THE UNIVERSITY OF MICHIGAN

Department Of Pathology

ANNUAL REPORT

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

1 July 1991 - 30 June 1992

THE UNIVERSITY OF MICHIGAN

Department Of Pathology

ANNUAL REPORT



1 July 1991 - 30 June 1992

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
Barnes, Barbara A.	Assistant Professor	The University of Michigan
Barr Jr., Mason+	Professor	The University of Michigan
Beals, Theodore F.	Assistant Professor	Veterans Administration Medical Center
Blaivas, Mila I.	Clinical Assistant Professor	The University of Michigan
Bonadio, Jeffrey	Assistant Professor	The University of Michigan
Capps, Rodney D.	Assistant Professor	The University of Michigan
Chensue, Stephen W.	Assistant Professor	Veterans Administration Medical Center
Courtney, Richard M.*	Assistant Professor	The University of Michigan
Crockett-Torabi, Elahe	Assistant Research Scientist	The University of Michigan
D'Amato, Constance J.	Assistant Professor	The University of Michigan
Davenport, Robertson	Assistant Professor	The University of Michigan
de la Iglesia, Felix**	Adjunct Research Scientist	Warner-Lambert;Parke Davis
Del Buono, Elizabeth	Assistant Professor	The University of Michigan
Dixit, Vishva M.	Associate Professor	The University of Michigan
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
Flint, Andrew	Associate Professor	The University of Michigan
Frank, Thomas S.	Assistant Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Friedman, Bruce A.	Professor	The University of Michigan
Giacherio, Donald	Assistant Professor	The University of Michigan
Gikas, Paul W.	Professor	The University of Michigan
Gordon, David	Associate Professor	The University of Michigan
Hanks, Carl T.*	Associate Professor	The University of Michigan
Hanson, Curtis A.	Assistant Professor	The University of Michigan
Headington, John T.	Professor	The University of Michigan
Heidelberger, Kathleen P.	Professor	The University of Michigan
Hendrix, Robert C.	Professor Emeritus	The University of Michigan
Hicks, Samuel P.	Professor Emeritus	The University of Michigan
Hinerman, Dorin L.	Professor Emeritus	The University of Michigan
Johnson, Kent J.	Professor	The University of Michigan
Judd, W. John	Professor	The University of Michigan
Killen, Paul D.	Assistant Professor	The University of Michigan
Kunkel, Steven L.	Professor	The University of Michigan
Lindsten, Tullia	Assistant Research Scientist	The University of Michigan
Lloyd, Ricardo V.	Professor	The University of Michigan
Lowe, John B.	Associate Professor	The University of Michigan
McClatchey, Kenneth D.	Professor	The University of Michigan
McKeever, Paul E.	Associate Professor	The University of Michigan
Midgley, A. Rees	Professor	The University of Michigan
Miller, Richard A.	Professor	The University of Michigan
Mitra, Raj S.	Assistant Research Scientist	The University of Michigan
Naylor, Bernard	Professor	The University of Michigan
Nickoloff, Brian J.	Associate Professor	The University of Michigan
Nunez, Gabriel	Assistant Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Oberman, Harold A.	Professor	The University of Michigan
Phan, Sem H.	Associate Professor	The University of Michigan
Pierson, Carl L.	Assistant Professor	The University of Michigan
Rachmaninoff, Nikolai	Lecturer	The University of Michigan
Rasche, Rodolfo	Lecturer	The University of Michigan
Remick, Daniel G.	Assistant Professor	The University of Michigan
Repola, Kenneth L.	Lecturer	The University of Michigan
Ross, Charles W.	Lecturer	The University of Michigan
Rowe, Nathaniel H.*	Professor	The University of Michigan
Schmidt, Robert W.	Professor Emeritus	The University of Michigan
Schnitzer, Bertram	Professor	The University of Michigan
Selvaggi, Suzanne M.	Assistant Professor	The University of Michigan
Shanberge, Jacob N.	Clinical Professor	William Beaumont Hospital
Sheldon, Susan	Assistant Professor	The University of Michigan
Shope, Thomas C.+	Associate Professor	The University of Michigan
Silverman, Eugene M.	Clinical Associate Professor	The University of Michigan
Sima, Anders A.F.	Professor	The University of Michigan
Smolen, James E.+	Assistant Research Scientist	The University of Michigan
Stoolman, Lloyd M.	Associate Professor	The University of Michigan
Till, Gerd O.	Professor	The University of Michigan
Varani, James	Professor	The University of Michigan
Ward, Peter A.	Professor and Chairman	The University of Michigan
Warren, Jeffrey S.	Assistant Professor	The University of Michigan
Weatherbee, Lee	Associate Professor	Veterans Administration Medical Center
Weiss, Bernard	Professor	The University of Michigan

Name	Rank	Institutional Affiliation
Weiss, Sharon W.	Professor and Director, Anatomic Pathology	The University of Michigan
Wolter, J. Reimer++	Professor Emeritus	The University of Michigan
Yabkowitz, Rachel	Assistant Research Scientist	The University of Michigan

* Joint Appointment, Dental School
** Clinical Appointment, Warner-Lambert, Parke Davis
\+ Joint Appointment, Department of Pediatrics and Communicable Diseases
++ Joint Appointment, Department of Opthalmology



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DEPARTMENTAL OVERVIEW

DEPARTMENTAL OVERVIEW
1991/92

Events and initiatives of the past year have had important impacts on the Department of Pathology. In the area of **education**, perhaps the most visible institutional event has been the introduction of the new Medical School curriculum which especially impacts on the first two years of Medical Student education and will result in a fundamental change in the manner by which Pathology is taught. The format entails a shift from the departmental block-type teaching to a broadly integrated "subject committee" type of presentation, emphasizing organ system pathology, physiology, biochemistry, etc. The new curriculum also involves diminished numbers of formal hours of interaction (e.g. lecture) as well as a better integration of the curriculum. On behalf of the Department of Pathology, Drs. Gerald Abrams and Joseph Fantone have major roles in development and coordination of the new curriculum. The graduate program in Experimental Pathology appears to be moving ahead on schedule and currently has eight graduate students (including two Medical Scientist Training Program individuals). The success in attracting MSTP students to the Department of Pathology is an important goal that is becoming increasingly recognized. The Department of Pathology has consistently been recognized for its excellence in the area of teaching at all levels within the institution, and this tradition can be expected to continue.

With respect to **clinical service**, this past year has had its share of challenges. The three issues most directly affecting the Department all deal with reimbursement and include imposition of the resource based/relative value scales (RB/RVS), a federally implemented schedule of reduction in professional fees in Pathology (as well as in other clinical disciplines). Since Pathology part B fees in the State of Michigan have historically been very low, the impacts of the RB/RVS system are so far marginal. A matter of considerable concern was the decision by Michigan Blue Shield in Spring, 1992, to reduce part B payments to pathologists by a mean of 8.5% in the State of Michigan. The Department is actively engaged in efforts to seek reversal of this initiative. Finally, we continue to struggle with a Hospitals-mandated successive and additive 6.5% cuts in the operating budget for each of four years. The operating budgets of the Clinical Laboratories have been trimmed to date by somewhat more than 2.4 million dollars. The Hospitals budget-based operations in the Department seem at present to be operating in a very lean fashion. Further reductions will inevitably require substantial decrements in available Clinical Laboratory services, to the point of affecting lengths-of-stay and specimen turn-around times.

An important initiative in the Clinical Pathology Division has been the program designed to reduce unnecessary use of blood products. Drs. Hanson, Davenport, Oberman and Friedman, working with Drs. Todd and Yamada in the Department of Internal Medicine, have developed criterion maps that must be filled out before the elective ordering of blood products. The purpose behind this program is to encourage physicians to be more judicious in the ordering of blood products. It is our hope that this program, which is being initially targeted in Medical Oncology, can be expanded to include all blood product usage and that such a program will result in significantly reduced utilization of blood products. The magnitude of this challenge cannot be underestimated, because it entails behavior modification in Medical attendings, house officers, and even medical students and nurses. This initiative is a very important one, success in which can be translated into many other areas of clinical activity (e.g. imaging, pharmacy, etc.).

A major change in the Division of Clinical Pathology in the Fall of 1991 was the naming of Dr. Curtis A. Hanson as Division Director. Dr. Hanson took over the duties from Dr. Kenneth D. McClatchey, whose service as Division Director for almost a decade greatly strengthened the Department. As part of the reorganization changes, Dr. Hanson has named Dr. Jeffrey S. Warren as Associate Director of the Division. This new administrative alignment has, among other things, resulted in the consolidation both administratively and geographically of Clinical Chemistry, Toxicology, and Immunology. These changes should make the new unit a very strong and highly efficient clinical

operation. Similar charges are underway in the area of cytogenetics. We continue to develop the area of Molecular Diagnostics, which bridges both Anatomic and Clinical pathology and is increasingly becoming an important departmental and institutional function. The Division of Anatomic Pathology continues to be a strong and widely respected unit, very capably directed by Dr. Sharon W. Weiss, who has just completed four years at the helm of this important Division. It should also be noted that the Residency Program is recruiting excellent house officers, the success probably being the reflection of the Department's broad strengths in service, teaching and research. The Surgical Pathology, Cytopathology and Hematopathology Fellowships continue to draw excellent individuals to our programs.

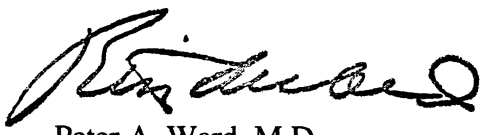
Research programs in the Department continue to prosper, the total (direct and indirect) incomes to the Department and institution being approximately $6,726,165 per annum. This also includes the recent award of a Program Project dealing with "Oligosaccharides as Antiinflammatory Agents". The breadth of the research programs in the Department of Pathology is reflected not only in the very strong intradepartmental research efforts but also by the key role that pathology faculty members play in other activities such as the Comprehensive Cancer Center, Renal Center, Diabetes Research and Training Center, Multipurpose Arthritis Center, Pulmonary Specialized Center of Research.

There are a few events worthy of note. As a result of the June, 1992, Department Retreat, which was very effectively developed and directed by Dr. Joseph C. Fantone, it became clear that a problem existed with respect to faculty development and the understanding of how the promotion system is defined and operates. To this end, after careful discussions the Department has put into place a system of annual review of all faculty members, featuring verbal as well as written communication regarding academic development. This process involves a key role for Division Directors who work closely with the Department Chair. In addition, the Department has developed a detailed document which outlines the criteria for appointment and promotion in each of the appointment tracts. Criteria for tenure nomination are also spelled out. By the publishing of these criteria as well as an annual review of the performance of each faculty member, this should result in a strengthening of our faculty. Also discussed in the Chairman's Advisory Committee as a follow-up to the June Retreat were additional issues, decisions for which will be formulated in the current calendar year.

It should also be noted that the Department is working in close alliance with the A. James French, M.D., Society in a fund raising effort to develop an Endowed Professorship in Dr. French's name. These efforts are being done in cooperation with the University's "Momentum Campaign" which seeks to raise $1 billion in gifts, representing the largest fund raising effort for any State University. As of the early Fall, 1992, the A. James French M.D. endowment account has pledges and contributions of approximately $260,000. We hope that the campaign target of $500,000 will be realized within the year. The intent of the endowment will be to support a position linked to the diagnostic field of pathology, which will reflect the interests of Dr. French when he was Chairman of the Department.

Although there is the constant need to respond to the ever changing environment, especially as this relates to state and federally directed changes in health care reimbursement, the Department is very strong and stands among the top academic Departments of Pathology in North America. There is still much to be done to strengthen the Department in its search for excellence.

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 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Services - 3 1/2 months.
B. Necropsy Service - on call.
C. Pathologist, Cardiac Transplant Team
D. Consultant for Gastrointestinal Pathology
E. Consultant for Cardiovascular Pathology

II. TEACHING ACTIVITIES:

A. Freshman Medical Class:
   1. ICS-500 Sequence Coordinator and Lecturer, "Basic Concepts of Disease" - 20 lecture hours.
   2. ICS 500, 501 - CPC's - 3 contact hours.
B. Sophomore Medical Class:
   1. ICS 600, 601 - CPC's - 3 contact hours.
   2. Pathology 600 - 6 lecture hours.
C. Senior Medical Class:
   1. Pathology Clerkship Mentor.
D. Graduate School
   1. Pathology 580 (Graduate School), Course Director, Lecturer - 36 lecture hours.
   2. Pathology 583 (Graduate School), Course Director, Instructor - 28 contact hours.
E. Hospital Conferences:
   1. Cardiovascular Pathology Conference - monthly.
   2. Internal Medicine CPC - occasional.
   3. Internal Medicine Necropsy Review - monthly.
F. House Officers:
   1. Training in Surgical and Necropsy Pathology.
G. Invited Lectures:
   1. 1992 Family Practice Review, March 18, 1992 - Towsley Center.
   2. Berrien County Medical Society, May 19, 1992.
   3. Student Biomedical Research Program, June 11, 1992.
   4. Northern Michigan Summer Conference, June 22-26, 1992.
H. Honors:
   1. Recognition Award, University of Michigan Learning Disabilities Society.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Evaluation of Cardiac Autonomic Innervation by PET. NIH 1-R01-HL 47543-1
B. SCOR Grant - Occupational and Immunologic Lung Diseases. NIH 1-P50 HL 46487-01.

PROJECTS UNDER STUDY:

A. Pathologic-Radiologic Correlation in Aortic Disease (with W. Williams).
B. Pathologic Aspects of Cardiac Autonomic Innervation (with M. Schwaiger).
C. Microbial Flora in Ulcerative Colitis (with J. Benentt, R. Freter).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

1. Member, Pathology Doctoral Program Committee.
2. Member, Pathology House Officer Selection Committee.
3. Member, Pathology Human Resources Committee.

MEDICAL SCHOOL/HOSPITAL:

1. Member, Historical Center for the Health Sciences Liaison Committee.
2. Member, Hospital Ethics Committee.
3. Member, Inteflex Policy Committee.
4. Member, Curriculum Policy Committee.
5. Director, Component II, Medical Curriculum.
6. Ombudsperson, Medical Faculty.
7. Member, Medical School Advisory Committee on Appointments, Promotions and Titles.

REGIONAL AND NATIONAL:

1. Editorial Board, "Modern Pathology".
2. Deputy Medical Examiner, Washtenaw County.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Williams, D.M., Kirsh, M.M. and Abrams, G.D.: Penetrating atherosclerotic ulcer with dissecting hematoma: control of bleeding with percutaneous embolization. Radiology 1991;181:85-88.
2. Williams, D.M., Marx, M.V., Andrews, J.C., Doenz, F. and Abrams, G.D.: Design and testing of a high-flow autoperfusion catheter: An experimental study. J. Vasc. Intervent. Radiol. 1992;3:285-290.
3. Bates, E.R., Walsh, D.G., MU, D.X., Abrams, G.D. and Lucchesi, B.R.: Sustained inhibition of the vessel wall - platelet interaction after deep coronary artery injury by temporary inhibition of the platelet glycoprotein IIb/IIIa Receptor. Cor. Art. Dis. 1992; 3:67-76.
4. Muller, D.W.M., Topol, E.J., Abrams, G., Gallagher, K. and Ellis, S.G.: Intramural methotrexate therapy for the prevention of neointimal thickening after balloon angioplasty. J. Amer. Coll. Cardiol. 1992, In press.
5. Rosenchein, U., Yakubov, S.J., Gubernich, D., Bach, D.S., Sonda, P.L., Abrams, G.D. and Topol, E,J.: Shock wave thrombus ablation, a new method for non-invasive mechanical thrombolysis. Amer. J. Cardiol. 1992, In press.

6. Punch, M.R., Hubbell, G.P., Elkins, T.E. and Abrams, G.D.: Conservative management of bilateral massive edema of the ovary. J. Reprod. Med. 1992, In press.
7. Schuger, C.D., McMath, L., Abrams, G., Spears, J.R., Boldea, D., Steinman, R.T., Meissner, M.D. and Lehmann, M.H.: Long term effects of percutaneous transcatheter laser balloon ablation (PTLBA) from the canine coronary sinus. _Circulation 1992, In press.

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

1. Abrams, G.D.: Review - "Cardiovascular Pathology", Virmani R, Atkinson JB and Fenoglio JJ. Editors, W.B. Saunders, 1991. Am. J. Surg. Path. 1992;16:428.
2. Abrams, G.D.: Infectious disorders of the intestines, in Ming SC and Goldman H. (eds.), "Pathology of the Gastrointestinal Tract", W.B. Saunders, 1992; 621-642.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Director, Drug Analysis and Toxicology Laboratory.
B. Section Head, Biochemistry Laboratories.
C. Consultant to Veterans Administration Hospital, Ann Arbor, Michigan.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students:
   1. Pathology 600 Course, Case Preparations.
   2. M1 Clerkship, Clinical Chemistry/Toxicology
B. House Officers:
   1. Lecturer, Clinical Pathology Grand Rounds.
   2. Lecturer, Clinical Pathology Didactic Lecture Series.
   3. Daily sign-out and interpretation of Laboratory Results.
C. Graduate Students:
   1. Thesis Committee, Biomedical Engineering.
      Se-Hwan Paek; "An Immunosensor with a Heterobifunctional Enzyme Conjugate as Signal Generator"

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Measurement of Drugs in Saliva. DHHS PHS Phase I Grant. Co-Investigator/Consultant. Allocated Support to Pathology/T. Annesley, $12,000.
B. "Multicenter Randomized Dose Ranging Study Comparing the Safety and Efficacy of OG37-325 Oral Solution to Sandimmune in Renal Transplant Patients". Sandoz Pharmaceuticals 1990-1992. Allocated Support to Pathology/T. Annesley, $63,000.

PROJECTS UNDER STUDY:

A. Metabolism, Analysis, and Therapeutic Effect of OG37-325 (CsG) in Renal Transplant Patients.
B. Distribution of cyclosporine and metabolites in blood and tissues.
C. Measurement of therapeutic drugs using alternative fluids beyond serum.
D. Esoteric analysis of drugs by gas chromatography/mass spectrometry.
E. Microbore Applications to the analysis of drugs.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Drug Analysis an Toxicology Laboratory.
B. M-Labs Technical Group.
C. Pathology Associates.

MEDICAL SCHOOL/HOSPITAL:

A. Standardization of Procedures Committee.
B. Pharmacokinetics Quality Improvement Team.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

OTHER

A. Clinical Chemistry, Reviewer.
B. Mayo Clinic Proceedings, Reviewer.
C. Journal of Clinical Immunoassay, Reviewer.
D. Journal of International Federation of Clinical Chemistry, Reviewer.

E. Biomedical Chromatography, Reviewer.
F. Therapeutic Drug Monitoring, Reviewer.

INVITED LECTURES/SEMINARS:

1. "Kinetic Interaction of Microparticles in Solution (KIMS). The On-Line Drugs Abuse Testing System". Roche Analytical Systems National Seminar, New York, New York, September, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Bolling, S.F., Lin, H., Annesley, T.M., Boyd, J.A., Gallagher, K. and Levy, R.: Local cyclosporine immunotherapy of cardiac transplants in rats enhances survival. J. Heart Transplant. 1991;10:577-583.
2. Schramm, W., Annesley, T.M., Siegel, G.J., Sackellares, J.C. and Smith, R.H.: Measurement of phenytoin and carbamazepine in an ultrafiltrate of saliva. Ther. Drug Monitor. 1991;13:452-460.
3. Annesley, T.M., Matz, K., and Leichtman, A.B.: High performance liquid chromatographic analysis of cyclosporine G (Nva-cyclosporine) in human blood. Ther. Drug. Monitor., In Press.
4. Turgeon, D.K., Normolle, D., Leichtman, A., Annesley, T.M., Smith, D.E., and Watkins, P.B.: Erythromycin breath test predicts oral clearance of cyclosporine in renal transplant patients. Clin. Pharmacol. Therap., accepted for publication.

BOOK CHAPTERS:

1. Annesley, T.M.: "Preanalytical Test Variables". Clinical Laboratory Medicine, Williams and Wilkins, New York, New York, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. General surgical pathology - 5 months.
B. Gastrointestinal and hepatic pathology consultation services - full time.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Medical Students.
   1. Pathology 600 - 8 full class lectures.
   2. Pathology 630 (dental) - 3 full class lectures.
   3. Senior medical student, elective rotation in pathology, supervisor 1 month.
B. House Officers:
   1. Autopsy service tutoring, 1 week
   2. Surgical pathology diagnosing room instruction for assigned house officer - 5 months.
   3. Gastrointestinal and hepatic pathology tutoring - full time.
   4. Mentor for two house officers and three fellows in gastrointestinal and liver pathology subspecialty rotations - 4 months total.
   5. Formal Lectures on GI and Liver Pathology - 3 hours.
C. Interdepartmental:
   1. Medical Gastrointestinal Pathology Biopsy Conference - 2nd and 4th Wednesday of each month.
   2. G-I Tumor Conference - 4th Tuesday of each month.
   3. Liver Transplant Conference - Every other Thursday.
   4. Liver Biopsy Conference - Every other Wednesday.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT: None.

PROJECTS UNDER STUDY:

A. Hepatic histopathologic changes in methotrexate - treated psoriatics, with A. Flint and members of the Gastroenterology Division.
B. Appendiceal epithelial neoplasia.
C. Peptic-associated and Helicobacter-associated gastritis and duodenitis with Grace Elta, Jeffrey Barnett and Tim Nostrant.
D. Interactive Computer Based Diagnostic Program in Colorectal, Appendiceal and Anal Pathology with Bharat Nathwani at USC, plus Intellipath.

E. Thymosin Treatment of Chronic Hepatitis B with Milton Mutchnick
F. Liver Transplantation for Hepatitis B Disease with Mike Lucey, Keith Henley Bob Merion and Dave Graham. (Paper accepted. See below.)
G. Chronic gasritis in Michigan, with Paul Mazzara.
H. The appendix in ulcerative colitis, with John Goldblum (Abstract published; Paper accepted, see below).
I. Morphologic expressions of achalasia, with John Goldblum.
J. PCNA in gastric and duodenal stromal tumors, with John Goldblum and Ric Lloyd.
K. Crohn's disease of the appendix, with Jane Huang.
L. Recurrent autoimmune hepatitis in the transplanted liver, with Michael Lucey and Kyle Carr.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITALS:

A. Member, Cancer Work Group, University Hospital.
B. Member, Tissue and Invasive Procedure Committee, University Hospital.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Short Course, "Inflammatory Conditions of the Esophagus, Stomach and Duodenum",USCAP, Atlanta, Georgia, March, 1992, with D. A. Antonioli.
2. Seminar, "The Biopsied Stomach Need Not Be a Diagnostic Nightmare, Although It Certainly Drives Us Crazy at Times", USCAP Course: Diagnostic Pathology '90, Ann Arbor, Michigan, August, 1991.

3. Lecture, Gastrointestinal Lymphomas Without Rearranging a Single Gene: An Anti-Intellectual Approach. Presented at Fall Meeting of Pacific Northwest Society of Pathologists, Victoria, BC, September 13, 1991.
4. Seminar, Gastrointestinal biopsies that annoy me, and how I decide to deal with them, so I can get on with the rest of my life, Fall Meeting of Pacific Northwest Society of Pathologists, Victoria, BC, September 14, 1991.
5. Lecture: Gastric Polyps and giant folds. Presented at symposium on Advances in the Diagnosis and Understanding of Upper Gastrointestinal Disorders, sponsored by the Gastrointestinal Pathology Society, Annual Meeting, American Society of Clinical Pathologists, New Orleans, Louisiana, September 21, 1991.
6. Lecture, A pathologist's view of the morphologic natural history of the bowel wall in ulcerative colitis. The 5th Annual Kangos Memorial Lecture, Children's Hospital of Pittsburgh, University of Pittsburgh, October 24, 1991.
7. Seminar, Gastrointestinal biopsies that drive me crazy. Connecticut Society of Pathologists, Rocky Hill, Connecticut, November 12, 1991.
8. Visiting Professor, Department of Pathology, Yale University Medical School, University of Connecticut School of Medicine, St. Francis Hospital of Hartford, November 12-13, 1991.
9. Visiting Consultant, Department of Pathology, Beaumont Army Medical Center, El Paso, Texas, February 12-14, 1992.
10. Seminar on problematic GI biopsies, Detroit Society of Pathologists, Detroit, Michigan, February 18, 1992.
11. Lecture: Acute versus chronic colitis. Presented at the Annual Gastrointestinal Pathology Society Meeting, Atlanta, Georgia, March 15, 1992.
12. Lectures: IAP 18th Annual Scientific Meeting, Sydney, Australia, June 14, 1992.
    1. "Stromal tumours of the upper gut: Do we need to know the cell of origin?"
    2. "Fighting your way through gastritis"
13. Slide Seminar on GUT Pathology, IAP 18th Annual Scientific Meeting, Sydney, Australia, June 14, 1992.
14. Visiting Lecturer: Department of Pathology, University of Adelaide, Adelaide, South Australia, June 16 & 17, 1992.
15. Visiting Professor, Department of Pathology, Flinders University, Adelaide, South Australia, June 16, 1992.
16. Slide Seminar on Gastrointestinal Pathology, Royal Melbourne Hospital, Melbourne, Australia, June 18, 1992
17. Seminar on neoplastic diseases of intestine, American Society of Clinical Pathologists, Santa Fe, New Mexico, June 26, 1992.

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

1. Mutchnick, M.G., Appelman, H.D. et. al.: Thymosin treatment of chronic hepatitis B: A placebo-controlled pilot trial. Hepatology 1991;14:409-415.
2. Barnett, J.L., Appelman, H.D. and Moseley, R.H.: A familial form of incomplete septal cirrhosis. Gastroenterology 1992;102:674-678.
3. Barnett, J.L., McDonnell, W.M., Appelman, H.D. and Dobbins, W.O.: Familial viceral neuropathy with neuronal intranuclear inclusions: Diagnosis by rectal biopsy. Gastroenterology 1992;102:684-691.
4. Goldblum, J. and Appelman, H.D.: The appendix in ulcerative colitis. Accepted for publication in Mod Pathol.

5. Lucey, M.R., Graham, D.M., Martin, P., DiBisceglie, A., Rosenthal, S., Waggoner, J.G., Merion, R.M., Campbell, D.A., Nostrant, T.T. and Appelman, H.D.: Recurrence of hepatitis B and delta hepatitis following orthotopic liver transplantation. Accepted for publication in GUT.
6. Henley, K.S., Lucey, M.R., Appelman, H.D., et al: Biochemical and histopathological correlation in liver transplant: the first one-hundred-eighty days. Acepted for publication in Hepatology.

BOOKS AND CHAPTERS IN BOOKS:

1. Appelman, H.D.: Mesenchymal Tumors of the GI Tract. Chapter 15, in, Ming, S-C and Goldman, H. (eds), Pathology of the Gastrointestinal Tract, W.B. Saunders, Philadelphia, 1992.

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

1. Goldblum, J.R. and Appelman, H.D.: Appendiceal involvement in ulcerative colitis. Am. J. Clin. Path. 1991;96:412.
2. Silverman, E.M., Appelman, H.D. and Sapala, J.A.: Regression of hepatic steatosis with weight loss after gastric exclusion for morbid obesity. Am J Clin Pathol 1992;97:446.
3. DelBuono, E.A., Appelman, H.D., Wilson, M. and Frank, T.S.: Diagnosis of cytomegalovirus (CMV) infecton in liver transplant patients: Role of the polymerase chain reaction (PCR). Mod Pathol 1992;5:96A.
4. DelBuono, E.A., Frank, T.S., Wilson, M. and Appelman, H.D.: Posttransplant minimicroabscess disease. Mod. Pathol. 1992;5:96A.
5. Elta, G., Barnett, J., Scheiman, J., Nostrant, T., Behler, E., Loeffler, K. and Appelman, H.: The effect of treatment for Helicobacter pylori on non-ulcer dyspepsia symptoms. Gastroenterol, 1992; 102:A63.
6. Henley, K.S., Brown, K.A., Appelman, H.D., et al.: Biochemical-histopathological correlation in liver transplants. Gastroenterol. 1992;102:A820.

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

ANNUAL DEPARTMENT REPORT
1 JULY, 1991 - 30 JUNE, 1992

I. CLINICAL ACTIVITIES:

A. Director, Histocompatibility and Immunogenetics Laboratory.

II. TEACHING ACTIVITIES:

A. Director, Basic Immunology Course for Allergy Fellows-In-Training.
B. Instructor, ICS Course 600-601.
C. Attending General Internal Medicine Service.
D. Instructed Pathology Residents, Renal Fellows and Allergy Fellows in HLA Typing.
E. Supervised Jodi Maastricht (M1), Mathew Waier (M1) and three undergraduate students in research.
F. Supervisor for Dr. Lawrence Hennessey's (Allergy Fellow) Research Project.
G. Internal Medicine Grand Rounds

III. RESEARCH ACTIVITIES

SPONSORED SUPPORT:

A. Characterization of Thyroid Autoantibodies and Antigens, NIH-NIAID, R29-AI 30501, May 1, 1992 - April 30, 1993, $70,000/year.
B. Characterization of Recognition Events Involved in the Genesis of Thyroid Autoimmunity, The Boots Company Foundation, 1990-1992, $14,375/year.
C. Core Co-Director, UM-MAC: Hybridoma Core, 5 P60 AR205572 04, NIH, January 1, 1992 - December 31, 1993, $42,853/year.
D. Core Co-Director, MDRTC: Hybridoma Core, 5 P60 DK20572- 4, NIH, April 15, 1992 - April 14, 1993, $171,413/year.
E. Endocrine Fellow Training Grant, Endocrine Society, 5 P32 DK07245 15, July 1, 1992 - June 30, 1993, $33,000/year.

IV. SERVICE ACTIVITIES

COMMITTEE and ADMINISTRATIVE SERVICES:

A. Planning Committee, Advances in Internal Medicine, University of Michigan Medical School, 1990-1992.
B. Histocompatibility Committee, Organ Procurement Agency of Michigan.
C. Immunology Subcommittee, Dean's Committee on Curriculum Improvement 1991-1992.

MILITARY SERVICE:

A. US Army Reserve Medical Corps. 1978-1992.

V. OTHER RELEVANT ACTIVITIES

INVITED LECTURES:

1. Consultant Visit, Allergy Division, Department of Medicine, Walter Reed Army Medical Center, Washington, DC.

SCIENTIFIC ACTIVITIES:

1. Editorial Board, Journal of Clinical Endocrinology and Metabolism.
2. Reviewer, Annals of Internal Medicine.
3. Reviewer, Journal of Clinical Investigation.
4. Reviewer, Endocrinology.
5. Reviewer, Journal of Leukocyte Biology.
6. Reviewer, Autoimmunity.
7. Consultant Director, HLA Laboratory, Walter Reed Army Medical Center, Washington, DC.
8. Director, Hybridoma Core, University of Michigan Medical School.

WORKSHOPS/PANEL DISCUSSIONS:

1. Current Use of Theophylline, American Academy of Allergy and Immunology, Orlando, Florida, March 1992
2. Drug Allergies, Allergy for the Primary Care Physician, Towsley Center, Ann Arbor, Michigan, March 1991

VI. PUBLICATIONS

ARTICLES PUBLISHED IN PEER REVIEWED JOURNALS:

1. Chowdhury, J.R, Grossman, M., Gupta, S., Chowdhury, N.R., Baker, J.R. Jr. and Wilson, J.M.: Long-term improvement of hypercholesterolemia after ex vivo gene therapy in LDLR-deficient rabbits. Science 1991;254:1802-1805.
2. Wortsman, J., McConnachie, P., Baker, J.R. Jr. and Mallette, L.E.: T-lymphocyte activation in adult-onset idiopathic hypoparathyroidism. American. J. Med. 1992;92:352-356.
3. Arscott, P., Rosen, E.D., Koenig, R.J., Kaplan, M.M., Ellis, T., Thompson, N. and Baker, J.R., Jr.: Immunoreactivity to Yersinia enterocolitica antigens in patients with autoimmune thyroid disease. J. Clin. Endo. & Metab. 1992;75 (1):295-300.
4. Maastricht, J., Koenig, R.J., Kaplan, M.M., Arscott, P., Thompson, N. and Baker, J.R., Jr.: Identification of localized autoantibody epitopes in thyroid peroxidase. J. Clin. Endo. & Metab. 1992;75 (1):121-126.

ARTICLES PUBLISHED IN NON PEER REVIEWED JOURNALS:

1. Baker, J.R. Jr. and Leigh, T.: The Immunopathogenesis of Aids. Derm. Clin. Jul. 1991;9 (3):403-413.

ARTICLES ACCEPTED FOR PUBLICATION:

1. Hansen, K.A., Opsahl, M.S., Nieman, L.K., Baker, J.R., Jr. and Klein, T.A.: Natural killer cell activity from pregnant subjects is modulated by RU 486. Amer. J. Obstet. Gynecol. 1991, In Press.
2. Peele, M.E., Carr, F.E., Baker, J.R. Jr., Wartofsky, L. and Burman, K.D.: TSH beta subunit gene expression in human lymphocytes. Amer. J. Med. Sci. 1991, Accepted.
3. Baker, J.R., Jr.: Review article, The immune response in chronic hepatitis B virus infection: The "core" of the Problem? Ehata, T., et. al. Variations in codons 84-101 in the core nucleotide sequence correlate with hepatocellular injury in chronic hepatitis B virus infection. (JCI 89:33, 1992) to be published in the "Elsewhere" of Hepatology, August, 1992.
4. Cai, W-Y., Lukes, Y.D., Burch, H.B., Djuh, Y-Y., Carr, F., Wartofsky, L., Rhooms, P., D'Avis, J., Baker, J.R., Jr. and Burman, K.D.: Analysis of human TSH receptor gene and RNA transcripts in patients with thyroid disorders. Autoimmunity, 1992.

BOOK CHAPTERS:

1. Baker, J.R., Jr.: Immunologic Aspects of Endocrine Diseases, in deShazo, R.D., (ed.) Primer of Allergic and Immunologic Diseases, JAMA 1991; Accepted.

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

1. Arscott, P.L., Maastricht, J., Koenig, R.J. and Baker, J.R., Jr.: Epitope specificity of thyroid peroxidase (TPO) autoantibodies in common-variable hypogammaglobulinemia (CVH) patients with Hashimoto's thyroiditis (HT). Presented, Annual Meeting of the American Academy of Allergy and Immunology, March 1992, Orlando, Florida.
2. Seifert, M.J., Arscott, P.L. and Baker, J.R., Jr.: The induction of heat shock protein 70 (HSP 70) on human thyroid cells and fisher rat thyroid (FRTL-5) cells. Presented, AAP/ASCI/AFCR Annual Meeting, May 1992, Baltimore, Maryland.
3. Bermann, M., Koenig, R.J., Maastricht, J.L., Kaplan, M., Arscott, P.L. and Baker, J.R., Jr.: The identification of two areas of human auto-antibody binding in thyroid peroxidase. Presentation scheduled, Endocrine Society Annual Meeting, June 1992, San Antonio, Texas.
4. Ross, P.V., Koenig, R.J., Ludgate, M., Nelson, C.C., Kaplan, M., and Baker, J.R., Jr.: Tissue specificity and serologic reactivity of an autoantigen associated with autoimmune thyroid disease. Presentation scheduled, American Thyroid Association Annual Meeting, September 1992, Rochester, Minnesotta.

ARTICLES SUBMITTED FOR PUBLICATION TO PEER REVIEWED JOURNALS:

1. Sack, J., Zilberstein, D., Geinski, P., Baker, J.R., Jr., Wartofsky, L. and Burman, K.D.: Thyrotropin binding sites in Yersina Enterocolitica. Submitted 1991.
2. Burman, K.D., Lukes, Y.G., Wartofsky, L. and Baker, J.R., Jr.: Iodiotypic anti-iodiotype immune complexes in Graves disease. Submitted 1991.
3. Baker, J.R., Jr., Dow, N., Toro, L., Clark, L. and Wright, D.C.: Identification of HIV-antigen positive lymphocytes using flow cytometry. Submitted 1991.
4. Salazar, R.O., Arscott, P., Klapper, D., Burge, H.B., Solomon, W.R. and Baker, J.R., Jr.: Detection and quantitation of airborne ragweed pollen using an immunoblotting technique. Submitted 1991.

5. Schaudies, R.P., Djuh, Y-Y., La Rocca, R.V., Wartofsky, L., Rhooms, P., Carr, F., Nicholson, D., D'Avis, J., Baker, J.R., Jr. and Burman, K.D.: Epidermal growth factor receptor gene in normal and pathologic tissue in patients with autoimmue thyroid disease, cancer and multinodular goiter: Correlation of unique genetic hybridization pattern with cellular responsiveness. Submitted 1991.
6. McClain, J.B. COL MC, Bharati, J., Baker, J.R., Jr. and Cross, A. COL MC.: Alternative pathway complement activity to E. Coli K1 and 25922 contrasted to Leptospira interrogans and Leptospira biflexa. Submitted 1991.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Medical Director, Myelodysplasia Unit: inpatient and outpatient services for children with spina bifida.
B. Teratology Unit (see Research Activities).
C. On Sabbatical leave - January 1 - June 30, 1992.

II. TEACHING ACTIVITIES:

A. Teratology-Obstetrics Conference: weekly case review meeting of Obstetrics, Teratology, Neonatology for planning management of fetuses with prenatally detected malformations.
B. Pediatrics-Pathology Conference: organize and present CPC-type conferences to the Department of Pediatrics; four per year.
C. Neonatology Pathology Conference: quarterly review and discussion of neonatal deaths.
D. Malformations lecture, Embryology (M-1) Course.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT: None.

TERATOLOGY UNIT (DIRECTOR):

A. Detailed postmortem investigations of abortuses, stillborns, and selected neonatal deaths for morphologic, pathologic, and growth characteristics, correlations with family and prenatal histories, and counseling for future reproductive decisions by the parents.
B. Continuing investigation of normal and abnormal patterns of somatic and visceral growth. Detection of patterns of growth abnormalities associated with specific syndromes, exposures, and obstetrical antecedents.
C. Quality control investigations for various prenatal diagnostic methodologies.
D. Teratology Unit Activities: 178 fetal/neonatal examinations (85 from UMMC, 93 referred from 14 outside hospitals)

COLLABORATIVE RESEARCH:

A. Collection and allocation of fetal tissues for research projects in the Departments of Pediatrics, Pathology, Obstetrics, Anatomy, Genetics, and Howard Hughes Institute. Loan of fetal material for research investigations in the Department of Radiology.
B. Collaborative research with Central Laboratory for Embryology at the University of Washington (T.H. Shepard, M.D.) and the Department of Pathology at the University of South Alabama (W.R. Blackburn, M.D.) on standards for normal fetal morphometrics.
C. Research with Wayne State University (M.P. Johnson, M.D.) on fetal growth assessment in aneuploid fetuses.
D. Investigation of ACE inhibitor fetopathy (with M. Michael Cohen, D.M.D., Dalhousie University, and Peter Pryde, M.D., Wayne State University, and unnamed investigators from the pharmaceutical industry).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Departmental - Pathology: none.
B. Departmental - Pediatrics: Editorial Board, Pediatric Round.
C. On sabbatical leave from various other committees.

REGIONAL AND NATIONAL:

A. Reviewer for journals: Teratology, Pediatric Pathology.
B. President Elect, Teratology Society (President 92-93).

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Ohio State University, Columbus, Ohio.
2. St. Joseph Mercy Hospital, Ann Arbor, Michigan.
3. Dental School, University of Michigan, Ann Arbor, Michigan.
4. All-Michigan OB/GYN Review Course, Livonia, Michigan.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Barr, M. and Cohen, M.M.: ACE inhibitor fetopathy and hypocalvaria: the kidney-skull connection. Teratology 1991;44:485-495.
2. Blane, C.E., Barr, M., DiPietro, M., Sedman, A.B. and Bloom, D.A.: Renal obstructive dysplasia: Ultrasound diagnosis and therapeutic implications. Pediatric Radiol. 1991;21:274-277.
3. Hartshorne, N., Shepard, T. and Barr, M.: Compensatory renal growth in human fetuses with unilateral renal agenesis. Teratology 1991;44:7-10.

4. Pridjian, G., Nugent, C.E. and Barr, M.: Twin gestation: influence of placentation on fetal growth. Am. J. Obstet. Gynecol. 1991;165:1394-1401.
5. Pryde, P.G., Nugent, C.E., Pridjian, G., Barr, M. and Faix, R.G.: Spontaneous resolution of nonimmune hydrops fetalis secondary to human parvovirus B19 infection. Obstet. Gynecol. 1992;79:859-861.
6. Martin, R.A., Jones, K.L., Mendoza, A., Barr, M. and Benirschke, K.: The effect of ACE inhibition on the fetal kidney: decreased renal blood flow. Teratology, In press.

