER RELEVANT ACTIVITIES:

A. Designed the T-shirt logo for The 9th International Congress of Immunology, 1995.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Crockett-Torabi, E., Smith, C.W., Sullenbarger, B. and Fantone, J.C.: Activation of human neutrophils through L-selectin and Mac-1 molecules. J. Immunol. 154:2291-2302,1995.
2. Crockett-Torabi, E., Sullenbarger, B. and Fantone, J.C.: Tyrosine phosphorylation is coupled to L-selectin-mediated signal transduction and superoxide release by human neutrophils. Submitted to J. Immunol.

BOOKS/CHAPTERS IN BOOKS:

1. Crockett-Torabi, E. and Fantone, J.C.: Signal transduction and adhesion molecules, in, Ward, P.A. and Fantone, J.C. (eds), Adhesion Molecules and the Lung, Marcel Dekker, Inc., New York, New York.

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

1. Crockett-Torabi, E.. Sullenbarger, B. and Fantone, J.C.: Tyrosine phosphorylation is coupled to L-selectin-mediated signal transduction and superoxide release in human neutrophils. FASEB J. 9:1315A, 1995. Experimental Biology 95. Invited Speaker, "Leukocyte activation and adhesion molecules", mini-symposium. ASIP.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

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

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. Co-coordinator for the Neuroscience Sequence.
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.
E. Teratology Society.

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:

1. Sima, A.A.F., Defendini, R., Keohane, C., D'Amato, C.J., Foster, N.L., Parachi, P., Gambetti, P., Lynch, T. and Wilhelmsen, K.C.: The neuropathology of chromosome 17-linked dementia. Annals of Neurology, 1996.
2. Albin, R.L., Minoshima, S., D'Amato, C.J., Frey, K.A., Kuhl, D.A. and Sima, A.A.F.: Fluoro-deoxyglucose positron emission tomography in diffuse Lewy body disease. Neurology, 1996.

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

1. Sima, A.A.F., Jones, M.Z., D'Amato, C.J. and Boyer, P.J.: Mesocorticolimbic dementia; DLBD without Lewy bodies or a separate entity? J. Neuropath. Exper. Neurol. 55:609, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

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

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: "Expanding Blood Bank Information Resources Through the Internet".
   2. Presented talk entitled: "What Leukoreduction Filters Really Do".
   3. Moderated session on Controversies and New Directions.
D. Clinical Pathology Grand Rounds: "Leukocyte Reduction Filters", May 10, 1996.
E. Clinical Pathology M-4 Elective:
   1. Lecture/Discussion: "Blood Component Utilization".
   2. Lecture/Discussion: "Transfusion Reactions".
   3. 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. Polymorphisms and function of CR1 on erythrocyte membranes.
D. Mechanisms of immune suppression by blood transfusion.
E. Mechanisms of action of leukoreduction filters.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Transfusion Committee.
B. Department of Pathology Internal Review 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.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Davenport, R.D,: Cytokines as intercellular signals in hemolytic transfusion reactions. J. Biol. Signals In Press.
2. Snyder, E.L., Mechanic, S., Baril, E. and Davenport, R.D.: Removal of soluble biologic response modifiers (complement and chemokines) by a bedside leukoreduction filter. Transfusion In Press.

ABSTRACTS, AND PRESENTED PAPERS:

1. Judd, W.J., Steiner, E.A., Knafl, P. and Davenport, R.D.: Failure to detect potentially significant antibodies in prewarmed tests. Transfusion 35:68S, 1995.

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 In Press.

PATENTS:

1. Davenport, R.D. and Haddock, T.F.: Leukocyte Filter Assembly, Media, and Method, U. S. Patent Number 08,607,089, Pending)

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 -30 JUNE 1996

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, Pennsylvania.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Editorial Board Member, Drug Metabolism Reviews.

INVITED LECTURES/SEMINARS:

1. "Regression of Multiorgan Cellular Hyperplasia Induced by Recombinant Human EGF 1-48 in Cynomolgus Monkeys," American College of Veterinary Pathologists, Atlanta, Georgia, November, 1995.
2. "Hypolipidemic-Induced Quantitative Microscopic Changes in Rat Liver Mitochondria," VII International Congress of Toxicology, Seattle, Washington, July, 1995.
3. "Subcellular Organelle Effects of Tacrine (Cognex) in Human and Rat Hepatocytes," VII International Congress of Toxicology, Seattle, Washington, July, 1995.
4. "Quantitative Changes by Epidermal Growth factor (EGF 1-48) on the Small Intestine of Cynomolgus Monkeys," American Society for Investigative Pathology, New Orleans, Louisiana, June, 1996.
5. "Quantitative Microscopic Changes of Cecal and Colonic Mucosa after EGF 1-48 in Non-human Primates," American Society for Investigative Pathology, New Orleans, Louisiana, June, 1996.
6. "Identification of Putative Protein Tyrosine Phosphatase Genes in Rat Regenerating Pancreas Using Polymerase Chain Reaction," American Association for Cancer Research, Toronto, Ontario, Canada, March, 1995.
7. "Modulation of Mercuric Chloride-induced Kidney Injury by Two Recombinant Human Epidermal Growth Factors," Society of Toxicology, Anaheim, California, March, 1996.
8. "Effect of Tacrine on Isolated Hepatic Mitochondria," Society of Toxicology, Anaheim, California, March, 1996.
9. "Localization of Cellular Proliferation in Marmosets Treated with Human Recombinant EGF 1-48," American College of Veterinary Pathologists, November, 1996.
10. "Is Mitochondrial Dysfunction the Basis for the Observed Hepatotoxicity of Tacrine?", American Association for the Study of Liver Diseases, Chicago, Illinois, November, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Breider, M.A., Bleavins, M.R., Reindel, J.F., Gough, A.W. and de la Iglesia, F.A.: Cellular hyperplasia in rats following continuous intravenous infusion of recombinant human epidermal growth factor. Vet. Path. 33:184-194, 1996.
2. de la Iglesia, F.A., McGuire, E.J., Haskins, J.R. and Lalwani, N.: Structural diversity of peroxisome proliferators and their effects on mammalian cells in vivo. Ann. N.Y. Acad. Sci., In Press, 1996.
3. Bleavins, M.R., de la Iglesia, F.A., McCay, J.A., White, K.L. and Munson, A.E.: Immunotoxicologic studies with CI-959: A novel benzothiophene cell activation inhibitor. Toxicology 98:111-123, 1995.
4. Lalwani, N.D., Dethloff, L.A., Haskins, J.R., Robertson, D.G. and de la Iglesia, F.A.: Increased nuclear ploidy, not cell proliferation is sustained in the early stages of peroxisome proliferation in rat liver. Toxicol. Pathol., In Press, 1996.
5. Reindel, J.F., Pilcher, G.D., Gough, A.W. and de la Iglesia, F.A.: Recombinant human EGF 1-48 induced morphologic changes in the digestive tract of cynomolgus monkeys. Toxicol. Pathol., In Press, 1996.
6. Dethloff, L.A., Graziano, M.J., Goldenthal, E., Gough, A.W. and de la Iglesia, F.A.: Perspective on the carcinogenic potential of phenytoin based on rodent tumor bioassays and human epidemiological data. Human Exper. Toxicol. 15:335-348, 1996.

ARTICLES SUBMITTED FOR PUBLICATION:

1. de la Iglesia, F.A., Di Fonzo, C.J., Martin, R.A., McGuire, E.J. and Feuer, G.: Quantitative microscopic changes of the functionally impaired hepatic endoplasmic reticulum in a proposed cholestasis rat model. Submitted for publication, 1996.
2. de la Iglesia, F.A., Martin, R.A., Walker R.M. and Feuer, G.: Metabolic effects of antiinfective agents on the liver of common marmosets (*Callithrix jacchus*). Submitted for publication, 1996.
3. McGuire E.J. and de la Iglesia, F.A.: Hypolipidemic effects on rat liver mitochondria studied by quantitative microscopy. Submitted for publication, 1996.
4. Monteith, D.K., Theiss, J. and de la Iglesia, F.A.: Subcellular organelle effects of tetrahydroaminoacridine (tacrine) on human and rodent liver cells. Sumitted for publication, 1996.
5. Robertson, D.G., Braden, T.K., Urda, E.R., Lalwani, N.D. and de la Iglesia, F.A.: Effects of tacrine on isolated mitochondria from liver cells. Submitted for publication, 1996.

BOOKS/CHAPTERS IN BOOKS:

1. Drug Induced Hepatotoxicity, in, Cameron, R., Feuer, G. and de la Iglesia, F.A. (eds), Handbook of Experimental Pharmacology, Springer Verlag Publishers, Berlin, 1996.
2. Feuer G., and de la Iglesia, F.A.: Subcellular biochemical and pathological correlates in experimental models of hepatotoxicity, in, Cameron, R.G., Feuer, G. and de la Iglesia, F.A. (eds),, Drug Induced Hepatotoxicity", Springer Verlag Publishers, Berlin, pp 43-73, 1996.
3. Cameron, R.G., de la Iglesia, F.A. and Feuer, G.: Hepatotoxicity of cardiovascular drugs, in, Cameron, F.G., Feuer, G. and de la Iglesia, F.A. (eds), Drug Induced Hepatotoxicity, Springer Verlag Publishers, Berlin, pp 477-513, 1996.

4. Metz, A.L., Gough, A.W., Robertson, D.G., de la Iglesia, F.A. and Bishop, S.P.: Agents associated with the development of cardiac hypertrophy and/or cardiac failure, in, Comprehensive Toxicology, Volume 6, Cardiovascular Toxicology. In Press, 1966.

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

1. Reindel, J., Pilcher, G., Walsh, K., Gough, A. and de la Iglesia, F.: Gross and histologic findings following intravenous administration of recombinant human epidermal growth factor 1-48 for two weeks in cynomolgus monkeys. Toxicol. Pathol. 22:646, 1994.
2. Breider, M., Bleavins, M., Reindel, J., Gough, A. and de la Iglesia, F.: Multisystemic cellular hyperplasia in Wistar rats induced by continuous IV infusion of human recombinant epidermal growth factor 1-48. Toxicol. Pathol. 22:645, 1994.
3. Reindel, J., Altrogge, D., Breider, M., Gough, A. and de la Iglesia, F.A.: Regression of multiorgan cellular hyperplasia induced by recombinant human EGF 1-48 in cynomolgus monkeys. Vet. Pathol. 32:599, 1995.
4. Lalwani, N.D., Haskins, J.R., Bleavins, M.R. and de la Iglesia, F.A.: Quantitative changes by epidermal growth factor (EGF 1-48) on the small intestine of cynomolgus monkeys. FASEB J. 10:1430, 1996.
5. Haskins, J.R., Lalwani, N.D., Bleavins, M.R. and de la Iglesia, F.A.: Quantitative microscopic changes of cecal and colonic mucosa after EGF 1-48 in nonhuman primates. FASEB J. 10:A1430, 1996.
6. McGuire, E.J., Haskins, J.R., Lucas, J.A. and de la Iglesia, F.A.: Hypolipidemic-induced quantitative microscopic changes in rat liver mitochondria. The International Toxicologist 7:47-P-7, 1995.
7. Bleavins, M.R., Johnson, K. and de la Iglesia, F.A.: Modulation of mercuric chloride-induced kidney injury by two forms of recombinant human epidermal growth factor. The Toxicologist 30:305, 1996.
8. Monteith, D.K., Theiss, J. and de la Iglesia, F.A.: Subcellular effects of tacrine in human and rat hepatocytes. The International Toxicologist 7:60-P-14, 1995.
9. Robertson, D.G., Braden, T.K., Urda, E.R., Lalwani, N.D. and de la Iglesia, F.A.: Effect of tacrine on isolated hepatic mitochondria. The Toxicologist 30:82, 1996.
10. Reindel, J., Lalwani, N., Haskins, J., Altrogge, D., Gough, A. and de la Iglesia, F.: Localization of cellular proliferation in marmosets treated with human recombinant EGF 1-48. Vet. Path., In Press, 1996.
11. Robertson, D.G., Monteith, D.K., Braden, T.K., Lalwani, N.D. and de la Iglesia, F.A.: Is mitochondrial dysfunction the basis for the observed clinical hepatotoxicity of tacrine? Hepatology, In Press, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Service - 15 weeks.
B. Primary Consultant for Bone and Joint Pathology.
C. Secondary Consultant for Soft Tissue Pathology.
D. Secondary Consultant for Head and Neck Pathology.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Sophomore Medical Class:
   1. Pathology 600 - lecture - six contact hours.
   2. Pathology 600- laboratory sessions- 19 contact hours.

B. Senior Medical Class:
   1. Pathology clerkship - 5 M4 students for four weeks (September 1995).
   2. Pathology clerkship with specialization in orthopaedic pathology-1 M4 student for four weeks (February 1996).

C. House Officers:
   1. Training in Surgical Pathology.
   2. Weekly Surgical Pathology Conference- "Pathology School"- 40 Hours.
   3. Lectures - three hours.
   4. Surgical Pathology Consultation Conference - four hours.
   5. Pathology Resident Elective in Musculoskeletal Research (M. Putzi, M.D.- August 1995) - four weeks.
   6. Pathology Resident Elective in Musculoskeletal Pathology (L. Su, M.D.- November 1995) - four weeks.
   7. Pathology Resident Elective in Musculoskeletal Pathology (V. K. Douglas, M.D.- February 1996) - four weeks.

D. Interdepartmental:
   1. Sarcoma conference - monthly: 32 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.

4. Oral and Maxillofacial Surgery Resident Elective in Head and Neck Pathology (E. Reinish, D.D.S.- July 1995) - two weeks.
5. Oral and Maxillofacial Surgery Resident Elective in Head and Neck Pathology (S. Davis, D.D.S.- September 1995) - two weeks.
6. Oral and Maxillofacial Surgery Resident Elective in Head and Neck Pathology (J. Glasser, D.D.S.- June 1996) - two weeks.

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 (1996 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 1996 Annual Meeting of the United States and Canadian Academy of Pathology (Washington, D.C.).

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURANALS:

1. Ferlito, A. and Devaney, K.: Developmental lesions of the head and neck: Terminology and biological behavior. Ann. Otol. Rhinol. Laryngol. 104:913-918, 1995.
2. Skodras, G., Snodgrass, J. and Devaney, K.: Bladder carcinoma with extensive choriocarcinomatous differentiation - whence the "primary choriocarcinoma of the bladder?" J. Urol. Pathol. 3:235-247, 1995.
3. Wenig, B.M., Devaney, K. and Bisceglia, M.: Inflammatory myofibroblastic tumor of the larynx: A clinicopathologic study of eight cases simulating a malignant spindle cell neoplasm. Cancer 76:2217-2229, 1995.
4. Beckwith, L., Devaney, K. and Kragel, P.J.: Perineurioma. Southern Med. J. 88:964-968, 1995.
5. Ferlito, A., Carbone, A, DeSanto, L.W., Barnes, L., Rinaldo, A., D'Angelo, L. and Devaney, K.O.: "Early" cancer of the larynx: the concept as defined by clinicians, pathologists, and biologists. Ann. Otol. Rhinol. Laryngol. 103:245-250, 1995.
6. Ferlito, A., Devaney, K., Rinaldo, A., Milroy, C.M. and Carbone, A.: Adenoid squamous cell carcinoma of the head and neck. Ann. Otol. Rhinol. Laryngol. 105:409-413, 1996.
7. Abbondanzo, S.L. and Devaney, K.: Hodgkin's disease involving bone and adjacent soft tissue in adults: A clinicopathologic and immunophenotypic study of 7 cases. Int. J. Surg. Pathol. 3:147- 154, 1996.
8. Devaney, K., Wenig, B.M. and Abbondanzo, S.L.: Olfactory neuroblastoma and related sinonasal round cell lesions - characterization by MIC2 antigen and bcl-2 detection by immunohistochemistry. Modern Pathol. 6:653-658, 1996.
9. Ferlito, A., Devaney, K. and Rinaldo, A: The squamous neoplastic component in unconventional squamous carcinomas of the larynx. Ann. Otol. Rhinol. Laryngol., In Press.
10. Devaney, K. and Ferlito, A.: Yolk sac tumors (endodermal sinus tumors) of the head and neck. Ann. Otol. Rhinol. Laryngol., In Press.
11. Milroy, C.M., Ferlito, A., Devaney, K.O. and Rinaldo, A.: The role of DNA measurements of head and neck tumors. Ann. Otol. Rhinol. Laryngol., In Press.
12. Ferlito, A., Devaney, K.O., Rinaldo, A., Milroy, C.M., Fenig, B.M. and McCabe, B.F.: Ear cholesteatoma versus cholesterol granuloma. Ann. Otol. Rhinol. Laryngol., In Press.
13. Terek, R.M., Schwartz, G.K., Devaney, K., Glantz, L., Huvos, A., Healey, J.H. and Albino, A.: Chemotherapy and multidrug resistance gene expression in chondrosarcoma. Cancer, In Press.

14. Ferlito, A., Weiss, L.M., Rinaldo, A., Carbone, A., Devaney, K.O., MacMillan, C and Barnes, L.: Lymphoepithelial carcinoma of the larynx, hypopharynx and trachea. Ann. Otol. Rhinol. Laryngol., In Press.
15. Ferlito, A., Rinaldo, A. and Devaney, K.O.: Syndrome of inappropriate antidiuretic hormone secretion associated with head and neck cancers. Ann. Otol. Rhinol. Laryngol., In Press.
16. Devaney, K., Hunter, B.C., Ferlito, A. and Rinaldo, A.: Pre-treatment pathologic prognostic factors in squamous carcinomas of the head and neck. Ann. Otol. Rhinol. Laryngol, In Press.
17. Devaney, K., Putzi, M.J., Ferlito, A. and Rinaldo, A.: Head and neck Langerhans cell histiocytosis. Ann. Otol. Rhinol. Laryngol., In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Devaney, K. and Popek, E.: Langerhans cell histiocytosis presenting with skeletal involvement in the first two years of life- a report of 22 cases. Human Pathology, Submitted.

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. Montgomery, E., Devaney, K. and Weiss, S.W.: Low grade fibroblastic sarcomas and their distinction from deep fibromatoses. Modern Pathol. 9:11A, 1996.
2. Putzi, M., Frank, T.S. and Devaney, K.: Cutaneous neuroendocrine carcinomas (Merkel cell tumors)- an analysis of MIC-2, MIB-1, Bcl-2, and p53 positivity by immunohistochemistry and comparison with extracutaneous small cell carcinomas. Modern Pathol. 9:44A, 1996.
3. Devaney, K.: Book review: Dahlin's Bone Tumors- General Aspects and Data on 11,087 Cases, by K.K. Unni. Am. J. Surg. Pathol., In Press.
4. 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., In Press.
5. Devaney, K.O. and Ferlito, A.: Clinicopathologic consultation: Cartilaginous tumors of the larynx. In Section Seven (Neoplastic and Inflammatory Diseases of the Head and Neck) of the 1996 Home Study Course of the American Academy of Otolaryngology- Head and Neck Surgery.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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:

A. Principal Investigator, "Signal Transduction by the Eck Receptor Tyrosine Kinase", NIH-GM/DK54386, 15% effort, Budget $137,000 current year, Period 04/01/96 - 03/31/00.
B. 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.
C. Principal Investigator, "Thrombospondin 2; Structure, Expression and Function", NIH-RO1 - CA58182-06, 20% effort, Budget $143,657 current year, $1,236,526 Total, 8/04/92 to 05/31/97.
D. Principal Investigator, "Erb-B2 Expression and Resistance to TNF Killing", NIH-LA-64803. 10% effort, Budget $148,779 current year, $858,304 Total, 07/01/94 - 06/31/98.
E. Principal Investigator, "Characterization of Fas associated Death Domain (FADD)", NIH-AG13671, 15% effort, Budget $107,000 current year, Period 04/01/96 to 03/31/99

PENDING:

F. Principal Investigator, "CD40 Signal Transduction", NIH-HD33881, 15% effort, Priorty Score: 121, Percentile Ranking: 3.3.
G. Principal Investigator, "Identification of Components of the Cell Death Pathway", NIH-ES08111, 15% effort, Priority Score: 102, Percentile Ranking: 0.2.

PROJECTS UNDER STUDY:

A. 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:

1. Invited Speaker, IDUN Pharmaceuticals, San Diego, California, 1995.
2. Invited Speaker, Mayo Clinic, Scottsdale, Arizona, 1995.
3. Invited Speaker, March Atherosclerosis Forum, Courchevel, Switzerland, 1995.
4. Invited Speaker, American Society of Investigative Pathology, Toronto, Canada, 1995.
5. Invited Speaker, Tularik, Inc., San Francisco, California, 1995.
6. Invited Speaker, Gordon Conference, New London, New Hampshire, 1995.
.7. Invited Speaker, Association of Pathology Chairs, Apoptosis Seminar, Vail, Colorado, 1995.
.8. Invited Speaker, University of Minnesota, Apoptosis Conference, Vail, Colorado, 1995.
9. Invited Speaker, Pfizer Pharmaceuticals, Groton, Connecticut, 1995.
10. Invited Speaker, University of Washington, Seattle, Washington, 1995.
11. Invited Speaker, Scripps Research Institute, La Jolla, California, 1995.
12. Invited Speaker, New England Immunology Conference, Woods Hole, Maine, 1995.
13. Invited Speaker, IBC Conference on Cell Death, San Diego, California, 1995.
14. Invited Speaker, International Titisee Conference on Angiogenesis, Titisee, Germany, 1995.
15. Invited Speaker, American Heart Association Scientific Sessions, Anaheim, California, 1995.
16. Invited Speaker, Pluto Society Meeting, San Juan, Puerto Rico, 1995.

17. Invited Speaker, La Jolla Cancer Research Foundation, La Jolla, California, 1995.
18. Invited Speaker, Tularik, Inc., San Francisco, California, 1996.
19. Invited Speaker, NIH, Bethesda, Maryland, 1996.
20. Invited Speaker, University of Texas, Dallas, Texas, 1996.
21. Invited Speaker, Rush Medical College, Chicago, Illinois, 1996.
22. Invited Speaker, Sixth International Conference on Lymphocyte Activation and Immune Regulation, Newport Beach, California, 1996.
23. Invited Speaker, St. Louis University, St. Louis, Missouri, 1996.
24. Invited Speaker, Washington University, St. Louis, Missouri, 1996.
25. Invited Speaker, Mayo Clinic, Scottsdale, Arizona, 1996.
26. Invited Speaker, University of North Carolina, Chapel Hill, 1996.
27. Invited Speaker, Tufts University, Boston, Massachusetts, 1996.
28. Invited Speaker, Memorial Sloan-Kettering Cancer Center, New York, New York, 1996.
29. Invited Speaker, National University of Singapore, 1996.
30. Invited Speaker, Harvard University, Cambridge, Massachusetts, 1996.
31. Invited Speaker, Boston University, Boston, Massachusetts, 1996.
32. Invited Speaker, TNF Congress, Rhodes, Greece, 1996.
33. Invited Speaker, Duke University, Durham, North Carolina, 1996
34. Invited Speaker, Mt. Sinai Medical Center, New York, New York, 1996.
35. Invited Speaker, ASBMB/ASIP Conference, New Orleans, Louisiana, 1996.
36. Invited Speaker, FASEB Summer Research Conference, Saxtons River, Vermont, 1996.
37. Invited Speaker, Hans Bloemendal Symposium, Netherlands, 1996.
38. Invited Speaker, NIAAA Symposium, Washington, D.C., 1996.
39. Invited Speaker, Human Genome Sciences, Rockville, Maryland, 1996.
40. Invited Speaker, Gordon Conference, Andover, New Hampshire, 1996.
41. Invited Speaker, SmithKline Beecham, Philadephia, Pennsylvania, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Shao, H., Lou, L., Pandey, A., Verderame, M.F., Siever, D.A. and Dixit, V.M.: cDNA cloning and characterization of a *Cek7* receptor protein-tyrosine kinase ligand that is identical to the ligand (ELF-1) for the Mek-4 and Sek receptor protein-tyrosine kinases. J. Biol. Chem. 270:3467-3470, 1995
2. Tewari, M. and Dixit, V.M.: Fas- and TNF-induced apoptosis is inhibited by the Poxvirus *crmA* gene product. J. Biol. Chem. 270:3255-3260, 1995.
3. Shao, H., Pandey, A., O'Shea K.S., Seldin, M. and Dixit, V.M. Characterization of B61, the ligand for the *Eck* receptor protein-tyrosine kinase. J. Biol. Chem. 270:5636-5641, 1995.
4. Sarma, V., Lin, Z., Clark, L., Rust, B.M., Tewari, M., Noelle, R.J. and Dixit, V.M.: Activation of the B-cell surface receptor CD40 induces A20, a Nnvel zinc finger protein that inhibits apoptosis. J. Biol. Chem. 270:12343-12346, 1995.

5. Chinnaiyan, A.M., O'Rourke, K., Tewari, M. and Dixit, V.M.: FADD, a novel death domain-containing protein, interacts with the death domain of Fas and initiates apoptosis. Cell 1:505-512, 1995.
6. Tewari, M., Quan, L.T., O'Rourke, K., Desnoyers, S., Zeng, Z., Beidler, D.R., Poirier, G.G., Salvesen, G. and Dixit, V.M.: Yama/Cpp32ß, a mammalian homolog of CED-3, is a CrmA-inhibitable protease that cleaves the death substrate poly(ADP-Ribose) polymerase. Cell 81:801-809, 1995.
7. Pandey, A., Shao, H., Marks, R.M., Polverini, P.J. and Dixit, V.M.: The role of B61, the ligand for the Eck receptor tyrosine kinase in TNF-α Induced angiogenesis. Science 268:567-569, 1995.
8. Qabar, A., Derick, L., Lawler, J. and Dixit, V.M.: Thrombospondin 3 is a pentameric molecule held together by interchain disulfide linkage involving two cysteine residues. J. Biol. Chem. 270:12725-12729, 1995.
9. Tewari, M., Wolf, F.W., Seldin, M.F., O'Shea, K.S., Dixit, V.M. and L.A. Turka: Lymphoid expression and regulation of A20, an inhibitor of programmed cell death. J. Immunol. 1699-1706, 1995.
10. Beidler, D.R., Tewari, M., Friesen, P.D., Poirier, G. and Dixit, V.M.: The baculovirus p35 protein inhibits Fas and tumor necrosis factor-induced apoptosis. J. Biol Chem. 270:16526-16528, 1995.
11. Pandey, A., Duan, H. and Dixit, V.M.: Characterization of a novel src-like adapter protein that associates with the *eck* receptor tyrosine kinase. J. Biol. Chem. 270:19201-19204, 1995.
12. Tewari, M., Beidler, D.R. and Dixit, V.M.: CrmA-inhibitable cleavage of the 70-kDa protein component of the U1 small nuclear ribonucleoprotein during Fas- and TNF-induced apoptosis. J. Biol. Chem. 270:18738-18741, 1995.
13. Jäättelä, M., Benedict, M., Tewari, M., Shayman, J.A. and Dixit, V.M.: Bcl-x and Bcl-2 inhibit TNF and Fas-induced apoptosis and activation of phospholipase A_2 in breast carcinoma cells. Oncogene. 10:2297-2305, 1995.
14. Pandey, A., Duan, H., Di Fiore, P.O. and Dixit, V.M.: The *ret* receptor protein tyrosine kinase associates with the SH2 containing adapter protein Grb10. J. Biol. Chem. 270:21461-21463, 1995.
15. Rothe, M., Sarma, V., Dixit, V.M. and Goeddel, D.V.: TRAF2 mediates activation of NF-κB by TNF receptor 2 and CD40. Science. 269:1424, 1995.
16. Tewari, M., Telford, W.G., Miller, R.A. and Dixit. V.M.: CrmA, a poxvirus-encoded serpin, inhibits cytotoxic T-lymphocyte-mediated apoptosis. J. Biol. Chem. 270:22705, 1995.
17. Numa, F., Hirabayashi, K., Tsunaga, N., Kato, H., O'Rourke, K., Shao, H., Stechmann-Lebakken, C., Varani, J., Rapraeger, A. and Dixit, V.M.: Elevated levels of Syndecan-1 expression confer potent serum-dependent growth in human 293T cells. Cancer Research 55:4676-4680, 1995.
18. Duan, H., Chinnaiyan, A.M., Hudson, P.L., Wing, J.P., He, W.-W. and Dixit, V.M.: 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.
19. Chinnaiyan, A.M., Tepper, C.G., Seldin, M.F., O'Rourke, K., Kischkel, F.C., Hellbardt, S., Krammer, P.H., Peter, M.E. and Dixit, V.M.: FADD/MORT1 is a common mediator of CD95 (Fas/APO-1)- and TNF-receptor-induced apoptosis. J. Biol. Chem. 271:4961-496, 1996.

20. Chinnaiyan, A.M., Orth, K., O'Rourke, K., Duan, H., Poirier, G.G. and Dixit, V.M.: 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
21. Pandey, A., Liu, X., Di Fiore, P.P., Dixon, J.E. and Dixit, V.M.: Direct association between the Ret receptor tyrosine kinase and the SH2-containing adapter protein Grb7. J. Biol. Chem. 271:10607-10610, 1996.
22. 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 Dixit, V.M.: 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.
23. Orth, K., Chinnaiyan, A.M., Garg, M., Froelich, C.J. and Dixit, V.M.: 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.
24. Chinnaiyan, A.M., Hanna, W.L., Orth, K., Duan, H., Poirier, G.G., Froelich, C.J. and Dixit, V.M.: Cytotoxic T-cell-derived granzyme B activates the apoptotic protease ICE-LAP3. Current Biology 6:897-899, 1996.
25. Vincenz, C. and Dixit, V.M.: 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., In Press.
26. Orth, K., O'Rourke, K., Salvesen, G.S. and Dixit, V.M.: Molecular ordering of apoptotic mammalian CED-3/ICE-like proteases. J. Biol. Chem., In Press.
27. Chinnaiyan, A.M., O'Rourke, K., Yu, G.-L., Lyons, R.H., Garg,M., Duan, D.R., Xing,L., Gentz, R., Ni, J. and Dixit, V.M.: Signal transduction by DR3: A death domain-containing receptor related to TNFR-1 and CD95. Science 274:990-992, 1996.
28. Duan, H. and Dixit, V.M.: RAIDD, A novel death adaptor molecule. Nature, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Guest Lecturer, Anatomy & Cell Biology course #580, 1995.
B. Guest Lecturer, Biology course #421, 1995.
C. Guest Lecturer, Biology course #405, 1996.

MEDICAL SCHOOL/HOSPITALS:

A. 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.

PENDING:

A. Co-Principal Investigator (Dr. Roger C. Wiggins, Principal Investigator), University of Michigan Nephrology Center Grant, NIH/NIDDK, "Signaling in Glomerular and Tubular Injury and Development", August 1, 1997-July 31, 2002. Dr. Dressler - Project 6 "GDNF and Branching Morphogenesis in the Kidney" (10%). Direct costs/year (Project 6 only) approximately $50,000.

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.

REGIONAL AND NATIONAL:

A. None.

V. OTHER RELEVANT ACTIVITIES:

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

INVITED LECTURES/SEMINARS:

1. Invited speaker, Sixth International Workshop on Developmental Nephrology, Airlie, Virginia, August 23-25, 1995.
2. Invited speaker for Midwest Society for Pediatric Research, Chicago, Illinois, September 28-30, 1995.
3. Invited speaker, Necker's Seminars in Nephrology, Paris, France, May 6-9, 1996.
4. Invited speaker at Hybridon, Inc., Worcester, Massachusetts, May 21-22, 1996

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Gnarra, J.R. and Dressler, G.R.: Expression of Pax-2 in renal cell carcinoma and growth inhibition by antisense oligonucleotides. Cancer Res. 55:4092-4098, 1995.
2. Torres, M., Gomez-Pardo, E., Dressler, G.R. and Gruss, P.: Pax-2 controls multiple steps of urogenital development. Development: 121:4057-4065, 1995.

3. Phelps, D.E. and Dressler, G.R.: Identification of novel Pax-2 binding sites by chromatin precipitation. J. Biol. Chem. 271:7978-7985, 1996.
4. Lechner, M.S. and Dressler, G.R.: Mapping of PAX-2 transcription activation domains. J. Biol. Chem., In Press, 1996.
5. Vega, Q.C., Worby, C.D., Lechner, M.S., Dixon, J.E. and Dressler, G.R.: Glial derived neurotrophic factor is a ligand for RET and promotes kidney morphogenesis. Proc. Nat. Acad. Sci. USA, In Press, 1996.
6. Winyard, P.J.D., Risdon, R.A., Sams, V.R., Dressler, G.R. and Woolf, A.S.: The PAX2 transcription factor is expressed in cystic and hyperproliferative dysplastic epithelia in human kidney malformations. J. Clin. Invest., In Press.

ARTICLES SUBMITTED FOR PUBLICATION IN REFEREED JOURNALS:

None.

BOOKS/CHAPTERS IN BOOKS:

1. Dressler, G.R.:. Developmental control genes, in, Schlondorff, D. and Bonventre, J. (eds), Molecular Nephrology: Kidney Function in Health and Disease, Mercel Dekker, New York , pp. 1-13, 1995.
2. Dressler, G.R. (1996) Contrôle génétique du développement rénal, in, Funck-Brentano, J.L., Bach, J.F., Kreis, H. and Grunfield, J.P (eds), Actualités Néphrologiques Jean Hamburger, Médecine-Sciences, Paris, France, pp.1-18, 1996.
3. Dressler, G.R.: Genetic control of renal development, in, Advances in Nephrology, Mosby-Year Book, Inc., Chicago, Illinois, In Press, 1996.

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

1. Dressler, G.R.: Pax-2, kidney development, and oncogenesis. Medical and Pediatric Oncology, In Press, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Director, Ligand Assay Laboratory.

II. TEACHING ACTIVITIES:

A. Instructor for Pathology House Officers Laboratory Rotation.
B. Instructor for Nuclear Medicine Residents Laboratory Rotation.
C. 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, $130,000/yr., 1993-1998.
B. USPHS (NICHD) 5T32HD07048-18: Training Program in Reproductive Endocrinology, Co-Investigator, $149,898/yr., 1990-1995.

IV. SERVICE 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.

V. OTHER RELEVANT ACTIVITIES:

A. Executive Committee Member of the Clinical Ligand Assay Society, 1995-1996.

B. Chairman of Scientific Program (Roundtables) of the 1996 Annual Meeting of the Clinical Ligand Assay Society held in Los Angeles, California.

C. Roundtable Presentor; Annual Meeting 1996 Los Angeles, California, Clinical Ligand Assay Society. Estradiol Calibration, What's Right?

D. Residents Award Winner For Platform Presentation at the Annual Meeting of the American Society of Clinical Pathologists, Boston, Massachusetts, April, 1996. Henricks, W.H., England, B.G., Giacherio, D.A., Oesterling, J.E. and Wojno, K.J.: Free to total PSA ratio does not predict extraprostatic spread of prostatic adenocarcinoma. Am. J. Clin. Pathol. 105:494, 1996.

E. Best Poster Award at the 22nd Annual Meeting Clinical Ligand Assay Society, Los Angeles, California, May 8 - 11, 1996. Smart, J.B., Giacherio, D.A., Henricks, W.H. and England, B.G.: A comparison of five chemiluminescent immunoassays for TSH. J. Clin. Ligand Assay. 19:96, 1996.

F. Best Poster in Session Award at the The American Urologic Association Meeting, Orlando, Florida, May, 1996. Oesterling, J.E., Wojno, K.J., Vashi, A. and England, B.G.: A comparison of free to total PSA (F/T) ratio to total PSA for distinguishing benign prostatic hyperplasia (BPH) from prostate cancer (CaP) using the Abbott AxSYM System. J. Urol. 155:370A, 1196.

G. Invited Manuscript that will appear in Hormones, Health, and Behavior: A Developmental And Ecological Perspective, Panter-Brick, C. and Worthman, C. (eds), Cambridge: Cambridge University press. Flinn., M.V., Quinlan, M., Quinlan, R., Turner, M.T. and England, B.G.: Glucocorticoid stress response, immune function, and illness among children in a rural Caribbean village. Amer. J. Human Biol. 7:122, 1995.

H. Invited Manuscript that will appear in Human Nature, and will be reprinted in Naturalistic Studies of Male Endocrinology, Campbell, B. (ed),. Hawthorne, New York, Aldine Press. Flinn, M.V., Decker, S.D., Tedeschi, D., Turner, M.T., Quinlan, R., Baerwald, C. and England, B.G.: Life history variation Of male hormone profiles in a rural Caribbean village. Amer. J. Physical Anthropol. Supplement 19:89, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Benghuzzi, H.A. and England, B.G.: Long-term sustained delivery of androgens by means of TCPL devices and the effect on high-density lipoprotein in castrated rams. Biomed. Sciences Instrumentation (ISA): IEEE, Vol.31, pp. 165-170, 1995.
2. Benghuzzi, H.A., and England, B.G.: The effect of sustained delivery of danazol and antioxidants on lipoprotein profiles of adult female mice. Biomed. Sci. Instrumentation (ISA): IEEE, Vol.31, pp. 171-176, 1995
3. Bush, D., England, B., Tucci, M., Cason, Z., Lemos, L. and Benghuzzi, H.: The effect of TCPL sevices on tissue-implant interface using adult sheep as a model. Biomed. Sci. Instrumentation (ISA): IEEE, Vol.31, pp. 147-152, 19951-R.
4. Flinn, M.V. and England, B.G.: Childhood stress and family environment. Current Anthropology 36:854-866, 1995

5. Flinn, M.V., Quinlan, R.J., Turner, M.T., Decker, S.A. and England, B.G.: Male-female differences effects of parental absence on glucocorticoid stress response. Human Nature 7:1125-1162, 1996.

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

1. Flinn, M.V., Quinlan, M., Quinlan, R., Turner, M. and England, B.G.: Glucocorticoid stress respons immune function, and illness among children in a rural Caribbean village (abstract). Amer. J. Physic Anthropol. Supplement 20, 1995.
2. Flinn, M.V., Quinlan, M., Quinlan, R., Turner, M.T. and England, B.G.: Glucocorticoid stress respo immune function, and illness among children in a rural Caribbean village (abstract). Amer. J. Huma Biol. 7:122, 1995. (Invited Ms. to appear in Hormones, Health, and Behavior: A developmental and ecological perspective, C. Panter-Brick and C. Worthman (Eds.). Cambridge: Cambridge University Press.
3. Flinn, M.V., Decker, S.D., Tedeschi, D., Turner, M.T., Quinlan, R., Baerwald, C. and B.G. England, (1995). Life history variation of male hormone profiles in a rural Caribbean village (abstract). Amer Physical Anthropol. Supplement 19:89, 1995. (Invited Ms. to appear in Human Nature, and to be re in Naturalistic Studies of Male Endocrinology, B. Campbell (ed), Hawthorne, New York, Aldine Pre
4. Turner, M.T., Flinn, M.V. and England, B.G.: Mother-infant glucocorticoidstress response in a rural Caribbean village. Amer. J. Physical Anthropol. Supplement 20, 1995
5. Benghuzzi, H.A., Bajpai, P.K., and England, B.: Morphological changes of male reproductive organ during sustained delivery of dihydrotestosterone and estradiol by biocompatible and biodegradable c implants. Paper presented at the Tenth Annual Scientific Session of the Academy of Surgical Resea September 22-24, 1994, Orlando, Florida, Published in J. Invest. Surg.. 7:p. 342, 1995.
6. Benghuzzi, H. and England, B.G.: TCP devices and sustained release of estradiol plus progesterone adult female rats. P3-313 10th International Congress Of Endocrinology June 12-15, 1996 Moscone Convention Center San Francisco, California.
7. Benghuzzi, H. and England, B.G.: Oral Presentation #1 Scanning Microscopoy International. May 1 1996, Hyatt Regency Hotel, Bethesda, Maryland.
8. Benghuzzi, H. and England, B.G.: Oral Presentation #2 Scanning Microscopoy International. May 1 1996 Hyatt Regency Hotel, Bethesda, Maryland.
9. Benghuzzi, H. and England, B.G.: TCPL Delivery System: The effect of various testosterone concentrations using adult castrated rams, 5th World Biomaterials Congress, Toronto, Ontario Canac 28 - June 2, 1996, Abstract # 920.
10. Benghuzzi, H. and England, B.G.: TCPL steroid delivery system and the analysis of fibrous tissue u adult rams as a model, 5th World Biomaterials Congress, Toronto, Ontario Canada May 28 - June 2, Abstract # 919.
11. Henricks, W.H., England, B.G., Giacherio, D.A., Oesterling, J.E. and Wojno, K.J.: Free to total PSA does not predict extraprostatic spread of prostatic adenocarcinoma. Am. J. Clin. Pathol. 105:494, 1 Annual Meeting of the American Society of Clinical Pathologists, Boston, Massachusetts, April, 199 **Residents Award Winner Platform Presentation**
12 Smart, J.B., Giacherio, D.A., Henricks, W.H. and England, B.G.: A comparison of five chemilumine immunoassays for TSH. J. Clin. Ligand Assay 19:96, 1996. 22nd Annual Meeting Clinical Ligand Society, Los Angeles, California, May 8-11, 1996. **Best Poster Award.**

13. Moyad, M.A., Oesterling, J.E. and England, B.G.: An evaluation of the IMx PSA immunoassay system: A complete lot-to-lot analysis in thel low range, 22nd Annual Meeting Clinical Ligand Assay Society, Los Angeles, California, May 8-11, 1996.
14. Henricks,W.H., Giacherio, D.A., Oesterling, J.E., Wojno, K.J. and England, B.G.: Performance of free/total PSA as measured by two investigational immunoassays in predicting the presence of prostatic adenocarcinoma. J. Clin. Ligand Assay 19:94, 1996. 22nd Annual Meeting Clinical Ligand Assay Society, Los Angeles, California, May 8-11, 1996.
15. Henricks, W.H., England, B.G., Giacherio, D.A., Oesterling, J.E. and Wojno, K.J.: A comparison of serum levels of total prostate specific antigen (PSA) and the free to total PSA ratio in detecting prostatic adenocarcinoma. Clin. Chem. 42:S263, 1996, 22nd Annual Meeting Clinical Ligand Assay Society, Los Angeles, California, May 8-11, 1996.
16. Henricks, W.H., Giacherio, D.A., Oesterling, J.E., Wojno, K.J. and England, B.G.: Extraglandular spread of prostatic adenocarcinoma: can it be predicted by free to total prostate specific antigen (PSA) ratio? J. Clin. Ligand Assay 19:94, 1996, 22nd Annual Meeting Clinical Ligand Assay Society, Los Angeles, California, May 8-11, 1996.
17. Oesterling, J.E., Wojno, K.J., Vashi, A. and England, B.E.: A comparison of free to total PSA (F/T) ratio to total PSA for distinguishing benign prostatic hyperplasia (BPH) from prostate cancer (CaP) using the Abbott AxSYM system. Presented at The American Urologic Association Meeting, Orlando, Florida, May, 1996. J. Urol. 155:370A, 1196. **Best Poster in Session Award**
18. Henricks, W.H., England, B.G., Giacherio, D.A., Oesterling, J.E. and Wojno, K.J.: Free to total PSA ratio does not predict extraprostatic spread of prostatic adenocarcinoma. Presented at The American Urologic Association Meeting, Orlando, Florida, May, 1996. J. Urol. 155:369A, 1996.
19. Richardson, T.D., Wojno, K.J., Liang, L.W., Giacherio, D.A., England, B.G., Henricks, W.H., Schork, A. and Osterling, J.E.: Serum half life determination of free prostate specific antigen. Presented at The American Urologic Association Meeting, Orlando, Florida, May, 1996. J. Urol. 155:698A, 1996.
20. England, B.G., Giacherio, D.G., Henricks, W.H. and Smart, J.B.: A comparison of five chemiluminescence immunoassays for thyroid stimulating hormone (TSH): ACS-TSH andACS-TSH3, access-TSH, Nichols-TSH3 and immulite-TSH3, The University of Michigan Medical Center, Ann Arbor, Michigan, ICCC MEETING July 8-12, 1996, London, England,

ARTICLES SUBMITTED FOR PUBLICATION:

1. Flinn, M.V. and England, B.G.: Family composition and childhood stress. Current Anthropology, In Press, 1996.
2. Flinn, M.V. and England, B.G.: The social economics of childhood glucocorticoid stress response and health. American Journal of Physical Anthropology, Submitted.
3. Flinn, M.V. and England, B.G.: Health condition and glucocorticoid stress response among children in a rural Dominican village. . Proc. Nat.l Acad. Sci, USA, Submitted.

MANUSCRIPTS IN PREPARATION:

1. Vashi, A.R., Wojno, K.J., England, B.G., Vessella, R.L., Lange P.H., Wright, G, Schellhammer, P.F., Weigand, R., Olson, R.M.,. Dowell, B.L. and Oesterling J.E.: Determination of the "reflex range" and

appropriate cutpoints for percent free PSA in 413 men referred for prostatic evaluation using the AxS system. In Preparation.

2. Seamus, A.D., Flinn, M.V. and England, B.G.: Salivary cortisol associates negatively with peer-rate social status among Dominican men. In Preparation.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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 (three).
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. Chairman's Advisory Committee.
B. Coordinator - Educational Programs.
C. Department ACAPT Committee.
D. Human Resource Committee.
E. Research Space Advisory Committee.
F. Faculty Sexual Harassment Contact Person.

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. NIH Site Visit, SCOR: Boogaloosa Heart Study, Washington, D.C., 1996.
B. AHA of Michigan, Grant Review Committee, 1995.
C. 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. Crokett-Torabi, E., Smith, C.W. and Fantone, J.C.: Activation of human neutrophils through L-selectin and Mac-1 molecules. J. Immunol. 154:2291-2302, 1995.
2. Brieland, J.K., Remick, D.G., Freeman, P.T., Hurley, M.C., Fantone, J.C. and Englebery, M.C.: In vivo regulation of replicative legionella pneumophila lung infection by endogenous tumor necrosis factor and nitric oxide. Infection and Immunity. 63:3253-3258, 1995.

3. Brieland, J.K., Flory, C.M., Jones, M.L., Miller, G.R., Remick, D.G., Warren, J.S. and Fantone, J.C.: Regulation of monocyte chemoattractant protein-1 gene expression and secretion in rat pulmonary alveolar macrophages by lipopolysaccharide tumor necrosis factor-α, and interleukin-1β. Am. J. Resp. Cell 12:104-109, 1995.
4. Crockett-Torabi, E. and Fantone, J.C.: The Selectins: Insight into Selectin Induced Intracellular Signaling in Leukocytes. Immunol Res. 14:237-251, 1995.
5. Robins, L.s., Fantone, J.C., Oh, M.S., Alexander, G.L., Shlafer, M. and Davis, W.K.: The effect of pass/fail grading and weekly quizes on first year edical students' performances and satisfaction. Acad. Med. 70:327-329, 1995.

BOOKS/CHAPETERS IN BOOKS:

1. Brieland, J.K. and Fantone, J.C.: Neutrophils and pulmonary fibrosis, in, Phan, S.H. and Thrall, R. (eds), Pulmonary Fibrosis. Lung Biology in Health and Disease, Volume 80, Marcel Dekker, New York, New York, pp. 383-404, 1995.
2. Crockett-Torabi, E. and Fantone, J.C.: Signal transduction and leukocyte adhesion molecules. in, Ward, P.A. and Fantone, J.D. (eds), Adhesion Molecules and the Lung, Lung Biology in Health and Disease, Volume 89, Marcel Dekker, New York, New York, New York, pp. 63-98, 1996..
3. Ward, P.A. and Fantone, J.C. (eds): Adhesion molecules and the lung; Lung Biology in Health and Disease, Marcel Dekker, N.Y., 1996. Mol. Biol. 1995; 12 (1): 104-109, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Rotations, July (2/4), August (1/4) September (2/4), November (2/4), December (2/4), January (2/4), February (2/4),March (2/4), June (2/4).
B. Estrogen and progesterone receptor analysis of paraffin embedded breast carcinomas by image analysis - 115 samples.
C. Ophthalmic Pathology Service, September 1995 - present.