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

1. Barr, M. and Cohen, M.M. Survival and performance with isolated alobar holoprosencephaly. Presented to David W. Smith Workshop on Malformations and Morphogenesis, Lake Arrowhead, California, September 27-October 1, 1991.
2. Martin, R.A., Jones, K.L., Benirschke, K., Mendoza, A. and Barr, M. Renal defects seen with prenatal exposure to angiotensin converting enzyme inhibitor: nonspecific consequences of decreased renal blood flow. Presented to David W. Smith Workshop on Malformations and Morphogenesis, Lake Arrowhead, California, September 27-October 1, 1991.
3. Pryde, P.G., Nugent, C.E., Sedman, A.B. and Barr, M. ACE inhibitor fetopathy. Presented to Society of Perinatal Obstetricians, Orlando, Florida, February 3-8, 1992. Am. J. Obstet. Gynecol. 1992;166:329.
4. Johnson, M.P., Barr, M., Treadwell, M.C., Isada, N.B., Pryde, P.G., Colton, D.B. and Evans, M.I. Foot: leg length and foot: femur length ratio in noninvasive screening for trisomy 21. Presented to Society of Perinatal Obstetricians, Orlando, Florida, February 3-8, 1992. Am. J. Obstet. Gynecol. 1992;166:329.
5. Cohen, S.R., Corrigan, M.L., Bookstein, F., Trotman, C.A. and Barr, M. Log linear allometric analysis of fetal craniofacial growth: I. Normative data. Presented to American Cleft Palate - Craniofacial Association, Portland, Oregon, May 14, 1992.
6. Cohen, S.R., Corrigan, M.L., Bookstein, F., Trotman, C.A. and Barr, M. Log linear allometric analysis of fetal craniofacial growth: II. Down's syndrome. Presented to American Cleft Palate - Craniofacial Association, Portland, Oregon, May 14, 1992.
7. Barr, M. and Sedman, A.B. ACE inhibitor fetopathy: an update. Presented to Teratology Society, Boca Raton, Florida, June 27-July 2, 1992. Teratology 1992;45:452.
8. Barr, M. and Cohen, M.M. Alobar holoprosencephaly: when is "lethal" lethal? Presented to Teratology Society, Boca Raton, Florida, June 27-July 2, 1992. Teratology 1992;45:459.
9. Barr, M. Meckel Mysteries. Presented to Teratology Society, Boca Raton, Florida, June 27-July 2, 1992. Teratology 1992;45:459.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Diagnostic Electron Microscopy, Veterans Affairs Medical Center, Director of Electron Microscopy Center of Excellence.
B. Cytopathology, Veterans Affairs Medical Center.
C. Coordinator of Decentralized Hospital Computer Program in Laboratory Service, Veterans Affairs Medical Center.
D. Fine Needle Aspiration, Veterans Affairs Medical Center.
E. Surgical/Autopsy Pathology, Veterans Affairs Medical Center.
F. Tumor Board, Veterans Affairs Medical Center.
G. Deputy Washtenaw County Medical Examiner.
H. Consultant: Diagnostic Electron Microscopy, Allen Park, VAMC and Danville, VAMC.

II. TEACHING ACTIVITIES:

A. Pathology House Officer monthly elective: Diagnostic Electron Microscopy, 10 months.
B. Diagnostic Electron Microscopy Case Conference, bi-weekly.
C. Pathology House Officers, fine needle aspiration technique and interpretation.
D. Pathology 600 Lab Section.
E. Microbiology 620 Small Group Sessions.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Pathologist for: Veterans Administration Cooperative Study #268. A New Strategy to Preserve the Larynx in the Treatment of Advanced Laryngeal Cancer.(G. Wolf, Principal Investigator).
B. Marijuana-Bronchoscopy Project (Fligiel/Gong/Tashkin), NIH.
C. A Prospective, Controlled, Randomized and Double-Blind Multi-Center Clinical Evaluation of Monoclonal Antibody 17.13.C1.10 for its Capability to Detect Head and Neck Squamous cell carcinoma in Primary Site Malignancies and Lymph Nodes.(Co-Investigators: Baker, Beals, Carey, Krause, McClatchey and Wolf).
D. Crescentic Nephritis -Core B- NIH Program Project, Consultant (Wiggins and Johnson).

PROJECTS UNDER STUDY:

A. Clinical Relevance of Ultrastructural Characteristics of Small Cell Carcinoma (with R. Green).
B. Role of Plastic Embedded Cell-Blocks and Electron Microscopy in Fine Needle Aspiration.

C. Morphometric Analysis of Cells and Tissue using the Scanning Light Microscope.
D. Growth of Cells on Microcarriers (with J. Varani)
E. Endothelial Cell Damage Caused by Oxidants (with D. Hinshaw).
F. DNA content as a Predictor of Chemotherapeutic Response And Prognosis in Squamous Cell Carcinoma of the Larynx (with C. Gregg and G. Wolf)
G. Differentiation of Isolated Renal Tubular Cells in Culture (with D. Humes).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Electron Microscopy Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Surgical Case Review Committee, Veterans Affairs Medical Center.
B. Electron Microscopy Committee, chair, Veterans Affairs Medical Center.
C. Medical Records Review Committee, Veterans Affairs Medical Center.
D. Automated Data Processing Committee, Veterans Affairs Center.
E. Medical School Admissions Committee.
F. Executive Admissions Committee, Medical School.

REGIONAL AND NATIONAL:

A. Association of Veterans Affairs PathologistsSecretary-Treasurer.
B. Veterans Affairs Central Office Electron Microscopy Review Group.
C. Veterans Affairs Representative on Scientific Advisory Board, Armed Forces Institute of Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Pulmonary Neoplasm: Diagnostic Problems and Ultrastructural Characteristics (Department of Internal Medicine, Pulmonary Conference).
2. Electron Microscopy as an Aid to Diagnostic Cytopathology. Henry Ford Medical Center

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1 Hinshaw, D.B., Burger, J.M., Beals, T.F., Armstrong, B.C. and Hyslop, P.A.: Actin polymerization in cellular oxidant injury. Arch. Biochem. Biophys. 1991;288:311-316.
2. Beals, T.F.: Ultrastruture of in situ hybridization. Ultrastructural Pathol. 1992;16:87-93.
3. Beals, T.F.: Scanning electron microscopy of body fluids. Diagnostic Cytopathol. 1992;8:266-271.

4. Mierau, G.W., Agostini, R., Beals, T.F., Carlen, B., Dardick, I., Henderson, D.W., Pysher, T.J., Weeks, D.A. and Yowell, R.: The role of electron microscopy in evaluating ciliary dysfunction: Report of a consensus workshop. Ultrastructural Pathol. 1992;16:245-254.
5. Truelson, J.M., Fisher, S.G., Beals, T.F., McClatchey, K.D. and Wolf, G.T.: DNA content and histologic growht pattern correlate with prognosis in patients with advanced squamous cell carcinoma of the larynx. Cancer, In press, 1992.

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

1. Gregg, C.M., Beals, T.F., Fisher, S.G. and Wolf, G.T. DNA content and tumor response to induction chemotherapy in patients with advanced laryngeal squamous cell carcinoma, Third Interal Conf. Head and Neck Cancer, 1992.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. M-LABS AP/CP coverage at Lapeer Community Hospital, Albion Community Hospital, Thorn Hospital, and The University of Michigan Hospital.
B. 8.5 months of Neuropathology Service. All inside muscle biopsies through-out the year.
C. Three rotations in Autopsy Service.
D. Muscle and nerve biopsies referred by other hospitals in and out of state throughout the year.
E. Consultations on brain biopsies and rheumatology cases.

II. TEACHING ACTIVITIES:

A. Taught residents, fellows and staff in Neurology, Rheumatology and Pediatrics and medical students on muscle and nerve biopsies.
B. Taught pathology residents how to perform and read out autopsies.
C. Lectured on muscle, nerve and brain pathology to residents in Pathology and Neurology
D. Monthly conference on muscle cases with Neurology department.
E. Monthly neuropathology cases review with pathology residents.
F. Weekly conference with Neuromuscular staff.
G. Bimonthly conference with Neuroradiology fellows and staff.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Histology and histochemistry of orbicularis muscle, normal, aging, diseased.
B. Embiology and pathology of soft palate muscles of human and mice.
C. Pathologic changes in rat brain induced by MK-801.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Supervision of the muscle histochemistry.
B. Continuing improvement of interdepartmental coordination of muscle biopsy service.

MEDICAL SCHOOL:

A. Member of the Admission Committee.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

A. Attended IAP, Peripheral Neuropathy Association and American Association of Neuropathologists meetings.

INVITED LECTURES/SEMINARS:

1. Lectured students and fellows in Toledo Medical College on muscle and nerve pathology.

VI. PUBLICATIONS:

ARTICLES ACCEPTED FOR PUBLICATIOM:

1. Drury, I., Blaivas, M., Aboy-Khalil, B.W. and Beydoun, A.: Biopsy results in a kindred with Lafora disease. Archives of Neurology.
2. Ike, R.W. and Blaivas, M.: Corticosteroid responsive puffy hands and occult vasculitic neuropathy: RS_3PE plus? Journal of Rheumatology.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Simmons, Z, Blaivas, M.B., Bromberg, M.B. and Feldman, E.L: Polyneuropathy associated with IgA monoclonal gammopathy. Neurology.
2. Simmons, Z., Blaivas, M.B., Bromberg, M.D. and Feldman, E.L.: Nondiagnostic sural nerve biopsy in patients with peripheral neuropathy and primary amyloidosis. Neurology.

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

1. Simmons, Z., Blaivas, M., Bromberg, M.B. and Feldman, E.L.: Polyneuropathy association with IGA monoclonal gammopathy. AAEN meeting in September 27-28, 1991.
2. Felice, K.J., Fratkin, J.D., Blaivas, M. and Feldman, E.L.: Sudden death due to respiratory failure in Dejerine-Sottas disease. ANN meeting in October 1991.

CHAPTER IN BOOKS

1. McKeever, P.E. and Blaivas, M.: The brain, spinal cord, and meninges (Chapter 9) in, Sternberg, S.S. (ed.), Diagnostic Surgical Pathology,, Raven Press, New York, New York. Updated for the 2nd Edition to be published, 1992/1993.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Inherited Connective Tissue Disease Diagnostic Service (Biochemical Analysis of Skin Biopsy Material).
B. Attending Staff, University of Michigan Autopsy Service.

II. TEACHING ACTIVITIES:

A. Graduate Student:
   a. Thesis Co-Chairman with Steven Goldstein: Mr.John Germiller (MSTP).
   b. Thesis Co-Chairman with Steven Goldstein: Mr. Karl Jepsen (Bioengineering).
   c. Thesis Co-chairman with Steven Goldstein: Ms. Patrician Sherman (Human Genetics).
   d. Thesis committee: Ms. Elizabeth Allen (Human Genetics).
   e. Thesis committee: Ms. Linda Kallikan (Cellular and Molecular Biology).
B. Supervision of four postdoctoral fellows: (David Bole, Ph.D., Marcy Wong, Ph.D., Wushan Yin, M.D., and Chiara Sanguineti, Ph.D.)
C. Mentor, Summer Medical Research Program, University of Michigan: (Arul Chinnaivan, Maurice Albright).
D. Courses:
   1. Lab Instructor, Pathology 600.
   2. Lecturer, Biochemistry 501.
   3. Course Co-Director, Pathology 581.
E. Continuing Medical Education:
   1. Genetics Grand Rounds, Department of Medicine, University of Michigan, 1991.
   2. Gene Therapy Seminar Series, Department of medicine, University of Michigan, 1991.
   3. Biomechanics 1000 Lecture Series, Department of Surgery, University of Michigan, 1992.
F. Invited Presentations:
   1. Gordon Research Conference, Structural Macromolecules, August, 1991.
   2. Plenary Session on Inherited Connective Tissue Diseases (Session co-chair), European Society for Pediatric Research Annual Meeting, Zurich, Switzerland, September, 1991.
   3. Instituto Nazionale per la Ricerca sul Cancro, Genoa, Italy, September, 1991.
   4. NIH Workshop on Transgenic Models of Human Disease, NIH, Bethesda, Maryland, September, 1991.
   5. Seminar Series, Department of Biochemistry, University of Nebraska, Omaha, Nebraska, October, 1991.
   6. Seminar Series, Department of Human Genetics, University of Nebraska, Omaha, Nebraska, October, 1991.

7. Orthopaedic Research Society Annual Meeting, Washington, D.C., February, 1992.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Transgenic Mouse Model of Osteogenesis Imperfecta Type I", NIAMSD, NIH, AR40679 (25% effort), $162,679.00/year direct costs $462,843.00/3 years 1991-1993.

PROJECTS UNDER STUDY:

A. Structure/function relationships in connective tissue.
B. Regulation of osteoblast gene expression.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

A. Member, Preclinical Advisory Program, University of Michigan Medical School.
B. Biomechanics Core Steering Committee, University of Michigan Multipurpose Arthritis and Musculoskeletal Diseases Center.

DEPARTMENTAL:

A. Oversight Committee, Graduate Program, Department of Pathology, University of Michigan.

V. OTHER RELEVANT ACTIVITIES:

A. Appointments:
   1. Assistant Investigator, Howard Hughes Medical Institute
   2. Faculty Member, Bioengineering Program, University of Michigan
B. Ad-hoc Reviewer
   1. American Journal of Human Genetics.
   2. The Journal of Clinical Investigation.
   3. The Journal of Biological Chemistry.
   4. The March of Dimes Grants Program.
   5. Genomics.
C. Consultant Editor: European Journal of Experimental Musculoskeletal Research, 1991-present.
D. Study Section:
   1. NIH, Site Visist Team, Ad Hoc Member, NIAMS, 1992.
   2. NIH, Program Project Review Ad Hoc Member, MIAMS, 1992.
   3. Department of Veterans Affiars, ACMD for Research and Development, Ad Hoc Reviewer, 1992.
E. Member

1. Multipurpose Arthritis Center.
2. Michigan Cancer Center.
3. Program in Bioengineering.
4. Rheumatology Fellowship Training Grant, University of Michigan, Multipurpose Arthritis and Musculoskeletal Diseases Center.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Cole, W.G., Patterson, E., Bonadio, J., Campbell, P.E. and Fortune, D.W.: The clinicopathological features of three babies with osteogenesis imperfecta resulting from the substitution of glycine by valine in the proα1(I) chain of type I procollagen. J. Med. Genet. 1992;29:112-118.
2. Wong, M., Lawton, T., Goetinck, P., Goldstein, S.A. and Bonadio, J.: Aggrecan core protein is expressed in membranous bone of the chick embryo: molecular and biomechanical studies of normal and Nanomelia embryos. J. Biol. Chem. 1992;267:5592-5598.
3. Niyibizi, C., Byers, P.H., Smiley, E., Bonadio, J. and Eyre, D.R.: Incorporation level of a mutant collagen α2(I) chain into bone matrix in a lethal case of osteogenesis imperfecta. J. Biol. Chem., In Press.
4. Biesecker, L.G., Erickson, R.P., Glover, T.W. and Bonadio, J.: Molecular and cytologic studies of Ehlers-Danols syndrome type VIII. Am. J. Hum. Genet. 1992;41:284-288.

BOOKS/CHAPTERS IN BOOKS:

1. Bonadio, J. and Goldstein, S.A.: Our understanding of inherited skeletal fragility and what this has taught us about bone structure and fuction, Molecular and Cellular Biology of bone, Noda, M., ed., Academic Press, Inc., San Diego, California, In Press.
2. Bonadio, J. and Goldstein, S.A.: Osteogenesis imperfecta: An inherited connective tissue disease of bone, in Carlson, D.S. and Goldstein, S.A., eds, Bone Biodynamics in Orthodontic and Orthopedic Treatment, Craniofacial Growth Series, Vol. 27, Center for Human Growth and Development, The University of Michigan, Ann Arbor, Michigan, In Press.

ABSTRACTS:

1. O'Donnell, L.R., Majmudar, G. and Bonadio, J.: Temporal and spatial distribution of mRNA for transforming growth factor-β types 1,2,3, and 4 in embryonic chick bone. Workshop on Osteobiology, Brindisi, Italy, 1991.
2. Wong, M., Lawton, T., Pasternak, A., Jepsen, K., Goetinck, P., Kuhn, J.L., Goldstein, S.A. and Bonadio, J.: Aggrecan is expressed in membranous bone of the chick embryo: molecular genetic and biomechanical studies of wild-type and Nanomelia embryos. Workshop on Osteobiology, Brindisi, Italy, 1991.
3. Jepsen, K., Kuhn, J.L., Goldstein, S.A., Mansoura, M. and Bonadio, J.: A geometrical adaptation effectively compensates skeletal fragility in heterozygous Mov13 mice. Workshop on Osteobiology, Brindisi, Italy, 1991.
4. Majmudar, G., Bole, D., Goldstein, S.A. and Bonadio, J.: Bone cell culture in a three-dimensional polymer bead stabilizes the differentiated phenotype and provides evidence that osteoblastic cells synthesize type III collagen and fibronectin. Workshop on Osteobiology, Brindisi, Italy, 1991.

5. Bonadio, J., Goldstein, S.A., Kuhn, J.L., Jepsen, K. and Mansoura, M.: Osteogenesis imperfecta: fragile molecules make brittle bones. European Society for Pediatric Research Annual Metting, Zurich, Switzerland, 1991.
6. Bonadio, J., Goldstein, S.A., Kuhn, J.L., Jepsen, K.A. and Mansoura, M.: Osteogenesis imperfecta type I in Mov13 transgenic mice. NIH Workshop: Transgenic Animal Models in Biomedical Research, Bethesda, Maryland, 1991.
7. Goldstein, S.A., Hollister, S.J., Kuhn, J.L., Bonadio, J. and Matthews, L.S.: Mechanical influences on bone adaptation. American Society of Mechanical Engineers Winter Meeting, Atlanta, Georgia, 1991.
8. Wong, M., Germiller, J., Goldstein, S.A. and Bonadio, J.: Altered pattern of gene expression in the neuromuscular-deficient chick embryo femur. Symposium on Transforming Growth Factor-β and Related Proteins in Development, Ames, Iowa, 1991.
9. Wong, M., Lawton, T., Goetinck, P.F., Goldstein, S.A. and Bonadio, J.: The contribution of aggrecan to the functional properties of membranous bone of the chick embryo. Ortho. Trans. 1992;17(1):27.
10. Wong, M., Bonadio, J. and Goldstein, S.A.: The effect of decreased mechanical loading on the growth and morphogenesis of the chick embryo long bone. Ortho. Trans. 1992;17(2):182.
11. Jepsen, K., Mansoura M., Kuhm, J.L., Jaenisch, R., Bonadio, J. and Goldstein, S.A.: An in vivo assessment of the contribution of type I collagen to the mechanical properties of cortical bone. Ortho. Trans. 1992;17(1):93.
12. Mansoura, M., Jepsen, K. and Bonadio, J.: Transcriptional regulation of type I collagen contributes to cortical bone adaptation. Ortho. Trans. 1992;17(1):187.
13. Germiller, J.A., Wong, M., Goldstein, S.A. and Bonadio, J.: Induced muscular atrophy in the chick embryo hindlimb alters gene expression in long bone. J. Cell. Biochemistry Suppl. 1992;16F:135.
14. Goldstein, S.A., Jepsen, K.J., Kuhn, J.L. and Bonadio, J.: Biomechanical assessment of the extracellular matrix of bone: the contribution of collagen type I. European Society of Biomechanics Annual Meeting, Rome, Italy, 1992.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Director, Clinical Laboratories, Veterans Affairs Medical Center, responsibilities include, new equipment and methodology evaluation, review and consultation regarding quality management programs, personnel evaluation, peronnel counseling and greivance procedures.
B. Hematology/Coagulation, daily evaluation of pathologist referred blood smears (500/yr), bone marrow smears (110/year) and interpretation of special coagulation studies (12 months/yr), Veterans Affairs Medical Center.
C. Surgical/Frozen Section Diagnosis, 2 days/week (12 months/yr), Veterans Affairs Medical Center. (approx. 2250 cases/year).
D. Autopsy Service, rotational basis, on call 18 weeks/year.
E. Special Chemistry/Immunology, daily interpretation of protein electrophoreses (800/yr), isoenzyme studies (2200/yr), and problem ligand studies Veterans Affairs Medical Center (12 months/year).
F. Blood Bank, consults and investigations, full time as needed, Veterans Affairs Medical Center.

II. TEACHING ACTIVITIES:

A. Medical School, Pathology 600 laboratory course, (1 semester, 40 contact hours).
B. Graduate course, Pathology 580, 1 lecture hour.
C. Graduate course, Epidemiology 570, 2 lecture hours.
D. Pathology house officers, Surgical Pathology/Autopsy supervision and instruction, 2 days/week (12 month/year).
E. Technologists and technicians, ongoing inservice instruction on clinical laboratory topics.
E. Physicians, educational lectures regarding aspects of clinical pathology (1-2 lectures/year).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, Cytokine Cascades in Granuloma Formation, VAMC Merit Review ($55,000 annual) 1990-1993.
B. Consultant on NIH-HL-R01-31237, Macrophage Function in Pulmonary Inflammation, Dr. S. Kunkel, Principal Investigator.

PROJECTS UNDER STUDY:

A. Role of chemotatic cytokines (MCP and MIP) in Schistosoma mansoni egg-induced granulomatous inflammation.
B. Role of interleukin-1 antagonist protein (IRAP) in the regulation of immune responses.
C. Regulation and orchestration of T helper cell cytokine production during granulomatous inflammation.
D. Analysis of eosinophil recruitment and chemotactic factors in Schistosoma mansoni egg-induced granulomatous inflammation.
E. In vivo and in vitro analysis of neutrophil and monocyte chemoattractant function and regulation.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Editorial Review:
   1. American Journal of Pathology.
   2. Journal of Immunology, Associate Editor.
   3. Clinical Immunology and Immunopathology.
   4. American Journal of Respiratory Cell and Molecular Biology.
   5. Agents and Actions, Section Editor.
B. Inspector, College of American Pathologists.
C. Reviewer and on site inspection for Merit Review Board.
D. Chair, Minisymposium session, FASEB, 1992.

V. OTHER RELEVANT ACTIVITIES:

A. Case presentations at Tumor Board, GI and Hematology Conferences.
B. Case presentations at Morbidity and Mortality Conferences.
C. Tissue evaluation for clinical researchers.
D. Invited lecture, Tri-County Clinical Microbiology Association.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Schmouder, R.L., Strieter, R.M., Wiggins, R.C., Chensue, S.W. and Kunkel, S.L.: In vitro and in vivo interleukin-8 production in human renal cortical epithelia. Kidney Internat. 1992;41:191.
2. Chensue, S.W., Terebuh, P.D., Warmington, K.S., Hershey, S.D., Evanoff, H.L., Kunkel, S.L. and Higashi, G.I.: Role of interleukin 4 and gamma-interferon in *Schistosoma mansoni* egg-induced hypersensitivity granuloma formation: orchestration, relative contribution, and relationship to macrophage function. J. Immunol. 1992;148:900.
3. Terebuh, P.D., Otterness, I.G., Strieter, R.M., Lincoln, P.M., Danforth, J.M., Kunkel, S.L. and Chensue, S.W.: Biologic and Immunohistochemical Analysis of Interleukin 6 expression in vivo. Constitutive and induced expression in murine polymorphonuclear and mononuclear phagocytes. Am. J. Pathol. 1992;140:649.
4. Chensue, S.W., Warmington, K.S., Berger, A.E. and Tracey, D.E.: Immunohistochemical demonstration of interleukin 1 receptor antagonist protein (IRAP) and IL-1 in human lymphoid tissue and granulomas. Am.J. Pathol. 1992;140:269.
5. Strieter, R.M., Kasahara, K., Allen, R.M., Standiford, T.J., Rolfe, M.W., Becker, F.S., Chensue, S.W. and Kunkel S.L.: Cytokine-induced neutrophil-derived interleukin 8. Am. J. Pathol. 1992;141, In Press.
6. Koch, A.E., Kunkel, S.L., Chensue, S.W., Haines, G.K. and Strieter, R.M.: Constituitive expression of interleukin-1 and interleukin-1 receptor antagonist protein by human rheumatoid synovial tissue macrophages. Clin. Immunol. Immunopathol. 1992, In Press.
7. Kunkel, S.L., Strieter, R.M., Lukacs, N. and Chensue, S.W.: Initiation and Maintenance of the Granulomatous Response. Chest 1993, In Press.

BOOKS AND CHAPTERS IN BOOKS:

1. Kunkel, S.L., Standiford, T.J., Chensue, S.W. and Strieter, R.M.: Interleukin-8 and the inflammatory response. In, Cytokines in Health and Disease, Kunkel, S. and Remick D. (eds.), Marcel Dekker, 1992.
2. Kunkel, S.L., Chensue, S.W. and Phillips, S.M.: Mechanisms of Immunopathology in parasitic infections. In, Parasitic Infections, S.M. Phillips (ed.), 1992.

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

1. Chensue, S.W., Kunkel, S., Hershey, S., Warmington, K. and Tracey, D.E.: Interleukin-1 antagonist protein (IRAP) abrogates foreign body but not hypersensitivity-type granulomas. FASEB J. 1992;6:A1330.
2. Chensue, S.W.: Cytokine cascades in macrophage recruitment and activation. 1992. FASEB Minisymposium Macrophage Biology/Effector Cell Activity.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Neural and Behavioral Sciences 600 (NBS 600), Neuropathology for second year medical students, 5 hours of lectures and 10 hours of brain cutting sessions. Sequence coordinator for NBS 600, Neuropathology; responsible for implementing general plan of course, selection of much of the teaching material, coordination and integration of the lectures of the course with other instructors, lecturing, and conducting the brain cutting sessions.
B. Neuropathology for Pathology house officers. This exercise is integrated with Clinical Activities A, B, and D.
C. Neuropathology 858. Intensive laboratory-lecture course for house officers and fellows, in Pathology and in the several clinical services concerned with the nervous system, and medical students, graduate students, and faculty; implement general plan of course and lecturing. Annual, 18 hours. One credit hour elective.
D. Neuropathology teaching for house officers and fellows from the several clinical services concerned with the nervous system, and medical students who take an elective rotation in Neuropathology.
E. Teach laboratory techniques and basic neuroanatomy and neuropathology to our laboratory technologists.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

None

PROJECTS UNDER STUDY:

A. The pathologic examination of human autopsy brains from patients with clinical diagnosis of Alzheimer's, Huntington's, Pick's and other dementing diseases is being done in collaboration with Drs A.B. Young, J.B. Penney, and R. Albin, in the University of Michigan Alzheimer Disease Research Center, who are examining the brains biochemically.
B. Growth, spread and antigenicity of ENU-induced gliomas in rats, in collaboration with Paul E. McKeever, M.D., Ph.D..

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Anatomic Pathology Committee.

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

A. Presentation: Alzheimer's Disease and other dementias for Eastern Michigan University students, March 1992.
B. Member: Dementia Subcommittee of the Chronic Disease Advisory Committee (State of Michigan).
C. Member: Executive Committee of the Postmortem Examination Work group of the Dementia Subcommittee (State of Michigan).
D. Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Committee.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Brunberg, J.A., DiPietro, M., Venes, J.L., Dauser, R., Muraszko, K.M., Berkey, J., D'Amato, C.J. and Rubin, J.M.: Intramedullary lesions of the pediatric spinal cord: Correlation of findings from MRI imaging, intraoperative sonography, surgery and histologic study. Radiology 1991;181:573-579.
2. Foster, N.L., Gilman, S., Berent, S., Sima, A.A.F., D'Amato, C.J., Koeppe, R.A. and Hicks, S.P.: Progressive subcortical gliosis and progressive supranuclear palsy can have similar clinical and PET abnormalities. J. Neurol. Neurosurg, Psychiatry, In press, July 1992.

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

1. Fratkin, J., Remick, D., D'Amato, C., Hogan, J., Shope, J., Izenson, S., Foster, N., Huang, L., Dragovic, L, Garcia, J., Ho, K., Sima, A., Lovell, K. and Jones, M.: Michgian postmortem examination network for dementia patients , J. Neuropathol. & Exper. Neurol. 1992;51:315.
2. D'Amato, C.J., Foster, N.L., Sima, A.A.F. and Hicks, S.P.: Swollen cortical neurons and Lewy bodies accompanying progressive supranuclear palsy and Creutzfeldt-Jakob's disease. J. Neuropathol. & Exper. Neurol. 1992;51:324.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Introductory course in Blood Banking/Transfusion Medicine for Pathology House Officers.
B. Daily teaching rounds for Pathology House Officers assigned to the Blood Bank.
C. Continuing education presentations for Blood Bank technologists.
D. Clinical Pathology Grand Rounds: Component therapy, May 22, 1992.
E. Clinical Pathology Grand Rounds: Applications of apheresis, June 28, 1992.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Biomedical Research Council - Biological Mediators of Transfusion Reactions; Principal Investigator.

PROJECTS UNDER STUDY

A. Cytokine production in hemolytic transfusion reactions.
B. Interleukin-8 and monocye chemoattractant protein production by monocytes in response to Fc receptor stimulation.
C. Leukocyte-associated procoagulant activity induction in whole blood in response to ABO incompatibility.
D. Endothelial cell responses in hemolytic transfusion reactions.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL

A. Transfusion Committee.

B. Quality Inprovement Team in Outpatient Care.

V. OTHER RELEVANT ACTIVITIES:

A. Reviewer, Chest.
B. Reviewer, Transfusion.
C. Reviewer, American Journal of Clinical Pathology.
D. Program committee, Michigan Association of Blood Banks

INVITED LECTURES AND SEMINARS:

1. Recent Advances in the Area of Transfusion Reactions. North Detroit General Hospital; August 16, 1991.
2. Appropriate Use of Plasma. Workshop: Transfusion Therapy, Guidelines for Practice. American Association of Blood Banks, Baltimore, Maryland; November 9-10, 1991.
3. Problem Solving in the Blood Bank. Workshop: Current Topics in Blood Banking, Ann Arbor, Michigan; June 3, 1992.
4. Know Your Hemoflagilates: The Other Transfsuion Transmitted Diseases. Current Topics in Blood Banking, Ann Arbor, Michigan; June 4, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Judd, W.J., Steiner, E.A., Abruzzo, L., Davenport, R.D., Oberman, H.A., Pehta, J. and Nance, S.: Anti-i causing acute hemolysis following a negative immediate-spin crossmatch. Transfusion, In press.
2. Davenport, R. D.: Predicting postprocedure bleeding in liver disease (editorial). Hepatology 1992;15:735-737.
3. Adams, P. T., Davenport, R. D., Reardon, D. A. and Roth, M. S.: Detection of circulating donor white blood cells in patients receiving multiple transfusions. Blood, In press.
4. Davenport, R. D., Burnie K. L. and Barr, R. M.: Transfusion management of patients with IgA deficiency and anti-IgA during liver transplantation. Vox Sang, In press.
5. Davenport, R. D., Burdick, M., Moore, S. A. and Kunkel, S. L.: Cytokine production in IgG mediated red cell incompatibility. Transfusion, In press.

ABSTRACTS:

1. Davenport, R. D., Burdick, M., and Kunkel, S. L.: Cytokine production in Rh incompatibility. Transfusion 1991;31:53S.
2. Burnie, K. L., Davenport, R. D. and Barr, R. M.: Transfusion management of IgA deficiency with anti-IgA during liver transplantation. Presented at American Association of Blood Banks, Baltimore, Maryland, November, 1991.
3. Burdick, M., Strieter, R. M., Kunkel, S. L. and Davenport, R. D.: Monocyte chemotactic protein production in red cell incompatibility. FASEB J. 1992;6:A1898.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1990 - 30 JUNE 1991

I. CLINICAL ACTIVITIES: None.

II. TEACHING ACTIVITIES:

A. Supervised the following undergraduate students: Kara Reynolds.
B. Supervised the following graduate students: Carol Laherty, Tony Opipari, Ron Katz, Muneesh Tewari.
C. Supervised the following post doctoral fellows: Larry Holzman, Vidya Sarma, Rachel Yabkowitz, Theresa Bacon-Baguely, Valarie Castle.
D. Graduate School Pathology Course. Lectures on Extracellular Matrix.
E. Cell and Molecular Biology course to clinical fellows.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

1. NIH-R01-39037-01 - "Structure and Regulation of Human Platelet Thrombospondin", Period 07/01/87 - 06/30/92, Budget - $105,621, Principal Investigator, 35% effort.
2. #89-217 - American Heart Association Established Investigatorship Award - "Structure and Function of Thrombospondin", Period 07/01/89-06/31/94, Budget $35,000 annually, Principal Investigator.
3. DK39255-03 - "Mechanisms of Glomerular and Tubular Injury", Period 09/01/87-07/31/92, Budget - $44,156, Co-Investigator, 10% effort, Roger C. Wiggins, Program Director.
4. American Heart Association - Grant-in-Aid - "Thrombospondin Heparin Binding Domain and Platelet Function", Period 07/01/90-06/30/93, $35,000 per year, Principal Investigator, 10% effort.
5. ACS-CD-466 - "Novel Thrombospondin Receptors on Squamous Carcinoma Cells", Period 07/01/90 - 06/30/92, Budget - $136,000, Principal Investigator, 10% effort.
6. NIH-HL45351-01 - "Cytokine Modulation of Endothelial Gene Expression", Response to RFA entitled "Developmental Biology of the Vessel Wall", Period 07/01/90 - 04/30/93, Budget $194,745, Principal Investigator, 15% effort.
7. NIH-CA51888 - "Novel Thrombospondin Receptors on Squamous Carcinoma Cells", Period 02/01/91 - 01/31/94, Budget $97,454, Principal Investigator, 20% effort.

PENDING GRANTS:

1. NIH-1-R01-HL47857-01 - "Heparin and Aortic Smooth Muscle Cell Proliferation", Response to RFA NIH-91-HL-02-H "Mechanisms of Restenosis After Coronary

Angioplasty", Period 09/01/91 - 08/31/96, Budget $150,476, Principal Investigator, 20% effort.

PROJECTS UNDER STUDY:

A. Structure/function relationships in thrombospondin.
B. Mechanisms of action of tumor necrosis factor.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interview prospective graduate students for a) Molecular and Cell Biology Program, and b) Medical Scientist Training Program.
B. Taught a graduate school course on Extracellular Matrix.
C. Taught a pathology resident course on molecular biology.
D. Participated in graduate school pathology program.

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Reviewer for the following journals: Journal of Biological Chemistry, Journal of Clinical Investigation.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Invited Speaker, The International Conference on Biological Treatment of Melanoma and Other Cancers, New Castle, Australia, 1990.
2. Invited Speaker, Cor Therapeutics, Inc., S. San Francisco, California, 1990.
3. Invited Speaker, NIEHS, Research Triangle Park, North Carolina, 1991.
4. Invited Speaker, FASEB, Atlanta, Georgia, 1991.
5. Invited Speaker, Wahsington University Medical Center, Respiratory and Critical Care Division, St. Louis, Missouri, 1991.
6. Invited Speaker, Mesangial Cells and Extracellular Matrix, International Society of Nephrology, Kloster Banz, Germany, 1991.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Dixit, V.M., Green, S., Sarma, V., Holzman, L., Wolf, F.W., O'Rourke, K., Ward, P.A., Prochownik, E.V. and Marks, R.M.: Tumor necrosis factor-α induction of novel genes in human endothelial cells including a macrophage specific chemotaxin. J. Biol. Chem. 1990;265:2973-2978.
2. Barker, J.N.W.N., Sarma, V., Mitra, R.S., Dixit, V.M. and Nickoloff, B.J.: Marked synergism between TNF-α and IFN-γ in regulation of keratinocyte-derived adhesion molecules and chemotactic factors. J. Clin. Invest. 1990;85:605-608.
3. Wolf, F.W. and Dixit, V.M.: Structure of the thrombospondin gene provides evidence for exon shuffling. Genomics 1990;6(4):685-691.
4. O'Shea, K.S., Rheinheimer, J.S.T. and Dixit, V.M.: Deposition and role of thrombospondin in the histogenesis of the cerebellar cortex. J. Cell. Biol. 1990;110(4):1275-1284.
5. Long, M.W. and Dixit, V.M.: Thrombospondin functions as a cytoadhesion molecule for human hematopoietic progenitor cells. Blood 1990;75(12):2311-2318.
6. Opipari, A.W., Boguski, M.S. and Dixit, V.M.: The A20 cDNA induced by tumor necrosis factor-α encodes a novel type of zinc finger protein. J. Biol. Chem. 1990;265:14705-14708.
7. Holzman, L.B., Marks, R.M. and Dixit, V.M.: A novel immediate-early response gene of endothelium is induced by cytokines and encodes a secreted protein. Mol. Cell. Biol. 1990;10:5830-5838.
8. O'Shea, K.S., Liu, L.-H.J., Kinnunen, L.H. and Dixit, V.M.: Role of the extracellular matrix protein thrombospondin in the early development of the mouse embryo. J. Cell Biol. 1990;111:2713-2723.
9. Schuger, L., Dixit, V.M., Carey, T.E. and Varani, J.: Modulation of squamous carcinoma cell growth, morphology, adhesiveness and extracellular matrix production by interferon-γ and tumor necrosis factor-α. Pathobiol. 1990;58:279-286.
10. Nickoloff, B.J., Karabin, G.D., Barker, J.N.W.N., Griffiths, C.E.M., Sarma, V., Mitra, R.S., Elder, J.T., Kunkel, S.L. and Dixit, V.M.: Cellular localization of interleukin-8 and its inducer-tumor necrosis factor-alpha in psoriasis. Am. J. Pathol. 1991;138(1):129-140.
11. Barker, J.N.W.N., Mitra, R.S., Griffiths, C.E.M., Dixit, V.M. and Nickoloff, B.J.: Keratinocytes as initiators of Inflammation. Lancet 1991;337:211-214.
12. Barker, J.N.W.N., Jones, M.L., Swenson, C.L., Sarma, V., Mitra, R.S., Ward, P.A., Johnson, K.J., Fantone, J.C., Dixit, V.M. and Nickoloff, B.J.: Monocyte chemotaxis and activating factor production by keratinocytes in response to IFN-γ. J. Immunol. 1991;146(4):1192-1197.
13. Tripathi, B.J., Tripathi, R.C., Yang, C., Millard, C.B. and Dixit, V.M.: Synthesis of a thrombospondin-like cytoadhesion molecule by cells of the trabecular meshwork. Invest. Ophthalmol. Vis. Sci. 1991;32:181-188.
14. Yabkowitz, R. and Dixit, V.M.: Human carcinoma cells express receptors for distinct domains of thrombospondin. Cancer Res. 1991;51:1645-1650.
15. Suchard, S.J., Burton, M.J., Dixit, V.M. and Boxer, L.A.: Human neutrophil adherence to thrombospondin occurs through a CD11/CD18-independent mechanism. J. Immunol. 1991;146:3945-3952.
16. Castle, V.P., Varani, J., Fligiel, S., Prochownik, E.V. and Dixit, V.M.: Antisense-mediated reduction in thrombospondin reverses the malignant phenotype of a human squamous carcinoma. J. Clin. Invest. 1991;87:1883-1888.
17. O'Shea, K.S., Liu, L-H.J. and Dixit, V.M.: Thrombospondin promotes neuron attachment and neurite outgrowth. Neuron 1991;7:231-237.

18. Yabkowitz, R. and Dixit, V.M.: Human carcinoma cells bind thrombospondin through a 80/105 kD receptor. Cancer Res. 1991;51:3648-3656.
19. Suchard, S.J., Boxer, L.A. and Dixit, V.M.: Human neutrophils express two distinct thrombospondin receptors. J. Immunol. 1991;147:651-659.
20. Bornstein, P., O'Rourke, K., Wikstrom, K., Wolf, F.W., Katz, R., Li, P. and Dixit, V.M.: A second, expressed thrombospondin gene (THBS2) exists in the mouse genome. J. Biol. Chem. 1991;266:12821-12824.
21. Wolf, F.W., Marks, R.M., Sarma, V., Byers, M.G., Katz, R.W., Shows, T.B. and Dixit, V.M.: Characterization of a novel tumor necrosis factor-α induced endothelial primary response gene. J. Biol. Chem., In Press.
22. Laherty, C.D., O'Rourke, K., Wolf, F.W., Katz, R., Seldin, M.F. and Dixit, V.M.: Characterization of mouse thrombospondin 2 sequence and expression during cell growth and development. J. Biol. Chem., In Press.

ARTICLES SUBMITTED FOR PUBLICATION

1. Johnson, K.J., Dixit, V.M. and Varani, J.: Role of thrombospondin in the acute inflammatory response. Am. J. Pathol., Submitted.
2. Sarma, V., Wolf, F.W., Marks, R.M., Byers, M.G., Shows,T.B. and Dixit, V.M.: Characterization from endothelium of a novel primary response gene induced by tumor necrosis factor-α. J. Biol. Chem., Submitted.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Instructor and Course Coordinator: "Advanced Topics in Toxicology: Toxicologic Pathology".
      b. Instructor: "Fundamentals in Electron Microscopy".
      c. Student Training and Doctoral Committees.
      d. Joint Student Training in Pharmacology and Toxicology with Florida A&M School of Pharmacy.
      e. Direct a Postdoctoral Research Fellowship Program in Experimental Pathology.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. All research activities are conducted with intramural support from Parke-Davis, including a co-sponsored program with the Medical Research Council of Canada.
B. Collaborates with K. Johnson in developing morphometric models for the evaluation of kidney pathology.
C. Consultation with Dr. Ward and colleagues regarding application of morphometric techniques.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Co-chair, Joint University of Michigan and Parke-Davis Pathology Program.

MEDICAL SCHOOL/HOSPITAL:

A. None.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

INVITED LECTURES/SEMINARS:

1. Liver Toxicity, International Training Course on Environmental and Industrial Toxicology, Chulaborn Research Institute, Bangkok, Thailand, November 19, 1991. 1990.
2. Skin Toxicity, International Training Course on Environmental and Industrial Toxicology, Chulaborn Research Institute, Bangkok, Thailand, November 19, 1991.
3. Integration of Toxicology and Pharmacokinetics/Drug Metabolism in Drug Development, Plenary Lecture, 2nd. International Conference on Pharmacokinetics, Basel, Switerzerland, March 23, 1992.
4. Toxicokinetics and the Impact on Toxicity Studies, Symposium on Recent Trends in Toxicology, Northwestern University Medical School, May 15, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Bleavins, M.R., de la Iglesia, F.A., Munson, A.E., McCay, J.A., Stern, M.L., Fuchs, B.A. and White, K.L.: Effects of CI-949, a novel antiallergy agent, on immune function of male Fischer 344 rats. J. Pharm. Exp. Ther. 1991;257:316-322.
2. Bleavins, M.R. de la Iglesia, F.A., Munson, A.E., McCay, J.A., Fouant, M.M. and White, K.L.: Effects of CI-949, a novel antiallergy agent, on host resistance in mice. Fund. Appl. Toxicol. 1991;17:723-732.
3. McGuire, E.J., Lucas, J.A., Gray, R.H. and de la Iglesia, F.A.: Peroxisome induction potential and lipid-regulating activity in rats: Quantitative microscopy and chemical structure-activity relationships. Amer. J. Path. 1991;189:217-229.
4. Watkins, J.R., Kim, S.N., Anderson, J.A., Rothwell, C.E. and de la Iglesia, F.A.: Long-term studies in rats and dogs with the antiarrhythmic agent Pirmenol Hydrochloride. Drug Invest. 1991;3:141-147.
5. de la Iglesia, F.A., Gray, R.,H. and McGuire, E.J.: Subcellular organelle biogenesis and dynamics in peroxisome proliferation. J. Am. Coll. Toxicol., In Press, 1992.

6. McGuire, E.J., Gray, R.H. and de la Iglesia, F.A.: Chemical structure-activity relationships of peroxisome proliferation and lipid regulation in rats. J. A. Coll. Toxicol., In Press, 1992.
7. Watkins, J.R., McGuire, E.J., Goldenthal, E. and de la Iglesia, F.A.: Calcium valproate-induced uterine adenocarcinomas in Wistar rats. Toxicology. 1991;71:35-47.
8. Dethloff, L. and de la Iglesia, F.A.: Cholecystokinin antagonists. A toxicologic perspective. Drug Metab. Rev. 1991;24:267-293.
9. Rothwell, C.E., McGuire, E.J., Margin, R.A. and de la Iglesia, F.A.: Chronic toxicity and carcinogenisity studies with the β-adrenoceptor antagonist levobunolol. Fund. Appl. Tox. 1992;18:353-359.

BOOKS/CHAPTERS IN BOOKS:

1. Welling, P.G., and de la Iglesia, F.A.: Toxicokinetics. (Editors), Marcel Dekker Publisher, 1992, In Press.
2. de la Iglesia, F.A.: Toxicokinetic perspective on Toxicity and Safety Evaluation Studies. In: Toxicokinetics. P.G. Welling and F.A. de la Iglesia (Eds.) Marcel Dekker Publisher, 1992, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Bleavins, M.R., Brott, D.A., Alvey, J.D. and de la Iglesia, F.A.: Lymphocyte subpopulation characterization in Cynomolgus monkeys. Vet. Immunol. Immunopath., Submitted, 1991.
2. Bleavins, M.R., de la Iglesia, F.A., White, K.L., McCay, J.A., Fouant, M.M., Stern, M.L., Fuchs, B.A. and Munson, A.L.: Innumotoxicologic Studies with the Novel Benzothiophene Cell Activation Inhibitor CI-959 in rats and Mice. Fund. Appl. Toxicol, Submitted, 1992.

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

1. Gough, A., Wojcinskl, Z., Courtney, C., McGuire E., and de la Iglesia, F.: Hepatocarcinogenicity of Perosixome Proliferator, a Phenylene (oxy)-bis 2,2-Dimethylpentanoic Acid, in Mice byt not in Rats. Abstracts, 195h Intl. symp. Toxicologic Pathologits. Toxicol. Pathol. 1991;19:622.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

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. Postdoctural Mentor for Hamed Benghuzzi, Ph.D.
D. Participant, Clinical Pathology Grand Rounds.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. USPHS (NIDDKD) 2P60AM20572-10: Michigan Diabetes Research and Training Center, Director Ligand Assay Core Facility, $129,322/yr., 1987-1992.
B. USPHS (NICHD) P30 HD18258: Center for the Study of Reproduction, Co-Director, Standards and Reagents Core Facility, $348,320/yr., 1989-1994.
C. USPHS (NICHD) 5T32HD07048-18: Training Program in Reproductive Endocrinology, Co-Investigator, $149,898/yr., 1990-1995.
D. Protocol to evaluate the transdermal delivery of estradiol-17B in postmenopausal women. Sponsor: Ciba-Geigy Corporation.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Director, Central Ligand Assay Laboratory.

MEDICAL SCHOOL/HOSPITAL:

A. Director, Chemistry Core Facility, Michigan Diabetes Research and Training Center.
B. Co-Director, Standards and Reagents Core Facility, Reproductive Sciences Program.
C. Member, Selection Committee, Reproductive Sciences Program.

V. OTHER RELEVANT ACTIVITIES:

1. Session Chairman, Therapeutics-I at the Seventh Annual Meeting of the Academy for Surgical Research, Sept. 26-29, 1992, Scottsdale, Arizona.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: The effects of long-term sustained delivery of DHT by polylactic acid impregnated and noncoated biodegradable ceramic devices in male rats. J. Bioactive and Compatible Polymers 1991;6:115-128.
2. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Sustained-release of norepinephrine by means of ceramic drug delivery devices. The Tenth Southern Biomedical Engineering Conference. October 18-21, 1991. Atlanta, Georgia. J. Toler (Editor), pp. 122-124, 1991.
3. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: TCPL delivery system: The effect of compression loads on the delivery of steroids. The Tenth Southern Biomedical Engineering Conference. October 18-21, 1991. Atlanta, Georgia. J. Toler (Editor), pp. 118-121, 1991.
4. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: The effects of various loaded doses of biologicals on the delivery rate by means of ceramic delivery devices. The Tenth Southern Biomedical Engineering Conference. Oct. 18-21, 1991. Atlanta, Georgia. J. Toler (Editor), pp. 125-128, 1991
5. Benghuzzi, H.A., England, B.G., and Bajpai, P.K.: Characterization of ceramic drug delivery devices: The effect of various temperature of incubation on the delivery of biological. Biomedical Medical Sciences Instrumentation (ISA, Paper #92-0131). 1992;28:129-134.
6. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Controlled release of hydrophilic compounds by resorbable and biodegradable ceramic drug delivery devices. Biomedical Sciences Instrumentation (ISA, Paper #92-0141)). 1991;28:179-182.
7. Benghuzzi, H.A., England, B.G., Bajpai, P.K. and Giffin, B.F.: Successful antidote of multiple lethal infections Using sustained delivery of difluromethylornithine by means of ceramic drug delivery devices. J. Clin. Materials (CMU-9201), In Press.
8. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: The effects of density of the ceramic delivery devices on dustained release of androgens in castrated rats. J. Clin. Materials, In Press
9. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Regulation of fertility in male rodents by sustained delivery of testosterone from biodegradable ceramic devices. Southern Biomedical Eng. Symp., In Press

10. Benghuzzi, H.A., England, B.G., Possley, R.M. and Bajpai, P.K.: The use of tricalcium-phosphate ceramic reservoirs to deliver testosterone in adult castrated rams. Southern Biomedical Eng. Symp., In Press

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

1. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Physiological response associated with sustained delivery of danazol and androgens in adult rats.. Seventh Annual Scientific Session of the Academy of Surgical Research , September 26-29, 1991, Scottsdale, Arizona.
2. Benghuzzi, H.A., England, B.G. and Bajpai, P. K.: An evaluation of the controlled release of azidothymidine (AZT) from TCP and ALCAP ceramic implants in male rodents. Seventh Annual Scientific Session of the Academy of Surgical Research , September 26-29, 1991, Scottsdale, Arizona.
3. Benghuzzi, H.A., England, B.G. and Bajpai, P. K.: Ceramic delivery system: Effects of sustained release of testosterone and estradiol on spermatogenesis of adult rats. Accepted for Oral Presentation and Publication (Abstract # 83) at The 47th Annual Meeting of The American Fertility Society, October 19-24, 1991, Orlando, Florida.
4. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: The effects of various loaded doses of biologicals on the delivery rate by means of ceramic delivery devices. Paper Accepted for Presentation and Publication at the Tenth Southern Biomedical Engineering Conference. October 18-21, 1991. Atlanta, Georgia. J. Toler (Editor).
5. Benghuzzi, H.A., England, B.G. and Bajpai, P. K.: England. Sustained-release of norepinephrine by means of ceramic drug delivery devices. Paper Accepted for Presentation and Publication at the Tenth Southern Biomedical Engineering Conference. October 18-21, 1991. Atlanta, Georgia. J. Toler (Editor).
6. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: England. TCPL DELIVERY SYSTEM: The effect of compression loads on the delivery of steroids. Paper Accepted for Presentation and Publication at the Tenth Southern Biomedical Engineering Conference. October 18-21, 1991. Atlanta, Georgia. J. Toler (Editor).
7. Possley, R.M., Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Control of reproductive function in adult ewes by means of progesterone and estradiol loaded ceramic implants. Paper Accepted for Presentation at the Federation of American Society for Experimental Biologists, April 5-9, 1992; Anaheim, California, FASEB J. p. A2031 (Abstract #6339).
8. England, B.G., Benghuzzi, H.A. and Brownlee, B.: Testosterone affects proliferation of endothelial and vascular smooth muscle cells. Paper Accepted for Presentation at the Federation of American Society for Experimental Biologists, April 5-9, 1992; Anaheim, California, FASEB J., p. A2032 (Abstract #6346).
9. Brownlee, B.E., Benghuzzi, H.A. and England, B.G.: Effects of antioxidants on LDL-induced cytotoxicity in cultured aortic smooth muscle and endothelial cells. Paper Accepted for Presentation at the Federation of American Society for Experimental Biologists, April 5-9, 1992; Anaheim, California, FASEB J., p. A1343, (Abstract #2355).

10. Benghuzzi, H.A., England, B.G., Possley, R.M. and Bajpai, P.K.: One year long term maintenance of testosterone levels in rams using an implantable ceramic delivery system. Paper Presented at the Federation of American Society for Experimental Biologists, April 5-9, 1992; Anaheim, California, FASEB Journal, p. A2031, (Abstract # 6338).
11. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Characterization of ceramic drug delivery devices: The effect of various temperature of incubation on the delivery of biological. Paper accepted for aresentation and publication at the Proceedings of the 29th Annual Meeting of the Rocky Mountain Bioengineering Symposium, Rochester, Minnesota. April 11-12, 1992. C. Ferris (Editor), Biomedical Sciences Instrumentation (ISA).
12. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Controlled release of hydrophilic compounds by resorbable and biodegradable ceramic drug delivery devices. Paper accepted for presentation and publication at the Proceedings of the 29th Annual Meeting of the Rocky Mountain Bioengineering Symposium, Rochester, Minnesota. April 11-12, 1992. C. Ferris (Editor), Biomedical Sciences Instrumentation (ISA).
13. Benghuzzi, H.A., England, B.G. and Bajpai, P.K.: Ultrastructure of the reproductive organs of adult male rat: Effect of sustained selivery of sestosterone. Scanning Electron Microscopy International: Cells and Materials, May 11-14, 1992, Chicago, Illinois (Invited).
14. Benghuzzi, H.A., England, B.G. and Possley, R.M.: Serum LH and FSH responses during sustained delivery of testosterone from ceramic delivery systems in adult castrated rams. Presented at the First Annual Michigan Forum On Reproduction, May 29, 1992, Ann Arbor, Michigan (#52)
15. Flinn, M.V., England, B.G. and Beer, T.: Health condition and corticosteroid stress response among children in a rural dominican village. American Association of Physical Anthropologists, April 3-5, 1992, Las Vegas, Nevada.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Autopsy Service.

II. TEACHING ACTIVITIES:

A. Director, Resident Training Program.
B. Graduate Program Committee (Chairman).
C. Course Director - Pathology 600.
D. Lecturer and Laboratory Instructor - Pathology 600.
E. Coordinator - Senior Medical Student Clerkships.
F. Sequence Coordinator and Lecturer - ICS-600: Immunopathology.
G. Associate Director - Sophomore Medical Student ICS Course (600/601).
H. Coordinator, Department of Pathology Summer Clinical Program for Minority Medical Students.
I. Pulmonary Pathology Conference (6 per year to Pulmonary Division - Internal Medicine).
J. Lecturer - Microbiology and Immunology 624.
K. Preceptor, Microbiology 620, Problem-Based Learning Tutorial.
L. Lecturer - Pathology 580.
M. Preceptor, Pathology 650
N. Preceptor - Undergraduate and Medical Student Research (5).
O. Graduate Student Ph.D. Thesis Committee (3).
P. Assistant Director - Medical Student Curriculum Component I.
Q. Faculty Mentor - Baccalaureate Program for Pre-Medical Minority Students.

III. RESEARCH ACTIVITIES:

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

SPONSORED SUPPORT:

A. Principal Investigator: Mechanisms of Myocardial Ischemia/Reperfusion Injury (NIH-R01-HL44085).
B. Principal Investigator: Myocardial Ischemia and Reperfusion Injury, (American Heart Association Grant-in-Aid).
C. Principal Investigator: Phagocytic Cell and Glomerular Injury. Section IV of Renal Center Grant (NIH-P50-DK39255).
D. Co-Investigator: Mechanisms and Genetic Regulation of Pulmonary Fibrosis. (S.H. Phan; Principal Investigator) (NIH-5-R01-HL-28737).

E. Co-Investigator: Pharmacologic Studies on the Ischemic Heart (B. Lucchesi, Principal Investigator) (NIH-R01-HL-19782).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chairman's Advisory Committee.
B. Coordinator - Educational Programs.
C. Department ACAPT Committee.
D. Coordinator, Department Faculty Retreat on Junior Faculty Development.
E. Human Resource Committee.
F. Research Space Advisory Committee.
G. Department Photography Committee.

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Reviewer, Searle's Pharmaceutical Company Research Grants, Chicago, Illinois, 1991.
B. NIH Site Visit, Program Project: Physical Properties and Biologic Functions of Lipids, Hormel Institute, Austin, Minnesota, 1991.
C. NIH Special Grant Review, 1991.
D. Reviewer, Veteran's Administration Research Grants.
E. USMLE, Pathophysiology Test Group.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Editorial Board, Infection and Immunity.
B. Editorial Board, Laboratory Investigation.
C. Editorial Board, Biological Signals

INVITED LECTURES AND SEMINARS:

1. Invited Speaker, American College of Sports Medicine, Dallas, Texas 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Barker, J.N.W.N., Jones, M.L., Mitra, R.S., Crockett-Torabe, E., Fantone, J.C., Kunkel, S.L., Warren, J.S., Dixit, V.M. and Nickoloff, B.J.: Modulation of keratinocyte-derived interleukin-8 which is chemotactic for neutrophils and T-lymphocytes. Am. J. Pathol. 1991;139:869-786.
2. Bosanko, C.M.M., Korobkin, M., Fantone, J.C., Rubin, S.B. and Lynch, J.P.: Lobar primary pulmonary lymphoma: CT findings. J. Computer Assisted Tomography 1991;679-682.
3. Crockett-Torabi, E., Smith, W.C., Kateley, J.R. and Fantone, J.C.: Insoluble immune complex-stimulated neutrophil LTB_4 production is dependent on FcγRII and FcγRIII and independent of pertussis toxin sensitive signal transduction pathways. Am. J. Pathol. 1992;613-620.
4. Coffey, M., Peters-Golden, M., Fantone, J.C. and Sporn, P.H.S.: Membrane association of active 5-lipoxygenase in resting cells: Evidence for novel regulation of the enzyme in the rat alveolar macrophage. J. Biol. Chem. 1992;267:570-576.
5. Brieland, J.K., Clarke, S.J., Karmiol, S., Phan, S.H. and Fantone, J.C.: Transferrin: A potential source of iron for oxygen free radical-mediated endothelial cell injury. Arch. Biochem. Biophys. 1992;294:265-270.
6. Coffey, M.J., Fantone, J. III, Stirling, M.C. and Lynch, J.P., III: Pseudoaneurysm of pulmonary artery in mucormycosis. Am. Rev. Respir. Dis. 1992;145:1487-1490.
7. Brieland, J., Jones, M., Clarke, S., Warren, J. and Fantone, J.C.: Expression of monocyte chemoattractant protein-1 (MCP-1) by rat pulmonary alveolar macrophages during acute inflammatory lung injury. Am. J. Resp. Cell Mol. Biol., In Press.
8. Werns, S.W., Fantone, J.C., Ventura, A. and Lucchesi, B.R.: Myocardial glutathione depletion impairs recovery of isolated, blood-perfused hearts after global ischemia. J. Mol. Cell. Cardiol., In Press.
9 Mickelson, J.K., Hoff, P.T., Homeister, J.W., Fantone, J.C. and Lucchesi, B.R.: High dose intravenous aspirin, not low dose intravenous or oral aspirin, inhibits thrombus formation and stabilizes blood flow in experimental coronary vascular injury. J. Am. Coll. Cardiol., In Press.
10. Lynch, J.P. III and Fantone, J.C.: Pulmonary granulomatous vasculitic Syndromes. In, Immunologically-Mediated Pulmonary Diseases. J.P. Lynch and R.A. DeRemee (Eds.) J.B. Lippincott, Co., New York, 1991.

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

1. Brieland, J., Jones, M., Clarke, S., Warren, J. and Fantone, J.C.: Expression of monocyte chemoattractant protein-1 (MCP-1) by rat pulmonary alveolar macrophages during acute inflammatory lung injury. 28th Annual Meeting of Society for Leukocyte Biology, Aspen, Colorado, 1991.
2. Crockett-Torabi, E., Smith, C.W., Kateley, J.R. and Fantone, J.C.: Fcθ receptor-mediated LTB_4 synthesis by human neutrophils. 28th Annual Meeting of Society for Leukocyte Biology, Aspen, Colorado, 1991.
3. DeForge, L.E., Bolgos, G., Fantone, J.C. and Remick, D.G.: Dimethyl sulfoxide (DMSO) inhibits interleukin 8 (IL-8) production in lipopolysaccharide (LPS)-stimulated human whole blood. FASEB, 1992.

4. Crockett-Torabi, E., Tsai, P. and Fantone, J.C.: Insoluble immune complexes-induced human neutrophil phospholipase D activation through a pertussis toxin insensitive pathway. FASEB, 1992.
5. Jones, M.L., Flory, C.M., Fantone, J.C., Ward, P.A. and Warren, J.S.: Cloning and expression of functional rat monocyte chemoattractant protein 1/JE in a baculovirus system. FASEB, 1992.
6. Cunningham, M.R., Driscoll, E.M., Mu, D.-X., Fantone, J.C., Patton, L.M., Kirschenheuter, G.P. and Lucchesi, B.R.: Infarct size reduction in experimental myocardial infarction - Assessment of an elastase inhibitor. FASEB, 1992.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Rotations, July (1/4), August (2/4), September (2/4), November (2/4). March (2/4), April (2/4), May (2/4), June (1/4); Autopsy rotation, August (1/4).

II. TEACHING ACTIVITIES:

A. Pathology 600 Lectures:
   1. Pulmonary Pathology I - February 28, 1992.
   2. Pulmonary Pathology II - February 19, 1992.
   3. Pulmonary Pathology III - February 20, 1992.
   4. Pulmonary Pathology IV - March 2, 1992.
   5. Gyn Pathology I - March 31, 1992
   6. Gyn Pathology II - April 1, 1992
   7. Pathology 600 Laboratory Instructor, January-April, 1992

B. Pathology 630:
   1. Respiratory Disease I - October 30, 1991.
   2. Respiratory Disease II - November 1, 1991.

C. Residency Training:
   1. Diseases of the Chest I - November 12, 1991.
   2. Diseases of the Chest II - November 19, 1991.
   3. Diseases of the Chest III - November 26, 1991.
   4. Surgical Pathology Consultant's Conference, April, 1991.

D. Other educational activities:
   1. M4 student elective mentor, March, 1992.
   2. Pulmonary Pathology - Radiology Conference, Department of Radiology, October, 1991.
   3. Pulmonary Pathology - Radiology Conference, Department of Radiology, December, 1991.
   4. Pulmonary Pathology - Radiology Conference, Department of Radiology, February, 1992.
   5. Anatomic Pathology Journal Club Discussion Leader, February, 1992.
   6. Department of Internal Medicine Seminar, "Pulmonary Pathology", November, 1991.
   7. Center for Research on Learning and Teaching Workshop: Leading Discussions I, February, 1992.
   8. Center for Research on Learning and Teaching Workshop: Leading Discussions II, February, 1992.
   9. Member, Required and Elective Clerkships Task Force Committee, DCCI, Summer, 1991.
   10. Member, M-2 Respiratory Sequence Committee, 1992.

11. Course Director, M-4 Student Pathology Clerkships.
12. Pathology Resident Mentor.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Pathology Consultant, Morphologic Studies of Diffuse Interstitial Lung Diseases, A Multi-Institution Project, Reuben M. Cherniak, M.D., National Jewish Hospital, Program Director.
B. Prognostic Markers of Urinary Bladder Cancer (RFACA 91-09), H. Barton Grossman, M.D., (Principal Investigator), Andrew Flint, M.D. (Co-Investigator).
C. Role of Urothelial Cell Activation in Interstitial Cystiltis (DK-91-04), Monica Liebert, Ph.D. (Principal Investigator), Andrew Flint, M.D. (Co-Investigator).
D. Interstitial Lung Diseases - Specialized Center of Research (1 P50 HL - 46487-01), Galen Toews, M.D. (Principal Investigator), Andrew Flint, M.D. (Co-Investigator).
E. Monoclonal Antibodies to Bladder Tumor Antigens, H. Barton Grossman, M.D. (Principal Investigator), Andrew Flint, M.D. (Co-Investigator).

PROJECTS UNDER STUDY:

A. Measurement of Proliferating Cell Nuclear Antigen of low stage renal cell carcinoma and correlation with ploidy measurement and clinical outcome.
B. Quantitation of immunochemically-determined estrogen and progesterone receptors of breast carcinomas.
C. Methotrexate-induced hepatic disease: an analysis of sequential liver biopsy samples.
D. Measurement of CEA expression in cytopathology samples as a diagnostic adjunct.
E. Airway inflammation of the lingula: can gender differences explain unusual localization of *m. avium* infection?
F. Interstitial lung disease: the influence of biopsy site on diagnosis.
G. The morphologic manifestations of metastatic renal cell carcinoma to the lung.
H. PCNA expression of preoperative esophageal biopsy samples: correlation with response to treatment and prognosis.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Interviewed House Officer Candidates (September, 1991-January, 1992).
B. Member, Residency Selection Committee
C. Coordinator, Senior Staff Service Rotations.
D. Director, Surgical Pathology Fellowship Program.
E. Member Credentials Committee (a Continuing Committee of the Medical Staff).

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

1. Reviewer, Annals of Thoracic Surgery.
2. Reviewer, American Journal of Pathology.

INVITED LECTURES/SEMINARS:

1. Guest Pathologist, Tri-State Thoracic Society, Orange Beach, Alabama, January, 1992.
2. "Drug and Chemical Induced Hypersensitivity Disorders" Environmental Pathology, UAREP, Sugarbush, Vermont, October, 1991.
3. "Applications of DNA Analysis to Diagnostic Cytology", Annual New Frontiers in Cytology Lecture, American Society of Cytology Annual Meeting, Los Angeles, California, November, 1991.

VI. PUBLICATIONS:

1. Flint, A.: The detection of pulmonary neoplasms by bronchial washings: Are cell blocks a diagnostic aid? Acta Cytol, In Press.
2. Flint, A.: Drug and chemical induced hypersensitivity disorders. Hum Pathol (in press).
3. Hyde DM, King TE, McDermott T, Waldron, Jr. JA, Colby TV, Thurlbeck MB, Flint A, Ackerson L, Cherniack RM: Idiopathic pulmonary fibrosis: comparison of a semi-quantitative versus a morphometric histopathologic scoring system in the quantitative assessment of lung pathology. Amer Rev Resp Med (in press).
4. Liebert M, Wedemeyer G, Stein JA, Washington, Jr. R, Faerber G, Flint, A, Grossman HB: Evidence of urothelial cell activation in interstitial cystitis. J Urol (in press).

SUBMITTED PUBLICATIONS:

1. Flint A: Interstitial Lung Disease. Advances in Pathology and Laboratory Medicine.
2. Drescher CW, Flint A, Hopkins MP, Roberts JA: Prognostic Significance of DNA content and nuclear morphology in borderline ovarian tumors. Gyn. Oncol.

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

1. Grossman HB, Liebert M, Flint A, Washington R: DD23: a monoclonal antibody reactive with bladder and breast cancer. Am Assoc Can Res, 1992.
2. Liebert M, Stein J, Wedemeyer G, Faerber G, Flint A, Grossman HB: Evidence for urothelial cell activation in interstitial cystitis. J Urol., 1992.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Surgical Pathology, including consultations on surgical gynecologic pathology from other hospitals and medical centers - 2139 cases.
B. Necropsy Service - one week.
C. Molecular Diagnostics for Anatomic Pathology.
D. Weekly interdisciplinary Gynecologic Oncology Tumor Board Review.

II. TEACHING ACTIVITIES:

A. Pathology 600 Lectures:
   1. Neoplasia (four hours), January 1992.
   2. Gynecology (two hours), March 1992.
B. Introduction to Clinical Sciences 601 Course (one hour), January, 1992.
C. Co-Director, Pathology 600 laboratory section.
D. Preceptor for medical student research project under auspices of Biomedical Research Program: Genetic alterations in gynecologic malignancy (Brad Slywka, B.A.).
E. Lecturer, two Anatomic Pathology Didactic Conferences.
F. Monthly Pathology-Gynecology teaching conference for house officers in Obstetrics and Gynecology.
G. Presentation of Grand Rounds to Department of Obstetrics and Gynecology: Pathology of the Endometrium, June 1992.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Linkage and Mapping of Breast Cancer to Chromosome 17, NIH Grant RO1 CA57601-01, 7/1/91-6/30/97. Barbara Weber, M.D. (Principal investigator), Francis Collins, M.D., Ph.D. (co-investigator), Judy Garber, M.D., M.P.H. (consultant), Thomas S. Frank, M.D. (consultant).
B. Significance of allelic loss of p53 tumor suppressor gene in endometrial neoplasia, University of Michigan Cancer Center Institutional Grant IRG-40-33, 4/1/92-3/31/93.
C. Molecular analysis of clonality, Horace H. Rackham Faculty Grant from the University of Michigan, 5/1/91-6/30/93.
D. Molecular analysis of clonality, Phoenix Memorial Research Grant from the University of Michigan, 4/18/91-6/30/92.
E. Genetic markers in gynecologic malignancy, Harris Foundation, 1/1/92-1/1/94.

PROJECTS UNDER STUDY:

A. Loss of heterozygosity of p53 gene in epithelial malignancies of ovary and endometrium (with James A. Roberts, M.D., Department of Obstetrics and Gynecology).
B. Retrospective analysis of somatic and tumor-associated alterations of p53 gene in familial breast carcinoma (with Barbara L. Weber, M.D. and Francis S. Collins, M.D., Ph.D, Department of Internal Medicine).
C. Diagnosis of histologically occult cytomegalovirus infection in immunocompromised patients using the polymerase chain reaction.
D. Identificiation of mycobacterial DNA in paraffin-embedded tissues using the polymerase chain reaction.
E. Mutations and gene loss of p53 locus in hepatocellular carcinoma.
F. Molecular analysis of clonality.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Surgical Pathology representative to the Departmental Quality Assurance/Quality Control Committee.

REGIONAL AND NATIONAL:

A. Member, American Association for the Advancement of Science.
B. Member, United States & Canadian Academy of Pathology (US-CAP).
C. Member, American Society of Clinical Pathologists.
D. Member, Amercian Society of Human Genetics.
E. Member, A. James French Society.

V. OTHER RELEVANT ACTIVITIES:

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

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Frank, T.S., Himebaugh, K.S. and Wilson, M.D.: Granulomatous endometritis associated with histologically occult cytomegalovirus in a healthy patient. Am. J. Surg. Pathol. 1992;16:716-720.

2. Frank, T.S, Cook, S.M., DelBuono, E.A. and Wilson, M.D.: A simplified method for detecting cytomegalovirus by polymerase chain reaction from histologic sections of small biopsies. Modern Pathol 1992;5:449-454.
3. Carr, K.A., Roberts, J.A. and Frank, T.S.: Progesterone receptros in bilateral ovarian ependymoma presenting in pregnancy. Human Pathol., In Press.
4. Helvie, M.A. and Frank, T.S.: Enhanscing breast metastases from bronchial neuroendocrine (carcinoid) carcinoma. Breast Diseases, an International Journal, In Press.
5. Frank, T.S., Reed, J.C. and Brooks, J.J.: Absence of c-*sis* and transforming growth factor-beta mRNA expression in malignant fibrous histiocytoma. Surg. Pathol., Accepted, July, 1992.
6. Pelkey, T.J., Frank, R.S., Frank, T.S., Stanley, J., Zelenock, G.B. and D'Alecy, L.G.: Minimal physiologic temperature variations during renal ischemia alter functinal and morphologic outcome. J. Vasc. Surg., Accepted, August, 1991.
7. Frank, R.S., Frank, T.S., Zelenock, G.B. and D'Alecy, L.G.: Intermittent reperfusion rduces functional and morphologic damage following renal ischemia. Ann. Vascular Surg., In Press.
8. Stanley, J.J., Goldblum, J.S., Frank, T.S., Zelenock, G.B. and D'Alecy, L.G.: Attenuation of renal reperfusion injury in rats by the 21-amino steroid U74006F. J. Vascular Surg., In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Frank, T.S., Haefner, H., Roberts, J.A., Hubbell, G. and Wilson, M.: Loss of heterozgosity of p53 tumor suppressor gene in ovarian carcinoma.
2. Helm, C.W., Kinney, W.K., Keeney, G., Lawrence, W.D., Frank, T.S., Gore, H., Reynolds, R.K., Soong, S.J., Partridge, E.E., Roberts, J.A., Podratz, K.C. and Shingleton, H.M.: A matched study of surgically treated IB adenosquamous carcinoma and adenocarcinoma of the cervix.
3. Cook, S.M., Himebaugh, K.S. and Frank, T.S.: Absence of cytomegalovirus in gestational tissue in recurrent spontaneous abortion.
4. Perosio, P.M. and Frank, T.S.: Detection of mycobacteria in paraffin-embedded lung biopsie s by the polymerase chain reaction.
5. Ikeda, D.M., Frank, T.S. and Marn, C.S.: Case report: lymphoma of the breast.
6. Ethier, S.P., Mahacek, M.L., Gullick, W.J., Frank, T.S. and Weber, B.L.: Differential isolation of normal luminal mammary epithelial cells and breast cancer cells from primary and metastatic sites using selective media.

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

1. Ikeda, D.M., Helvie, M.A., Frank, T.S., Anderson, I., Linnell, F. and Chapel, K.: Paget's disease of the nipple: Radiologic/pathologic correlation. 77th Scientific Assembly of the Radiologic Society of North America, 1991.
2. Helm, C.W., Soong, S-J., Partridge, E.E., Shingleton, H.M., Reynolds, R.K., Frank, T.S. and Roberts, J.A.: A matched study of surgically treated IB adenosquamous carcinoma and adenocarcinoma of the cervix. Annual Meeting of the Society of Gynecologic Oncologists (1992).
3. Haefner, H., Roberts, J.A., Wilson, M., Hubbel, G. and Frank, T.S.: Loss of heterozygosity of p53 tumor suppressor gene in ovarian carcinoma. Modern Pathol., 1992;5(1):64A.
4. DelBuono, E.A., Frank, T.S., Wilson, M. and Appelman, H.D.: Posttransplant minimicroabescess disease (PTMMD). Modern Pathol., 1992;5(1):96A.
5. DelBuono, E.A., Appelman, H.D., Wilson, M. and Frank, T.S.,: Diagnosis of cytomegalovirus (CMV) infection in liver thansplant patients: role of the polymerase chain reaction. Modern Pathol., 1992;5(1):96A.

6. Cook, S., Himebaugh, K. and Frank, T.S.: Cytomegalovirus is not associated with recurrent spontaneous abortion. Modern Pathol., 1992;5(1):62A.
7. Perosio, P. and Frank, T.S.: Detection of mycobacteria in paraffin-embedded lung biopsies by the polymerase chain reaction. Modern Pathol., 1992;5(1):93A.
8. Book Review: Pathology of Reproductive Failure (Kraus, Damjanov, and Kaufman). Am. J. Surg. Pathol., 1992, In Press.
9. Moderator, Infectious Diseases Platform Session, 1992 Annual Meeting, United States and Canadian Academy of Pathology.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

DEPARTMENT:

A. Co-Director of a laboratory section for Pathology 600.
B. Course Co-Director, Pathology 631 (Dental School, Sophomore Pathology), 1991-.
C. Teaching and supervision of three Pathology house officers through two-week Pathology Data Systems rotations.

MEDICAL SCHOOL/HOSPITALS:

A. Program Director of the Tenth Annual Clinical Laboratory Computer Symposium at the Towsley Center for Continuing Medical Education, June 10-12, 1992. Symposium attracted 175 registrants and 34 vendors.

III. WORK IN PROGRESS:

1. Information systems in hospitals: technical, political, and transaction cost explanations for departmental success and interdepartmental failure.
2. Informating versus informationalizing: the information product of pathology.
3. Alliances between for-profit reference laboratories and tertiary care hospital laboratories.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Quality Assurance Committee.
B. Editor, Pathology Electronic News (PEN).

HOSPITAL:

A. ITN (Information Technology and Networking) Steering Committee.
B. Chairman, Committee on Blood Products Utilization (1991-1992); helped to develop a system of criteria maps to optimize ordering of blood and blood products.

UNIVERSITY OF MICHIGAN:

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

REGIONAL AND NATIONAL:

A. Council on Medical Informatics of the American Society of Clinical Pathologists.
B. Chairman of the Executive Council, Cerner Users' Group.
C. Editorial Advisory Board, Clinical Laboratory Management Review.
D. Co-Editor of a special focus issue of *Clinical Laboratory Management Review* of a special edition devoted to laboratory information systems (January-February, 1992).
E. Ad Hoc Committee on Laboratory Management/Medical Informatics of the American Board of Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. "Towards the Development of a New Model for the Management of Clinical Information in Hospitals", A lecture presented at Pathology Grand Rounds, Department of Pathology, Duke University Medical Center, Durham, North Carolina, July 10, 1991.
2. "Managing the Information Product of Pathology", A workshop presented with J. R. Beck, M.D., at the ASCP National Meeting, New Orleans, Louisiana, September 22, 1991.
3. "The Laboratory Information System as a Strategic Tool", A one-hour teleconference presented for the American Society of Clinical Pathologists with 70 participating sites, November 12, 1991.
4. "The Role of Physicians in the Deployment and Management of Clinical Information Systems", The Harry J. Sacks Lecture in Clinical Pathology at Cedars-Sinai Medical Center, Los Angeles, California, January 24, 1992.
5. "The Role of Pathology Informatics in a Tertiary Care Medical Center. The Nitty-Gritty of Hospital Computer Politics", Two lectures delivered while a visiting professor in the Department of Laboratory Medicine and Pathology, the University of Minnesota Medical School, Minneapolis, Minnesota, February 12-13, 1992.
6. "The Hospital Clinical Laboratory in the Year 2001: An Information Technology Perspective", A lecture presented to the Diagnostics Division, Abbott Laboratories, Abbott Park, Illinois, March 5, 1992.
7. "Integrating Medical Information in the 1990s", A workshop presented at the ASCP Spring Meeting, Boston, Massachusetts, April 8, 1992.
8. "Medical Complications of Venipuncture", A lecture delivered at a symposium entitled "The Phlebotomy Team: Technical and Management Perspectives" presented at the University of Michigan Medical School, Ann Arbor, Michigan, April 25, 1992.
9. "The Clinician's Role in Health Information Systems", A lecture presented at a symposium entitled "The Information Management Executive" sponsored by HIMMS, CHIM, and the University of Michigan Department of Health Services Management and Policy, the University of Michigan, Ann Arbor, Michigan, April 30, 1992.
10. "Managing a Laboratory Information System: An Operational and Strategic Approach. The LIS Symposium: A Ten-Year Perspective", A lecture and workshop presented to the Tenth Annual Laboratory Information System Symposium, Ann Arbor, Michigan, June 10, 1992.
11. "Fundamentals of Clinical Laboratory Computing", A lecture presented to the Pathology and Experimental Toxicology Section, Parke-Davis Pharmaceutical Research Division, Ann Arbor, Michigan, June 26, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Friedman, B.A. and Mitchell, W.: The deployment of information technology in the clinical laboratories and its impact on professional roles. Clin. Lab. Manage. Rev. 1992;6:87-93.
2. Friedman, B.A. and Dito, W.R.: Managing the information product of the clinical laboratories. [Editorial] Clin. Lab. Manage. Rev. 1992;6:5-8.
3. Friedman, B.A., and Mitchell, W.: An analysis of the relationship between a department of pathology and the vendor of its laboratory information system. Am. J. Clin. Pathol. 1992;97:363-368.
4. Pierson, C.L. and Friedman, B.A.: Comparison of susceptibility to beta-lactam antimicrobics among bacteria isolated from different intensive care units. Diag. Micro. Infec. Dis. 1992;15:19S-30S.
5. Friedman, B. and Mitchell, W.: Integrating information from decentralized laboratory testing sites: the creation of a value-added network Amer. J. Clin. Pathol., In Press.

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

1. Friedman, B.A.: Information management truths in small bytes. Medical Laboratory Observer (MLO) 1992;24:52-54.
2. Friedman, B.A. and Barnes, B.W.: Who will deliver the integration solution for hospitals? Computers in Healthcare, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Director, General Chemistry Laboratory.
B. Daily sign-out and interpretation of electrophoresis results.
C. Direct operation of blood gas-electrolyte analyzers in operating rooms of Main and Mott Hospitals.
D. Direct work group for the establishment of a quality assurance program for bedside blood glucose testing.
E. Planning group for establishment of alternate site testing and near the patient testing programs.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Medical School:
   1. Developed case presentation on acute myocardial infarction for Path 600 Laboratory.
B. Pathology House Officers:
   1. Lecturer, Clinical Pathology Rounds (two lectures).
   2. Coordinator, Pathology House Officer rotation through General Chemistry Lab.
   3. Review daily sign-out and interpretation of electrophoresis results.
   4. Review of selected topics in Clinical Chemistry.
C. Medical Technologists:
   1. Program Director, Continuing Education Series for Medical Technologists.

III. RESEARCH ACTIVITIES:

A. Evaluation and standardization of an assay for Lipoprotein (a).
B. Evaluation of new methods for drugs of abuse testing.
C. CRC Protocol: Hourly variation in serum potassium and magnesium concentrations in patients with congestive heart failure (with J. Nicklas).
D. IDMH Study. Changes in serum lipids, apolipoproteins, and lipoprotein (a) in hypercholesterolemic patients following dietary therapy (with C. Orringer).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Quality Assurance Committee.
B. M-Labs/M-Care Quality Assurance Group.
C. Co-Director, M-Care Site Laboratory Advisory Group.
C. Coordinator, Chemistry Lab Supervisors Meetings.
D. Biochemistry Section Directors Group.

E. Coordinator, Clinical Chemistry In-Service Education Program.

MEDICAL SCHOOL/HOSPITAL:

A. Pathology representative to the "Standardization and Product Evaluation Committee".
B. Chair, Task Force on Standardization of Blood Glucose Testing.

REGIONAL AND NATIONAL:

A. Coordinator, College of American Pathologists Clinical Chemistry Standards Assay Laboratory.
B. Chair-Elect, Michigan Section, AACC.
C. Education Committee Chair, Michigan Section, AACC.
D. Lipids and Lipoproteins Subgroup, AACC.