II. TEACHING ACTIVITIES:

A. Pathology 600 Lectures:
   1. Obstructive Lung Disease - November 15, 1995.
   2. Neoplasms - November 17, 1994.
   3. Pathology of ARDS - November 21, 1995.
   4. Tissue Reactions to Infectious Agents - November 16, 1995.
   5. Laboratory Instructor, September, 1995 - May, 1996.
   6. Student question and answer sessions, afternoons, October, 1995 - May, 1996.
B. Pathology 630:
   1. Respiratory Disease I - October 23, 1995.
   2. Respiratory Disease II - November 3, 1995.
C. Residency Training:
   1. Diseases of the Chest I - October 31, 1995.
   2. Diseases of the Chest II - November 21, 1995.
   3. Diseases of the Chest III - November 28, 1995.
   4. Surgical Pathology Consultant's Conference, December, 1995; June, 1996.
D. Inteflex 211:
   1. The Pathologist as Physician - September 26, 1995.
   2. The Physician as Scientist - November 28, 1995.
E. Other educational activities:
   1. M4 student elective mentor, August 1995, February, 1996, March 1996.
   2. Center for Research on Learning and Teaching Workshop: Techniques for enhancing student comprehension of material, February 7, 1996.
   3. Member, M-2 Respiratory Sequence Committee, 1995-1996.
   4. Course Director, M-4 Student Pathology Clerkships.
   5. Participant, Thoracic Surgery Residents Core Curriculum, 1995 - 1996.
   6. Opthalmic Pathology, AFIP Course, August, 1995.

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. Monoclonal Antibodies to Bladder Tumor Antigens, H. Barton Grossman, M.D. (Principal Investigator), Andrew Flint, M.D. (Co-Investigator).
C. National Cancer Institute Study Section on Lung Cancer November 12 -14, 1995.

PROJECTS UNDER STUDY:

A. Analysis of TGF-β and its binding protein, decorin, in lung tissue of ARDS patients.
B. Histologic predictors of obliterative bronchiolitis in lung transplant patients.
C. Histologic prognostic indicators of survival in ARDS patients treated with ECMO.
D. Correlation of TGF-β levels in BAL specimens with histochemical demonstration of TGF-β in lung tissue sections
E. Ploidy analysis and P53 expression in Barrett's esophagus.
F. Pathologic effects of perfluorocarbon liquid ventilation of ARDS patients.
G. The clinical usefulness of the abnormal nondiagnostic lung biopsy sample.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interviewed House Officer Candidates (October, 1995-January, 1996).
B. Member, Admissions Committee of the University of Michigan Medical School, 1995 - present

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Reviewer, Human Pathology.
B. Reviewer, Annals of Thoracic Surgery

INVITED LECTURES/SEMINARS:

1. Co-Director, Short Course on Closed Lung Biopsy Interpretation, USCAP meeting, Washington, D. C., March, 1996.

VI. PUBLICATIONS:

1. Pickhardt, P.J., Kazerooni, E.A, and Flint, A.: Diagnosis of lymphangioleiomyomatosis by CT-guided retroperitoneal lymph node biopsy. J Thoracic Imaging, Accepted.
2. Keane, M.P., Meaney, J.F.M., Kazerooni, E.A., Whyte, R.I., Flint, A. and Martinez, F.J.: Accessory cardiac bronchus presenting with haemoptysis. Thorax, Accepted.
3. Lee, C., Liebert, M., Washington, R., Wedemeyer, G., Flint, A. and Grossman, H.B.: Expression of MUC1 antigens in human prostate cancer. J Urol., Accepted.

SUBMITTED PUBLICATIONS:

1. DiGiovine, B., Lynch,, III, J.P., Martinez, F.J., Flint, A., Whyte, R.I., Iannettoni MD, et al: Bronchoalveolar lavage neutrophilia is associated with obliterative bronchiolitis after lung transplantation: Role of interleukin- 8. J. Immunology.
2. Brown, R.S., Leung, J.Y., Flint, A. and Wahl, R.L.: Expression of glucose transporters in human lung cancer. Can. Res.
3. DiGiovine, B., Lynch, III, J.P., Martinez, F.J., Flint, A., Whyte, R.I., Iannettoni, M.I., et al: Neutrophilic alveolitis inobliterative bronchiolitis after lung transplantation: role of interleukin-8. J. Clin. Invest.
4. Flint, A., Lynch, III, J.P., Martinez, F.J. and Whyte, R.I.: Pulmonary smooth muscle proliferation occuring after lung transplantation. Chest.
5. Bruch, L.A., Flint, A. and Hirschl, R.B.: Pulmonary pathology of patients treated with perfluorocarbon partial liquid ventilation. Modern Pathol.

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

1. Gay, S.E., Kazerooni, E.A., Gross, B., Hariharan, K., Spizarny, D., Cascade, P.N., Popovich, J., Hyzy, R., Major, M., Flint, A., Whyte, R.I., Toews, G.B., Lynch, III, J.P. and Martinez: High resolution computed tomography (HRCT) as predictor of response and/or death in idiopathic pulmonary fibrosis. Chest.
2. Michae,l C.W. and Flint, A.: Cytologic features of Wegener's granulomatosis. Acta Cytol.
3. DiGiovine, B., Lynch, J.P., Martinez, F.J., Flint, A., Whyte, R.I., Iannettoni, M.D., et al: Interleukin-1 receptor antagonist is elevated in lung transplant recipients with obliterative bronchiolitis. Chest.
4. Kazerooni, E.A., Greenberger, M., Martinez, F.J., Flint, A., Lynch, J.P. snf Toews, G.B.: Composite clinical, radiographic and physiologic score in the initial evaluation of idiopathic pulmonary fibrosis: Contribution of thin-section CT. Radiology.
5. Brown, R.S., Leung, J.Y., Zasadny, K.R., Flint, A. and Wahl, R.L.: Relationship between SUV-lean and Glut-1 expression in untreated human lung and breast cancer. Society of Nuclear Medicine.
6. Kazerooni, E.A., Martinez, F.J., Flint, A., Cascade, P.N., Gross, B.H. and Lynch, J.P.: HRCT at 10 mm increments versus 3-level HRCT in idiopathic pulmonary fibrosis: correlation with pathologic scoring. Radiology.

7. Kazerooni, E.A., Martinez, F.J., Flint, A., Gross, B.H., Cascade, P.N. and Toews, G.B.: Correlations of HRCT and pathologic scoring systems for idiopathic pulmonary fibrosis. Radiology.
8. DiGiovine, B., Lynch, J.P., Martinez, F.J., Flint, A., et al: IL-8 is elevated in lung transplant recipients with obliterative brochiolitis. Amer. Thorac. Soc.
9. Greenberger, M., Martinez, F.J., Kazerooni, E., Hampton, J., Popovich, J., Hyzy, R., Major, M., Flint, A., et al: Composite clinical, radiographic and physiologic (CRP) score in the initial evaluation of patients with IPF: the contribution of high resolution CT Scan. Amer. Thorac. Soc.
10. Gay, S.E., Kazerooni, E., Gross, B., Sizarny, D., Hampton, J., Martinez, F., Popovich, J., Hyzy, R., Major, M., Flint, A., et al: High resolution chest CT as a predictor of response to high dose corticosteroid therapy in IPF. Amer. Thorac. Soc.
11. Gay, S.E., Martinez, F., Kazerooni, E., Gross, B., Hampton, J., Flint, A., et al.: HRCT, CRP and pathologic fibrosis score as predictors of mortality in IPF. Amer. Thorac. Soc.
12. Greenberger, M.J., Kazerooni, E., Gross, B., Hampton, J., Spizarny, D., Popovich, J., Hyzy, R., Major, M., Curtis, J., Flint, A., et al.: High resolution correlates with pathologic scoring systems in idiopathic pulmonary fibrosis. Amer. Thorac. Soc.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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. Teaching and supervision of Walter Henricks, fellow in Chemical Pathology and Informatics.

MEDICAL SCHOOL/HOSPITALS:

A. Program Director of the Fourteenth Annual Symposium on Automated Information Management in the Clinical Laboratory (AIMCL) at the Towsley and Power Center, Ann Arbor, Michigan, June 5-7, 1995. The symposium attracted 276 registrants and 37 system vendors.
B. Two hours of programming from AIMCL were transmitted on June 5 as a realtime audioconference to 53 pathology training programs in the U.S. and Canada. Two additional hours of programming were transmitted on June 6 as an audioconference to laboratory managers located at 70 sites around the country in collaboration with the Clinical Laboratory Management Association.
C. Two additional standalone audioconferences were developed and offered to pathology training programs in the U.S. and Canada on October 23, 1995, and March 12, 1996. Both of these audioconferences attracted a registration of about 45 sites.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. The major research activity underway at the present time is the development and analysis of a virtual clinical laboratory and virtual department of pathology which consists of a set of teaching and research activities that are information technology enabled and span

distance barriers. The prime example of this is a relationship that is developing with the pathology informatics program in the Department of Pathology, University of Pittsburgh Medical Center, that is being referred to as the Pathology Information Exchange (PIX).

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), The University of Michigan, 1991-1998.

REGIONAL AND NATIONAL:

A. College of American Pathologists (CAP) Committee on Informatics.
B. Guest Editor of a Pathology Patterns (AJCP) supplement on informatics published in April, 1996.
C. Editorial Advisory Board, Clinical Laboratory Management Review.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. "Leveraging the Laboratory Database for Strategic Advantage," a lecture delivered at the annual meeting of the Clinical Laboratory Management Association, Minneapolis, Minnesota, August 29, 1995.
2. "(1) A Modus Operandi for Healthcare CIOs and Pathologists; and (2) The Politics of Managing a Hospital LIS," two lectures presented at the Fall Meeting of the College of American Pathologists, New Orleans, Louisiana, September 17-18, 1995.
3. "Delivering Continuing Medical Education to Heathcare Professionals Via the Internet and Web," a lecture delivered as part of a symposium sponsored by the Healthcare Advisory Council, the International Quality and Productivity Center, Nashville, Tennessee, September 27, 1995.
4. "The Future of Laboratory Information Systems: An Urgent Mandate for Managed Care," a lecture delivered at the Laboratory Institute, Washington G2 Reports, Washington, D.C., September 28, 1995.

5. "LISs and Managed Care: A Strategic and Management Overview," a teleconference lecture presented under the auspices of the Virtual Department of Pathology, University of Michigan Medical School, Ann Arbor, Michigan, October 23, 1995.
6. "Healthcare Computing in the U.S.: Systems and Trends," A lecture presented at the International Conference on Computing in the Clinical Laboratory, Barcelona (Sitges), Spain, November 4, 1995.
7. "The Community Health Information Network (CHIN): Managing Healthcare and Laboratory Information on a Regional Basis," an ASCP audioconference presented to about 60 sites, March 19, 1996.
8. "Phlebotomy and Managed Care," lecture presented at a conference entitled "The Phlebotomy Team: Technical and Management Perspectives," Ann Arbor, Michigan, April 19, 1996.
9. "Integrating Medical Information in the 1990s," a workshop presented at the ASCP Spring Meeting, Boston, Massachusetts, April 20, 1996.
10. "A Modus Operandi for Healthcare Organization Chief Information Officers and Pathologists," a lecture presented at the CAP Spring Meeting, Boston, Massachusetts, April 21, 1996.
11. "Defining the Laboratory Information Space as Healthcare Goes Regional: A Strategic Viewpoint," a lecture presented at the 14th annual Symposium on Automated Information Management in the Clinical Laboratories (AIMCL), Ann Arbor, Michigan, June 5-7, 1996.
12. "Pathology Informatics and the Evolution of the Clinical Laboratory," an audioconference for approximately 50 sites sponsored by the Clinical Laboratory Management Association and the Catholic University of America, June 19, 1996.

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 1995 - 30 JUNE 1996

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

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Medical School:
   1. Developed Chemistry Laboratory Presentations for the M4 Laboratory Medicine Elective.
B. Pathology House Officers:
   1. Lecturer, Clinical Pathology Rounds lecture series.
   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. Doctoral Thesis Committee for Aaron Smith, Chemistry Department, University of Michigan.

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 immuno-rate assays for the determination of phenobarbital and carbamazepine on the Ektachem 250 analyzer.
D. Evaluation of the interfernce in routine serum chemistry analyses from hemoglobin based blood substitutes.
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.

REGIONAL AND NATIONAL:

A. Executive Committee, Michigan Section AACC.
B. Chair, Program Committee, Michigan Section AACC.
C. Lipids and Lipoproteins Division Member, AACC
D. Consultant, Parke-Davis.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "Evaluation of the Ektachem Immuno-Rate Assays for Digoxin and Phenytoin," AACC National Meeting, Anaheim California, July, 1995.
2. "Point of Care Testing: The Future with Immunoassays," CLAS National Meeting, Los Angeles, California, May, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Annesley, T.A., Hunter, B.C. and Giacherio, D.A.: Stability of Tacrolimus (FK506) and Cyclosporin G in whole blood. Therapeutic Drug Monitoring. 17:361-365, 1995.
2. Bleske, B.E., Rice, T.L., Warren, E.W., Giacherio, D.A., Gilligan, L.J., Massey, K.D. and Tait, A.R.: Effect of vehicle on the nasal absorption of epinephrine during cardiopulmonary resuscitation. Am. J. Emerg. Med. 14:133-138, 1996.

ARTICLES SUBMITTED FOR PUBLICATION:

1. 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. Submitted for Publication.
2. 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. J. Urology, Submitted.

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

1. Henricks, W.H., England, B.G., Giacherio, D.A., Oesterling, J.E. and Wojno, K.J.: Free to total PSA ratio does not predict extraprostatic spread of prostatic adenocarcinoma. Am. J. Clin. Pathol. 105:494, 1996.
2. Smart, J.B., Giacherio, D.A., Henricks, W.H. and England, B.G.: A comparison of five chemiluminescent immunoassays for TSH. J. Clin. Ligand Assay. 19:96, 1996.
3. Henricks, W.H., Giacherio, D.A., Oesterling, J.E., Wojno, K.J. and England, B.G.: Performance of free/total PSA as measured by two investigational immunoassays in predicting the presence of prostatic adenocarcinoma. J.Clin. Ligand Assay. 19:94, 1996.
4. Henricks, W.H., Giacherio, D.A., Oesterling, J.E., Wojno, K.J. and England, B.E.: Extraglandular spread of prostatic adenocarcinoma: Can it be predicted by free to total prostate specific antigen (PSA) ratio? J. Clin. Ligand Assay. 19:94, 1996.
5. Richardson, T.D., Wojno, K.J., Liang, L.W., Giacherio, D.G., England, B.G., Henricks, W.H., Schork, A. and Oesterling, J.E.: Serum half life determination of free prostate specific antigen. J. Urol. 155:698A, 1996.
6. Henricks, W.H., England, B.G., Giacherio, D.A., Oesterling, J.E. and Wojno, K.J.: A comparison of serum levels of total prostate specific antigen (PSA) and the free to total PSA ratio in detecting prostatic adenocarcinoma. Clin. Chem. 42:S263, 1996.
7. Henricks, W.H., England, B.G, Giacherio, D.A., Oesterling, J.E. and Wojno, K.J.: Free to total PSA ratio does not predict extraprostatic spread of prostatic adenocarcinoma. J. Urol . 155:369A, 1996.
8. Davenport, R.D. and Giacherio, D.G.: Removal of potassium from red blood cells and whole blood by ion exchange. AABB National Meeting, 1996.
9. O'Reilly, M.O., Shoff, B.A., Wahr, J., Giacherio, D.A. and Tremper, K.: Bedside monitoring of PT and aPTT in patients undergoing liver transplantation.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Pathology Lab Section for M-1 students, twelve contact hours, Winter term 1996.

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. Consultant to Scientific Advisory Council, The Humane Society of the United States.

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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.
E. Dermatopathology - one month.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. Component II Endocrine Sequence - two lectures on Endocrine Pathology.
   2. Endocrine Pathology Laboratories - preparation of course materials.
B. House Officers:
   1. General Surgical Pathology - four 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.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, University of Michigan Phoenix Project, "Differential Gene Expression in Adrenal Cortical Neoplasms, $6,000.

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, "Thyroglobulin Expression in Anaplastic Thyroid Carcinoma."
D. Principal Investigator, "Proliferation Studies of Papillary Thyroid Carcinoma During Pregnancy."
E. Co-Investigator, "Pathology of Multiple Endocrine Neoplasia, Type 1," with Dr. Norman Thompson, Department of Surgery.
F. Co-Investigator, "Histologic-Radiologic Correlation of Pulmonary Metastases of Papillary Thyroid Carcinoma," with Dr. James Sissons, Department of Internal Medicine.
G. Co-Investigator, "Pitfalls in the Surgical Treatment of Sporadic Insulinoma," with Dr. Norman Thompson, Department of Surgery.
H. Co-Investigator, "Preclinical Studies on New Drugs for Adrenal Cancer," with Dr. David E. Schteingart, Department of Internal Medicine.
I. Co-Investigator, "Molecular Genetic Analysis of an Unusual Case of Adrenal Cortical Carcinoma," with Dr. David E. Schteingart, Department of Internal Medicine.
J. Co-Investigator, "CD95 Expression in Graves Disease and Thyroiditis," with Dr. James Baker, Department of Internal Medicine.
K. Co-Investigator, "Somatostatin Receptor Analysis in Merkel Cell Carcinoma," with Dr. Rick Kloos, Department of Internal Medicine, University of Alabama, Birmingham.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. House Officer Candidate Interviews.
B. Faculty Candidate Interviews.

REGIONAL AND NATIONAL:

A. Consultant, U.S. Surgical Corporation.
B. Co-Chair of Proffered Endocrine Papers, 1995 United States and Canadian Academy of Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Workshop entitled, "Practical Endocrine Pathology," American Society of Clinical Pathologists (ASCP), Spring Meeting, Boston, Massachusetts.

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. and Spaulding, R.T.: Treatment of micronodular pulmonary metastases from papillary thyroid cancer treated with 13-I. Cancer, In Press, 1996.
2. Korobkin, M., Giordano, T.J., Brodeur, F.J., Francis, I.R., Spiegelman, E.S., Qjint, L.E., Dunnick, N.R., Heiken, J.P. and Wang, H.H.: The relationship between histologic lipid and CT/MR findings in adrenal adenomas. Radiology 200:743-747, 1996.
3. Giordano, T.J., Medeiros, L.J., Monterroso, V., Linehan, W.M. and Merino, M.J.: Immunohistochemical analysis of transthyretin (prealbumin) in renal cell carcinoma and other neoplasms. Int. J. Surg. Pathology, In Press, 1996.
4. Panico, L., D'Antonio, Salvatore, G., Mezza, E., Tortora, G., De Laurentiis, M., De Placido, S., Giordano, T., Merino, M., Salomon, D.S., Gullick, W.J., Pettinato, G., Schnitt, S.J., Bianco, A.R. and Ciardiello, F.: Differential immunohistochemical detection of transforming growth factor a, amphiregulin and cripto in human normal and malignant breast tissues. Int. J. Cancer 65:51-56, 1996.

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, N.W., 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.

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

1. Few, J., Thompson, N.W., Angelos, P., Simeone, D., Giordano, T. and Reeve, T.: Riedel's thyroiditis: Treatment with tamoxifen. Presentated at the 1996 Conference of the American Association of Endocrine Surgeons.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

A. Patterns of growth factor/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.

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. Dean's Diversity Advisory Group.
D. Dean's Faculty Affairs Advisory Group.

REGIONAL AND NATIONAL:

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

INVITED LECTURES/SEMINARS:

1. "Cell Proliferation and Collagen Gene Expression in Human Atherosclerosis," talk given to Gladstone Institute of Cardiovascular Disease, San Francisco, California, July 24, 1995.
2. "Cell Proliferation and Collagen Gene Expression in Human Atherosclerosis," talk given to Texas Biotechnical Institute, Houston, Texas, October 13, 1995.
3. "Cell Proliferation and Collagen Gene Expression in Human Atherosclerosis," talk given to Vascular Medicine Program, the University of Michigan, Ann Arbor, Michigan, February 6, 1996.
4. "Cell Proliferation and Collagen Gene Expression in Human Atherosclerosis," talk given to Department of Surgery, at the University of Arizona, Tucson, Arizona, March 8, 1996.
5 "The Growth of Human Atherosclerosis: Cell Proliferation and Collagen Synthesis," U.S. and Canadian Association of Pathologists meeting (Society for Cardiovascular Pathology), Washington, D.C., March 24, 1996.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Rekhter, M.D. and Gordon, D.: Active proliferation of different cell types, including lymphocytes in human atherosclerotic plaques. Am. J. Pathol. 147:668-677, 1995.
2. Kolpakov, V., Gordon, D. and Kulik, T.J.: Nitric oxide-generating compounds inhibit total protein and collagen synthesis in cultured vascular smooth muscle cells. Circ. Res. 76:305-309, 1995.

3. Pompili, V.J., Gordon, D., San, H., Yang, Z., Muller, D.W.M., Nabel, G.J. and Nabel, E.G.: Expression and function of a recombinant PDGF B gene in porcine arteries. Arterioscler. Thromb. Vasc. Biol. 15:2254-2264, 1995.
4. Kolpakov, V., Rekhter, M.D., Gordon, D., Wang, W.H. and Kulik, T.J.: Effect of mechanical force on growth and matrix protein synthesis in the in vitro pulmonary artery: Analysis of the role of individual cell types. Circ Res. 77:823-831, 1995.
5. Thackray, B.D., Burns, D.H., Fergurson, M.S., Gordon, D., Beach, K.W., Hatsukami, T., Detmer, P.R., Primozich, J.F. and Strandness, D.E.. A new method of studying plaque morphology. Amer. J. Cardiac Imaging. 9:149-156, 1995.
6. Kang, S., Kim, K.J., Griffiths, C.E.M., Wong, T.Y., Talwar, H.S., Fisher, G.J., Gordon, D., Hamilton, T.A., Ellis, C.N. and Voorhees, J.J.: Topical tretinon (retinoic acid) improves early stretch marks. Arch. Dermatol. 132:519-526, 1996.
7. Schwartz, S.M., Gordon, D., Mosca, R.S., Bove, E.L., Heidelberger, K.P. and Kulik, T.J.: Collagen content in normal, pressure and pressure-volume overloaded developing human hearts. Amer. J. Cardiol. 77:734-738, 1996.
8. Simari, R.D., San, H., Rekhter, M., Ohno, T., Gordon, D., Nabel, G.J. and Nabel, E.G.: Regulation of cellular proliferation and intimal formation following balloon injury in atherosclerotic rabbit arteries. J Clin. Invest. 98:225-235, 1996.
9. Yang, Z.Y., Simari, R.D., Perkins, N.D., San, H., Gordon, D., Nabel, G.J. and Nabel, E.G.: Role of the p21 cyclin-dependent kinase inhibitor in limiting intimal cell proliferation in response to arterial injury. Proc. Natl. Acad. Sci. USA 93:7905-7910, 1996.
10. Sarkar, R., Meinberg, E.G., Stanley, J.C., Gordon, D. and Webb, R.C.: Nitric oxide reversibly inhibits the migration of cultured vascular smooth muscle cells. Circ Res 78:225-230, 1996.
11. Rekhter, M.D., O'Brien, E., Schwartz, S.M., Simpson, J.B. and Gordon, D.: Collagen I gene expression occurs in specific regions of the arterial intima in human coronary atherosclerosis. Accepted, in Cardiovascular Research, 1996.
12. Sarkar, R., Gordon, D., Stanley, J.C. and Web, R.C.: Cell cycle effects of nitric oxide on vascular smooth muscle cells, Submitted.
13. Sarkar, R., Gordon, D., Stanley, J.C. and Webb, R.C.: Dual cycle-specific mechanisms mediate the antimitogenic effects of nitric oxide in vascular smooth muscle cells, Submitted.
14. Sarkar, R., Gordon, D., Stanley, J.C. and Webb, R.C.: Cell cycle effects of nitric oxide on vascular smooth muscle cells. Amer. J. of Path., Submitted.

BOOKS AND CHAPTERS IN BOOKS:

1. Gordon, D. and Nable, E.G.: Growth factors as inducers of neointimal hyperplasia, in, Orosz, Sedmak and Ferguson (eds.), Transplant Vascular Sclerosis, 1995.
2. Kohler, T. and Gordon, D.: Cerebrovascular atherosclerosis, in, Zierler (ed.), Surgical Management of Cerebrovascular Disease, 1995.
3. Gordon, D.: Human carotid artery atherosclerosis, in, Ernst and Stanley (eds.), Current Therapy in Vascular Surgery, 1995.
4. Gordon, D.: Transplant arteriosclerosis, in, Ross and Topol (eds.). Atherosclerosis and Coronary Artery Disease, 1996.

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

1. Yang, Z., Perkins, N.D., Simari, R.D., San, H., Gordon, D., Nabel, G.J. and Nabel, E.G.: p21 cyclin-dependent kinase inhibitor inhibits intimal lesions through cell cycle arrest and differentiation of vascular cells. Circulation, 68th Scientific Session of the American Heart Association 92:2381, October, 1995.

2. Simari, R.D,, San, H., Ohno, T., Gordon, D., Nabel, G.J. and Nabel, E.G.: Regulation of cellular proliferation and intimal formation following balloon injury in hyperlipidemic rabbit arteries. Circulation, 68th Scientific Session of the American Heart Association 92:2393, October, 1995.
3. Rekhter, M.D., Simari, R.D., Work, C., Nabel, E.G. and Gordon, D.: Adenovirus-mediated gene transfer into human coronary arteries and rabbit aorta. Circulation, 68th Scientific Session of the American Heart Association 92:2397, October, 1995.
4. Shah, N., Rekhter, M.D., Andreeva, E.R. and Orekhov, A.N.: Fibrin is associated with arterial mesenchymal cell proliferation in human aortas: Implications for developments and progression of atherosclerosis. FASEB J., 809, June, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. General surgical pathology - four months.
B. Gastrointestinal and hepatic pathology consultation services - six months.
C. Liver transplant pathology - six months.
D. Dermatopathology sign-out - eight days

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, 1.5 hour full class lecture (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, 1995.
   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 - 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) ÒDDT and Related Compounds and Pancreas CancerÓ, 5% salry support, David H. Garabrant, M..D. Principal investigator.

PROJECTS UNDER STUDY:

A. Focal active colitis study with Rob Stern and Jeff Barnett from the Division of Gastroenterology.
B. Pancreatic carcinoma study with Margaret Anderson and Henry Appelman.
C. Study of COX-2 expression in H. pylori gastritis with Division of Rheumatology.
D. Study of recurrent hepatitis C in liver transplant biopsies with Tom Frank, and Bob Merion from the Division of Transplantation Surgery.
E. Study of mini-microabscess disease in liver transplant patients with Henry Appelman, Tom Frank, and Grahame Macdonald, Division of Gastroenterology.
F. Study of liver transplant rejection with Keith Henley, Division of Gastroenterology.
G. Study of MALT lymphomas arising in Helicobacter pylori gastritis with Eric Hsi and Charlie Ross.
H. Study of LOH of the DCC gene in Dukes B colon cancers with Richard Boland and John Carruthers, Division of Gastroenterology, UC San Diego.
I. Study of colorectal carcinoma metastases with collaborators at Ohio State University.
J. Study of ishemic colitis with Caroline Reilly.
K. Study of small bowel stromal tumors with Joseph Tworek and Henry Appelman.
L. Study of cytokines in experimental colitis model with Dan Remick.
M. Study of PET scans in detecting metastases in breast cancer with Richard Wahl, Division of Nuclear Medicine.
N. Study of etiology of pancreas cancer with David Garabrandt, School of Public Health.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Surgical Pathology Fellowship Program.
B. Coordinator, Surgical Pathology Staff Service Rotations.
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.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Speaker, "Growth Patterns and Sites of Origin of Pancreatic Cancer", Wayne State University Pancreas Cancer Research Group, Detroit, Michigan.
2. Invited Speaker, "Hepatitis 1996", Central Ohio Society of Pathology, Annual President's Lecture.
3. Visiting Professor, "Gastritis 1996", and Difficult Case Seminar, Ohio State University.
4. Invited Speaker, "Pathology and the World Wide Web", Michigan State Pathology Society.
5. Invited Speaker, Gastroesophageal Reflux Disease (GERD) Symposium, Macomb Hospital Center.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Cote, R.J., Houchens, D.P., Saad, A.D, Nines, R.G., Sampsel, J.W., Greenson, J.K., et al: Intraoperative detection of occult colon cancer micrometastases using ^{125}I-radiolabeled monoclonal antibody CC49. Cancer 77:613-20, 1996.
2. Hsi, E.D., Greenson, J.K., Singleton, T.P., Siddiqui, J., Schnitzer, B. and Ross, C.W.: Detection of immunoglobulin heavy chain rearrangement by polymerase chain reaction in chronic active gastritis associated with helicobacter pylori. Human Pathol 27:290-96, 1996.
3. Greenson, J.K., Svoboda, S.M., Merion, R.M. and Frank, T.S.: The histologic progression of recurrent hepatitis C in liver transplant allografts. Am. J. Surg. Pathol. 20:730-38, 1996.

ARTICLES SUBMITTED FOR PUBLICATION IN PEER-REVIEWED JOURNALS:

1. Macdonald, G.A., Greenson, J.K., Saito, K., Appelman, H.D. and Boland, C.R.: Loss of the DNA mismatch repair genes hMSH2 and/or hMLH1 is an early event in hepatic carcinogenesis. Submitted to PNAS.
2. Greenson, J.K., Stern, R.A., Carpenter, S.L. and Barnett, J.L.: The clinical significance of focal active colitis. Submitted to Human Pathol.
3. Greenson, J.K,: Macrophage infiltrates in cytomegalovirus esophagitis. Submitted to Human Pathol.
4. Scheiman, J.,.Meise, K., Greenson, J.K. and Coffey, R.J.: Transforming growth factor alpha (TGFα) levels in the human proximal gastrointestinal epithelium: Effect of mucosal injury and acid inhibition. Submitted to Digestive Diseases and Sciences.
5. Svoboda, S.M., Greenson, J.K., Singleton, Sun, R. and Frank, T.S.: Detection of hepatitis C in paraffin sections of formalin fixed liver using RT-PCR. Submitted to Diagnostic Molecular Pathology.
6. Hsi, E.D., Greenson, J.K., Singleton, T.P., Eisbruch, A., Ross, C.W. and Schnitzer, B.: Classification of primary gastric lymphomas according to histologic features. Submitted to American Journal of Surgical Pathology.
7. Dignan, C.R. and Greenson, J.K.: Can ischemic colitis be differentiated from Clostridium Diffficile colitis in biopsy specimens? Submitted to American Journal of Surgical Pathology.
8. Greenson, J.K.: Collagenous colitis and lymphocytic colitis. Submitted to Pathology Case Reviews.

BOOK CHAPTERS:

1. Greenson, J.K.: Pathology of the colon and rectum, in, Boland, C.R. (ed), Gastroenterology and Hepatology. The Comprehensive Visual Reference, Vol 2, Colon, Rectum, and Anus Current Medicine, Philadelphia, Pennsylvania, p 11.1-11.19, 1996. Also CD-ROM and kodachrome slide set.

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

1. Greenson, J.K.: (Book review). Liver biopsy interpretation. Am. J. Surg. Pathol. 19:1338, 1995.
2. Macdonald, G.A., Greenson, J.K., Saito, K., Appelman, H.D. and Boland, C.R.: Loss of the DNA mismatch repair genes hMSH2 and/or hMLH1 is an early event in hepatic carcinogenesis. Platform presentation at AASLD Meeting, November, 1995. Hepatology 22:219A, 1995.
3. Anderson, M.M., Appelman, H.D., Eckhauser, and Greenson, J.K.: The origins and growth patterns of adenocarcinomas in the head of the pancreas. Platform presentation, USCAP Meeting, 1996. Modern Pathol. 9:133A, 1996.
4. Svoboda, S.M., Greenson, J.K., Singleton, T.P., Sun, R. and Frank, T.S.: Detection of hepatitis C in paraffin sections of formalin fixed liver using RT-PCR. Platform presentation, USCAP Meeting, 1996. Modern Patho. 1 9:137A, 1996.
5. Stern, R.S., Carpenter, S.L., Barnett, J.L.and Greenson, J.K.: The clinical significance of focal active colitis. Platform presentation, USCAP Meeting, 1996. Modern Pathol. 9:66A, 1996.
6. Tworek, J.A., Appelman, H.D., Singleton, T.P. and Greenson, J.K.: Stromal tumors of the jejunum and ileum. Platform presentation, USCAP Meeting, 1996. Modern Pathol. 9:67A, 1996.
7. Reilly, C.R. and Greenson, J.K.: Can ischemic colitis be differentiated from C. Difficile colitis in biopsy specimens?" Poster, GI Pathology Resident Project Award Winner, USCAP Meeting, 1996. Modern Pathol. 9:64A, 1996.
8. Hsi, E.D., Greenson, J.K., Singleton, T.P., Eisbruch, A., Ross, C.W. and Schnitzer, B.: Classification of primary gastric lymphomas according to histologic features. Poster, USCAP Meeting, 1996. Modern Pathol. 9:59A, 1996.
9. Greenson, J.K., Merion, R.M. and Henley, K.S.: Liver transplantation (OLT) for sequelae of hepatitis. Reproducibility of the diagnosis of acute cellular rejection (ACR) and recurrent hepatitis (RC). Poster Presentation at the AGA Digestive Disease Week, 1996.
10. Greenson, J.K.: (Book review). Differential Diagnosis in Pathology: Liver Disorders. Am J Surg. Pathol. 20:777, 1996

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Dermatopathology, private consultations.
B. Dermatopathology, M-Labs.
C. Dermatopathology, UMH.
D. Dermatopathology, tutorials.

II. TEACHING ACTIVITIES:

A. Medical Students: (second year):
   1. Dermatopathology lectures.
B. Pathology and Dermatology House Officers:
   1. Dermatopathology.
C. Dermatology House Officers:
   1. Clinical Dermatology.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Pigmented Neurocristic Hamartomas.
B. Hair loss in utero.
C. Atlas: The Histology of Alopecia.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Consultant, Pigmented Lesion Clinic.

MEDICAL SCHOOL/HOSPITAL:

A. Director, Dermatopathology Unit.

REGIONAL AND NATIONAL:

A. Board of Directors, National Alopecia Areata Foundation.

INVITED LECTURES AND SEMINARS:

1. Sacramento Valley Dermatologic Society Meeting, February, 1996.

V. PUBLICATIONS:

1. Pearson, J.P., Weiss, S.W. and Headington, J.T.: Cutaneous malignant melanotic neurocristic tumors arising in neurocristic hamartomas. Am. J. Surg. Pathol. 665-677, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Surgical Pathology reading, six weeks.
B. Pediatric Necropsies, daily, twelve months.
C. Pediatric Consultation Cases, daily, twelve months.
D. Adult Necropsy Service, ten weeks.
E. Continued to organize and maintain the Michigan Cardiac Registry, twelve months.
F. Teratology Unit, histology, as necessary, approximately 40 cases per year.
G. Children's Cancer Study Group, coordinate pathological material and data necessary for all children registered in national tumor protocols. (Collaborating investigator, NCI #2-U10-CA-02971-33, CCSG, R. Hutchinson, M.D., P.I.).

II. TEACHING ACTIVITIES:

A. M2: Pathology 600, two hours with class as part of Congenital Heart Sequence of new curriculum.
B. M4: Pathology clerkship mentor, three students.
C. House Officers in Pathology, six weeks in surgical reading rooms.
D. House Officers in Pathology, gross and microscopic supervision of most pediatric necropsies, twelve months, and adult cases, ten 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 Pathology elective period.
H. Two lectures on Pediatric Pathology as part of the core curriculum for Pathology Residents.
I. Conferences: Faculty, house staff and students:
    1. Pediatric Cardiology Death Conference, monthly, twelve months.
    2. Pediatric Tumor Conference, twice monthly, twelve months.
    3. Pediatrics CPC/General Death Conference, quarterly, at least.
    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. Ongoing study with pediatric cardiologists and thoracic surgeons of effects of various stents and therapeutic manipulations on different stenotic vessels.
C. Histopathological component of lung changes associated with various cardiopulmonary therapeutic support mechanisms.

PROJECTS UNDER STUDY:

A. Review of the predictive value of pre-ECMO lung biopsy in determining survival and recovery of pulmonary function (Group study, pathologists, surgeons, pediatricians).
B. Continuing correlation of histopathologic classification of neuroblastoma cell/tumor maturity with different tissue gene expressions.
C. Study of myocardial ventricular fibrosis in various congenital heart defects, with pediatric cardiologists. (Published - See section IV, #3).
D. Review of predictive value of heart biopsies for death in pediatric transplant patients. (Manuscript submitted).

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. Interviewing fellowship candidates for Surgical Pathology (ad hoc).

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Member, Abstract Review Board, United States and Canadian Academy of Pathology.
B. Co-Chair: Pediatric Pathology Scientific Session , United States and Canadian Academy of Pathology 85th Annual Meeting, Washington, D.C., March, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Elhalaby, E.A., Teitelbaum, D.H., Coran, A. G. and Heidelberger, K.P.: Entercolitis associated with Hirschsprung's disease: A clinical histopathological correlative study. J. Ped. Surg. 301:1023-1027, 1995.
2. Barr, M., Jr., Heidelberger, K.P. and Comstock, C.H.: Craniomicromelic Syndrome: A newly recognized lethal condition with craniosynostosis, distinct facial anomalies, short limbs and intrauterine growth retardation. Am. J. Med. Genetics. 58:348-352, 1995.
3. Schwartz, S.M., Gordon, D., Mosca, R.S., Bove, E.L., Heidelberger, K.P. and Kulik, T.J.: Collagen content in normal, pressure, and pressure-volume overloaded developing human hearts. Am. J. Cardiol. 77:734-738, 1996.

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

1. Hutchins, G.M. and The Autopsy Committee of the College of American Pathologists (Kathleen P. Heidelberger, Member): Practice Guidelines for Autopsy Pathology: Autopsy Reporting., College of American Pathologists, Northfield, Illinois, 1995.
2. Powers, J.M. and The Autopsy Committee of the College of American Pathologists (Kathleen P. Heidelberger, Member): Practice Guidelines for Autopsy Pathology: Autopsy Procedures for Brain, Spinal Cord, and Neuromuscular System., College of American Pathologists, Northfield, Illinois, 1995.
3. Goldberg, C.S., Heidelberger, K.P., Caplan, M.J. and Dick, M.: Dimensions of the Triangle of Koch in Children. Abstract: International Society of Electrocardiology, Cleveland, Ohio, July, 1996. Accepted for presentation.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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/five years.
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.

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.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hirschl, R.B., Parent, A., Tooley, R., McCrachen, M., Johnson, K.J., Schaffer, T.H., Walfson, M.R. and Bartlett, R.H.: Liquid ventilation improves pulmonary function, gas exchange and lung injury in a model of respiratory failure. Annal. Surg. 221:79-88, 1995.
2. Messana, J.M., Johnson, K.J. and Mihatsch, M.J.: Renal structure and function effects after low dose cyclosporin in psoriasis patients: a preliminary report. Clin. Nephrol. 43:150-153, 1995.
3. Varani, J., Perone, P., Inman, D., Burmeister, W., Schallenberger, S., Fligiel, S.E.G., Sitrin, R.G. and Johnson, K.J.: Elaboration of proteolytic enzymes in the presence of factors which do not promote invasion. Am. J. Pathol. 146:210-217, 1995.
4. Yung, R.L., Quddus, J., Chrisp, C., Johnson, K.J. and Richardson, B.C.: Mechanisms of drug induced lupus ± cloned TH2 cells modified with DNA methylation inhibitors *in vitro* cause autoimmunity *in vivo.* J. Immunol. 154:3025-3035, 1995.
5. Shayevitz, J.R., Rodriguez, J.L., Gilligan, L., Johnson, K.J. and Tait, A.R.: Volatile anesthetic modulation of lung injury and outcome in a murine model of multiple organ dysfunction syndrome. Shock 4:61-67, 1995.
6. Varani, J., Burmeister, W., Perone, P., Bleavins, M. and Johnson, K.J.: Retinoic acid interferes with movements of Ca2+ across the plasma membrane of human dermal fibroblasts. FASEB J. 9:581, 1995.
7. Shayevitz, J.R., Miller, C., Johnson, K.J. and Rodriguez, J.L.: Multiple organ dysfunction syndrome: End organ and systemic inflammatory response in a bacteria-independent mouse model. Shock 4:389-396, 1995.
8. Hirschl, R.B., Tooley, R., Parent, A., Johnson, K.J. and Bartlett, R.H.: Partial liquid ventilation: A study model in a setting of severe respiratory failure. Chest. 109":500-508, 1995.
9. Varani, J., Burmeister, B., Perone, P., Bleavine, M. an Johnson, K.J.: All-trans retinoic acid inhibits fluctuation in intracellular Ca^{2+} resulting from change in extracellular Ca^{2+}. Amer. J. Pathol. 147:718-727, 1995.
10. Yung, R.L., Johnson, K.J. and Richardson, B.C.: New concepts in the pathogenesis of drug-induced lupus. Lab Invest. 73:746-759, 1995.
11. Shayevitz, J.R., Rodriguez, J.L., Gilligan, L., Johnson, K.J. and Tait, A.R.: Volatile anesthetic modulation of lung injury and outcome in a murine model of multiple organ dysfunction syndrome. Shock. 4:61-7, 1995.
12. 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.
13. 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.
14. Ward, P.A. and Johnson, K.J.: Lung inflammatory mechanisms. J. of Human Path., In Press.

15. Ward, P.A., Warren, J.S., Remick, D., Varani, J., Gannon, D. and Johnson, K.J.: Cytokines and oxygen radical mediated tissue injury, in Shoemaker, W.C. (ed), New Horizons III, Critical Care Medicine, In Press.
16. Ward, P.A., Johnson, K.J. and Till, G.O.: Mechanisms of lung injury. Prax. Klin. Pneumonol., In Press.
17. 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.
18. Johnson, K.J., Sulavik, C. and Rehan, A.: Role of oxygen radicals in autologous anti-GBM nephritis. Inflammation, In Press.
19. Mulligan, M.S., Sulavik, C., Ward, P.A., Kunkel, R.G. and Johnson, K.J.: The delayed phase of anti-GBM nephritis is deferoxamine sensative but catalase insensitive. Inflammation, In Press.
20. 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.
21. Lowe, N.J., Wieder, J.M., Rosenbach, A., Johnson, K.J., Kunkel, R., Bainbridge, C., Baurget, T., Demovy, I., Simpson, K., Glass, E. and Grabie, M.T.: Chronic low dose cyclosporin therapy for severe psoriasis: Effects on renal function and structure. J. Invest. Derm., In Press.
22. 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, In Press.
23. 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., In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Ward, P.A., Till, G.O., Kunkel, R.G. and Johnson, K.J.: Protection against neutrophil-mediated lung injury by platelet depletion. Submitted for publication.
2. Ginsburg, I., Schuger, L., Gibbs, F., Johnson, K.J., Ryan, U.S., Ward, P.A. and Varani, J.: Endothelial cell killing by polymorphonuclear leukocytes: independent and synergistic roles for oxygen radicals and proteases. Submitted for publication to Am. J. Pathol.
3. Varani, J., Jones, J., Gibbs, D.F., Sulavik, C., Dame, M. and Johnson, K.J.: In vitro and in vivo modulation of the acute inflammatory response by all-trans retinoid acid. Submitted for publication.
4. Johnson, K.J., Dixit, V.M. and Varani, J.: Role of thrombospondin in the acute inflammatory response. Submitted for publication.
5. Messana, J.M., Johnson, K.J., Leichtman, A.B., Ellis, C.N., Mihatsch, M.J., Hamilton, F.A., Groisser, D.S., Gartside, M.S. and Voorhees, J.J.: A prospective study of the effects of low dose cyclosporin in renal structure and function in psoriasis patients. Submitted for publication.
6. Kershaw, D.B., Bunchman, T.E, Johnson, K.J., Sedman, A.B. and Kelsch, R.C.: Crescentic glomerulonephritis with subsequent hemolytic uremic syndrome in a child. Submitted for publication.
7. Lowe, N.J., Weider, J.M., Rosenbach, A., Kunkel, R.G., Johnson, K.J., Simpson, K., Glass, F. and Grabie, M.T.: Chronic cyclosporin for severe psoriasis: effects on renal function and structure. Submitted for publication.

8. Hirschl, R.B., Overbeck, M.C., Parent, A., Hernandez, R., Schwartz, S.S., Dosanjh, A., Johnson, K.J. and Bartlett, R.H.: Perfluorocarbon liquid ventilation provides uniform distribution of ventilation in the setting of respiratory failure. Submitted for publication.
9. 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.
10. Mulligan, M.S., Shanley, T.P., Jones, M.L., Johnson, K.J., Bonish, B.K. and Ward, P.A.: Cytokine and adhesion molecule requirements in lung injury induced by anti-glomerular molecule requirements in lung injury induced by anti-glomerular basement membrane antibody. Submitted for publication.
11. 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.
12. 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.
13. Yung, R.L., Johnson, K.J. and Richardson, B.C.: New concepts in the pathogenesis of drug-induced lupus. Lab. Invest., Submitted.
14. 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.
15. 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.
16. 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.
17. 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.
18. 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.
19. 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.
20. 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.
21. 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.
22. 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.
23. 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.

24. Yung, R., Williams, R., Johnson, K.J., Stoolman, L., Change, S. and Richardson, B.: Mechanisms of drug-induced lupus. III. gender-specific differences in splenic T cell homing explain increased disease severity in female mic. J. Clin. Invest., Submitted.
25. 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*. Submitted for publication.

BOOKS AND CHAPTERS IN BOOKS

1. Warren, J.S., Johnson, K.J. and Ward, P.A.: Phagocytes and reactive oxygen substances as mediators of acute lung injury, in, Hyers, T. (ed), Diffuse Alveolar Damage and Respiratory Failure, Futura Press, New York, In Press.
2. Till, G.O., Johnson, K.J. and Ward, P.A.: Oxygen free radicals in inflammation, in, Messmer, K. and Hammersen, F. (eds), Prog. Appl. Microcirc., Volume 9, Karger, Basel, In Press.
3. Ward, P.A., Johnson, K.J. and Till, G.O.: Leukocyte oxygen radicals and acute lung injury, in, Proceedings of a Symposium on "Acute Lung Injury", PSG Publishing Co., Littleton, Massachusetts, In Press.
4. Warren, J.S., Ward, P.A. and Johnson, K.J.: Oxygen radicals as "mediators of inflammation", Volume 6, in, Henson, P.M. (ed), The Handbook of Inflammation, Volume 6, Elsevier Biomedical Division, Amsterdam, The Netherlands, In Press.
5. Warren, J.S., Ward, P.A. and Johnson, K.J.: The respiratory burst and mechanisms of oxygen radical mediated tissue injury, in, Sbarra, A.J. and Strauss, R.P. (eds), The Respiratory Burst and its Physiological Significance in Medicine, Plenum Press, New York, New York, In Press.
6. Warren, J.S., Johnson, K.J. and Ward, P.A.: Consequences of oxidant injury, in, Crystal R.G. and West, T.B. (eds), The Lung: Scientific Foundations, In Press.
7. Ward, P.A., Warren, J.S., Johnson, K.J. and Varani, J.: Cytokines and oxygen radical responses, in, Maier, R. (ed), Proceedings of the International Congress on the Immune Consequences of Trauma, Shock and Sepsis: Mechanisms and Therapeutic Approaches, In Press.
8. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Free radicals in lung disease, in, Rice-Evans, C. (ed), Free Radicals, Diseased States and Anti-Radical Interventions, Proceedings of the Special Colloquium, London, England, In Press.
9. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines toxic oxygen products and cell injury, in, Molecular Aspects of Medicine, Proceedings of the VIIth Annual Inflammation Meeting, Birmingham, U.K., Pergammon Press, In Press.
10. Ward, P.A., Warren, J.S. and Johnson, K.J.: Oxygen radicals, inflammation and tissue injury, in, Pryor, W. and Godber, S.L. (eds), Free Radical Biology and Medicine, In Press.
11. Warren, J.S., Ward, P.A., and Johnson, K.J.: Oxygen radicals as "mediators of inflammation", in, Volume 6, Henson, P. (ed), The Handbook of Inflammation, Elsevier Biomedical Division, Amsterdam, The Netherlands, In Press.
12. Ward, P.A., Warren, J.S., Johnson, K.J. and Varani, J.: Inflammation, oxygen radicals and tissue injury, in, Oxidative Damage and Repair: Clinical, Biological and Medical Aspects, In Press.
13. Johnson, K.J., Chensue, S.W., Kunkel, S.L. and Ward, P.A.: Immunopathology, in, Rubin, E. and Farber, J.L. (eds) Textbook of Pathology, Second Edition, J.B. Lippincott Inc., New York, New York, In Press.