V. INVITED LECTURES:

1. "Evaluation of the Roche OnLine Drugs of Abuse Testing Procedure for Cocaine and Opiates." Roche Diagnostic Systems, Nutley, New Jersey. September 1991.
2. "The Status of Clinical Laboratory Testing in the United States." Japanese Association for Medical Technology, Osaka, Japan. November 1991.
3. "Strategies for Controlling Laboratory Test Utilization." Nikkei Medical Supplement Discussion Group, Tokyo, Japan. December 1991.
4. "STAT Testing in the United States." Japanese Association for Medical Technology, Tokyo, Japan. December 1991.

VI. PUBLICATIONS:

ARTICLES SUBMITTED FOR PUBLICATION:

1. Annesley, T. and Giacherio, D.: Evaluation of the TRIAGE test kit system for the detection of drugs of abuse in urine. Clin Chem.

ABSTRACTS:

1. Giacherio, D. and Matz, K.: Comparison of three immunoturbidimetric assays for the quantitation of apolipoproteins A1 and B. Clin. Chem. 1992;38:1062.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Surgical Pathology - Room I and Room II, 13 weeks.
B. Diagnostic electron microscopy - share nephropathology work with Dr. K. Johnson and Dr. Killen.
C. Consultation service for Uropathology.
D. Conduct monthly conference in Urologic Pathology with Urology Section.
E. Participate in weekly Renal Biopsy Conference for Nephrology Section with Dr. K. Johnson and Dr. Killen.
F. Frozen Section "on call" Rotation.
G. Consultant, Veterans Administration Hospital.
H. Autopsy Service, 1 week

II. TEACHING ACTIVITIES:

A. Lectures to sophomore Pathology 600 students:
   1. Death certification and forensic pathology.
   2. Pathogenesis of highway injuries.
   3. Renal neoplasms and renal allograft rejection.
   4. Diseases of prostate and external genitalia.
   5. Testicular disease.
B. Lecture on Urologic Pathology to Dental Pathology 630 students.
C. Pathology Resident Teaching. Recipient of Resident Teaching Award for 1992.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Collaborating with urology staff and a pathology resident (Cheryl Utiger) on a study to estimate the size of prostatic adenocarcinoma based on the number of random needle biopsy cores involved.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Assistant Dean for Medical School Admissions.

UNIVERSITY:

A. None.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS

None.

BOOK REVIEW

None.

ABSTRACT

None.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Supervision of Autopsies (6 weeks).
B. Cardiovascular Pathology Consultation.
C. Cardiovascular Surgical Pathology.

II. TEACHING ACTIVITIES:

A. Lecturer, Biomedical Summer Research Program for Minority Students.

III. RESEARCH ACTIVITIES:

A. Patterns of growth factor gene expression and cell proliferation in human atherosclerosis.
B. Patterns of collagen type gene expression in human atherosclerosis.
C. Patterns of growth factor gene expression and cell proliferation in transplant arteriosclerosis (human and rat models).
D. Patterns of collagen type gene expression in transplant arteriosclerosis (human and rat models).
E. Evaluation of the effects of specific genes transferred into the artery wall (collaborative research with Gary and Betsy Nabel, Department of Internal Medicine.
F. Immunosuppressive modifications of transplant rejection (collaborative research with Larry Turka and Hua Lin in Departments of Internal Medicine and Surgery).
G. The pathobiology of arterial stenting (collaborative research with David Muller, Division of Cardiology).

SPONSORED SUPPORT:

A. Principal Investigator, "Proliferation and Growth Factors in Atherosclerosis National Institutes of Health, HL42119, five years, $710,820, 1988-1993.
B. Principal Investigator (Michigan Subcontract), "Cells and Molecules Mediating Graft Atherosclerosis." HL43322, five years $284,743, 1989-1994.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Cardiovascular Research Center, Executive Committee

REGIONAL AND NATIONAL:

A. National American Heart Association Grant-in-Aid review committee (Vascular Biology).
B. National American Heart Association Fellowship review committee.

INVITED LECTURES/SEMINARS:

1. Invited speaker: Society for Cardiovascular Pathology, Atlanta, March 1992.
2. Invited speaker: Div. of Hematology, Emory University, Atlanta, March 1992.
3. Invited speaker: Div. of Cardiology, Tufts University (St. Elizabeth's Hospital) Boston, April, 1992.
4. Invited speaker: Div. of Cardiology, Indiana University, Indianapolis, April 1992.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nelken, N., Coughlin, S., Gordon, D., and Wilcox, J.N.: Monocyte chemoattractant protein-1 in human atheromatous plaques. J. Clin. Invest. 1991;88:1121-1127.
2. O'Brien, K.D., Gordon, D.. Deeb, S., Ferguson, M., and Chait, A.: Lipoprotein lipase is synthesized by macrophage-derived foam cells in human coronary atherosclerotic plaques. J. Clin. Invest. 89:1544-1550, 1992.
3. Isik, F.F., Ferguson, M., Yamanaka, E., and Gordon, D.: Proliferating cell nuclear antigen: a marker for cell proliferation in autopsy tissue. Arch. Path. Lab. Med. 1992, In Press..
4. Carlos, T., Gordon, D., Fishbein, D., Himes, V., Coday, A., Ross, R., and Allen, M.D.: Vascular cell adhesion molecule-1 is induced on endothelium during acute rejection in human cardiac allografts. J. Heart Transplant 1992, In Press.
5. Isik, F.F., McDonald, T.O,, Ferguson, M., Yamanaka, E., and Gordon, D.: Transplant arteriosclerosis in a rat aortic model. Am. J. Pathol, 1992, In Press.
6. Urieli-Shoval, S., Meek, R.L., Hanson, R.H., Ferguson, M., Gordon, D., and Benditt, E.P.: Preservation of RNA and protein for *in situ* hybridization and immunocytochemistry. J. Histochem. Cytochem. 1992, In Press.

ABSTRACTS:

1. Rekhter, M., Nichols, S., Ferguson, M., and Gordon, D.: Cell proliferation in human arteriovenous shunts used for hemodialysis. Presented at the 1992 Restenosis Summit, Cleveland.

CARL T. HANKS, D.D.S.
PROFESSOR OF DENTISTRY
DEPARTMENT OF ORAL PATHOLOGY
ASSOCIATE PROFESSOR OF ORAL PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES: None.

II. TEACHING ACTIVITIES:

A. D.D.S. Level:
   a. Oral Pathology 694.(Sophomore Core Course)

B. Graduate Dental Level:
   a. Oral Pathology 694 (Graduate Core Course)
   c. Oral Pathology 624.(Graduate Core Course)

C. Dental Hygiene Level:
   a. Dental Hygiene 494 (Clinical Oral Pathology).
   b. Dental Hygiene 293 (General/Oral Pathology)

B. Graduate Level Advisement:
   a. John Wataha - Ph.D. Program (Oral Biology and Materials Sci-Engineering) - 4 years.
   b. Celeste Swamidoss - MSD Program (Oral Pathology) - 2.5 years.
   c. Rod Parsell - DDS program - 4 years.
   d. Fawzi El Shefei - MSD Program (Biomaterials) - 2.0 years.
   e. John C. Fat - MSD Program (Endodontics) - 2.5 years.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Specialized Materials Science Research Center"
Co-director as well as principal investigator for one of four projects.; R.G. Craig, P.I.
25% for this last year (10% of this is cost-shared with the dental school). NIDR 9/29/89-9/28/94.
$2,657,883 for direct costs, total period; $115,113 direct costs for Biocompatibility Group for the year.

B. "Restorative Dental Materials" ---Training Grant
Participating Investigator; R.G. Craig-P.I.
10% for this last year. NIDR 7/1/91-6/30/95
$258,586 for direct costs, total period

IV. ADMINISTRATIVE ACTIVITIES:

UNIVERSITY OF MICHIGAN, SCHOOL OF DENTISTRY AND DEPARTMENT OF ORAL PATHOLOGY:

A. Admissions Committee, School of Dentistry, 1985-1992.
B. Hazardous Waste Committee, School of Dentistry, 1987-1992 (Chairman).
C. Table Clinics Committee, 1989-1992.
D. Search Committees for faculty for Department of Prosthodontics, 1990-1992.
E. Director of Research, School of Dentistry, 1989-1992.
F. Vice-Chairman, Department of Oral Medicine, Pathology and Surgery, School of Dentistry, 1990-1992.
G. Organizer of Specialized Materials Center Fall Conference, 1990 -1992.
H. Biomedical Research Council, University of Michigan Medical School, 1990-1993.
I. Research Advisory Committee, Department of Surgery, University of Michigan Medical School, 1990-1992.
J. Research Dean's Committee (OVPR, U/M), 1989-1992.
K. Medical Affairs Advisory Committee to Vice Provost Zuidema, 1989-1992.
L. Chair, Search Committee for Biomaterials faculty, 1992.
M. Research Space Utilization Committee, Dental School, 1991-92.
N. Special Review Committee for DRDA Operations, 1992.

REGIONAL AND NATIONAL:

A. ADA Subcommittee on Biological Evaluation of Dental Materials (Committee Member), 1987-1992.
B. U.S. Technical Advisory Group for International Standards Organization Tissue Culture Group 194: Biological Evaluation of Medical and Dental Materials and Devices (Nominated Member), 1989-1992.
C. Constitution Committee for American Association for Dental Research, 1991-1994.
D. External Review Board for NIDR Program Project in Materials Science, University of Missouri at Kansas City.

V. OTHER RELEVANT ACTIVITIES:

A. Consultant: W. R. Grace Co.
B. Consultant: Kerr Manufacturing Co.
C. Consultant: Paladin Medical (Baxter).
D. Special Study Sections, NIDR, 1988-1991.

PROFESSIONAL ORGANIZATIONS:

A. International Association for Dental Research.
B. American Academy of Oral Pathology.
C. American Association for the Advancement of Science.
D. Omicron Kappa Upsilon.
E. Tissue Culture Association (National).
F. New York Academy of Sciences.
G. Sigma Xi.
H. American Association of Dental Schools

EDITORIAL REVIEW BOARDS:

A. Journal of Dental Research.
B. Journal of the American Dental Association.
C. Journal of Periodontal Research.

INVITED LECTURES/SEMINARS: None

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wataha, M.C., Craig, R.G. and Hanks, C.T.: The release of elements of dental casting alloys into cell-culture medium. J. Dent. Res. 1991;70(6):1014-1018.
2. Hanks, C.T., Strawn, S.E., Wataha, J.C. and Craig, R.G.: Cytotoxic effects of resin components on cultured mammalian fibroblasts. J. Dent. Res. 1991;70(11):1450-1455.
3. Wataha, J.C., Hanks, C.T. and Craig, R.G.: The in vitro effects of metal cations on eukaryotic cell metabolism. J. Biomed. Mater. Res. 1991;25(9):1133-1150.
4. Wataha, J.C., Craig, R.G. and Hanks, C.T.: The precision of and new methods for testing in-vitro alloy toxicity. Dental Mater. 1992;8:65-71.

ARTICLES IN PRESS OR ACCEPTED BY PEER-REVIEWED JOURNALS:

1. Hanks, C.T., Parsell, R.R., Strawn, S.E. and Wataha, J.C.: Delineation of cytotoxic concentrations of two dentin bonding agents in vitro. (Accepted by J.Endodon. for publication in 1992).
2. Wataha, J.C., Craig, R.G. and Hanks, C.T.: The effects of cleaning on the kinectics of in vitro metal release from dental casting alloys. (Accepted by J.Dent.Res. for publication in 1992).
3. Wataha, J.C., Hanks, C.T. and Craig, R.G.: In vitro synergistic, antagonistic, and duration of exposure effects of metal cation on eucaryotic cells. (Accepted by J.Biomed.Mater.Res. for publication in 1992).

ARTICLES SUBMITTED TO PEER-REVIEWED JOURNALS: None

ABSTRACTS:

1. Wataha, J.C., Craig, R.G. and Hanks, C.T.: Precision of new methods for testing in vitro alloy toxicity. J. Dent. Res. 1991;70(sp.iss.):361(abst. 766).
2. Nassiri, M.R., Cameron, M.J., Strawn, S., Wataha, J.C., Hanks, C.T. and Craig, R.C.: Metal ion affects the cell cycle progression. J. Dent. Res. 1991;70(sp.iss.):361(abst. 767).
3. Hanks, C.T., Parsell, R.R., Strawn, S.E. and Wataha, J.C.: Cytotoxicity of dentin bonding agents with monolayer and dentin diffusion. J. Dent. Res. 1991;70(sp.iss.):361(abst.947).
4. Strawn, S.E., Nassiri, M.R., Hanks, C.T., Cameron, M.J., Wataha, J.C. and Craig, R.G.: Bis-GMA and UDMA effects on cell metabolism and cell cycle. J. Dent. Res. 1991;70(sp.iss.):361(abst. 948).
5. El-Shafei, F.A., Nassiri, M.R., Hanks, C.T. and Craig, R.G.: Cytotoxic evaluation of heat-treated composite resin inlay by flow cytometry. J. Dent. Res. 1991;70(sp.iss.):361(abst.1051).
6. Dahlgren, J.A., Syed, S.A. and Hanks, C.T.: In vitro adhesion of oral bacteria to three biomaterials. Annual Meeting of the American Society of Microbiologists, abstract at 1991 meeting.

CURTIS A. HANSON, M.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DIRECTOR, CLINICAL PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Clinical Flow Cytometry Laboratory.
B. Clinical Hematology Laboratory.
C. Diagnostic Surgical Pathology, Hematopathology.
D. Consultant for Hematopathology cases.
E. Clinical Molecular Diagnostics Laboratory.
F. Director, Clinical Pathology Laboratories
G. Medical Director, Medical Technology Program, Eastern Michigan Univeristy

II. TEACHING ACTIVITIES:

A. Medical Students and Graduate Students:
   1. Three lectures, Hematopathology - Pathology 600 course.
   2. Laboratory Instructor (2 sessions), Hematopathology - Pathology 600 course.
   3. M4 Clerkship, Hematology portion of Clinical Pathology Rotation.
   4. M4 elective in Laboratory Medicine (in planning).
B. House Officers:
   1. Sign-out of bone marrow biopsies and aspirates.
   2. Review of blood smears and body fluids in Hematology Laboratory.
   3. Review of Flow Cytometry results and correlation with hematologic diagnosis.
C. Hematopathology teaching:
   1. Hematopathology Lectures/biweekly.
   2. Hematopathology unknown conferences/biweekly.
D. Clinical Pathology Grand Rounds (two lectures).
E. Clinical Pathology Case Conference (weekly).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Clinical Oncology Fellowship Program, American Cancer Society, 1991 - 1992 ($10,000).

PROJECTS UNDER STUDY:

A. Acute Biphenotypic Leukemias.
B. Immunophenotyping in Chronic Lymphoproliferative Disorders.
C. CD2-Positive Acute Myeloid Leukemia.
D. CD7 Expression in Acute Leukemias.
E. Cytogenetic Abnormalities in Myeloproliferative and Myelodysplastic Syndromes.

F. Automated Blood Differential Counts.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Quality Assurance Committee, Department of Pathology, 1991-present.
B. Co-Director, Clinical Hematology Laboratory, The University of Michigan Hospitals, 1987-present.
C. Co-Director, Flow Cytometry Laboratory, The University of Michigan Hospitals, 1991-present.
D. Leukemia Conference, biweekly.
D. Chairman's Advisory Committee, The University of Michigan Hospitals, 1990-present.
E. Director, Hematopathology Fellowship Program, The University of Michigan Hospitals, 1989-present.
F. Director, Clinical Pathology/Clinical Laboratories, The University of Michigan Hospitals, 1991-present.

REGIONAL AND NATIONAL:

A. Associate Editor of Pathology Patterns (American Journal of Clinical Pathology, Supplement).
B. Editorial Board, American Journal of Clinical Pathology
C. Council for New Scientific Technology in Clinical Pathology, American Society of Clinical Pathologists.
D. Ad hoc reviewer of articles for Blood, American Journal of Pathology, Laboratory Medicine and Clinical Immunology and Immunopathology.
E. Review of Southwest Oncology Group (SWOG) leukemia cases

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Lecturer, Automated Differential Counts in the Hematology Laboratory, Internal Medicine Grand Rounds, Department of Internal Medicine, University of Michigan, September 12, 1991.
2. Lecturer, Flow Cytometry and Southern Blotting in the Diagnosis of Leukemia and Lymphoma, course presented at the American Society of Clinical Pathologists (ASCP), New Orleans, Louisiana, September 23, 1991.
3. Lecturer, Acute Lymphocytic Leukemia, Course presented at the American Society of Clinical Pathologists (ASCP), New Orleans, Louisiana, September 26, 1991.
4. Lecturer, Automated Leukocyte Differentials in a University Setting, Coulter Corporation, Romulus, Michigan, October 10, 1992.
5. Co-Chairman, Hematopathology platform session, United States and Canadian Academy of Pathology (USCAP), Atlanta, Georgia, March 16, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chan, L.S., Hanson, C.A. and Cooper, K.D.: Concurrent eosinophilic fascitis and cutaneous T-cell lymphoma: eosinophilic fascitis as a paraneoplastic syndrome of T-cell malignant neoplasms? Arch. Dermatol. 1991;127:862-865.
2. Grossman, D.M., Hanson, C.A. and Schnitzer, B.: Simultaneous lymphocyte predominant Hodgkin's disease and large cell lymphoma. Am. J. Surg. Pathol. 1991;15:668-676.
3. Reardon, D.A., Roskos, R. and Hanson, C.A.: Viral-associated hemophagocytic syndrome in bone marrow transplantation. Am. J. Ped. Hem. Onc. 1991;13:305-309.
4. Keuck, B.D., Parkin, J., Peterson, L.C., Hanson, C.A. and Smith, R.E.: Eosinophilic leukemia - A myeloproliferative disorder distinct from the hypereosinophilic syndrome. Hematol. Pathol. 1991;5:195-205.
5. Hanson, C.A., Bockenstedt, P.L., Schnitzer, B., Fox, D.A., Keuck, B. and Braun, D.K.: S100-positive, T-cell chronic lymphoproliferative disease: Possible association with human herpes virus-6. Blood 1991;78:1803-1813.
6. Hanson, C.A.: Immunophenotyping of immunologic malignancies: to flow or not to flow. (Editorial) Am. J. Clin. Pathol. 1991;96:295-298.
7. Farnen, J.P., Tyrkus, M., Hanson, C.A., Cody, R.L. and Emerson, S.G.: Characterization of a new human multiple myeloma cell line, UMJF-2 which suppresses antibody production by T-lymphocytes in-vitro. Leukemia 1991;5:574-584.
8. Hanson, C.A., Ross, C.W. and Schnitzer, B.: Anti-CD34 immunoperoxidase staining in paraffin sections of acute leukemia: Comparison with flow cytometric immunophenotyping. Human Pathol. 1992;23:26-32.
9. Baddoura, F.K., Hanson, C.A. and Chan, W.C,: Plasmacytoid T-zone lymphoma in myelofibrosis with myeloid metaplasia. Cancer 1992;69:1457-1467.
10. Nowell, P.C., Kant, J.A., Finan, J.B., Cassileth, P. and Hanson, C.A.: Marrow fibrosis associated with a Philadelphia chromosome. Cancer Genet. Cytogenet. 1992;59:89-92.
11. Hanson, C.A.: Book Review on "Lymphoid Malignancy: Immunocytology and cytogenetics", Hanoaka M, Kadin ME, Mikata A, Watanabe S. Am. J. Surg. Pathol., In Press.
12. Hanson, C.A.: Book Review on "Diagnostic Flow Cytometry", by John S. Coon and Ronald S. Weinstein, Lab. Med., In Press.
13. Ross, C.W., Hanson, C.A. and Schnitzer, B.: CD30 (Ki-1)-positive, large cell lymphoma mimicking gastrointestinal carcinoma. Cancer, In Press.
14. Ross, C.W., Schlegelmilch, J.A., Grogan, T.M., Weiss, L.M., Schnitzer, B. and Hanson, C.A.: Detection of Epstein-Barr virus genome in Ki-1 (CD30)-positive, large cell anaplastic lymphomas using the polymerase chain reaction. Am. J. Pathol., In Press.
15. Kaminski, M.S., Fig, L.M., Zasadny, K.R., Koral, K.F. et al.: Imaging, Dosimetry, and Radioimmunotherapy with iodine-131-labeled anti-CD37 (MB-1) antibody in B-cell lymphoma. J. Clin. Oncol., In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Hanson, C.A., Swanson, P.E., Gajl-Peczalska, K.J., Jaszcz, W., Frizzera, G. and Wick, M.R.: Immunohistochemical analysis of "true histiocytic" lymphoma in paraffin sections.
2. Abruzzo, L.V., Thornton, A.J., Hanson, C.A., Evanoff, H., Westwick, J., Emerson, S. and Kunkel, S.L.: Chemotactic cytokine gene expression in human bone marrow stromal cells.
3. Miesfeldt, S., Hanson, C.A., Crist, W.M., Bohjanen, P.R,, Kim, S. and Thompson, C.B.: Lack of translocation breakpoints in the promoter region of Ets-1 in cases of acute leukemia involving 11q23.
4. Hanson, C.A., Abaza, M., Sheldon, S., Ross, C.W,, Schnitzer, B. and Stoolman, L.M.: Acute biphenotypic leukemia: immunophenotypic and cytogenetic analysis.

BOOKS AND CHAPTERS IN BOOKS:

1. Keren, D.K., Hanson, C.A. and Hurtubise P (eds), Clinical Applications in Flow Cytometry. ASCP Press, Chicago Illinois, In Press.
2. Hanson, C.A.: Reticulocyte analysis by flow cytometry, in, Keren, D.K., Hanson, C.A. and Hurtubise, P. (eds), Clinical Applications in Flow Cytometry, ASCP Press, Chicago, Illinois, In Press.
3. Carey, J.L. and Hanson, C.A.: Flow Cytometry Analysis of Leukemia & Lymphoma, in, Keren, D.K., Hanson, C.A. and Hurtubise, P. (eds), Clinical Applications in Flow Cytometry, ASCP Press, Chicago, Illinois, In Press.
4. Hanson, C.A.: The acute leukemias and myelodysplastic syndromes, in, McClatchey, K.D. (ed) Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, In Press.
5. Hanson, C.A. and Ross, C.W.: Clinical applications of molecular biology: Hematopoietic disorders, in, McClatchey, KD (ed), Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, In Press.
6. Hanson, C.A.: Peripheral blood and bone marrow: morphology, counts and differentials, and reactive disorders, in, McClatchey, K.D. (ed), Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, In Press.

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

1. Ross, C.W., Hanson, C.A., Schnitzer, B. and Sheldon, S.: Chronic myeloid neoplasia associated with eosinophilia and abnormalities of chromosome 12p. Lab. Invest. 1992;66:86A.
2. Hanson, C.A., Ross, C.W., Abaza, M. and Schlegelmilch, J.A.: CD45 expression in acute leukemias (AL) and chronic lymphoproliferative disorders (CLPD). Lab. Invest. 1992;66:78A.
3. Abaza, M.A., Ross, C.W., Sheldon, S., Stoolman, L.M., Schlegelmilch, J.A., Schnitzer, B. and Hanson, C.A.: CD7-positive acute leukemias: morphology, immunophenotype (IPH), and cytogenetics. Lab. Invest. 1992;66:73A.
4. Fivenson, D,P., Hanson, C.A. and Nickoloff, B.J.: Specific localization of the malignant clone to the epidermal compartment in cutaneous T-cell lymphoma. Amer. Fed. Clin. Res., In Press.
5. Sheldon, S. and Hanson, C.: Two histologically and cytogenetically distinct populations of cells in a patient with acute promyelocytic leukemia. Amer. J. Human Genet., In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Unclassified malignant cutaneous neoplasms of neural crest origin.
B. Genetic Changes in Melanoma (with J. Trent)
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. Editorial Board, Archives of Dermatology.
B. Test Committees For Dermatopathology. (American Boards of Pathology and Dermatology).
C. Board of Directors, National Alopecia Areata Foundation.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. American Society of Dermatopathology, Dallas, Texas, December 1991.
2. Midland Hospital, Midland, Michigan, April 1992.
3. Munson Medical Center, Traverse City, Michigan, May 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Lefell, D.S., Headington, J.T., Wong, D.S. and Swanson, N.A.: Aggressive Growth Basal Cell Carcinoma in Young Adults. Arch. Dermatol. 1991;127:1663-1667.
2. Cornblath, W.T., Dotan, S.A., Trobe, J.D. and Headington, J.T.: Varied Clinical Spectrum of Necrobiotic Xanthogranuloma. Ophthalmology 1991;99:103-107.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Pediatric Surgical and Placental Pathology, daily, twelve months.
B. Pediatric Necropsies, daily, twelve months.
C. Pediatric Consultation Cases, daily, twelve months.
D. Adult Necropsy Service, 0.75 months.
E. Continued to organize and maintain the Michigan Cardiac Registry, twelve months.
F. Teratology Unit, histology, as necessary, approximately 40 cases per year.
G. Children's Cancer Study Group, coordinate all pathological material and data necessary for all children registered in national tumor protocols. (Collaborating investigator, NCI #2-U10-CA-02971-33, CCSG, R. Hutchinson, M.D., P.I.)

II. TEACHING ACTIVITIES:

A. M2: Pathology 600, three whole class lectures on Pediatric Pathology.
B. M4: Pediatric Surgical Pathology, twelve months, while they were on their pathology electives.
C. Supervised M4s on Pathology elective, one rotation (four weeks).
D. House Officers in Pathology, daily reading of pediatric surgicals, twelve months.
E. House Officers in Pathology, gross and microscopic supervision of most pediatric necropsies, twelve months and adult cases 0.75 months plus on-call weekends.
F. Surgical Pathology Conference, one hour/week, twelve months.
G. Lectures on Pediatric Necropsy Pathology in Core Curriculum Series for House Officers in Pathology.
H. Lectures on Pediatric Surgical Pathology in Core Curriculum Series for House Officers in Pathology.
I. Gross Necropsy Conference, one hour/week, twelve months.
J. Supervised Pediatric Hematology Fellows (two) for AP elective period.
K. Conferences:
    1. Pediatric Cardiology Death Conference, monthly, all year.
    2. Pediatric Tumor Conference, twice monthly, all year.
    3. Pediatrics CPC/General Death Conference, quarterly.
    4. Pediatric Liver-GI Conference, twice a month.
    5. Pediatric General Surgery Conference monthly.
L. Lecture: Classification and Histopathology of Pulmonary Artery Hypertension for Pediatric Cardiology Division.

III. RESEARCH ACTIVITIES:

A. Continued study of effects of various congenital heart defects on the pulmonary vasculature.
B. Study with pediatric cardiologists 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 neoplasms in post transplant patients.
B. Study of the differential development of renal tubules and glomeruli in twin fetuses and newborns with Mason Barr, M.D.
C. Continued study of the effect of ACE inhibitors on renal tubular maldevelopment with Mason Barr, M.D. (Earlier work resulted in FDA drug warning).
D. Correlation of x-rays, operative findings and histologic features of osteoblastoma and osteoid osteoma of the spine with orthopedic surgeons (see abstracts and papers).
E. Review of the predictive value of pre-ECMO lung biopsy in determining recovery of pulmonary function (Group study, pathologists, surgeons, pediatricians).
F. Correlating clinicopathologic study of histopathology of pediatric aneurysmal bone cysts with clinical recurrence risk, with pediatric orthopedic surgeons.
G. With pediatric hematologists/oncologists: histopathology slide correlation of neuroblastoma maturity with tissue gene expression.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Executive Committee for Mott/Women's/Holden/Psychiatric Hospitals.
B. Interviewing Pediatric Cardiology fellowship candidates.
C. Dean's External Review Committee for Department of Physical Medicine and Rehabilitation. (Completed, Fall 1991).

REGIONAL AND NATIONAL:

A. Member, CAP Council on Anatomic Pathology's Autopsy Committee.
B. Appointed member, Nominating Committee, Society for Pediatric Pathology.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Grossman, D.M, Long, J., Heidelberger, K.P. and Lloyd, R.V.: Expression of tyrosine hydroxylase protein and chromogranin A protein and messenger RNA in paraffin-embedded sections of neuroendocrine neoplasms. Endocrine Pathology 1991;2:148-154.
2. Minich, L., Beekman, R.H., Rocchini, A.P., Bove, E.L. and Heidelberger, K.P.: Surgical repair is safe and effective after unsuccessful angioplasty of native coarctation. J. Am. Coll. Cardiol. 1991;19:389-393
3. Frommelt, M.A., Snider, A.R., Crowley, D.C., Meliones, J.N. and Heidelberger, K.P.: Echocardiographic indexes of cardiac allograft rejection in transplant recipients. Echocardiogr. 1992;5:41-47.

4. Heidelberger, K.P.: Paediatric Pathology, 2nd Edition. Book Review. Arch. Path. Lab. Med. 1992;116:302. (Invited review; Journal is refereed).
5. Raskas, D.S., Graziano, G.P., Herzenberg, J.E., Heidelberger, K.P. and Hensinger, R.N.: Osteoid osteoma and osteoblastoma of the spine in children. J. Spinal Disorders 1992;5:204-211.

ABSTRACTS:

1. Raskas, D.S., Graziano, G.P., Herzenberg, J.E., Heidelberger, K.P. and Hensinger, R.N.: Osteoid osteoma and osteoblastoma of the spine in children. Presented at 59th Annual Meeting American Academy of Orthopedic Surgeons, Washington D.C., February, 1992.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. With C.J. D'Amato prepare microscopic descriptions of most UM autopsy brains for the Pathology House Officers which after review with the officers are incorporated into the final autopsy report. We also examine many of the brains sent to the Department for diagnosis, and prepare gross and microscopic descriptions. Many of these brains are from patients with clinical dementia.

II. TEACHING ACTIVITIES:

A. Review microscopics of some of the above brains with house officers in Pathology and other house officers spending time in the department of Pathology.
B. Neural and Behavioral Sciences 600 for second year medical students: two hours of lecture on neuropathology.
C. Neuropathology 858, a laboratory - lecture course for house officers in Pathology, Neurology, Neurosurgery, and other neural areas, graduate students and occasionally faculty and undergraduate students. 18 hours including two lectures.

III RESEARCH ACTIVITIES:

Pathologic studies of the autopsy brains of people with various forms of dementia and related nervous diseases in collaboration with members of the Deparment of Neurology and others.

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

A. American Association of Neuropathologists.
B. American Academy of Neurology.
C. Society of Neuroscience.
D. American Society of Human Genetics.

V. OTHER RELEVANT ACTIVITIES:

None

VI. PUBLICATIONS:

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

ABSTRACTS:

1. D'Amato, C.J., Foster, N.L., Sima, A.A.F. and Hicks, S.P.: Swollen cortical neurons and Lewy bodies accompanying progressive supranuclear palsy and Creutzfeldt-Jakob's disease. J. Neuropathol. & Exper. Neurol. 1992;51:324.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVTIES:

SPONSORED SUPPORT:

A. "Oxidants and Protease Interaction in Acute Lung Injury". National Institutes of Health. Principal Investigator. $834,625 for five years.
B. "Oxidants and Glomerular Injury", Project V, Renal Center Grant. National Institutes of Health. Principal Investigator, $246,585 for five years.
C. "Mechanisms of Glomerular and Tubular Injury", Core B, Renal Center Grant. National Institutes of Health, Principal Investigator, $147,795.
D. "Inflammatory Cells and Lung Injury", Core C, National Institutes of Health, Principal Investigator, $291,025.
E. "Crescentic Nephritis Program Project", Core B, Principal Investigator, National Institutes of Health, $204,490.

PENDING SUPPORT:

A. "Aging, Anesthesia and Influenzia Infection", with Paul Knight, Anesthesia and Dan Remick, Pathology. National Institutes of Health, Co-Investigator.
B. "DNA Methylation and SLE", with Bruce Richardson, Rheumatology. National Institutes of Health, Co-Investigator.
C. "Amino Acids and Cell Injury", with Joel Weinberg, Nephrology and James Varani, Pathology. National Institutes of Health, Co-Investigator.

PROJECTS UNDER STUDY:

A. Pathogenesis of IgG and IgA Immune Complex Lung Injury.
   1. Role of oxygen radicals.
   2. Role of proteases.

3. Role of terminal components of the complement system.
B. Oxidant and protease interaction in inflammation.
C. Pathogenesis of aspiration pneumonitis.
D. Pathogenesis of viral pneumonitis.
E. Pathogenesis of pancreatitis and pancreatitis Induced ARDS.
F. Adhesion molecules and cytokines in inflammation.
G. Cyclosporine induced nephrotoxicity.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

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

V. INVITED LECTURES AND SEMINARS:

1. Invited Speaker, "Metalloproteinases in Inflammation", AMGEN Corporation.
2. Invited Speaker and Symposium Moderator, Cyclosporine and Autoimmune Diseases, Bad Zurzach, Switzerland.
3.. Visiting Professor, University of Basle, Basle, Switzerland.

VI. OTHER RELEVANT ACTIVITIES:

A. Consultant on Dermatology and Nephrology training grants.

VII. PUBLICATIONS:

ARTICLES PUBLISHED IN REFEREED JOURNALS:

1. Weinberg, J.M., Varani, J., Johnson, K.J., Rosser, N.F., Dame M.K., Davis, J.A. and Venkatachelam, M.S.: Protection of human umbilical vein endothelial cells of glycine and structurally similar amino acids against calcium and hydrogen peroxide-induced lethal cell injury. Am. J. Pathol. 1992;140:457-471.
2. Weinberg, J.M., Venkatachalam, M.A., Roeser, N.F., Davis, J.A., Varani, J. and Johnson, K.J.: Amino acid protection of cultured kidney tubule cells against calcium ionophore-induced lethal cell injury. Lab. Invest. 1991;65:671-678.

3. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines, toxic oxygen products and cell injury. Mol. Asp. Med. 1991;12:169-174.
4. Barker, J.N.W.N., Jones, M.L., Swenson, C.L., Sarma, V., Mitra, R.S., Ward, P.A., Johnson, K.J., Fantone, J.C., Dixit, V.M. and Nickoloff, B.J.: Monocyte chemotaxis and activating factor production by keratinocytes in response to IFN-g. J. of Immunol. 1991;146:1192-1197.
5. Schmeling, D.J., Oldham, K.T., Guice, K.S., Kunkel, R.G. and Johnson, K.J.: Experimental obliterative cholangitis. A model for the study of biliary atresia. Ann. Surg. 1991;213:350-355.
6. Varani, J., Stoolman, L., Wang, T., Schuger, L., Flippen, C., Dame, M., Dixit, V.M., Johnson, K.J., Todd, R.F., Ryan, U.S. and Ward, P.A.: Thrombospondin production and thrombospondin mediated adhesion on U937 cells. Exp. Cell Res. 1991;195:177-182.
7. Varani, J., Gibbs, D.F., Johnson, K.J., Weinberg, J.M., Ryan, U.S., Ginsburg, I. and Ward, P.A.: Hydrogen peroxide-induced cell and tissue injury: protective effects of MN^{2+}. Inflammation 1991;15:291-301.
8. Varani, J., Jones, J., Dame, M.K., Sulavik, C., Gibbs, D.F. and Johnson, K.J.: Effects of all-trans retionic acid on neutrophil-mediated endothelail cell injury and immune complex injury in rats. Am. J. Pathol. 1991;139:901-910.

ARTICLES ACCEPTED FOR PUBLICATION:

1. Ward, P.A. and Johnson, K.J.: Lung inflammatory mechanisms. J. Human Path., In Press.
2. 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.
3. Ward, P.A., Johnson, K.J. and Till, G.O.: Mechanisms of lung injury. Prax. Klin. Pneumonol., In Press.
4. 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.
5. Huber, A.R., Ellis, S., Johnson, K.J., Dixit, V.M. and Varani, J.: Monocyte diapedesis through an *in vitro* vessel wall construct: Inhibition with monoclonal antibodies to thrombospondin. J. Leuk. Biol., In Press.
6. Knight, P.R., Druskovich, G., Tait, A.R. and Johnson, K.J.: The role of neutrophils, oxidants and proteases in the pathogenesis of acid pulmonary injury. Anesthesiology, In Press.
7. 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.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Tait, A.R., Davidson, B.A., Johnson, K.J., Remick, D.G. and Knight, P.R.: Halothine alters the cellular immune response to influenza virus infection in mice. Submitted for publication.
2. Tait, A.R., Davidson, B.A., Johnson, K.J., Remick, D.G. and Knight, P.R.: Production of tumor necrosis factor following influenza infection in mice: The effect of Halothine Anesthesia. Submitted for publication.
3. 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.
4. Shayevitz, J.R., Johnson, K.J., Knight, P.R.: Halothane-oxidant interactions in the ex vivo perfused rabbit lung: edema formation and eicosanoid production. Submitted for publication.
5. Ginsburg I., Schuger L., Gibbs, F., Johnson, K.J., Ryan, U.S., Ward, P.A. and Varani, J.: Endothelial cell killing by polymorphonuclear leukocytes: Independent and synergistic roles for oxygen radicals and proteases. Am. J. Pathol., Submitted.
6. Chan, L.S., Hammerberg, C., Soong, H.K., Johnson, K.J. and Cooper, K.D.: Cicatricial pemphigoid: Its clinical spectrum and its distinction from bullous pemphigoid. Submitted.
7. 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.

8. Quddus, J., Johnson, K.J., Gavalchin, J., Amento, E., Crisp, C. and Richardson, B.: Mature T cells treated with a DNA methylation inhibitor induce a lupus-like disease in syngeneic mice. Submitted for publication.
9. Johnson, K.J., Dixit, V.M. and Varani, J.: Role of thrombospondin in the acute inflammatory response. Submitted for publication.
10. Johnson, K.J., Sulavik, C. and Rehan, A.: Role of oxygen radicals in autologous anti-GBM nephritis. Submitted for publication.
11. Mulligan, M.S., Johnson, K.J., Smith, C.W., Anderson, D.C. and Ward, P.A.: Requirements for CD18 and TNFa in Nephrotoxic Nephritis. J. Clin. Invest. Submitted for publication.
12. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines, toxic oxygen products and cell injury. Submitted for publication.
13. Huber, A.R., Johnson, K.J. and Varani, J.: Monocyte diapedesis through an in vitro vessel wall construct: Inhibition with monoclonal antibodies to thrombospondin. Submitted for publication.
14. Messana, J.M., Johnson, K.J., Leichtman, A.B., Ellis, C.N., Mihatsch, M.J., Hamilton, F.A., Groisser, O.S., Gartside, M.S. and Voorhees, J.J.: A prospective study of the effects of low dose cyclosporine on renal structure and function in psoriasis patients. Submitted for publication.
15. 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.
16. Richardson, B., Buckmaster, T., Keren, D. and Johnson, K.J. Evidence that macrophages are programmed to die after activating cloned, antigen specific CD4+ T cells. Submitted for publication.
17. Zador, I.Z., Deshmukh, G.O., Kunkel, R. and Johnson, K.J., Radin, N.S., Sheyman, J.A.: A role for gylycosphingolipid accumulation in the renal hypertrphy of streptozotocin-induced diabetes mellitus. Submitted for publication.
18. Richardson, B.C., Buckmaster, T., Keren, D.F. and Johnson, K.J.: Evidence that macrophages are programmed to die after activating autologous, cloned antigen specific, CD4+ T cells. Submitted for publication.
19. Gilardy, A., Dysko, R.C., Spilman, S.C., Kunkel, R.G., Brammer, D.W. and Johnson, K.J.: Immune complex vasculitis with secondary ulcerative dermatitis in aged C57BL/6NNia mice. Submitted for publication.
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. 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.), Progress in Applied Microcirculation, Vol. 9, Karger, Basel, In Press.
3. Ward, P.A., Johnson, K.J. and Till, G.O.: Leukocyte oxygen radicals and acute lung injury, in, Proceedings of a Symposium on "Acute Lung Injury", PSG Publishing Co., Littleton, Massachusetts, In Press.
4. Warren, J.S., Ward, P.A. and Johnson, K.J.: The inflammatory response, Chapter 8, in, Williams W.J. (ed), Hematology, 4th Edition, 1991.
5. Warren, J.S., Ward, P.A. and Johnson, K.J.: Oxygen radicals as Mediators of inflammation', Volume 6, in, Henson, P.M. (ed.), The Handbook of Inflammation, Vol.6, Elsevier Biomedical Division, Amsterdam, The Netherlands, In press.
6. 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, NY, In Press.

7. Warren, J.S., Johnson, K.J. and Ward, P.A.: Consequences of oxidant injury, in, The Lung: Scientific Foundations, Crystal, R.G. and West, T.B. In Press.
8. 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 Approches, In Press.
9. 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.
10. 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.
11. Ward, P.A., Till, G.O., Gannon, D.E., Varani, J.A. and Johnson, K.J.: The role of iron in injury of endothelial cells *in vitro* and *in vivo*, in, Simic, M.D., Taylor, K.A., Ward, J.F. and Sonntag, C.C. (eds), Oxygen-Radicals in Biology and Medicine, 4-ICOR Conference, Plenum Press, New York, pp. 969-974, 1989.
12. 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.
13. Warren, J.S., Johnson, K.J. and Ward, P.A.: 7.5.2 Immunoglobulin and complement mediated immune injury, in, Crystal, R.G., West, J.B., Barnes, P.J., Cherniack, N.S. and Weibel, E.R. (eds), The Lung: Scientific Foundations, Raven Press, New York, pp. 1939-1946. 1991.
14. Warren, J.S., Ward, P.A. and Johnson, K.J.: Oxygen radicals as "mediators of inflammation", Volume 6, Henson, P. (ed), The Handbook of Inflammation, Elsevier Biomedical Division, Amsterdam, The Netherlands, In Press.
15. 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.
16. 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.
17. Johnson, K.J., Chensue, S.W., Kunkel, S.L. and Ward, P.A.: Immunopathology in essential pathology, in, Rubin, E. and Farber, J.L. (eds.), J.B. Lippincott Inc., Philadelphia, 1991.
18. 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.
19. 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.
20. Warren, J.S., Johnson, K.J. and Ward, P.A.: Consequences of oxidant injury, Crystal, R.G., West, J.B., Bames, P.J., Cherniack, N.S. and Weibel, E.R. (eds), The Lung: Scientific Foundations, Raven Press, New York, pp.1829-1838. 1991.
21. Warren, J.S., Ward, P.A. and Johnson, K.J.: The respiratory burst and mechanisms of oxygen radical mediated tissue injury, in, Sbarra, A.J. and Strauss, R.P. (eds), The Respiratory Burst and its Physiological Significance in Medicine, Plenum Press, New York, New York, In Press.

ABSTRACTS, PRELIMINARY COMMUNICATIONS, PANEL DISCUSSIONS

1. Johnson, K.J., Sulavik, C., Gibbs, D. and Varani, J.: In vivo suppression of immune complex injury by all-trans retinoic acid. FASEB J. 1991;5:5207.
2. 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 lethel injury. FASEB J. 1991;5:3008.
3. Sulavik, C. and Johnson, K.J.: The role of oxygen radicals in autologous anti-GBM glomerulonephritis. FASEB J. 1991;5:5299.

4. Johnson, K.J., Jones, J., Dame, M., Gibbs, D.F. and Varani, J.: *In vitro* and *in vivo* modulation of the acute inflammatory response of all-trans retinoic acid. J. Cell Biochem. 1991;150:220(cc200).
5. Varani, J., Gibbs, D.F., Mukhopadhyay, P.S., Sulavik, C., Johnson, K.J., Weinberg, J.M., Ginsburg, I. and Ward, P.A.: Hydrogen peroxide-induced cell and tissue injury; Protective effects of manganese. J. Cell Biochem. 1991;150:223(cc210).
6. Gilardy, A.K., Johnson, K.J., Brammer, D.W., Spilman, S.C. and Dysko: Immune complex vasculitis and glomerulonephritis with secondary ulcerative dermatitis in aged C57B1/6 mice. AALAS, 1991.
7. Coleman, B.S., Rutler, T., Tait, A.R., Johnson, K.J. and Knight, P.R.: The effect of duration of anesthetic exposure on pulmonary acid injury. ASA, 1991.
8. Knight, P.R., Tait, A.R., Druskovich, G. and Johnson, K.J.: Pathogenesis of pulmonary acid injury. ASA, 1991.
9. Knight, P.R., Tait, A.R., Davidson, B., Remick, D. and Johnson, K.J.: Pulmonary production of tumor necrosis factor during halothine anesthesia in mice. ASA, 1991.
10. Mulligan, M.S., Johnson, K.J., Smith, C.W., Anderson, D.C. and Ward, P.A.: Requirements for CD18 and TNFa in nephrotoxic nephritis. ASN, 1991.
11. Mulligan, M.S., Johnson, K.J., Smith, C.W., Anderson, D.C. and Ward, P.A.: Nephrotoxic nephritis: role of TNFa and adhesion molecules. JASN 1991;2(3):555.
12. Rutter, T., Knight, P., Tait, A., Coleman, E. and Johnson, K.J.: Pathogenesis of gastric particulate lung injury. FASEB, 1992.
13. Knight, P., Tait, A. and Johnson, K.J.: The role of neutrophils, oxidants, and proteases in pulmonary acid injury. FASEB, 1992.
14. Kunkel, R.G., Mulligan, M.S., Johnson, K.J., Riggs, L.K., Riggs, L.K. and Ward, P.A.: Morphologic studies on inhibition of acute glomerulonephritis by TNFa. FASEB, 1992.
15. Mulligan, M.S., Johnson, K.J., Tamatini, T., Miyasaka, M., Anderson, D.C., Smith, C.W. and Ward, P.A.: Requirements for CD18 and ICAM.1 in nephrotoxic nephritis. FASEB, 1992.
16. Johnson, K.J., Varani, J., Mulligan, M., Smith, C.W., Anderson, D.C. and Ward, P.A.: The role of adhesion molecules in leukocyte mediated glomerular injury. Keystone Symposium, 1992.
17. Young, E.W., Johnson, K.J., Leichtman, A.B., Mihatsch, M.J., Messana, J.M., Ellis, C.N. and Voorhees, J.J: Progressive renal interstitial fibrosis in psoriasis patients treated with low-dose maintenance cyclosporine. ASN, 1992.

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

ANNUAL DEPARTMENT REPORT
1 JULY, 1991 - 30 JUNE, 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Directed weekly 1991-92 Clinical Pathology Grand Rounds.
B. Coordinated weekly 1991-92 Anatomical Pathology Conferences.
C. Coordinated Core-Lecture Series in Blood Banking for 1st-year Pathology House Officers.
D. Attended and participated in weekly Clinical Pathology Case Study Conferences.
E. Made two presentations at Clinical Pathology Grand Rounds:
   1. Immune hemolysis.
   2. Rh blood groups.
F. Trained Pathology and Pediatric Hematology Residents in Immunohematology.
G. Provided instruction to Pathology Residents during their Blood Bank Rotation.
H. Director, Current Topics in Blood Banking Conference, Towsley Center for Continuing Medical Education:
   1. Planned and coordinated the June, 1992 Current Topics in Blood Banking Symposium and Preconference Workshops
   2. Presented Workshop entitled: Serological Testing in the Detection, Diagnosis and Transfusion Management of Immune Hemolysis
   3. Presented talk entitled: Pitfalls in Pretransfusion Testing.
   4. Moderated morning session on Transfusion Management.
I. Provided experience in pretransfusion testing to 10 1st-year minority medical students.

III. RESEARCH ACTIVITIES:

1. Alloanti-N in an *MS^{u}/MsHe* individual. ME Reid, F. Alexander, M. Yacob, R, Oyen, K. Lee, and W.J. Judd. Submitted for presentation at the 1992 Annual Meeting of the American Association of Blood Banks, San Francisco, November, 1992.
2. State association sponsored program for SBB Candidates. W.J. Judd, L. Eisenbrey and M. Weaver. Submitted for presentation at the 1992 Annual Meeting of the American Association of Blood Banks, San Francisco, November, 1992.
3. The computer crossmatch. S.H. Butch, W.J. Judd, E.A. Steiner, M. Stoe and H.A. Oberman. Submitted for presentation at the 1992 Annual Meeting of the American Association of Blood Banks, San Francisco, November, 1992.
4. Anti-Vw hemolytic disease of the newborn with a negative direct antiglobulin test. W.J. Judd, J.A. Hoschner, S.R. Kahn, E. A. Steiner, J. Poole, L. Sausis and M.E. Reid. Submitted for presentation at the 1992 Annual Meeting of the American Association of Blood Banks, San Francisco, November, 1992.

5. In vitro hemolytic autoanti-M: the second example. W.J. Judd, E.A. Steiner, P. Knafl and C. Hunter. Submitted for presentation at the 1992 Annual Meeting of the American Association of Blood Banks, San Francisco, November, 1992.
6. Know your monoclonals: an absolute must for the effective resolution of blood typing problems. W.J. Judd, T. Annesley, J. Kirkegaard and M.L. Beck. Submitted for presentation at the 1992 Annual Meeting of the American Association of Blood Banks, San Francisco, November, 1992.
7. Genetic basis for weak expression of B in a group A Korean family. F. Yamomoto and S. Hakomori, Judd, W.J., Davenport, R.D. University of Washington, Seattle, WA and University of Michigan, Ann Arbor, MI. 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:

A. Michigan Association of Blood Banks:
Chairman, Advanced Lectures in Blood Banking Program - coordinated a series of 60 lectures and two full-day workshops for MABB members seeking Certification as a Specialist in Blood Banking.
B. American Association of Blood Banks:
Board of Directors, North Central District Representative.
Technical Manual Committee - Editor, Special Methods Section for 11th edition.
C. Reviewer of articles submitted for publication in Transfusion and Immunohematology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES:

1. When the urine is red. Annual Meeting of the Michigan Association of Blood Banks, Dearborn, Michigan, September, 1991.
2. Are there better ways than the crossmatch to detect ABO errors? Annual Meeting of the Michigan Association of Blood Banks, Dearborn, Michigan, September, 1991.
3. Pretransfusion testing: what else can go? Philadelphia Area Antibody Club, Philadelphia, Pennsylvania, October 1991.
4. The Electronic Crossmatch. Annual Meeting of the Pennsylvania Association of Blood Banks, Atlantic City, New Jersey, April, 1992.
5. Prenatal Testing. Annual Meeting of the California Blood Bank Society, Sacramento, California, May, 1992.
6. The Rh Blood Groups. Michigan Association of Blood Banks Advanced Lecture Series. William Beaumont Hospital, Troy, Michigan.
7. The MN Blood Groups. Michigan Association of Blood Banks Advanced Lecture Series. William Beaumont Hospital, Troy, Michigan.

PANEL DISCUSSIONS/WORKSHOPS

1. Monoclonal antibodies: boon or burden? Teleconference: American Society for Clinical Pathology, June, 1992.

2. Appropriate serological testing. Kansas Society for Medical Technology, Wichita, Kansas, April, 1992.

VI. PUBLICATIONS:

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

1. Judd, W.J., Steiner, E.A. and Oberman, H.A.: Can the reading for serological reactivity following 37°C incubation be omitted? Transfusion 1992;32:304-8.
2. Nugent, C.E., Gelinas, J.R., Judd, W.J. and Steiner, E.A.: Anti-Yt^a does not cause hemolytic disease of the newborn. Obst. Gynecol. 1992;79:872-3.
3. Judd, W.J., Steiner, E.A., Abruzzo, L.V., Davenport, R.D., Oberman, H.A., Pehta, J.C and Nance, S.J.: Anti-i causing acute hemolysis following a negative immediate-spin crossmatch. Transfusion, Accepted for publication.
4. Chenoweth, C.E., Judd, W.J., Steiner, E.A. and Kauffman, C.A.: Cefotetan-induced immune hemolytic anemia. Clinical Infectious Diseases, Accepted for publication.
5. Judd, W.J.: Polyagglutination (editorial). Immunohematology; Accepted for publication.

CHAPTERS IN BOOKS:

1. Judd, W.J.: Pretransfusion testing, in, McClatchey, K.D. (ed), Clinical Laboratory Medicine, Williams and Wilkins, Co., Baltimore, Maryland.

ABSTRACTS/LETTERS:

1. Judd, W.J.: On proper terminology (letter). Transfusion 1992;32:88.
2. Beck, M.L. and Judd, W.J.: Increased incidence of acquired-B associated with use of monoclonal typing reagents. Accepted for presentation at the Annual Meeting of the British Blood Transfusion Society, York, 1992.
3. Reid, M.E., Yacob, M., Oyen, R. and Judd, W.J.: Alloanti-N in an $MS^u/MsHe$ individual. Accepted for presentation at the Annual Meeting of the British Blood Transfusion Society, York, 1992.
4. Judd, W.J., Steiner, E.A. and Nugent, C.E.: Appropriate Serological Testing in Pregnancy (letter). Accepted for publication in Vox Sanguinus.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Board Certification, Anatomic Pathology.
B. Autopsy Pathology.
C. Diagnostic Renal Biopsy Service.

II. TEACHING ACTIVITIES:

A. Pathology 631 - Pathology Laboratory for Dental Student. Approximately 60 contact hours.
B. Pathology 580 - three contact hours.
C. Gross Pathology Conference.
D. Renal Pathology Conference.
E. Renal Pathology for Nephrology Fellows (20 contact hours).
F. Post Doctoral Fellows (4).
G. Graduate Students (3).
H. Dissertation Committees (9).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH-P01-HL31963, Principal Investigator, Project VI "Molecular Biology of Alveolar Wall Injury", (40% Effort) $87,140/year, 3/1/89 - 2/28/94.
B. NIH-P50-DK39225, Principal Investigator, Project XI "Monokine-Mediated Matrix Biosynthesis by Mesangial Cells", (10% Effort) $39,110/year, 8/1/88-7/30/93.
C. NIH-RO1-DK44848, Principal Investigator, "Collagen IV Gene Transcription in cpk/cpk Mice", (25% Effort) $143,000/first year, 9/30/91-9/29/96.
D. American Heart Association-Grant-in-Aid, Principal Investigator, "Collagen IV Gene Regulation During Renal Development", $25,500, 7/01/91-9/30/92.

PENDING SUPPORT:

A. NIH-P50-DK39225, Principal Investigator, Project VI "TGF-β Induced Collagen IV Gene Transcription" (10% Effort) $49,822/year 8/1/92-7/30/97.
B. NIH-RO1, Co-Investigator, "Renal Fibrosis" (10% Effort) $198,213/first year, 4/1/93-3/30/98.
C. NIH-RO1-DK40042, Co-Investigator, "Role of EDRF in the Juxtaglomerular Apparatus", (10% Effort) $181,858/first year, 4/1/93-3/30/98.
D. NIH-Physician Scientist Award, Co-Sponsor, "Aldose Reductase Expression in Diabetes", $60,429/year, 4/1/93-3/30/98.

PROJECTS UNDER STUDY:

A. Structure and function of collagen IV.
B. Regulation of collagen IV gene expression during development.
C. Localization of nephron segment-specific genes by PCR.
D. Role of aldose reductase in diabetic complications.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Post-doctoral candidate recruitment, Immunopathology Training Grant.
B. Anatomic Pathology Accessioning Committee.

MEDICAL SCHOOL/HOSPITAL:

A. Faculty recruitment - Department of Pathology.
B. Faculty recruitment - Department of Internal Medicine.
C. Curriculum development-M1 Pathology.
D. Curriculum development-M2 Urinary System.

REGIONAL AND NATIONAL:

A. Planning Committee, Genetic Basis of Renal Disease. NIDDK, NIH.
B. Ad hoc reviewer, Division of Extramural Activities, NIDDK, NIH.
C. Ad hoc Reviewer, Juvenile Diabetes Foundation.
D. Reviewer, Laboratory Investigation, American Journal of Pathology, Journal of Clinical Investigation. Journal of Cell Biology, Journal of Biological Chemistry, Journal of American Soc. of Nephrology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Speaker, "Regulation of Collagen IV Transcription", Forefronts in Nephrology, Banz, Germany, 1991.
2. Invited Speaker, "Regulation of Collagen IV Transcription", International Symposium Cell and Molecular Biology of Basement Membranes in Health and Disease, Airlie, Virginia, 1991.
3. Invited Speaker, "Collagen IV Expression in Normal and Pathological States" Leiden, The Netherlands, 1992.
4. Invited Speaker, "Collagen Expression in Glomerular Disease", Molecular Approaches to Nephrology: Prospects in Diagnosis and Management, Bari, Italy, 1992.
5. Symposium Organizer and Invited Speaker, "Interstitial Scarring in the Kidney", 25th Meeting of the American Society of Nephrology, 1992.
6. Invited Speaker, Department of Anatomy and Cell Biology, Univ. of Kansas, Kansas City Kansas, 1993.
7. Advisory Committee, and invited speaker VIth International Symposium on Basement Membranes, Hakone Japan, May 1993.
8. Invited Speaker, XIIth International Congress of Nephrology, Jerusalem, Israel, June 1993.
9. Invited Speaker, "Mechanisms of Glomerulonephritis and Glomerulosclerosis, Leiden, The Netherlands, June 1993.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Wolf, G., Killen, P.D. and Neilson, E.G.: Intracellular signalling of transcription and secretion of type IV collagen after angiotensin II-induced cellular hypertrophy in cultured proximal tubular cells. Cell Regulation 1991;2:219-217.
2. Chen, M., Schnermann, J., Malvin, R.L., Briggs, J.P. and Killen, P.D.: Time course of stimulation of renal renin mRNA by furosemide. Hypertension, In Press.
3. Varani, J., Taylor, C.G.,Riser, B., Shumaker, D.K., Yeh, K-Y, Dame, M., Gibbs, D.F., Todd, R.F.,Dumler, F., Bromberg, J. and Killen, P.D.: Mesangial cell lilling by leukocytes: Role of oxidants and proteolytic enzymes. Kidney Int. 1992, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Schuger, L., Varani, J., Killen, P.D., Skubitz, A.P.N. and Gilbride, K.: Laminin expression in the mouse lung increases with development and stimulates spontaneouse organotypic rearrangement of mixed lung cell cultures. Submitted.
2. Simon, R.H., Scott, M.J., Reza, M.M. and Killen, P.D.: Type IV collagen production by rat pulmonary epithelial cells. Submitted.
3. Kuncio, G.S., Alvarez, R., Li, S., Haverty, T., Killen, P.D. and Neilson, E.G.: Cytokine modulation of the a1(IV) collagen gene in murine renal tubular epithelial cells. Submitted.
4. Henry, D.N., Del Monte, M., Greene, D.A. and Killen, P.D.: Altered aldose reductase gene regulation in cultured human retinal pigment epithelial cells. Submitted.
5. Wiggins, R., Goyal, M., Merritt, S. and Killen, P.D.: Vascular adventitial cell expression of collagen I in experimental anti-GBM antibody-induced crescentic nephritis in the rabbit. Submitted.
6. Grande, J.P., Melder, D. and Killen, P.D.: TGF-b1 induces collagen IV gene transcription in NIH-3T3 Cells. Submitted.
7. Todd-Turla, K., Schnermann, J., Briggs, J.P. and Killen, P.D.: Distribution of mineralocorticoid and glucocorticoid receptor mRNA along the rat nephron. Submitted.

BOOKS/CHAPTERS IN BOOKS:

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

1. Wiggins, R.C., Goyal, M., Merritt, S.E. and Killen, P.D.: Localization of $\alpha 2(I)$ collagen mRNA by *in situ* hybridization to the periarterial and periglomerular regions in anti-GBM crescentic nephritis in the rabbit. American Society of Nephrology, accepted, 1991.
2. Hansch, G.M., Wagner, C., Stoeck, M., Killen, P.D. and Rother, K.: TGF-β_1 induces collagen IV expression in cultured human glomerular mesangial cell. American Society of Nephrology, accepted, 1991.
3. Chen, M., Schnermann, J., Killen, P.D. and Briggs, J.P.: Assessment of rennin mRNA in isolated JC cells by competitive PCR. American Heart Association, accepted, 1991.
4. Chen, M., Schnermann, J., Killen, P.D. and Briggs, J.P.: Cyclic amp-mediated regulation of renin mRNA in cultured juxtaglomerular cells. American Society of Nephrology, accepted, 1991.
5. Todd-Turla, K.M., Briggs, J.P., Smart, A., Killen, P. and Schnermann, J.: Distribution of mineralocorticoid and glucocorticoid receptor mRNA along the rat kidney nephron. American Society of Nephrology, accepted, 1991.

6. Killen, P.D.: Regulation collagen IV gene expression. Cell and Molecular Biology of Basement Membranes in Health and Disease. An International Symposium, Arilie, Virginia, September 20-21, 1991.
7. Gattone, V.H. II, Kraybill, A.L., Calvet J.P. and Killen, P.D.: Extracellular matrix expression in inherited rodent models of polycystic kidney disease. Cell and Molecular Biology of Basement Membranes in Health and Disease. An International Symposium, Airlie, Virginia, September 20-21, 1991.
8. Funabiki, K., Togawa, M., Chapo, J.A. and Killen, P.D.: Expression of the Murine α3(IV) Collagen Gene is Regulated in a Tissue-specific Fashion. Am. Society of Nephrology, June 1992, (abs).
9. Todd-Turla, K.M., Briggs, J.P., Smart, A.M., Killen, P.D. and Schnermann, J.B.: β-Actin mRNA distribution along the rat nephron. Am. Society of Nephrology, June 1992, (abs).
10. Chapo, J.A., Grande, J.P. and Killen, P.D.: Transcriptional regulation of collagen IV gene expression during renal development. Am. Society of Nephrology, June 1992, (abs).
11. deMiguel, M., Killen, P., Goyal, M. Merritt, S. and Wiggins. R.: Comparison of α1(IV) collagen, α1(1) and α2(1) procollagen mRNA distribution during evolution of crescentic nephritis in the rabbit using *in situ* hybridization. Am. Society of Nephrology, June, 1992 (abs).
12. Bergijk, E.C., Bacide, J.J., de Heer, E., Killen, P.D. and Bruijn, J.A. (intr. by Hoedemaeker, Ph. J.): Specific accumulation of exogenous fibronectin plays a major role in the development of experimental glomerulosclerosis. Am. Society of Nephrology, June, 1992.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES: None.

II. TEACHING ACTIVITIES:

A. Inflammation/Immunopathology Series ICS-600.
B. Pathology 581.
C. Course co-director "Cellular and Molecular Basis of Disease" (with Dr. Jeffrey Bonadio).
D. Epidemiology 570.
E. Member, Pathology Graduate Program Committee.
F. Member, Molecular Pathogenesis Training Grant (Microbiology).
G. Member, Immunopathology Training Grant (Pathology).
H. Member, Operating Committee, Systems and Intergrative Biology Training Grant (Physiology).
I. Teaching/Research Seminars in various departments.
J. Supervised the following postdoctoral fellows and graduate students: Drs. Kim Brown, Amanda Thornton, Mark Rolfe, Robert Schmouder, Charles Dibb, Andy Metinko, Tsyoshi Kasama, Susan Moore, Rob Smith, and Ron Allen.
K. Undergraduate students: Mark Milia, Andy Gilbert, Paul Holman, Rick Dwyer, and Dan Scharbaum.
L. Doctoral Committee Member/Oral Presentation Committee for the following graduate students: Susan Moore, Ron Allen, Cindy Hoorn and Paul Bohjanen.
M. Mentor for Dr. Janice Liebler, University of Oregon Health Science Center; sabbatical leave.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH - Macrophage/Monocyte Signals in Lung Granuloma Formation; HL-R01-35276; Principal Investigator.
B. NIH - Monokine Gene Expression/Regulation in Lung Injury; HL-R01-31237; Principal Investigator.
C. NIH - Inflammatory Cells and Lung Injury; Program Project HL-31963; Principal Investigator for Section II and Core II.
D. NIH - Crescentic Nephritis; Program Project P01-DK38149; Principal Investigator - Section II.
E. Tobacco Research Institute - Principal Investigator.

PROJECTS UNDER STUDY:

A. Regulation of macrophage signals that dictate immune responsiveness.
   1. Tumor necrosis factor production.
   2. Chemotactic cytokines.

3. Endogenous regulators of cytokine expression.

B. Role of macrophages - lymphocyte interactions in the initiation, maintenance, and resolution of chronic immune response.

C. Regulation of macrophage gene expression.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Operating Committee Graduate Program.
B. Space Utilization and Research committee.
C. Program Committee for 1992 Pathology Faculty Retreat
D. Interview Candidates for Residency Program/Graduate Program.

MEDICAL SCHOOL/HOSPITAL:

A. Member, University Senate Assembly.
B. Committee on Medical Student Research.
C. Medical School Admission Interview Committee.
D. Medical School Admissions Executive Committee.
E. Medical Scientist Training Program Interview Committee.
F. Biomedical Research Council Committee (Vice-Chair).
G. Member, Michigan Cancer Center.

REGIONAL AND NATIONAL:

A. Associate Editor, *American Journal of Pathology.*
B. Section Editor, *Journal of Immunology.*
C. Associate Editor, *American Journal of Respiratory Cell and Molecular Biology.*
D. Associate Editor, *Pathobiology.*
E. Editorial Board Rapid Communications, *Mediators of Inflammation.*
F. Program Advisory Committee, Third International Workshop on Cytokines.
G. Organizing Committee, 1994 International Cytokine Symposium.
H. Organizing Committee, 3rd International Conference on Chemotactic Cytokines.
I. Organizer/Session Chair, International Conference on Interleukins and Other Cytokines.
J. Member, American Association of Pathology Program Committee.
K. Reviewer for the following journals: *American Journal of Pathology, American Review of Respiratory Disease, Circulation, Clinical Immunology and Immunopathology, Infection and Immunity, Journal of Rheumatology, Laboratory Investigation, Science, Journal Immunology, American Journal of Respiratory Cell and Molecular Biology.*
L. Grant Reviewer, United States Department of Agriculture.
M. Grant Reviewer, The Arthritis Society.
N. Grant Reviewer, Veterans' Administration.
O. Grant Reviewer, The Scleroderma Foundation.
P. Grant reviewer, Canadian Cystic Fibrosis Foundation.
Q. Session Chair, 3rd International Workshop on Cytokines.
R. Session Chair, ATS, Cytokines in Lung Inflammation.
S. Session Chair, FASEB, Novel Neutrophil Activating Factors.
T. Session Chair, 3rd International Conference on Tumor Necrosis Factor.
U. Session Chair, Australian Inflammatory Symposium.
V. Long-Range Planning Committee, American Association of Pathology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Invited Speaker, 17th International Congress on Chemotherapy, Berlin, Germany, July, 1991.
2. Invited Speaker/Faculty, 1st Annual Congress of European Respiratory Society, Brussels, Belgium, September, 1991.
3. Invited Speaker, Bayer AG, Wuppertal, Germany, September, 1991.
4. Invited Speaker, Lung Cell Biology Symposium at Woods Hole, "Signal Transduction in Lung Cells," Woods Hole, MA, October, 1991.
5. Invited Speaker, Cleveland Clinic Research Institute, Immunology Section, Cleveland, Ohio, October, 1991.
6. Invited Faculty/Lecturer, American Association for the Study of Liver Diseases, 1991 Workshop, "Role of Cytokines in inflammation," Chicago, Illinois, November, 1991.
7. Invited Speaker/Chair, Third International Workshop on Cytokines, Stresa, Italy, November, 1991.
8. Invited Speaker, "Cellular Aspects of Impaired Heart Function: Sepsis versus Ischemia," Wuppertal, Germany, November, 1991.
9. Invited Speaker, Keystone Symposia, "Inflammation, Growth Regulatory Molecules and Atherosclerosis," Keystone, Colorado, January, 1992.
10. Invited Speaker, Hanson Center for Cancer Research, Institute for Medical and Veterinary Science, Adelaide, Australia, February, 1992.
11. Invited Speaker/Chair, Australian Inflammatory Symposium, St. Vincent's Hospital, Sydney, Australia, February, 1992.
12. Invited Speaker/Chair, International Conference on Interleukins and Other Cytokines, London, England, February, 1992.
13. Invited Speaker, Keystone Symposia, "Recognition of Endotoxin in Biological Systems," Lake Tahoe, Nevada, March, 1992.
14. Invited Speaker, National Cancer Institute, Frederick, Maryland, March, 1992.
15. Invited Speaker, Biochemistry Lecture Series, University of Kansas, Lawrence, Kansas, April, 1992.
16. Invited Speaker/Chair, Symposium on Novel Chemotactic Cytokines, FASEB, Anaheim, California, April, 1992.
17. Invited Speaker/Chair, 3rd International Conference on Tumor Necrosis Factor, Veldhoven, Netherlands, May, 1992.
18. Invited Speaker/Chair, American Thoracic Society, Miami, Florida, May, 1992.
19. Invited State-of-the-Art Speaker, Aspen Lung Conference, Aspen, Colorado, June, 1992.
20. Invited Speaker, Xoma, Inc., San Francisco, California, June, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Chavin, K.D., Bromberg, J.S. and Kunkel, S.L.: Effects of a polyclonal anti-TNF antibody on cell mediated immunity. Transplant. Proc. 1991;23:847-848.
2. Standiford, T.J., Kunkel, S.L. and Strieter, R.M.: Elevated serum levels of tumor necrosis factor post-bronchoscopy with bronchoalveolar lavage. Chest. 1991;99:1529-1530.
3. Krasnow, S.W., Zhang, L., Leung, K., Osborn, L., Kunkel, S.L. and Nabel, G.J.: Tumor necrosis factor, Interleukin-1, and phorbol myoristate acetate are independent activators of NF-κB which differentially activate T cells. Cytokine. 1991;3:1-5.

4. Elner, S.G., Strieter, R.M., Elner, V.M., Rollins, B.J., Del Monte, M.A. and Kunkel, S.L.: Monocyte chemotactic protein gene expression by cytokine-treated retinoid pigmented epithelial cells. Lab. Invest. 1991;64:819-825.
5. Brown, Z., Strieter, R.M., Chensue, S.W., Ceska, M., Lindley, I., Neild, G.H., Kunkel, S.L. and Westwick, J.: Cytokine-activated human mesangial cells generate the neutrophil chemoattractant-interleukin 8. Kidney Intern. 1991;40:86-90.
6. Ham, J.M., Kunkel, S.L., Dibb, C.R., Standiford, T.J., Rolfe, M.W. and Strieter, R.M.: Chemotactic cytokine (IL-8 and MCP-1) gene expression by human whole blood. Immunol. Invest. 1991;20:387-394.
7. Remick, D.G., Nguyen, D.T., Eskandari, M.K. and Kunkel, S.L.: Interleukin-2 induces tumor necrosis factor gene expression *in vivo*. Immunol Invest. 1991;20:395-402.
8. Davenport, R.D., Strieter, R.M. and Kunkel, S.L.: Tumor necrosis factor production in hemolytic transfusion reactions: An *in vitro* model. Br. J. Hematol. 1991;78:540-544.
9. Huber, A.R., Kunkel, S.L., Todd, R.F. and Weiss, S.J.: Regulation of transendothelial neutrophil migration by endogenous interleukin-8. Science, 1991;254:99-102.
10. Griffin, G.E., Leung, K., Folks, t.M., Kunkel, S.L. and Nabel, G.J.: Induction of NF-κB during monocyte differentiation is associated with activation of HIV-gene expression. Res. Virol. 1991;142:233-238.
11. Koch, A.F., Kunkel, S.L., Burrows, J.D., Evanoff, H.L., Haines, G.K., Pope, R.M. and Strieter, R.M. The synovial tissue macrophage as a source of the chemotactic cytokine interleukin-8. J. Immunol. 1991;147:2187-2195.
12. Elner, V.M., Strieter, R.M., Pavilack, M.A., Elner, S.G., Remick, D.G., Danforth, J.M. and Kunkel, S.L.: Human corneal interleukin-8: IL-1 and TNF-induced gene expression and secretion. Am. J. Pathol. 1991;139:977-988.
13. Barker, J.N.W.N., Jones, M.L., Mitra, R.J., Crockett-Torabe, E., Fantone, J.C., Kunkel, S.L., Warren, J.S., Dixit, V.M. and Nickoloff, B.J.: Modulation of keratinocyte-derived interleukin-8 which is chemotactic for neutrophils and T lymphocytes. Am. J. Pathol. 1991;139:869-876.
14. Walz, A., Buregener, R., Car, B., Baggiolini, M., Kunkel, S.L. and Strieter, R.M.: Structure and neutrophil-activating properties of a novel inflammatory peptide (EMA-78) with homology to interleukin-8. J. Exp. Med. 1991;174:1355-1362.
15. Thornton, A.J., Ham, J. and Kunkel, S.L.: Kupffer cell-derived cytokines induce the synthesis of a leukocyte chemotactic peptide, interleukin-8, in human hepatoma and primary hepatocyte cultures. Hepatology 1991;14:1112-1122.
16. Rolfe, M.W., Kunkel, S.L., Standiford, T.J., Chensue, S.W., Allen, R.M., Evanoff, H.L., Phan, S.H. and Strieter, R.M.: Pulmonary Fibroblast Expression of Interleukin-8: A Model for Alveolar Macrophage-derived Cytokine Networking. Am. J. Resp. Cell Mol. Biol. 1991;5:493-501.
17. Standiford, T.J., Kunkel, S.L., Kasahara, K., Milia, M.J., Rolfe, M.W. and Strieter, R.M.: IL-8 gene expression from human alveolar macrophages: The role of adherence. Am. J. Resp. Cell Mol. Biol. 1991;5:579-585.
18. Standiford, T.J., Kunkel, S.L., Rolfe, M.W., Evanoff, H.L., Allen, R.M., and Strieter, R.M.: Regulation of human alveolar macrophage and blood monocyte-derived interleukin-8 by prostaglandin E_2 and dexamethasone. Am. J. Respir. Cell Mol. Biol. 1992;6:75-81.
19. Evanoff, H.L., Burdick, D., Moore, S.A., Kunkel, S.L. and Strieter, R.M.: A sensitive ELISA for the detection of human monocyte chemoattractant protein (MCP-1). Immunol. Invest. 1992;1:39-45.
20. Phan, S.H. and Kunkel, S.L: Lung cytokine production in bleomycin-induced pulmonary fibrosis. Exp. Lung Res. 1992;18:29-43.
21. Abruzzo, L.V., Thornton, A.J., Liebert, M., Grossman, B.H., Evanoff, H.L., Westwick, J., Strieter, R.M. and Kunkel, S.L.: Cytokine-induced gene expression of interleukin-8 in human transitional cell carcinoma and renal cell carcinomas. Am. J. Path. 1992;140:365-373.
22. Schmouder, R.L., Strieter, R.M., Wiggins, R.C., Chensue, S.W. and Kunkel, S.L.: *In vitro* and *in vivo* interleukin-8 production in human renal cortical epithelia. Kidney International 1992;41:191-198.

23. Chensue, S.W., Terebuh, P., Evanoff, H.L., Kunkel, S.L. and Higashi, G.I.: Role of interleukin-4 and γ interferon in Schistosoma mansoni egg-induced hypersensitivity granuloma formation: Orchestration, relative contribution and relationship to macrophage function. J. Immunol. 1992;148:900-906.
24. Standiford, T.J., Lindsten, T., Thompson, C.B., Strieter, R.M. and Kunkel, S.L.: Interleukin-4 differentially regulates tumor necrosis factor-α gene expression by human T lymphocytes and monocytes. Pathobiol. 1992;60:100-107.
25. Bolling, S.F., Kunkel, S.L. and Lin, H.: Prolongation of cardiac allograft survival in rats by anti-TNF and cyclosporin combination therapy. Transplantation 1992;53:283-286.
26. Terebuh, P.D., Otterness, I.G., Strieter, R.M., Lincoln, P.M., Danforth, J., Kunkel, S.L. and Chensue, S.W.: Biologic and immunohistochemical analysis of IL-6 expression *in vivo*. Constitutive and induced expression in murine polymorphonuclear and mononuclear phagocytes. Am. J. Pathol. 1992;140:649-657.
27. Dibb, C.R., Strieter, R.M., Burdick, M. and Kunkel, S.L.: Expression of interleukin-8 by LPS-stimulated bone marrow-derived mononuclear cells. Infect. Immun. 1992;60:141-157.
28. Lynch, J.P., Standiford, T.J.., Role, M.W., Kunkel, S.L. and Strieter, R.M.: Neutrophilic alveolitis in idiopathic pulmonary fibrosis: The role of interleukin-8. Am. Rev. Respir. Dis. 1992;145:1433-1439.
29. Rolfe, M.W., Kunkel, S.L., Rowens, B., Standiford, T.J., Cragoe Jr., E.J. and Strieter, R.M.: Suppression of Human Alveolar Macrophage-derived Cytokines by Amiloride. Am. J. Respir. Cell Mol. Biol 1991;6:576-582.
30. Lin, H., Chensue, S.W., Strieter, R.M., Remick, D.G., Gallagher, K.P., Bolling, S.F. and Kunkel, S.L.: Antibodies against tumor necrosis factor prolongs allograft survival in the rat. J. Heart and Lung Transplant. 1992;11:330-335.
31. Zamir, O., Hasselgren, P., Kunkel, S.L., Frederick, J. Higashiguchi, T. and Fischer, J.E.: Evidence that tumor necrosis factor (TNF) participates in the regulation of muscle proteolysis during sepsis. Archives of Surgery. 1992;127:170-174.
32. Negussie, Y., Remick, D.G., DeForge, L.E., Kunkel, S.L., Eynon, A. and Griffin, G.E.: Detection of plasma tumor necrosis factor, interleukin-6, and interleukin-8 during the Jarisch-Herxheimer reaction of relapse fever. J. Exp. Med. 1992;127:1207-1212.
33. Moore, S.A., Strieter, R.M., Rolfe, M.W., Standiford, T.J., Burdick, M. and Kunkel, S.L: The expression and regulation of human alveolar macrophage-derived interleukin-1 receptor antagonist. Am. J. Respir. Cell Mol Biol. 1992;6:569-575.

BOOKS AND CHAPTERS IN BOOKS:

1. Kunkel, S.L., Chensue, S.W. and Phillips, S.M.: Mechanisms of Immunology, in, Parasitic Infections.
2. Kunkel, S.L., Standiford, T.J., Rolfe, M.W. and Strieter, R.M.: Expression and regulation of chemotactic cytokine genes by non-immune pulmonary cells, in, Brody, A., Cester, D. and Kachak, V.T. (eds), Signal Transduction in Lung Cells, Marcel Dekker, New York, New York.
3. Kunkel, S.L., Standiford, T.J., Rolfe, M.W. and Strieter, R.M.: The role of chemotactic cytokines in diverse pathophysiologic diseases, in, Mantovani, A. and Ghezzi, P. (eds), Pathophysiology of Cytokines, Biomedical Press.
4. Strieter, R.M., Standiford, T.J., Rolfe, M.W., Lynch, J.P. III, Metinko, A.P. and Kunkel, S.L: Cytokines in Pulmonary Injury, in, Kunkel, S.L. and Remick, D.G (eds), Cytokines in Health and Disease, Marcel Dekker, Inc., New York, New York, pp. 397-411.
5. Kunkel, S.L., Standiford, T.J., Chensue, S.W. and Strieter, R.M.: Interleukin-8 and the Inflammatory Response,in, Kunkel, S.L. and Remick, D.G.(eds), Cytokines in Health and Disease," Marcel Dekker, Inc., New York, New York, pp. 121-130.
7. Cytokines in Health and Disease. Edited by S. L. Kunkel and D. G. Remick, Marcel Dekker, Inc., New York, New York.
8. "Chemotactic Cytokines." in, Westwick, J., Lindley, I.S.D. and Kunkel, S.L. (eds), Biology of the Inflammatory Peptide Supergene Family, Plenum Press, New York, New York.

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

1. Strieter, R.M., Standiford, T.J., Scales, W., Rolfe, M. and Kunkel, S.: Regulation of inflammatory cytokines by PGE_2, dexamethasone and pentoxifylline. Second International Conference on Shock, Vienna, Austria, June 1991.
2. Brown, Z., Strieter, R.M., Fairbanks, L.D., Neild, G.H., Kunkel, S.L. and Westwick, J.: Interleukin-1 induced IL-8 generation by mesangial cells involves a pertussin-toxin-sensitive guanine nucleotide binding component. Symposium of the International Society of Nephrology, University of Erlangen, Nurnberg, Germany, June 1991.
3. Kunkel, S.L., Standiford, T.J. and Strieter, R.M.: Cellular and molecular regulation of cytokine networks: Induction and regulation of distal cytokines. 17th International Congress of Chemotherapy, Berlin, Germany, June 1991.
4. Strieter, R.M., Standiford, T.J., Role, M., Kasahara, K. and Kunkel, S.L. Regulation of Human alveolar macrophage and blood monocyte-derived TNF and IL-8: The role of PGE2, dexamethasone, Amiloride and IL-4. XII World Congress on Sarcoidosis and Other Granulomatous Disorders, Kyoto, Japan, September, 1991.
5. Schmouder, R.L., Strieter, R.M., Wiggins, R.C. and Kunkel, S.L.: Disparate IL-8 and MCP-1 expression in human renal cortical epithelial cells stimulated with interferon-γ. The American Society of Nephrology, 25th Annual Meeting, November, 1991.
6. Standiford, T.J., Kunkel, S.L., Gromer, K.G., Gruenert, D., Evanoff, H.L. and Strieter, R.M.: Interleukin-8 gene expression from human tracheal explant epithelial cells is regulated by dexamethasone. Clin. Res. 1991;39:728A.
7. Metinko, A.P., Kunkel, S.L., Standiford, T.J. and Strieter, R.M. Endothelial cell expression of interleukin-8 in response to oxidant stress. Clin. Res. 1991;39:707A.
8. Rolfe, M.W., DeMeester, S.R., Kunkel, S.L., Deeb, M.G., Lupinetti, F.M. and Strieter, R.M. Compartmentalization of tumor necrosis factor-α during rat lung allograft rejection. Clin. Res. 1991;39:3278A.
9. Dibb, C., Strieter, R.M. and Kunkel, S.L.: Primary induction of bone marrow mononuclear cell-derived IL-8 by LPS. American Society of Hematology Annual Meeting, Denver, Colorado, December 1991.
10. Koch, A.E., Kunkel, S.L., Burrows, J.C., Evanoff, H.L., Haines, G.K., Pope, R.M. and Strieter, R.M.: The synovial tissue (ST) Macrophage (MO) as a source of interleukin-8. Arth. Rheum. 1991;34:S60.
11. Koch, A.E., Kunkel, S.L., Chensue, S.W., Haines, G.K. and Strieter, R.M.: Constitutive expression of interleukin-1 (IL-1 and interleukin-1 receptor antagonist protein by human rheumatoid (RA) ST macrophages (MOs). Arth. Rheum. 1991;34:S156.
12. Kunkel, S.L. and Strieter, R.M.: Mechanisms that regulate the expression of chemotactic cytokines: Potential role in atherosclerosis and DTH. J. Cell. Biochem. 1991;16A;4.
13. Rolfe, M., Kunkel, S.L., Standiford, T.J., Becker, F., Gilbert, A., Evanoff, H.L., Burdick, M. and Strieter, R.M.: Human pulmonary fibroblasts express monocyte chemoattractant peptide-1 (MCP): A model of cellular communication. FASEB J. 1992;6:A941.
14. Burdick, M., Strieter, R.M., Kunkel, S.L. and Davenport, R.D.: Monocyte chemotactic protein production in red cell incompatibility. FASEB J. 1992;6:A1898.
15. Smith, R., Kashahara, K., Kunkel, S.L., Kasama, T. and Strieter, R.M.: Potentiation of human neutrophil-derived interleukin-8 gene expression by cholera toxin. FASEB J. 1992;6:A1895.
16. Liebler, J.M., Kunkel, S.L., Dwyer, R.E. and Strieter, R.M.: Disparate chemotactic cytokine production by monocytes in response to phytohemagglutinin (PHA) in combination with LPS, IL1-β or TNF-α. FASEB J. 1992;6:A1606.
17. Brown, K.A., Strieter, R.M., Evanoff, H.L. and Kunkel, S.L.: SK hepatoma cell production of monocyte chemotactic peptide-1 (MPC) in response to interleukin-1- beta (IL-1β), tumor necrosis factor-alpha (TNF-α), and gamma-interferon (IFN-ψ). FASEB J. 1992;6:A1026.