14. Varani, J. and Johnson, K.J.: Modulation of endothelial cell injury by all-trans retinoic acid: Role of the anti-inflammatory effects of RA, in, Jesaitis, A. (ed), Molecular basis of oxidative damage by leukocytes. CRC Press, In Press.
15. Johnson, K.J., Varani, J. and Smolen, J.E.: Neutrophil activation and function in health and disease, in, Coffey, R.G. (ed), Granulocyte Responses to Cytokines: Basic and Clinical Research, Marcel Dekker, Inc., New York, In Press.

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

1. Richardson, B.C., Lalwani, N.D., Johnson, K.J. and Marks, R.M.: Ligation of FAS is sufficient to trigger apoptosis in macrophages but not in cultured human endothelial cells. Clin. Res., 1995
2. Colton. D., Hirschl, R., Till, G.O., Johnson, K.J., Metzger, R., Dean, S. and Bartlett, R.: The pathophysiology of respiratory failure following systemic complement activation. E. Soc. Crit. Care Med., 1995.
3. Leggat, J.E., Johnson, K.J., Kolars, J.C., Schmiedlin-Ren, P., Watkins, P.B. and Leichtman, A.B.: Immunohistochemical localization of cytochrome P450 3A in normal and neoplastic kidney and urinary bladder epithelium. Exp. Biol., 1995.
4. Richardson, B.C., Johnson, K.J. and Lalwani, N.D.: Macrophage apoptosis in active lupus. Ninth International Congress of Immunology, 1995.
5. Bleavins, M., Johnson, K.J. and de la Iglesia, F.A.: Comparative effects of two recombinant human epidermal growth factors (EGF) in mercuric chloride-induced kidney injury. ICT, Seattle, Washington, 1995.
6. Davidson, B.A., Nader-Djalal, N., Jones, M.L., Johnson, K.J. and Knight, P.R.: The proinflammatory cytokine, TNF is required for full expression of gastric inspiration lung injury. ASA, 1995.
7. Nader-Djalal, N., Davidson, B.S., Helinski, M.S., Shanley, T.P., Johnson, K.J. and Knight, P.R.: Is interleukin-10 invited to the feast in aspiration pneumonitis? ASA, 1995.
8. Foreman, K.E., Till, G.O., Johnson, K.J, and Ward, P.A.: Complement Activation, endothelial cell P-selectors and the role of C5b-C9. FASEB J. 9:198, 1995.
9. Varani, J., Burmeister, W., Perone, P., Bleavins, M., and Johnson, K.J.: Retinoic acid interferes with movement of Ca across the plasma membrane of human dermal fibroblasts. FASEB J. 9:3366, 1995.
10. Gipson, T.S., Shanley, T.P., Jones, M.L., Ward, P.A. and Johnson, K.J.: Molecular cloning and in vivo transcriptional expression of rat TIMP-2 in lung inflammation. FASEB J. 9:4339, 1995.
11. Leggat, J.E., Jr., Johnson, K.J., Kolars, J.C., Schmiedlin-Ren, P., Watkins, P.B. and Leichtman, A.B.: Immunohistochemical localization of cytochrome P450 3A in normal and neoplastic kidney and urinary bladder epithelium. FASEB J. 9:5604, 1995.
12. Johnson, K.J, Swanson, P.C., Yung, R.L., Blatt, N.B., Eagan, M., Norris, J., Richardson, B.C. and Glick, G.D.: Anti-DNA antibodies structure-function and pathogenicity. Amer. Soc. Nephrol., 1995.
13. Yung, R.L., Johnson, K.J, and Richardson, B.C.: LFA-1 overexpression on T cells causes autoimmunity *in vivo.* Amer. Coll. Rheum., 1995.

14. Colton, D.M., Johnson, K.J. and Hirschl, R.B.: Lung vascular permeability is reduced during partial liquid ventilation (PLV) in the setting of respiratory failure. Amer. Thoracic Soc., 1995.
15. Colton, D.M., Till, G.O., Johnson, K.J., Gator, J., Brent, D.O. and Hirschl, R.B.: Partial liquid ventilation (PLV) decreases intraveolar hemorrhage during acute respiratory failure. Amer. Coll. Surg., 1995.
16. 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.
17. 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.
18. 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. Submitted to: FASEB, 1996.
19. 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. Submitted to FASEB, 1996.
20. 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
21. 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.
22. 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.
23. Yung, R., Johnson, K. and Richardson, B.: DNA methylation inhibitors cause lupus by inducing T cell LFA-1 overexpression. FASEB J. 10:A1307, 1996.
24. 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.
25. 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.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Clinical Pathology Grand Rounds:
   1. Program Director.
   2. Presented lecture entitled: "Blood groups and disease".
B. Anatomical Pathology Conferences:
   1. Program Coordinator.
C. Core-Lecture Series in Blood Banking for 1st-year Pathology House Officers:
   1. Program Coordinator.
   2. Presented lectures on:
      a. Pretransfusion testing.
      b. Prenatal/perinatal testing.
      c. Immune hemolysis.
D. Clinical Pathology Case Study Conference:
   1. Program Coordinator.
   2. Participant.
E. Hematology/Oncology Fellows:
   1. Provided instruction in immunohematology to Dr. Afshin Ameri(ten 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).
G. Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
   1. Program Director - Planned and coordinated theMay, 1996 Current Topics in Blood Banking Symposium and Preconference Workshops.
   2. Presented Workshop entitled: "Maternal-Fetal Immunohematology".
   3. Presented talk entitled: "What is the Best Method for Antibody Detection?".
   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, Knafl P. Validation of the gel test. Accepted for presentation at the Annual Meeting of the American Association of Blood Banks, Orlando, October, 1996
B. Judd WJ, Steiner EA, Davenport RD. Time of sample receipt and ability to batch tests. In preparation.

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, Advanced Lectures in Blood Banking Program - coordinated a series of 60 lectures, two full-day workshops and a two-day review session for technologists seeking Certification as a Specialist in Blood Banking.
   2. Member, Annual Meeting Program Committee.
B. American Association of Blood Banks:
   1. Member, Awards Committee.
C. Member, Editorial Board, Transfusion.
D. Reviewer of articles submitted for publication in Transfusion, Immunohematology, Transfusion Medicine Reviews, Vox Sanguinus and the ASCP Check Sample Program
E. International Society of Blood Transfusion
   1. WHO Committee on Blood Group Nomenclature

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

1. "101 Ways with a Wet Noodle!", Michigan Association of Blood Banks Fall Lecture Series, Traverse City, Michigan, October, 1995.
2. "Approaches to Antibody Identification", Michigan Association of Blood Banks Fall Lecture Series, Traverse City, Michigan, October, 1995.
3. "101 Ways with a Wet Noodle!", Michigan Association Of Blood Banks Fall Lecture Series, Houghton, Michigan, October, 1995.
4. "Approaches to Antibody Identification", Michigan Aassociation of Blood Banks Fall Lecture Series, Houghton, Michigan, October, 1995.
5. A Seminar to Honor E. Hackel and R. Walker. Michigan Association of Blood Banks, Dearborn, Michigan, October, 1995. *Director and Moderator.*
6. Session Moderator, "Red Cells and Serological Methods", American Association of Blood Banks Annual Meeting, New Orleans, Louisians, November, 1995.
7. Speaker, "The perfect crossmatch", AABB Annual Meeting, New Orleans, Louisiana, November, 1995.

8. "Partner's in Productivity", Ortho Diagnostic Systems, Inc. New Orleans, Louisiana, November, 1995. *Moderator.*
9. "New Strategies for Pretransfusion Testing", American Red Cross, Miami, Florida, February, 1996.
10. "The Electronic Crossmatch", Second Congress of Medical Technology, San Juan, Puerto Rico, April, 1996.
11. "What is the Best Method for Antibody Detection?", Second Congress of Medical Technology, San Juan, Puerto Rico, April, 1996.
12. "New Strategies for Pretransfusion Testing", Ohio Society for Medical Technology, April, 1996
13. "New Strategies for Pretransfusion Testing", Hoxworth Blood Center, Cincinnati, Ohio, May, 1995.
14. "Computer Applications in Transfusion Medicine", Michigan Association of Blood Banks, Lansing, Michigan, May, 1996.
15. Videoconference: The Perfect Crossmatch. American Red Cross, Washington DC, March, 1996.
16. Teleconference: The Perfect Crossmatch. American Society of Clinical Pathology, April, 1996.
    A. Safety and Efficacy of Blood Bank Testing in Hospital Transfusion Services", International Society of Blood Transfusion, Tokyo, Japan, April, 1996.

VI. PUBLICATIONS:

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

1. Judd, W.J. and Annesley, T.M.: The acquired-B phenomenon. Trans. Med. Rev. 10:111-7, 1996.

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

1. Butch, S.H. and Judd, W.J.: Experience with the electronic crossmatch: errors and suggested improvements. 48th Annual Meeting of the American Association of Blood Banks, New Orleans, Louisiana. Transfusion 35(S):25, 1995.
2. Judd, W.J., Steiner, E.A., Knafl, P. and Davenport, R.D.: Failure to detect potentially significant antibodies in prewarmed test. 48th Annual Meeting of the American Association of Blood Banks, New Orleans, Louisiana. Transfusion 35(S):68, 1995.
3. Judd, W.J.: Attack on prewarmed tests - too much hot air (letter). Transfusion 36:192-3, 1996.
4. Judd, W.J.: Laboratory management of antibodies to blood group antigens in pregnancy (letter). Lancet 347:1412-3, 1996.
5. Judd, W.J.: Safety and efficacy of blood bank testing in hospital transfusion services. Vox Sang., In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Director, Molecular Diagnostics, 1993-present.
B. Director, Clinical Chemistry Section, 1993-present.
C. Interpretation and sign-out of protein electrophoretic analyses (Immunology Laboratory), 1993-present.

II. TEACHING ACTIVITIES:

A. Lectures to Medical Students in M4 Laboratory Medicine Elective.
B. Lectures to House Staff on Block B, Clinical Pathology.
C. Protein Sign-Out in Immunology Laboratory with one-two residents for four-six 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. Lisa Passmore (Undergraduate, now accepted for medical school at the University of Alabama, Birmingham, Alabama). Research advisor to Ms. Patricia Polaczyk, Undergraduate.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Identification of genes activated by mineralocorticoid hormones.
B. Quantitative analytical technologies for nucleic acids.

SPONSORED SUPPORT:

A. American Heart Association (Michigan Chapter) 7/1/95-6/30/96, $27,600, "Identification of Mineralocorticoid Response Genes", Principal Investigator.
B. Michigan Phoenix Memorial Project. 7/1/95-6/30/96, $4,900 "Identification of Mineralocorticoid Response Genes", Principal Investigator.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Molecular Diagnostics Laboratory.
B. Director, Clinical Chemistry Section.
C. Member, Pathology Resident Selection Committee.
D. Obtained ACGME Certification for the Fellowship Program in Chemical Pathology for the Department of Pathology.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Patient Care Information Systems (PCIS) Committee.

REGIONAL AND NATIONAL:

A. Program Chair, Association for Molecular Pathology Annual Meeting, 1996 (to be held in Baltimore, November 1996).
    1. Editor of ACLPS Newsletter.
    2. Chair, ACLPS Taskforce on Networking.
B. Member, AACC, ASHG, CAP, ACLPS, AMP.
C. Manuscript Reviewer, Clinical Chemistry, and Molecular Diagnosis

V. INVITED LECTURES AND SEMINARS:

1. "Congenital Adrenal Hyperplasia: Clinical, Biochemical, and Molecular Aspects", Fifth Annual Symposium on Molecular Pathology, William Beaumont Hospital, Royal Oak, Michigan, March, 1996.
2. "Molecular Biology Applicants in Pathology", Ohio Society for Clinical Laboratory Sciences Annual Meeting, Toledo, Ohio, April, 1996.
3. "Surfing the Net in Laboratory Medicine", Academy of Clinical Laboratory Scientists and Pathologists Annual Meeting, Roundtable Discussion, St. Louis, Missouri, June, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Killeen, A.A.: A visible spectrophotometric assay for submicrogram quantities of DNA, including PCR-amplified DNA. Microchemical Journal 52:333-340, 1995.
2. Hitomi, Y., McDonnell, W.M., Killeen, A.A. and Askari, F.K.: Hepatitis C virus core gene sequence fidelity confirms core protein as an appropriate target for HCV vaccine strategies. J Viral Hepatitis 2:235-241, 1995.
3. Killeen, A.A.: Quantification of nucleic acids. Clinics in Laboratory Medicine, In Press.

4. Killeen, A.A.: An overview of current internet resources for pathology. J Clin Lab Analysis, In Press.
5. Passmore, L.J. and Killeen, A.A.: Toluidine blue dye-binding method for measurement of genomic DNA extracted from peripheral blood leukocytes. Mole Diag, In Press.

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

1. Jone, C. and Killeen, A.A.: Monitoring of bone marrow engraftment by PCR with product detection and quantitation by capillary electrophoresis. Clin. Chem. 42:S201.
2. Killeen, A.A.: A visible spectrophotometric dye binding method for measurement of genomic DNA. Clin. Chem. 42:S201.
3. Bavikatty, N.B. and Killeen, A.A.: Aldosterone increases citrate synthase activity in human mononuclear leukocytes. Presented at the ACLPS meeting, June 1995, Syracuse, New York. Am. J. Clin. Path. 104:227-228, 1995.
4. Noorhdoek, G.T,, van Embden, J.D.A. and Kolk, A.H.J.: Reliability of nucleic acid amplification for detection of M. Tuberculosis: An international collaborative study among 30 laboratories. Association for Molecular Pathology Annual Meeting, Minneapolis, Minnesota, November 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Board Certification, Anatomic Pathology.
B. Autopsy Pathology (11 days).
C. Diagnostic Renal Biopsy Service (six months).
D. Chief Renal Consultant.

II. TEACHING ACTIVITIES:

A. M2 Pathology Lecture - Renal Sequence (three hours).
B. M2 Pathology Laboratory- Renal Sequence (16 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 contact hours).
H. Renal Pathology Fellow - Carrie Phillips - (300 hours).
I. Autopsy Pathology (five hours).
J. Undergraduate Students (one).
K. Dissertation Committees (one).
L Post Doctoral Fellows (two).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Collagen IV Gene Transcription in cpk/cpk Mice", NIH-RO1-DK44848, (25% Effort) $143,000/first year, 9/30/91-9/29/95.
B. Principal Investigator, Project VI, "TGF-β Induced Collagen IV Gene Transcription", NIH-P50-DK39225, (10% Effort) $49,822/year, 8/1/92-7/30/97.
C. Co-Investigator, "Renal Fibrosis", NIH-RO1, (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, 1/1/97-12/31/01.
B. Co-Investigator, "IGF-I is an Osmoprotectant in Neuroglial Cells", NIH-R01-DK38304, (5% Effort) $103,045 direct costs/year, 1/1/97-12/31/00.
C. Co-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. Postdoctoral fellow recruitment, Immunopathology Training Grant.
B. Anatomic Pathology Accessioning Committee.
C. Assistant Director, Diagnostic Renal Biopsy Service.

MEDICAL SCHOOL/HOSPITAL:

A. Faculty recruitment - Department of Internal Medicine.
B. Faculty recruitment - Department of Surgery.
C. Curriculum development-M2 Urinary System.

REGIONAL AND NATIONAL:

A. Planning Committee, Genetic Basis of Renal Disease. NIDDK, NIH.
B. Ad hoc reviewer, Division of Extramural Activities, NIDDK, NIH.
C. Ad hoc Reviewer, Juvenile Diabetes Foundation.
D. Reviewer:
    1. Laboratory Investigation.
    2. American Journal of Pathology.
    3. American Journal of Physiology.
    4. Journal of Clinical Investigation.
    5. Journal of Biological Chemistry.
    6. Journal of American Society of Nephrology.
E. AHA-National Cardio-Renal Study Section, 1992-1996.

V. INVITED LECTURES AND SEMINARS:

1. Invited Speaker, "Advances in the Interpretation of Renal Biopsies", Xth Congress of the International Pediatric Nephrology Association, Santiago, Chile, August 1995.
2. Invited Speaker, "Cytokines and Growth Factors in Fibrosis Symposium", Annual Meeting of the American Society of Nephrology, November, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Singh, I.J., Killen, P.D. and Leichtman, A.: Cholesterol emboli presenting as acute allograft dysfunction after renal transplantation. J. Amer. Soc. Nephrol. 6:165-170, 1995.
2. Bergijk, E.C., Baelde, H.J., de Heer, E., Killen, P.D. and Bruijn, J.A.: Specific accumulation of exogenous fibronectin in experimental glomerulosclerosis. J. Pathol. 176:191-199, 1995.
3. Bergijk, E.C., Baelde, J.J., de Heer, E., Killen, P.D. and Bruijn, J.A.: Role of the extracellular matrix in the development of glomerulosclerosis in experimental chronic serum sickness. Exp. Nephrol. 3:338-347, 1995.
4. Enders, G.C., Kahsai, T.Z., Lian, G., Funabiki, K., Killen, P.D. and Hudson, B.G.: Developmental changes in seminiferous tubule extracellular matrix component expression in the mouse testis: α3(IV) collagen chains expressed at the initiation of spermatogenesis. Biol. Reprod. 53:1489-1499, 1995.
5. 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., In Press, 1996.
6. 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., In Press, 1996.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Todd-Turla, K.M., Schnermann, J.B., Briggs, J.P. and Killen, P.D.: Regulation of renal mineralocorticoid and glucocorticoid receptor mRNA in response to adrenalectomy and corticosteroid hormone replacement. Submitted.
2. Wu, K., Setty, S., Mauer, S.M., Killen, P.D., Nagase, H., Michael, A.F. and Tsilibury, E.C.: Altered kidney matrix gene expression in experimental diabetes. Submitted.
3. Porcellati, F., Hlaing, T., Togawa, M., Stevens, M.J., Larkin, D., Glover, T.W., Henry, D.N., Greene, D.A. and Killen, P.D.: The human sodium-myo-inositiol cotransporter gene: Differential exon utilization results in multiple RNA transcripts. Submitted.
4. Togawa, M., Maeda, S., Henry, D.N., Greene, D.A. and Killen, P.D.: Characterization of an osmotic enhancer of human aldose reductase gene transcription. Submitted.
5. Lee, S.K., Wiggins, R., deMiguel, M., Goyal, M., Wharram, B. and Killen, P.D.: Development of a quantitative RT-PCR method for measurement of collagen I gene expression. Submitted.

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

1. Sharif, K., Goyal, M., Killen, P., Thomas, P., Wharram, B. and Wiggins, R.: GLEPP1 expression and distribution in glomeruli in idiopathic nephrotic syndrome (INS). American Society of Nephrology, 1995.

2. Maeda, S., Togawa, M., Greene, D. and Killen, P.D.: A 13 bp sequence is critical for the osmotic activation of aldose reductase (AR) gene transcription. American Society of Nephrology, 1995.
3. Lee, S.K., Wiggins, R., Goyal, M., Dysko, R. and Killen, P.D.: Renal biopsy collagen I (CI) mRNA predicts renal scarring in a model of crescentic nephritis in rabbits. American Society of Nephrology, 1995.
4. Schieren, G., Gattone II, V.H. and Killen, P.D.: Increased expression of extra-cellular matrix (ECM) genes occurs early in polycystic kidney disease (PKD) in CD1-*pcy/pcy* mice. American Society of Nephrology, 1995.
5. Gattone II, V.H., Schieren, G. and Killen, P.D.: Aberrant expression of extra-cellular matrix in infantile-type polycystic kidney disease (PKD) in *cpk/cpk* mice. American Society of Nephrology, 1995.
6. Funabiki, K., Yamamoto, M., Fukui, M., Shirato, I., Tomino, Y. and Killen, P.D.: Dissociated expression of the collagen type IV subchains in the diabetic Kkay mouse kidneys. American Society of Nephrology, 1995.
7. Bergijk, E.C., Baelde, J.J., de Heer, E., Killen, P.D. and Bruijn, J.A.: Differential expression of collagen type IV subchains in experimental glomerulosclerosis. Kidney Int. 47:698, 1995.
8. Bergijk, E., Baelde, J.J., Ileer, B., Killen, P.D. and Bruijn, J.: Differential mRNA and protein expression of collagen type IV (col IV) subchains in experimental glomerulosclerosis. J. Amer. Soc. Nephrol. 6:892, 1995.
9. Minto, A.W.M., Killen, P.D., Funabiki, K., Bergijk, E.C. and Salant, D.J.: Increased abundance of a 4 type IV collagen mRNA in passive Heymann nephritis: Role of complement. J. Amer. Soc. Nephrol. 6:902, 1995.
10. Feldman, E.L., Greene, D.A., Stevens, M. and Killen, P.D.: IGF-I prevents gloctoxicity in neuroglial cells. EASD, Submitted, 1996.
11. 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.
12. 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.
13. 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.
14. 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.
15. 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.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Epidemiology 570.
B. Host Defense Sequence, First Year Medical School.
C. Lecture in didactic seminar series, Internal Medicine (Rheumatology).
D. Member, Pathology Graduate Program Committee.
E. Member, Lung Immunopathology Postdoctoral 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:
    1. Dr. Doug Arenberg, Postdoctoral Fellow.
    2. Dr. Betsy Parks, Postdoctoral Fellow.
    3. Dr. Ken Simpson, Postdoctoral Fellow.
    4. Dr. Cary Caldwell, Postdoctoral Fellow.
    5. Dr. Bruno DiGiovine, Postdoctoral Fellow.
K. Undergraduate students:
    1. Kolby Keefer.
    2. Laural Goldstein.
    3. Harold Schock.
    4. Drew Pullen.
    5. Matt Steinhouse.
    6. Eric Strieter.
    7. Scott Lipinski
    8. Carrie Zickus.
L. High school students: Jamal Bufford
M. Doctoral Thesis Committee Member/Orals Committee for the following graduate students:
    1. Andrew Merry (Pathology).
    2. Jami Foreback (Pathology).

3. Arul Chinnaiyan (Pathology).
4. Hangjun Duan(Pathology).
5. Fran Wolber(Pathology).
6. Jim Parks (Pharmacology).
7. Jeffrey Ruth (Public Health).
8. Mei-Chen Kuo (Public Health).
9. Joyce J. Lai (Public Health).

N. Sabbatical supervisor for Dr. Keith Walley, University of British Columbia.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Macrophage/MonocyteSignals in Lung Granuloma Formation", HL-RO1-35276; National Institutes of Health.
B. Principal Investigator, "Monokine Gene Expression/Regulation in Lung Injury", HL-RO1-31237, National Institutes of Health.
C. "Inflammatory Cells and Lung Injury", Program Project HL-31963; Principal Investigator for Section II, National Institutes of Health.
D. "The role of TNF and ICAM-1 in Lung Allograft Rejection", Co-Investiagator, HL-50057, National Institutes of Health.
E. NIH-RO1, "The Role of C-X-C Chemokines in Lung Cancer, Co-Investigator.
F. SCOR, "Occupational and Immunological Lung Disease", Co-Investigator, P50HL-46487, Effect of Alcohol on Cytokine Mediated Lung Host Defense", Co-Investigator AA-10571

PATENTS:

A. "Labelled Monocyte Chemotactic Protein-1 and Medical Uses Thereof", # 5,413,778 issued May 9, 1995.

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. Medical School Admission Interview Committee.
C. Medical Scientist Training Program Interview Committee.
D. Member, Research Council of the Office of the Vice President for Research.
E. Member, Michigan Cancer Center.
F. Grant Reviewer, Biomedical Research Counci.
G. Member, Advisory Committee Cancer Center Animal Core.
H. Member, Panel of Inquiry into Federally-Sponsored Human Radiation Research at the University of Michigan in the Post-World War II Era.
I. Member, Search committe, Computational Biology.
J. Member, Search Committee, Department of Microbiology/Immunology.
K. Associate Dean, Rackham Graduate School.

REGIONAL AND NATIONAL

A. Senior Associate Editor, American Journal of Pathology.
B. Associate Editor, American Journal of Respiratory Cell and Molecular Biology.
C. Associate Editor, Pathobiology.
D. Associate Editor, Shock.
E. Editoral Board, Mediators of Inflammation.
F. Vice-Chair, 1998 Gordon Conference on Chemokines.
G Member Program Committee, American Society of Investigative Pathology.
H. Reviewer for the following journals:
    1. American Journal of Pathology.
    2. American Review of Respiratory Disease.
    3. Circulation.
    4. Infection and Immunity.
    5. Laboratory Investigation.
    6. Science.
    7. Journal of Immunology.
    8. American Journal of Respiratory Cell and Molecular Biology.
I. Grant Reviewer, The Arthritis Society.
J. Grant Reviewer, Veterans Administration.
K. National Institute of Health Study Section, Lung Biology and Pathology, Ad Hoc, 1995.
L. National Institute of Health Study Section, Bacteriology & Mycology-1, Ad Hoc, 1996
M. National Cancer Institute Site Visit Team, Laboratory for Molecular Immunoregualtion, 1996.
N. Scientific Advisory Council, American Lung Association.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Invited Chair/Speaker, The 9th International Congress of Immunology, San Francisco, California, July, 1995.
2. Invited Speaker, World Congress on Immunology, Brighton United Kingdom, September, 1995.
3. Invited Speaker, World Association of Sarcoidosis and other Granulomatous Disorders, London, United Kingdom,October, 1995.
4. Invited Speaker, Hammersmith Hospital, Department of Infectious Diseases, London, United Kingdom, October, 1995.
5. Invited Speaker, Gene I. Higashi Memorial Lecture, School of Public Health, University of Michigan, Ann Arbor, Michigan, November, 1995.
6. Visiting Professor, University of Toronto Immunology Center, Toronto, Ontario, Canada, January, 1996.
7. Invited Speaker, Department of Pathology, University of Virginia, Charolesville, Virginia, January, 1996.
8. Invited Speaker, Canadian Association of Gastroentrology, Banff, Alberta, March, 1996.
9. Invited Speaker, Experimental Biology '96 Symposium, "Molecular Biology of Leukocyte Recruitment and Activation in Inflammation", New Orleans, Louisiana, June, 1996.
10. Invited Speaker, Special Emphasis Planel, NHLBI, Lung Biology and Disease, Bethesda, Maryland, June, 1996.
11. Invited Speaker, "Adhesion Molecules and Cytokines Symposium", Ann Arbor, Michigan, June, 1996.
12. Invited Speaker, Gordon Conference on Chemokines, Holderness School, Plymouth, New Hampshire, June 1996.

VI. PUBLICATIONS

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lukacs, N.W., Strieter, R.M. and Kunkel S.L.: Leukocyte infiltration in allergic airway 1995; inflammation. Am. J. Respir. Cell Mol. Biol. 13:1-6, 1995.
2. Standiford, T.J., Kunkel, S.L., Lukacs, N.W., Greenberger, M.J., Danforth, J.M., Kunkel, R.G. and Strieter, R.M.: Macrophage inflammatory protein-1 alpha mediates lung leukocyte recruitment, lung injury, and early mortality in murine endotoxemia. J. Immunol. 155:1515-1524, 1995.
3. Standiford, T.J., Strieter, R.M., Lukacs, N.W. and Kunkel, S.L.: Neutralization of IL-10 increases lethality in endotoxemia: Cooperative effects of macrophage inflammatory protein-2 and tumor necrosis factor. J. Immunol. 155:2222-2229, 1995.
4. Strieter, R.M., Polverini, P.J., Arenbergd D.A. and Kunkel, S.L. The role of CXC chemokines as regulators of angiogenesis. Shock 4:155-160, 1995.
5. Koch, A.E., Kunkel, S.L., Shah, M.R., Hosaka, S., Halloran, M.M., Haines, G.H., Burdick, M.D., Pope, R.M. and Strieter, R.M.: Growth-related gene product α: A

chemotactic cytokine for neutrophils in rheumatoid arthritis. J. Immunol. 155:3660-3666, 1995.

6. Chensue, S.W., Ruth, J.H., Warmington, K., Lincoln, P. and Kunkel, S.L.: In vivo regulation of macrophage IL-12 production during type 1 and type 2 cytokine-mediate granuloma formation. J. Immunol. 155:3546-3551, 1995.
7. Lukacs, N.W., Strieter, R.M., Elner, V., Evanoff, H.L., Burdick, M.D. and Kunkel, S.L.: Production of chemokines, IL-8, MCP-1 during monocyte:endothelial cell interactions. Blood 86:2767-2773, 1995.
8. Karpus, W.J., Lukacs, N.W., McRae, B.L., Strieter, R.M., Kunkel, S.L. and Miller, S.D.: An important role for the chemokine macrophage inflammatory protein-1 alpha in the pathogenesis of the T cell mediated autoimmune disease, experimental autoimmune encephalomyelitis. J. Immunol. 155:5003-5010, 1995.
9. Huffnagle, G.B., Strieter, R.M., Standiford, T.J., McDonald, R.A., Burdick, M.D., Kunkel S.L. and Toews, G.B.: The role of monocyte chemotactic protein-1 (MCP-1) in the recruitment of monocyte and CD4+ T cell during a pulmonary *Crytococcus neoformans* infection. J. Immunol. 155:4790-4797, 1995.
10. Strieter R.M., Polverini P.J., Kunkel S.L., Arenberg, D.A., Burdick, M.D., Kasper, J., Dzuiba, J., VanDamme, J., Walz, A., Marriott, D., Chan, S-Y., Roczniak, S. and Shanafelt, A.B.: The functional role of the 'ELR' motif in CXC chemokine-mediated angiogenesis. J. Biol. Chem. 270:27348-27357, 1995.
11. Elner, S.G., Elner, V.M., Jaffe, G.J., Stuart, A., Kunkel, S.L. and Strieter, R.M.: Cytokines in proliferative diabetic retinopathy and proliferative vitreoretinopathy. Current Eye Research 14:1045-1053, 1995.
12. Kunkel, S.L., Strieter, R.M., Lindley, I.J.D. and Westwick, J.: Chemokines: New ligands, receptors, and activities. Immunol Today 16:559-561, 1995.
13. Kunkel, S.L., Lukacs, N.W. and Strieter, R.M.: Expression and biology of neutrophil and endothelial cell-derived chemokines. Seminars in Cell Biol. 6:327-336, 1995.
14. Driscoll, K.E., Hassenbein, D.G., Carter, J.M., Kunkel, S.L., Quinlan, T.R. and Mossman, B.T.: TNF alpha and increased chemokine expression in rat lung after particle exposure. Toxicology Letters 83:483-489, 1995.
15. Koch, A.E., Kunkel, S.L., Shah, M.R., Fu, R., Mazarakis, D.D., Haines, G.K., Burdick, M.D., Pope, R.M. and Strieter R.M.: Macrophage inflammatory protein-1β: A C-C chemokine in osteoarthritis. Clin. Immunol. Immunopathol. 77:307-314, 1995.
16. Schmouder, R.L. and Kunkel, S.L.: The cytokine response in renal allograft rejection. Nephrol. Dial. Transplant. 10: 36-43, 1995.
17. Conlon, K., Lloyd, A., Chattopadhyay, U., Lukacs, N., Kunkel, S.L., Schall, T., Taub, D., Morimoto, C., Osbourne, J. and Oppenheim, J.J.: CD8+ and CD45RA+ human periheral blood lymphocytes are potent sources of macrophages inflammatory protein-1 alpha, interleukin-8, and RANTES. Eur. J. Immunol. 25:751-756, 1995.
18. VanOtteren, G.M., Standiford, T.J., Kunkel, S.L., Danforth, J.M. and Strieter, R.M.: Alterations of ambient oxygen concentration modulate the expression of tumor necrosis factor and macrophage inflammatory protein-1 alpha from murine alveolar macrophages. Am. J. Respir. Cell Mol. Biol. 13:399-409, 1995.

19. Massey, K.D., Strieter, R.M., Kunkel, S.L., Danforth, J.M. and Standiford TJ. Cardiac myocytes release leukocyte stimulating factors. Am J. Physiol: Heart and Circ. 269:2767-2773, 1995.
20. Greenberger, M.J., Strieter, R.M., Kunkel, S.L., Danforth, J.M., Laichalk, L.L. and Standiford T.J. Neutralization of macrophage inflammatory protein-2 attenuates neutrophil recruitment and bacterial clearance in murine Klebsiella pneumonia. J. Infect. Dis. 173: 159-165, 1996.
21. Standiford, T.J., Kunkel, S.L., Greenberger, M.J., Laichalk, L.L. and Strieter, R.M.: Expression and regulation of chemokines in bacterial pneumonia. J. Leukocyte Biol. 59:24-28, 1996.
22. Shanely, T., Peters, J.L., Jones, M.L., Chensue, S.W., Kunkel, S.L. and Ward, P.A.: Regulatory effects of interleukin-1 receptor antagonist protein in immunoglobulin immune complex-induced lung injury. J. Clin. Invest. 97:963-970, 1996.
23. Ruth, J.H., Bienkowski, M., Warmington, K.S., Lincoln, P.M., Kunkel, S.L. and Chensue, S.W.: IL-1 receptor antagonist (IL-1ra) expression, function, and cytokine-mediated regulation during mycobacterial and schistosomal antigen-elicited granuloma formation. J. Immunol. 156:2503-2509, 1996.
24. Strieter, R.M., Standiford, T.J., Huffnagle, G.B., Colletti, L.M., Lukacs, N.W. and Kunkel, S.L.: Commentary: "The good, the bad, and the ugly": The role of chemokines in models of human disease. J. Immunol. 156:3583-3586, 1996.
25. Lukacs, N.W., Strieter, R.M., Lincoln, P.M., Brownell, E., Pullen, D.M., Schock, H.J., Chensue, S.W., Taub, D.D. and Kunkel, S.L.: Stem cell factor (c-kit ligand) influences eosinophil recruitment and histamine levels in allergic airway inflammation. J. Immunol. 156:3945-3951, 1996.
26. Glabinski, A.R., Balasingam, V., Tani, M., Kunkel, S.L., Strieter, R.M., Wee Yong, V. and Ransohoff, R.M.: Chemokine monocyte chemoattractant protein-1 (MCP-1) is expressed by astrocytes after mechanical injury to the brain. J. Immunol. 156:4363-4368, 1996.
27. Colletti, L.M., Kunkel, S.L., Walz, A., Burdick, M., Kunkel, R.G., Wilke, C.A. and Strieter, R.M.: The role of cytokine networks in the local liver injury following hepatic ischemia/reperfusion in the rat. Hepatology 23:506-514, 1996.
28. Murphy W.J., Tian, Z.G., Asai, O., Funakoshi, S., Rotter, P., Henry, M., Strieter, R.M., Kunkel, S.L., Longo, D.L. and Taub, D.D.: Chemokines and T lymphocyte activation II. Facilitation of human T cell trafficking in severe combined immunodeficient mice. J. Immunol. 156:2104-2111, 1996.
29. Kunkel, S.L., Lukacs, N., Kasama, T. and Strieter, R.M. The role of chemokines in inflammatory joint disease. J. Leuk. Biol. 59:6-12, 1996.
30. Donnelly, S.C., Strieter, R.M., Reid, P.T., Kunkel, S.L., Burdick, M.D., Armstrong, I., Mackenzie, A. and Haslett, C.: The association between motality rates and decreased concentration of interleukin-10 and interleukin-1 receptor antagonist in the lung fluids of patients with the adult respiratory distress syndrome. Ann. Inter. Med. 125:191-196, 1996.

BOOKS AND CHAPTERS IN BOOKS:

1. Walz, A., Kunkel, S.L. and Strieter, R.M.: CXC chemokines: An Overview, in, Koch, A.E. and Strieter, R.M. (eds), The Role of Chemokines in Disease, R.G. Landes Co., Biomedical Publishers, Austin, Texas.

2. Strieter, R.M., Kunkel, S.L., Shanafelt, A.B., Arenberg, D.A., Koch, A.E. andPolverini, P.J.: The role of CXC chemokines in regulation of angiogenesisin, in, Koch, A.E. and Strieter, R.M. (eds), The Role of Chemokines in Disease, R.G. Landes Co., Biomedical Publishers, Austin, Texas.
3. Strieter, R.M., Standiford, T.J., Colletti, L.M. and Kunkel, S.L.: Neutrophil recruitment in acute lung injury: The interplay of early response cytokines, adhesion molecules, and CXC chemokines in, Koch, A.E. and Strieter, R.M. (eds), The Role of Chemokines in Disease, R.G. Landes Co., Biomedical Publishers, Austin, Texas.
4. Kunkel, S.L., Chensue, S.W., Lukacs, N.W. and Strieter, R.M.: Macrophage-derived cytokines in lung inflammation, in, Lipscomb, M. and Russell, S. (eds), Lung Macrophages and Dendritic Cells, Marcel Dekker, New York, New York.
5. Kunkel, S.L.: An introduction to cytokine biology, n, Davenport, R.(ed), Cytokines and Biological Response Modifiers. A Transfusion Medicine Primer, American Association for Blood Banking.
6. Lukacs, N.W., Strieter, R.M. and Kunkel, S.L.: Adhsion molecules, cytokines, and chemokines in allergic airway inflammation, in, Bochner, B. (ed), Adhsion Molecules in Allergic Disease, Marcel Dekker, New York, New York.

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

1. Greenberger, M.J., Kunkel, S.L., Danforth, J.M., Strieter, R.M. and Standiford, T.J.: Interleukin-10 and interleukin-12 differentially influence survivial in murine Klebsiella pneumonia. J. Invest. Med. 43:479A, 1995.
2. Arenberg, D.A., Kunkel, S.L., Burdick, M.D., Polverini, P.J., Strieter, R.M.: Treatment with anti-IL-8 inhibits non-small cell lung cancer tumor growth. J. Invest. Med. 43:479A, 1995.
3. Colletti, L.M., Kunkel, S.L., Green, M., Burdick, M. and Strieter, R.M.: C-X-C chemokines may be important molecules for hepatocyte proliferation, Presented at the Surgical Forum, New Orleans, Louisiana, October, 1995.
4. Arenberg, D., Kunkel, S., DiGiovine, B., Whyte, R., Iannetoni, M., Smith, D., Glass, M., Burdick, M. and Strieter, R.: CC chemokine levels are elevated in human lung cancer. J. Invest. Med 44:276A, 1996.
5. Walley, K.R., Lukacs, N.W., Standiford, T.J., Strieter, R.M. and Kunkel, S.L.: Balance of pro-- and anti-inflammatory cytokines regulates inflammation and mortality in sepsis. Am. J. Respir. Crit. Care Med. 153:A834, 1996.
6. Walley, K.R., Lukacs, N.W., Standiford, T.J., Strieter, R.M. and Kunkel, S.L.: Pattern of chemokine expression in murine sepsis. Am. J. Respir. Crit. Care Med. 153:A834, 1996.
7. Driscoll, K.E., Carter, J.M., Howard, B.W., Kunkel, S.L. and Strieter, R.M.: Role of interleukin-10 (IL-10) in silica-induced pulmonary inflammation in rats. Am. J. Respir. Crit. Care Med. 153:A288, 1996.
8. Arenberg, D., Kunkel, S.L., Polverini, P.J., Whyte, R.I., Iannetoni M, Burdick, M.D., Glass, M., Morris, S., DiGiovine, B. and Strieter, R.M.: Interferon g-inducible protein 10 (IP-10) is a potent angiostatic factor present in non-small cell lung cancer (NSCLC). Am. J. Respir. Crit. Care Med. 153:A672, 1996.

9. Greenberger, M.J., Kunkel, S.L., Strieter, R.M., Gauldie, J., Bramson, J., Lukacs, N.W., Danforth, J.M. and Standiford, T.J.: Transient lung interleukin-12 transgene expression increases survival in murine Klebsiella pneumonia. Am. J. Respir. Crit. Care Med. 153:A694, 1996.
10. Lukacs, N.W., Kunkel, S.L., Chensue, S.W. and Strieter, R.M.: Differential recruitment of leukocyte populations by CC chemokines during allergic airway inflammation. Am. J. Respir. Crit. Care Med. 153:A219, 1996.
11. DiGiovine, B., Lynch, J.P., Martinez, F.J., Flint, A, Whyte, R.I., Iannettoni, M.D., Arenberg, D.A., Burdick, M.D., Glass, M.C., Morris, S.B., Kunkel, S.L. and Strieter, R.M.: IL-8 is elevated in lung transplant recipients with obliterative bronchiolitis. Am. J. Respir. Crit. Care Med. 153:A152, 1996.
12. Morrison, D., Strieter, R.M., Donnelly, S., Burdick, M.D., Kunkel, S.L. and MacNee, W.: Epithelial permeability *in vivo* and *in vitro* and TNFa in bronchoalveolar lavage fluid and leucoyte conditioned medium from non smokers and smokers. Am. J. Respir. Crit. Care Med. 153:A505, 1996.
13. Strieter, R.M., Polverini, P.J. and Kunkel, S.L.: The role of CXC chemokines in regulation of angiogenesis, Submitted to the 1996 Eric K. Fernström Symposium on "Cytokines and Anticytokines, Cytokines in Hematopoiesis, Inflammation, and Matrix Biology", Lund, Sweden, June 2-5, 1996.
14. Simpson, K.J., Lukacs, N., Strieter, R.M. and Kunkel, S.L.: Monocyte adhesion to HepG2 cells stimulates the production of CXC and CC chemokines. FASEB J. 10:A1426, 1996.
15. Lukacs, N.W., Strieter, R.M., Karpus, W.J., Keefer, C., Lincoln, P., Chensue, S.W. and Kunkel, S.L.: FASEB J. 10:A1036, 1996.
16. Strieter, R.M., Kunkel, S.L., Chensue, S.W., Burdick, M.D., Evanoff, H.L. and Lukacs, N.W.: Mast cell-derived ENA-78 functions as a potent neutrophil chemoattractant during allergic airway inflammation. FASEB J. 10:A1217, 1996.
17. Polak, T., Kunkel, S.L., Strieter, R.M., Marin, E. and Lukacs, N,W.: C-C chemokines augment allogeneic responses. FASEB J. 10:A1319, 1996.
18. Parks, E., Lukacs, N.W., Strieter, R.M. and Kunkel, S.L.: Differential regulation of chemokines by monocytes and endothelial cells. FASEB J. 10:A1293, 1996.
19. Sullivan, T.D., Kunkel, S.L., Burdick, M.D., Glass, M.C., Arenberg, D.A., DiGiovine, B., Morris, S.B. and Strieter, R.M.: Prostaglandin E2 augments the prodcution of two pro-inflammatory chemokines (ENA-78 and GRO-a). FASEB J. 10:A1485, 1996.
20. DiGiovine, B., Lynch III, J.P., Martinez, F.J., Flint, A., Whyte, R.I., Iannettoni, M.D., Arenberg, D.A., Burdick, M.D., Glass, M.C., Morris, S.B., Kunkel, S.L. and Strieter, R.M.: Neutrophilic alveolitis in obliterative bronchiolitis after lung transplantation: Role of interleukin-8. FASEB J. 10:A1194, 1996.
21. Arenberg, D.A., Kunkel, S.L., Polverini, P., Whyte, R., Iannettoni, M., Burdick, M., Glass, M., Morris, S., DiGiovine, B. and Strieter, R.: Interferon-g-inducible protein 10 (IP-10) inhibits tumor growth of non-small cell lung cancer (NSCLC). FASEB J. 10:A1472, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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 nine postdoctoral fellows (Aron Thall, Ph.D., Peter Smith, Ph.D., E. Paul Scheidegger, M.D., Kazuhiro Yago, M.D.,. Daniel Legault, M.D., Steven Domino, M.D., Ph.D., Jonathon Homeister, M.D., Ph.D., Petr Maly, Ph.D., and Hedwig Murphy, M.D., Ph.D.).
B. Lecturer - Postdoctoral Research Training Program.
C. Member of three Ph.D. thesis committees (Akhilesh Pandey, George Pipia, and Vance H. Thomas).
D. Oral preliminary 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), $481,355/five years direct cost), 09/01/92 - 04/30/97.
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. Resident Selection Committee.
B. Chair, Neuropathology Faculty Search Committee.

REGIONAL AND NATIONAL:

A. Member, Pathobiochemistry Study Section, Division of Research Grants, National Institutes of Health.
B. Member, Scientific Advisory Board, The Ara Parseghian Medical Research Foundation (Niemann-Pick disease type C).
C. Co-chair, Unified Graduate Admission Program Task Group, University of Michigan Medical School.
D. Member, Editorial Board of the Journal of Biological Chemistry.
E. Member, Editorial Board of Glycobiology.
F. Member, Editorial Board of Archives of Biochemistry and Biophysics.
G. Consulting Reviewer for Proceedings of the National Academy of Sciences USA, Journal of Clinical Investigation, 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, Associate Investigator.

VI. INVITED LECTURES AND SEMINARS:

1. "Ablation of murine glycosyltransferase genes", Federation of the European Biochemical Societies, Basel, Switzerland, August, 1995.
2. "Deletion of selectin ligand expression by fucosyltransferase gene ablation in the mouse", Genzyme Corporation, Cambridge, Massachusetts, September, 1995.

3. "Ablation of murine glycosyltransferase genes", Phillipe Laudat Conference on Glycoconjugates, Aix-les-Bains, France, October, 1995.
4. "Deletion of selectin ligand expression by fucosyltransferase gene ablation in the mouse", University of California at San Diego, San Diego, California, January, 1996.
5. Keynote Lecture: "Structure and function of glycosyltransferases", 1996 Keystone Symposium: The extracellular matrix of plants. Tamarron, Colorado, March, 1996.
6. "Fucosyltransferases required for selectin ligand expression", University of Michigan Department of Medicinal Chemistry and Pharmaceutics Ann Arbor, Michigan, May, 1996.
7. "Defective leukocyte recruitment, lymphocyte homing," and "E-, P-, and L-selectin ligand expression, in mice deficient in the α(1,3)fucosyltransferase Fuc-TVII", University of Michigan Division of Rheumatology, Ann Arbor, Michigan, May, 1996.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Masteller, E., Larsen, R.D., Carlson, L.M., Pickel, J.M., Nickoloff, B., Lowe, J., Thompson, C.B. and Lee, K.P.: The selectin ligand sialyl Lewis x is developmentally regulated during chicken B cell development and appears to direct lymphocyte homing to the bursa of Fabricius. Development 121:1657-1667, 1995.
2. Thall, A.D., Maly, P. and Lowe, J.B.: Oocyte Galα1,3Gal epitopes implicated in sperm adhesion to the zona pellucida glycoprotein ZP3 are not required for fertilization in the mouse. J. Biol. Chem. 270:21437-21440, 1995.
3. Scheidegger, E.P., Sternberg, L.R., Roth, J. and Lowe, J.B.: A human STX cDNA confers polysialic acid expression in mammalian cells. J. Biol. Chem. 270:22685-22688, 1995.
4. Gersten, K.M., Natsuka, S., Trinchera, M., Petryniak, B., Kelly, R.J., Hiraiwa, N., Jenkins, N.A., Gilbert, D.J., Copeland, N.G. and Lowe, J.B.: Molecular cloning, expression chromosomal assignment, and tissue-specific expression of a murine α(1,3)fucosyltransferase locus corresponding to the human ELAM-1 Ligand Fucosyl Transferase (ELFT/Fuc-TIV). J. Biol. Chem. 270:25047-25056, 1995.
5. Henry, S., Mollicone, R., Lowe, J.B., Samuelsson, B. and Larson, G.: A second non-secretor allele of the blood group α(1,2)fucosyltransferase (FUT2). Vox Sang. 70:21-25, 1996.
6. Smith, P.L., Gersten, K.M., Petryniak, B., Kelly, R.J., Rogers, C., Natsuka, Y., Alford, J.A. III, Natsuka, S., and Lowe, J.B.: Expression of the α(1,3)fucosyltransferase Fuc-TVII in lymphoid aggregate high endothelial venular endothelial cells correlates with expression of L-selectin ligands. J. Biol. Chem. 271:8250-8259, 1996.
7. Knibbs, R.N., Craig, R.A., Natsuka, S., Chang, A., Cameron, M., Lowe, J.B. and Stoolman, L.M.: The fucosyltransferase Fuc-TVII regulates E-selectin ligand synthesis in human T-cells. J. Cell. Biol. 133:911-920, 1996.
8. Thall, A.D., Murphy, H. and Lowe, J.B.: α(1,3)Galactosyltransferase deficient mice produce naturally occurring cytotoxic anti-Gal antibodies. Transplantation Proc. 28:556-557, 1996.
9. Wagers, A.J. Lowe, J.B. and Kansas, G.S.: An important role for the α1,3fucosyltransferase Fuc-TVII in leukocyte adhesion to E-selectin. Blood In Press, 1996.

10. Maly, P., Thall, A.D., Petryniak, B., Rogers, C.E., Smith, P.L., Marks, R.M., Kelly, R.J., Gersten, K.M., Cheng, G., Saunders, T.L., Camper, S.A., Camphausen, R.T., Sullivan, F.X., Isogai, Y., Hindsgaul, O., von Adrian, U.H. and Lowe, J.B.: The α(1,3)fucosyltransferase Fuc-TVII controls leukocyte trafficking through an essential role in L-, E-, and P-selectin ligand expression. Cell In Press, 1996.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Prieto, P.A., Larsen, R.D., Rivera, H.N., Shilatifardi, A., Lowe, J.B., Cummings, R.D. and Smith, D.F.: Expression of the human H-type α1,2fucosyltransferase encoding for blood group H(O) antigen in Chinese hamster ovary cells: evidence for potential fucosylation and truncation of polylactosamine sequences. Submitted.
2. Fuhlbrigge, R.C., Alon, R., Puri, K.D., Lowe, J.B. and Springer, T.A.: Sialylated, fucosylated ligands for L-selectin expressed on leukocytes mediate tethering and rolling adhesions in physiologic flow conditions. Submitted.
3. Thall, A., von Adrian, U.H., Cheng, G., Petryniak, B., Camper, S., Saunders, T. and Lowe, J.B.: 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.
4. Domino, S., Hiraiwa, N. and Lowe, J.B.: Structure and tissue-specific expression of a murine α(1,2) fucosyltransferase gene. In Preparation.
5. Hiraiwa, N., Domino, S., Saunders, T. and Lowe, J.B.: Dominant pre-implantation lethality in mice directed by aberrant expression of an α(1,2)fucosyltransferase cDNA. In Preparation.
6. Smith, P.L., Phillips, M.L., Ketchum, K., Paulson, J.C. and Lowe, J.B.: 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:

1. Lowe, J.B.: The carbohydrate components of selectin ligands, in, Vestweber, D. (ed), The Selectins: Initiators of Leukocyte Endothelial Adhesion, Harwood Academic Publishers, Reading, United Kingdom, 1996.

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

ANNUAL DEPARTMENT REPORT
1 JULY 1995-30 JUNE 1996

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. "Immune mechanisms of Disease", Epidemiology 570, Course Instructor, Fall, 1995.
B. Immunovirogy lectures, Epidemiology, School of Public Health, Lecturer, Winter, 1996.
C. Supervised Undergraduate students: Kolby Keifer, Matt Steinhauser, Scott Lipinski, Carrie Zickus, and Eric Strieter.

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, May 1, 1996 to April 30, 2001.
B. Principal Investigator, "Leukocyte recruitment in eosinophilic inflammation", American Lung Association Research Grant, July 1 1995 to June 30, 1997.
C. Prinicipal Investigator, "Production of Chemokines During Monocyte:Endothelial Cell Interactions", American Heart Association of Michigan Grant-in-Aid, July 1, 1995 to June 30, 1996.
D. Co-Investigator, "The Role of Chemokines in Autoimmune Encephalomyelitis", NIH RO1 NS34510-01, with William J. Karpus, Ph.D. Microbiology/Immunology, Northwestern University, Chicago, Illinois, September, 1995 to August, 1999.

PENDING SUPPORT:

A. Principal Investigator, "SCF and Mast Cells in Allergic Airway Inflammation", RO1 December 1, 1996 - November 30, 2001, National Institutes of Health.
B. 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.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

None

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Reviewer for the following Journals:
   1. American Journal of Pathology
   2. Journal of Immunology
   3. American Journal of Respiratory Cell and Molecular Biology
   4. Infection and Immunity
   5. Immunology Today

INVITED LECTURES/SEMINARS:

1. "Participation of Chemokines in Inflammatory Lung Inflammation", Wayne State University School of Medicine, Department of Immunology/Microbiology. Detroit, Michigan, October 3, 1995.
2. "Cytokines and Leukocyte Recruitment in a Murine Model of Allergic Airway inflammation", Fifth annual lung cell biology symposium at Woods Hole, Cape Cod, Maine, November 5-8, 1995.
3. "The Role of Cytokines in Allergic Airway Inflammation", Michigan State University, Department of Veterinary Medicine. January 11, 1996.
4. "Non-traditional Academic Positions in Academics", University of Michigan Graduate School. Ann Arbor, Michigan, January 29, 1996.
5. "Cytokines and Leukocytes in Allergic Airway Inflammation", The 4th Annual Midwest Inflammation Research Assoc. Conference. Chicago, Illinois, March 6, 1996.
6. "The Role of Chemokines in Inflammation and Disease", University of Sheffield, Department of Clinical Sciences, Sheffield, England, U.K., April 15, 1996.
7. "Inflammatory and Chemotactic Cytokines in Animal Models of Disease", British Society of Immunology, Spring Meeting, Bristol, England, U.K., April 18, 1996.

8. "Chemokine Activation and Regulation in Animal Models of Disease", Louisiana State University Medical School, Department of Microbiology and Immunology, New Orleans, Louisiana, May 13th, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERREED JOURNALS:

1. Lukacs, N.W., Strieter, R.M., Elner, V., Evanoff, H., Burdick, M.D. and Kunkel, S.L.: Production of chemokines, IL-8 and MCP-1, during monocyte:endothelial cell interactions is induced via matrix protein interactions. Blood 86:2767-2773, 1995.
2. Standiford, T.J., Strieter, R.M., Lukacs, N.W. and Kunkel, S.L.: Neutralization of IL-10 increases lethality in endotoxemia: Cooperative effects of macrophage inflammatory protein-2 and tumor necrosis factor. J.Immunol. 155:2222-2229, 1995.
3. Standiford, T.J., Kunkel, S.L., Lukacs, N.W., Greenberger, M.J., Danforth, J.M., Kunkel, R.G. and R.M. Strieter: Macrophage inflammatory protein-1a mediates lung leukocyte recruitment, lung capillary leak, and early mortality in murine endotoxemia. J. Immunol. 155:1515-1524, 1995.
4. Karpus, W.J., Lukacs, N.W., McRae, B.L., Strieter, R.M., Kunkel, S.L. and Miller, S.D.: An essential role for chemokines in the pathogenesis of T cell-mediated autoimmune disease. J. Immunol. 155:5003-5110.
5. Colon, K., Lloyd, A., Chattopadhyay, U., Lukacs, N., Kunkel, S., Schall, T., Taub, D., Morimoto, C., Osborne, J., Oppenheim, J. et al.: . CD8+ and CD45RA+ human peripheral blood lymphocytes are potent sources of macrophage inflammatory protein-1 alpha, interleukin-8, and RANTES. Eur. J. Immunol. 25:751-756, 1995.
6. Lukacs, N.W., Strieter, R.M., Chensue, S.W. and Kunkel, S.L.: Activation and regulation of chemokines in allergic airway inflammation. J. Leuk. Biol. 59:13-18, 1996.
7. Strieter, R.M., Standiford, T.J., Huffnagle, G.B., Colletti, L.M., Lukacs, N.W. and Kunkel, S.L.: The good, the bad, and "the ugly": The role of chemokines in models of human disease. J. Immunol. 156:3583-3586, 1996.
8. Lukacs, N.W., Strieter, RM., Lincoln, P.M., Brownell, E., Pullen, D.M., Schock, H.J., Chensue, S.W., Taub, D.D. and Kunkel, S.L.: Stem cell factor (c-kit ligand) influences eosinophil recruitment in allergic airway inflammation. J. Immunol. 156:3945-3951, 1996.
9. Karpus, W.J. and Lukacs, N.W.: 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, 1996.
10. Lukacs, N.W., Kunkel, S.L., Strieter, R.M., Evanoff, H., Key, M.L. and Taub, D.D.: The role of stem cell factor (c-kit ligand) and inflammatory cytokines in pulmonary mast cell activation. Blood, In Press, 1996.
11. Goldstein, L.A., Strieter, R.M., Evanoff, H.L, Kunkel, S.L. and Lukacs, N.W.: TNF-induced IL-8 and MCP-1 production in eosinophilic cell line, EOL-1. Mediators in Inflammation, In Press.
12. Lukacs, N.W.: Cytokines in allergic eosinophilic airway inflammation. Biological Signals, In Press.

13. Greenberger, M.J., Kunkel, S.L., Strieter, R.M., Lukacs, N.W., Bramson, J., Gauldie, J., Graham, F.L., Hitt, M., Danforth, J.M. and Standiford, T.J.: Transient lung IL-12 transgene expression increases survival in murine Klebsiella pneumonia. J. Immunol., In Press.

BOOKS/CHAPTERS IN BOOKS

1. Lukacs, N.W. and Ward, P.A.: Inflammatory mediators, cytokines, and adhesion molecules in pulmonary inflammation and injury. Advances Immunol., In Press.
2. Kunkel, S.L., Lukacs, N.W. and Strieter, R.M.: Expression and biology of neutrophil and endothelial cell-derived chemokines. Sem. in Cell Biol. 6:327-336, 1995.
3. Lukacs, N.W. and Ward, P.A.: . Chemotactic molecules and cellular activation, in, Kaplan, A.P. (ed), Allergy, Second Edition, In Press.
4. Kunkel, S.L., Chensue, S.W., Lukacs, N.W. and Strieter, R.M.: Macrophage-derived cytokines in lung inflammation, in, Lipscomb, M.F. and Russell, S. (eds), Lung Macrophages and Dendritic Cells, Marcel Dekker, Inc. New York, New York.
5. Kunkel, S.L., Lukacs, N.W., Strieter, R.M. and Chensue, S.W.: TH1 and TH2 responses regulate experimental lung granuloma development. Sarcoidosis, Submitted.
6. Lukacs, N.W., Strieter, R.M. and Kunkel, S.L.: Adhesion molecules, cytokines, and chemokines in allergic airway inflammation, in, Bochner, B.S. (ed), Adhesion Molecules in Allergic Diseases, Marcel Dekker, Inc. New York, New York.

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

1. Lukacs, N.W., Kunkel, S.L., Evanoff, H., Strieter, R.M., Key, M.L., Kunkel, R.G. and Taub, D.D.: The role of stem cell factor (C-kit ligand) and inflammatory cytokines in pulmonary mast cell activation. International Immunol. Conference, 1995.
2. Wallace, L., Lukacs, N.W. and Brownell, E.: Effects of bronchoalveolar lavage (BAL) fluids on mast cell proliferation. AAAI Annual Meeting, 1994.
3. Lukacs, N.W., Kunkel, S.L., Strieter, R.M., Karpus, W.J., Keefer, C., Lincoln, P. and Chensue, S.W.: C-C chemokines differentially alter IL-4 production from lymphocytes. FASEB J. A1036, 1996.
4. Strieter, R.M., Kunkel, S.L., Chensue, S.W., Burdick, M.D., Evanoff, H.L. and Lukacs, N.W.: Mast cell-derived ENA-78 fuctions as a potent neutrophil chemoattractant during allergic airway inflammation. FASEB J. A1217, 1996.
5. Parks, E., Lukacs, N.W., Strieter, R.M. and Kunkel, S.L.: Differential regulation of chemokines by monocytes and endothelial cells. FASEB J. A1293, 1996.
6. Polak, T., Kunkel, S.L., Strieter, R.M., Marin, E. and Lukacs, N.W.: C-C chemokines augment allogeneic responses. FASEB J. A1319, 1996.
7. Simpson, K.J., Lukacs, N., Strieter, R.M. and Kunkel, S.L.: Monocyte adhesion to HepG2 cells stimulates the production of C-X-C and C-C chemokines. FASEB J. A1426, 1996.
8. Walley, K.R., Lukacs, N.W., Standiford, T.J., Strieter, R.M. and Kunkel, S.L.: Pattern of chemokine expression in murine sepsis. Am. Thoracic Soc. Int. Meeting, 1996.

9. Walley, K.R., Lukacs, N.W., Standiford, T.M., Strieter, R.M. and Kunkel, S.L.: Balance of pro- and anti-inflammatory cytokines regulates inflammation and mortality in sepsis. Am. Thoracic Soc. Int. Meeting, 1996.
10. Lukacs, N.W., Kunkel, S.L., Chensue, S.W. and Strieter, R.M.: Differential recruitment of leukocyte populations by C-C chemokines during allergic airway inflammation. Am. Thoracic Soc. Int. Meeting, 1996.
11. Greenberger, M.J., Kunkel, S.L., Strieter, R.M., Gauldie, J., Bramson, J., Lukacs, N.W., Danforth, J.M. and Standiford, T.J.: Transient lung interleukin-12 transgene expression increases survival in murine klebsiella pneumonia. Am. Thoracic Soc. Int. Meeting, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Surgical Pathology, consultant on head and neck pathology cases, 1983-June 30, 1996.
B. Autopsy, 1983-present:
   1. Consultant on forensic odontology cases.
   2. Assistant Medical Examiner, Washtenaw County.
C. Director of Clinical Microbiology\Virology Laboratory, 1978-March, 1996.
D. Ann Arbor Veterans Administration Medical Center - monthly consultant, 1978-June 30, 1996.
E. Associate Chief of Clinical Affairs, 1990-1995.
F. Staff, Oral Pathology Laboratory, School of Dentistry, 1973-June 30, 1996.
G. Professor, Department of Otorhinolaryngology, 1991-1995.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Pathology 630/580/631; Course Director, 1983-June 30, 1996.
B. Otorhinolaryngology Pathology 856, Director, 1979-June 30, 1996.

III. RESEARCH ACTIVITIES:

A. Consultant, "Impact of Follow-Up on Control of High Blood Pressure and Cholesterol," Principal Investigator, Andrea Foote, Ph.D., Institute of Labor and Industrial Relations, the University of Michigan, 1988-1995.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Clinical Microbiology/Virology Laboratory, 1978-March, 1996.

MEDICAL SCHOOL/HOSPITAL:

A. Medical Liability Review Committee, 1992-June 30, 1996.
B. Member, Patient Care Advisory Committee, The University of Michigan Hospitals, 1989- June 30, 1996.
C. Member, Technical Advisory Committee, State of Michigan, Department of Health, Bureau of Laboratory and Epidemiological Services, 1987-June 30, 1996.
D. Chairman, Standardization and Product Evaluation Committee (SPEC), The University of Michigan Medical Center, 1991-June 30, 1996.
E. Associate Chief of Clinical Affairs, The University of Michigan Hospitals, 1990-1995.
F. Member, Executive Committee on Clinical Affairs, The University of Michigan Medical Center, 1990-1995.

G. Vice Chairman, Claims Control Committee, The University of Michigan Hospitals, 1990-1995.
H. Clinical Practice Work Group, University of Michigan, 1993-June 30, 1996.
I. Health Services Research Coordinating Committee, University of Michigan, 1993-June 30, 1996.

REGIONAL AND NATIONAL:

A. College of American Pathologists:
   1. Member, Standards Committee, 1986-present.
   2. Council on Scientific Affairs, 1987-present.
   3. Chairman, International Committee, 1993-present.
B. National Committee for Clinical Laboratory Standards:
   1. Council of the National Reference System for the Clinical Laboratory, 1983-present.
   2. International Relations Committee, member, 1988-present.
   3. Committee on Standardization of the PAP Technique, Chairman, 1988-present.
   4. Committee on Standardization of FNA Technique, Chairman, 1992-present.
   5. Area Committee on Alternate Site Testing, member, 1993-present.
   6. Subcommittee on Point of Care Testing, member, 1993-present.
   7. Member, Board of Governors.
C. American Society of Clinical Pathologists:
   1. ASCP Advisory Council, 1984-1995.
   2. Contributor, Laboratory Management, Resident Examination, 1992-present.
D. Technical Advisory Committee, State of Michigan Department of Health, Bureau of Laboratory and Epidemiological Services, 1987-1996.
E. American Society for Testing Materials (ASTM):
   1. Committee F31 on Health Care Services, member, 1988-present.

INTERNATIONAL:

A. Secretariat, Commission on World Standards of World Association of Societies of Pathology, 1987-present.
B. Chair, Committee on Management of the Blood System, Committee on Blood Safety. Government of Canada, 1993-1995.
C. International Organization for Standardization Technical Committee 212, 1995-present.
D. Pan American Health Organization, Advisory Committee, 1995-present.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Quality Management, World Association of Societies of Pathology, Biennial Meeting, Auckland, New Zealand, October, 1995.
2. Worldwide Standards, Local Impact, National Committee for Clinical Laboratory Standards, Annual Conference, Atlanta, Georgia, March, 1996.
3. International Laboratory Standardization, National Committee for Clinical Laboratory Standards, Annual Conference, Atlanta, Georgia, March, 1996.

VI. PUBLICATIONS

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Sassler, A.M., McClatchey, K.D., Wolf, G.T., Fischer, S.G. and the Laryngeal Cooperative Study Group: Eosinophilic infiltration in advanced laryngeal squamous cell carcinoma. Laryngoscope 105:1-4, 1995.
2. Beck, J.C., McClatchey, K.D., Lesperance, M.M., Esclamado, R.M., Carey, T.F. and Bradford, C.R.: Presence of human papillomavirus predicts recurrence of inverted papilloma. Otolaryngol. Head & Neck Surgery 113:49-55, 1995.
3. Strome, S.E., McClatchey, K.D., Kileny, P and Koopman, C.F. Jr.: Neonatal choristoma of the tongue containing glial tissue: Diagnosis and surgical considerations. Int. J. Ped. Otohinolaryngol. 33:265-273, 1995.
4. Beck, J.C., McClatchey, K.D., Lesperance, M.M., Esclamado, R.M., Carey, T.E. and Bradford, C.R.: HPV types important in progression of inverted papilloma. Otolaryngol. Head & Neck Surgery 113:558-563, 1995.

ARTICLES SUBMITTED FOR PUBLICATION

1. Frank, C.J., McClatchey, K.D., Devaney, K.O. and Carey, T.E.: Squamous carcinomas cell lines accurately reflect in vivo loss of 18 q. Advances in Brief. Cancer Research, July, 1996.

BOOKS AND CHAPTERS IN BOOKS

1. Travers, E.M. and McClatchey, K.D.: Laboratory Management, Travers, E.M. (ed), Waverly Press, Baltimore, Maryland, 1996.

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

1. McClatchey, K.D.: The reference system for the clinical laboratory: Criteria for development and credentialing of methods and materials for harmonization of results; Accepted guideline, National Committee for Clinical Laboratory Standards, 1995.
2. Clinical Laboratory Medicine, Videodisc Program, Clinical Laboratory Medicine, Wilkins & Wilkins, Inc., 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1994 - 30 JUNE 1995

I. CLINICAL ACTIVITIES:

A. Daily surgical neuropathology and electron microscopic neuropathology - four months.
B. Consultations on surgical neuropathology from other hospitals.
C. Weekly Brain Tumor Board, review of neurosurgical, neuroradiologic, neuropathologic and clinical-pathologic correlation - six months.
D. Diagnostic neuropathology consultant, Veterans Administration Hospital - four months.
E. Examination of autopsy neuropathologic material - staff rotation and consults to faculty.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Neuroscience Sequence, Neuropathology for Second Year Medical Students.
B. House Officers:
   1. Individual daily instruction of Pathology House Officers over microscope.
   2. Review of neuropathologic postmortem material - staff rotation and consults to residents.
   3. Review all neurosurgically removed material in this hospital in CME-approved biweekly conference - six months.
   4. Shared consultations in conference.
   5. Invited presentations of neuropathologic observations at joint clinical conferences.
   6. Pathology Resident's monthly Neuropathology Conference - four months.
C. Two Pathology House Officers: Scott Silveira and Walter Henricks, and one Neurosurgery House Officer, Michael Polinsky: One month electives in neuropathology.
D. Teach laboratory techniques to Neurohistologists and Research Staff.

REGIONAL AND NATIONAL:

A. Nelson, J.S. and McKeever, P.E.: Clinical Neuropathology. Laser videodisk medical education reference, In Press.
B. 33rd Faculty Annual AFIP Neuropathology Review, Armed Forces Institutes of Pathology, New Orleans, Louisiana.

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. Co-Investigator, "PET Study of Biochemistry and Metabolism of the CNS," (Program Title), "Glioma Imaging with Benzodiazepine Analogs." (Section Title), National Institute of Health Program Project NS-15655, 1 December 1989-30 November 1994.
C. Co-Investigator, "PET, Growth Kinetics and Neuropathology of Brain Tumors," National Institutes of Health Grant, NIH, CA54104, 1 May 1991-30 April 1995.

PROJECTS UNDER STUDY:

A. Glioma tissue marker potential diagnostic and prognostic value with Drs. Mila Blaivas, Thomas W. Glover, David Gordon, Harry S. Greenberg, Robert Jones, Larry Junck, Anthony A. Killeen, Hernando Mena, James S. Nelson, Donald Ross, Susan Sheldon, Myla Strawderman, Jeffrey M. Trent and Sharon W. Weiss. Submitted to NCI.
B. Growth, spread and antigenicity of ENU-induced gliomas in rats with Constance D'Amato and Dr. Terry Hood, submitted to J. Neuro-oncology.
C. Quantitative analysis of DNA in fresh and cultured cells of brain tumors, with Drs. Karin Muraszko, Donald Ross, William Chandler and James Varani.
D. Extracellular matrix products and plasminogen activators of gliomas with Drs. James Varani, Robert Sitrin, Dario Caccamo and Suzanne Fligiel.
E. Magnetic resonance diffusion and cross relaxation of brain tumors with Drs. James Brunberg, Thomas Chenevert and Brian Ross.
F. Characterization of Rosai-Dorfman disease in brain with Drs. Michael Boland and Karin Muraszko.
G. Combined ultrastructural and karyotypic analysis of the VX-2 tumor with Dr. Thomas E. Carey, submitted to Int. J. Cancer.
H. Viral vectors in glioma therapy with Drs. Julian Hoff, Brian Ross and Donald Ross.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chief, Section of Neuropathology.
B. Member, Photography Committee.
C. Member, Immunoperoxidase Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Organization and scheduling of Pathology, Neurology, Neuroradiology and Neurosurgery House Officer Neuropathology teaching conferences, individual instruction and consultation review.
B. Organization of call logistics, specimen handling, and schedules for coverage of diagnostic neuropathology by staff.
C. Supervision of Neurohistologists and Neuropathology Laboratories, and quality control of histologic preparations.
D. Interaction with Chiefs and Staff of other clinical services, particularly Neurosurgery, Neurology, Nuclear Medicine, Radiation Oncology, Neuro-oncology and Neuro-radiology.
E. 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. Primary Review Pathologist, Children's Cancer Study Group CCG 9891 nationwide study of childhood low grade gliomas.
B. Reviewer for various pathology, neuroscience and neuro-oncology journals.
C. M-Labs Neuropathology Services.

V. OTHER RELEVANT ACTIVITIES:

PROFESSIONAL ORGANIZATIONS:

A. Faculty of Graduate Program of Department of Pathology.
B. Member of the University of Michigan Cancer Center.
C. Member, International Academy of Pathology, 1972--.
D. Member, Alpha Omega Alpha, Eta Chapter, 1972--.
E. Member, American Association of Neuropathologists, 1978--.
F. Member, Society of Neuroscience, 1983--.
G. Member, American Association of Pathologists, 1984--.
H. Member, Children's Cancer Study Group, 1985--.
   1. Pathology Committee, 1989--.
I. Member, Histochemical Society, 1989--.
   2. Councilor, 1994--.
J. Member, Constitution Committee, American Association of Neuropathologists, 1990- .

INVITED LECTURES/SEMINARS:

1. Chairperson, scientific session on brain tumors, American Association of Neuropathologists, and International Society of Neuropathologists, Toronto, Ontario, 1994.
2. Chairperson, scientific session, Brain tumors, United States and Canadian Academy of Pathology, Toronto, Ontario, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Sweasey, T.A., Brunberg, J.A., McKeever, P.E., Sandler, H.M. and Chandler, W.F.: Cystic cervical intramedullary ependymoma with previous intracyst hemorrhage: MR imaging at 1.5T. J. Neuroimaging 4:11-113, 1994.
2. Caccamo, D., Keohane, M.E. and McKeever, P.E.: Plasminogen activators and inhibitors in gliomas: An immunohistochemical study. Modern Pathology 7:99-104, 1994.
3. Meyer, J.R., Quint, D.J., McKeever, P.E., Boland, M. and Ross, D.A.: Giant Rathke's cleft cyst. Am. J. Neuroradiol.. 15:533-536, 1994.
4. Greenberg, H.S., Chandler, W.F., Ensminger, W.D., Sandler, H., Junck, L., Page, M.A., Crane, D., McKeever, P.E., Tankanow, R. and Bromberg, J.: Radiosensitization with carotid intra-arterial bromodeoxyuridine ± 5-fluorouracil biomodulation for malignant gliomas. Neurology 44:1715-1720, 1994.
5. McKeever, P.E., Varani, J., Papadopoulos, S.M., Wang, M. and McCoy, J.P.: Products of cells from gliomas: IX. Evidence that two fundamentally different mechanisms change extracellular matrix expression by gliomas. J. Neuro-Oncol. 1995, In Press.
6. Roberson, P.L., Ten Haken, R.K., McKeever, P.E. and Ensminger, W.D.: Nonuniform liver dose for yttrium-90-microsphere therapy in a rabbit model. J. Nucl. Med., In Press.

7. Levy, R.A., Allen, R. and McKeever, P.E.: Pleomorphic xanthoastrocytomas presenting with massive intracranial hemorrhage. Am. J. Neuroradiol.., In Press.
8. Brunberg, J.A., Chenevert, T.L., McKeever, P.E., Ross, D.A., Junck, L.R., Muraszko, K.M., Dauser, R., Pipe, J.G. and Betley, A.T.: *In vivo* MR determination of water diffusion coefficients and diffusion anisotrophy: Correlation with structural alterations in gliomas of the cerebral hemispheres. Amer. J. Neuroradiol. 16:361-371, 1994.
9. McKeever, P.E., Dennis, T.R., Burgess, A.C., Meltzer, P.S., Marchuk, D.A. and Trent, J.M.: Chromosomal breakpoint at 17q11.2 and insertion of DNA from three different chromo- somes in a glioblastoma with exceptional GFAP expression. Cancer Genet. Cytogenet, In Press.

BOOKS/CHAPTERS IN BOOKS:

1. McKeever, P.E. and Lloyd, R.V.: Pituitary adenomas and related lesions, in, Garcia, J.H. (ed), Diagnostic Neuropathology, Vol IV, Mosby, In Press.
2. McKeever, P.E. and Blaivas, M. : The brain, spinal cord, and meninges, in, Sternberg. S.S., Antonioli, D.A., Carter, D., Mills, S.E., and Oberman, H.A. (eds), Diagnostic Surgical Pathology, Raven Press, Ltd., New York, New York, pp. 409-492, 1994.
3. McKeever, P.E.: Molecular neuropathology in brain tumor diagnosis, in, Kornblith, P.L., Walker, M., and Korn, S.E. (eds), Advances in Neuro-Oncology, Vol 2, Futura, San Diego, California.
4. McKeever, P.E.: Glial cell cathology, in, Smith, B.H. and Adelman, G. (eds), Encyclopedia of Neuroscience, Elsevier, Amsterdam, In Press.

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

1. Junck, L., McKeever, P.E., Ross, D.A., Brunberg, J.A., Greenberg, H.S., Betley, A.T. and Grube, S.: Glucose metabolism and cell kinetics in untreated human gliomas studied *in vivo*. Amer. Acad. of Neurology, 1994.
2. McKeever, P.E., Junck, L., Ross, D.A., Brunberg, J.A., Bromberg, J., Wang, M., Onda, K., Grube, S.V. and Greenberg, H.S.: Comparison of MIB-1, BUDR and PCNA labeling index markers of cellular proliferation in grading astrocytic gliomas. Brain Pathol. 4:412, 1994.
3. McKeever, P.E. and Wang, M.: Numerical variations in chromosome specific satellite DNA distinguish glioblastoma, lower grade gliomas and brain. Brain Pathol. 4:412, 1994.
4. McKeever, P.E., Dennis, T.R., Burgess, A.C., Meltzer, P.S. and Trent, J.M.: Chromosomal breakpoint at 17q11.2 and DNA insertion near the NF-1 and c-erB-2 gene loci corresponds with expression of glial fibrils in a glioblastoma. FASEB J. 8:A392, 1994.
5. McKeever, P.E., Lawrence, T.S., Davis, M.A., Genik, S.J. and Ensminger, W.D.: Quantitative immunohistochemistry (QIHC) reveals topographic differences in iodode- oxyuridine (IdUrd) uptake by tumor cells. J. Histochem. Cytochem. 42:978; 1994.
6. McKeever P.E. and Wang M.: Internal standardization of archival tissue sections enables evaluation of chromosomal abnormalities by *in situ* hybridization, United States and Canadian Academy of Pathology Meeting, 1995.
7. Junck, L., Strawderman, M., Ross, D.A., Betley, A.T., Brunberg, J.A., Greenberg, H.S. and McKeever, P.E.: Prognostic value of PET-FDG scans in untreated gliomas. Neurol. 45: A387, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995- 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Cytopathology - six months.
B. Breast Cytopathology (transfer cases) and back-up Breast Pathology - twelve months.
C. Consultation Service, Department of Pathology:
    1. Cytopathology - 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 - one/year.
B. Other Education Activities:
    1. Cytotechnologists - Cytopathology Conferences - three/year.
    2. Visiting Cytopathologist - two weeks.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. The cytologic spectrum of mesothelioma in situ, with Dr. C.W.M. Bedrossian, Wayne State University.
B. Can true papillary neoplasms and their mimickers be distinguished cytologically?, with B. Buschmann, University of South Alabama.
C. The differential diagnosis of Psammoma bodies on cervical smears.
D. The cytologic spectrum of apocrine lesions of the breast.
E. Mammographic demonstration of transient microcalcifications in postpartum state: A case report, with D.M. Gomez, and M. Roubidoux, Department of Radiology.
F. Mammographic identification of microinvasive carcinoma (in conjunction with M. Roubidoux, Department of Radiology).
G. Mammographic evaluation of simple versus complex fibroadenoma (in conjunction with M. Roubidouz, Department of Radiology).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Associate Director, Cytopathology Laboratory.

MEDICAL SCHOOL/HOSPITAL:

None.

REGIONAL AND NATIONAL:

A. Reviewer, Diagnostic Cytopathology.
B. Member, Quality Control Committee, Papanicolaou Society of Cytopathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. King, J., Hester, R., Titford, M. and Michael, C.W.: Psammoma Bodies: Confocal microscopy with 3-D reconstruction of two-color fluorescence on paraffin-embedded sections and cytology smears. Cell Vision 2:420-424.
2. Michael, C.W., Lawrence, W.D. and Bedrossian, C.: Intraoperative consultation in ovarian lesions: A comparison between cytology and frozen sections. Diagn. Cytopathol., In Press.
3. Michael, C. and Esfahani, F.M.: Pregnancy related changes: A retrospective review of 278 patients. Diagn. Cytopathol., In Press.
4. Richardson, P., Muller, A., Elkhalifa, M. and Michael, C.W.: Bronchus-associated lymphoma (Baltoma), Submitted to Acta Cytol.
5. Michael, C.W., King, J. and Hester, R.: Confocal laser scanning microscopy (CLSM) and three-dimensional reconstruction of serous fluids, Submitted to Diagn Cytopathol.

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

1. King, J. Elkhalifa, M. and Michael, C.W.: Malignant lymphoma identified on a cervical cytologic smear with immunophenotypic analysis, Letter to the Editor, Acta Cytol., In Press.
2. Michael, C.W. and Esfahani, F.M.: Pregnancy-related changes: A retrospective of 278 cervical smears. Acta Cytol. 39:980, 1995.

3. Michael, C.W., King, J. and Hester, R.: Confocal laser scanning microscopy (CLSM) and three-dimensional reconstruction of serous fluids. Acta Cytol. 39:1051, 1995.
4. Richardson, P., Elkhalifa, M., Bozner, P. and Michael, C.W.: Malignant lymphomas and reactive lymphocytosis in effusions. Acta Cytol. 39:1041, 1995.
5. Buschmann, B. and Michael, C.: The significance of reporting atypical squamous metaplasia: A retrospective review of 913 cases. Acta Cytol. 39:970, 1995.
6. Rochester, A., Roubidoux, M., Michael, C.W. and Helvie, M.A.: Mammographic location of small ductal carcinomas in situ. Platform presentation, Society of University Radiologists, Birmingham, Alabama, April, 1996.
7. Michael, C.W. and Flint, A.: Cytologic features of Wegener's granulomatosis: A retrospective review, Accepted, Acta Cytol.
8. Bedrossian, C., Fawaz Dawamneh, M., Nelson, J. and Michael, C.W.: Morphologic and immunocytochemical study of serous fluids in cell blocks and thin preps, Accepted, Acta Cytol.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

CLINICAL RESEARCH-RELATED ACTIVITIES:

A. Laid groundwork for transition to new leadership: initiated multiple discussions with Reproductive Sciences Program Executive Committee and Membership and held two retreats.

B. Stabilized core laboratory with implementation of state-of-the art procedures for assay performance. This involved moving to new, expanded quarters; introducing a high degree of automation; implementing QC and reagent control systems good for multi-year studies; acquiring a major new supplemental grant; implementing GLP-type practices; and establishing new methods.

C. Generated interest and initial planning towards development of a hypermedia-based learning system re. human reproduction with an aim to be of value to persons at a wide range of ages and with knowledge ranging from middle school years through residency training.

II. TEACHING ACTIVITIES:

A. Lectures:
   1. Served as a primary instructor for a full semester four hours/week laboratory course for dental and health professional students, Pathology 630/631, Fall 1995.
   2. Lectured for Bioengineering 500, Dynamics of Cellular Response.

B. Graduate Students:
   1. Karen Heinze, Bioengineering - Doctoral Student transferred supported on NCIR Grant.
   2. William Lemon, Bioengineering, supported on NCIR Grant.

C. Undergranduate Students:
   1. Marjorie Dugué, post-baccalaureate student, Pre-Medical Student.
   2. Jasmin Ghuznavi, Pre-Medical Student.
   3. Chris Liu, Pre-Medical Student.
   4. Carla O'Neal, post-baccalaureate student, Pre-Medical Student.
   5. Mona Prasad, Pre-Medical Student.

D. Dissertation Committees:
   1. Michael Poplawski, Electrical Engineering and Computer Science, Current.
   2. David Mauger, Biostatistics, Ph.D. awarded.

E. Worked with Visiting Scientist:
   1. Bent G. Boving, Ph.D., Extramural Associate, Department of Embryology, Carnegie Institute of Washington.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH, P30 HD 18258, A.R. Midgley, Principal Investigator, "Center for the Study of Reproduction," 04/01/94 - 03/31/99, $3,039,072, 10%.
B. NIH, U54-HD 29184-04, N. Reame, Principal Investigator, "National Center for Infertility Research at Michigan," 09/01/91 - 08/31/96, $5,496,007, 28%.
C. NIH, U01-AG 12495, A.R. Midgley, Principal Investigator, "Menopause and Aging in Women: Central Laboratory," 10/01/94 - 09/30/99, $1,465,338, 20%.
D. NIH, U01-AG 12495 Supplement, A.R. Midgley, Principal Investigator, "Hormonal Predictors of Perimenopausal Morbidity,"05/29/96 - 07/31/99, $2,894,204.
E. NIH, 1RO1-MH 03204, E. Young, Principal Investigator, "Stress and Reproductive Hormones in Depressed Women," 08/01/94 - 07/31/95, $661,569, 5%.
F. NIH, T32-HD 07048, D. Foster, Principal Investigator, "Training Program in Reproductive Endocrinology," 07/01/95 - 06/30/00, $1,354,407, 5%, (no salary support).
G. SBIR, R43-HD 33776, S. Pincus, Principal Investigator, "Does FSH Secrete More Irregularly than LH in Humans?," 03/15/96 - 09/14/96, $99,918 ($29,840 subcontract to the University of Michigan).
H. SBIR, R43-HD 29654, J. Erb, Principal Investigator, "Fertile Period Identification with a TIRF Biosensor," $562,968 (consultant).

PENDING:

A. NIH, U54-HD 29184-04, N. Reame, Principal Investigator, "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).
B. NIH, R01-HD-34732-01, A.R. Midgley, Principal Investigator, "Dynamic Mechanisms of Neuroendocrine Feedback in PCOS," 12/01/96 - 11/30/01, $1,204,357, 20%.
C. NIH, R01, A.R. Midgley (June 1, 1996 submission), "Mechanisms Responsible for the LH Surge," 04/01/97 - 03/31/02, $1,247,332 (estimated direct), 20%.

SCIENTIFIC COLLABORATIONS:

A. 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.
B. 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 and Gynecology).
C. Obstetrics and Gynecology; John Randolph and Greg Christman: Analysis of hormonal time series profiles in control women and women with polycystic ovarian syndrome.
D. 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.

E. Innovation Associates, Ann Arbor, Michigan, 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.
F. Massachusetts General Hospital: Pat Sluss, Reproductive Biologist: development of assays for inhibin, follistatin and activin.
G. Yale University: Steve Pincus, a 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:

A. Neuroendocrine causation of polycystic ovarian syndrome; mechanisms controlling pituitary gonadotropin secretion.
B. Dynamics and modes of regulatory communication among cells.
C. Development and utilization of a computer-controlled perifusion system for on-line analysis of cellular responses to pulsatile and other controlled signaling.
D. Modeling of the LH surge as a preclude to modeling the reproductive cycle of the sheep.
E. Development of novel biosensors and immunoassays.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Director, Center for the Study of Reproduction (NIH P30).
B. Associate Director, National Center for Infertility Research at Michigan (NIH NCIR).
C. Director, Standards and Reagents Core Facility (NIH P30 Center).
D. Director, Assay Development Core (NIH U01 NCIR).
E. Director, Central Laboratory, Study of Women Across the Nation (NIH SWAN).

UNIVERSITY:

A. Director, Reproductive Sciences Program.
B. Member, Scientific Advisory Board, Child/Adolescent Health Behavior Research Center, the University of Michigan, 1991-.
C. Member, Michigan Cancer Center, 1993-.
D. Interviewing candidates for Obstetrics/Gynecology, Internal Medicine, Institute of Gerontology.
E. OVPR Unit Value Centered Management Advisory Committee, 1995-.

REGIONAL AND NATIONAL:

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

REPRODUCTIVE SCIENCES PROGRAM:

A. Developing an immunoassay analysis system with potential to assist many investigators.
B. Implementing ELISA and chemiluminescence-based, solid state, two site immunoassays in Standards and Reagents Core as partial replacement for radioimmunoassays (and thereby reduction in usage of radioactive isotopes).

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. U01 Perimenopause Meeting, San Francisco, California, July 5-7, 1995.
2. Annual Meeting of the Society for the Study of Reproduction, University of California, Davis, Davis, California, July 9-12, 1995.
3. Meeting of Directors of NICHD P30 Centers, San Francisco, California, July 13, 1995.
4. U01 Perimenopause Stress Markers Meeting, Pittsburgh, Pennsylvania, July 25-26, 1995.
5. U01 Laboratory Meeting, Boston, Massachusetts, July 27, 1995
6. U01 Perimenopause Training Session, Boston, Massachusetts, September 29-30, 1995.
7. Chaired, NIH Site Visit, University of Illinois, Urbana, Illinois, October 11-13, 1995.
8. Reverse Site Visit for U01 Supplement, Bethesda, Maryland, October 22-24, 1995.
9. RSP Poster Day, November 3, 1995.
10. NIH Special Review Committee Meeting, Bethesda, Maryland, November 9-10, 1995.
11. Annual Meeting of the Society for Neuroscience, San Diego, California, November 10-15, 1995.
12. National Cooperative Program for Infertility Research Meeting, Boston, Massachusetts, November 29-December 1, 1995.
13. Lecture, "Bioengineering 500, Dynamics of Cellular Response", U01 Perimenopause Meeting, Bethesda, Maryland, January 10-12, 1996.
14. National Cooperative Program for Infertility Research Meeting, Ann Arbor, Michigan, April 22-24, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Dabbs, J.M., Jr., Campbell, B.C., Gladue, B.A., Midgley, A.R., Navarro, M.A., Read, G.F., Susman, E., Swinkels, L.M.J.W and Worthman, C.M.: Reliability of salivary testosterone measurements: A multicenter evaluation. Clin. Chem., In Press.
2. Ulloa-Aguirre, A., Midgley, A.R.M., Beitins, I.Z. and Padmanabhan, V.: Follicle stimulating isohormones: Biological characterization and physiological relevance. Endocrine Reviews 16:765-787, 1995.
3. Wang, Q.F., Khuory, R.H., Smith, P.C., McDonnell, 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., In Press.
4. 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, In Press, July, 1996.
5. McConnell, D.S., Padmanabhan, V., Pollak, T.B., Groome, N.P., Ireland, J.J. and Midgley, A.R., Jr.: Development of a two-site solid phase immunochemiluminescent assay for

measurement of dimeric inhibin in human serum and other biological fluids. Clin. Chem., In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Midgley, A.R., Brand, R.M., Favreau, P.A., Boving, B.G., Ghazzi, M.N., Padmanabhan, V., Young, E.Y. and Cantor, H.C.: Monitoring dynamic responses of perifused neuroendocrine tissues to stimuli in real time, in, Veldhuis, J.D. and Johnson, M.L. (eds), Quantitative Neuroendocrinology, a volume in the series Methods in Neurosciences, Volume 28, pp. 188-219, 1995.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Midgley, A.R., Jr., McFadden, K., Ghazzi, M., Karsch, F.J., Brown, M.B., Mauger, D.T. and Padmanabhan, V.: Secretory dynamics of luteinizing hormone in ovariectomized ewes: Characterization near site of secretion, Submitted.

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

1. Midgley, A.R., McConnell, D.S., Wyman, T.L., Randolph, J.F., Pincus, S.M. and Padmanabhan, V.: Differential control of LH and FSH during the menstrual cycle and involvement of episodic inhibin B during the follicular phase. 10th International Congress of Endocrinology, San Francisco, California, 1996, Submitted.
2. Padmanabhan, V.P., Favreau,P.A., Van Cleeff, J., Mucci, N.M. and Midgley, A.R.: Activin and follistatin modulate FSH by regulating basal expression. 10th International Congress of Endocrinology, San Francisco, California, 1996, Submitted.
3. Padmanabhan, V., Midgley, A.R., McConnell, D.S., Randolph, J.F., Moghissi, K. and Reame, N.E.: Pattern of circulating dimeric inhibin-A during the luteal phase is episodic but differs in young cylcing and premenopausal cycling women. 10th International Congress of Endocrinology, San Francisco, California, 1996, Submitted.
4. Padmanabhan, V., Karsch, F.J. and Midgley, A.R.: Complementary neuroendocrine regulation of follicle stimulating hormone secretion: Hypothalmic and pituitary control. IXth World Congress on Human Reproduction, 1996, Submitted.

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 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Thirteen sessions Pathology 850 (Miller).
   2. Program Director, "Experimental Immunopathology Training Grant."
   3. Ph.D. Dissertation Committees, University of Michigan:
      a. Ann Jackson.
      b. Alex Greenwood.
   4. Ph.D. Dissertation Advisor:
      a. Michael Eisenbraun.
      b. Chris Kirk.
      c. Neil Faulkner (co-sponsor).
   5. Summer Rotations:
      a. Meryem Koker, Med I.
      b. Andrew Sword, Med I.

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.

PENDING:

A. Principal Investigator, "Wild Derived Mouse Stocks: New Models for Aging Research", NIA R01-AG13711 (5%), $187,826 direct costs requested/year, 4/1/96 - 3/31/01.

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.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Journal of Gerontology: Biological Sciences.
B. Journal of the American Geriatrics Society. (Section Editor).

INVITED LECTURES/SEMINARS:

1. III European Congress on Gerontology, Amsterdam, Netherlands, "Signal Transduction Defects in T Cells from Old Mice.", August 30 to September 2, 1995.
2. Symposium on the Calcium Hypothesis of Brain Aging, Heidelberg, Germany, "Calcium in Aged Lymphocytes", October 23-25, 1995.
3. Gerontological Society of America Annual Meeting, Los Angeles, California, (Session Chair). "Functionally Distinct T Cell Subsets that Differ in Expression of P-glycoprotein", November 16-19, 1995.
4. Gerontology Division, Dept. of Medicine, Beth Israel Hospital, Boston, Talk 1: "Gerontometrics: Do People Age at Different Rates? and Can Biomarkers Measure Aging?" Talk 2: "Subset Changes and Signalling Defects in T Cells from Old Mice." January 16 and 17, 1996.
5. Picower Institute for Medical Research, Manhasset, New York, "Subset Changes and Signalling Defects in T Cells from Old Mice." February 20, 1996.
6. Geron Corporation, Menlo Park, California, "Gerontometrics: Do All Mice Age at the Same Rate?", March 29, 1996.
7. British Society for Immunology Annual Meeting, Bristol, England, "Activation Defects in T Cells from Aging Mice", April 18 - 20, 1996.
8. University of Washington, Seattle, Washington, "T Cell Subset Counts as Biomarkers of Aging in Mice", May 1, 1996.

9. University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, "T Cell Aging: Subsets, Signals, and Survival." May 30, 1996.
10. Fourth Annual Summer Training Course in Experimental Aging Research, Ann Arbor, Michigan, Course Director. "Aging and Immune Function" and "Animal Models for Aging Research", June 9 - 13, 1996.
11. First International Conference on Immunology and Aging, Washington, D.C., Plenary Lecture: "Mechanisms of Immune Senescence", Research Talk: "Geroncology: Mouse Models for Dissection of the Aging/Cancer Nexus", June 16 - 19, 1996.
12. Aging and Mobility Summer Research Retreat, Ann Arbor, Michigan, "Research Funding: The Steep and Thorny Path", June 25, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Li, S. P., Verma, S. and Miller, R.A.: Age-related defects in T cell expression of CD40 ligand and induction of in vitro B cell activation. Aging: Immunology and Infectious Disease 6:79-93, 1995.
2. Tewari, M., Telford, W.G., Miller, R.A. and Dixit, V.M.: CrmA, a poxvirus-encoded serpin, inhibits cytotoxic T-lymphocyte-mediated apoptosis. J. Biol. Chem. 270:22705-22708, 1995.
3. Witkowski, J. M., Gorgas, G. and Miller, R.A.: Reciprocal expression of P-glycoprotein and TAP1 accompanied by higher expression of MHC Class I antigens in T cells of old mice. J. Gerontology: Biological Sciences 51A:B76-B82, 1996.
4. Dozmorov, I. M., Lutsenko, G. V., Sidorov, I. A. and Miller, R.A.: Analysis of cellular interactions in limiting dilution cultures. J. Immunological Methods 189:183-196, 1996.
5. Telford, W. G. and Miller, R.A.: Detection of plasma membrane Ca^{2+}-ATPase activity in mouse T lymphocytes by flow cytometry using Fluo-3 loaded vesicles. Cytometry 24:243-250, 1996.
6. 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, In Press.
7. Dozmorov, I. M. and Miller, R.A.: Regulatory interactions between virgin and memory CD4 T lymphocytes. Cellular Immunology, In Press.
8. 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., In Press.
9. Miller, R. A.: The aging immune system: primer and prospectus. Science 273:70-74, 1996.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Bining, N. and Miller, R.A.: Production of IL-5 and IL-10 by age-sensitive subsets of CD4 memory T cells differing in P-glycoprotein expression. Submitted for publication.
2. Garcia, G. G. and Miller, R.A.: Differential tyrosine phosphorylation of zeta-chain dimers in mouse CD4 T lymphocytes: effect of age. Submitted for publication.