18. Kasama, T., Strieter, R.M., Moore, S.A., Becker, F.S. and Kunkel, S.L.: Neutrophil production of interleukin-1 receptor antagonist (IRAP). FASEB J. 1992;6:A1897.
19. Standiford, T.J., Strieter, R.M., Allen, R., Burdick, M.D., Gilbert, A.R. and Kunkel, S.L.: IL-7 upregulates the expression of IL-8 from resting and stimulated human blood monocytes. FASEB J. 1992;6:A1204.
20. Metinko, A.P., Kunkel, S.L., Wharram, B.L. and Strieter, R.M.: Structure and characterization of a new member of the interleukin-8-like neutrophil-activating peptides. FASEB J 1992;6:A938.
21. Walz, A., Burgener, R., Car, B., Baggiolini, M., Kunkel, S.L. and Strieter, R.M.: Structure and characterization of a new member of the interleukin-8-like neutrophil-activating peptides: ENA-78. FASEB J. 1992;6:A1780.
22. Fick, R.B., Shaw, R.N., Kunkel, S.L. and Strieter, R.M.: Pro-inflammatory cytokines in cystic fibrosis (CF) lung disease. FASEB J. 1992;6:A1781.
23. Koch, A.E., Kunkel, S.L., Polerini, P.J., Harlow, L.A., DiPietro, L.A., Elner, V.M. and Strieter, R.M. Interleukin-8 is a potent human macrophage-derived mediator of angiogenesis that is blocked by interleukin-8 antibody and antisense oligonucleotide. Clin Res 1992;40:186A.
24. Koch, A.E., Kunkel, S.L., Harlow, L.A., Johnson, B., Evanoff, H.L., Haines, G.K., Burdick, M.D., Pope, R.M. and Strieter, R.M.: The synovium and synovial fluid as a source of monocyte-chemoattractant protein-1. Clin. Res. 1992;40:228A.
25. Kunkel, S.L., Rolfe, M. and Strieter, R.M.: TNF expression and associated pathologic conditions. 4th International TNF Conference, Veldhoven, The Netherlands, May, 1992.
26. Kunkel, S.L. and Strieter, R.M.: The expression of chemotactic cytokines via IL-1 and TNF-dependent networks. 4th International TNF Conference, Veldhoven, The Netherlands, May, 1992.
27. Metinko, A.P., Schumacher, R.E., Kunkel, S.L. and Strieter, R.M.: Meconium stimulates release of interleukin-8 from mononuclear phagocytes. Am Rev Respir Dis 1992;145:A345.
28. Metinko, A.P., Kunkel, S.L., Wharram, B.L. and Strieter, R.M.: Anoxia-hyperoxia: An ischemia-reperfusion model for interleukin-8 expression by endothelial cells. Am Rev Respir Dis 1992;145:A235.
29. Liebler, J.M., Strieter, R.M., Dwyer, R.E. and Kunkel, S.L.: The production of monocyte-derived monocyte chemotactic protein-1` is signal specific. Am Rev Respir Dis 1992;145:A697.
30. Liebler, J.M., Kunkel, S.L., Dwyer, R.E. and Strieter, R.M.: Disparate chemotactic cytokine production by monocytes in response to phytohemagglutinin and lipopolysaccharide. Am Rev Respir Dis 1992;145:A235.
31. Rolfe, M.W., DeMeester, S.R., Kunkel, S.L., Lincoln, P.M., Deeb, G.M., Lupinetti, F.M. and Strieter, R.M.: Interleukin-6 and tumor necrosis factor-alpha expression during rat lung allograft rejection. Am Rev. Respir Dis 1992;145:A308.
32. Rolfe, M.W., Rowens, B., Kunkel, S.L., Standiford, T.J. and Strieter, R.M.: Suppression of human alveolar macrophage-derived cytokines by amiloride. Am Rev Respir Dis 1992;145:A181.
33. Rolfe, M.W., Standiford, T.J., Kunkel, S.L., Becker, F.S., Evanoff, H.L., Burdick, M.D. and Strieter, R.M.: Expression and regulation of human pulmonary fibroblast-derived monocyte chemotactic peptide-1. Am Rev Respir Dis 1992;14:A235.
34. Standiford, T.J., Rolfe, M.W., Kunkel, S.L., Becker, F.S., Lynch, J.III, Orringer, M., Phan, S.H. and Strieter, R.M.: Altered production and regulation of monocyte chemoattractant protein-1 from pulmonary fibroblasts isolated from patients with idiopathic pulmonary fibrosis. Thomas L. Petty Aspen Lung Conference, June, 1992.
35. Rolfe, M., DeMeester, S., Kunkel, S., Lincoln, P., Deeb, M., Lupinetti, F. and Strieter, R.M.: Lung allograft rejection: The role of tumor necrosis factor-alpha and interleukin-6. Thomas L. Petty Aspen Lung Conference, June, 1992.

TULLIA LINDSTEN, M.D., PH.D.
ASSISTANT RESEARCH SCIENTIST
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Pathology 581.
B. Doctoral Committee Member: Paul Bohjanen.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Tullia Lindsten, "Lymphokine-specific RNA binding proteins, NIH CA54521 (50%). $70,717/year ($350,000/five years). 4/15/91 - 03/31/96.

IV. ADMINISTRATIVE ACTIVITIES:

A. Reviewer for Journal of Immunology.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

None.

INVITED LECTURES/SEMINARS:

None.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Standiford, T.J., Lindsten, T., Thompson, C.B., Strieter, R.M. and Kunkel, S.L.: Interleukin 4 differentially regulates tumor necrosis factor-alpha gene expression by human T lymphocytes and monocytes. Pathobiology 1992;60:100-107.
2. Bohjanen, P.R., Petryniak, B., June, C.H., Thompson, C.B. and Lindsten, T.: AU RNA-binding factors differ in their binding specificities and affinities. J. Biol. Chem. 1992;267:6302-6309.

3. Mao, X., Green, J.M., Safer, B., Lindsten, T., Frederickson, R.M., Miyamoto, S., Sonenberg, N. and Thompson, C.B.: Regulation of translation initiation factor gene expression during human T cell activation. Submitted for publication.
4. Boise, L.H., Petryniak, B., Mao, X., June, C.H., Wang, C.Y., Lindsten, T., Bravo, R., Kovary, K., Leiden, J.M. and Thompson, C.B.: The NFAT-1 DNA-binding complex in activated T cells contains Fra-1 and JunB. Submitted for publication.

RICARDO V. LLOYD, M.D., PH.D.
PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES

A. Surgical pathology - 12 weeks.
B. Autopsy Pathology - one week.
C. Consultant for endocrine lesions.
D. Consultant to Veterans Administration Medical Center, Ann Arbor, Michigan.
E. Consultant for immunochemistry cases.

II. TEACHING ACTIVITIES:

A. Lectures to sophomore medical students - Pathology 600.
B. Fourth Year medical student rotation in Pathology - one month.
C. Lecture to dental students - Pathology 630.
D. Lectures to pathology house officers.
E. Immunoperoxidase Rounds - Monthly.
F. Supervision of three postdoctoral fellows in research laboratory (Dr. L. Jin, Dr. E. Kulig, Dr. T. Maeda).
G. Honors Elective Course for undergraduate student (Annie Chang)- one semester.
H. Medical Student Summer Research Program Mentor (Chris Antczak).
I. High School Minority Summer Research Program Mentor (Ameer Daniels).
J. Resident elective rotation in immunohistochemistry (Drs. Phil Perkins, Eric Kaldjian and Cindy Hegg).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Regulation of Rat Pituitary Hyperplasia and Neoplasia. NIH CA 37238, 12/1991-11/1994, (Principal Investigator - R. Lloyd).
B. Studies of Normal and Neoplastic Human Pituitary Tissues. NIH Grant CA 42951, 7/90 - 6/95 (Principal Investigator - R. Lloyd).

PROJECTS UNDER STUDY:

A. Regulation of pituitary growth and differentiation in humans, rats and mice.
B. Applications of immunochemical and molecular biological techniques to diagnostic pathology.
C. Hormonal regulation of mammary tumor development in transgenic mice and in humans.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director of Immunohistochemistry Service.
B. Coordinator of Anatomic Pathology Journal Club.

MEDICAL SCHOOL/HOSPITAL:

A. Endocrine Surgery Conference.
B. Pathology presentations at General Endocrine Conference.
C. Curriculum Revision Committee - Endocrine Section.

REGIONAL AND NATIONAL:

A. Editorial Board - American Journal of Pathology.
B. Editorial Board - Endocrine Pathology.
C. Editorial Board - American Journal of Surgical Pathology.
D. Editorial Board - Modern Pathology.
E. Editorial Board - Applied Immunohistochemistry.
F. Reviewer of articles for Laboratory Investigation, Journal of the American Medical Association, Journal of Histochemistry and Cytochemistry, the American Journal of Medical Sciences, New England Journal of Medicine, Journal of Clinical Endocrine Metabolism, and others.
G. Pathology B Study Section, National Cancer Institute, Member 1987 - June 1991.
H. NIH - Reviewer Reserve (NRR, July 1991 - June 1995).

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURE AND SEMINARS

1. Ultrastructural and *In Situ* Hybridization Studies of Human Pituitary Tumors. Midwest Electron Microscopy Group. October, 19, 1991.
2. Florida Society of Pathologist Seminar Presentation. January 26-27, 1992.
3. Visiting Professor. University of Toronto. Toronto Society of Pathologists. February 24, 1992.
4. Course Presentation at US-Canadian Academy of Pathology Meeting "Neuroendocrine Neoplasms". March 16, 1992.
5. Lecture on Immunohistochemistry in Pathology. Washington, D.C. May 2, 1992.
6. Invited Lecture. Sendai University. Sendai, Japan. May 25, 1992.
7. Invited Lecture. Tokai University. Japan. May 27, 1992.
8. Plenary Lecture. Japan Endocrine Society. Tokushima, Japan. May 28, 1992.
9. Pathology Lectures. Pathologists Overseas Program. Nairobi, Kenya. June 8-18, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Lloyd, R.V.: Ultrastructure of spontaneous and transplanted tumors in laboratory animals. J. Electron Micro. Tech. 1991;19:64-79.
2. Lloyd, R.V., Jin, L., Fields, K. and Kulig, E.: Regulation of estrogen receptor mRNA in normal and neoplastic rat pituitary tissues. Endocr. Pathol. 1991;2:74-82.

3. Graham, D.M., Jin, L. and Lloyd, R.V.: Detection of estrogen receptor in paraffin-embedded sections of breast carcinoma by immunohistochemistry and *in situ* hybridization. Am. J. Surg. Pathol. 1991;15:475-485.
4. Kovacs, K.., Stefaneanu, L.., Horvath, E.., Lloyd, R.V., Lancronjan, I., Buchfelder, M. and Fahlbusch, R: Effect of dopamine agonist medication on prolactin-producing pituitary adenomas. A morphologic study including immunocytochemistry, electron microscopy and *in situ* hybridization. Virch. Arch. A Pathol. Anat. 1991;418:439-446.
5. Kulig, E., Landefeld, T.D. and Lloyd, R.V.: Estrogen regulates prolactin gene methylation in transplantable rat pituitary tumors. Am. J. Pathol. 1992;140:207-214.
6. Flint, A. and Lloyd, R.V.: Pulmonary metastases of colonic carcinoma. Distinction from pulmonary adenocarcinoma. Arch. Pathol. Lab. Med., In Press.
7. Lloyd, R.V., Jin, L. and Chandler, W.F.: In situ hybridization in the study of pituitary tissues. Pathol. Res. Pract. 1991;187:552-555.
8. Lloyd, R.V., Jin, L., Fields, K. and Kulig, E.: Effects of estrogens on pituitary cell and pituitary tumor growth. Pathol. Res. Pract. 1991;187:584-586..
9. Stefaneanu, L., Kovacs, K., Horvath, E. and Lloyd, R.V.: In situ hybridization study of proopiomelanocortin (POMC) gene expression in human pituitary corticotrophs and their adenomas. Virch. Arch. Pathol. 1991;419:107-113.
10. Grossman, D., Jin, L., Heidelberger, K.P. and Lloyd, R.V.: Expression of chromogranin A protein and messenger RNA and tyrosine hydroxylase protein in paraffin-embedded sections of neuroendocrine neoplasms. Endocrine Pathol. 1991;2:148-154.
11. Lloyd, R.V., Jin, L., Fields, K., Chandler, W.F., Horvath, E., Stefaneanu, L. and Kovacs, K.: Analysis of pituitary hormones and chromogranin A mRNAs in null cell adenomas, oncocytomas and gonadotroph adenomas by in situ hybridization. Am. J. Pathol. 1991;139:553-564.
12. Lloyd, R.V., Hawkins, K., Jin, L., Fields, K. and Kulig, E.: Chromogranin A and B and secretogranin II in the pituitary and adrenal medulla. Lab. Invest., In Press.
13. Kendall, S.K., Sauders, T.L., Jin, L., Lloyd, R.V., Glode, L.M., Nett, T.M., Nilson, J.H. and Camper, S.A.: Targeted ablation of pituitary gonadotrophs in transgenic mice. Mol. Endocrinol. 1991;5:2025-2036.
14. Flint, A. and Lloyd, R.V.: Colonic carcinoma metastatic to lung: cytologic manifestation and distinction from primary pulmonary adenocarcinoma. Arch. Pathol. Lab. Med. 1992, In Press.
15. Wang, X., Tafra, L., Berezmiak, R., Lloyd, R.V., Muraike, L. and Dafoe, D.C.: Co-transplanted fetal liver (FL) benefits fetal pancreas (FP) isografts. Transplantation 1992;53:272-276.
16. Lloyd, R.V., Jin, L., Kulig, E., Fields, K., Camper, S.A. and Frohman, L.A.: Pituitary hyperplasia and neoplastic development in mice with the GHRH transgene. Am. J. Pathol., In Press.
17. Lloyd, R.V., Jin, L., Kulig, E. and Fields, K.: Molecular approaches for the analysis of chromogranins and secretogranins. Diagnostic Mol. Pathol. 1992;1:2-15.
18. Erickson, J.D., Lloyd, R.V., Trojanowski, J.Q., Iacangelo, A. and Eiden, E.: Sites of synthesis of chromogranins A and B in the human brain. Neuropeptides 1992;21:239-244.
19. Kovacs, K., Stefaneanu, L., Horvath, E., Lloyd, R.V., Lancranjan, I., Buchfelder, M. and Fahlbusch, R.: Effect of dopamine agonist medication on prolactin producing pituitary adenomas. Virch. Archiv. Pathol. 1991;418:439-446.
20. Jay, V., Kovacs, K., Horvath, E., Lloyd, R.V. and Smyth, H.S.: Idiopathic prolactin cell hyperplasia of the pituitary mimicking prolactin cell adenoma: a morphological study including immunocytochemistry electron microscopy and *in situ* hybridization. Acta Neuropathol. 1991;82:147-151.
21. Zhang, K., Kulig, E., Jin, L. and Lloyd, R.V.: Effects of estrogen and epidermal growth factor on prolactin and Pit-1 mRNA in GH_3 cells. Proc. Soc. Biol. Med., 1992, In Press.
22. Jin, L., Maeda, T., Chandler, W.F. and Lloyd, R.V.: Protein kinase C (PKC) activity and PKC messenger RNA in human pituitary adenomas. Am. J. Pathol., In Press.

23. Stefaneanu, L., Kovacs, K., Lloyd, R.V., Sano, T. and Scheithauer, B.W.: Pituitary lactotrophic and somatotroph in pregnancy: An ***in situ*** hybridization and immunocytochemical study. Virch. Arch., In Press.
24. Perkins, P.L., McLeod, M.K., Jin, L., Fukuuchi, A., Cho, K.J., Thompson, N.W. and Lloyd, R.V.: Analysis of gastrinomas by immunohistochemistry and *in situ* hybridization histochemistry. Diag. Mol. Pathol., In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Maeda, T. and Lloyd, R.V.: Protein kinase C activity and messenger RNA modulation by estrogen in normal and neoplastic rat pituitary tissue. Lab. Invest., Submitted.
2. Fields, K., Kulig, E. and Lloyd, R.V.: Detection of ectopic prolactin in normal and neoplastic tissues by PCR. Lab. Invest., Submitted.
3. Shulkin, B.L., Koeppe, R.A., Francis, I.R., Deeb, G.M., Lloyd, R.V. and Thompson, N.W.: PET FDG localization of pheochromocytomas which fail to accumulate MIBG. Submitted.
4. Kaldjian, E.P., Jin, L., Davenport, R.D. and Lloyd, R.V.: Immunohistochemical analysis of hormone receptor, tumor vascularity and proliferative activity in paraffin-embedded sections of breast carcinoma tissues. Submitted.
5. Jin, L. and Lloyd, R.V. Neural cell adhesion molecule (NCAM) expression in human and rat pituitary cells. Regulation by nerve growth factor. In Press.
6. Jin, L., Stone, M., Chandler, W.F. and Lloyd, R.V. Neural cell adhesion molecular (NCAM) in normal and neoplastic human pituitary tissues. Analysis by immunohistochemistry and *in situ* hybridization. Endocrine Pathol., In Press.
7. Jin, L., Chandler, W.F., Smart, J.B., England, B.G. and Lloyd, R.V.: Differentiation of human pituitary adenomas determines the pattern of chromogranin/secretogranin mRNA expression. Submitted to J. Clin. Endocrinol. Metab.
8. Jin, L., Landefeld, T., Camper, S. and Lloyd, R.V.: Regulation of Pit-1 transcription factor by bFGF and estrogen in normal and neoplastic rat pituitary tissues. Submitted.
9. Jin, L. and Lloyd, R.V.: Basic fibroblast growth factor protein and mRNA in human pituitary tissues. Submitted.
10. Lloyd, R.V., Jin, L. and Kulig, E.: Human pituitary adenomas and normal pituitary tissues express Pit-1 transcription factor mRNA. Submitted.

BOOKS/CHAPTERS IN BOOKS

1. Lloyd, R.V.: Morphologic Methods, in, Kovacs and Asa S. (eds), Functional Endocrine Pathology, Blackwell Scientific Publishers, Boston, Massachusetts, 1991, pp. 94-103.
2. Chandler, W.F. and Lloyd, R.V.: Surgical Endocrinology--Pituitary, in. Greenfield, L.J., Mulholland, M.W., Oldham, K.T., Zelenock, G.B. (eds.), Surgery Scientific Principles and Practice, J. B. Lipincott Co. 1992, In Press.
3. McKeever, P. and Lloyd, R.V.: Pituitary adenomas and selected intracranial tumor, in, Garcia, J.H., Escabona-Zapata, J., Sandback, V., Cervas-Nararra, J. (eds), Diagnostic Neuropathology, Vol IV, Field and Wood Medical Publisher Inc., 1992, In Press.
4. Lloyd, R.V.: Embryology and anatomy of the pituitary gland, in, Lloyd, R.V. (ed), Surgical Pathology of the Pituitary Gland, W. B. Saunders, Chapter 1, 1992, In Press.
5. Lloyd, R.V.: Cytology and Function of the Pituitary Gland, in, Lloyd, R.V. (ed), Surgical Pathology of the Pituitary Gland, W. B. Saunders, Chapter 2, 1992, In Press.
6. Lloyd, R.V.: Practical Approaches to the diagnosis of pituitary lesions, in, Lloyd, R.V. (ed), Surgical Pathology of the Pituitary Gland, W. B. Saunders, Chapter 3, 1992, In Press.
7. Lloyd, R.V.: Frozen sections in the diagnosis of pituitary lesions, in, Lloyd, R.V. (ed), Surgical Pathology of the Pituitary Gland, W. B. Saunders, Chapter 4, 1992, In Press.
8. Lloyd, R.V.: Non-neoplastic pituitary lesions including hyperplasia, in, Lloyd, R.V. (ed), Surgical Pathology of the Pituitary Gland, W. B. Saunders, Chapter 5, 1992, In Press.

9. Lloyd, R.V.: Molecular biological analysis of pituitary disorders in, Lloyd, R.V. (ed), Surgical Pathology of the Pituitary Gland, W. B. Saunders, Chapter 8, 1992, In Press.
10. Lloyd, R.V. Ectopic Pituitary Adenomas, in Lloyd, R.V. (ed), Surgical Pathology of the Pituitary Gland, W. B. Saunders, Chapter 11, 1992, In Press.
11. Jin, L. and Lloyd, R.V., Metastatic neoplasms to the pituitary gland, in, Lloyd, R.V. (ed), Surgical Pathology of the Pituitary Gland, W. B. Saunders, Chapter 12, 1992, In Press.
12. Lloyd, R.V.: Future prospects in the diagnosis and treatment of pituitary adenomas, in, Lloyd, R.V. (ed), Surgical Pathology of the Pituitary Gland, W. B. Saunders, Chapter 16, 1992, In Press.
13. Lloyd, R.V.: Adrenal medulla and paraganglia, in, Gould, V. and Lechago, J. (eds), Bloodworth's Endocrine Pathology, 3rd Edition. Williams & Williams, 1992, In Press.
14. Lloyd, R.V. and Jin, L.: Regulation of chromogranin A and B gene expression in human pituitary adenomas, in, 5th European Workshop on Pituitary Adenomas, Venice, 17-20 March 1991, Elsevier Science Publishers 1991, pp. 87-94.

BOOKS:

1. Surgical Pathology of the Pituitary Gland. Saunders, Lloyd, R.V. (ed) (In Press) .

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

1. Lloyd, R.V.: The polymerase chain reaction in the study of endocrine diseases. Endocrine Pathology. February, 1992 (Editorial).
2. Lloyd, R.V.: Markers of the diffuse neuroendocrine system. Japan Endocrine Society Publication.
3. Kaldjian, E., Jin, L. and Lloyd, R.V.: Immunohistochemical analysis of breast carcinomas. Correlation of estrogen and progesterone receptor, proliferative activity, tumor vascularity and lymph node metastasis. Lab. Invest. 1992;66:14A. Abstract 74.
4. Fields, K., Kulig E., Jin, L. and Lloyd, R.V.: Detection of ectopic prolactin expression in normal and neoplastic tissues by the polymerase chain reaction. Lab. Invest. 1992;66:36A. Abstract 204.
5. Hegg, C., Jin, L., Sisson, J., Thompson, N. and Lloyd, R.V.: Relationship of antigen of messenger RNA expression to biological behavior in sporadic and familial medullary thyroid carcinoma. Lab. Invest. 1992;66:36A. Abstract 207.
6. Maeda, T., Jin, L., Chandler, W. and Lloyd, R.: Protein kinase C activity in human and rat pituitary tissues. Lab. Invest. 1992;66:37A. Abstract 210.
7. Perkins, P., Jin, L., McLeod, M., Fukuuchi, A., Cho, K., Thompson, N. and Lloyd, R.V.: Analysis of gastrinomas by immunohistochemistry and *in situ* hybridization histochemistry. Lab. Invest. 1992;66L:38A. Abstract 215.
8. Stefaneanu, L., Scheithauer, B.W., Lloyd, R.V., Sano, T. and Kovacs, K.: Pituitary lactotroph hyperplasia in human pregnancy. Lab. Invest. 1992;66:38A. Abstract 219.
9. Jin, L., Chandler, W.F. and Lloyd, R.V.: Localization of specific growth factors (GF) in normal and adenomatous human pituitaries. The Endocrine Society, 74th Ann Meeting, San Antonio, Texas, July 24-27, 1992, p. 315, Abstract 1056.
10. Kulig, E. and Lloyd, R.V.: Molecular mechanisms regulating estrogen-induced rat pituitary proliferation and PRL expression. The Endocrine Society, 74th Ann Meeting, San Antonio, Texas, July 24-27, 1992, p. 315, Abstract 1053.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Supervision of seven postdoctoral fellows (Robert Larsen, Ph.D., Nozomu Hiraiwa, M.D., Ph.D., Brent Weston, M.D., Marco Trinchera, M.D., Aron Thall, Ph.D., Peter Smith, Ph.D., and Daniel LeGault, M.D.) and one M.D., Ph.D. thesis student, (Mr. Kevin Gersten).
B. Lecturer - Pathology 581.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "Analysis of the roles of oligosaccharides during murine embryogenesis". Source of award: Howard Hughes Medical Institute.
B. Principal Investigator, "The Molecular Biology of Intracellular Lipid Transport", NIH DK-38482 (50% effort), $57,297/year direct cost ($317,737/five years), 8/1/86 - 7/31/92.
C. Sponsor, NRSA Postdoctoral Fellow, Brent Weston, M.D. "The Lewis Blood Group a(1,3/1,4) Fucosyltransferase Gene". Inclusive dates of funding: 12/1/90 - 11/30/92. Source of award: National Institutes of Health. Total direct costs = $62,300.00.
D. Principal Investigator, "Molecular genetics of the human Lewis and Lewis-related blood group loci". (5% effort), Source of Award: National Blood Foundation. Inclusive dates of funding: 7/1/91 - 6/30/93. Total direct costs = $19,500.00.
E. Principal Investigator, "Molecular biology of human a1,3 fucosyltransferase", NIH GM47455-01 (25% effort), $71,951/year direct cost ($632,749/five years), 5/1/92 - 4/30/97.
F. Subcontract Principal Investigator, "Controlled expression of neoglycans in animal cells", NIH GM45914 (5% effort), $27,740/year direct cost ($89,334/two years), 8/1/91 - 7/31/93.
G. Sponsor, American Society of Nephrology/Marion Merrell-Dow Fellow "Structure-function relationships of fucosyltransferases". Daniel J. Legault, M.D. Inclusive dates of funding: 7/1/92 - 7/1/94 Source of award: National Kidney Foundation, Inc.

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

1. Resident Selection Committee.

REGIONAL AND NATIONAL:

1. Member, Editorial Board, Journal of Biological Chemistry.

V. OTHER RELEVANT ACTIVITIES:

1. Howard Hughes Medical Institute, Assistant Investigator.

INVITED LECTURES AND SEMINARS:

1. Molecular biology of mammalian glycosyltransferase genes, 11th International Symposium on Glycoconjugates, Toronto, Canada, July, 1991.
2. Recombinant mammalian glycosyltransferases in science and industry, International Perspectives in Glycobiology, University of Oxford, Oxford, England, September, 1991.
3. Cloned human fucosyltransferase genes and oligosaccharide ligands for cell adhesion molecules, Scripps Research Institute, La Jolla, Califoria, October, 1991.
4. Genes that determine terminal glycosylation events in mammalian cells, IBEX Biotechnology Expo and Scientific Conference, San Francisco, California, October, 1991.
5. Molecular genetics of the human H blood group locus, American Society of Hematology, December, 1991.
6. Molecular biology of fucosyltransferases, Georgetown University, Washington, DC, January, 1992.
7. Mammalian glycosyltransferase genes that determine selectin-dependent cell adhesion, Mucin and Other Cancer-associated Carbohydrate Antigens in Cell Biology, US-Japan Cancer Program. Oahu, Hawaii, February, 1992.
8. Structure and function of mammalian glycosyltransferase genes, Glycobiology II Keystone Symposia, Park City, Utah, March, 1992.
9. Mammalian genes that determine glycosylation events, FASEB Meeting, April, 1992.
10. Human fucosyltransferase genes and cell adhesion, Ciba-Geigy, Summit, New Jersey, April, 1992.
11. Mammalian genes that determine terminal glycosylation event, University of Alabama, Birmingham, Alabama, May, 1992.
12. Molecular structure and function of mammalian glycosyltransferases, First IUBMB Conference Biochemistry of Diseases, Nagoya, Japan, June, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Lowe, J.B., Kukowska-Latallo, J.F., Nair, R.P., Larsen, R.D., Marks, R.M., Macher, B.A., Kelly, R.J. and Ernst, L.K.: Molecular cloning of a human fucosyltransferase gene that determines expression of the Lewis x and VIM-2 epitopes but not ELAM-1-dependent cell adhesion. J. Biol. Chem. 1991:266;17467-17477.

2. Dumas, D.P., Ichikawa, Y., Wong, C.-H., Lowe, J.B. and Nair, R.P.: Enzymatic synthesis of sialyl Le^x and derivatives based on a recombinant fucosyltransferase. Bio. Med. Lett. 1991:1;425-428.
3. Lowe, J.B., Stoolman, L.M., Nair, R.P., Larsen, R.D., Behrend, T.L. and Marks, R.M.: A transfected human fucosyltransferase cDNA determines biosynthesis of oligosaccharide ligand(s) for endothelial-leukocyte adhesion molecule 1. Biochem. Soc. Trans. 1991:19;649-653.
4. Lowe, J.B.: Molecular cloning, expression, and uses of mammalian glycosyltransferases. Advances in Glycobiology, Seminars in Cell Biology. W.B. Saunders Company, United Kingdom, 1991, 2:289-307.
5. Weston, B.W., Nair, R. and Lowe, J.B.: Isolation of a novel human a(1,3)fucosyltransferase gene and molecular comparison to the human Lewis blood group a(1,3/1,4)fucosyltransferase gene. Syntenic, homologous, non-allelic genes encoding enzymes with distinct acceptor substrate specificities. J. Biol. Chem. 1992:267;4152-4160.
6. Ball, G.E., O'Neill, R., Schultz, J.E., Lowe, J.B., Weston, B.W., Nagy, J.O., Brown, E.G., Hobbs, C. and Bednarski, M.D.: Synthesis and structural analysis using 2-D NMR of sialyl Lewis X (SLe^x) and Lewis X (Le^x) oligosaccharides: ligands related to E-selectin (ELAM-1) binding. J. Am. Chem. Soc., In Press.
7. Wong, C.-H., Dumas, D.P., Ichikawa, Y., Koseki, K., Danishefsky, S.J., Weston, B.W. and Lowe, J.B.: Specificity, inhibition and synthetic utility of a recombinant human a1,3 fucosyltransferase. J. Am. Chem. Soc., In Press.

ARTICLES SUBMITTED OR IN PREPARATION:

1. Kelly, R.J., Ernst, L.K., Larsen, R.D., Bryant, J.G., Robinson, J.S. and Lowe, J.B.: Molecular basis for H blood group deficiency in Bombay (O_h) and para-Bombay individuals.
2. Gersten, K.M., Trinchera, M. and Lowe, J.B.: Identification and characterization of a murine a1,3 fucosyltransferase gene: comparison to its orthologous human homologue Fuc-TIV.
3. Weston, B.W., Smith, P.L., Kelly, R.J. and Lowe, J.B.: Molecular cloning of a fourth member of a human a(1,3)fucosyltransferase gene family: Multiple homologous sequences that determine expression of the Lewis x, sialyl Lewis x, VIM-2, and difucosyl sialyl Lewis x epitopes.

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

1. Lowe, J.B.: Molecular Biology: Basic Concepts. Clinical Laboratory Medicine, K.D. McClatchey (ed.) Williams & Wilkins, Baltimore, Maryland, 1992, in press.
2. Lowe, J.B.: Oligosaccharide-dependent mechanisms of leukocyte adhesion. Homing Mechanisms and Cellular Targeting. B.R. Zetter (ed.) Marcel Dekker, New York, 1992, in press.
3. Lowe, J.B.: Specificity and expression of carbohydrate ligands. Handbook of Immunopharmacology - Adhesion Molecules. C.D. Wegner(ed.) Academic Press, London, 1992, in press.

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

ANNUAL DEPARTMENTAL REPORT
July 1, 1991 - June 30, 1992

I. CLINICAL ACTIVITIES

A. Surgical Pathology, consultant on all head and neck pathology cases.
B. Autopsy:
   1. Consultant on forensic odontology cases.
   2. Assistant Medical Examiner, Washtenaw County.
C. Director of Clinical Microbiology\Virology Laboratory.
D. Medical Director of Medical Technology Program; Eastern Michigan University.
E. Ann Arbor Veterans Administration Medical Center - monthly consultant.
F. Associate Chief of Medical Affairs.
G. Director of Pathology Laboratory, School of Dentistry.

II. TEACHING ACTIVITIES

MEDICAL SCHOOL/HOSPITALS

A. Pathology 630/631; Course Director:
   1. Five hours credit (Monday and Wednesday, 2-4:00 p.m.)
   2. 100 dental students, 25 medical illustration and graduate students.
B. Oral Diagnosis 644; lecturer.
C. Pathology 600; lecturer, head and neck pathology.
D. Oral Pathology 695, Course Director.

III. RESEARCH ACTIVITIES

A. Consultant, Serologic Studies of Squamous Cell Carcinoma of the Head and Neck. Principal Investigator: Thomas E. Carey, Ph.D., Department of Otorhinolaryngology, The University of Michigan. NCI CA-49708-01, 6/1/89-3/31/92.
B. Consultant, Impact of Follow-Up on Control of High Blood Pressure and Cholesterol. Principal Investigator: Andrea Foote, Ph.D., Institute of Labor and Industrial Relations, The University of Michigan, 1988-present.
C. Veterans Administration Co-operative Studies Program, Executive Committee. G.T. Wolf, T.F. Beals, A.A. Forastiere, T. Carey, K.D. McClatchey, A. Flint, and J.L. Hudson: A New Strategy to Preserve the Voice Box in Advanced Laryngeal Cancer. Protocol 582-C, Clinical Research Center, The University of Michigan, 1985-present.
D. Consultant, Impact of Follow-up on Control of High Blood Pressure and Cholesterol. Principal Investigator, Andrea Foote, Ph.D., Institute of Labor and Industrial Relations, The University of Michigan, 1988-present.
E. Co-Investigator, Enzyme Tagging of Malignant Cervical Epithelial Cells. Principal Investigator, Daisy S. McCann, Ph.D., McCann Associates, Wayne, Michigan, 1991-present.

PENDING SUPPORT

A. Consultant, Head and Neck Cancer in Young Patients. Principal Investigator, Thomas E. Carey, Ph.D., Department of Otorhinolaryngology, The University of Michigan, 1988-present.

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL

A. Medical Service Plan Executive Committee, 1979-present.
B. Chairman's Advisory Committee.

MEDICAL SCHOOL/HOSPITAL

A. Ambulatory Care Committee, The University of Michigan Hospitals, 1980-1991.
B. Advisor, Medical and Biological Illustration Program, The University of Michigan Medical School, 1986-present.
C. Member, Infection Control Committee, The University of Michigan Hospitals, 1978-present.
D. Chairman, Laboratories Committee of the Medical Staff, The University of Michigan Hospitals, 1987-present.
E. Chairman, Quality Assurance Committee, The University of Michigan Hospitals, 1989-present.
F. Vice Chairman, Claims Control Committee, The University of Michigan Hospitals, 1990-present.
G. Member, Patient Care Advisory Committee, The University of Michigan Hospitals, 1989-present.
H. Member, Transplant Program Task Force, The University of Michigan Hospitals, 1990-present.
I. Chairman, Standardization and Product Evaluation Committee (SPEC), The University of Michigan Medical Center, 1991-present.

REGIONAL AND NATIONAL

A. College of American Pathologists, Fellow, 1975-present.
   1. Board of Governors, 1986-present.
   2. Members, Standards Committee, 1986-present.
   3. Chairman, Commission on Anatomic Pathology, 1986-present.
   4. Council on Scientific Affairs, 1987-present.
B. National Committee for Clinical Laboratory Standards, Corresponding Membership, 1987-present.
   1. Council of the National Reference System for the Clinical Laboratory, 1987-present.
   2. International Relations Committee, member, 1988-present.
   3. Subcommittee on Standardization of the PAP Technique, 1988-present.
C. American Society of Clinical Pathologists, 1975-present.
   1. ASCP Advisory Council, 1984-present.
   2. ASCP Advisory Council, State Councilor, 1987-present.
D. Michigan Society of Pathologists, 1982-present.
   1. Editor, Newsletter, 1988-1991.
   2. Nominating Committee, 1990-present.

E. Technical Advisory Committee, State of Michigan Department of Health, Bureau of Laboratory and Epidemiological Services, 1987-present.
F. American Society for Testing Materials (ASTM)
1. Committee F31 on Health Care Services, member, 1988-present.
G. Member, National Fetal-Infant Mortality Review Program Steering Committee, 1990-present.

INTERNATIONAL

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

V. OTHER RELEVANT ACTIVITIES

INVITED LECTURES/SEMINARS

1. Quality Assurance in the Practice of Pathology. 96th Annual Convention and Scientific Seminar of the American Osteopathic Association, New Orleans, Louisiana, November 4, 1991.
2. Clinicopathologic Correlations in Head and Neck Pathology, University of Vermont, Burlington, Vermont, January, 1992.
3. Clinicopathologic Correlations in Head and Neck Pathology, Loyola University, Chicago, Illinois, April, 1992.
4. Head and Neck Pathology. 96th Annual Convention and Scientific Seminar of the American Osteopathic Association, New Orleans, Louisiana, November 4, 1991.

VI. PUBLICATIONS

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Zappia, J.J., Sullivan, M.J. and McClatchey, K.D.: Unilateral multicentric Warthin's tumors. J. Otolaryngol. 1991;20:93-96.
2. Wells, M.D., Hoffman, H.T. and McClatchey, K.D.: An uncommon case of parotid sialolithiasis. Ann. Dent. 1991;50:23-24.
3. Dept. of Veterans Affairs Laryngeal Cancer Study Group, Authors: Randomized Trial of Induction Chemotherapy for Larynx Preservation in Patients With Advanced Laryngeal Cancer. N. Engl. J. Med. 1991;324:1685-1690.
4. Grenman, R., Carey, T.E., McClatchey, K.D., Wagner, J.G., Pekkola-Heino, K., Schwartz, D.R., Wolf, G.T., Lacivita, L.P., Ho, L., Baker, S.R., Krause, C.J. and Lichter, A.S.: In vitro radiation resistance among cell lines established from patients with squamous cell carcinoma of the head and neck. Cancer. 1991;67:2741-2747.
5. Zappia, J.J. and McClatchey, K.D.: Mucoepidermoid carcinoma associated with acute lymphoblastic leukemia. J. Ped. Otorhinolaryngology 1991;23:85-89.
6. Zappia, J.J., Wolf, G.T. and McClatchey, K.D.: Signet ring cell adenocarcinoma metastatic to the maxillary Sinus. Oral Surg., Oral Med., Oral Pathol. 1991;73:89-90.
7. Carroll, W.R., Niparko, J.K., Zappia, J.J. and McClatchey, K.D.: Primary adenocarcinoma of the temporal bone. A case with forty year follow-up. Arch. Otolaryngology - Head Neck Surg. 1991;117:439-441, 1991.
8. Zappia, J.J., Telian, S.A. and McClatchey, K.D.: Pathologic quiz case 2. Angiolymphoid hyperplasia with eosinophilia. Arch. Otolaryngol - Head Neck Surg. 1991;117:110-113.
9. Zappia, J.J., Bradford, C.R., Winter, P.H. and McClatchey, K.D.: Olfactory neuroblastoma associated with Kallman's syndrome. J. Otolaryngol. 1992;21:1.