BOOKS/CHAPTERS IN BOOKS:

1. Miller, R. A.: Cellular and biochemical changes in the aging mouse immune system. Nutrition Reviews 53: S8-S17, 1995.
2. Miller, R. A.: Gerontology as oncology. Aging: Clinical and Experimental Research 7:66-67, 1995.
3. Miller, R. A: Aging and the immune response, in, Schneider, E.L. and Rowe, J.W. (eds), Handbook of the Biology of Aging, 4th Edition, , Academic Press, New York, Chapter 16, pp 355-392, 1996.
4. Miller, R. A.: Calcium signals in T lymphocytes from old mice. Life Sciences 59:469-475, 1996.
5. Miller, R. A.: Mini-review: Aging and cancer — one side of the same coin, (In Italian and English), Giornale di Gerontologia, In Press.
6. Miller, R. A.: The biology and genetics of aging and longevity, in, Kelley, W.N. (ed), Textbook of Internal Medicine. 3rd Edition, J. B. Lippincott, New York, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Students:
1. Aalyeha Koreshi (Biology Undergraduate Research Rotation).
2. Meryem Koker (Medical Student Summer Research Rotation).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Frequency and Expansionary Potential of Postthymic T Stem Cells from Aged Mice", American Federation for Aging Research (AFAR), $40,000, July 1, 1995-June 30, 1996.
B. 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.

PENDING:

A. Principal Investigator, "Skewed T Cell Repertoires in Aged Mice", 1RO3AG14178-01, Pilot project research grant program for the NIA, $50,000, September 1, 1996-August, 1997. Under Review.

SUBMITTED PROPOSALS NOT FUNDED:

A. Principal Investigator, "Age Related Effects on Postthymic T Stem Cell Populations", Sandoz Foundation for Gerontological Research
B. Principal Investigator, "Postthymic T Stem Cell Frequency and Characterization", 1R29AI40258-01, R29 FIRST Application.

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.

IV. ADMINISTRATIVE ACTIVITIES:

A. None.

V. OTHER RELEVANT ACTIVITIES:

A. Ad hoc reviewer, Journal of Gerontology.
B. Participant, Mock Study Section, Comprehensive Cancer Center and Geriatrics Center, University of Michigan Medical School, Ann Arbor, Michigan.
C. Participant, Ninth Annual AFAR Grantee Conference, Harriman, New York, May 31-June, 1996.
D. Trainee, Fourth Annual Summer Training Course in Experimental Aging Research by The National Institute of Aging, held at the University of Michigan Medical School, Ann Arbor, Michigan, June 9-13, 1996.

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "Careers in Research and Teaching", Graduate Career Fair '96, University of Michigan Medical School, March 26, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Teitelbaum, D.H., Reyas, B., Merion, R.M. and Mosley, R.L.: Intestinal intraepithelial lymphocytes: Identification of an inhibitory subpopulation. J. Surg. Res. 63:123-127, 1996.
2. Teitelbaum, D.H., Del Valle, J., Reyes, B., Gupta, A., Mosley, R.L. and Merion, R.M.: Intestinal intraepithelial lymphocytes (IEL) influence the production of somatostatin. Surgery, In Press, 1996.

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

1. Gough, A., Breider, M. and Mosley, R.L.: Early pathological changes in dextran sodium sulphate-induced colitis in mice. Vet. Pathology 32:588.

2. Mosley, R.L. and Miller, R.A.: Repopulation kinetics and T cell repertoire analysis of athymic mice reconstituted with limiting number of peripheral T lymphocytes. Research abstracts of the Ninth Annual AFAR Grantee Conference. 9:15, 1996.
3. Mosley, R.L.: Skewed T cell repertoires in aged mice. Abstracts of the Fourth Annual Summer Training Course in Experimental Aging Research, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NHLBI Clinical Investigator Development Award KO8 HL03181-01:Structure and Function of Recombinant Selectin Ligands, 09/01/94-08/31/99, $402,916.

PROJECTS UNDER STUDY:

A. Structure and function of recombinant glycoproteins.
B. Endothelial cell expression of selectin ligands, function and mechanism of generation of superoxide, signal transduction.
C. Properties of endothelial cells derived from macro- and microvasculature.

IV. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A Clinical Immunology and Immunopathology.
B. Biochemical Pharmacology.
C. Shock.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Thall, A.D., Murphy, H.S. and Lowe, J.: α1,3-Galactosyltransferase deficient mice produce naturally occurring cytotoxic anti-Gal antibodies. Trans. Proceed. 28:561-562, 1996.

BOOKS/CHAPTERS IN BOOKS:

1. Ward, P.A. and Murphy, H.S.: Role of complement activation products in endothelial cell activation, in, Koch, K. (ed),. Cell Adhesion and Migration, Am. Chemical Society Press, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Cytopathology - Consultation Service, 12 months.

II. TEACHING ACTIVITIES:

A. Pathology residents - Lecture seminar.
B. Sophomore medical students: Instructor (Pulmonary sequence), Pathology 600 laboratory.

III. RESEARCH ACTIVITIES:

A. Cytopathology, with particular reference to serous fluids.

PROJECTS UNDER STUDY:

A. None.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Advisory Committee on Appointments and Promotions.

REGIONAL AND NATIONAL:

A. North American Review Board, Acta Cytologica.
B. Associate Editor, Acta Cytologica.
C. Editorial Board, Cytopathology.
D. Editorial Consultant, Diagnostic Cytopathology.
E. Chairman, Publications Committee, International Academy of Cytology.
F. Membership Committee, International Academy of Cytology.
G. Budget and Finance Committee, American Society of Cytology.
H. Chairman, Awards Committee, American Society of Cytology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Naylor, B.: Lecturer to cytotechnology trainees, Cytotechnology Training Program, Henry Ford Hospital, Detroit, Michigan, January and February 1996.
2. Naylor, B.: a). Moderator, Diagnostic panel, b). Lecturer, "Pleural, Peritoneal, and Pericardial Fluids: Technical Approaches and Diagnostic Problems," Michigan Society of Cytology, Ann Arbor, Michigan, June, 1996.

HONORS AND AWARDS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

None.

BOOKS/CHAPTERS IN BOOKS:

1. Naylor, B.: Cytopathology: The past, the present and a glimpse into the future, in, Gray, W. (ed), Diagnostic Cytopathology, London, Churchill Livingstone; 1995, pp 3-9.

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

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Supervised Maribel Gonzalez-Garcia, Didier Grillot, Naohiro Inohara, Ramon Merino, Philip Simonian,and Dayang Wu, Postdoctoral Fellows.
B. Supervised Mary Benedict, Brian Bonish, Diane Maestos, and Herschell Wallen, graduate students.
C. Supervised Vindhyo Cuddapha, Chaim Hyman, Miguel Suarez and Kevin Winer, undergraduate students
D. Laboratory Instructor, Pathology 630/631. Full semester, two hours/week.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Function of the Bcl-2 Proto-Oncogene During B Cell Development," The Council for Tobacco Research, $264,709.
B. Principal Investigator, "Genetic Regulation of Apoptotic Cell Death," National Institutes of Health, $813,000 (total direct costs).
C. Principal Investigator, Research Career Development Award, "Genetic Regulation of Apoptotic Cell Death," National Institutes of Health, $315,000 (total direct costs).
D. Principal Investigator, "Bcl-xS Mediated Apoptosis of Kaposi's Sarcoma Cells," National Institutes of Health, $2,282,648 (total direct costs).
E. Principal Investigator, "Regulation and Function of Bcl-2 proto-Oncogene in Germinal Centers," American Cancer Society, $169,896 (total direct costs).
F. Principal Investigator, "Molecular Analysis of Bcl-xS induced Apoptosis in Breast Cancer," U.S. Army Medical Research and Material Command, Fort Detrick, Frederick, Maryland, $801,917 (total direct costs).

PROJECTS UNDER STUDY:

A. Functional characterization of Bcl-2 and Bcl-x genes during lymphoid development.
B. Molecular interactions among Bcl-2 family members.

C. Gene therapy using Bcl-2 proteins as targets for cancer cell killing.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Member, Preliminary Examination Committee, Training Program in Pathology.
B. Interviewer, faculty, postdoctoral, and graduate student candidates for research fellowships.
C. Interviewer, MSTP Candidates.

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, Ann Arbor, Michigan.
G Committee Member, Thesis committee for Pan Quintin, Pharmacology, May 23, 1996.
H. Committee Member, Thesis committee for Jordan Fridman, Pharmacology, May 29, 1996.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Reviewer for the following journals:
   1. American Journal of Pathology.
   2. Journal of Immunology.
   3. Oncogene.
   4 Journal of Cell Biology.
   5. Laboratory Investigation.
   6. Cancer Research.
   7. Proceedings of National Academy Science.
   8. Science.
B. Ad Hoc reviewer: Research grants, National Institute of Health.
C. Ad Hoc reviewer: American Cancer Society.

INVITED LECTURES AND SEMINARS

UNIVERSITY OF MICHIGAN

1. Invited Speaker, "Bcl-2 Family and Apoptosis," Boehringer-Mannheim Symposium on Apoptosis, University of Michigan Medical Center, October 17, 1995.
2. Invited Speaker, "Regulation of Cell Death by the Bcl-2 Family," Division of Hematology/Oncology Research Seminar, University of Michigan Medical Center, December 7, 1995.
3. Invited Speaker, "Control of Cell Death by the Bcl-2 Gene Family," Cancer Biology Research Seminar, Comprehensive Cancer Center, University of Michigan Medical Center, June 12, 1996.

NATIONAL AND INTERNATIONAL

1. Invited Speaker and Chairperson, Symposium on "Cancer and Apoptosis," National Congress of Spanish Society for Cancer Research, Barcelona, Spain, September 26, 1995.
2. Invited Speaker, "Regulation of Apoptosis by the Bcl-2 Family," Swiss National Science Foundation, Vallars, Switzerland, September 24-28, 1995.
3. Invited Speaker, "Regulation of Lymphoid Cell Death by the Bcl-2 Family," Department of Microbiology and Immunology, Wayne State University, Detroit, Michigan, November 15, 1995.
4. Invited Speaker, University of St. Andrews, Scotland, December 1995.
5. Invited Speaker, Sixth International Conference on Lymphocyte Activation and Immune Regulation, "Cell Cycle and Programmed Cell Death in the Immune System," Newport Beach, California, February 22, 1996.
6. Invited Speaker, "The Bcl-2 Family of Proteins: Regulators of Cell Death and Survival," University of Rochester, Medical Center, Rochester, New York, March 14, 1996.
7. Invited Speaker, Symposium on Apoptosis, Keystone, Colorado, April 17, 1996.
8. Invited Speaker, Wound Healing Society, Annual Meeting, Minneapolis, Minnesota, May 1, 1996.

9 Invited Speaker, "The Bcl-2 Family of Proteins," Nikolas Symposium, Athens, Greece, Immunology Study Section, May 11, 1996..

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFERRED JOURNALS.

1. Gonzalez-Garcia, M., Garcia, I., Ding, L., O'Shea, S., Boise, L.H., Thompson, C.B. and Núñez, G: Bcl-x is expressed in embryonic and postnatal neural tissues and functions to prevent neuronal cell death. Proc. Natl. Acad. Sci., USA 92:3404-3408.
2. Merino, R., Grillot, D.A.M., Simonian, P.L., Muthukkumar, S., Fanslow, W.C., Bondada, S. and Núñez, G.: Modulation of anti-IgM-induced B cell apoptosis by Bcl-x_L and CD40: Dissociation from cell cycle arrest and dependence on the avidity of the antibody-IgM receptor interaction. J. Immunol. 155:3830-3838, 1995.

3. Wrone-Smith, T., Johnson, T., Nelson, B., Boise, L.H., Thompson, C., Núñez, G. and Nickoloff, B.J.: Discordant expression of Bcl-x and Bcl-2 by keratinocytes in vitro and psoriatic keratinocytes in vivo. Am. J. Pathol. 146:1079-1088, 1995.
4. Fukunaga-Johnson, N., Ryan, J.J., Wicha, M., Núñez, G. and Clark MF: Bcl-2 protects murine erythroleukemia cells from p53-dependent and -independent radiation-induced cell death. Carcinogenesis 16:1761-1767, 1995.
5. Grillot, D., Merino, R-M and Núñez G: Bcl-x_L displays restricted distribution during T cell development and inhibits multiple forms of apoptosis but not clonal deletion in transgenic mice. J. Exp. Med. 182:1973-1983, 1995.
6. Schott, A.F., Apel, I.J., Núñez, G. and Clarke, M.F.: Bcl-x_L protects cancer cells from p53-mediated apoptosis. Oncogene 11:1389-1394, 1995.
7. Benito, A.., Silva, M., Grillot, D., Núñez, G., Fernández-Luna, J.L., Grillot, D.A.M., Merino, R., Pena, J.C., Fanslow, W.C., Finkelman, F.D., Thompson, C.B. and Núñez, G.: Bcl-x exhibits regulated expression during B cell development an activation and modulated lymphocyte survival in transgenic mice. J. Exp. Med. 284:1852-1862, 1996.
8. Middleton, G., Núñez, G. and Davies, A.: Bax promotes neuronal survival and antagonizes the survival effects of neurotrophic factors. Development 122:695-701, 1996.
9. Gibson, L.F., Piktel, B.S., Narayanan, R., Núñez, G. and Landreth, K.S.: Stromal cells regulate Bcl-2 and expression in pro-B cells. Exp. Haematol. 24:628-637, 1996.

ARTICLES ACCEPTED FOR PUBLICATION:

1. Foreman, K.E., Clarke, M.F., Wrone-Smith, T., Boise, L.H., Thompson, C.B., Polverini, P.J., Apel, I.J., Simonian, P.L., Núñez, G. and Nickoloff, B.J.: 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., In Press.
2. Dole, M.G., Clarke, M.F., Eipers, P., Jasty, R., Thompson, C.B., Rhode, C., Bloch, C., Núñez, G. and Castle, V.P.: Bcl-x_S induces apoptosis in neuroblastoma cells even in the presence of high levels of Bcl-x_L and Bcl-2. Cancer Research, In Press.
3. Lopez-Hoyos, M., Carrió, R., Merino, R., Buelta, L., Izui, S., Núñez, G. and Merino, J.: Constitutive expression of Bcl-2 in B cells causes a lethal form of lupus-like autoimmune disease after induction of neonatal tolerance to $H2^b$ alloantigen. J. Exp. Med., In Press.
4. Simonian, P.L., Grillot, D.A.M., Merino, R. and Núñez, 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., In Press.
5. Carrió, R., López-Hoyos, M., Jimeno, J., Benedict, M.A., Merino, R., Benito, A., Fernández-Luna, J.L., Núñez, G., Garcia-Porrero, J.A. and Merino, J.: *A1* demonstrates restricted tissue distribution during embryonic development and functions to protect against cell death. Am. J. Path., In Press.
6. Silva, M., Grillot, D., Benito, A., Richard, C., Núñez, G. and Fernandez-Luna, J.L.: Apoptosis induced by erythroid differentiation of human erythroleukemia cell lines is inhibited by Bcl-x_L. Blood 11:3837-3843, 1996.

7. Silva, M., Grillot, D., Benito, A., Richard, C., Nuñez, G. and Fernandez-Luna, J.L.: .Erythropoietin promotes erythroid progenitor survival by repressing apoptosis through Bcl-x_L and Bcl-2. Blood, In Press.
8. Varani, J., Dame, M.K., Taylor, C.G., Sarma, V., Merino, R., Kunkel, R.G., Núñez, G. and Dixit, V.M.: Age-dependent injury to human umbilical vein endothelial cells: Relationship to apoptosis and correlation with a lack of A20 expression. Lab Invest., In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Simonian, P.L., Grillot, D.A.M. and Núñez, G.: Bax homodimerization is not required for Bax to accelerate chemotherapy induced cell death. Submitted.

BOOK CHAPTERS

1. Evans, G.I., Harrington, E., McCarthy, N., Gilbert, C., Benedict, M.A. and Núñez, G.: The integrated control of cell proliferation and apoptosis by oncogenes, in, Thomas, N.S.G. (ed), Apoptosis and Cell Cycle Control in Cancer, Bios. Scientific Publishers Ltd., Oxford, United Kingdom, pp. 109-129, 1995.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Director, Blood Bank and Transfusion Service, University Hospitals.
B. Diagnosis of surgical specimens from University Hospital patients.
C. Diagnosis of surgical specimens from M-Labs.
D. Diagnosis of consultation breast cases from pathologists elsewhere in the United States.
E. Medical direction of Transfusion Service.
F. Medical coverage of Necropsy Service (Quality Control Review).
G. 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. Weekly teaching ward rounds covering Hematology, Bone Marrow Transplantation and Transfusion Medicine for Hematology and Pathology house officers.
F. Lecture-Discussion (two) on Transfusion Medicine to senior student elective course in Laboratory Medicine.
G. Postgraduate Course, "Current Topics in Blood Banking", Planning Committee.
H. Lectures on Transfusion Medicine presented to Pathology and Hematology/Oncology house officers.
I. Seminars and lectures on Pathology of Breast to Pathology House Officers.
J. Lectures on Transfusion Medicine to Pharmacology and Therapeutics senior student elective course, February 10, 1995.
K. Planning committee for curriculum in hematology for sophomore medical students.
L. Lecture, Pathology of the Breast, to Dental Pathology Course.
M. Presentation of consultation slide conferences (four) on pathology of the breast to pathology house officers.
N. Presentation of Clinical Pathology Grand Rounds. Appropriate Use and Complications of Fresh Frozen Plasma and Cryoprecipitate, May 3, 1996.
O. Tutoral experience, "Diagnosis of Breast Lesions," Dr. Nicholas Sellas, July 6-13, 1995.

UNIVERSITY:

A. Doctoral committee for Midori Koga, candidate for Doctor of Musical Arts in Piano, School of Music.

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 U.S. Army medical research acquisition activity ($605,849/four years) (T. Chenevert, Principal Investigator, with members of Department of Radiology).
B. New Ultrasound Methods for Cancer Diagnosis and Treatment (three-five years at 5% effort).
C. Microvascular and Structural Imaging of Breast Cancer (three-five years at 3% effort).
D. Adenoid cystic carcinoma of the breast (with C. Kleer).
E. Microinvasive carcinoma of the breast (with L. Pierce).
F. Analysis of epidemiologic and pathologic risk factors for subsequent presentation of breast cancer (D. Schottenfeld, Principal Investigator).

IV. ADMINISTRATIVE ACTIVITIES:

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. AIDS Task Force.
E. Hospital Program for Excellence Advisory Committee.
F. Task Force on Medical Center Governance, Medical Center Clinicians' Group.
G. Haematology Sequence Advisory Committee, M-2 year.
H. University of Michigan Senate Assembly.

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, Veterans 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, 1996-1997.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

INVITED LECTURES/PAPERS/SEMINARS:

1. "Diagnotic Problems in Surgical Pathology of the Breast", Course presented with S. Silverberg at annual meeting of American Society of Clinical Pathologists, Orlando, Florida, September 19, 1995.
2. "Pathology of Non-Invasive Breast Cancer", Course: Multimodality Treatment of Breast Cancer, sponsored by the Department of Radiation Oncology, University of Michigan, Pinehurst, North Carolina, April 19, 1996.
3. "Pathology of Invasive Breast Cancer", Course: Multimodality Treatment of Breast Cancer, sponsored by the Department of Radiation Oncology, Pinehurst, North Carolina, April 20, 1996.
4. "The Role of the Pathologist in Assessing Prognosis of Breast Cancer", Course: Modality Treatment of Breast Cancer, sponsored by the Department of Radiation Oncology, University of Michigan, Pinehurst, North Carolina, April 21, 1996.
5. "Problem Solving in the Blood Bank", Workshop, Current Topics in Blood Banking, 22nd Annual Symposium, University of Michigan, Ann Arbor, Michigan, May 29, 1996.
6. "Appropriate Use of Plasma and Components", Current Topics in Blood Banking, 22nd Annual Symposium, University of Michigan, Ann Arbor, Michigan, May 31, 1996.
7. "Legal Aspects of Transfusion Medicine", with E.B. Goldman, Current Topics in Blood Banking, 22nd Annual Symposium, University of Michigan, Ann Arbor, Michigan, May 30, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Popovsky, M., Benson, K., Glassman, A., Hume, H., Oberman, H.A., Pisciotto, P. and Anderson, K.: Transfusion practices in HIV-infected patients. Transfusion. 35:612-616, 1995.
2. Butch, S.H., Knafl, P., Oberman, H.A. and Bartlett, R.H.: Blood utilization for adult patients undergoing extracorporeal membrane oxygenation therapy. Transfusion 36:61-63, 1996.
3. Pierce, L.J., Oberman, H.A., Strawderman, M.S. and Lichter, A.S.: Microscopic extracapsular extension in the axilla: Is this an indication for axillary radiotherapy? Int. J. Rad. Oncol. 33:253-259, 1995.
4. Hume, H., Popovsky, M., Benson, K., Glassman, A.B., Oberman, H.A., Pisciotto, P.T. and Anderson, K.: Hypotensive reactions: A previously uncharacterized complication of platelet transfusion? Transfusion, In Press.
5. Oberman, H.A. and Henson, D.E.: Protocol for the examination of specimens removed from patients with breast cancer. AMA Arch. Pathol. Lab. Med., In Press.

6. Wilson, T., Helvie, M., Oberman, H.A. and Joynt, L.K.: Mucinous carcinoma of the breast: Mammographic appearance with histopathologic correlatoin. Am. J. Roentgenol. 165:285-289, 1995.
7. Hume, H., Benson, K., Oberman, H., Glassman, A.B. and Pisciotto, P.T.: Hypotensive reactions: A previously uncharacterized complication of platelet transfusion. Transfusion, In Press.

CHAPTERS IN BOOKS:

1. Oberman, H.A.: The history of transfusion medicine, in, Petz, L.D., Swisheer, S.N., Kleinman, A., Spence, R.K. and Strauss, R.G. (eds), Clinical Practice of Transfusion Medicine, Ed. 3, Churchill Livingston, New York, New York, 1996.

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

1. Book Review Editor, American Journal of Surgical Pathology.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES

A. Autopsy Service.

II. TEACHING ACTIVITIES:

A. Hong-yu Zhang, M.D., Ph.D., Postdoctoral Fellow.
B. Kai Zhang, M.D., Postdoctoral Fellow.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Mechanisms of Pulmonary Fibrosis," NIH, RO-1, HL 28737, (25% 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).
F. Co-investigator, "Renal fibrosis," (R. Wiggins, Principal Investigator), NIH, 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 macrophages, eosinophils, and fibroblasts, and its regulation by bleomycin and cytokines.

F. Regulation of cytokine gene expression in fibrotic tissues.
G. Mechanism 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. Member, Lung Biology and Pathology Study Section, National Institutes of Health.
B. Review for the following journals:
   1. American Journal of Respiratory and Critical Care Medicine.
   2. American Journal of Pathology.
   3. American Journal of Immunology.
   4. American Journal of Physiology.
   5. American Journal of Respiratory Cell and Molecular Biology.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Zhang, K., Flanders, K.C. and Phan, S.H : Cellular localization of transforming growth factor β expression in bleomycin-induced pulmonary fibrosis. Am. J. Pathol. 147:352-361, 1995.
2. Zhang, H., Gharaee-Kermani, M., Zhang, K. and Phan, S.H.: Lung fibroblast contractile and α-smooth muscle actin phenotypic alterations in bleomycin-induced pulmonary fibrosis. Am. J. Pathol. 148:527-537, 1996.
3. Gharaee-Kermani, M., Wiggins, R., Wolber, F., Goyal, M. and Phan, S.H.: Fibronectin is the major fibroblast chemoattractant in anti-GBM disease. Am. J. Pathol. 148:961-967, 1996.
4. Gharaee-Kermani, M., Denholm, E.M. and Phan, S.H.: Co-stimulation of fibroblast collagen and transforming growth factor β_1 gene expression by monocyte chemoattractact protein-1 via specific receptors. J. Biol. Chem. In Press, 1996.
5. Shanley, C.J., Charaee-Kermani, M., Sarkar, R., Welling, T.H., Kriegel, A., Ford, J., Stanley, J.C. and Phan, S.H.: Transforming growth factor-β_1 increases lysyl oxidase enzyme activity and mRNA in rat aortic smooth muscle cells. Vascular Surgery In Press, 1996.
6. Zhang, K. and Phan, S.H.: Cytokines and pulmonary fibrosis. J. Biol. Signals. In Press, 1996.

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

1. Phan, S.H., Gharaee-Kermani, M. and Denholm, E.: Monocyte chemotactic protein-1 stimulates lung fibroblast collagen synthesis via transforming growth factor β. Europ. Resp. J. 8:141s, 1995.
2. Gharaee-Kermani, M., McGarry, B. and Phan, S.H.: Lung interleukin-5 expression in bleomycin-induced pulmonary fibrosis. FASEB J. 10:A811, 1995.
3. Zhang, K., Gharaee-Kermani, M., McGarry, B., Remick, D. and Phan, S.H.: Role of tumor necrosis factor α (TNF α) in lung eosinophil recruitment in pulmonary fibrosis. Am. J. Respir. Crit. Care Med. 153:A221, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Associate Director, Clinical Microbiology/Virology Laboratories.
B. Director, UMMC Ypsilanti Pediatrics Health Care Center Laboratory.
C. Director, UMMC Ypsilanti Family Practice Health Care Center Laboratory.
D. Director, UMMC -Medsport Laboratory.
E. Coordinator, Infectious Disease Microbiology Laboratory Rounds.
F. Technical Consultant - M-Labs.
G. Hospital Cost Effectiveness Program.
H. New clinical test development.

II. TEACHING ACTIVITIES:

A. Coordinator, 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. Co-coordinator, Clinical Pathology Visiting Professor program, 1996.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Trends in Antimicrobial Resistance for Cllinical Isolates of *Bacteroides sp.*", Principal Investigator: D. R. Snydman, New England Medical Center, Boston, Massachusetts.
B. "Comparative Evaluation of Roche Amplicor and GenProbe for the Detection of *Chlamydia trachomatis* in urogenital specimens", Roche Diagnostic Systems, Research Triangle Park, North Carolina.
C. "Evaluation of the Abbott LCx for the Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in Male Urine Specimens", Abbott Laboratories, North Chicago, Illinois.
D. "Use of the BacT/Alert for Culture of Sterile Body Fluids Other Than Blood", Co-Investigator: P. Bourbeau: Geisinger Medical Center, Danville, Pennsylvania, Organon-Teknika, Durham, North Carolina.

E. "Protective Activity of Allguard- Assessment of *in vitro* Activity", American Medical Industries, Inc., Atlanta, Georgia.

PROJECTS UNDER STUDY:

A. PCR for detection of HSV in spinal fluid.
B. Detection of the mec A resistance gene in staphylococci growing in blood culture bottles.
C. Characterization of the beta lactamase produced by *Pseudomonas aeruginosa* that destroys ticarcillin-clavulanate.
D. Epidemiologic studies of *Pseudomonas aeruginosa* using pulse-field gel electrophoresis.
E. Evaluation of the GenProbe TMA system to detect *Mycobacterium tuberculosis* in AFB smear-negative specimens.
F. Detection of *Escherichia coli* SLT I & II in fecal specimens by EIA.
G. Evaluation of DFA methods to detect CMV pp65 antigen in blood leukocytes.
H. Susceptibility of respiratory bacterial pathogens using the E-test strips.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Clinical Pathology Laboratory Director's Committee.
B. Chair, Clinical Microbiology/Virology Senior Staff meeting.
C. Chair, Clinical Microbiololgy/Virology Advisory Committee.
D. UMMC Health Care Centers Laboratory Committee.

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL/NATIONAL:

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

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. "Application of Automated Blood Culture Systems for the Detection of Pathogenic Organisms in Sterile Body Fluids Other Than Blood," Metropolitan Hospital, Cleveland, Ohio.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lockhart, S.R., Reed, B.D., Pierson, C.L. and Soll, D.R.: Most frequent scenario for recurrent *Candida* vaginitis is strain maintenance with "substrain shuffling": Demonstration by sequential DNA fingerprinting with probes Ca3, C1, and CARE2." J. Clin. Microbiol. 34:767-777, 1996
2. Snydman, D.R., McDermott, L., Cuchural Jr., G.J., Hecht, D.W., Iannini, P.B., Harrell, L.J., Jenkins, S.G., O"Keefe, P., Pierson, C.L., Rihs, J.D., Yu, V.L., Finegold, S.M. and Gorbach, S.L.: Analysis of trends in antimicrobial resistance for clinical isolates of *Bacteroides fragilis* group species from 1990-1994." Clinical Infectious Diseases, In Press, 1996.
3. Eyler, A.E., Pierson, C.L. and Reed, B.D: Improved diagnosis of *Candida* vulvovaginitis using Diamond's modified media." J of Women's Health, In Press, 1996.

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. Blackwood, R.A., Rode, C.K., Pierson, C.L. and Block, C.A.: Pulse-field gel electrophoresis genomic fingerprinting of hospital *E. coli*-bactereia isolates."
3. Marinella, M.A., Pierson, C.L. and Chenoweth, C.: The stethoscope: a potential source of nosocomial infection.

BOOKS/ CHAPTERS IN BOOKS:

None.

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

1. Grossman, S., Hankerd, R., and Pierson, C.L.: Anaerobe E-Test, agar dilution and the NCCLS interpretation standards. Abstracts, 96th American Society for Microbiology General Meeting, p 58.

2. Bourbeau, P., Riley, J., Heiter, B.J., Master, R., Young, C. and Pierson, C.: Use of the BacT/Alert for culture of sterile body fluids other than blood. Abstracts, 96th American Society for Microbiology General Meeting, p 54.
3. Blythe, L.K., Debusscher, J., Hankerd, R. and Pierson, C.L.: Comparison of Amplicor polymersase chain reaction to Syva Direct Fluorescent Antibody Test for detection of *Chlamydia trachomatis* in male urine specimens." Abstracts, 96th American Society for Microbiology General Meeting, p 6.
4. Varney, G., Zientak, C., Reed, A., Turner, N. and Pierson, C.L.: Automation of viral antibody tests utilizing the Gull Solus Omni System. Abstracts, 1996 Clinical Virology Symposium. Clearwater Beach, Florida.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

OVERVIEW:

I continued to devote my efforts predominantly to the M-Labs program. We were able to add more hospitals to our list of clients (Community Health Center of Branch County in Coldwater, Botsford Hospital in Farmington Hills and Hurley Hospital in Flint) and as a result our revenues continued to increase. A marketing plan was developed to increase our activity in Michigan and Ohio, 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 number of surgical pathology cases increased as we added several satellite clinics or acquired physician offices to the cases from Albion and Addison Hospitals. The M-Labs Symposium for pathologists continues to be successful. The seventh was held in April, 1996. My commitment to help the Cytopathology Lab continued, as well as my participation in the autopsy coverage.

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. These stat-consults rely on our courier and provide test turnaround time. Most of these cases are shown in consultation to other faculty.
C. Cytopathology: reviewing and verifying cases from the University of Michigan Health Service and other M-Labs clients.
D. Autopsy coverage at the University Hospitals five weeks a year and six week-ends a year.
E. Pathologist, on site coverage for Albion and Addison Community Hospitals.

II. TEACHING ACTIVITIES:

A. Read out autopsies with house officers.
B. Organize and lecture at the M-Labs Symposium, 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.

III. RESEARCH ACTIVITIES:

Utility of urine cultures-study in progress, with the medical and laboratory staff at the University Health System. To develop criteria for ordering urine cultures.

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.
C. Monthly colposcopy meeting with Gynecology staff at the University of Michigan Health Service.

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. Started a Quality Assurance program for client pathologists with AP faculty approval.
E. Participated in a week-long meeting on networking, managed care and legal issues, in addition to Diagnostic Pathology sponsored by the College of American Pathologists, in Boston.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Director, Autopsy Service.
B. Supervision of Autopsies-11 weeks, signed out 96 autopsies.
C. Coordinator of Senior Staff Autopsy Call Schedule.
D. Deputy Medical Examiner for University Hospitals (16 weeks).
E. Director, Electron Microscopy Service.

II. TEACHING ACTIVITIES:

A. Coordinator, Biweekly Pathology Gross Conference.
B. Lectures to Pathology House Officers in Anatomic and Clinical Pathology.
C. Lecturer, Pathology 600 Course.
D. Pathology 600, Provided written critiques of student autopsy write-ups (200).
E. Laboratory Instructor, Histopathology Laboratory for M1 students.
F. Thesis Committee - Andrew Merry.
G. Directed research of Jorge Rodriguez, M.D. (Department of Surgery); Michael O'Reilly, M.D. (Department of Anesthesiology), Stewart Wang, M.D., Ph.D. (Department of Surgery), House Officers - Devina Prakash (Pediatrics) Postdoctoral fellows, Lorelie Villarete, Ph.D.;Samuel Ebong, Ph.D. Graduate Students - Jami Foreback, Medical Students - Sunir Garg, Liza Green, Undergraduate Students - David Newcomb.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Regulation of gene expression of soluble mediators of inflammation using the following models:
   1. Endotoxin-stimulated human whole blood.
   2. Endotoxin injection in mice.
   3. Cecal ligation and puncture.
B. Toxic effects of immunomodulators.
C. Pathophysiology of septic shock.
D. Quantitation of mediators in septic shock.
E. Cloning, sequencing, and expressing cytokines including mTNF, hTNF, mIL-6, hIL-8, MCP, JE.

F. 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.

SPONSORED SUPPORT:

A. Principal Investigator, "The Role of Cytokines in Sepsis and Trauma", GM44918 $906,182, 1990-1996.
B. Principal Investigator, "The Effects of IL-10", $31,500, 1994-96.
C. Scientific Reviews:
   1. NIH phone conference November, 1995.
   2. NIH phone conference June, 1996.
   3. Ad hoc reviewer, Surgery, Anesthesiology and Trauma, Februry, 1996.
D. Pricipal Investigator, "Regulation of IL-8 gene expression: four years, GM50401 $870,822, 1995-1999.
E. G. Burroughs Wellcome Travel Fund, $3,890.00, 1995.
F. Co-Investigator, "Local Tissue Responses After Thermal Injury", American College of Surgeons, $60,000, 1996 - 1998.

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, Medical School Admissions Committee.
B. Member, Michigan Cancer Center.
C. Reviewer, Biomedical Research Council grants.
D. Reviewer, Department of Surgery grants.

REGIONAL AND NATIONAL:

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

E. Member, Executive Committee, Michigan Association of Medical Examiners.
F. 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. Reviewer, Veterans Administration Merit grants.
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. Circulatory Shock.
7. Journal of Clinical Investigations.
8. Infection and Immunity.
9. Blood.
10. Shock.
11. American Journal of Physiology.
12. Journal of Immunology.
13. Journal of Gerontology.

INVITED LECTURES/SEMINARS

1. Visiting Professor, Royal Hammersmith Hospital, London, England, September 3-17, 1996.
2. Visitng Professor, St. George's Medical School, London, England, September 18-24,1996.
3. Program Director, 1995 Michigan Association of Medical Examiners Meeting, Midland Michigan, October 13-15, 1995.
4. Invited speaker, "Animal Models of Sepsis," Michigan Laboratory Animal Medicine Society, Ann Arbor, Michigan, November 8, 1995.
5. Invited participant, Washtenaw County Medical Examiners Roundtable Discussion, Ann Arbor, Michigan, November 29, 1995.
6. Invited speaker, "Anti-TNF Antibodies Reduces the Lethality of Sepsis But Not True Sepsis," Sepsis/SIRS, Reducing the Mortality to Patients and Suppliers, Washington D.C., February 11-13, 1996.
7. Ad Hoc Reviewer, NIH, Surgery, Anesthesiology and Trauma Study Section, Washington, D.C., February 21-22, 1996.
8. Invited participant, "Lysofylline," Cell Therapeutics Incorporated, San Fransisco, March 8-9, 1996.
9. Invited participant, G-CSF, Amgen Inc, Santa Monica, California, April 21-22, 1996.

10. "Pentoxyfylline fails to prevent the Jarisch-Herxheimer Reaction associated with treatment of relapsing fever," 6th International Congress on Tumor Necrosis Factor, Rhodes, Greece, May 8 - 11, 1996.
11. Invited Discussant, Moses Gunn Conference, University of Michigan Medical School, Ann Arbor, Michigan, May 23rd, 1996.
12. Invited participant, Upjohn Seminar on Adhesion Molecules and Cytokines, Ann Arbor, Michigan, June 19, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Remick, D.G. and Villarete L: Regulation of cytokine gene expression by reactive oxygen and reactive nitrogen intermediates. J. Leukoc. Biol. 59:471-5, 1996.
2. Biswas, S., Friedland, J.S., Remick, D.G., Davies, E.G. and Sharland, M.: Elevated plasma interleukin 8 in respiratory syncytial virus bronchiolitis. Pediatr. Infect. Dis. J. 14:919 1995.
3. Brieland, J.K., Flory, C.M., Jones, M.L., Miller, G.R., Remick, D.G., Warren, J.S. and Fantone, J.C.: Regulation of monocyte chemoattractant protein-1 gene expression and secretion in rat pulmonary alveolar macrophages by lipopolysaccharide, tumor necrosis factor-alpha, and interleukin-1 beta. Am. J. Respir. Cell Mol. Biol. 12:104-9, 1995.
4. Brieland, J.K., Remick, D.G., Freeman, P.T., Hurley, M.C., Fantone, J.C. and Engleberg, N.C.: In vivo regulation of replicative Legionella pneumophila lung infection by endogenous tumor necrosis factor alpha and nitric oxide. Infect. Immun. 63:3253-8, 1995.
5. Hsi, E.D. and Remick, D.G.: Monocytes are the major producers of interleukin-1 beta in an ex vivo model of local cytokine production. J. Interferon Cytokine Res. 15:89-94, 1995.
6. Olson, A.D., DelBuono, E.A., Bitar, K.N. and Remick, D.G.: Anti-serum to tumor necrosis factor and failure to prevent murine colitis. J. Pediatr. Gastroenterol. Nutr. 21:410-8, 1995.
7. Remick, D., Manohar, P., Bolgos, G., Ropdriguez, J., Moldawer. L. and Wollenberg, G.: Blockade of tumor necrosis factor reduces lipopolysaccharie lethality, but not the lethality of cecal ligation and puncture. Shock 4:89-95, 1995.
8. Remick, D.G.: Cytokines: a primer for plastic surgeons. Ann. Plast. Surg. 35:549-59, 1995.
9. Rogy, M.A., Auffenberg, T., Espat, N.J., Philip, R., Remick, D., Wollenberg, G.K., Copeland, E.M., 3rd, Moldawer, L.L. and Copeland, E.M.: Human tumor necrosis factor receptor (p55) and interleukin 10 gene transfer in the mouse reduces mortality to lethal endotoxemia and also attenuates local inflammatory responses. J. Exp. Med. 181:2289-93, 1995.
10. Tang, W.W., Yi, E.S., Remick, D.G., Wittwer, A., Yin, S., Qi, M. and Ulich, T.R.: Intratracheal injection of endotoxin and cytokines. IX. Contribution of CD11a/ICAM-1 to neutrophil emigration. Am. J. Physiol. 269:L653-9, 1995.
11. Ulich, T.R., Howard, S.C., Remick, D.G., Wittwer, A., Yi, E.S., Yin, S., Guo, K., Welply, J.K. and Williams, J.H.: Intratracheal administration of endotoxin and cytokines. VI. Antiserum to CINC inhibits acute inflammation. Am. J. Physiol. 268:L245-50, 1995.
12. Villarete, L.H. and Remick, D.G.: Nitric oxide regulation of IL-8 expression in human endothelial cells. Biochem. Biophys. Res. Commun. 211:671-6, 1995.

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

1. Balazovich, K.J., Succhard, S.J., Remick, D.G. and Boxer, L.A.: TNFα and FMLP receptors are functionally linked during FMLP-stimulated activation of adherent human neutrophils. 37th Annual Meeting of ASH, 1995.
2. Remick, D.G., Negussie, Y., Fekade, D. and Griffin, G.: Pentoxifylline fails to prevent the Jarisch-Herxheimer reaction or associated cytokine release. 6th International TNF Congress, 1996.
3. Remick, D.G., Mulligan, M., Newcomb, D., Huie, T. and Bolgos, G.: Endogenous or exogenous IL-10 fails to modulate sepsis. Nineteenth Annual Conference on Shock, 1996.
4. Bolgos, G., Rodriguez, J., Huie, T., Sunir, G. and Remick, D.: Effect of human IL-8 transgene on the murine CLP model of sepsis. Nineteenth Annual Conference on Shock.
5. Taheri, P.A., Ferrara, J.J., Wang, S.C., Cardellio, A., Remick, D.G., Till, G. and Rodriguez, J.L.: Loco-regional cytokine production following thermal injury. Shock, 1996.
6. Essani, N.A., Remick, D.G., Fisher, M.A. and Jaeschke, H.: Galactosamine primes the liver for production of the chemokine KC/GRO during endotoxin shock. Shock, 1996.
7. Foreback, J.L., Remick, D.G. and Ward, P.A.: Cytokine production by human PBMC in response to solid phase human IgG subclasses. ASBMB/ASIP/AAI Joint Meeting, 1996.

BOOKS AND CHAPTERS IN BOOKS

1. Editor, Cytokines in Health and Disease, second edition. Anticipated publication date, 1997.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995- 30 JUNE 1996

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 (two lectures).
E. Clinical Pathology Case Conference/weekly.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None

PROJECTS UNDER STUDY:

A. Immunophenotyping in acute and chronic leukemias.
B. Phenotyping and genotyping of lymphomas.
C. Detection of immunoglobulin gene rearrangements by the polymerase chain reaction.
D. Effects of radioimmunotherapy in B-cell lymphoma.
E. Detection of infectious agents in lymphoid lesions by polymerase chain reaction.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Clinical Flow Cytometry Laboratory.
B. Coordinator, CP resident teaching program.
C. Resident Selection 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, American Society of Clinical Pathology.
C. Ad hoc manuscript reviewer, Blood.
D. Ad hoc manuscript reviewer, Cancer Investigation.

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, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Alkan, S., Schnitzer, B., Thompson, J.L., Moscinski, L.C. and Ross, C.W.: Cyclin D1 protein expression in mantle cell lymphoma. Annals of Oncology 6:567-570, 1995.
2. Hoyer, J.D., Ross, C.W., Li, C.Y., Witzig, T.E., Gascoyne, R.A., Dewald, G.W. and Hanson, C.A.: True T-cell chronic lymphocytic leukemia: A morphologic and immunophenotypic study of 25 cases. Blood 86:1163-1169, 1995.
3. Metzman, M.S., Stevens, S.R., Griffiths, C.E., Ross, C.W., Barnett, J.M. and Cooper K.D.: A clinical and histologic mycosis fungoides simulant occurring as a T cell infiltrate coexisting with B cell leukemia cutis. J. Am. Acad. Dermatol. 33:341-345, 1995.
4. Hsi, E.D., Greenson, J.K., Singleton, T.P., Siddiqui, J., Schnitzer, B. and Ross, C.W.: Detection of immunoglobulin heavy chain gene rearrangement by polymerase chain reaction in chronic active gastritis associated with Helicobacter pylori. Hum. Pathol. 27:290-296, 1996.
5. Alkan, S., Ross, C.W., Hanson, C.A. and Schnitzer, B.: Follicular lymphoma with involvement of the splenic marginal zone: A pitfall in the differential diagnosis of splenic marginal zone cell lymphoma. Hum. Pathol. 27:503-506, 1996.

6. Kaminski, M.S., Zasadny, K.R., Francis, I.R., Fenner, M.C., Ross, C.W., Milik, A.W., Estes, J., Tuck, M., Regan, D., Fisher, S., Glenn, S. and Wahl, R.L.: 131-I-Anti-B1 Radioimmunotherapy for B-Cell Lymphoma. J. Clin. Oncol., In Press.
7. 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., In Press.
8. Anderson, M.M., Ross, C.W., Singleton, T.P., Sheldon, S. and Schnitzer, B.: Ki-1 anaplastic large cell lymphoma with a prominent leukemic phase. Hum. Pathol., In Press.

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. McCarthy, C.J., Sheldon, S., Ross, C.W. and McCune, W.J.: Cytogenetic abnormalities and therapy-related myelodysplastic syndromes in rheumatic disease.
3. Hsi, E.D., Eisbruch, A., Greenson, J.K., Singleton, T.P., Ross, C.W. and Schnitzer, B.: Classification of primary gastric lymphomas according to histologic features.

BOOKS AND CHAPTERS IN BOOKS:

1. Ross, C.W., Sadler, D.A. and Keren, D.F.: Flow cytometric evaluation of immunodeficiency diseases, in, Bauer, K.D., Duque, R.E. and Shankey, T.V. (eds), Flow Cytometry: Principles and Clinical Applications, Williams and Wilkins, In Press.

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

1. Tworek, J.A., Singleton, T.P., Schnitzer, B., Hsi, E.D. and Ross, C.W.: Immunophenotypic analysis of small lymphocytic lymphoma (SLL), plasmacytoid SLL (SLLP), and mantle cell lymphoma (MCL). Mod. Pathol. 9:124A, 1996.
2. Poston, C.D., Ross, C.W., Schnitzer, B. and Singleton, T.P.: Phenotypic analysis of acute leukemias by immunohistochemistry (IHC) on bone marrow, flow cytometry (FC), and morphology. Mod. Pathol. 9:120A, 1996.
3. Hsi, E.D., Greenson, J.K., Singleton, T.P., Eisbruch, A., Ross, C.W. and Schnitzer, B.: Classification of primary gastric lymphomas according to histologic features. Mod. Pathol. 9:59A, 1996.
4. Hsi, E.D., Singleton, T.P., Frank, T.S., Svoboda, S.M., Ross, C.W., and Schnitzer, B.: Immunoglobulin heavy chain gene rearrangement in spleens with expanded marginal zones: Detection of low stage splenic marginal zone lymphoma? Am. J. Clin. Pathol. 105:513, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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. "Hodgkin's Disease 160 Years Later: A Practical Approach to its Diagnosis", Society for Hematopathology, New Orleans, Louisiana, September 1995.
2. "A Practical Approach to the Diagnosis of Extranodal Lymphomas", ASCP Workshop, New Orleans, Lousiana, September, 1995.
3. "Diagnosis and Classifications of Lymphomas in 1996", Florida Society of Pathologists, Orlando, Florida, January, 1996.
4. "Reactive Lymphadenopathies",Tutorial on Neoplastic Hematopathology, Department of Laboratory Medicine and Pathology, University of Minnesota, San Diego, California, February, 1996.
5. Slide Seminar, Severance and Associate, San Antonio, Texas, March 1996.
6. Cancer Update: A.O. Severance Pathology Lecture, "Unusual Clinical Presentations of Lymphoma", San Antonio, Texas, March 1996.
7. Schnitzer, B., Ross, C.W. and Singleton, T.: "Hematologic Coups", ASCP Workshop, Boston, Massachusetts, April, 1996.
8. "Acute Lymphoproliferative Disorders", ASCP Workshop, Boston, Massachusetts, April, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Alkan, S., Schnitzer, B., Thompson, L., Moscinski, C. and Ross, C.W.: Cyclin D1 protein expression in mantle cell lymphoma. Ann. Oncol. 6:567-570, 1995.
2. Hsi, E.D., Zukerberg, L.R., Schnitzer, B. and Harris, N.L.: Development of extrasalivary gland lymphoma in myoepithelial sialadenitis. Mod. Pathol. 8: 817-24, 1995.

3. Hsi, E.D., Greenson, J.K., Singleton, T.P., Siddiqui, J., Schnitzer, B. and Ross, C.W,: Detection of immunoglobulin heavy chain gene rearrangement by polymerase chain reaction in chronic active gastritis associated with helicobacter pylori. Human Pathol. 27:290-296, 1996.
4. Alkan, S., Ross, C.W., Hanson, C.A. and Schnitzer, B.: Follicular lymphoma with involvement of the splenic marginal zone: A pitfall in the differential diagnosis of splenic marginal zone cell lymphoma. Human Pathol. 27:503-506, 1996.
5. 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. In Press.

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.

BOOKS AND CHAPTERS IN BOOKS:

1. Schnitzer, B., Chan, W. and Weiss, L: Pathology of lymph nodes, in, Anderson's Pathology, 10th Edition, C.V. Mosby,Co., 1995.

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

1. Hsi, E.D., Greenson, J.K., Singleton, T.P., Eishbruch, A., Ross, C.W. and Schnitzer, B.: Classification of primary gastric lymphoma according to histologic features. Modern Pathol. 9:59A, 1996.
2. Grogan, T., Miller, T., Dahlberg, S., Braziel, R., Banks, P., Nathwani, B., Kjeldsberg, C., Tubbs, R., Foucar, K., Leith, C., Spier, C., Schnitzer, B., Gulley, M. and Fisher, R.: Morphologic review of 2100 SWOG patients supports the REAL classification of lymphomas as clinically useful. Modern Pathol. 9:120A, 1996.
3. Poston, C.D., Ross, C.W., Schnitzer, B. and Singleton, T.P.: Phenotypic analysis of acute leukemias in bone marrow by immunohistochemistry, flow cytometry and morphology. Modern Pathol. 9:120A, 1996.
4. Tworek, J.A., Singleton, T.P., Schnitzer, B., Hsi, E.D. and Ross, C.W.: Immunophenotypic analysis of small lymphocytic (SLL), plasmacytoid SLL (SLIP), and mantle cell lymphoma (MCL). Modern Pathol. 9:124A, 1996.
5. Hsi, E.D., Singleton, T.P., Frank, T., Svoboda, S., Ross, C.W. and Schnitzer, B.: Immunoglobulin heavy chain gene rearrangement in spleens with expanded marginal zones: Detection of low stage splenic marginal zone lymphoma? Am. J. Clin. Pathol. 105:513, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Cytopathology - 23 weeks.
B. Gynecologic Pathology (transfer cases) - 12 months.
C. Consultation service, Department of Pathology:
    1. Cytopathology and Gynecologic Pathology - 12 months.
D. Necropsy Service - One week.

II. TEACHING ACTIVITIES:

A. Medical Students:
    1. Pathology laboratory instructor, April, 1996.
    2. Reproductive sequence lecture: Gynecologic Pathology, April 1, 1996.
B. Residents and Cytopathology Fellow:
    1. Sign-out; gynecologic and non-gynecologic cytology cases.
    2. Instruction in the performance and interpretation of fine needle aspirates.
    3. Monthly Cytopathology Conference.
    4. Lecture-Obstetric/Gynecologic Pathology - one hour.
    5. Consult Case Conference - one/year.
C. Other Education Activities:
    1. Cytotechnologists-Cytopathology conferences - monthly.
    2. Obstetric/Gynecologic Colposcopy/Pathology Conference - monthly.

III. GRANT SUPPORT

CURRENT

A. National Institute of Health, Co-investigator (1 UO1 CA68291-01), "Retinoids and Intermediate Biomarkers for CIN II and III", 09/01/95 - 08/31/2000 ($2,610,213 - direct cost), (8% effort).

IV. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Cervical atypia in women with SLE treated with intravenous cyclophosphamide (in conjunction with Dr. J. McCune, Dept. of Internal Medicine/Rheumatology).

B. Genital infections as risk factors for low grade squamous intraepithelial lesion progression (in conjunction with Dr. Barbara Reed, Department of Family Practice).
C. Retinoids and Intermediate Biomarkers for CIN II and III. (In conjunction with Dr. Mack Ruffin, Department of Family Practice).

V. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Cytopathology Laboratory.
B. Director, Cytopathology Fellowship Program.
C. Member, Resident Selection Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Member, Quality Assurance/Quality Control Committee.
B. Member, M II Curriculum Committee-Reproduction Sequence.

REGIONAL AND NATIONAL:

A. Editorial Review Board, Diagnostic Cytopathology.
B. Editorial Review Board, Cancer Cytopathology.
C. Member, Cytopathology Committee, College of American Pathologists.
D. Member, Cervical Cancer Advisory Committee, Michigan Department of Public Health, Lansing, Michigan.

VI. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. "The Significance of ASCUS on Cervical Smears", Keynote Speaker; Illinois Society of Cytology. Chicago, Illinois, September 29, 1995.
2. Cytopathology workshop, "Fine Needle Aspiration Cytology of Cystic Ovarian Lesions in Conjunction with Peritoneal Washing Cytology", Forty-second Annual Scientific Meeting of the American Society of Cytology, Chicago, Illinois, November 10, 1995.

VII. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Selvaggi, S.M., Haefner, H.K., Lelle, R.J., Pearl, M.K. and Roberts, J.A.: Neovaginal cytology following total pelvic exenteration for gynecologic malignancies. Diagn. Cytopathol. 13:22-25, 1995.

2. Selvaggi, S.M. and Haefner, H.K.: Reporting of ASCUS on cervical smears: Is it significant? Diagn. Cytopathol. 13:352-356, 1995.
3. Mikhail, A.A., Haefner, H.K. and Selvaggi, S.M.: Endocervical polyps as a source of ASCUS and AGUS on cervical smears. Diagn. Cytopathol., In Press.
4. Selvaggi, S.M. and Haefner, H.K.: Microglandular endocervical hyperplasia and tubal metaplasia: Pitfalls in the diagnosis of adenocarcinoma on cervical smears. Diagn. Cytopathol., In Press.
5. Schemmel, M., Haefner, H.K., Selvaggi, S.M., Warren, J.S. and Hurd, W.W.: Comparison of the ultrasonic scalpel to CO2 laser and electrocautery in terms of tissue injury and adhesion formation in a rabbit model. Fertility and Sterility, in Press.

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

1. Selvaggi, S.M. and Lawrence, W.D.: Cytopathology of the uterine cervix, in, Shingleton, H.M., Fowler Jr., W.C., Jordan, J.A., and Lawrence, W.D. (eds.), Gynecologic Oncology: Current Diagnosis and Treatment, W.B. Saunders Co., pp. 9-24, 1996.
2 Selvaggi, S.M.: On the American Scene: The American Society of Cytopathology and the Papanicolaou Society of Cytopathology. Diagn. Cytopathol. 14:96, 1996.
3. Selvaggi, S.M.: Cervical cancer screening and detection in Michigan, Recommendations to Reduce Mortality, Contributing Author. From the Cervical Cancer Advisory Committee, Department of Public Health, Lansing, Michigan, March, 1996.
4. Greenbaum, E., Selvaggi, S.M. and Lerner, J.: Fine needle aspiration of cystic ovarian lesions, in, Schmidt, W.A., Miller, T.R. (eds), Cytopathology Annual, ASCP Press, In Press.
5. Stern, R. and Selvaggi, S.M.: Book Review: The Art and Science of Cytopathology: Exfolitive Cytology and Aspiration Cytology, DeMay, R.M., ASCP Press, 1995; Am. J. Surg. Pathol., In Press.
6. Check Samples Series, American Society of Clinical Pathologists: Selvaggi, S.M. Aspiration Cytology of Neoplastic Ovarian Cysts, In Press.
7. Selvaggi, S.M.: Guides to Clinical Aspiration Biopsy: Female Pelvic Organs, Igaku-Shoin, In Preparation.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Chief, Hemostasis and Coagulation Laboratory, William Beaumont Hospital, Royal Oak, Michigan.
B. Hematopathology, Bone Marrow Service, William Beaumont Hospital, Royal Oak, Michigan.
C. Clinical Consultant, Problems in Bleeding and Thrombosis, William Beaumont Hospital, Royal Oak, Michigan.

II. TEACHING ACTIVITIES:

A. Daily "plasma" rounds, monitoring blood component usage, William Beaumont Hospital.
B. Periodic lectures to ICU residents on blood component therapy, William Beaumont Hospital.
C. Clinical Pathology Grand Rounds, General Principles of Hemostasis, University of Michigan Medical Center.
D. Coagulation conferences for pathology residents, William Beaumont Hospital.
E. Seven lectures for Medical Technology Students - Coagulation and Hemostasis, William Beaumont Hospital.
F. Participated in Clinical Pathology Elective for Senior Medical Students - Lecture on Approach to Bleeding Disorders plus case presentations and discussions, University of Michigan.
G. Weekly conferences on Coagulation, Thrombosis and Component Therapy for Blood Bank Residents, University of Michigan.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Investigator, "Protamine Filter for Extracorporeal Heparin Removal," University of Michigan College of Pharmacy, NIH-NHLBI HL-38353 (5%), $204,000, 01/01/95-12/31/95.

IV. PUBLICATIONS:

A. None.

V. MISCELLANEOUS:

A. On June 15, 1996, Dr. Shanberge resigned his position in the Department of Pathology at William Beaumont Hospital and became an Emeritus Member of the Medical Staff.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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. Pathology Graduate Course, three lectures.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Clinical Cytogenetics Laboratory.

REGIONAL AND NATIONAL:

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. University of Michigan Comprehensive Cancer Center Colleagues in Care, June, 1996 CCG.
2. Pediatric (Hematology/Oncology) June, 1996.
3. Tutorial Southeast Michigan Cytogenetics Conference, August, 1995.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Flejter, W., Bennett-Baker, P., Ghaziuddin, M., McDonald, M., Sheldon, S. and Gorski, J.: Cytogenetic and molecular analysis of inv dup (15) chromosomes observed in two patients with autistic disorder and mental retardation. Am. J. Med. Genet. 61:182, 1996.

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

1. Griffiith, A., Downs, C., Innis, J., Shepard, N., Gebarski, S., Sheldon, S. and Arts, H.: Familial inheritance of the large vestibular aqueduct syndrome. Laryngoscope (Abstract).
2. Wilke, C.M., Cox, B.A., Yanik, G.A., Miller, D.E., Glover, T.W. and Sheldon, S.: Fluorescence in-situ hybridization characterization of a 3q amplification in a Fanconi Anemia patient. AJHG 1996. (Abstract).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

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

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

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

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

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

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

G. Surgical Pathology "Quickie" Anatomic Pathology consults for 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 Albion Community Hospitals.

III. RESEARCH ACTIVITIES:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. 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 at the end of the last fiscal year and the one hired in the middle of this fiscal year have added to the effectiveness of our highly motivated and talented M-Labs team. We are now able to deal with support of existing clients as well as marketing. Operations are now

dealt with in a more coordinated fashion. The M-Labs office has been reorganized. The operations representative has prepared a manual with specific client issues and requirements for the M-Labs office and accessioning personnel.

b. Problems with our report formats have been ameliorated by changes in format accomplished with assistance from laboratory personnel and PDS.

c. Accessioning errors have not increased despite cutbacks in personnel, partly because of the client handbook and a "client exception list" prepared by M-Labs operations for CD personnel.

d. Through the efforts of PDS, we have our first fully operational interface between the University of Michigan laboratory computer system and a client hospital's computer system. Two others are under development and two more are planned.

3. Growth. M-Labs has experienced a 23% increase in net revenues from billings to clients for clinical pathology services and a 344% increase in net billings to patients for clinical pathology services. The number of M-Labs surgical pathology cases has also increased by 16% . Billing for these cases have increased by 22%.

a. In this fiscal year we added the reference laboratory work of a 500 bed hospital, a 130 bed hospital, the health service of a nearby university, and several large group practices and individual physicians' offices.

b. We lost one large group practice because of difficulties with TAT, reporting, and differences in test profiles from those desired by that physician group.

c. We are finalizing agreements to provide reference lab testing to another large hospital and a small hospital which will begin in the next few months.

d. We have submitted proposals to a 150 bed hospital in northern Ohio and to an entity that includes 2 large hospitals in northwestern Ohio.

4. Managed Care Contracts. We have succeeded in contracting with MCare to provide outpatient laboratory testing for its soon to be introduced Medicare product. We are subcontracting the work to a group of hospitals. M-Labs will manage the revenue distribution to the subcontractors based on the relative-value weighted volume of testing furnished by each provider.

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 been accepted for membership in JVHL, a network of major hospital laboratories in the Detroit area.

b. We are exploring the possibility of providing reference laboratory work to a developing 13 hospital laboratory network in Central Michigan.

B. Director, Laboratory at Albion Community Hospital, Albion, Michigan.

C. Chairman, Tissue/Transfusion Committee, Albion Community Hospital, Albion, Michigan.

D. Chairman, Infection Control Committee, Albion Community Hospital, Albion, Michigan.

E. Director of Laboratories, Addison Community Hospital, Addison, Michigan.

F. Chair, Tissue Transfusion and Infection Control Committees, Addison Community Hospital, Addison, Michigan, 9/92 -.

G. Plan and review Laboratory QA and CQI at Albion and Addison Community Hospitals.

H. Review Quality Control of Clinical Pathology tests at Albion and Addison Community Hospitals.

V. OTHER RELEVANT ACTIVITIES:

None.

VI. PUBLICATIONS:

None.

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

ANNUAL DEPARTMENTAL REPORT
1 AUGUST 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Sign-out lymph node and bone marrow biopsies, peripheral blood smears and body fluids.
B. Sign-out flow cytometry.
C. Quality control and antibody development for clinical immunohistochemistry laboratory.
D. Review material for interdepartmental conferences.
   1. Weekly lymphoma conference.
   2. Biweekly leukemia conference
   3. Biweekly non-neoplastic hematology conference.
   4. On occasion, fill in for monthly cutaneous lymphoma conference.

II. TEACHING ACTIVITIES:

A. Medical students, first two years:
   1. Lecture, Lymphoprolifertive Disorders.
   2. Laboratory, Hematology.
B. Medical students, last two years:
   1. Lecture, Red Cell Disorders.
   2. Laboratories, Hematology
   3. Review biopsies at sign-out.
C. Dental students, first two years
   1. Lecture, Leukocyte Disorders
C. Residents and fellows in pathology and other departments:
   1. Review of biopsies at sign-out.
   2. Bimonthly unknown conference in hematopathology.
   3. Bimonthly conference in immunohistochemistry.
   4. Grand Rounds Lecture, Myeloid Leukemias.

III. RESEARCH ACTIVITIES:

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

IV. ADMINISTRATIVE ACTIVITIES:

A. Assistant Director, Hematology Laboratory.
B. Assistant Director, Immunohistochemistry Laboratory for Anatomic Pathology's Special Studies Laboratory.

V PRESENTATIONS:

1. "Coups in Hematopathology", Course presented at the American Society for Clinical Pathology, April, 1996.
2. "Classification of Non-Hodgkin's Lymphoma", Lecture and slide review, presented at University of Michigan's M-Labs Symposium, 1996.
3. "Classification of Non-Hodgkin's Lymphoma", Lecture presented at the Fourth Annual Cancer Care Symposium, Mercy Hospita, Port Huron, Michigan, November, 1995

V. PUBLICATIONS:

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

1. Hsi, E., Greenson, J., Singleton, T., Siddiqui, J., Schnitzer, B. and Ross, C.: Detection of immunoglobulin heavy chain (IgH) gene rearrangement by polymerase chain reaction in chronic active gastritis associated with Helicobactor pylori. Hum. Pathol. 27:290-6, 1996.
2. Cooney, K.A., Wetzel, J., Merjaver, S.D., Macoska, J.A., Singleton, T.P. and Wojno, K.J.: Loss of heterozygosity involving chromosome 13q14.3 in sporadic prostate cancer. Cancer Res. 56:1142-45, 1996.

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

1. Book Review: Surgical Pathology of the Lymph Nodes and Related Organs by ES Jaffe, Second Edition, in Am. J. Surg. Pathol. 20:775, 1996.
2. Poston, C.D., Ross, C.W., Schnitzer, B. and Singleton, T.P.: Phenotypic analysis of acute leukemias by immunohistochemistry on bone marrow, flow cytometry and morphology, United States and Canadian Academy of Pathology, 1996.
3. Tworek, J.A., Singleton, T.P., Schnitzer, B., Hsi, E.D. and Ross, C.W.: Immunophenotypic analysis of small lymphocytic lymphoma (SLL), plasmacytoid SLL (SLLP), and mantle cell lymphoma (MCL), United States and Canadian Academy of Pathology, 1996.
4. Khalidi, H.S., Singleton, T.P., and Weiss, S.W.: Do leukocyte markers distinguish inflammatory malignant fibrous histiocytoma from Hodgkin's and non-Hodgkin's Lymphoma?, United States and Canadian Academy of Pathology, 1996
5. Singleton, T.P., Frank, T.S., Field, K., Sun, R. and Wojno, K.J.: Immunohistochemistry (IHC) for estrogen receptor using an automated stainer: comparison with IHC by hand and with cytosol assay, United States and Canadian Academy of Pathology, 1996.

6. Hsi, E.D., Greenson, J.K., Singleton, T.P., Eishbruch, A., Ross, C.W. and Schnitzer, B.: Classification of primary gastric lymphoma according to histologic features, United States and Canadian Academy of Pathology, 1996
7. Svoboda, S.M., Greenson, J.K., Singleton, T.P., Sun, R. and Frank, T.S.: Detection of hepatitis C in paraffin sections of formalin fixed liver using RT-PCR, United States and Canadian Academy of Pathology, 1996
8. Tworek, J.A., Appelman, H.D., Singleton, T.P. and Greenson, J.K.: Stromal tumors of the jejunum and ileum, United States and Canadian Academy of Pathology, 1996
9. Lee, C.T., Wojno, K.J., Oesterling, J.E., Singleton, T.P., McCauley, L., Jehr, J., Monti, J.E. and Pienta, K.: Expression of parathyroid hormone-like protein in prostate cancer and prostatic intraepithelial neoplasia, Presented at AACR. Cancer Res. (Resident Award Poster).
10. Cooney, K.A., Wetzel, J., Merjaver, S.D., Macoska, J.A., Singleton, T.P. and Wojno, K.J.: Loss of heterozygosity involving chromosome 13q14.3 in sporadic prostate cancer, American Cancer Society, April, 1995.
11. Blaivas, M., Mikhail, A., Perry, A., McKeever, P.E., Singleton, T. and Scheithauer, B.W.: Macrophages in high grade gliomas with or without associated infarct, American Association of Neuropathologists, 1996.

DENISE SULAVIK, M.D.
LECTURER
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

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

B. Autopsy service.

II. TEACHING ACTIVITIES:

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

1. Randall Knibbs, Ph.D., Research Scientist (January, 1994-present) - Dr. Knibbs recently 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. Recently completed studies show 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 will next focus on the structure of the carbohydrate portion of the selectin ligands on T-cells and on the signalling pathways controlling FucT-VII activity.
2. Francis Wolber, Ph.D. candidate in Experimental Pathology (July, 1992-present) - Ms. Wolber's thesis project focuses on the role of adhesion receptors in the leukocyte recruitment in murine hypersensitivity pneumonitis. 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 developed assays which permit the evaluation of selectin and integrin adhesive interactions during T-lymphoblast recruitment into the lung. This effort resulted in the first direct evidence that both selectins and the β1-integrin VLA-4 contribute to T-cell recruitment in hypersensitivity pneumonitis.
3. Neil Faulkner (July, 1995-present), MD., Ph.D. student - Mr. Faulkner's project focus on the regulation of selectin ligand synthesis by the FucT-VII enzyme during antigen-driven T-cell proliferation. Mr. Faulkner will determine whether FucT-VII activity is controlled at the transcriptional levels in T-cells.

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. Developed new lecture series on the growth, differentiation and normal physiology of leukocytes and autoimmune diseases.

F. Lecturer, Host-Defense Sequence in Component I - developed new lecture series on leukocyte recruitment and the clinical uses of flow cytometry.

G. Daily sign-out of cases in flow cytometry with pathology residents and medical students.

H. Attending, Autopsy Service.

III. RESEARCH ACTIVITIES:

ACTIVE SUPPORT:

A. Principal Investigator, Project 4, "Leukocyte-Microvascular Adhesive Interactions in Rheumatoid Arthritis", NIH, P50AR41703 (SCOR in Rheumatoid Arthritis; Josi Holoshitz, M.D., Program Director), 25% effort, $398,269; 30 Sepember 1992 - 31 August 1995.

B. Principal Investigator, Project 3- "Selectin Binding Sites on Leukocytes and Inflamed Venules", NIH, PO1AI33189 (Oligosaccharides as Anti-inflammatory Agents; PA Ward, Program Director), 20% effort, $347,950; 1 September 1992- 31 August 1996.

C. Co-Principal Investigator, (J. Curtis, Principal Investigator), Project 4, "Mechanisms of Lymphocyte Recruitment to the Lungs", NIH, P50HL46487 (SCOR in Pulmonary Fibrosis; G. Toews, M.D., Program Director), 15% effort, $650,000; 1 December 1991 - 31 November 1996.

D. Principal Investigator, Project 5, "Mononuclear Leukocyte Adhesion and Recruitment in Chronic Inflammatory Disease", NIH, P01, HL31963 (Inflammatory Cells and Lung Injury; PA Ward, M.D., Program Director), 20% effort, $500,000; 1 February 1994 - 29 January 1999.

PENDING SUPPORT:

A. Principal Investigator, Project III, "Structure of Selectin-Ligands Synthesized by Human T-Lymphoblasts", NIH, PO1AI33189 (Competitive renewal of Oligosaccharides as Anti-inflammatory Agents; PA Ward, Program Director), 15% effort, submitted 7/1/95: This project will determine whether mammalian cells which synthesize high avidity selectin ligands on their surface can be used to generate soluble recombinant glycoprotein inhibitors of the selectins. In addition, the activities of monomeric and multimeric selectin inhibitors will be compared using a novel in vitro assay which allows one to measure the impact of inhibitors on leukocyte-endothelial interactions at physiologic levels of linear shear-stress.

B. Principal Investigator, "Structure-Function Studies of Selectin Ligands on T-lymphoblasts", 25% effort, submitted 10/1/95: Studies in this area have been hampered by the difficulty of collecting sufficient starting material for structural studies on authentic ligands. We have overcome this obstacle through the development of a growth protocol which allows the production of $>10^{11}$ human T-cells expressing high levels of functional ligands for the selectins. Viable lymphocytes from any source can be used with a 100-1000 fold increase in cell number achieved over two weeks. These ligands

are indistinguishable from those on circulating T-cells. This proposal seeks funding for structural analysis of the selectin ligands on human T-cells.

C. Principal Investigator, "T-Cell Trafficking in Adoptive Cellular Immunotherapy", NIH, RO1CA73059, 30% effort, submitted 2/1/96: This project builds on the discovery that the protocols used to expand vaccine-derived and tumor-infiltrating lymphocytes prior to infusion into patients dramatically alter the prevalence and function of adhesion receptors used by the infused cells to gain access into tissues. Current protocols generate cells which require expression of the selectin family for optimal adhesion at physiologic levels of shear. However, studies in animal models show virtually no induction of these molecules in the vascular beds of experimental tumors. If this is true in human neoplasms then a "mismatch" between the adhesion molecules on the infused cells and the adhesion molecules expressed on the vasculature in the tumor bed may account for the poor recruitment of cells into tumors during adoptive immunotherapy. This proposal will define the adhesion molecules used by circulating cells to enter tumor-bearing organs and determine whether upregulation of selectin expression on the vasculature in the tumor bed will augment the therapeutic effect of adoptively transferred cells.

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 the 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.

B. Co-Director, Hematology Sequence in Component II of Medical School Curriculum - design and implement laboratory exercises, oversee lecture development for leukocyte disorders, co-edit/author exams and provide quality control for sequence.

C. Co-Director, General Pathology Course for Dental and Graduate Students (580/630) - re-design laboratory exercises, compose new lecture series on leukocyte physiology and autoimmune diseases, co-edit/author exams and provide quality control for sequence.

D. Cancer Center Executive Committee - departmental representative.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL ACTIVITIES:

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Carr, K., Lowry. T., Li, L.L., Tsai, C., Stoolman, L. and Fox, D.A.: Expression of CD60 on multiple cell lineages in inflammatory synovitis. Lab. Invest. 73:332-338. 1995.
2. Varani, J., Dame, M.K., Diaz, M. and Stoolman, L.M.: Deferoxamine interferes with adhesive functions of activated human neutrophils. Shock. 5:395-401, 1996.
3. Knibbs, R.N., Craig, R.A., Natsuka, S., Chang, A., Cameron, M., Lowe, J.B. and Stoolman, L.M.: The fucosyltransferase FucT-VII regulates E-selectin ligand synthesis in human T-Cells. J. Cell Biol. 133:911-920, 1996

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, 1996.
2. Stoolman, L.M., Craig, R.A., Wolber, F., Abbassi, O., Smith, C.W., McIntire, L.V. and Ballew, J.R.: α4-integrin mediated T-cell tethering to endothelium: activation requirements and efficiency relative to the selectins, 1996.
3. Stoolman, L.M., Craig, R., Cameron, M., Reddy, V., Liu, J., Ballew, J. and Chang, A.E.:. *Ex vivo* expansion of lymphocytes for adoptive-immunotherapy alters the prevalence and function of adhesion receptors involved in T-cell recruitment, 1996.
4. Wolber, F., Curtis, J., Kim, S. and Stoolman, L.M.: Lymphocyte recruitment and the kinetics of adhesion receptor expression in murine hypersensitivity pneumonitis, 1996.
5. Wolber, F., Stoolman, L.M and Curtis, J.: The effects of α4-integrin and L-selectin blockade on leukocyte recruitment in murine hypersensitivity pneumonitis,, 1996.
6. Wolber, F., Curtis, J., Maly, P., Thall, A., Lowe, J.B. and Stoolman, L.M.: Selectin and α4-integrin mediated T-cell recruitment in murine hypersensitivity pneumonitis, 1996.
7. Snapp, K.R., Wagers, A.J., Craig, R., Stoolman, L.M. and Kansas, G.S.: Leukocyte P-selectin glycoprotein ligand 1 (PSGL-1) is essential for adhesion to P-selectin but not E-selectin, 1996.
8. Yung, R., Williams, R., Johnson, K., Stoolman, L.M., Chang, S. and Richardson, B.: Mechanisms of drug-induced Lupus. III. Gender-specific differences in splenic T-cell homing explain increased disease severity in female mice, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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 undergraduate and graduate students and for postdoctoral investigators
   1. Maria-Thereza S. Piccolo, M.D.
   2. Elisabeth Schmid, M.D.
   3. Aresh Monem, Pharm. D.
   4. Dorothy Pao, Medical Student.
   5. Serge Verbrugge, Medical Student.
   6. Minh Nguyen, Undergraduate Student.

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 ocular ischemia-reperfusion injury.

C. Functional responses of retinal pigment epithelial (RPE) cells in vitro.

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. Member NIH Study Section Surgery, Anesthesiology and Trauma, 1996.
B. Member Honors and Awards Committee of the American Shock Society, 1995-present.

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. American Journal of Physiology.
    3. Blood.
    4. Circulation.
    5. Free Radical Biology and Medicine.
    6. Journal of Biological Chemistry.
    7. Journal of Leukocyte Biology.
    8. Shock.

INVITED LECTURES/SEMINARS:

1. Speaker at a Seminar on Experimental Studies in Thermal Injury I, University of Michigan Hospitals Burn Unit, Ann Arbor, Michigan, February 6, 1996.
2. Speaker at a Seminar on Experimental Studies in Thermal Injury II, University of Michigan Hospitals Burn Unit, Ann Arbor, Michigan, March 12, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Liu, Z., Giudice, G.J., Swartz, S.J., Fairley, J.A., Till, G.O., Troy, J.L. and Diaz, L.A.: The role of complement in experimental bullous pemphigoid. J. Clin. Invest. 95:1539-44, 1995.
2. 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. In Press, 1996.
3. Lai, J.C., Johnson, M.W., Martonyi, C.L. and 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, 1996
4. Colton, D.M., Hirschl, R.B., Till, G.O., Johnson, K.J., Patel, S., Dean, S.B. and Bartlett, R.H.: Partial liquid ventilation (PLV) decreases neutrophil infiltration in the setting of acute lung injury. Amer. J. Resp. Crit. Care Med. In Press, 1996.
5. Colton, D.M., Till, G.O., Johnson, K.J., Dean, B.S. and Hirschl, R.B.: Neutrophil accumulation is reduced during partial liquid ventilation. Crit. Care.Med. In Press, 1996.
6. 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, 1996.
7. Winn, W.C., Davis, G.S., Durda, J.P. and Till, G.O.: The effect of neutropenia on experimental Legionella pneumonia. Infec. Immun. In Press, 1996.
8. Seekamp, A., Schmal, H., Friedl, H.P., Hultquist, D.E., Ward, P.A. and Till, G.O.: Protection by vitamin B2 against oxidant-mediated acute lung injury. Free Radic. Biol. Med. In Press, 1996.

BOOKS AND CHAPTERS IN BOOKS:

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

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

1. Mulligan, M.S., Piccolo T., Wang, Y., Till, G.O. and Ward, P.A.: Roles of TNF, IL-1 and IL-8 in lung and dermal vascular injury following thermal trauma of skin. Shock 5:19A, 1996.
2. Schmid, E., Friedl, H.P., Warner, R.L., Ward, P.A. and Till, G.O.: C5a is required for the development of acute lung injury secondary to skin burns. Shock 5:23A, 1996.
3. Taheri, P.A., Ferrara, J.J., Wang, S.C., Cardellio, A., Remick, D., Till, G. and Rodriguez, J.L.: Loco-regional cytokine production following thermal injury. Shock 5:24A, 1996.
4. Czermak, B., Schmal, H., Shanley, T.P., Friedl, H.P., Till, G.O. and Ward, P.A.: Northern blot and quantitative PCR analysis of IgG immune complex -mediated lung injury. Shock 5:151A, 1996.

5. Younger, J., Tagi, A., Till, G. and Hirschl, R.: Peep reduces ventilator-induced lung injury in rats. Shock 5:174A, 1996.
6. Warren, J.S., Kilgore, K.S., Powers, K., Schmid, E., Friedl, H.P. and Till. G.O.: Complement plays a role in glucan-induced pulmonary granuloma formation in the rat. FASEB J. 10:A1007, 1996.
7. Schmid, E., Crouch, L.D., Friedl, H.P., Bless, N.M., Till, G.O. and Ward, P.A.: Complement levels in acute inflammatory lung injury. FASEB J. 10:A1008, 1996.
8. Younger, J.G., Taqi, A., Till, G.O., Stern, S.A. and Hirschl, R.B.: Pulmonary neutrophil infiltration is decreased during partial liquid ventilation in a model of hemorrhagic shock. Proceedings Acad.Emerg.Med. In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Member, Dissertation Committee of Douglas F. Gibbs (Pathology).
B. Member, Dissertation Committee of Mike Model (Biophysics).
C. Member, Dissertation Committee of Thomas Cheng (Neurosciences).
D. Mentor for students who worked in my laboratory over the past year including one visiting scientist, two post-doctoral fellows, one pathology graduate student, one medical student, and five undergraduate students.
E. Member, University of Michigan Minority Student Research Opportunities Program.
F. Member, University of Michigan Student Research Opportunities Program.

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, 7-1-91-6/30/2001.
E. Principal Investigator, "Perfluorocarbon and Acute Lung Injury," Alliance Pharmaceutical Co., 7-01-94-6/30/97.
F. Co-Investigator, "Erb-b-2 Expression and Resistance to TNF Killing," NIH CA 64803, 9/01/94-8/30/98.
G. Co-Investigator, "Protease-Oxidant Interactions in Lung Inflammation," NIH HL42607, 7/1/94-6/30/98.

PROJECTS UNDER STUDY;

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

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. Pittsburgh Biotechnology Conference on Opportunities in Tissue Engineering, Pittsburgh, Pennsylvania, September 19, 1995.
2. Cell Culture Engineering V. San Diego, California, January 28-February 2, 1996.
3. Department of Laboratory Medicine, M.D. Anderson Cancer Center, Houston, Texas, February 15, 1996.
4. Molecular Design International, Memphis, Tennessee, March 7, 1996.
5. Society for Investigative Dermatology, Washington D.C., May 1-4, 1996.
6. Johnson & Johnson Retinoid Symposium, Short Hills, New Jersey, May 23, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS.

1. Varani, J., Fligiel, S.E.G., Inman, D.R., Beals, T.F. and Hillegas, W.J.: Modulation of adhesive properties of DEAE-dextran with laminin. J. Biomed. Materials Res. 29:993-997, 1995.
2. McKeever, P.E., Varani, J., Papodopoulous, S.M., Wang, M. and McCoy, J.P.P.: Products of cells from gliomas: IX. Evidence that two fundamentally different mechanisms alter extracellular matrix expression by gliomas. J. Neuro-Oncol. 24:267-280, 1995.
3. Varani, J., Burmeister, B., Perone, P., Bleavins, M. and Johnson, K.J.: All-trans retinoic acid inhibits fluctuations in intracellular Ca^{2+} resulting from changes in extracellular Ca^{2+}. Am J. Pathol. 147:718-729, 1995.
4. 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, In Press.
5. 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.
6. 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, In Press.
7. 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.
8. Varani, J., Dame, M.K., Taylor, C.G., Sarma, V., Merino, R., Kunkel, R.G., Nunez, G. and Dixit, V.M.: Age-dependent injury in human umbilical vein endothelial cells: Relationship to apoptosis and correlation with a lack of A20 expression. Lab. Invest. 73:851-858, 1995.
9. Numa, F., Hirabayashi, K., Tsunaga, N., Kato, H., O'Rourke, K., Shao, H., Stechmann-Lebakken, C., Varani, J., Rapraeger, A. and Dixit, V.M.: Elevated levels of syndecan-1 expression confer potent serum-dependent growth in human 293T cells. Cancer Res. 55:4676-4680, 1995.

10. 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.
11. Varani, J., Josephs, S. and Hillegas, W,J.: Human diploid fibroblast growth on polystyrene microcarriers in aggregates. Cytotechnology, In Press.
12. Varani, J., Dame, M.K., Diaz, M. and Stoolman, L.: Deferoxamine interferes with adhesive functions of activated human neutrophils. Shock 5:395-401, 1996.
13. 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. Shock, In Press.
14. 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, In Press.
15. 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, In Press.
16. 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., 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, eds. Mosbey, St. Louis, Missouri, In Press.
3. Varani, J.: Human skin in organ culture: A Model for the Study of Normal and Pathological Responses of Skin, in, Histology and Histopathology, In Press.

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

1. Varani, J., Josephs, S. and Hillegas, W.J.: High cell density growth on microcarrier aggregates. Cytotechnology 17: MO14, 1995.
2. Zeigler, M.E., Krause, S., Dutcheshen, N.T., Perone, P., Gibbs, D.F,, Karmiol, S. and Varani, J.: Growth factor-induced epidermal invasion of the dermis in organ culture. AACR Proceed. 1996.
3. Varani, J., Kang, S., Datta, S.C. and Voorhees, J.J.: Natural aging reduces human skin proliferative capacity, reduces fibronectin production, increases matrix metalloproteinase activity but allows a normal response to retinoic acid. J. Invest. Dermatol. 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Beatrice Beck-Schimmer, M.D., Postdoctoral Fellow.
      b. Nicolas Bless, M.D., Postdoctoral Fellow.
      c. Larry Crouch, Ph.D., Postdoctoral Fellow.
      d. Boris Szermak, M.D., Postdoctoral Fellow.
      e. Jami Foreback, Pathology Graduate Program Student (MSTP student) (mentor).
      f. Teletha Gipson, Ph.D., Postdoctoral Fellow.
      g. Michael S. Mulligan, M.D., Postdoctoral fellow.
      h. Elizabeth Schmid, M.D., Postdoctoral Fellow.
      i. Ralph C. Schimmer, M.D., Postdoctoral Fellow.
      j. Hagen Schmal, M.D., Postdoctoral Fellow.
      k. Thomas Shanley, M.D.. Postdoctoral Fellow.
      l. David Tung, Ph.D., Postdoctoral Fellow.
      m. Roscoe Warner, Ph.D., Postdoctoral Fellow.
      n. UROP Undergraduate Students:
         - Hillary Cohen, Senior.
         - Karen Rosner, Sophomore.
         - Richard Carter, Freshman.
      o. Morgan Althoen, Medical Student.
   2. Indirect 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, March 29, 1995, three hours.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Lung Immunopathology" (Training Grant), NHLBI-NIH-HL-07517 (5%), $235,013/year ($2,693,183/ten years), June 1, 1996 -May 31, 1997. (Renewed for another five years, June 1, 1996 to May 31, 2001.)

B. Principal Investigator, "Lung Injury by Oxygen Metabolites", NIGMS-NIH-5-R37-GM-29507 (20%), $262,568/year ($1,271,378/five years), July 1, 1996 - June 30, 1997.
C. Principal Investigator, "Inflammatory Cells and Lung Injury", NHLBI-HL-31963 (29%), Section I - $189,794, Core A -$38,431/year ($1,010,734/five years), March 1, 1989-February 28, 1997.
D. Co-Investigator, "Mechanisms of Glomerular and Tubular Injury" (R. Wiggins, Principal Investigator), NIADDK-NIH-DK-39255 (5%), Section 1 - $48,000/year, August 1, 1995 - July 31, 1996.
E. Principal Investigator, "Oligosaccharides as Inflammatory Agents" NIH-AI33189-01 (Core - 10%; Administrative Core - 5%), $449,661/year ($2,192,155/four years), September 1, 1992-June 30, 1996. No Cost Extension.

PENDING:

A. Co-Investigator, "The Role of Cytokines and Adhesion Molecules in Thermal Injury", (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. Dean's Cabinet, 1993--.
B. Advisory Committee for the Howard Hughes Medical Institute, 1984--.
C. Clinical Council, 1993--.
D. Conflict of Interest Committee, 1993--.
E. Dean's Advisory Council, 1985--.
F. Geriatric Center Executive Committee.
G. Howard Hughes Medical Institute Dean's Advisory Committee.
H. Internal Medicine Advisory Committee for the University of Michigan George M. O'Brien Renal and Urologic Center, 1991--.
I. Michigan Eye Bank Research Review Committee, 1980--.
J. Presidential Initiatives Fund, The University of Michigan, March, 1987--.
K. Undergraduate Research Opportunity Program, University of Michigan, 1992--.
L. University of Michigan Cancer Center Executive Committee.

UNIVERSITY OF MICHIGAN:

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

REGIONAL AND NATIONAL:

A. American Association for Advancement of Science.
B. American Association of Immunologists.
C. American Association of Pathologists.
    1. Nominating Committee, 1985-present.
    2. Executive Committee, Intersociety Pathology Council and Universities Associated for Research and Education in Pathology, Inc.

3. Representative to the Universities Associated for Research and Education in Pathology, 1988-89.
4. Steering Committee for the Federal Demonstration Project, 1990-1992.
5. Future Directions Committee, 1989--.

D. American Board of Pathology, effective January 1, 1988:
1. President, 1996
2. Vice-President, 1995
3. Trustee, 1980--.
4. Immunopathology Test Committee, 1980-85, 1988--. Vice-Chairman.
5. Anatomic Pathology Examination Committee, 1988--.
6. By-Laws Committee, 1988--.
7. Examination Evaluation Committee, 1988--.
8. Professional Qualification/Competence Committee, 1988--.
9. ABP/ABPRF Research Committee, 1989--.
10. Residency Review Committee for Pathology.
11. Building Committee, 1992--.
12. Planning and Development Committee, 1992--.
13. Test Committee for Molecular Pathology, 1993--.

E. American Federation for Clinical Research.
F. American Heart Association, Cardiopulmonary Division.
G. American Lung Association.
H. American Society for Clinical Investigation.
I. American Pathology Foundation.
J. American Thoracic Society.
K. Association of American Physicians.
L. Association of Pathology Chairmen.
M. Center for Alternatives to Animal Testing, Johns Hopkins University.
N. A. James French Society of Pathologists, 1988--.
O. Health Policy Agenda for the Amerian People, Advisory Committee.
P. Institute of Medicine, July 1, 1990.
Q. United States and Canadian Academy of Pathology, Inc.
1. Council Member, April 1, 1986-1989.
2. Member, Finance Committee, April 1, 1986-1990.
3. Vice-President, 1990.
4. President-Elect, 1991.
5. President, 1992.
6. Past-President, 1993.

R. Michigan Society of Pathologists.
S. Michigan Thoracic Society, 1988--.
T. National Research Council
1. Institute of Laboratory Animal Resources.
2. Committee on Human Rights, Correspondent.

U. The Oxygen Society, 1988--.
V. Phi Rho Sigma, President, The University of Michigan Chapter, September, 1988.
W. Society of Medical Consultants to the Armed Forces:
1. President, 1988.

X. Universities Associated for Research and Education in Pathology, Inc., Board of Directors.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. American Journal of Pathology, Editorial Board, 1982--.
B. American Review of Respiratory Diseases, Consulting Editor, 1977--.
C. Biological Signals, Consulting Editor.
D. Clinical Immunology and Immunopathology, Consulting Editor, 1977--.
E. CRC Critical Reviews in Free Radical Research, Advisory Board, 1986--.
F. CRC Critical Reviews in Toxicology, Advisory Board, 1986--.
G. Journal of Critical Care, Editorial Board.
H. Toxicologic Pathology, Editorial Board, 1988--.

HONORS AND AWARDS

A. Rous-Whipple Award, American Society for Investigative Pathology, Hilton Hotel, New Orleans, Louisiana, June 5, 1996.

PATENTS:

A. Sulfatides as Anti-Inflammatory Compounds, U.S. Patent No. 5,486,36, UM File #914, January 23, 1996.

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "The Selectins in Animal Models of Acute Inflammation", in Symposium on Glycoconjugates and Contract Structures of the Cell Surface in Bonn, Germany, July 11-16, 1995.
2. Invited Lecturer, "Nitric Oxide and Inflammation", Aspen Allergy Conference, Given Institute of Pathobiology, Aspen, Colorado, August 3-5, 1995.
3. Invited Lecturer, "Molecular Regulation of Lung Inflammation", First International Ringberg Symposium on "Molecular Mechanisms of Inflammation", Ringberg Castle, Tegernsee, Germany, September 5-9, 1995.
4. Invited Lecturer, "Cytokine Regulation of Lung Inflammation", Alliance Pharmaceutical Corporation, San Diego, California, October 13, 1995.
5. Invited Lecturer, "Cytokines, Adhesion Molecules and Pulmonary Injury (Overview Lecture)", the Charles G. Cochrane Festschrift and Immunopathology Symposium, Sheraton Grande Torrey Pines, La Jolla, California, October 14, 1995.
6. Invited Lecturer and Chairperson, "Chemokines in Lung Inflammatory Reactions", IBC Conference on Chemotactic Cytokines: Targets for Novel Therapeutic Development, Philadelphia, Pennsylvania, October 25-26, 1995.
7. Invited Lecturer, "Cytokines in Infection", Bayer Pharmaceutical Conference on the Interaction Between Defences and Bacteria in the Pathogenesis of Infection - Time for a Reappraisal, Hanbury Manor, Ware, Hertfordshire, United Kingdom, November 13-16, 1995.
8. Visiting Professor, "Role of Nitric Oxide and Role of Lung Injury", Searle Research and Development, Monsanto Company, St. Louis, Missouri, December 1, 1995.
9. Invited Founder's Day Speaker, "Regulation of Lung Inflammatory Responses", Tanabe Research Laboratories, USA, Inc., San Diego, California, December 5-6, 1995.
10. Invited Lecturer, "Regulation of Inflammatory Responses", Parke-Davis Pharmaceutical Research Division Immunopathology Seminar, Ann Arbor, Michigan, December 22, 1995.

11. Invited Lecturer, "Cytokines in Lung Inflammatory Reactions", Second Annual "Anti-Inflammatory Drug Discovery Summit", sponsored by Strategic Research Institute, New Brunswick, New Jersey, February 12-13, 1996.
12. Invited Lecturer, "Regulation of Lung Inflammation", Department of Immunology/Microbiology, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illlinois, February 19, 1996.
13. Invited Speaker, "Cytokines and Lung Inflammation", Bernie B. Carter Center for Immunology Research Spring 1996 Seminar Series, University of Virginia Health Sciences Center, Charlottesville, Virginia, April 1, 1996.
14. Invited Lecturer, "Cytokines and Adhesion Molecules in the Inflammatory Response", William Harvey Research Conference on New Targets in Inflammation: Inhibitors of COX-2 or Adhesion Molecules, Sheraton New Orleans Hotel, New Orleans, Louisiana, April 15-16, 1996.
15. Invited Lecturer, "Activation and Regulation of Lung Inflammation", Montreal GeneralHospital Research Institute, Montreal, Quebec, Canada, April 25, 1996.
16. Invited Lecturer, "How the Inflammatory System Works", Biological Sciences Lecture Series, University of Kansas, Kansas City, Kansas, May 8, 1996.
17. Invited Lecturer, "Cytokine Regulation of Pulmonary Inflammation", American Thoracic Society Symposium, "The Molecular Basis of Neutrophil and Macrophage Activation", New Orleans, Louisiana, May 12, 1996.
18. Invited Lecturer, "Cytokine and Complement Mediated Regulation of Inflammation", Gordon Research Conference on Vascular Cell Biology, Proctor Academy, Andover, New Hampshire, June 26-27, 1996.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Eppinger, M.J., Jones, M.L., Deeb, M., Bolling, S.F. and Ward, P.A.: Pattern of injury and the role of neutrophils in reperfusion injury in rat lung. J. Surg. Res. 58:713-718, 1995.
2. Eppinger, M.J., Ward, P.A., Jones, M.L., Bolling, S.F. and Deeb, G.M.: Disparate effects of nitric oxide on lung ischemia-reperfusion injury. Amer. Thorac. Surg. 60:1169-1175, 1995.
3. Foreman, K.E., Glovsky, M.M., Warner, R.L., Horvath, S.J. and Ward, P.A.: Does complement activation control "tissue trafficking" by C3a and C5a anaphylotoxin generation? Int. Arch. Allergy Immunol. 107:394-395, 1995.
4. Kilgore, K.S., Shen, J.P., Miller, B.F., Ward, P.A. and Warren, J.S.: Enhancement by the complement membrane attack complex of tumor necrosis factor-α induced endothelial cell expression of E-selectin and ICAM-1. J. Immunol. 155:1434-1441, 1995.
5. Kim, J.S., Gautam, S.C., Chopp, M., Zaloga, C., Jones, M.L., Ward, P.A. and Welch, K.M.A.: Expression of monocyte chemoattractant protein-1 and macrophage inflammatory protein-1 after focal cerebral ischemia in the rat. J. Neuroimmunol. 56:127-134, 1995.
6. Mulligan, M.S., Miyasaka, M., Suzuki, Y., Kawashima, H., Lizuka, M., Suzuki, T., Hasegawa, A., Kiso, M., Warner, R.L. and Ward, P.A.: Anti-inflammatory effects of sulfatides in selectin-dependent acute lung injury. Inter. Immunol. 7:1107-1113, 1995.
7. Mulligan, M.S., Schmid, E., Beck-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., 98:503-512, 1996.
8. Mulligan, M.S., Vaporciyan, A.A., Warner, R.L., Jones, M.L., Foreman, K.E., Miyasaka, M., Todd, R.F., III and Ward, P.A.: Compartmentalized roles for leukocytic adhesion molecules in lung inflammatory injury. J. Immunol. 154:1350-1363, 1996.
9. Shanley, T.P., Jones, M.L., Schmal, H., Friedl, H.P. and Ward, P.A.: Role of macrophage inflammatory protein-1α (MIP-1α) in acute lung injury in rats. J. Immunol. 154:4793-4802, 1995.