10. Truelson, J.M., Fisher, S.G., Wolf, G.T., Beals, T.E. and McClatchey, M.D.: DNA content and histologic growth pattern correlate with prognosis in patients with advanced squamous cell carcinoma of the larynx. Cancer 1992;70:56-62.
11. Creps, L.B., Coffey, R.J., Warner, P.A. and McClatchey, K.D.: Improvement of quality through the integration of total quality and quality assessment. J. Quality Improvement: Review Bulletin, 1992, Accepted.

ARTICLES SUBMITTED FOR PUBLICATION

1. Carroll, W.R., Niparko, J.K., Zappia, J.J. and McClatchey, K.D.: Primary adenocarcinoma of the temporal bone: A case with forty year follow-up. Arch. Otolaryngology - Head and Neck Surg., July, 1990.
2. Carroll, W.R., Zappia, J.J. and McClatchey, K.D.: Branchiogenic carcinoma. Laryngoscope, November, 1991.

BOOKS AND CHAPTERS IN BOOKS

1. McClatchey, K.D. and McMahon Jr., L.F.: Laboratory Medicine, in Textbook of Internal Medicine, Kelley (ed), (2nd Edition), J. B. Lippincott, Philadelphia, Pennsylvania, Published, 1991.
2. McClatchey, K.D., et al.: Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, 1989-92 (Publication, February, 1993).
3. McClatchey, K.D.: The Oral Cavity, Sinuses, Tongue and Minor Salivary Gland, in, Histology for Pathologists, Sternberg (ed), Raven Press, New York, New York, 1989, Revised, 1991.
4. McClatchey, K.D. and Peterson, T.: The Laboratory Information System, in. Clinical Laboratory Medicine, Kenneth D. McClatchey (ed), Williams and Wilkins, Baltimore, Maryland, 1992, In Press.
5. Travers, E.M., and McClatchey, K.D.: Laboratory Management, in, Clinical Laboratory Medicine, Kenneth D. McClatchey (ed), Williams and Wilkins, Baltimore, Maryland, 1992, In Press.
6. Pierson, C.L. and McClatchey, K.D.: Automation, in, Encyclopedia of Microbiology, 1992, Academic Press, Inc., San Diego, Califoria, In Press.

PAMPHLETS

1. McClatchey, K.D., Dawson, J.B., Bernacki Jr., E.G., Kurtycz, D., Lukeman, J.M., Noller, K.L., Perna, V.P., Plott, A.E., Plowden, K. and Richart, R.: Papanicolau Technique, NCCLS Tentative Guideline, NCCLS Publication GP15, Villanova, Pennsylvania, 1991.
2. Travers, E.M., Delahunty, D.C., Flanagan, J., McClatchey, K.D., Meyer, D. and Rudar, J.M.: Cost Accounting in the Clinical Laboratory; Tentative Guidelines, Vol. 10, No. 13 (NCCLS Publication GP11-P), National Committee for Clinical Laboratory Standards, Villanova, Pennsylvania, 1991.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR

1. Alford, E. and McClatchey, K.: Effects of therapeutic irradiation on vessels used as recipients in revascularized free tissue transfer, Lambertson Lectures, Ann Arbor, Michigan, May 28, 1992.
2. Wolf, G., Hong, W., Fisher, S., Spaulding, M., Endicott, J., Laramore, G., Hillman, R., McClatchey, K., Frye, C., and the VA Laryngeal Cancer Study Group: Larynx Preservation with Induction Chemotherapy (CT) and Radiation (XRT) in Advanced Laryngeal Cancer: Final Results of the VA Laryngeal Cancer Study Group Cooperative Trial, ASCO Annual Meeting, San Diego, California, May 17-19, 1992.

PAUL E. MCKEEVER, M.D., PH.D.
ASSOCIATE PROFESSOR OF PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Neural and Behavioral Sciences 600, Neuropathology for Second Year Medical Students.
B. House Officers:
   1. Individual daily instruction of Pathology House Officers over microscope.
   2. Review of neuropathologic postmortem material - staff rotation and consults to residents.
   3. Review all neurosurgically removed material in this hospital in CME-approved biweekly conference - three months.
   4. Shared consultations in conference.
   5. Invited presentations of neuropathologic observations at joint clinical conferences.
   6. Pathology Resident's monthly Neuropathology Conference - three months.
C. Neurology resident, Norman Pflaster: One month elective in neuropathology.
D. Teach laboratory techniques to Neurohistologists and Research Staff.

REGIONAL AND NATIONAL:

A. 30th Annual AFIP Neuropathology Review, Armed Forces Institutes of Pathology, Washington, D.C., "New Methods of Brain Tumor Analysis", 1992.
B. Clinical Neuro-Oncology Course, University of Michigan Towsley Center, "Neuropathology and Labeling Index of Gliomas", 1991.
C. Nelson, J.S. and McKeever, P.E.: Clinical Neuropathology. Laser videodisc medical education reference, In Press.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. National Institutes of Health Grant NIH CA-47558, "Antigenic Instabilities and Clonal Heterogeneity in Human Gliomas", Principal Investigator. Changes in malignancy and resistance to treatment of human gliomas, the most common and devastating group of brain tumors, are thought to be related in part to antigenic instabilities of these cells. Antigenic instabilities are followed upon explantation of human glioma cells *in vitro* and

correlated with studies designed to determine the mechanism of these instabilities. The extent of changes in antigens are studied. Antigenic changes are correlated with changes in cellular DNA over time intervals and correlated with changes in clones of cells from the gliomas of individual patients. 5/1/88 - 4/30/93.

B. National Institutes of Health Program Project NIH CA-42761, "Antimetabolite Selectivity: Regional Treatment and Modulation", Principal Investigator of Pathology Core Grant. 4/1/93 - 3/31/96 (Pending).

C. National Institute of Health Program Project NS-15655, "PET Study of Biochemistry and Metabolism of the CNS" (Program Title). "Glioma Imaging with Benzodiazepine Analogs" (Section Title), Co-investigator. 12/1/89-11/30/94.

D. National Institutes of Health Grant NIH CA54104, "PET, Growth Kinetics and Neuropathology of Brain Tumors", Co-investigator. 5/1/91-4/30/95.

PROJECTS UNDER STUDY:

A. Growth, spread and antigenicity of ENU-induced gliomas in rats with Constance D'Amato and Dr. Terry Hood, Submitted to J. Neuro-oncology.

B. Quantitative analysis of DNA in fresh and cultured cells of brain tumors, with Drs. William Ensminger, Parvin Shakui, William Chandler, and James Varani.

C. Extracellular matrix products and plasminogen activators of gliomas with Drs. James Varani, Robert Sitrin, Dario Caccamo, and Suzanne Fligiel.

D. Magnetic resonance diffusion and cross relaxation of brain tumors with Drs. James Brunberg, Thomas Chenevert and Brian Ross.

E. Clinical-pathologic correlations of intracystic hemorrhage in cervical ependymoma with Drs. Thomas Sweasy and William Chandler.

F. Characterization of Rosai-Dorfman disease in brain with Drs. Michael Boland and Karin Muraszko.

G. Prognostic potential of nuclear organizers in myxopapillary ependymoma with Dr. Donald Ross.

H. Combined ultrastructural and karyotypic analysis of the VX-2 tumor with Thomas E. Carey. Submitted to Int. J. Cancer.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chief, Section of Neuropathology.

B. Member, Photography 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 and postmortem neuropathology by staff.

C. Supervision of Neurohistologists and Neuropathology Laboratories, and quality control of histologic preparations - six months.

D. Interaction with Chiefs and Staff of other clinical services, particularly Neurosurgery, Neurology, Nuclear Medicine, Radiation Oncology, Neuro-oncology and Neuroradiology - six months.

E. Quality control of ultrastructural and immunodiagnostic neuropathology. This included scheduled twice monthly meetings and various ad hoc reviews requested by faculty.

REGIONAL AND NATIONAL:

A. Editorial Board, Critical Reviews in Neurobiology.
B. International Editorial Board, Cellular and Molecular Biology.
C. Primary Review Pathologist, Children's Cancer Study Group CCG 9891 nationwide study of childhood low grade gliomas.
D. Reviewer, for various pathology, neuroscience and neurooncology journals.
E. M-Lab Neuropathology Services.

V. OTHER RELEVANT ACTIVITIES:

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

SABBATICAL

A1. DNA extraction, quantitation, purification and electrophoresis.
B. Southern and Northern blots.
C. DNA radiolabeling and hybridization.
D. Plasmid preparation.
E. High resolution G-banding of chromosomes.
F. Karyotyping.
G. Fluorescent in situ hybridization to chromosomal DNA.
H. Preparation of two manuscripts and three chapters.

INVITED LECTURES AND SEMINARS

1. Invited Lecture, Clinical Neuro-Oncology Course, University of Michigan Towsley Center: "Neuropathology and Labeling Index of Gliomas", Ann Arbor, Michigan, June 27, 1991.
2. Chairperson, Scientific Session, Neuronal and Nerve Sheath Tumors, American Association of Neuropathologists, Annual Meeting, St. Louis, Missouri, June 20, 1992.
3. Faculty, 30th Annual AFIP Neuropathology Review, Armed Forces Institutes of Pathology, Washington, D.C.: "New Methods of Brain Tumor Analysis", March 3, 1992.
4. Faculty, Neuropathology Specialty Conference, USCAP, Atlanta, Georgia, March 16, 1992.
5. Lecturer, Interdepartmental Immunology Research Seminar, Phenotypic Alterations in Gliomas, University of Michigan, Ann Arbor, Michigan, March 25, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Davenport, R.D., O'Donnell, L.J., Schnitzer, B. and McKeever, P.E.: Non-Hodgkin's lymphoma of the brain following Hodgkin's disease: An immunohistochemical study. Cancer 1991;67:440-443.
2. Lawrence, T.S., Davis, M.A., McKeever, P.E., Maybaum, J., Stetson, P.L., Normolle, D.P. and Ensminger, W.D.: Fluorodeoxyuridine-mediated modulation of iododeoxyuridine incorporation and radiosensitization in human colon cancer cells *in vitro* and *in vivo*. Cancer Res. 1991;51:3900-3905.
3. Pillai, K.M., McKeever, P.E., Knutsen, C.A., Terrio, P.A., Prieskorn, D.M. and Ensminger, W.D.: Microscopic analysis of arterial microsphere distribution in rabbit liver and hepatic VX2 tumor. Selective Cancer Therapeutics 1991;7:39-48.
4. Jonston, M.V., McDonald, J.W., Sackellares, J.C., Hood, T., Gilman, S., Garafalo, E., McKeever, P.E. and Troncoso, J.: Altered excitatory and inhibitory amino acid receptor binding in hippocampus of patients with temporal lobe epilepsy. Annals Neurol. 1991;29:529-541.
5. Roberson, P.L., Ten Haken, R.K., McShan, D.L., McKeever, P.E. and Ensminger, W.D.: Three-dimensional tumor dosimetry for hepatic Yttrium-90-microsphere therapy. J. Nuclear Med. 1992;33:5.
6. Lawrence, T.S., Davis, M.A., Maybaum, J., Mukhopadhyay, S.K., Stetson, P.L., Normolle, D.P., McKeever, P.E. and Ensminger, W.D.: The potential superiority of bromodeoxyuridine to iododeoxyuridine as a radiation sensitizer in the treatment of colorectal cancer. Cancer Res. 1992;526:3698-3704.
7. McKeever, P.E.: Computerized image analysis of distinct cell marker parameters of glial fibrillary acidic protein: Intensity of immunofluorescence and topography in human glioma cultures. Cell. Molec. Biol. 1992;38:175-180.

BOOKS AND CHAPTERS IN BOOKS:

1. McKeever, P.E., Davenport, R.D. and Shakui, P.: Patterns of antigenic expression in cultured glioma cells in, Nelson, J.S. (ed), Critical Reviews in Neurobiology, CRC Press, Boca Raton, Florida, 1991, Vol. 6, pp. 119-147.
2. Greenberg, H.S., Chandler, W.F., Ensminger, W.D., Junck, L., Thornton, A., Sandler, H., Page, M.A., McKeever, P., Gebarski, S., Liang, B. and Tankanow, R.: Radiosensitization with carotid arterial infusion of bromodeoxyuridine (BUdR) $\pm$ 5 fluorouracil (5FU) biomodulation with focal external beam radiation (FEBT) for malignant gliomas, Neuro-Oncology, Kluwer Academic Publish., Netherlands, 1991, pp. 217-219.
3. McKeever, P.E., Sima, A.A.F. and Blaivas, M.: Neoplasms of the sellar region, in, Lloyd, R.V. (ed), Surgical Pathology of the Pituitary Gland, Major Problems in Pathology series, W.B. Saunders, In Press.
4. McKeever, P.E.: Human astrocytic neoplasms, in Murphy, S. (ed), Astrocytes: Pharmacology and Function, Academic Press, New York, 1992, In Press.
5. McKeever, P.E. and Lloyd, R.V.: Pituitary ademomas and related lesions, in, Garcia, J.H. (ed), Diagnostic Neuropathology, Vol. IV, Field and Wood, New York, In Press.
6. Greenberg, H.S., Chandler, W.F., Ensminger, W.D., Junck, L., Page, M.A., Gebarski, S.S., Hood, T.W., Stetson, P.L., Diaz, R.F., Hegarty, T., Thornton, A., Lichter, A.S., McKeever, P.E. and Tankanow, R.: Radiosensitization with constant intra-arterial infusion of bromodeoxyuridine (BUDR) and focal external beam radiation in the treatment of malignant astrocytoma, Infusion Systems in Medicine, In Preparation.

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

1. Rowe, J.M., Hemperly, J.J., Sima, A.A.F., Gillard, M., Ross, D.A. and McKeever, P.E.: Localization of neural cell adhesion molecules in human brain tumors. J. Neuropathol. Exp. Neurol. 1991;50:366.
2. McKeever, P.E., McLaughlin, P.W., Lawrence, T.S., Rowe, J.M., Stetson, P.L., Mukhopadhyay, S.K. and Ensminger, W.D.: Partial growth arrest of glial fibrillary acidic protein (GFAP) positive cells in a solid human tumor. J. Neuropathol. Exp. Neurol. 1991;50:369.
3. Shakui, P., McKeever, P.E. and Papadopoulos, S.M.: Separation of heterogeneous phenotypes of cells from human glioma tissue. Fed. Am. Soc. Exp. Biol. J. 1991;5:A1261.
4. McKeever, P.E., Rowe, J.M., McLaughlin, P.W., Genik, S.J. and Ensminger, W.D.: Double immunoperoxidase staining for bromodeoxyuridine and iododeoxyuridine. Soc. Neurosci. Abstracts 1991;374:8.
5. Sondak, V.K., Stetson, P.L., McKeever, P.E., Change, A.E. and Lawrence, T.S.: IURD incorporation and washout in normal human tissues after intravenous infusion. Amer. Assoc. Cancer Res. San Diego, May 20, 1992.
6. McKeever, P.E. and Gammons, D.T.: Review of book titled, Textbook of Neuropathology (2nd ed), by Richard L. Davis and David M. Roberston. Amer. J. Surg. Path. 1992;16:210-211.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

CLINICAL RESEARCH-RELATED ACTIVITIES:

A. Assisted as a Co-Principal investigator in preparation of a an NIH proposal for studying the effects of clinical depression on the human reproduction.

B. Developed a method for continuous, integrated sampling from human subjects involving collection into a refrigerated fraction collector and continuous monitoring of oxidizable molecules.

C. Developed an approach for generating protocols and bar-coded labels to facilitate analysis of samples for a large clinical study.

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 1991.
2. Taught portion of Mammalian Reproductive Endocrinology, Physiology 541 (6 hrs lecture; ten contact hours).
3. October 9, 1991, Bioengineering 890 lecture: Cellular communication by extracellular signals.
4. November 26, 1991, Bioengineering 495 lecture: Monitoring the activity of living cells in real time.
5. January 16, 1992, Obstetrics and Gynecology.
6. Taught portion of Mammalian Reproductive Endocrinology, Physiology 581 (6 hrs lecture; ten contact hours).
7. April 3, 1991, Bioengineering 890 lecture: Real time monitoring of cellular activity: Aiming towards integrative biology.

B. Primary supervision of two postdoctoral fellows:
1. Beverly Strassman - postdoctoral fellow working on F32 fellowship. Appointed as Assistant Professor of Anthropology at the University of Michigan.
2. Daniel McConnell - postdoctoral fellow working on chemiluminescence-based assays (Support received from the TLindbergh Fund).

C. Primary supervision of eight graduate students:
1. Mahmoud Ghazzi, Bioengineering (recipient of an NIH Physician Scientist Award) - successfully defended on 7/3/91; now working as Assistant Research Scientist in RSP.
2. Craig Halberstadt, Bioengineering - successfully defended on 7/25/91; now employed by a biotechnology firm in California.
3. Rhonda Brand, Bioengineering - successfully defended on 11/6/91.
4. Jane Wiesen, Cellular and Molecular Biology (presented at the Society for the Study of Reproduction) - defense scheduled for August, 1992, supported on RO1 & RSP training grants.
5. Hal Cantor, Bioengineering - defense probably in Spring, 1993, supported on NSF sensor grant.

6. Sharolyn Belzer, Education with Biology Concentration - working for two semesters on research project involving hormones and behavior in preadolescent children, volunteering services.
7. Karen Heinze, Bioengineering - first year doctoral student transferred from Northwestern, supported on NCIR grant.
8. William Lemon, Bioengineering, supported on Cellular Biotechnology Training Grant.

D. Primary supervision of two pre-medical students:
1. Kristin McFadden (May, 1991-October, 1992).
2. Michael Lee (May, 1992).

E. Service on Other Dissertation Committees.
1. Kevin Ferreri, Biochemistry - successfully defended on 1/30/92.
2. Howard Goldberg, Electrical Engineering Computer Science - to defend in September, 1992.
3. John Bendell, external examiner, University of Toronto, 10/1/92.
4. Dan Burdick (current; Music).

F. Worked with two Visiting Scientists:
1. Bent G. Boving, Ph.D. Extramural Associate, Dept. of Embryology, Carnegie Institute of Washington.
2. Robert J. Carrico, Ph.D., President, Software Technologies, Inc., Franklin, Michigan 48025.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH, P30 HD18258, "Center for the Study of Reproduction", $337,266 TDC year #3, 3/1/89-2/28/94, Principal Investigator, 10% effort (5% as director of Administrative Core; 5% as Director, Standards and Reagents Core).

B. NIH, T32 HD-07048, "Training Program in Reproductive Endocrinology", $186,439 direct and stipends, 7/1/90-6/30/95, Mentor, 5% maximum effort.

C. NSF ECS-8915497, "Site-directed bioreagent immobilization for development of microbiosensor arrays", 9/1/89-8/31/92, $181,811 3rd year total costs, 6% effort (cost-shared), PI: Richard Brown (Dept. Electrical Engineering and Computer Science) Role: Co-investigator. My annual support from this grant, $13,199, is for one graduate research assistant, Hal Cantor.

D. NIH F32 HD07480, "The reproductive endocrinology of the Dogon." Individual postdoctoral fellowship for Beverly I. Strassmann, 02/01/91-01/31/93. Role: mentor, 5% maximum effort, cost shared.

E. NIH U54 Cooperative Center, "National Center for Infertility Research". $624,096 year 01. 9/30/91-08/31/96 PI: Nancy Reame (School of Nursing). Role: Associate Director of Center, 3% effort (cost shared); Director of "Assay Development Core," 5% effort (2% cost shared), $34,094 and PI of one project, "Gonadotrope response to ovulation-controlling signals." 15% effort year 01 (10% cost shared), $84,934.

F. Office of Vice President for Research, "University of Michigan Women's Health Initiative", Principal Investigator with Patricia Levine, 2% effort, cost shared, $5,840, 4/1/92-9/30/92.

G. Office of Vice President for Research, "Hormones and Behavior: An Interdisciplinary Study of Women and Adolescents", Principal Investigator, 5% effort, cost shared, $7,000, 6/15/92-9/30/92.

PROPOSAL WRITING:

A. Submitted to NIMH, "Stress and Reproductive Hormones in Depressed Women". $165,357 year 1 TDC, $708,446 years 1-4. PI: Elizabeth Young (MHRI & Psychiatry). Role: Co-PI, 10% effort. 12/1/92-11/30/96. Pending.
B. Prepared request to Cellular Biotechnology Training Grant, Aug 1991, traineeship for Karen Heinze. Not funded.
C. Assisted on behalf of RSP in development of a new training grant application for six predoctoral fellowships from the NSF.
D. Prepared request to Cellular Biotechnology Training Grant, Aug 1991, traineeship for Hal Cantor. Funded for six months.
E. Assisted on behalf of the Bioengineering Program in the development of a proposal to the Whitaker Foundation (we are now among the finalists).
F. Assisted three individuals in three firms (Innovation Associates, Software Technologies, Inc. and Wolpert Polymers) to develop SBIR grants which, if successful, will involve the University as a sub-contractor.
G. Submitted supplemental application for the NICHD to support the development of an immunoassay for follistatin which will be funded on October 1, 1992.

SCIENTIFIC COLLABORATIONS:

A. Biostatistics: Morton Brown and Dan Normolle: Development and implementation of a new robust method for analysis of immunoassays involving maximum likelihood estimators.
B. Chemistry: Mark Meyerhoff: (with Richard Brown) NSF-funded project aimed at developing multisite, antibody-based solid state microelectrodes.
C. Electrical Engineering: Richard Brown: (with Mark Meyerhoff) NSF-funded project aimed at developing multisite, antibody-based solid state microelectrodes.
D. Internal Medicine: David Humes: continuing to study the ability of kidney stem cells to form tubules and perhaps form an artificial kidney using our patented three dimensional bioreactor (we are getting kidney tubules to form from dissociated rabbit kidney cells).
E. Nursing: Nancy Reame: joint involvement in developing the NIH U54 National Center for Infertility Research.
F. 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.
G. Psychology: Jacquelynne Eccles: returning this fall to the University of Michigan. Completing a long term, longitudinal study concerning hormones and behavior in adolescents.
H. Carnegie Institute of Washington, Embryology and WSU, Anatomy: Bent Boving (retired): co-investigator in artificial organ development and perifusion programs.
I. Innovation Associates, Ann Arbor, MI: Judith Erb, Immunoassayist: assisted in development of a to-be-funded SBIR concerning the development of simplified immunoassays able to evaluate fertility.
J. Michigan State University, Animal Science: James Ireland, Reproductive Biologist: development of a solid state, two site chemiluminescence-based immunoassay for inhibin.
K. Software Technologies, Inc., Franklin, Michigan 48025: Robert J. Carrico, Statistician, Assisted in development of an SBIR proposal submitted June 15, 1992 concerning the development of a new computer interface to assist scientists in their access of statistical programs.
L. Wolpert Polymers, Inc., Southfield, Michigan 48037: Stephen M. Wolpert, Polymer Chemist formerly with Gelman Sciences and KMS Fusion. Helping him develop an

SBIR focused on creating a novel affinity matrix-membrane for immunoassays, blotting experiments, etc.

M. Wayne State University, Obstetrics and Gynecology:: Kamran Moghissi: Co-Associate Director of the NCIR grant and Key Investigator of one of its projects.

N. Wayne State University, Chemistry: Paul Schaap: with Dan McConnell, development of new approaches for chemiluminescent immunoassays.

INTELLECTUAL PROPERTIES ACTIVITY:

A. Halberstadt, C.R. and Midgley, A.R. Bioreactor System, Continuation of Serial No. 07/654,418, April 18, 1988, abandoned. Filed February 11, 1991, Issued on January 14, 1992, United States Patent Number 5,081,035.

B. Responding to first office action on patent application, Bioreactor system with alginate matrix (SN 07/744,109; UM#136c1 RM-6HM).

PROJECTS UNDER STUDY:

A. Development of a computer-controlled perifusion system for on-line analysis of cellular responses to pulsatile and other controlled signaling.

B. Analysis of dynamic control of pituitary function by GnRH: the role of intercellular signaling.

C. Localization and regulation of mRNAs in rat granulosa cells.

D. Application of principles of cellular bioengineering to the growth and function of mammalian cells and the development of artificial organs.

E. Development of novel biosensors and immunoassays.

F. Examination of the relationships between changes in hormones, behavior and peer reactions during pre-adolescent development of children.

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL/HOSPITAL:

A. Director, Center for the Study of Reproduction.

B Associate Director, National Center for Infertility Research at Michigan (NCIR).

C. Director, Standards and Reagents Core Facility.

D. Director, Assay Core, NCIR.

E. Member, RSP Selection Committee.

UNIVERSITY:

A. Director, Reproductive Sciences Program.

B. Member, Committee to Review IOG, CHGD and RSP.

C. Proposed the establishment of a Women's Health Initiative.

D. Initiated the establishment of a Michigan Reproductive Medicine Consortium (This led to submission of the U54 Consortium Center grant).

E. Interviewing candidates for Internal Medicine, Ob-Gyn, Perinatal Medicine.

REGIONAL AND NATIONAL:

A. Member, NIDDK Endocrinology Research Program Advisory Committee, 1986-.

B. Member, NIDDK Hormone Distribution Program Subcommittee, 1986-.

C. Member, NIH Reviewers Reserve, 1989-.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Member, Site visit team, P01 Center grant application, Cornell University, July 10-12, 1991.
2. 24th Annual meeting of the Society for the Study of Reproduction, Vancouver, July 27-August 1, 1991.
3. Presented opening RSP seminar, September 10, 1991.
4. Member, Site visit team, P30 Center grant application, University of North Carolina, September 4-6, 1991.
5. Give seminar and explore possibility of developing assays by chemiluminescence at Ciba Corning, Boston, Massachusetts, October 28-October 30, 1991.
6. Member, Site visit team, P30 Center grant, Harvard University, October 30-November 1, 1991.
7. Annual meeting of the Society for Neuroscience, November 10-15, 1991.
8. Phone review of grant, Cornell University, November 19, 1991.
9. Bi-annual meeting of the Steering Committee of the National Collaborative Program for Infertility Research, Boston, Massachusetts, November 20-21, 1991.
10. NIH Workshop on Gonadotropin Releasing Hormone, Bethesda, Maryland, November 25-27, 1991.
11. Visit Boehringer Mannheim, Indianapolis to explore applicability of automated ELISA methods to our NCIR grant, December 5, 1991.
12. Visit Ciba Corning, Boston to learn capabilities of and receive proprietary information on the ACS:180 automatic immunoassay analyzer, December 11-12, 1991.
13. Phone review of grant, Cornell University, January 6, 1992.
14. Seminar, Dept. of Obstetrics and Gynecology, January 16, 1992.
15. NIDDK Endocrine Research Program Advisory Committee, Bethesda, Maryland, March 15-16, 1992.
16. NIDDK Hormone Distribution Program Committee, Bethesda, Maryland, March 16, 1992.
17. Review of Hormone Distribution Contract, Bethesda, Maryland, March 17, 1992.
18. Review of SBIR grants, Bethesda, Maryland, March 18, 1992.
19. Seminar, Dept. of Physiology, Wayne State University, Detroit, Michigan, April 14, 1992.
20. Presented lecture at All Michigan Obstetrics/Gynecology Course, Livonia, Michigan, May 8, 1992.
21. Hosted bi-annual meeting of the Steering Committee of the National Collaborative Program for Infertility Research, May 11-13, 1992.
22. Endocrine Society Meeting, San Antonio, Texas, June 23-28, 1992.

RELEVANT ACTIVITIES:

1. Developing an immunoassay analysis system (LigAnal) that will assist many investigators and possibly the Department of Pathology Ligand Assay Laboratory.
2. Implementing ELISA and chemiluminescence-based, solid state, two site immunoassays in Standards and Reagents Core as a partial replacement for radioimmunoassays (and thereby reduction in usage of radioactive isotopes).
3. Met with Board of Directors or Scientific Advisory Board of BioQuant, Inc. on July 18, October 10, November 27, and December 17, 1991, and January 14 and 28, and May 13, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Cantor, H.C. and Midgley, A.R.: Development of an active biosensor for real-time monitoring of neuroendocrine and gonadal humoral activity. Sensors and Actuators B: Chemical, In Press.

2. Cha, G.S., Liu, D., Meyerhoff, M.E., Cantor, H.C., Midgley, A.R., Goldberg, H.D. and Brown, R.B.: Electrochemical performance, biocompatibility, and adhesion of new polymer matrices for solid-state ion sensors. Analytical Chemistry 1991;63:1666-1672.
3. Moenter, S.M., Brand, R.M., Midgley, A.R. and Karsch, F.J.: Dynamics of GnRH release during a pulse. Endocrinology, 1992;130:503-510.

ARTICLES SUBMITTED:

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

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

1. Cantor, H.C., Brand, R.M., Boving, B.G., Ghazzi, M.N. and Midgley, A.R.: Monitoring dynamic responses of perifused tissue to hormonal stimuli instantaneously in real time. 24th Annual Meeting, Society for the Study of Reproduction, July 28-31, 1991.
2. Ghazzi, M.N., Wise, K.D., Anderson, D.J., Newman, S.W. and Midgley, A.R. Jr.: Use of silicon-based multichannel microelectrodes to characterize single-unit activity of neurons in the rat suprachiasmatic nucleus. Society for Neuroscience, November, 1991.
3. Wiesen, J.F. and Midgley, A.R. Jr.: Loss of c43 GAP junction mRNA during follicular atresia. 24th Annual Meeting, Society for the Study of Reproduction, July 28-31, 1991.
4. Midgley, A.R., Jr., McFadden, K. and Padmanabhan, V.: Non-GnRH-dependent episodic release of FSH into the hypophyseal portal blood of sheep. 74th Annual Meeting, Endocrine Society, June 24-27, 1992.
5. Wiesen, J.F. and Midgley, A.R., Jr.: Expression of c43 (a1) Gap junction mRNA and protein during rat ovarian follicular development and atresia. 25th Annual Meeting, Society for the Study of Reproduction, July 13-16, 1992.
6. McFadden, K., Padmanabhan, V. and Midgley, A.R.: Secretory dynamics of luteinizing hormone and GnRH as assessed by analysis of jugular and hypophyseal portal blood. 25th Annual Meeting, Society for the Study of Reproduction, July 13-16, 1992.
7. Strassmann, B.I. and Midgley, A.R. The reproductive endocrinology of the Dogon of Mali. Annual Meeting, Human Behavior and Evolution Society, 1992.

THESIS-RELATED MANUSCRIPTS NEARLY READY FOR SUBMISSION:

1. Halberstadt, C.R., Palsson, B.O. Midgley, A.R., Jr. and Curl, R.L.: Optimization of the Transtubular Bioreactor for the Production of Monoclonal Antibodies in a Serum-free, Low-protein Medium.
2. Brand, R.M., Cantor, H.C., Ghazzi, M.N., Favreau P.A., Boving B.G. and Midgley A.R., Jr.: Use of Continuous, On-Line Hydrogen Ion Monitoring To Examine the Flow Dynamics of Perifusion Systems and Cellular Metabolism.
3. Brand, R.M., Williams, W.J. and Midgley, A.R., Jr.: Convolution: A method for data analysis in perifusion systems.
4. Brand R.M., Lyons, R.H., and Midgley A.R., Jr.: Understanding the dynamics of HeLa cell responsiveness to modifications of metabolic substrates in perifusion.

5. Ghazzi, M.N., Wise, K.D., Anderson, D.J. and Midgley, A.R. Jr.: Computer-Assisted Approach for Analysis of Single Unit Nerve Cell Activity Extracted from Multichannel, Microprobe Data.
6. Ghazzi, M.N., Wise, K.D., Najafi, K. and Midgley, A.R. Jr.: Performance of Silicon-based Multichannel Microprobes in recording from deep brain structures.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES

None

II. TEACHING ACTIVITIES

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Two sessions Pathology 581 (Kunkel).
      b. Four sessions Pathology 620 (Miller).
      c. Six sessions Cellular and Molecular Biology 850.
   2. Ph.D. Thesis sponsor for Jia Shi (Pathology Department, Boston University).
   3. Laboratory Rotation, Heidi Michaels (Cell and Molecular Biology).
   4. Program Director, "Experimental Immunopathology Training Grant" submitted 6/92.

B. Undergraduate students:
   1. Meredith Pfifer, Minority High School Summer Research Program.

C. Postdoctoral fellows:
   1. Duaine Jackola, Ph.D.
   2. Li Shaokang, U.S.
   3. Jacek Witkowski, Ph.D.
   4. Jagadananda Ghosh, Ph.D.
   5. Paul Turke, Ph.D.

III. RESEARCH ACTIVITIES

SPONSORED SUPPORT:

A. Principal Investigator, "Activation Defects in Aging T Cells", NIH AG-09801 (30%), $126,107 direct costs/year, 8/1/90-7/31/95. MERIT award.

B. Principal Investigator, "T Cell Repopulation After Bone Marrow Transplantation", NIH CA-42148 (15%), $63,400 direct costs/year, 9/30/90 - 3/31/92.

C. Principal Investigator, "Aging Effects on IL-2 Secreting Helper T Cells", NIH AG-03978 (21%), $110,581 direct costs/year, 8/1/91 - 7/31/94.

D. Training Supervisor, "Research Training Agreement: Postdoctoral Training in Aging and Growth Control", Boston University (NIH/NIA Prime) (0%), $20,304 direct costs/year, 10/1/91-9/30/92.

E. Core Director, "Core Facility for Aged Rodents", NIH AG-08808 (10%), $66,755 direct costs/year, 9/1/89 - 8/30/94. (Component of Geriatric Research and Training Center, J. Halter, Program Director).

PENDING

A. Principal Investigator, "Immune and Muscle Function Assays as Biomarkers of Aging", NIH AG-11067 (15%), $149,000 direct costs/year, 4/1/93 - 3/31/98.
B. Program Director, "Research Training in Experimental Immunopathology", NIH AI-07413, $117,126 direct costs/year, 4/1/93-3/31/98.
C. Principal Investigator, "Summer Training Course in Aging Research", NIH AG-unassigned (2.5%), $33,651 direct costs, 4/1/93 - 6/30/93.
D. Principal Investigator, "T Cell Repopulation After Human Bone Marrow Transplantation, NIH CA-42148 (15%), $112,483 direct costs/year, 4/1/93 - 3/31/98.

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL

A. Committee on Master Planning Analysis.
B. Graduate Education Committee.
C. Qualifying Examination Committee.

MEDICAL SCHOOL/HOSPITAL

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

REGIONAL AND NATIONAL

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Journal of Immunology.
B. Aging: Immunology and Infectious Disease.
C. Journal of Gerontology: Biological Sciences.

INVITED LECTURES/SEMINARS:

1. International Conference on Biogerontology, Bologna, Italy, July, 1991.

2. Workshop on Aging, Cell Proliferation and Cancer (Session Chair), Montreal, Canada, October, 1991.
3. Gerontology Society of America Annual Meeting (Session Chair), San Francisco, November, 1991.
4. Keystone Symposium on Cytokines (Session Chair), Taos, Febuary, 1992.
5. Dept. of Immunology, Scripps Clinic and Research Foundation, February, 1992.
6. Andrus Gerontology Center, University of Southern California, February, 1992.
7. Jackson Laboratories, Bar Harbor, Maine, March, 1992.
8. Lecture, "Biology of Aging," Beaumont Hospital Intensive Review of Geriatric Medicine, April, 1992.
9. American Association of Pathologists (FASEB) Annual Meeting, April, 1992.
10. NIA Workshop on Genetically Heterogeneous Mice, Bethesda, April, 1992.
11. Division of Hematology, University of Michigan, May, 1992.
12. Division of Rheumatology, University of Michigan, June, 1992.
13. Gerontology Research Center, Baltimore (Nathan Shock Award Lecture), June, 1992.
14. Minority High School Summer Research Program (Univ. Michigan), June, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Miller, R. A., Flurkey, K., Molloy, M., Luby, T. and Stadecker, M. J.: Differential sensitivity of virgin and memory T lymphocytes to calcium ionophores suggests a buoyant density separation method and a model for memory cell hyporesponsiveness to Con A. J. Immunol. 1991;147:3080-3086.
2. Flurkey, K., Stadecker, M. and Miller, R.A.: Memory T lymphocyte hyporesponsiveness to non-cognate stimuli: A key factor in age-related immunodeficiency. Eur. J. Immunol. 1991;22:931-935.
3. Miller, R. A.: Gerontology as oncology: research on aging as the key to the understanding of cancer. Cancer 1991;68:2496-2501.
4. Holmes, F. F., Wilson, J., Blesch, K.S., Kaesberg, P.R., Miller, R.A. and Sprott, R.: Biology of cancer and aging. Cancer 1991;68:2525-2526.
5. Miller, R. A.: Caloric restriction and immune function: developmental mechanisms. Aging: Clinical and Experimental Research 1991;3:395-398.
6. Miller, R. A.: Of time, tumors, and T cells. Gerontology Society of America News, February, 1992, p. 4.
7. Jenkins, M. K. and Miller, R.A.: Memory and anergy: challenges to traditional models of T lymphocyte differentiation. FASEB J. 1992;6:2428-2433.
8. Patel, H. and Miller, R.A.: Age-associated changes in mitogen-induced protein phosphorylation in murine T lymphocytes. Eur. J. Immunol. 1992;22:253-260.
9. Flurkey, K., Miller, R.A. and Harrison, D.E.: Cellular determinants of age-related decrements in the T cell mitogen response of B6CBAF1 mice. J. Gerontol. Biol. Sci., In Press.
10. Shi, J. and Miller, R.A.: Tyrosine-specific protein phosphorylation in response to anti-CD3 antibody is diminished in old mice. J. Gerontology: Biological Sciences, In Press.

ARTICLES SUBMITTED FOR PUBLICATION

1. Witkowski, J. M. and Miller, R.A.: Increased function of P-Glycoprotein in T lymphocyte subsets of aging mice.
2. Warner, H., Campisi, J., Cristofalo, V., Miller, R.A., Papaconstantinou, J. Pereira-Smith, O., Smith, J. and Wang, E.: Meeting report: Control of cell proliferation in senescent cells.
3. Miller, R. A.: Aging and immune function: cellular and biochemical analyses.
4. Miller, R. A.: Aging and cancer: another perspective.

BOOKS/CHAPTERS IN BOOKS

1. Miller, R. A.: Accumulation of malfunctioning cells in a complex network: lessons from immunology for experimental gerontology. Proceedings of the First International Congress on Biomarkers in Gerontology, Bologna, Italy, In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. None.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Co-Investigator, "Role of Adhesion Molecules in Psoriasis", National Institute of Health, Grant 1-RO1-AR40065, $416,759, direct cost, three years. (B.J. Nickoloff, Principal Investigator).
B. Co-Investigator, "Role of Adhesion Molecules in skin Diseases", National Institutes of Health, (B.J. Nickoloff, Principal Investigator), July 1991-June 1994.
C. Co-Investigator, "Dermal Dendrocytes and AIDS-Related Psoriasis", National Institutes of Health, Grant 1-RO1-AR-40488, $573,176, direct cost, three years, (B.J. Nickoloff, Principal Investigator).

PENDING:

A. Safety Testing: Skin Irritation and Contact Sensitization, to be submitted to Proctor and Gamble, (R.S. Mitra, Principal Investigator; B.J. Nickoloff, Co-Investigator)

PROJECTS UNDER STUDY:

A. Characterization of gamma interferon receptor on normal and psoriatic keratinocytes.
B. Characterization of epidermal growth factor receptor on normal and psoriatic keratinocytes.
C. Role of Gamma interteron in modulating adherence reactions between resting and activated mononuclear leukocytes and keratinocytes.
D. Role of Urocanic acid and histidine metabolites on tumor necrosis factor alfa induced ICAM-1 expression in cultured keratinocytes.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Responsible for teaching theoretical as well as technical to newcomers to the laboratory.