10. Shanley, T.P., Schmal, H., Friedl, H.P., Jones, M.L. and Ward, P.A.: Regulatory effects of intrinsic IL-10 in IgG immune complex-induced lung injury. J. Immunol. 154:3454-3460, 1995
11. Shanley, T.P., Schmal, H., Friedl, H.P., Jones, M.L. and Ward, P.A.: Role of macrophage inflammatory protein-1α (MIP-1α) in acute lung injury in rats. J. Immunol. 154:4793-4802, 1995.
12. Shanley, T.P., Warner, R.L. and Ward, P.A.: The role of cytokines and adhesion molecules in the development of inflammatory injury. Molecular Med. Today 1:40-45, 1995.
13. Vaporciyan, A.A., Mulligan, M.S., Warren, J.S., Barton, P.A., Miyasaka, M. and Ward, P.A.: Up-regulation of lung vascular ICAM-1 in rats is complement dependent. J. Immunol. 155;1442-1449, 1995.
14. Ward, P.A.: Adhesion molecule knockouts: One step forward and one step backward. (Editorial) J. Clin. Invest. 95:1425, 1995.
15. Warner, R.L., Paine, R., III, Christensen, P.J., Marletta, M.A., Richards, M.K., Wilcoxen S.E. and Ward, P.A.: Lung sources and cytokine requirements for *in vivo* expression of inducible nitric oxide synthase. Amer. J. Resp. Cell and Molec. Biol. 12:649-661, 1995.
16. Crockett-Torabi, E. and Ward, P.A.: The role of leukocytes in tissue injury. Europ. J. Anaesthesiol. 13:235-246, 1996.
17. Kubo, H., Morgenstern, D., Quinlan, W.M., Ward, P.A., Dinauer, M.C. and Doerschuk, C.M.: Preservation of complement-induced lung injury in mice with deficiency of NADPH oxidase. J. Clin. Invest. 92;2680-2684, 1996.
18. Foreman, K.E., Glovsky, M.M., Warner, R.L., Horvath, S.J. and Ward, P.A.: Comparative effect of C3a and C5a on adhesion molecule expression on neutrophils and endothelial cells. Inflam. 20:1-9, 1996.
19. Mulligan, M.S., Miyasaka, M. and Ward, P.A.: Protective effects of combined adhesion molecule blockade in models of acute lung injury. Proc. Assoc. Amer. Physicians 108:198-208, 1996.
20. Schmal, H., Shanley, T.P., Jones, M.L., Friedl, H.P. and Ward, P.A.: Role for macrophage inflammatory protein-2 in lipopolysaccharaide-induced lung injury in rats. J. Immunol. 156:1963-1972, 1996.
21. Shanley, T.P., Jones, M.L., Schmal, H., Friedl, H.P. and Ward, P.A.: Regulatory effects of intrinsic interleukin-10 in IgG immune complex-induced lung injury. J. Immunol. 154:3454-3460, 1996.
22. Shanley, T.P., Peters, J.L., Jones, M.L., Chensue, S.W., Kunkel, S.L. and Ward, P.A.: Regulatory effects of endogenous interleukin-1 receptor antagonist protein in IgG immune complex-induced lung injury. J. Clin. Invest. 97:963-970, 1996.
23. Shanley, T.P., Schrier, D., Kapur, V., Kehoe, M., Musser, J.M. and Ward, P.A.: Streptococcal cysteine protease augments lung injury induced by products of *Group A Streptococci*. Infection and Immunity 64:870-877, 1996.
24. Mulligan, M.S., Johnson, K.J., Smith, C.W., Todd, R.F., Miyasaka, M., Tamatani, T., Issekutz, T.B., Anderson, D.C. and Ward, P.A.: Role of β2 integrins, VLA-4 and ICAM-1 in nephrotoxic nephritis. J. Clin. Invest., In Press.
25. Mulligan, M.S., Polley, M.J., Paulsen, J.C. and Ward, P.A.: Evidence for a role of P-selectin in lung injury developing after systemic complement activation. J. Biol. Chem., In Press.
26. Mulligan, M.S., Sulavik, C., Ward, P.A., Kunkel, R.G. and Johnson, K.J.: The delayed phase of anti-GBM nephritis in deferoxamine sensitive but catalase-insensitive. Inflammation, In Press.
27. Murphy, H.S., Seiler, A. and Ward, P.A.: Relationship of protein kinase C activity to 0_2^- production by rat pulmonary artery endothelial cells. Amer. J. Physiol., In Press.
28. Rao, N.A., Sevanian, A., Faure, J.-P., Kozak, Y., Ward, P.A., Till, G.O. and Marak, G.E.: The participation of reactive oxygen metabolites in the pathogenesis of experimental allergic uveitis. Invest. Ophthalmol. Vis. Sci., In Press.
29. Seekamp, A., Hultquist, D.E., Xu, F., Ward, P.A. and Till, G.O.: Protection by vitamin B2 against oxidant-mediated acute lung injury. Free Rad. Biol. Med., In Press.

30. Seekamp, A., Mulligan, M.S., Till, G.O. and Ward, P.A.: Role of oxygen radicals, nitric oxide and complement in ischemia reperfusion injury. Submitted to the Americal Journal of Pathology.
31. Seekamp, A. and Ward, P.A.: Ischemia - reperfusion injury. Agents in Actions (Supplement), In Press.
32. Till, G.O., Friedl, H.P. and Ward, P.A.: Role for histamine and xanthine oxidase in complement- and oxidant-mediated acute lung injury. Free Rad. Biol. Med., In Press.
33. Till, G.O., Lee, S., Mulligan, M.S., Wolter, J.R., Smith, C.W., Ward, P.A. and Marak, G.E.: Adhesion molecules in experimental phacoanaphylactic endophthalmitis. Invest. Ophthalmol. Vis. Sci., In Press.
34. Till, G.O. and Ward, P.A.: Immunologic and phagocytic cell defects in thermally injured patients. J. Crit. Care Med., In Press.
35. Vaporciyan, A.A. and Ward, P.A.: Induction by C5a of P-selectin dependent endothelial adhesiveness for neutrophils. J. Immunol., In Press.
36. Varani, J., Ginsburg, I., Johnson, K.J., Gibbs, D.F., Weinberg, J.M. and Ward, P.A.: Amino acids and metal ions protect endothelial cells from lethal injury. FASEB J., In Press.
37. Ward, P.A.: The wound environment - Local and systemic perturbations: Inflammation and the burn wound. J. Burn Care & Rehab. In Press.
38. Ward, P.A.: Free radicals and lung injury: Implications for therapy. Proceedings of the International Conference on Oxygen Free Radicals in Health and Disease, In Press.
39. Ward, P.A.: Oxidant damage. Submitted to the Task Force on Allergy and Immunology, National Institutes of Health.
40. Ward, P.A. and Johnson, K.J.: Lung inflammatory mechanisms. J. Human Path., In Press.
41. Ward, P.A., Johnson, K.J. and Till, G.O.: Mechanisms of lung injury. Prax. Klin. Pneumonol., In Press.

BOOKS/CHAPTERS IN BOOKS:

1. Kunkel, S.L., Driscoll, K.E., Ward, P.A., Nickoloff, B. and Strieter, R.M.: Immunopathology of environmental and occupational disease, Chapter 24, in, Craighead, J.E. (ed), The Pathology of Human Environmental and Occupational Disease, Mosby Yearbook, St. Louis, pp. 385-395, 1995.
2. Ward, P.A.: Interventional approaches in vivo for selectin-dependent inflammatory injury, in, Seiss, W., Lorenz, R. and Weber, P.C. (eds), Topics in Molecular Medicine, Volume 1, Adhesion Molecules and Cell Signaling: Biology and Clinical Applications, Raven Press, Ltd., New York,, pp. 243-249, 1995.
3. Ward, P.A.: Adhesion molecules and cytokines in experimental inflammatory disease, Chapter 14, in, Horton, Michael A. (ed), Adhesion Receptors as Therapeutic Agents, CRC Press, Boca Raton, Florida, pp. 273-279, 1995.
4. Ward, P.A.: Approaches to *in vivo* blocking of adhesion molecules, in, Schlossman, S.F., Boumsell, L., Gilks, W., Harlan, J.M., et al (eds), Leukocyte Typing V: White Cell Differentiation, Proceedings of the Fifth International Workshop and Conference, Volume Two, Oxford University Press, Oxford, pp. 1504-1507, 1995.
5. Ward, P.A. and Mulligan, M.S.: Role of adherence molecules in lung inflammation, Chapter 16, in, Granger, D.N. and Schmid-Schonbein, G.W. (eds), Physiology and Pathophysiology of Leukocyte Adhesion, Oxford University Press, New York, New York, pp. 313-322, 1995.
6. Chensue, S.W. and Ward, P.A.: Inflammation, Chapter 18, Volume 1, in Damjanov, I. and Linder, J. (eds), Anderson's Pathology, 10th Editio, Mosby Year Book, Philadelphia, Pennsylvania, pp. 387-415, 1996.
7. Lukacs, N.W. and Ward, P.A.: Inflammatory mediators, cytokines, and adhesion molecules in pulmonary inflammation and injury, Chapter 7, in, Dixon, F.J. (ed), Advances in Immunology (Vol. 62), Academic Press, Orlando, Florida, pp. 257-304, 1996.

8. Ward, P.A.: Immune complex-induced lung inflammatory injury in rats, in, Peltz, G. (ed), Leukocyte Recruitment in Inflammatory Disease, R.G. Landes Co., Austin, Texas, pp. 155-164, 1996.
9. Ward, P.A., Mulligan, M.S., Vaporciyan, A.A. and Eppinger, M.J.: Adhesion molecules in experimental lung inflammatory injury, in, Ward, P.A. and Fantone, J.C. (eds),.Adhesion Molecules and the Lung (Lung Biology in Health and Disease Series/89), Marcel Dekker, Inc., New York, New York, pp.159-176, 1996.
10. Ward, P.A., Seekamp, A. and Mulligan, M.S.: Acute inflammatory lung injury: Mechanisms and interventions, in, Catravas, J.D., Callow, A.D. and Ryan, U.S. (eds), Vascular Endothelium, Responses to Injury (Series A: Life Sciences Vol. 281), Plenum Press, New York, New York, pp. 131-137, 1996.
11. Fantone, J.C. and Ward, P.A.: Mechanisms of inflammation, in, Cohen, A.S. (ed), Rheumatology and Immunology, Grune and Stratton, In Press.
12. Johnson, K.J., Chensue, S.W., Kunkel, S.L. and Ward, P.A.: Immunopathology, in, Rubin, E. and Farber, J.L. (eds), Textbook of Pathology, Second Edition, J.B. Lippincott Inc., New York, New York, In Press.
13. Kunkel, S.L. and Ward, P.A.: The complement system, in, Bellanti, J.A. (ed), Immunology, 3rd Ed, In Press.
14. 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, Florida, In Press.
15. Maderazo, E.G. and Ward, P.A.: Leukocyte chemotaxis, in, Manual of Clinical Laboratory Immunology, 3rd Ed., American Society for Microbiology, Washington, D.C., In Press.
16. Maderazo, E.G., Woronick, C.L. and Ward, P.A.: Inhibitors of chemotaxis, in, Methods in Enzymology, Academic Press, Orlando, Florida, In Press.
17. Morganroth, M.L., Till, G.O. and Ward, P.A.: Pathophysiology of ischemia-reperfusion lung injury, in, Das, D.K. (ed), Pathophysiology of reperfusion Injury, CRC Press, Inc., In Press.
18. Mulligan, M.S. and Ward, P.A.: Inflammatory mechanisms of cellular and tissue damage, in, Cooper, G., Dudley, H.A.F., Gann, D.S., Little, R.A. and Maynard, R.L. (eds), Mechanisms of Cellular Damage for the Volume on Scientific Foundations of Trauma, Heinemann Medical Books, London, England, In Press.
19. Mulligan, M.S. and Ward, P.A.: Molecular Mechanisms in Acute Lung Injury", in, August, J.T., Anders, M.W. and Murad, F. (eds), Advances in Pharmacology, Volume 24, Academic Press, Orlando, Florida, In Press.
20. Mulligan, M.S. and Ward, P.A.: Mechanisms of cellular damage, Chapter 37, in, Gann, D.S. (ed), Scientific Foundations of Trauma, Butterworth Heinemann, Boston, Massachusetts, In Press.
21. Till, G.O., Friedl, H.P. and Ward, P.A.: Histamine-dependent modulation of oxygen radical production, in, Farr, C.H. (ed), Proceedings of the Second International Conference of Bio-Oxidative Medicine, In Press.
22. Till, G.O., Johnson, K.J. and Ward, P.A.: Oxygen free radicals in inflammation, in, Messmer, K. and Hammerson, R. (eds), Progress in Applied Microcirculation, Volume 9, Karger, Basel, In Press.
23 Till, G.O. and Ward, P.A.: Role of complement and neutrophils in experimental acute lung injury, in, Nuki, G. and Zvaifler, N. (eds) The Lungs and Rheumatic Disease, Butterworths International Medical Reviews, Rheumatology 3, Butterworth and Co., England, In Press.
24. Till, G.O. and Ward, P.A.: The lung and rheumatic disease: Role of complement. Butterworth's International Medical Reviews, Rheumatology 3, In Press.
25. Till, G.O. and Ward, P.A.: Thermal injury and lung tissue damage, in, Critical Topics in Pulmonary Pharmacology and Toxicology, In Press.

26. Till, G.O. and Ward, P.A.: Complement-induced lung Injury, in, Said, S.I. (ed), The Pulmonary Circulation and Acute Lung Injury, 2nd Edition, Futura Publishing Co., Mount Kisco, New York, In Press.
27. Vaporciyan, A.A. and Ward, P.A.: The inflammatory response, in, Beutler, E., Lichtman, M.A., Coller, B.S. and Kipps, T.J. (eds), Williams Hematology, McGraw-Hill, Inc., New York, In Press.
28. Varani, J., McCoy, J.P. and Ward, P.A.: The attraction of wandering metastatic cells, in, Kaiser, H. (ed), Progressive Stages of Neoplastic Growth, In Press.
29. Varani, J. and Ward, P.A.: The immunobiology of tumor cell chemotaxis, in, Waters, H. (ed), Handbook of Cancer Immunology, Garland STPM Press, In Press.
30. Ward, P.A.: Inflammation, Chapter 12, in, Bellanti, J.A. (ed), Immunology in Medicine, W.B. Saunders Company, Philadelphia, Pennsylvania, In Press.
31. Ward, P.A.: Overview, in, Kinney, J.M. and Tucker, H.N., Oxygen Metabolism and Nutrition: Ideas for Future Critical Care, Raven Press, New York, In Press, 1994.
32. Ward, P.A.: Adesion molecules and cytokines in experimental inflammatory disease, in, Adhesion Receptors as Therapeutic Targets, CRC Press, Boca Raton, Florida, In Press, 1995.
33. Ward, P.A.: Inflammation: Basic concepts, in, Barnes, P.J., Grunstein, M.M., Leff, A. and Woolcock, A.J. (eds), Asthma, Raven Press, New York, In Press, 1995.
34. 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, Chur, Switzerland, In Press.
35. Ward, P.A.: Cytokines, in, Monograph in the Series Issues in Infection, The Interaction Between Lung Defences and Bacteria in the Pathogenesis of Infection - Time for a Re-appraisal, Hanbury Manor, United Kingdom, 14-15 November 1995.
36. Ward, P.A.: Cytokines and adhesion molecules in the lung inflammatory response, in, Johnstone, D. (ed), William Harvey Research Conference Proceedings, New Targets in Inflammation: Inhibitors of COX-2 or Adhesion Molecules, New Orleans, Louisiana, April 15-16, 1996, Kluwer Academic Publishers, Lancaster, United Kingdom, In Press, 1996.
37. Ward, P.A.: Role of complement, chemokines, and regulatory cytokines in acute lung injury. New York Academy of Sciences, New York, New York, In Press, 1996.
38. Ward, P.A., Friedl, H.P. and Till, G.O.: Role of oxygen radicals in experimental shock, in, Coran, A.G. and Harris, B.H. (eds), 3rd National Conference on Pediatric Trauma, In Press.
39. Ward, P.A., Johnson, K.J. and Sulavik, M.D.: Lung injury produced by oxygen derived free radicals from leukocytes, in, Mechanisms of Lung Injury Symposium, given at the Graduate Hospital, Philadelphia, Pennsylvania, 1986, In Press.
40. Ward, P.A., Johnson, K.J. and Till, G.O.: Tissue injury as a consequence of oxygen radicals produced by phagocytic cells, in, Proceedings of Symposium by Comparative Respiratory Society, Anaheim, California, In Press.
41. Ward, P.A., Johnson, K.J. and Till, G.O.: Leukocyte oxygen radicals and acute lung injury, in, Proceedings of a Symposium on "Acute Lung Injury", PSG Publishing Co., Littleton, Massachusetts, In Press.
42. Ward, P.A., Johnson, K.J. and Till, G.O.: Animal models of oxidant lung injury, in, Proceedings of Stressa Symposium in Zambon, Italy, In Press.
43. Ward, P.A. and Mulligan, M.S.: The role of cytokines and adhesion molecules in lung inflammation, in, Schlag, G. (ed), Third Wiggers Bernard Conference on Shock, Sepsis, and Organ Failure, Hotel Schloff Obermayerhofen, Vienna, Austria, May 16-21, 1992, In Press.
44. Ward, P.A. and Murphy, H.S.: Complement activation products in endothelial cell activation, in, Koch, K. (ed), American Chemical Society Symposium series book on Cell Adhesion and Migration, In Press.
45. Ward, P.A. and Till, G.O.: The autodestructive consequences of thermal injury, in, Ninnemann, J. (ed), the Immune Consequences of Thermal and Traumatic Injuries, In Press.
46. 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.

47. Ward, P.A., Warren, J.S., Johnson, K.J. and Varani, J.: Cytokines and oxygen radical responses, in, Maier, R. (ed), Proceedings of the International Congress on The Immune Consequests of Trauma, Shock and Sepsis: Mechanisms and Therapeutic Approaches, In Press.
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50. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Free radicals in lung disease, in, Rice-Evans, C. (ed), Free Radicals, Diseased States and Anti-Radical Interventions, Proceedings of the Special Colloquium, London, England, In Press.
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52. Ward, P.A., Mulligan, M.S. and Vaporciyan, A.A.: Leukocyte adhesion molecules, cytokines, and tissue injury, in, Faist, E. (ed), The Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches, Pabst Science Publishers, Berlin, Germany, In Press.
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55. Warren, J.S., Johnson, K.J. and Ward, P.A.: Phagocytes and reactive oxygen substances ad mediators of acute lung injury, in, Hyers, T. (ed), Diffuse Alveolar Damage and Respiratory Failure, Futura Press, New York, In Press.
56. Warren, J.S. and Ward, P.A.: Consequences of oxidant injury, Chapter 7.2.4, in, Crystal, R.G. and West, J.B. (eds), The Lung: Scientific Foundations, Second Edition, Raven Press, New York, In Press.
57. Warren, J.S. and Ward, P.A.: Immunoglobulin and complement mediated immune injury, in, Crystal, R.G. and West, J.B. (eds), The Lung: Scientific Foundations, Second Edition, Raven Press, New York, In Press.
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60. Warren, J.S., Ward, P.A. and Johnson, K.J.: Oxygen radicals as "Mediators of Inflammation", Volume 6, in, Hensom, P.M. (ed), The Handbook of Inflammation, Elsevier Biomedical Division, Amsterdam, The Netherlands, In Press.
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1. Beck, B., Jones, M.L., Schimmer, R.C., Schmal, H., Friedl, H.P. and Ward, P.A.: Cloning and expression of rat intercellular adhesion molecule-1 (ICAM-1) in the pET and baculovirus systems. FASEB J. 9:A37, 1995.

2. Doyle, N.A., Quinlan, W.M., Bullard, D.C., Vestweber, D., Jones, M.L., Ward, P.A., Beudet, A.L. and Doerschuk, C.M.: P-selectin and ICAM-1 in cobra venom factor-induced lung injury: Anti-adhesion molecule antibodies and mutant mice. Amer. J. Resp. & Critic. Care Med. 151:A455, 1995.
3. Eppinger, M.J., Jones, M.L., Deeb, G.M., Bolling,. S.F. and Ward, P.A.: Acute phase lung ischemia-reperfusion injury is macrophage mediated. FASEB J. 9:A961, 1995.
4. Eppinger, M.J., Ward, P.A., Jones, M.L., Bolling, S.F. and Deeb, G.M.: Inhaled nitric oxide reduces lung ischemia-reperfusion injury. Soc. Thoracic Surgeons, January, 1995.
5. Foreman, K.E., Till, G.O., Johnson, K.J. and Ward, P.A.: Complement activation, endothelial cell P-selectin and the role of C5b-C9. FASEB J. 9:A34, 1995.
6. Gipson, T.S., Shanley, T.P., Jones, M.L., Ward, P.A. and Johnson, K.J.: Molecular cloning and *in vivo* transcriptional expression of rat TIMP-2 in lung inflammation. FASEB J. 9:A748, 1995.
7. Kubo, H., Quinlan, W.M., Doyle, N.A., Kutkoski, G., Jones, M.L., Ward, P.A., Dinauer, M.C. and Doerschuk, C.M.: Cobra venom factor-induced injury in mice with chronic granulomatous disease. Amer. J. Resp. & Crit. Care Med. 151:454, 1995.
8. Schimmer, R.C., Schrier, D.J., Flory, C.M., Conroy, M.C., Metz, A., Beck, B., Friedl, H.P., Jones, M.L. and Ward, P.A.: The role of the VLA-4/VCAM-1 adhesion pathway in SCW-induced monarthritis in rats. FASEB J. 9:A270, 1995.
9. Shanley, T.P., Schmal, H., Friedl, H.P., Jones, M.L. and Ward, P.A.: Regulatory effects of intrinsic IL-10 in IgG immune complex-induced lung injury. FASEB J. 9:A960, 1995.
10. Warner, R.L., Paine, III, R., Christensen, P.J., Marletta M.A., Richards, M.K., Wilcoxen, S.E. and Ward, P.A.: *In vivo* sources and regulation of iNOS in rat lung. FASEB J. 9:A853, 1995.
11. Mulligan, M.S., Ward, P.A. and Whyte, R.I.: Role of IL-10 in obliterative bronchiolitis in transplanted rat airways. 1996 Annual Meeting of the American Association for Thoracic Surgery, San Diego, California, April 28-May 1, 1996.
12. Kubo, H., Morgenstern, D., Ward, P.A., Dinauer, M.C. and Doerschuk, C.M.: Alternative pathway of oxygen radical production during CVF-induced lung injury in mice with genetic deletion of NADPH oxidase. Amer. J. Respir. & Critical Care Med. 153:A284, 1995.
13. Mulligan, M.S., Ward, P.A. and Bolling, S.F.: *In vivo* regulatory role of TH-2 cytokines in allografts. Int. Society for Heart and Lung Transplantation,. New York, New York, March 15-18, 1996.
14. 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:A1007, 1996.
15. Forebeck, J.L., Remick, D.G. and Ward, P.A.: Cytokine production by human PMC in response to solid phase human IgA and human IgG subclasses. FASEB J. 10:A1433, 1996.
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17. Mulligan, M.S., Warner, R.L., Bolling, S.F. and Ward, P.A.: Protective role of IL-10 in cardiac allograft rejection. FASEB J. 10:A1279, 1996.
18. Schmid, E., Crouch, L.D., Friedl, H.P., Bless, N.M., Till, G.O. and Ward, P.A.: Complement levels in acute inflammatory lung injury. FASEB J. 10:A1008, 1996.
19. Warner, R.L., Mulligan, M.S., Lowe, J., Suzuki, Y. and Ward, P.A.: Protective effects of sulfatides and neuraminic acid derivatives in selectin-dependent acute lung injury and blocking of P and E-selectin binding. FASEB J. 10:A1149, 1996.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. CLINICAL ACTIVITIES:

A. Director, Division of Clinical Pathology/Clinical Laboratories, May 1993-present.
B. Director, Clinical Immunopathology Service; September 1989-present.

II. TEACHING ACTIVITIES:

A. "Current Topics in Immunopathology" series: pathology residents, M4 students; (25 contact hours).
B. Clinical Pathology Grand Rounds:
   1. "The Inflammatory Response" (1/6/95).
C. Immunopathology journal club: EMU medical technology students, medical technologists, pathology residents (one hour; biweekly, September-June).
D. Immunopathology signout: pathology residents, M-4 medical students, EMU medical technology students (three times/week; 26 weeks/year).
E. M-4 Laboratory Medicine Elective; 4th year medical students, four week block; (eight contact hours).
F. M-1 Histopathology sequence (shared section with J.C. Fantone, M.D.); 1st year medical students; (four contact hours).
G. Supervision of Research activities for:
   1. Kenneth Kilgore, Ph.D. (Postdoctoral Fellow); (1/1/94-6/30/96) (supported by American Heart Association of Michigan Fellowship).
   2. Brigitt Casselman (Undergraduate, University of Michigan); (5/1/94 - 4/30/96).
   3. Douglas Allen (Undergraduate, University of Michigan); (9/1/94-12/1/95) (sponsored in UROP).
   4. 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).
   5. Jennifer Beyer (Undergraduate, Texas Technical University); (5/1/95-8/15/95).
   6. Vipul Maheswari (Undergraduate, University of Michigan); (6/15/95-present); (sponsored by American Heart Association of Michigan Fellowship).
   7. Karen Powers (Undergradate, University of Michigan); (9/1/95-present).
   8. Anjali Desai, Ph.D. (Postdoctoral Fellow); (6/15/96-present).
   9. Hernan Gomez, M.D. (Assistant Professor; Emergency Medicine, University of Michigan); (6/1/96-present).
H. Ph.D. Thesis Committees:
   1. Michael Gralinski, Department of Pharmacology, University of Michigan Medical School (completed Ph.D. 6/1/96).
   2. James Park, Department of Pharmacology, University of Michigan Medical School (6/2/95-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).
C. Role of MCP-1 in luteolysis (collaboration with Landis Keyes, Ph.D., Department of Physiology, University of Michigan Medical School).
D. Role of MCP-1 in PAN-induced interstitial nephritis (collaboration with Allison Eddy, M.D., Department of Pediatrics, University of Toronto, Canada).
E. Pathogenesis of extrinsic allergic enephalomyelitis (collaboration with Joan Berman, Ph.D., Department of Neurology, Albert Einstein, New York).
F. Ischemia-reperfusion injury in perinatal rat brain (collaboration with Faye Silverstein, M.D., Departments of Pediatrics and Neurology, University of Michigan Medical School).
G. Role of MCP-1 in cutaneous delayed type hypersensitivity (collaboration with Douglas Ringler, V.M.D., LeukoSite, Inc., Cambridge, Massachusetts).
H. MCP-1 in arterialized vein grafts (collaboration with John Hoch, M.D., Department of Surgery, University of Wisconsin, Madison, Wisconsin).
I. P-selectin antagonists in glucan-induced granulomatous vasculitis (collaboration with Mark Anderson, Ph.D., GlycoMed Corp., Alameda, California).
J. MCP-1 antagonists in granulomatous vasculitis (collaboration with Kurt Jarnagin, Ph.D, Roche Bioscience, Palo Alto, California).
K. 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).

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. Incentive Task Group, advisory to Medical Service Plan Executive Committee, 1994-1996.
D. Co-convener, Laboratory Services Team, advisory to Mission Health and University of Michigan Clinical Delivery System Operational Integration Task Force, 1995-1996.
E. Medical Leadership Council, University of Michigan Medical Center, 1996-present.
F. Cancer Center Clinical Leadership Committee, 1996-present.
G. Representative, National Committee for Clinical Laboratory Standards, 1996-present.
H. Member, Standardization and Product Evaluation Committee, 1996-present.
I. Clinical Council (ad hoc substitute for Dr. Ward), 1996-present.
J. 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.

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.

SECTION REPORTS

ANATOMIC PATHOLOGY

DIVISION OF ANATOMIC PATHOLOGY

ANNUAL REPORT
DEPARTMENT OF PATHOLOGY
1 JULY 1995 - 30 JUNE 1996

The division faced one of its greatest challenges in years with the mandated cost efficiency program. In concert with the global departmental plan the division merged its laboratories into a single laboratory placing a greater emphasis on cross training of personnel and sharing of space and commodities. In this effort, we greatly acknowledge the contributions of our newly appointed supervisor Diana Souza who brings strong administrative skills from her clinical pathology background. This reorganization is an evolutionary process which will rely heavily on increased computerization of all aspects of specimen handling and reporting as well as on strong educational initiatives in helping our residents and faculty understand the need for better use of ancillary tests in daily practice.

Our faculty continues to thrive despite the stringent climate. They participate in numerous short course offerings for both the American Society of Clinical Pathology and the United States Academy of Pathology from topics ranging from the applications in molecular diagnostics to diagnosis of bone tumors. Over a dozen abstracts were presented at the USCAP meeting, one of which won the Stowell Orbison Prize for best resident research project. In addition two of our faculty were cited for exceptional contributions in the teaching arena. Drs. Caplan and Devaney shared the annual resident teaching award. Drs. Appelman, Headington, and Weiss were listed among the best doctors in the midwest and Dr. Weiss was elected Vice-President of the US-CAP. Dr. Thomas Frank in conjunction with Drs. Wojno and Singleton redefined the role that pathology will play in the successful competing renewal for the Cancer Center. The Tissue Procurement Core accordingly was expanded to include histology and immunohistochemistry services with ultimate plans that these activities will be relocated and housed in dedicated space in the Cancer Center. Our fellowship rograms graduated 3 residents in surgical pathology (Drs. Khalidi, Reith and Silvera), 1 in cytopathology (Dr. Stern), and 1 in soft tissue pathology (Dr.Lane). Dr.Mark Wielk (Barnes Hospital) served as our Annual Residents Visiting Progressor and lectured on "Algorithmic Approach to Diagnosis using Immunohistochemistry".

The closure of this academic year witnessed the departure of two valued faculty members: Dr. Bernard Naylor and Dr. Thomas Frank. Dr. Frank, a product of Washington University and University of Pennsylvania, was responsible for the development of the molecular diagnostic laboratory in anatomic pathology and will be especially remembered for the numerous resident projects he mentored during his seven years in the department. He leaves to assume the position as Vice President of Medical Education for Myriad Genetics. Dr. Bernard Naylor retired after more than thirty years, bringing to a close an end an epoch in cytology in this department. He was the consummate diagnostic cytopathologist outstanding in nearly every area but identified closely with pulmonary cytopathology, asbestosis, and mesothelioma. He served with distinction in the past as the President of the American Society of Cytology. He is equally known throughout the department for his teaching skills both at the medial student and resident level. Hardly a resident leaves this program without remembering Dr. Naylor's words of wisdom on the importance of delivering an oral presentation properly, "Just remember the next time I listen to you speak, I may not care so much what you are saying, but I will remember how you said it."

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

AUTOPSY SERVICE
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. TIMELY COMPLETION OF AUTOPSY REPORTS:

Autopsies are still not completed in a timely fashion, and this has resulted in an interim CAP inspection citation. We are continuing to make improvements in the management of cases. Particular, the typing has been revamped so that house officers and staff may make their own corrections. This has completely removed this portion of the processing from causing delays. The table below indicates the improvements in turnaround time.

Year	Total # autopsies	Average days to completion	# >60 days to completion %
1994	496	176	448 (90%)
1995	566	112	406 (72%)
1996 (first six months only of 1996)	249	91	160 (64%)

While there has been substantial improvement in our ability to complete the cases, we have not yet achieved the final goal of having virtually all of our cases completed within 60 days. Beginning July 1, 1996, we have incorporated an incentive clause for completion of autopsies. Any autopsy reports that are not completed within 60 days will result in $500.00 per case reduction in pay for the staff person.

II. MORGUE RENOVATIONS:

The refrigerator in the morgue has been completely replaced. This renovation has upgraded the backup capacity of the refrigeration unit, improved the ability to service the refrigeration components, brought us into compliance with environmental regulations for the refrigerant, and increased the storage capacity. A new floor was also installed. While there have been some difficulties with the storage racks and initial performance of the cooling unit, these issues are being resolved. This new refrigerator doubles the storage capacity of the refrigerator.

We are in the process of acquiring a new room contiguous to the present facility. This will increase the office area to accommodate the greater the number of presentations which are being performed in the morgue. These presentations include review of cases with other house officers at the University of Michigan.

III. MEDICAL EXAMINER CASES:

We have concluded a contract with the Washtenaw County Medical Examiners Office which includes substantial improvements in reimbursement. We will be paid for past work that we performed for the county, and the new contract provides enhanced reimbursement for future years. However, there is a penalty clause which reduces reimbursement to the Department if there is a delay in the final report. If a report is 60 days late, there will be a 50% reduction, if it is 90 days late, 75% reduction, and if 120 days late, 100% reduction. Also new in the contract is the requirement that all autopsies be performed by forensic pathologists, which relieves the general pathology faculty of the need to staff these cases. Additionally, the Chief Medical Examiner of Washtenaw County, Bader Cassin, M.D.,will perform medical examiner autopsies at the University of Michigan, with administrative and technical support from the University. The pathology house officers will not participate in these autopsies, although they may. This decompresses the service commitments on the pathology house officers.

	1995 (6 months)	1993 (6 months)
Total ME autopsies	126	87
U of M hospital cases, or death at scene	101	73
Transfer from other hospital	25	14
Injury in Washtenaw County	74	
Injury outside Washtenaw County	28	
Medical Examiner's case, but autopsy requested by family and not ME	14	

We have completed an extensive analysis of the medical examiner caseload. We reviewed all of the ME autopsies performed, and the ME cases investigated from July 1, 1995 to December 31, 1995, i.e., a six month time interval. For comparison, the figures for the first six months of 1993 are included.

There are several important pieces of information in this table.

The number of medical examiner cases has increased, but this has primarily been due to either University of Michigan Hospital deaths, or deaths at the scene. We are getting very few cases transferred from other hospitals (only 11 such cases in the last six months of 1995). This indicates that the growth of the medical examiner work is due to the increased activity at the University, primarily because of the success of the Trauma/Burn Unit.

A. In most situations, the injury or violent act occurred in Washtenaw County.
B. Several medical examiner's cases are accepted, but an autopsy is not ordered by the medical examiner. However, the family will still request an autopsy (14 cases).

We also evaluated the utilization of the autopsy service by the medical examiner during this same time period.

Total number of in-hospital deaths investigated	179
Investigated deaths with no ME ordered autopsy	78
Investigated deaths with autopsy	101
Autopsy percentage	56%

IV. STATISTICS:

All of these are for the time period July 1, 1995 to June 30, 1996.

Total number of U of M deaths		1088
Total number of autopsies performed	541	
Total number of medical examiner cases		219

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

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1995 - 30 JUNE 1996

This past year has brought several new developments to the division of Cytopathology. Due to the increasing demands for cost containment in the health care industry, reorganization of the Cytopathology Laboratory with the Histology Laboratory will occur in the near future.

Gynecologic specimens numbered 31,913 and non-gynecologic specimens 5,603 of which 30% were fine needle aspirates. The increasing number of aspirates represents the main area of growth in cytopathology. Drs. Selvaggi and Michael in conjunction with representatives from the Cancer Center were fortunate to acquire space in the building for a fine needle aspiration clinic. Recruitment of an additional cytopathologist will ensure continuous staffing.

In the tenth year of our Cytopathology Fellowship Program, Dr. Robert Stern completed his training with distinction. Due to the demand for cytopathologists in the community, he received several job offers.

The division has continued to refine its computer program for the reporting of cervicovaginal cytology and will begin to develop a software package for non-gynecologic cytology in conjunction with Pathology Data Systems. Ms. Belinda Davis is working with representatives from Cerner to develop a working quality assurance/quality control software program for cervicovaginal cytology.

The cytotechnologists have been actively involved in the regional cytology society. Ms. Belinda Davis is the current Vice President of the Michigan Society of Cytology and serves as a screener for the College of American Pathologists Cytopathology Committee. Drs. Naylor, Selvaggi, and Michael have presented papers and workshops at various national meetings and cytologic societies. Henry Ford Hospital programs of Cytotechnology and have presented several workshops and papers at various national meetings and cytology societies.

Gynecologic specimens numbered 31,913 and non-gynecologic specimens 5,603 of which 30% were fine needle aspirates. The increasing number of aspirates represents the main area of growth in cytopathology. It is anticipated that the demand for aspirates will continue to increase in the new health care era and with the opening of the Cancer Center.

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

DERMATOPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1995- 30 JUNE 1996

The Dermatopathology Service receives diagnostic case material from six different sources: (1) UMMC (ID) cases; (2) outside contractual (MD) cases; (3) personal consultations (HE and NI) cases; (4) outside slides reviewed for referred patients (TD) cases; (5) miscellaneous intramural referrals (IE, IF, IS, ME, SC, TS) cases; (6) and informal consultations (intramural, VAH and MU).

Work load volume is as follows:

	1991-1992	1992-1993	1993-1994	1994-1995	1995-1996
HE	731	981	694	569	639
ID	5651	4255	4791	4759	4787
MD		1347	1663	2240	2560
TD		550	709	553	578
Misc			71	218	300
Informal	300	225	254	106	125

The total case numbers for 1995-1996 are somewhat inaccurate because of inability to include cases reported by General Surgical Pathologists during periods of absence by Dermatopathologists.

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.

As noted for the previous year the workload in the Dermatopathology service continues to be significantly impacted by the growth of Cutaneous Oncology services. The number of patients being seen in the Melanoma Clinic increased this year to almost 400 and bi-weekly conferences including 15 to 20 patients or more are not exceptional. The Otolaryngology and Plastic Surgery services have also been contributing complex cases for microscopic study.

Dermatopathology teaching in the Department of Dermatology remains unchanged.

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

Formal presentations were made to both the medical and dental students.

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

NEUROPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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

I. CLINICAL ACTIVITIES:

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

1. There were 695 neurosurgical cases including CNS, pituitary, muscle and nerve examined this year, with 79 of these cases coming from outside hospitals in consultation. A portion of these were part of an interdepartmental study of PET/BUDR and neuropathology funded by NIH. Approximately 300 surgical specimens required special neurohistologic procedures.
2. There were 300 brains out of 556 autopsies processed in the hospital neuropathology laboratory. This is 54% of the total autopsies. Five brains were also processed from other institutions. In addition, the Diagnostic Unit of the Neuropathology Core Laboratory of the MADRC processed 46 hospital dementia brains which is 8% of the total autopsies. Fifteen additional brains were processed by the Core Laboratory from the Michigan Dementia Network Program.
3. There were 239 muscle biopsies (122 inside, 117 outside) 87 processed through M-Labs, nearly all with histochemistry, 20% with electron microscopy. There were 97 (57 internal, 40 external) peripheral nerve biopsies. There were 50% with teased fiber preparations, all with thick plastic sections and 30% had electron microscopy performed. The combination of nerve teasing, muscle histochemistry, electron microscopy and morphometry make the service regionally competitive for diagnostic consultation.
4. Faculty interpreted 231 cases in semithin or thin section from electron microscopy. The majority of these cases were nerve, pediatric muscle, and neurosurgical biopsy cases.
5. The ceroid service, buffy coat division, reported 10 cases.
6. The Brain Tumor Board of the University of Michigan Cancer Center and Hospitals, supported weekly by a neuropathologist, reviewed neuropathology and clinical aspects of more than 130 difficult neuro-oncology cases.
7. One brain was examined for research purposes.
8. There are two neuropathology quality assurance meetings each month. Attendees include neuropathologists from nearby institutions.

II. TEACHING ACTIVITIES:

1. Medical Students: This year the neuropathology faculty taught in the eight week neuroscience sequence of our 2nd year medical curriculum. There were fourteen hours of neuropathology taught: six hours of lecture and eight hours in the laboratory.
2. House Officers, Graduate Students, Postgraduate and other students and faculty: These include periodic conferences with Neurology; twice monthly Continuing Medical Education (CME) accredited conferences where all biopsies are presented and interpreted; a weekly conference where abnormal brains are examined with all clinicians invited; monthly nerve and muscle

biopsy conferences accredited for CME; individual instruction on autopsies and biopsy material; Neuropathology 858, an 8 hour laboratory course; bimonthly conferences with Neuroradiology, conferences for neuromuscular disease and bi-weekly Neuropathology seminars for Neurosurgery and Neuroradiology House staff. Weekly seminars are provided to neurological and neurosurgical house staff on clinico-pathological correlations.

3. Electives: Two Pathology Residents, one Neurosurgery and one Neurology Resident chose elective rotations on the Neuropathology Service.

III. RESEARCH ACTIVITIES:

1. Dr. Hicks, Dr. Sima and Ms. D'Amato provided neuropathologic support for MADRC. Ms. D'Amato is Core Coordinator of the Diagnostic Neuropathology Unit of the Neuropathology Core of the MADRC. Ms. D'Amato is also Co-Investigator with Dr. Anders Sima on the MADRC Project: The Pathology of Diffuse Lewy Body Disease.
2. Dr. Blaivas and associates investigate: 1) ocular muscle (aging and botulinum effect), 2) musculature related to cleft palates in children 3) histology of animal model of rheumatoid arthritis, 4) histochemistry and morphometry of muscle in patients with hypertension and diabetes.
3. Dr. Sima's laboratory was investigating pathogenetic mechanisms involved in experimental and human diabetic neuropathies. In particular, the laboratory is focusing on the molecular, structural, and functional abnormalities of the nodal apparatus of myelinated fibers in diabetic nerve. The laboratory is also investigating trophic and immunological factors governing nerve fiber regeneration in diabetes. The Morphometric Imaging Core, directed by Dr. Sima, served as an international reading laboratory for nerve biopsies obtained from several ongoing multicenter clinical trails of drugs designed to ameliorate and halt the progression of diabetic neuropathy. Dr. Sima moved to Wayne State University in February.
4. Dr. McKeever and associates are determining the extent and cause of differences in gene product expression in brain tumor tissue versus cells in culture. These differences may result from a separate population of cells within brain tumors or from genetic instability in neoplastic cells. They are 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 *in vivo* and *in vitro*. He is 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 astrocytomas. He is studying receptor-ligand interactions and neuropathology of epilepsy with colleagues in Neurology.
5. Groups of the University of Michigan Cancer Center faculty and staff with clinical research interests in brain tumors, met and generated a number of project considerations from Pathology, Neurosurgery, Nuclear Medicine, Neuropathology, Neurology and Neuroradiology collaborations.
6. Collaboration with Neurology, Michigan State University, The State of Michigan Department of Public Health, the Alzheimer's Association, Henry Ford Hospital, Beaumont Hospital 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
Neuropathology Section

SPECIAL FUNCTIONS LABORATORY (IMMUNOPEROXIDASE, IMMUNOFLORESCENCE, NEURAL MUSCULAR STUDIES, AND ELECTRON MICROSCOPY) DEPARTMENT OF PATHOLOGY ANNUAL DEPARTMENTAL REPORT 1 JULY 1995 - 30 JUNE 1996

The immunoperoxidase laboratory has changed substantially over the last year. The major impetus for these changes being the cost efficiency program. To maximize use of personnel and resources the following services were combined under a single umbrella; immunoperoxidase, immunoflorescence, nerve teasing, muscle histochemistry, electron mycoscpoy, special histochemistry, and anatomic pathology molecular diagnostics. We have initiated the process of cross training personnel and have already realized the saving from this more efficient use of personnel in that we have not had to reduce the services provided in any substantial way with implementation of the cost efficiency program.

The immunohistology lab has continued to offer over 75 different immunohistochemical stains for paraffin and frozen tissues and perform approximately 650 test each month or over 7500 during the year. This is a substantial reduction from previous years and is mainly due to the decreased utilization of redundant antibodies on individual cases. During this time period we are not aware of a single incidence where this reduced redundant ordering of 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.

As part of continued efforts at cost efficiency we are planning to merge all of the anatomic pathology laboratories including cytology, histology, and the special studies mentioned above in order to maximize cross training and personnel utilization. These plans will be enhanced by the implementation of the new Cerner operating system (V500). The efficient use of this computer technology to eliminate manual logs and manual quality assurance records has the potential to increase productivity. This combined anatomic laboratory will be overseen by a single supervisor (Diana Souza) who will begin on July 1, 1996. We also plan to completely separate the research activities of this laboratory form the hospital service work. The research activities will be shunted to the Cancer Center Core histopathology and immunoperoxidase core facility as well as the research histology that is provided by the department (Cathy McClinchey). This initiative will remove a tremendous burden from the service lab and allow us the flexibility for cross training of personnel to maximize productivity. In conclusion we have made significant inrodes into the establishment of a cost efficient system over the past year and will continue our efforts in the coming year while trying to maintain the excellent quality of work for which this laboratory is known.

Kirk J. Wojno, M.D.
Director

Timothy P. Singleton, M.D.
Assistant Director

SURGICAL PATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

The surgical pathology service remains an active University service with in-house accessions approximating 30,000 and personal consultations 6000. The cases continue to demand increasingly higher levels of diagnostic sophistication coupled with more sophisticated ancillary procedures. More emphasis than ever is placed on STAT biopsy interpretations to facilitate treatment plans and diminish hospital stay. Consequently the staff has worked very conscientiously to improve turn around times (TAT) in order to better assist our clinical colleagues. Our current TAT for biopsies is 2.4 days, a figure which compares very favorably with the CAP guideline of 3.0 days. The Tissue Procurement Core, administered jointly by the Cancer Center and Surgical Pathology Service, distributes several thousand specimens per year to investigators throughout the medical center.

In concert with the departmental cost efficiency program the surgical pathology service has merged its histopathology laboratory with that of cytology and with time will integrate fully with immunohistochemistry. The consolidation of these three units will allow better cross training of individuals so as to acclimate to personnel reductions. We continue to work closely with Pathology Data Systems to complete full computerization of functions. Automatic SNOMED coding was added to our capability this year with future plans to adopt a computerized means of tracking slides and blocks.

Our fellowship programs remain robust. Drs. Hassan Khalidi (University of Texas), John Reith (Cleveland Clinic) and Scott Silvera completed their training in surgical pathology and Dr. Kathryn Lane (Duke University) finished a year of specialty training in soft tissue pathology. This coming year we look forward to three internal fellows: Drs. Lyndon Su, Steve Ramsburgh, and Joseph Tworek. Dr. Gelareh Farshid (Stanford University) will severe as the Soft Tissue Fellow. Dr. Joel Greenson is to be complimented for his direction of this program.

The surgical pathology service welcomes Dr. Lori Lowe as our new dermatopathology faculty member to assist Dr. Headington. Dr. Lowe joins us from Henry Ford Hospital where she had previously been the Director of Dermatopathology. In the coming year we will complete our recruitment for a new director of dermatopathology as Dr. Headington looks toward his retirement after an illustrious career in the department. Finally, we wish to acknowledge the retirements of Ada Tillman and Gwen Long from our Histopathology Laboratory. "Ada" and "Gwen", as we all called them, served as Supervisor and Assistant Supervisor of the laboratory for many years. Both were outstanding histotechnologists and fine, dependable individuals whose expertise will be missed.

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

CLINICAL PATHOLOGY

DIVISION OF CLINICAL PATHOLOGY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

Despite a continuing, institution-wide mandate to reduce operating budget the Clinical Laboratories continued to provide excellent, full-spectrum service. In 1995-96 the Clinical Labs performed approximately 3.2 million billable analyses. The reduction in cost per unit of activity provided by the Clinical Labs, in the face of rising overall health care costs, 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 and, with the oversight of Clinical Laboratory personnel, the UMMC - acquired physician office practices and satellite facilities received COLA certification. 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.

1995-96 was marked by three major initiatives. In response to pressures to reduce our cost/unit of laboratory service and to improve our 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 phlebotomy services. Major future cost efficiencies were gained through new 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 reorganization will be completed by autumn. The present reorganization will entail 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 successfully reallocated the resources necessary to meet the continuing and marked increase in transplantation activity (especially bone marrow) experienced in 1995-96. Integral to this programmatic demand was implementation of DNA-based high resolution class II antigen typing and DNA sequencing as clinical assays. Augmentation of the capabilities of the Blood Bank, Tissue Typing, and Cytogenetics Laboratories was contributory to the approval of the UMMC as a participant in the National Allogeneic Bone Marrow Transplantation Program. Finally, the Clinical Laboratories have responded to the institutional initiative to acquire broader primary care capabilities within the region. Specifically, nine medical practices and two UMMC satellite facilities that maintain on-site laboratory testing were added to the overall UMMC laboratory network. This activity was coupled with a robust 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, 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 1995-96. For instance, the 27th annual Blood Bank/Transfusion Medicine course and the Laboratory Information Systems course were each attended by more than 200 registrants making them among the most visible courses of their kind in the United States. 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 over 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 1995 - 30 JUNE 1996

PATIENT CARE:

Blood component utilization continued to grow during the year, approximating 100,000 units. This was related to further expansion of the liver and bone marrow transplantation programs and the need to provide support for patients prior to the actual procedure, as well as to growth in areas such as trauma care, extracorporeal membrane oxygenation and thoracic surgical operations. This growth occurred despite efforts to contain blood utilization in University Hospital.

Component utilization increased particularly in the areas of platelet and plasma transfusion. The requests for platelet transfusions were monitored by laboratory medical staff to ensure their appropriateness. A new initiative to monitor plasma and cryoprecipitate transfusions was instituted in hopes of ensuring appropriateness of utilization.

The Transfusion and Apheresis area, in an effort to meet the increased demands for therapeutic plasma exchange and for stem cell harvesting, modified its approach to blood transfusion and collection. An additional blood cell separator was obtained, allowing for a 50 per cent increase in apheresis procedures. This was accommodated by transferring hematology and oncology outpatient transfusions to an area elsewhere in the hospital. It is hoped that the introduction of the Cancer Center will allow improved relocation of some of the outpatient transfusion activity, perhaps associated with relocation of some of the I.V. immune serum globulin infusions.

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. Ms. Steiner 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, related to modification in the training program schedule. 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.

Lectures on Transfusion Medicine were given to clinical departments in University Hospital, including the Section of Thoracic Surgery and the Departments of Anesthesiology and Pediatrics.

The 23rd annual postgraduate course, "Current Topics in Blood Banking", was held on May 29-31, 1996. 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. Steiner, Ms. Butch, Mr. Judd 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 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, Ms. Steiner and Ms. Butch were active in education programs of the Michigan Association of Blood Banks and provided invited lectures throughout the country. Mrs. Knafl was active in organization of 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. Ms. Steiner served as chairperson of the AABB Committee on Reference Laboratories and Rare Donor File, co-edited the newsletter of the Michigan Association of Blood Banks and chaired the By-laws and Policy Manual Committee of the MABB. In addition, members of the technical staff participated in the Inspection and Accreditation program of the American Association of Blood Banks. Dr. Oberman's, Dr. Davenport's, and Mr. Judd's activities are further noted in their individual faculty reports.

RESEARCH ACTIVITIES:

The individual reports of Drs. Oberman, Davenport and a Mr. Judd record their publications and investigative efforts related to blood banking and Transfusion Medicine. In addition, Mr. Judd and Ms. Steiner studied the appropriateness of implementation of a gel-based system for pretransfusion blood testing.

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

CHEMICAL PATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
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1 JULY 1995 - 30 JUNE 1996

The Chemical Pathology Laboratory completed a stressful, but ultimately successful year that saw multiple changes in the lab operation. The focus of the year clearly was on reorganization and continued automation of manual assays in an attempt 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 into Chemistry. The implementation of this consolidation and cross-training of personnel in the coming year should allow for greater flexibility and potential further budget reductions. The Chemistry Laboratory experienced an approximate 2.0 % increase in test volume, performing nearly 3.5 million tests this past fiscal year. The laboratory is projecting it will finish 4.0 % under budget for this same time period.

The Chemistry lab undertook a series of instrument changes and upgrades aimed at increasing the number of tests performed on automated, random access analyzers. The major chemistry instruments were upgraded to Ektachem 950IRC analyzers. This allows for faster throughput, easier processing of both of urine chemistries and dilutions on serum samples, and the capability of performing more therapeutic drug monitoring assays on these systems. Cortisol, testosterone, estradiol, and progesterone were moved from manual RIA's to the automated Ciba Corning ACS-180 immunoassay analyzer. A super sensitive TSH assay was evaluated and implemented on the ACS-180. The lab evaluated and initiated testing on the Abbott AxSYM immunoassay analyzer. Testing for PSA, beta-HCG, CEA, AFP, and CK-MB were all switched to the AxSYM following extensive correlation studies. Correlations for many of the therapeutic drug monitoring assays were also performed in preparation for the planned consolidation of the Drug Analysis Laboratory with Chemistry.

The laboratory directors and staff participated in a significant number of evaluations and research studies. These included:

1. Comparison of multiple super sensitive TSH methods.
2. Evaluation of methods for measuring the free fraction of PSA and the use of percent free PSA as an improved marker of prostate cancer.
3. Evaluation of the performance of phenobarbital and carbamazepine determinations by the Ektachem dry slide technology.
4. Beta site evaluator of new software for the Abbott AxSYM.
5. Alpha site evaluation of a new prototype whole blood glucose meter.
6. Evaluation of Troponin I as a marker of myocardial injury following cardiac catheterization.
7. Interference of a polymerized hemoglobin based blood substitute on laboratory testing.

The Chemistry Laboratory continued its active role in Point of Care testing both within the hospitals and at the off-site health care centers. As part of a multi-departmental initiative to reduce blood product utilization, Chemistry personnel were responsible for the evaluation, implementation, and

ongoing management of a program that will bring rapid delivery of platelet counts, prothrombin time, and APTT to the operating rooms. A small Coulter MD8 hematology analyzer and portable Coagucheck Plus whole blood coagulation analyzers have been placed in the operating rooms. Testing is performed by Anesthesiology Department staff, with chemistry lab personnel doing all training, quality control evaluation, and ongoing competency assessment of all operators.

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. Pregnancy tests are being performed in Mott OR and in the OB-GN Clinic, with results collected and entered into Pathnet by Chemistry personnel. Cholesterol testing is being performed on select patients at the MedSport Clinic, and Hemoglobin A_{1c} is being performed in the Diabetes Clinic. In both of these programs, clinic personnel perform the tests, and Chemistry Lab staff are reponsible for training, quality assurance, and proficiency testing.

The labs role in managing small laboratories at off-site clinics has also continued to grow. The opening of Health Care Centers in Saline and West Ann Arbor, plus the aquisition of a group physician practices in Chelsea and Monroe have added to the management load of the Point of Care testing group. All of the sites have passed COLA accreditation inspections of their on-site laboratory functions with no deficiencies.

Donald Giacherio, Ph.D.

CLINICAL CYTOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
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The Clinical Cytogenetics Laboratory has maintained its plateau in volume in some areas, while others have continued to expand. In the area of prenatal diagnosis, just over 760 amniotic fluid specimens, 85 chorionic villus biopsies and 70 tissues were analyzed; this is approximately the same number as last year. 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 70 enumerated above. The bone marrow specimens continue to skyrocket, from under 400 three years ago, to 573 in the last year to 707 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 150 requests which were declined for one or more reasons. In addition, 523 peripheral blood specimens were analyzed, a five percent increase from last year. 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 two 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 dMYC amplification for neuroblastoma. In situ hybridization is performed on at least a weekly basis.

The Laboratory hosted the Southeastern Michigan Cytogenetics Meeting this year. Speakers included members of the Laboratory staff, as well as faculty from Child Psychiatry, Pediatric Genetics, and a Pathology Resident, Leslie Bruch. Approximately 50 people from six institutions attended the meeting.

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

DRUG ANALYSIS AND TOXICOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

The Drug Analysis and Toxicology Laboratory continues to maintain its prominent role as an active, progressive, and vital contributor to the success of the Department of Pathology and the University of Michigan. The volume of assays performed in support of the M-Labs program continues to remain strong. The types of tests being referred to DATL are typically the more labor intensive, specialized assays. While the overall activity for the laboratory was similar to the previous year, decreases in the volume of routine or automated assays were balanced by increases in volume for some specialized tests.

During the last year the Department of Pathology decided not to continue forensic urine drug testing in the laboratory, so that re-certification was not sought for 1996. DATL was one of the initial laboratories to be certified by the College of American Pathologists and the efforts made by the laboratory staff in achieving and maintaining the certification for over 6 years should be lauded.

One positive improvement made during the last year was the development and implementation of a new cyclosporine assay. Larry Clayton served as lead of the development of the assay, with contributions from a number of the laboratory staff. This assay uses a novel analytical column (prepared in-house) as well as the ability to use autoinjection of samples, both of which have reduced personnel time required for performance and maintenance of the assay. Because of the high volume of the assay, this assay advancement has allowed the laboratory to adjust to changes in staffing and volume without a loss of service to the transplant program. Savings in commodities are also being realized.

Much of the last year was spent in preparation for the Cost Efficiency Program mandated throughout the medical center. As part of the program a consolidation of personnel and testing into the Chemical Pathology workspace has been requested. The ability to efficiently consolidate and integrate laboratory services will require a major renovation of space, which we are currently awaiting. Goals for the next year will be to contribute to the departmental program of laboratory consolidations. The environment surrounding academic medical centers continues to change and the laboratory will continue to contribute to the challenge of making the medical center successful in the future.

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

CLINICAL FLOW CYTOMETRY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1995-30 JUNE 1996

The Clinical Flow Cytometry Laboratory processed approximately 3400 immunophenotyping specimens, a volume increase of 9% from the previous year. This included approximately 800 specimens submitted for leukemia/lymphoma immunophenotyping, 1250 specimens for monitoring of acquired and inherited immunodeficiencies, and 350 specimens for T-cell subset monitoring in organ transplant recipients. Anti-platelet and anti-neutrophil antibody assays were performed on approximately 350 specimens. Reticulocyte analysis was transferred to the main hematology laboratory in November 1995.

The laboratory has continued to increase its volume of work through the M-Labs Program. The comprehensive hematopathology consultation service provided by the laboratory has helped to attract this enlarging referral base. For the past year, M-Labs referrals comprised 39% of all acute leukemia immunophenotyping panels, 46% of all chronic leukemia/lymphoma profiles, and 44% of all non-transplant immunodeficiency monitoring.

The laboratory works in close cooperation with clinical services to enhance efficiency and control costs. Working in conjunction with the bone marrow transplant service, the laboratory now provides same-day reports of stem cell quantitation from apheresis products, peripheral blood, and bone marrow. Approximately 380 stem cell quantitations were performed in the last year, an increase of 155% from the previous year.

A major area of utilization management continues to be the close monitoring of all requests for leukemia/lymphoma immunophenotyping. The hematopathologists staffing the laboratory must screen all requests for these extensive antigen profiles. Of the 800 specimens submitted for leukemia/lymphoma immunophenotyping, pathologist review lead to cancellation of 310 of these requests.

The clinical data base stored in the laboratory has served as a resource for collaborative projects on immunophenotyping in chronic lymphoproliferative disorders and bclx expression in acute myeloid leukemias. The laboratory has also participated in collaborative efforts with the hematology laboratory for testing methods of CD4 lymphocyte counting.

Quality assurance conferences enable medical and technical staff to review leukemia/lymphoma cases reported by the laboratory. These meetings entail a comprehensive review of each case to assure such things as appropriateness of the test request, technical quality of the analysis, clerical quality of the reports, and consensus regarding final diagnosis. Teaching activities in the laboratory include daily case sign-out with the residents and hematopathology fellow. Continuing medical education for the technologists and house staff is also offered at the biweekly leukemia conference, an interdisciplinary conference held in conjunction with the Division of Hematology, Internal Medicine.

Charles W. Ross, M.D.
Director

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

CLINICAL HEMATOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. LABORATORY ACTIVITIES:

A. Competency testing:
   1. differentials, fluid differentials, and urine microscopics.
   2. differential slide preparation.

B. Implemented reticulocyte count on STKS in November, 1995.

C. Beta site for CD4/CD8 on STKS.

D. Continued to prepare for Cancer/Geriatric Center opening.

E. Reduction of 5 FTE's.

F. Several internal quality improvement teams dealt with such laboratory problems as work flow on different shifts, EMU students, implementation of new policies, etc.

G. Began plans to merge Flow Cytometry and Hematology, including cross-training of personnel and meetings with architects.

H. Discontinued differential counts when WBC <0.5.

I. Began labeling of bone marrow aspirate slides with surgical pathology numbers to facilitate storage.

J. Daily bone marrow and lymph node signout with House Officers, Hematology Fellows and Fellows from Adult and Pediatric Hematology/Oncology as well as visiting pathologists from other institutions.

K. Daily signout of in-house and UM clients' cases of abnormal smears and body and joint fluids takes place 7 days per week.

II. TEACHING ACTIVITIES:

A. Pathology House Officers and Hematopathology Fellows, Fellows from Pediatric and Adult Hematology/Oncology and visitors from other institutions (Dr. Felicitas Hitz, University of Zurich, Switzerland and Dr. Sun-Hee Kim from Korea) participated in the following activities:
   1. Daily review of abnormal blood smears, body fluids, joint fluids for crystals, bone marrow aspirates, smears and bone marrow biopsies.
   2. Daily review of in-house and transfer consultation cases in hematopathology (lymph node biopsies, bone marrow biopsies, aspirates, splenectomy specimens, etc.).
   3. Daily review of outside consultation cases of Dr. Schnitzer .
   4. Correlation of morphology with special studies (cytochemistry, flow cytometry, immunoperoxidase and occasionally electron microscopy).
   5. Daily review of abnormal blood smears from M-Labs clients.
   6. A formal teaching conference for House Officers has been continued.
   7. Weekly review of cases to be presented at Lymphoma Conference (Hematopathologists, Fellows, and house officers).
   8. Review of SWOG cases.
   9. Weekly Interdepartmental Lymphoma Conference.
   10. Biweekly Interdepartmental Leukemia Conference.
   11. Biweekly Interdepartmental Non-neoplastic Hematology Conference.
   12. Pediatric and Adult Hematology/Oncology Fellows participate in signouts.

B. Hematopathology Fellowship Program.
C. Continuing medical education for medical technologists - monthly.
D. Senior Student Clerkship Elective.
E. Summer Clinical/Research Program for Under-represented Minority Students.

III. FISCAL YEAR 1996/1997 GOALS:

A. Complete merger between flow cytometry and hematology including laboratory reorganization and movement of flow cytometry from Medical Science I to the Hospital.
B. Implement Coulter Gen-S for improved laboratory efficiency.
C. Schedule bone marrow biopsies, to facilicate more efficient utilization of personnel.
D. Prepare for the opening of the laboratory in the Cancer/Geriatric Center.
E. Continuation of cost-containment programs.
F. Continue to review and develop of laboratory utilization.
G. Continue to liberalize automated differential criteria.
H. Continue studies of limiting WBC requests from intensive care units.
I. Continue to enhance the overall efficiency of the laboratory operation.

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

Timothy P. Singleton, M.D.
Assistant Director, Clinical Hematology Laboratory

HISTOCOMPATIBILITY AND IMMUNOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY
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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.

I. 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 DR§ 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.

I. TEACHING ACTIVITIES:

Every member of the Laboratory was involved in the teaching activities of the Laboratory and they were effective in their work. The laboratory was involved in the instruction of Pathology Residents, Allergy Fellows, Renal Fellows and Postdoctoral Candidates from the Department of Hematology. Dr. Baker, the Laboratory Director, took an active role in ASHI. 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.

III. 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 hoped 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

DEPARTMENT OF PATHOLOGY
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I. OVERVIEW:

The Immunopathology Laboratory experienced a 3% increase in overall test volume in 1995-96. Anthony A. Killeen, M.D., Ph.D. and John Lowe, M.D. provided invaluable service commitments to the laboratory in the interpretation of protein electrophoresis studies. Kent Johnson, M.D., and Glen Bowen, M.D. (Dermatology) continued to signout tissue immunofluorescence studies under the auspices of the Anatomic Pathology Division. Paul Killen, M.D., Ph.D. and Dr. Johnson, also under the auspices of Anatomic Pathology, continued to enhance the renal biopsy service. Dr. Killen provided invaluable technical oversight of tissue immunofluorescence studies and leadership in the area of case-handling and tracking. Drs. Johnson, Killen, and Killeen also provided cross coverage of anti-neutrophil cytoplasmic antibody (ANCA) and anti-GBM studies.

II. CLINICAL SERVICES:

As the fiscal year approached its conclusion, the laboratory had experienced a modest increase in overall volume (approximately 3%). Particularly gratifying was the continued growth in several specialized assays; most notably the ANCA test and the anti-GBM indirect immunofluorescence test. Neutrophil cytoplasic antibody determinations increased from approximately 125/month to more than 150/month. More than 200 indirect immunofluorescence assays for anti-glomerular basement membrane antibodies were interpreted in 1995-96. 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. Most notable in this regard is sendout assays of circulating immune complexes, at a cost of $180/test. By instituting necessary approval by IP laboratory professional staff the number of these requests declined 5-fold, resulting in more than $12,000 saved. 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). Finally, we recently added the capability of determining specific IgG and IgM anti-cardioplipin antibody concentrations. This assay has relevance to the "anti-phospholipid antibody syndrome" which has been associated with thrombosis, thrombocytopenia, and fetal wastage. Several commercially-financed methods evaluations were also carried out. These studies involved anti-streptolysin O and anti-cardiolipin antibody measurements.

IV. QUALITY ASSURANCE:

The laboratory participated in two departmental QA projects. These related to a project that addressed transmission of laboratory testing data from point of order to medical record and 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 biweekly 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). Dr. Keren was appointed as a Clinical Professor of Pathology and 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

LIGAND ASSAY LABORATORY

DEPARTMENT OF PATHOLOGY
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CLINICAL ACTIVITIES:

The clinical laboratories continue to undergo sweeping changes. This year saw the consolidation of the following laboratories into one functional entity: Chemistry, Immunology, Ligand and Toxicology. An integral part of this consolidation has been the conversion of many immunoradioassay methods to non-radioisotopic methods that lend themselves to automation. This provides a two-fold improvement, (1) increased laboratory efficiency with the same or decreased staffing levels and (2) improved turnaround time for the availability of specimen results.

Volume of current laboratory analyses continues to increase, as does the number of different analytes offered to the clinical staff. A total of 171,585 specimens were processed during the 95-96 fiscal year, an increase of 6.6% over the previous year.

Barry G. England, Ph.D.
Director

CLINICAL MICROBIOLOGY/VIROLOGY LABORATORIES

DEPARTMENT OF PATHOLOGY
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I. CLINICAL ACTIVITIES:

The laboratories experienced a modest (2.9%) increase in specimen volume compared to fiscal year 1994-95. Efforts were made to decrease specimen volume for certain tests such as bacterial antigen testing and urinary CMV culture in cooperation with the appropriate clinical services. Other tests such as antibiotic susceptibilities, fecal cultures and viral serologies increased in volume. Several new tests were introduced resulting in a decreased number of tests that were being sent out to reference laboratories, including tests for *Helicobacter pylori* antibody, *Pneumocystis carinii* DFA, ligase chain reaction testing of urine for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* STDs, *Legionella* urinary antigen and, more recently, mec A gene detection in staphylococci using PCR. New instrumentation (Omni-Solus) was introduced in Virology to increase efficiency and testing spectra for viral antibodies and selected antigens. At the request of Pulmonary Medicine, new quantitative procedures were added for specified pulmonary specimens to assist in differentiating contaminating flora from potential pathogens. Other new tests are currently undergoing validation which will further decrease our sendout volume.

Considerable effort was directed toward reaching our CEP goals . This required a considerable amount of cooperation among our staff members while maintaining or improving our lab functions. Also, much time and effort was expended working with PDS and the PCIS team. Fortunately much of this information will be useful for converting to Cerner Version 500.

We continued to focus on Total Quality Improvement tasks by working with various clinical departments on specimen collection and handling issues as well as reporting quality issues. The Microbiology/Virology QI Team completed a multi-year program working with unit 6C to improve specimen quality. We monitored our antibiotic resistance rates for *Streptococcus pneumoniae* and *Enterococcus* spp. and reported these results to the Michigan Community Public Health Agency at the Michigan Department of Public Health as part of a state-wide surveillance program.

II. RESEARCH ACTIVITIES:

The Laboratory completed a multi-center evaluation of the BacT/Alert automated blood culture system for detecting organisms in sterile body fluids other than blood. The system is now being used for this purpose. The results of this study were presented at the ASM General Meeting and will soon be published.

A comparative evaluation of antimicrobic susceptibility testing methods for anaerobes was completed and reported at the same meeting. The E-test methods was found to be comparable to the more cumbersome conventional standard method (agar dilution) and will become our test method.

In cooperation with the UMMC Infectious Disease Section and our Cytology Lab, we evaluated the sensitivity and specificity of a DF monoclonal antibody assay method to detect *Pneumocystis carinii* in induced sputum specimens collected from AIDS patients. This method was found to be superior to cytology for detecting *P carinii* in this specimen type and has been implemented.

We continue to focus on rapid methods to detect *Mycobacterium tuberculosis* in pulmonary specimens. We successfully evaluated the GenProbe TMA system and have implemented the method after it received FDA approval. This method has displaced our in-house PCR method.

Phenotypic detection of methicillin resistance in staphylococci has been an inefficient process. We successfully tested and implemented a PCR method that allows for more rapid and sensitive detection of this form of resistance. We expect this to result in decreased vancomycin usage.

We have assisted residents and staff members from the departments of Pharmacy, Infection Control Services and Internal Medicine by performing culture analysis for their specific projects which have resulted in revised procedures and/or articles submitted for publication. One such project, the contribution of contaminated stethoscopes to nosocomial infections, received a departmental award for best research project.

Several projects are underway to determine the clinical utility of various molecular techniques to detect selected bacterial and viral pathogens in tissues and body fluids. Comparative testing of bacterial isolates to various new antimicrobics is ongoing.

III. ABSTRACTS PRESENTED:

1. Grossman, S., Hankerd, R. and Pierson, C.L.: "Anaerobe E-Test, Agar Dilution and the NCCLS Interpretation Standards." Abstracts, 96th American Society for Microbiology General Meeting, p 58.
2. Bourbeau, P., Riley, J., Heiter, B.J., Master, R., Young, C. and Pierson, C.: "Use of the BacT/Alert for Culture of Sterile Body Fluids Other Than Blood." Abstracts, 96th American Society for Microbiology General Meeting, p 54.
3. Blythe, L.K., Debusscher, J., Hankerd R., and Pierson, C.L.: "Comparison of Amplicor Polymersase Chain Reaction to Syva Direct Fluorescent Antibody Test for Detection of *Chlamydia trachomatis* in Male Urine Specimens." Abstracts, 96th American Society for Microbiology General Meeting, p 6.
4. Varney, G., Zientak, C., Reed, A., Turner, N. and Pierson, C.L.: "Automation of Viral Antibody Tests Utilizing the Gull Solus Omni System." Abstracts, 1996 Clinical Virology Symposium. Clearwater Beach, Florida.

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

MOLECULAR DIAGNOSTICS LABORATORY

DEPARTMENT OF PATHOLOGY
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The Molecular Diagnostics Laboratory continued its growth in activities in 1995-1996. The recruitment of a new Senior Clinical Technologist and a new Medical Technologist were significant factors in the laboratory this year. We are particularly fortunate in our recruitment of Ms. Nahida Akel as Senior Clinical Technologist. Ms. Akel has been in the field of molecular diagnostics for several years in positions at Dianon in Massachusetts, and at the William Beaumont Hospital in Royal Oak. Ms. Akel previously worked at the University of Michigan Medical Center.

The growth of the bone marrow transplant program has led to our bringing up DNA based tests for monitoring bone marrow engraftment by microsatellite analysis. The other tests that we began to offer this year were detection of the Factor V Leiden mutation and apo E genotyping.

We find ourselves under constant pressure to implement new diagnostic tests. Because of our small staff we have limited resources to devote to clinical R & D. This forces us to carefully select those tests we offer. Our position to this point has been to select those assays which we expect to have higher volume demand. Although we have not developed infectious disease testing this year, almost certainly we will move in that direction next year. In the area of infectious disease testing, we decided in conjunction with the Microbiology Laboratory to drop the routine testing of all specimens for M. Tb. By PCR. The decision was taken because we found that very few cases were being detected by PCR that were not detected by conventional acid-fast stains of sputum. If the case mix of patients attending the University of Michigan Medical Center were to alter so that more patients with Tb were being seen here, we would re-consider the decision.

The field is still in need of automation. Delays in getting diagnostic instrumentation approved by the FDA have resulted in a shortage of useful instruments on the market. One of our purchases this year was a capillary electrophoresis instrument which we intend to use for microsatellite analysis.

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 1995-1996:

- Readjustment of Phlebotomy and Central Distribution services providing the same services with fewer employees during the hiring freeze of November 1995 to June 1996 due to attrition. No services were cut during this time.

- 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 two phlebotomists to one phlebotomist. Approximately 82 patients are drawn in one day.

- 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 1996, 742,010 tests were entered, creating a revenue for the hospital of over 2.8 million dollars.

- Supporting the MCare off sites for blood drawing and bench testing back up with the development of an on-call system for phlebotomists working also in the inpatient setting.

- Cyclosporin specimens drawn outside the hospital are now received in Central Distribution instead of the transplant offices. These specimens come without requisitions. Information for handling these specimens must be obtained from the transplant office.

- Drawing the average of eight patients from children/adolescents at the Hawthorn Center in Northville Township two days per week, was started July, 1995. Stat service is provided 24 hours/day, seven days/week.

- MCare specimens increased from approximately 9600 patients for the month of July, 1995 to 10,731 for the month of June, 1996.

- 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 inhouse downsizing of number of tests offered. Billable tests for the 1996 fiscal year was 29,438, up from 1995 fiscal year of 20,815.

Suzanne Johnson

GENERAL PATHOLOGY

ELECTRON MICROSCOPY SERVICE

DEPARTMENT OF PATHOLOGY
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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.

This past year there has been a continuing major effort to maintain the low turnaround time required to complete specimens. Using the successful changes implemented last year, the turnaround time has routinely been within departmental guidelines (seven working days for completion of prints for kidney, 14 days for all other cases).

We are attempting to upgrade the present Zeiss electron microscope by installing a digitizing camera interfaced with the scope, and a laser printer. This will further decrease turnaround time since most cases will be capable of analysis using the laser prints, rather than using the labor intensive process of printing the film images. The EM staff have already evaluated several electron microscopes, and have found the quality to be very satisfactory. We have also explored the option of using the services of the Department of Anatomy and Cell Biology, but there are significant questions concerning that proposal.

The following table indicates the activity of the EM Service. The column "submitted" indicates the number of specimens submitted, to the lab. The column "semi-thin" 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. It should be noted that the Department of Pathology was reimbursed for all of the research cases.

	Submitted	Semi-thin	Thin/Scope
Neuro	275	143	95
Renal	276	254	219
Other	35		25
Research	8	8	7
Total Cases	594	430	340

There has been a 12% increase in activity on the EM service. This table provides a breakdown of the types of cases and change from last year. It would appear that we will have another increase this year based on the volume of material submitted to date.

	1995	1996	Increase # of cases
Neuro	252	275	+ 23 (9%)
Renal	256	276	+ 20 (8%)
Other, including research	23	43	+ 20 (87%)
Total Cases	531	594	+ 63 (12%)

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

M-LABS

DEPARTMENT OF PATHOLOGY
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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.
   - 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.
   - Reduced 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 USML as the primary 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 this fiscal year 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 able to deal with the support of existing clients as well as marketing to new clients, especially the previously neglected area of group practices and physician's offices. Operations functions are now being addressed in a more coordinated fashion. The operations manager has developed a Unit Orientation Manual outlining departmental policies and procedures and has developed a Client Manual which lists all the specific information for each individual client. The M-Labs office has been reorganized. Problems with our report formats have been ameliorated by changes in format accomplished with the assistance of Pathology Data Systems and individual laboratory personnel.

III. GROWTH:

- CP client billing net revenue increased 23% over FY 95.
- CP third party payor billing increased 344% over FY 95.
- AP surgical pathology cases increased by 16% over FY 95.
- Billing for these AP cases increased by 22%.

New MLabs accounts during FY 96 include:

- Hurley Medical Center - 500 bed hospital located in Flint, Michigan.
- Community Health Center of Branch County - 130 bed hospital in Coldwater, Michigan.
- Eastern Michigan University Health Center - Ypsilanti, Michigan.
- Several large group practices and individual physician's offices.
- Lost - one large group practice (because of difficulties with TAT, reporting format, and differences in test profiles from those desired by that physician group.

IV. INTERFACES:

Support of our efforts by Pathology Data Systems this fiscal year has been superb. We have achieved our first fully operational interface between the University of Michigan laboratory computer system and Mount Clemens General Hospital's laboratory computer. Two others are under development and two more are planned.

V. MANAGED CARE CONTRACTS:

We have succeeded in contracting with M-Care to provide outpatient laboratory testing for its soon-to-be introduced Medicare Product. We are subcontracting the work to a group of hospitals. M-Labs will manage the revenue distribution to the subcontractors based on the relative-value weighted volume of testing furnished by each provider. We will also be involved with quality assurance for the contracted services. We will gain a small management fee and considerable experience and standing in the laboratory managed care arena. It is our goal to ultimately contract with M-Care for the outpatient laboratory services of its main product which would be provided for by a network or networks of hospital laboratories who also provide the rest of the care for their subscribers.

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 been accepted for membership in JVHL, a network of major hospital laboratories in the Detroit area. 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 are actively pursuing the possibility of joining a developing 13 hospital laboratory network in the Central Michigan area where a significant portion of our client base is located.

VII. PROSPECTS:

This fall we will begin providing reference laboratory service to Botsford General Hospital and Eaton Rapids Hospital. The Toledo Hospital and Flower Hospital have merged and M-Labs has submitted a proposal for the reference laboratory work of these institutions. If our bid is successful, there will be a significant increase in revenues generated from that region. M-Labs efforts in Northern Ohio also include a proposal to St. Lukes Hospital and a proposal in preparation to Defiance Hospital, both located in the northern area of that state.

VIII. CLINICAL TRIALS LABORATORY TESTING:

There has been slow growth in the volume of work generated from a local large pharmaceutical firm. We plan on developing contact with other pharmaceutical firms and clinical research organizations to increase our currently very small market share in this field. We received our first request for proposal from a clinical research organization and hope to increase our contacts in this area.

IX. IMPEDIMENTS TO GROWTH:

- **External:**

- Revenues can be expected to decrease from:
  - Increased penetration of managed care.
  - Continued erosion of pricing.
  - Outpatient DRGs.

- **Internal:**

- Maintaining a broad test menu and rapid turnaround times in spite of internal demands for cost reduction.
- Accessioned tests have increased by 20,000 tests over FY 95 but the accessioning staff has been reduced. There are no plans as yet, to address the increased testing due to arrive soon from Botsford Hospital and Eaton Rapids, and from other clients should our proposals to Promedica, or St. Lukes Hospital 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. The M-Labs group believes that the success of the outreach effort is necessary for the continued viability of the hospital clinical laboratories. Although some faculty and staff are anxious to help and plan for growth of the outreach, others seem unwilling to do anything extra to accommodate the extra concerns and needs of "external" clients. This lack of commitment makes the addition of each new client more of a strain on the M-Labs marketing and operations teams than it needs to be and hinders our ability to market the services of the hospital clinical laboratories. We will be better able to accomplish our goals if we can concentrate on external marketing rather than on changing the corporate culture in the labs. The importance of outreach should be emphasized in the Pathology Department and the Clinical laboratories and contributions to our outreach effort should be recognized in performance evaluations of staff and faculty.
- 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 to participate in M-Care's newly developed Medicare product. This puts our relationship with these clients at risk.
- M-Care's relationship with Michigan Capital Medical Center (Columbia HCA) Health System in Lansing, Michigan and lack of participation of Sparrow Hospital and other small hospitals in Central Michigan has put one-third of our client base at risk. (M-Care may not have had a choice in this case.)

Eugene M. Silverman, M.D.
Director, M-Labs Program

PATHOLOGY DATA SYSTEMS

DEPARTMENT OF PATHOLOGY
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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 1995 through June 1996:

Improvements in daily operational support to the clinical laboratories

- Improved the system downtime record from last year to the current performance of less than 1% downtime, calculated on a 7/24 basis.
- Modified the PDS Help Desk rotation with participation by more PDS personnel. This change necessitated PC cross-training which will enhance the effectiveness of the unit as V. 500 of PathNet is installed which is a client-server architecture with a PC user-interface.
- The Cerner WPLink was replaced by the APLink/Word application which is a superior product with fewer training barriers.
- Anatomic pathology statistics are now being gathered on an ongoing basis and entered into a Microsoft Access database, enabling accurate workload and TAT measurements for the division for the first time.
- The on-call policy for PDS was revamped as part of the CEP effort in the unit, requiring three additional personnel to be trained in PathNet on-call operations.
- The DNA database application for the Tissue Laboratory was activated.

Interface engine (hub) enhancements and deployment of new interfaces to foreign systems

- Implemented an HL7 interface between the enterprise interface engine (hub) and the current version of PathNet. This is strategically important because it will avoid the development of complex and costly point-to-point interfaces in the future.
- Extensive work was performed on an interface with the Mayo reference laboratory that will save Central Distribution and the Blood Bank several hours of work per day in the manual data entry of Mayo reference laboratory results.

PathNet enhancements, upgrades, and preparation for V. 500 of the software

- Extensive training and system design in preparation for the installation of V. 500 of Cerner PathNet in the Fall of 1997. V. 500 of PathNet will utilize a modern client -server architecture and allow for the deployment of a web-base system for viewing laboratory results enterprise-wide and by MLabs clients.
- Implemented security measures for Window NT servers and also deployed software for the automated installation of Windows NT software. Extensive training on the Windows NT operating system was also completed by 10 personnel. in PDS. This is in preparation for the installation of V. 500 of Cerner PathNet.

M-Labs-related activities

- Implemented an HL7 based interface between the hospital interface engine and Mount Clemens General Hospital, an important Mlabs client.
- Database synchronization is nearly complete for two MLabs clients, Bottsford and Hurley Hospitals, in anticipation of the installation of host-to-host interfaces to the two sites. One of these two interface will require a very creative conversion of HL7 to ASTM data, two entirely different interface protocols.
- Completed a series of major format changes for presenting test results to MLabs clients.
- Installed 12 new remote printers at MLabs sites.
- Installed a FAX server on PathNet so that test results can be automatically transmitted to MLabs clients.

Web-based initiatives

- Developed a prototype web-based data browser that was then presented to Cerner development personnel. This prototype will be used by Cerner as a model for the creation of a viewer for test results in V. 500 of PathNet.
- Worked in collaboration with MCIT developmental personnel to integrate the browser development in pathology with similar activities relating to the browser to be used in conjunction with the clinical data repository.
- Developed PathNet linkage to the departmental web site to disseminate antimicrobic susceptibility data for the institution

Enterprise-wide information technology activities

- Participated in the planning, implementation and validation of the clinical data repository (CDR) to which test results will be replicated from the PathNet database to achieve integration with clinical, administrative, and financial information.
- PDS personnel worked actively with the DEC/Alpha consortium, culminating in the installation of two large DEC Alpha CPUs connected to the FDDI network in the hospital. The Alpha system used by the department of Internal Medicine's alpha physically located in the PDS machine computer room

Educational and committee activities

- The fourteenth annual symposium of automated information management in the clinical laboratory (AIMCL) was presented at the Power Center last June. More than 40 vendors attended the meeting and about 280 paid registrants. Two two-hour sessions were broadcast as audioconferences to 50 training programs in pathology and 90 CLMA chapters on the first two afternoons of the plenary conference.
- PDS personnel hosted a meeting of the Cerner Great Lakes Regional User Group at the Towsley center in November, 1997

Bruce A. Friedman, M.D.
Laboratory Director

PATHOLOGY EDUCATION OFFICE

DEPARTMENT OF PATHOLOGY
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1 JULY 1995 - 30 JUNE 1996

The Department of Pathology continues to offer a number of diverse programs within the Medical School, Dental School, School of Public Health, College of Literature, Science and the Arts, and the Rackham School of Graduate Studies. These include: courses requiring formal lecture and laboratory exercises, senior medical student Pathology clerkships, and research training for undergraduate, graduate and medical students, as well as postdoctoral fellows. Within the Medical Center, Departmental teaching activities extend not only to medical students but also house officers and the staff of 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 Canadian Academy of Pathologists (USCAP).

I. MEDICAL AND DENTAL STUDENT PROGRAMS:

Department faculty continue to fulfill significant teaching and leadership roles in the medical school curriculum. Multiple faculty within the Department have teaching responsibilities in both the first and second year courses and sequences including: Molecular and Cell Biology, Histology, Host Defense, Introduction to Pathology, and each of the second year organ system sequences including 46 pathology laboratories. In addition, faculty serve as directors and co-directors of several first and second year courses while Dr. Joseph Fantone serves as Director of the first and second year curriculum. The Department offers four elective clerkships to fourth year students with approximately 30% of each class electing at least one of the clerkships. Overall, formal student evaluations of faculty teaching throughout the medical curriculum have noted it to be excellent.

The summer clinical program for underrepresented minority medical students continues to attract between eight and ten students annually. The goal of this program is to provide medical students, who have completed their first year, the opportunity to participate in departmental clinical activities and promote the integration of basic science studies with patient-oriented clinical problems. In addition, it is hoped that the early exposure to the multiple opportunities available in Pathology will encourage students to consider careers in the specialty. Formal evaluations indicate that the program is viewed very positively by the students and has been successful in encouraging one to two students per class to chose pathology for their residency training.

The Department of Pathology continues to have primary responsibilities for the teaching of general and systemic pathology to dental students. This includes the presentation of formal lectures (Pathology 630) and preceptors of laboratory sessions (Pathology 631). Formal student evaluation indicates that the course functions smoothly and is well received by the students.

II. DOCTORAL PROGRAM:

The Graduate Program in Pathology, which was initiated seven years ago currently has eight students enrolled. The primary goal of the Doctoral Program in Pathology is to train individuals for careers as independent scientific investigators with a focus on the study of the cellular and molecular basis of disease processes. Five graduate level courses are offered by the Department. Four students are enrolled in combined M.D./Ph.D. programs and five students have achieved candidacy status. Four students have received their doctoral degree since the programs reactivation in 1989. One student received the prestigious Experimental Pathologist in Training Award from the American Society of Investigative Pathology this past year. An Immunopathology Training Grant within the Department provides support for both graduate students and postdoctoral fellow training.

III. GRADUATE EDUCATION:

The Department of Pathology provides formal advanced training to M.D.'s and Ph.D.'s through the Residency Training Program, clinical fellowships and postdoctoral research fellowships. These programs are integrated to provide trainees the greatest opportunity for clinical and research training in their chosen discipline and to foster academic excellence.

Clinical Fellows:

The Department provides advanced training in surgical pathology, cytopathology, hematology, neuropathology and transfusion medicine through formal fellowship programs. Three positions are currently supported with the clinical fellowships closely integrated with the Residency Training Programs (see Anatomic and Clinical Pathology Sections).

Postdoctoral Research Fellowships:

The Department of Pathology provides advanced research training for approximately 40 postdoctoral fellows which includes Pathology residents seeking training in experimental pathology. Fellows are located within the faculty research laboratories of the Department. Support is provided by an NIH-funded Lung Immunopathology Training Grant (HL-07517, P.A. Ward, Principal Investigator), an Immunopathology Training Grant (NIH AI-07413, R. Miller, Principal Investigator), and externally funded faculty research grants.

Residency Training:

The Department offers resident training in both anatomic and clinical pathology with opportunities to pursue basic research training in experimental pathology. The program continues to be exceedingly competitive with over 100 completed applications received, and 32 candidates invited to interview in the Department this past year. Five outstanding residents were recruited to the Department: Mariko Suchi, M.D., Ph.D., Rachael Vidal, M.D., Luzette Kuizon, M.D., Peter Lucas, M.D., Ph.D., and Christine Petricek, M.D.

Currently, there are 25 residents in the Department, 23 of whom are receiving training in both anatomic and clinical pathology and two receiving training in anatomic pathology. A significant number of residents continue to be involved in both clinical and experimental research projects which have resulted in the presentation of their work at national meetings, as well as publications in peer-reviewed journals. Six residents graduated from the program this past year. Three assumed positions as staff pathologists at large community hospitals in Michigan, Arizona, and Texas. Three residents are continuing training, in a Chemistry and Informatics Fellowship (University of Michigan), a Neuropathology Fellowship (Massachusetts General Hospital), and a Renal Pathology Fellowship (University of Michigan).

I. Courses in the Medical Curriculum:

A. First year courses:

1. Molecular and Cell Biology.
2. Host Defense.
3. Introduction to Pathology.
4. Histology.
5. Multidisciplinary conferences.

B. Second year organ system sequences.

C. Fourth year clinical clerkships:

1. General Pathology.
2. Laboratory Medicine.
3. Special Topics in Pathology.
4. Pathology Research.

D. Summer Clinical Program in Pathology for Underrepresented Minority Students.

II. Courses in the Dental Curriculum:

A. Pathology 630: General Pathology Lectures (45 contact hours).
B. Pathology 631: Pathology Laboratory.

III. Graduate Courses in Pathology:

A. Pathology 580: General Pathology for Biologic Scientists.
B. Pathology 581: Cellular and Molecular Basis of Disease.
C. Pathology 620: Genetics and Cell Biology of Aging.
D. Pathology 850: Research Colloquium.
E. Pathology 599: Non-Dissertation Research.
F. Pathology 990: Pre-Candidate Dissertation Research.
G. Pathology 995: Candidate Dissertation Research.

IV. Postgraduate ;Medicine/Continuing Medical Education:

A. Current Topics in Blood Banking Symposium, June, 1996.
B. Clinical Laboratory Computers Symposium, June, 1996.
C. Pathology 858: Neuropathology.

V. Clinical Conferences:

The Department of Pathology provides an important educational service to many other clinical departments through regular participation in interdepartmental working/teaching conferences. The Department is involved in many such conferences on a weekly, biweekly, and monthly basis. The unites served include:

Internal Medicine

- Gastroenterology
- Nephrology
- Hematology/Oncology
- Nuclear Medicine
- Pulmonary Medicine
- Cardiology
- General (Necropsy Review, CPC)

Pediatrics

- Cardiology
- Oncology
- Gastroenterology
- General (Mortality Conf., CPC)

Dermatology

Obstetrics and Gynecology

Thoracic Surgery

Oral Surgery

Urology

General Surgery

Otorhinolaryngology

Joseph C. Fantone, M.D.
Director, Educational Program

DEPARTMENT OF VETERANS AFFAIRS MEDICAL CENTER
PATHOLOGY AND LABORATORY MEDICINE SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

I. INTRODUCTION:

The Department of Veterans Affairs Medical Center (VAMC) is a Dean's Committee tertiary health care provider for veterans, affiliated with the University of Michigan. The VAMC Pathology and Laboratory Medicine Service maintains a close relationship with the University of Michigan 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 are currently filled and the fourth is slatted for filling in October, 1996. Three resident training positions have been maintained at the VAMC for university pathology residents. They 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, is a voting member of the Dean's Committee. During this reporting period the full laboratory was inspected by the College of American Pathologists and received full accreditation. The VA Medical Center is inspected by the Joint Commission 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. Data storage for all components of pathology and the clinical laboratories contains full patient information for more than a decade.

II. ANATOMIC PATHOLOGY:

A. **Surgical Pathology:** 4,536 surgical pathology cases have been accessioned and reported during this period of time. The resident assigned to surgical pathology, usually a first year resident, acts as coordinator of the section and in that capacity has the opportunity to examine all of the specimens grossly and microscopically under close one-to-one supervision by the staff pathologist. The resident interacts with the clinical 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 Anatomic Pathology, including regular consultations with the Armed Forces Institute of Pathology, University of Michigan, and other outside consultants. There is extensive review and analysis of frozen sections, amended diagnoses, surgical appropriateness, turnaround times and follow-up of positive diagnoses, within the medical center. The surgical and cytology readout stations are fully integrated into a

hospital digital imaging system. Routine images are captured on cases of interest. These are particularly useful in presentations to clinical teams reviewing specimens from their patients with the pathology staff and residents.

B. **Autopsy Pathology:** 47 autopsies were performed during this year; that is a rate of approximately 28% 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:** 2,325 cases were examined and diagnosed during this period. This is an increase of 132 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 to cytology within the VAMC, the cytological material is readily available and is used as correlative information for surgical and autopsy pathology. This laboratory is a "Center of Excellence" in cytology.

D. **Electron Microscopy:** 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 biweekly electron microscopy seminars at the University of Michigan. This VAMC is a "Center of Excellence" in electron microscopy and serves as consultant to other VA Medical Centers, to the University of Michigan Medical Center and to other hospitals by contact.

III. CLINICAL PATHOLOGY:

During the period of this report 887,605 clinical pathology procedures were done in the laboratory. In Chemistry there were 726,858; in Hematology 112,809; in Microbiology 28,322; and in Blood Bank 19,616. 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 other 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 entire staff participate in the laboratory and lecture portions of the second year medical students at the University of Michigan. Lectures in bone pathology are also given to the dental students. The VA staff also participate in other ad hoc lectures and in a moderate number of seminars for the resident staff, most often given at the University of Michigan. Both Drs. Beals and 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 for four years in October, 1993. 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 participate in various clinical studies and collaborate with a variety of investigators. The laboratory in general serves the VAMC research program by providing considerable technical support for clinical research and, in some cases, for more basic research in both anatomic and clinical pathology. The staff also serves as consultants and advisors for a number of research programs. Dr. Peter Brawn 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. Lee Weatherbee, who had been the Chief of the Service for 30 years died. In the interim Dr. Beals is serving as acting Chief. 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 the 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 the 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 for the Diagnostic Service Strategic Healthcare Group in this capacity, serving as the leader of the Veterans Health Administration Headquarter's administrative 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 at 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.

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 in patient care. All staff members are privileged and evaluated in accordance with their training, experience, continuing education and participation in high 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

FINANCE AND ADMINISTRATION

DIVISION OF FINANCE AND ADMINISTRATION

DEPARTMENT OF PATHOLOGY
ANNUAL DEPARTMENTAL REPORT
1 JULY 1995 - 30 JUNE 1996

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

B. ADMINISTRATIVE SUPPORT CENTER - MEDICAL SCHOOL ACTIVITIES:

David R. Golden, Clinical Department Associate
John E. Harris, Administrative Assistant

C. OFFICE OF RESEARCH AND EDUCATION ADMINISTRATION:

Maydis Caldwell Skeete, Research and Education Administrator
Susan M. Hunter, Student Services Assistant

D. OFFICE OF THE CHAIRMAN

Laura D. Blythe, Staff Assistant
Mary Anne Tishma, Staff Assistant

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. Mrs. Mary Anne Tishma has announced that she will retire effective 31 August 1996 after 38 years of service.

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). Our RCG mandated staff reduction, based upon MECON data, was 96.8 FTEs - equal to $3,150,000. In addition to this figure, we were required to meet a CEP reduction of $1,051,000. This involved a major restructuring of our laboratory system. Mr. Morrow is responsible for analyzing the MECON data for comparison of our laboratory productivity with similar academic institutions. This tool was used by Departmental Administration to develop and implement a plan to reduce costs. Key administrative support staff, 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 which underwent major reorganization with the implementation of the Cost Efficiency Program.

Billing Coordinator: This individual, Ms. Nancy Coray, is responsible for auditing all laboratory charges, 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 Hospital paid 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.

ADMINISTRATIVE SUPPORT CENTER/MEDICAL SCHOOL ACTIVITIES:

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 (with the exception of sponsored research); professional fee billing operations; general funds and teaching and administration funds; departmental renovation and remodeling; and management of the Word Processing Center.

The impact of the CDS was substantial to this unit's operation. In March 1996, the PPFBO (back end functions) became part of the CDS centralized billing department. Two of the four billing clerks were relocated to the new facility. The two remaining clerks were assigned other duties and responsibilities and are now concerned with charge capture for all professional fees. They also capture all technical fees for Hospital and MLabs patients.

The Pathology Wing of the Medical Science I Building was rekeyed in September 1995. The planning and distribution of keys for this project was handled by the administrative staff in this unit. In addition, the installation of a new HVAC unit necessary to augment the present building system was coordinated in this unit and completed in July 1995.

OFFICE OF RESEARCH AND EDUCATION ADMINISTRATION:

This unit, managed by Mrs. Maydis Caldwell Skeete assists the Chairman, Administrator and Principal Investigators with the business and administrative functions associated with our sponsored research and education programs. 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 the responsibility of 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.

In addition, 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.

SUMMARY OF FINANCIAL DATA:

1. Grants and Contracts:

128 active grants, contracts and other accounts

Total Direct Expenditures:	$ 6,323,397
Indirect Research Expenditures:	$ 2,430,609
Total Sponsored Projects:	$ 8,754,006

2. Faculty Group Practice Plan - Pathology:

15,352 active accounts (average number)

Number of charge entries:	106,655
Gross Billings - Anatomic and Clinical Pathology:	$ 15,169,777
Net Collections - Anatomic and Clinical Pathology:	$ 5,354,064
Part A Payment:	$ 2,572,667
M-Labs Transfer:	$ 731,225

3. Pathology Laboratories:

Number of fee code procedures:	2,466,586
Number of billed tests reported to MECON:	2,426,029
Total Gross Revenue - Pathology Laboratories:	$122,307,130
Total Direct Expenses Pathology Laboratories:	$ 38,001,610

Eugene J. Napolitan
Administrator