MEDICAL SCHOOL/HOSPITAL:

A. None.

REGIONAL AND NATIONAL:

A. None.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nickoloff, B.J., Karabin, G.D., Barker, J.N.W.N., Griffiths, C.E.M., Sarma, V., Mitra, R.S., Elder, J.T., Kunkel, S.L. and Dixit, V.M.: Cellular localization of interleukin-8 and its inducer tumor necrosis factor in psoriasis. Am. J. Pathol. 1991;138:129-140.
2. Barker, J.N.W.N., Mitra, R.S., Griffiths, C.E.M., Dixit, V.M. and Nickoloff, B.J.: Keratinocytes as initiators of inflammation: A unifying explanation for diverse array of environmental stimuli to produce cutaneous inflammation. Lancet 1991;337:211.
3. Barker, J.N.W.N., Jones, M.L., Swenson, C.L., Sarma, V., Mitra, R.S., Ward, P.A., Johnson, K.J., Fantone, J.C., Dixit, V.M. and Nickoloff, B.J.: Monocyte chemotaxis and activating factor production by keratinocytes in response to γ-IFN. J. Immunol. 1991;146:1192.
4. Barker, J.N.W.N., Jones, M.L., Mitra, R.S., Fantone, J.C., Kunkel, S.L., Dixit, V.M. and Nickoloff, B.J.: Modulation of keratinocyte-derived interleukin-8 which is chemotactic for neutrophils and T lymphocytes. Am. J. Pathol. 1991;139:869.
5. Ribeiro, P.L., Mitra, R.S. and Bernstein, I.A.: Assessment of the role of DNA damage and repair in the survival of primary cultures of rat cutaneous keratinocytes exposed to Bis - (2-chloroethyl) sulfide. Toxicol. Appl. Pharmacol. 1991;111:342.
6. Stoof, T.J., Mitra, R.S., Sarma, V., Dixit, V.S. and Nickoloff, B.J.: Keratinocyte activation following T lymphocyte binding. J. Invest. Dermatol. 1992;98:92
7. Mitra, R.S. and Nickoloff, B.J.: Epidermal growth factor and transforming growth factor-alpha decrease gamma interferon receptors and intercellular adhesion molecule on cultured keratinocytes. J. Cell. Physiol. 1992;150:264.
8. Nickoloff, B.J., Mitra, R.S., Shimizu, Y., Barker, J.N.W.N., Karabin, G., Stoof, T. and Stoolman, L.M.: HUT 78 T cells bind to noncytokine - stimulated keratinocytes using a non-CD18-dependent adhesion pathway. Am. J. Pathol. 1992;140:1365

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

BOOKS/CHAPTERS IN BOOKS:

1. Nickoloff, B.J., Varani, J. and Mitra, R.S.: Modulation of keratinocyte biology by gamma interferon: Revelance to cutaneous wound healing, in, Barbul, A. (ed), Clinical and Experimental Approaches to Dermal and Epidermal Repair: Normal and Chronic Wounds, Alan R. Liss, Inc., New York, New York, pp. 141-154, 1991.
2. Barker J., Griffiths C., Mitra R.S., Dixit V.M., Nickoloff B.J.: Human epidermal keratinocyte derived interleukin-8: Elevance to contact dermatitis, in, Czemielewski J.M. (ed), Immunological and Pharmacological Aspects of Atopic and Contact Eczema, Karger, Basal Vol 4, pp94-99, 1991

ABSTRACTS:

1. Mitra, R.S. and Nickoloff, B.J.: Epidermal growth factor decreases gamma interferon receptors and induction of intercellular adhesion molecule-1. J. Invest. Dermatol. 1991;96,554.

2. Nickoloff, B.J., Stoof, T.J., Mitra, R.S., Griffiths, G.E.M., Aulieino, M. and Stoolman, L.M.: CD-18 (LFA-1) and CD-492 (VLA-4) mediate lymphocyte adherence to endothelial cells in rhus dermatitis. J. Invest. Dermatol. 1991;96,538.
3. Mitra, R.S., Barker, J.N.W.N., Stoof, T.J., Stoolman, L.M. and Nickoloff, B.J.: Comparison of lymphocyte adhesion to keratinocyte, fibroblast, melanocytes CD-18 (LFA-1) dependent and independent pathways. Clinical Research 1991;39.
4. Nickoloff B.J. and Mitra R.S.: Keratinocytes derived from psoriatic plaques treated with phorbol ester plus gamma interferon stimulate lymphocyte proliferation. Clin Res 1991;39:740A.
5. Mitra, R.S., Stoof, T.J., Sarma, V.J., Dixit, V.M. and Nickoloff, B.J. Keratinocyte activation following T cell adhesion. International symposium on irritant contact dermatitis. Groningen, Holland, October, 1991.
6. Nickoloff, B.J., Mitra, R.S., Leek, Zell T., Thompson C. and Shimizu Y.: Gamma interferon does not induce expression on keratinocytes of the CD28-ligand B7/BB-1. Clin. Res. 1992;40:238.
7. Nickoloff, B.J., Mitra, R.S., Varani, J., dixit, V.M. and Polverini, P.: Psoriatic keratinocyte induced angiogenesis is inhibited by thrombospondin. J. Invest. Dermatol. 1992;98:560.
8. Mitra, R.S., Shimizu, Y. and Nickoloff, B.J.: Histamine synergistically augments tumor necrosis factor alpha mediated induction of keratinocytes ICAM-1 expression. Arch. Dermatol. Res., In Press, 1992.
9. Nickoloff, B.J., Mitra, R.S., Green, J., Shimizu, Y. and Thompson, C.: Gamma interferon treated keratinocytes present bacterial-derived superantigens to T cells which is blocked by LFA-1/ICAM-1 antibodies. Clin Res, In Press, 1992.

LETTERS TO THE EDITOR:

1. Nickoloff, B.J. and Mitra, R.S.: Intraepidermal psoriatic cytokine network involves gamma interferon, transforming growth factor-alpha and their cell surface receptors: Dysregulation rather than deficiency. J. Invest. Dermatol., In Press, 1992.

VI. OTHER RELEVANT ACTIVITIES:

1. Visiting Scientist, Free University Hospital, Amsterdam, The Netherlands. 6 October - 12 October, 1991.
2. Guest Lecturer:
   1. Modulation of ^{125}I-EGF ligand binding to cultured keratinocytes by antiproliferative agents.
   2. Epidermal growth factor and transforming growth factor - alpha decrease gamma interferon receptors and induction of ICAM-1 on cultured keratinocytes.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Pathology residents - supervision and teaching during cytopathology rotation and when covering necropsies.
B. Pathology residents - biweekly cytopathology conferences.
C. Senior medical students during pathology electives.
D. Sophomore medical students: class lectures, ICS course.
E. Sophomore medical students: Instructor, Pathology 600 laboratory.

III. RESEARCH ACTIVITIES:

A. Cytopathology, with particular reference to serous fluids, cytologic technique, and aspiration cytology.

PROJECTS UNDER STUDY:

A. Cross contamination in the cytologic staining circuit.
B. Cytomegalovirus infection of the uterine cervix.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director and Co-Director, Cytopathology Laboratory.
B. Chairman's Advisory Committee.
C. Advisory Committee on Appointments and Promotions.
D. Department of Pathology Medical Service Plan Executive Committee.

REGIONAL AND NATIONAL:

A. Secretary-Treasurer, American Society of Cytology.

B. North American Review Board, Acta Cytologica.
C. Associate Editor, Acta Cytologica.
D. Editorial Board, The ASC Bulletin.
E. Editorial Board, Cytopathology.
F. Chairman, Editorial and Publications Committee, International Academy of Cytology.
G. Membership Committee, International Academy of Cytology.
H. Budget and Finance Committee, American Society of Cytology.
I. Committee on Commemoration, American Society of Cytology.
J. State of Michigan Cervical Cytology Task Force. Interim Report and Recommendations, September, 1991.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Naylor, B.: Fine-needle aspiration cytology of the breast: Obtaining the specimens, what they show, and is it worth it? Lecture, Symposium on Breast Disease: Diagnostic Imaging and Current Management, The University of Michigan, Grand Traverse Village, Michigan, July 1991.
2. Naylor, B.: Pearls from the cytopathologist: Fascinomas and the mundane. Lecture, Update on Pulmonary and Critical Care Medicine, The University of Michigan, Ann Arbor, Michigan, September, 1991.
3. Wojcik, E.M. and Naylor, B.: "Collagen balls" in peritoneal washings: Prevalence, morphology, origin and significance. Paper, Annual Scientific Meeting of The American Society of cytology, Los Angeles, California, November, 1991.
4. Naylor, B.: Cytopathology of non-neoplastic entities. Lecture, University of California Irvine Medical Center and California Association of Cytotechnologists, Orange, California, January, 1992.
5. Naylor, B.: Seven lectures, Diagnostic cytopathology course, Pathology Education Incorporated, Snowmass, Colorado, February, 1992.
6. Naylor, B.: Perspectives in cytology: From Battle Creek to Oxford. Lecture, Thames Valley, South West and Wales Cytology Societies, Oxford, England, March, 1992.
7. Naylor, B.: a) Cytopathology: Its origins, fads, and fashions, and a glimpse into the future (lecture), b) Diagnostic seminar, c) Non-neoplastic entities in routine cytologic specimens (lecture). Ohio Society of Cytology, Cleveland, Ohio, March, 1992.
8. Naylor, B.: a) Ian Black Memorial Lecture, Cytopathology: Its beginnings, its fads and fashions, and a glimpse into the future, b) Diagnostic slide seminar. The Pacific Northwest Society of Pathologists, Seaside, Oregon, May, 1992.
9. Naylor, B: Asbestos and the pathologist. Lecture, Michigan Occupational and Environmental Medicine Association, Grand Rapids, Michigan, June, 1992.

HONORS AND AWARDS:

None

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Naylor, B.: Cytologic aspects of pleural, peritoneal and pericardial fluids from patients with systemic lupus erythematosus. Cytopathology 1992;3:1-8.
2. Grant, R., Naylor, B., Junck, L. and Greenberg, H.S.: Clinical outcome in aggresively treated meningeal gliomatosis. Neurology 1992;42:252-254.

BOOKS/CHAPTERS IN BOOKS:

1. Kim, K. and Naylor, B.: Practical Guide to Surgical Pathology with Cytologic Correlation. A Text and Color Atlas. New York, Springer-Verlag, 1991, pp 376.

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

None

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Dermatopathology, University of Michigan Hospitals.
B. Dermatopathology, M-Labs.
C. Dermatopathology, Private Consultations.
D. Dermatology, Melanoma Clinic.

II. TEACHING ACTIVITIES:

A. Pathology and Dermatology House Officers Lecture Series.
B. Clinical Pathology Orientation Lecture and Laboratory.
C. Five Week Medical Student (Year 2) Research Elective.
D. Year One Medical Student Dermatopathology Lecture Series.
E. Dermatology Grand Rounds - Dermatopathology Presentations.
F. Ten Week Undergraduate Student Research Elective.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. NIH RO-1 (40% effort: $147,702 Direct Costs; June 1991-July 1992): Role of Adhesion Molecules in Psoriasis.
B. NIH RCDA (50% effort: $60,000 Direct Costs; July 1991-June 1994). Role of Adhesion Molecules in Skin Diseases.
C. NIH RO-1 (10% effort: $184,727 Direct Costs; July 1991-June 1994). Role of Dermal Dendrocytes in AIDS-Related Psoriasis.

PROJECTS UNDER STUDY:

A. Role of gamma interferon in modulating adherence reactions between resting and activated mononuclear leukocytes and keratinocytes.
B. Characterization of gamma interferon receptor on normal and psoriatic keratinocytes.
C. Gamma interferon activation of protein kinase C in benign and malignant keratinocytes.
D. Binding of lymphocytes to epidermis and vessels of frozen sections of psoriatic skin and other dermatoses.
E. Characterization of type of Beta Interferon produced by virally infected keratinocytes.
F. Interrelationship between gamma interferon, and tumor necrosis factor and PGE_2 and IL-1 production by keratinocytes and monocytes.
G. Characterization and biological significance of thrombospondin production by keratinocytes and melanocytes.
H. Role of extracellular matrix in adherence reactions involving resting and activated mononuclear leukocytes.

I. Characterization of epidermal growth factor receptor on normal and psoriatic keratinocytes.
J. Characterization of effect of cyclosporin A on phorbol ester induced cutaneous inflammation and hyperplasia.
K. Role of endothelial cell adhesion molecules (ICAM-1, ELAM-1, VCAM-1) in cutaneous leukocyte trafficking.
L. Role of Factor XIII a positive dermal dendrocytes in AIDS-related psoriasis.
M. Dissection of cytokine networks in psoriasis, allergic contact dermatitis to poison ivy, and mycosis fungoides.

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

A. Editorial Board - American Journal of Dermatopathology, Journal of Cutaneous Pathology, Autoimmunity Forum In Dermatology. Journal of American Academy of Dermatology, Journal o Dermatological Science, American Journal of Pathology.
B. Reviewer of articles for: Journal of Investigative Dermatology, Journal of Cutaneous Pathology, American Journal of Pathology, American Journal of Dermatopathology, Archives of Dermatology, Journal of American Academy of Dermatology, American Journal of Plastic Surgery, Journal of Cellular Physiology, American Journal of Pathology, British Journal of Dermatology, New England Journal of Medicine, Journal of National Cancer Institute, Journal of Clinical Investigation, Journal of Dermatological Science, Journal of Immunology.
C. Member-General Medicine A Study Section, Subcomittee-1; NIH.
D. Ad-hoc Reviewer: University of Michigan Multipurpose Arthritis Center.
E. Ad-hoc Reviewer: University of Michigan Department of Surgery.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Topobiology and Investigative Dermatopathology, Invited Speaker, Howard Fox Lecture Series, Dept of Dermatology, New York University, June 7, 1991, New York, New York.
2 The Cytokine Network in Psoriasis. Invited Speaker, Fifth International Psoriasis Symposium-Plenary Lecture, July 12, 1991, San Francisco, California.
3. Keratinocyte Gene Activation in Psoriatic Epidermis: Molecular Basis of Increased Growth and Inflammation. Invited Speaker and Session Co-Chairman, 5th Japan-US Joint Seminar-The Biology of the Epidermis. July 21-25, 1991, Sapporo, Niseko, Hokkaido, Japan.
4. CD-34 Expression in Kaposi's Sarcoma, Annual Meeting-The Laboratory of Tumor Cell Biology-National Cancer Institute, September 3, 1991, Bethesda, Maryland.
5. Cytokine Networks in Skin Disease, Invited Speaker, Ocular Inflammation-Today and Tomorrow, University of Illinois Annual Meeting, September 14, 1991, Chicago, Illinois.
6. Cytokine Networks in Psoriasis, Invited Speaker and Visiting Professor, Zurich University Hospital, Dept of Dermatology, Zurich, Switzerland, September 30, 1991.
7. Molecular and Cellular Determinants of Cutaneous T-cell Lymphoma, Invited Speaker and Session Chairman, NATO Advanced Research Workshop, Basic Mechanisms of Physiological and Aberrant Lymphoproliferation in the Skin, San Mineato (Pisa), Italy, October 2, 1991.
8. The Cytokine Network in Psoriasis and Poison Ivy Dermatitis, Invited Speaker, Biological Responses to External Stimuli and Stress Symposium. Bausch and Lomb. October 10, 1991, Rochester, New York.

9. Mechanisms of Allergic Contact Dermatitis, Invited Speaker, Contact Dermatitis: State of The Art Issues, American Contact Dermatitis Society Symposium. October 25, 1991, Hotel Hershey, Hershey, Pennsylvania.
10. Keratinocytes Derived from Psoriatic Plaques Stimulate Lymphocyte Proliferation, Midwestern AFCR/SID Meeting, Nov 8, 1991, Chicago, Illinois.
11. Cytokine Network In Psoriasis, Invited Speaker, Dept of Biology; Kalamazoo College, Nov 26, 1991, Kalamazoo, Michigan.
12. Keratinocytes as Initiators of Inflammation, Invited Speaker, Advanced Immunology Seminar-Annual Meeting: American Academy of Dermatology, Dec 7, 1991, Dallas, Texas.
13. Cytokine Network in Psoriasis, Invited Speaker, Departs of Molecular Biology and Medicinal Chemistry, ISIS Pharmaceuticals, Dec 9, 1991, Carlsbad, California.
14. Cytokine Network in Psoriasis, Visiting Professor, Dept of Dermatology, Cleveland Clinic, April 2, 1992, Cleveland, Ohio.
15. Psoriatic Keratinocyte induced Angiogenesis is Inhibited by Thrompospondin, Annual Meeting-Society for Investigative Dermatology, April 30, 1992, Baltimore, Maryland.
16. Role of Adhesion Molecules in Psoriasis, Invited Speaker and Workshop Co-Chairman, Adhesion Molecules: 18th World Congress of Dermatology, June 13, 1992, New York, New York.
17. Role of Keratinocytes in Cutaneous Inflammation, Invited Speaker, Contact Hypersensitivity Workshop, 18th World Congress of Dermatology, June 13, 1992, New York, New York.
18. Role of Growth Factors in Kaposi's Sarcoma, Invited Speaker, Growth Factor Workshop, 18th World Congress of Dermatology, June 15, 1992, New York, New York.
19. Pathophysiology of Cutaneous Inflammation, Invited Speaker, Perspectives in Cutaneous Inflammation Symposium. 18th World Congress of Dermatology, June 17, 1992, New York, New York.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nickoloff, B.J., Karabin, G.D., Barker, J.N.W.N., Griffiths, C.E.M., Sarma, V., Mitra, R.S., Elder, J.T., Kunkel, S.L. and Dixit, V.: Cellular localization of interleukin-8 and its inducer tumor necrosis factor-alpha in psoriasis. Am. J. Path. 1991;138:129-140.
2. Mahoney, S.E., Duvic, M., Nickoloff, B.J., Minshall, M., Smith, L.L., Griffiths, C.E.M., Paddock, S.W. and Lewis, D.E.: HIV transcripts indentified in HIV-related psoriasis and Kaposi's sarcoma lesions. J. Clin. Invest., 1991;88:174-185.
3. Griffiths, C.E.M. and Nickoloff, B.J.: Induction, distribution, and diminution of leukocyte adhesion molecules (ELAM-1, ICAM-1, VCAM-1) T-cell chemotaxin (IL-8), and a modulatory cytokine (TNF-α) during the evolution of allergic contact dermatitis (Rhus Dermatitis). Br. J. Dermatol. 1991;124:519-526.
4. Nickoloff, B.J.: The human progenitor cell antigen (CD-34) is localized on endothelial cells, dermal dendritic cells, and perifollicular cells in formalin-fixed normal skin, and on proliferating endothelial cells and stromal spindle-shaped cells in Kaposi's Sarcoma. Arch. Dermatol. 1991;127:523-529.
5. Barker, J.N.W.N., Karabin, G.D., Stoof, T., Mitra, R.S., Sarma, V., Dixit, V.M. and Nickoloff, B.J.: Detection of gamma interferon mRNA in psoriatic epidermis by polymerase chain reaction. J. Dermatol. Sci. 1991;2:106-111.
6. Nickoloff, B.J.: Anti-β4 Integrin prominently stains nerves in psoriatic skin. Arch. Dermatol. 1991;127:271-272.
7. Barker, J.N.W.N., Jones, M.L., Swenson, C.L., Sarma, V., Mitra, R.S., Ward, P.A., Fantone, J.C. and Nickoloff, B.J.: Regulation of keratinocyte-derived monocyte chemotaxis and activating factor (MCAF) by interferon-gamma. J. Immunol. 1991;146:1192-1197.

8. Nickoloff, B.J. and Griffiths, C.E.M.: Aberrant intercellular adhesion molecule-1 (ICAM-1) by hair follicle epithelial cells and endothelial leukocyte adhesion molecule-1 (ELAM-1) by vascular cells are important adhesion molecule alterations in alopecia areata. J. Invest. Dermatol. 1991;96:91s-92s.
9. Barker, J.N.W.N., Mitra, R.S., Griffiths, C.E.M., Dixit, V. and Nickoloff, B.J.: Keratinocytes as initiators of inflammation: A unifying explanation for diverse array of environmental stimuli to produce cutaneous inflammation. Lancet 1991;337:211-214.
10. Nickoloff, B.J.: Cytokine network in psoriasis: Molecular pathway pointing to the psoriasis gene in mutant clones of epidermal keratinocytes. Arch. Dermatol. 1991;127:871-884.
11. Barker, J.N.W.N., Jones, M.L., Mitra, R.S., Fantone, J.C., Kunkel, S.L., Dixit, V.M. and Nickoloff, B.J.: Modulation of keratinocyte-derived interleukin-8 which is chemotactic for neutrophils and T lymphocytes. Am. J. Pathol. 1991;139:869-876.
12. Fivenson, D.P. and Nickoloff BJ: Immunodiagnosis in Cutaneous T cell Lymphoma: How does gene expression of the variable region of the T cell receptor fit into the diagnostic and pathophysiological picture of T cell neoplasia? J. Cut. Pathol. 1992;19:1-5.
13. Nickoloff, B.J., Mitra, R.S., Barker, J.N.W.N., Karabin, G., Stoof, T. and Stoolman, L.M.: A comparative study of lymphocyte adhesion to keratinocytes, fibroblasts, and melanocytes reveal both LFA-1 (CD-18) dependent and independent pathways. Am. J. Pathol. 1992;140:1365-1374.
14. Nickoloff, B.J.: Role of epidermal keratinocytes as key initiators of contact dermatitis due to allergic sensitization and initiation. Am. J. Contact Dermatitis. 1992;3:65-69.
15. Mitra, R.S. and Nickoloff, B.J.: Epidermal growth factor and transforming growth factor-alpha decreases gamma interferon receptors and induction of intercellular adhesion molecule (ICAM-1) on cultured keratinocytes. J. Cell Physiol. 1992;150:264-268.
16. Stoof, T., Mitra, R.S., Dixit, V.M. and Nickoloff, B.J.: Keratinocyte activation following binding of T lymphocytes. J. Invest. Dermatol. 1992;98:92-95.
17. Fivenson, .D.P., Becker, R., Dunstan, R.W., Nickoloff, B.J. and Moore, P.F.: Dermal dendrocytes and T cells in mycosis fungoides: Support for an animal model of human cutaneous T cell lymphoma. J. Cancer Res., In Press, 1992.
18. Fivenson, D.P., Douglass, M.C. and Nickoloff, B.J.: Thy-1 positive dermal dendrocytes are increased in mycosis fungoides. Am. J. Pathol., In Press, 1992.
19. Bruynzeel, I., Nickoloff, B.J., Van der Raaij, E.M.H., Boorsma, D.M., Stoof, T.J. and Willemze, R.: Induction of ICAM-1 expression by keratinocytes via a paracrine pathway involving dermal dendritic cells. Arch. Dermatol. Res., In Press, 1992.
20. Carr, K.A., Bulengo, S., Weiss, L.M. and Nickoloff, B.J.: Lymphoepithelioma-like carcinoma of the skin: a case report with immunophenotypic analysis and in-situ hybridization for Epstein-Barr viral genome. Am. J. Surg. Pathol., In Press, 1992.
21. Altman, D.A., Nickoloff, B.J. and Fivenson, D.P.: Demonstration of a relationship between factor XIIIa positive and CD34 positve dendrocytes in mesenchymal skin tumors. J. Cut. Pathol., In Press, 1992.
22. Nickoloff, B.J.: PECAM-1 (CD31) is expressed on proliferating endothelial cells, stromal spindle-shaped and dermal dendrocytes in Kaposi's sarcoma. Arch. Dermatol., In Press, 1992.

BOOKS/CHAPTERS IN BOOKS:

1. Nickoloff, B.J.: Interferons and cutaneous metabolism, in, Biochemistry and Physiology of the Skin, Oxford University Press, New York, pp1200-1221, 1991.
2. Nickoloff, B.J.: Role of epidermal T-cell migration in Parapsoriasis and Cutaneous T-cell Lymphoma, in, Muller, A.S. (ed.), Proceedings of the First International Parapsoriasis Symposium, Mayo Clinic Press, pp. 85-93. 1991.
3. Nickoloff, B.J., Varani, J. and Mitra RS: Modulation of keratinocyte biology by gamma interferon: Revelance to cutaneous wound healing, in, Barbul, A. (ed.), Clinical and Experimental Approaches to Dermal and Epidermal Repair: Normal and Chronic Wounds, Alan R. Liss Inc., New York, New York, pp. 141-154, 1991.

4. Nickoloff, B.J., Editor: Dermal Immune System (CRC Press), Inc. In Press, 1992.
5. Barker, J., Griffiths, C., Mitra, R.S., Dixit, V.M. and Nickoloff, B.J..: Human epidermal keratinocyte derived interleukin-8: Elevance to Contact dermatitis, in, Czemielewski, J.M. (ed.), Immunological and Pharmacological Aspects of Atopic and Contact Eczema. Karger, Basal Vol 4, pp. 94-99, 1991.
6. Nickoloff, B.J: Cytokine Networks in Skin Disease, in, Kunkel, S. and Remick, D. (eds.), Cytokines in Health and Disease: Physiology and Pathophysiology, New York, New York, pp. 413-432, 1992.
7. Barker, J.N.W.N. and Nickoloff, B.J.: Leukocyte-Endothelium Interactions in Cutaneous Inflammatory Processes, in, Hausar, C. (ed.), Springer Seminars in Immunopathology, Springer International, In Press, 1992.
8. Fivenson, D.P. and Nickoloff, B.J.: Cell Trafficking Networks in Cutaneous T Cell Lymphoma. NATO meeting-Basic Mechanisms of Physiological and Aberrant Lymphoproliferation in the Skin, in, Lambert, W.C. (ed.), Plenum Publishing, New York, In Press, 1992.
9. Stoof, T., Boorsma, D. and Nickoloff, B.J.: Immunological Cytokines of Epidermis. in, Leigh, I. (ed.), Keratinocyte Handbook, Cambridge University Press, Submitted, 1992.
10. Nickoloff, B.J.: The Immunobiology of Dermis, in, Nickoloff, B.J. (ed.), Dermal Immune System, CRC Press, Inc, Boca Ratan, Florida, In Press, 1992.

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

1. Nickoloff, B.J., Fivenson, D.P., Griffiths, C.E.M. and Modlin, R.: Perferential but not unique cutaneous endothelial cells epression of ELAM-1. Clin. Res. 1991;39:153.
2. Mitra, R.S., Barker, J.N.W.N., Stoof, T.J., Stoolman, L.M. and Nickoloff, B.J.: Comparison of lymphocyte adhesion of keratinocytes, fibroblasts, melanocytes: CD18 (LFA-1) dependent and independent pathways. Clin. Res. 1991;39;243.
3. Stoof, T.J., Mitra, R.S., Sarma, V., Dixit, V.M. and Nickoloff, B.J.: Binding by T lymphocytes triggers keratinocyte activation. J. Invest. Dermatol. 1991;96:1015.
4. Fivenson, D.P. and Nickoloff, B.J.: Adhesion molecule expression by Thy 1+/FXAAA at dermal dendrocytes in mycosis fungoides. Clin. Res. 1991;39:153.
5. Nickoloff, B.J.: CD-34 antigen expression in Kaposi's Sarcoma. NIH-NCI Laboratory of Tumor Cell Biology Lab Meeting, 1991.
6. Nickoloff, B.J. and Mitra, R.J.: Keratinocytes derived from psoriatic plaques treated with phorbol ester plus gamma interferon stimulate lymphocyte proliferation. Clin Res 1991;39:740A.
7. Nickoloff, B.J., Regezi, J.A. and Headington, J.T.: Immunophenotypic characterization of submucosal dendrocytes in eight different oral tumors. J. Clin. Path. 1991;18:382.
8. Brunzeel, I., Nickoloff, B.J., Van der Raaj, E., Boorsman, D., Stoof, T. and Willemze, R.: Induction of ICAM-1 expression by epidermal keratinocytes via a paracrine pathway involving dermal dendrocyte cells. Brit. J. Dermatol., In Press, 1992.
9. Nickoloff, B.J., Mitra, R., Leek, Zell, T., Thompson, C. and Shimizu, Y.: Gamma interferon does not induce expression on keratinocytes of the CD28-ligand B7/BB-1. Clin. Res. 1991;40:238.
10. Fivenson, D.P., Hanson, C.A. and Nickoloff, B.J.: Specific localization of the malignant clone to the epidermal component in cutaneous T-cell lymphoma. Clin. Res. 1992;40:308.
11. Koch, A.E., Haines, C.K. and Nickoloff, B.J.: Monoclonal antibody 4A11 detects a novel antigen epressed on abnormal vascular endothelium: Upregulation in a human in-vivo model of contact dermatitis. Clin. Res. 1992;40:268.
12. Huang, Y.Q., Li, J.J., Nickoloff, B.J. and Friedman-Kien, .A: Four different cultured Kaposi's sarcoma cell lines express several monocyte/macrophage antigens. J. Invest. Dermatol. 1992;98:618.
13. Nickoloff, B.J., Mitra, R.J., Varani, J., Dixit, V.M. and Polverini, P.: Psoriatic keratinocyte induced angiogenesis is inhibited by thrombospondin. J. Invest. Dermatol. 1992;98:560.

14. Fivenson, D.P. and Nickoloff, B.J.: CD1B and CD1c expression by dermal dendrocytes and epidermal Langerhans cells in mycosis fungoides and psoriasis. Clin. Res. 1992;40:499.
15. Mitra, R.S., Shimizu, Y. and Nickoloff, B.J.: Histamine synergiestically augments tumor necrosis factor alpha mediated induction of keratinocytes ICAM-1 expression. Arch. Dermatol. Res., In Press, 1992.
16. Nickoloff, B.J., Mitra, R.S., Green, J., Shimizu, Y. and Thompson, C:. Gamma interferon treated keratinocytes present bacterial-derived superantigens to T cells which is blocked by LFA-1/ICAM-1 antibodies. Clin. Res., In Press.
17. Saed, G., Fivenson, D.P., Naidu, Y. and Nickoloff, B.J.: Mycosis fungoides and psoriasis exhibit a TH-1 type cell mediated response while Sezary syndrome expresses a TH-2 type response. Clin. Res., In Press.
18. Barker, J.N.W.N., Griffiths, C.E.M. and Nickoloff, B.J.: NAP/IL-8 immunoreactivity in normal and psoriatic skin. J. Invest. Dermatol. 1991;97:607.
19. Nickoloff, B.J., Huang, Y.Q., Li, J. and Friedman-Kien, A.: Immunohistochemical detection of papilloma virus antigens in Kaposi's Sarcoma. Lancet 1992;339:548-549.
20. Nickoloff, B.J. and Mitra, R.J.: Intraepidermal psoriatic cytokine network involves gamma interferon, transforming growth factor-alpha and their cell surface receptors: Dysregulation rather than deficiency. J. Invest. Dermatol., In Press, 1992.
21. Nickoloff, B.J.: Book Review: Differential Diagnosis in Dermatopathology, by AB Ackerman. N. Eng. J. Med., In Press 1992.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Director, Molecular Diagnostics Laboratory.
B. Autopsy Service (two weeks).

II. TEACHING ACTIVITIES:

A. Supervised Dr. Maribel Gonzalez-Garcia (Postdoctoral Fellow).
B. Speaker, Rheumatology Teaching Conference and Research Seminar.
C. Coordinator, Molecular Diagnostics Conference (weekly) and Grand Rounds.
D. Clinical Pathology Grand Rounds (one lecture).

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Functional Role of Bcl-2 and Antigenic Stimulation in the Development of Lymphoma," The University of Michigan Cancer Research Committee, 5% effort, $7,500, 7/1/91 - 7/1/92.
B. Principal Investigator, "Development of a Genotyping core for CF Mutations," Cystic Fibrosis Foundation, (Core facility for the project "Gene Transfer Approaches to Cystic Fibrosis"), 10% effort, $25,000/year ($75,000/3 years) 9/1/91 - 8/31/94.

PENDING:

A. Principal Investigator, "Regulation and Function of Bcl-2 in T cell Development." NIH, Multi-purpose Arthritis Center, Development and Feasibility Grant ($150,000/3 years) 1/1/93 - 12/31/95.
B. Principal Investigator, "Regulation of Bcl-2 Proto-oncogene in Germinal Centers." American Cancer Society, ($352,928/3 years) 7/1/93 - 6/30/96.

PROJECTS UNDER STUDY

A. Functional role of Bcl-2 in lymphocyte development and neoplasia.
B. Molecular cloning of genes involved in programmed cell death of B lymphocytes.
C. Regulation and role of Bcl-2 in Neuroblastoma.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, Molecular Diagnostics Laboratory.
B. Interviewer, postdoctoral candidates for fellowship in Anatomic Pathology.
C. Interviewer, postdoctoral candidates for research fellowships.

MEDICAL SCHOOL/HOSPITAL:

A. Director, Genotyping Core for Cystic Fibrosis Rotations.
B. Member, Transgenic Core Facility Committee, Multi/purpose Arthritis Center.
C. Reviewer, Departmental Grants.
D. Inerviewer, Faculty and Pre-doctoral Candidates.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Speaker, Department of Human Genetics, Wayne State University, Detroit, Michigan, December 1991.
2. Speaker, Department of Microbiology and Immunology, Michigan State University, East Lansing, Michigan, February 1992.
3. Speaker, Symposium on Oncogenes, Madrid, Spain, April 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Nuñez, G., Hockenberry, D., McDonnell, T.J. and Korsmeyer, S.J.: Bcl-2 maintains B cell memory. Nature (London) 1991;353:71-73.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Gratiot-Deans, J., Ding, L., Turka, L. and Nuñez, G.: Immature human cortical thymocytes expressing high levels of proto-oncogene Bcl-2 are resistant to glucocorticoid-induced apoptosis.
2. Ales, J-E. Cuende, E., Ding, L., Martinez, C. and Nuñez, G.: Bcl-2 differentially regulates cell death in WEHI-231 B cells.
3. Ding, L., Kenny, J., Horton, K., Korsmeyer, S. and Nuñez, G.: Expression of Bcl-2 in M167 μ/κ transgenic mice: Expansion of receptor-positive B cells and rescue from Ig-induced apoptosis. In preparation.

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

1. Ding, L., Horton, K. and Nuñez, G.: Bcl-2 alters B cell development in μ/κ PC transgenic mice. FASEB, Anaheim, California, April, 1992.

HAROLD A. OBERMAN, M.D.
PROFESSOR OF PATHOLOGY
CO-DIRECTOR OF CLINICAL PATHOLOGY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Co-Director, Section of Clinical Pathology, University Hospitals (to 9/91).
B. Director, Blood Bank and Transfusion Service, University Hospitals.
C. Diagnosis of surgical specimens from University Hospital patients.
D. Diagnosis of surgical specimens from M-Labs.
E. Diagnosis of consultation cases from pathologists elsewhere on surgical pathology of breast.
F. Medical coverage of Transfusion Service.
G. Medical coverage of Necropsy Service (Quality Control review).
H. Member, University of Michigan Breast Care Center.
I. Member, Committee on Guidelines for Blood Product Utilization.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Lectures on breast pathology (two) and transfusion medicine (three) to sophomore class.
B. Postgraduate course, "Current Topics in Blood Banking", Planning Committee.
C. Course on Transfusion Medicine presented to Pathology and Hematology/Oncology House Officers.
D. Seminars and lectures on Pathology of Breast to Pathology House Officers.
E. Director, Pathology clerkship for senior medical students, October-November, 1991.
F. Presentation of Grand Rounds to Department of Surgery: Appropriate use of blood components". October 5, 1991.
G. Presentation of Grand Rounds to Department of Obstetrics and Gynecology: "Appropriate use of blood components". October 31, 1991.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. New Ultrasound Methods for Cancer Diagnosis and Treatment (3-5 years at 5% effort).
B. Microvascular and Structural Imaging of Breast Cancer (3-5 years at 3% effort).
C. Specialized Program of Research Excellence (SPORE) in Breast Cancer. Member, Advisory Board of proposal from Allegheny-Singer Research Institute, Pittsburgh, Pennsylvania (Dr. Stanley E. Shackney, Principal Investigator).

IV. ADMINISTRATIVE ACTIVITIES:

REGIONAL AND NATIONAL:

A. American Association of Blood Banks:
   1. Awards Committee, Chairman.
   2. Publications Committee.
B. American Society of Clinical Pathologists:
   1. Expert Review Panel in Anatomic Pathology.
C. International Academy of Pathology:
   1. Abstract Review Board.
D. Michigan Society of Pathologists.
E. Southeastern Michigan Red Cross Blood Program:
   1. Board of Directors.
F. Consultant, Veterans Administration Hospital, Ann Arbor.
G. Test Committee on Blood Banking/Transfusion Medicine, American Board of Pathology.
H. Breast Cancer Task Force, Michigan Department of Public Health.

DEPARTMENTAL:

A. Director, Transfusion Medicine program.
B. M-Labs Operation Committee.
C. Chairman's Advisory Committee.
D. Director, Fellowship Program in Blood Banking/Transfusion Medicine.

MEDICAL SCHOOL/HOSPITAL:

A. Transfusion Committee, Chairman.
B. Breast Care Center.
C. Bone marrow homotransplantation task force.
D. AIDS task force.
E. Hospital Quality Assurance Committee.
F. Committee for development of guidelines for use of blood products.
G. Haematology sequence advisory committee, M-2 year.

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

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

INVITED LECTURES/SEMINARS:

1. Appropriate use of plasma and plasma derivatives. Annual meeting, American Association of Blood Banks. Baltimore, Maryland, November 10, 1991.
2. Interdisciplinary seminar on breast cancer: Pathologic aspects. Rochester Academy of Medicine. Rochester, New York, November 15, 1991.

3. "Problems in the Diagnosis and Management of Breast Cancer". American Society of Clinical Pathologists. Three-day course organized and presented by Drs. Oberman and P.P. Rosen. Sarasota, Florida, December 5-7, 1991.
4. Blood component therapy. Flint Osteopathic Hospital. Flint, Michigan, December 12, 1991.
5. Optimal blood transfusion, 1992. Invited Basic Science Lecture, Annual Meeting, Society of Thoracic Surgeons. Orlando, Florida, February 2, 1992.
6. Appropriate use and complications of blood components. Department of Pediatrics postgraduate course. Towsley Center, Ann Arbor, Michigan, March 28, 1992.
7. Infectious disease testing and the blood supply. Invited lecture. Michigan Association of Blood Banks seminar on risks of blood transfusion. Detroit Red Cross, April 2, 1992.
8. Risks and benefits of blood transfusion: Medical and legal issues. Advances in Internal Medicine postgraduate course. Towsley Center, Ann Arbor, Michigan, April 29, 1992.
9. Lecture, "Medical-Legal Aspects of Blood Banking", University of Michigan postgraduate course, "Current Topics in Blood Banking", Ann Arbor, Michigan, June 4, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Adler, D.D., Helvie, M.A., Oberman, H.A., Ikeda, D.M. and Bhan. A.O..: Radial sclerosing lesion of the breast: Mammographic features. Radiology 1990;176:737-740.
2. Goldman, E.B. and Oberman, H.A.: Legal aspects of transfusion of Jehovah's Witnesses. Trans. Med. Rev. 1991;5:263-270.
3. Oberman, H.A.: A modest proposal (Editorial on use of frozen sections). Am. J. Surg. Pathol. 1992;16:69-70.
4. Judd, W.J., Steiner, E.A., Oberman, H.A. and Nance, S.J.: Can the reading for serologic reactivity following 37 C incubation be omitted? Transfusion 1992;32:304-308.
5. Judd, W.J., Steiner, E.A., Abruzzo, L.V., Davenport, R.D., Oberman, H.A. and Pehta, J.C.: Anti-i causing acute hemolysis following a negative immediate-spin crossmatch. Transfusion, In press.
6. Helvie, M.A., Paramagul, C., Oberman, H.A. and Adler, D.D.: Invasive lobular carcinoma: Imaging features and clinical detection. Investigative Radiology, In press.

BOOKS/CHAPTERS IN BOOKS:

1. Goulet, J.A. and Oberman, H.A.: Blood and Blood Products, in, Chapman, M.J. (ed.), Operative Orthopedics, Lippincott Co. Philadelphia, 1991.
2. Rosen, P.P. and Oberman, H.A.: Tumors of the Breast. Fascicles of Tumor Pathology. Armed Forces Institute of Pathology. Universities Associated for Research and Education in Pathology, Inc., In Press.
3. Oberman, H.A.: Section editor, Immunohematology. In, McClatchey, K.D. (ed.), Clinical Laboratory Medicine, Williams and Wilkins Co. Baltimore, Maryland, In Press.
4. Oberman, H.A.: Organization, Functions, Regulation and Legal Concerns of Blood Banks, in, McClatchey, K.D. (ed.), Clinical Laboratory Medicine, Williams and Wilkins Co. Baltimore, Maryland, In Press.

ABSTRACTS, BOOK REVIEWS, LETTERS TO THE EDITOR,

1. Book Review Editor, American Journal of Surgical Pathology.
2. Oberman, H.A.: Follies and Fallacies in Medicine. Book review. Am. J. Surg. Path. 1991;15:1019.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Autopsy Service.

II. TEACHING ACTIVITIES:

A. Course Director, Pathology 650.
B. Soverin Karmiol, Ph.D. - Postdoctoral Fellow.
C. Kai Zhang, M.D. - Postdoctoral Fellow.
D. Young Choi, Undergraduate/Research.
C. Ravis Curry, Summer Undergraduate Research Program.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Mechanisms and Genetic Regulation of Pulmonary Fibrosis", R01-HL28737-09.
B. Principal Investigator, "Macrophage Function in Lung Injury and Fibrosis", P01-HL31963, Section IV.
C. Principal Investigator, "Fibroblast Heterogeneity in Pulmonary Fibrosis", R01-HL39925.
D. Principal Investigator, "Crescentic Nephritis", P01-DK38149, Section IV.
E. Co-Investigator, "Hepatic Ischemia-Induced TNF and Multiorgan injury", RO1-DK42455, Principal Investigator, D.G. Remick.
F. Co-Investigator, "Lung Fibrosis," HL46487, Project 1.

PROJECTS UNDER STUDY:

A. Lung macrophage/monocyte, recruitment and activation during lung injury and fibrosis.
B. Cytokine regulation of fibroblast function - in terms of chemotaxis, collagen metabolism and proliferation in fibrotic lesions of lung, kidney and skin.
C. Isolation and characterization of lung fibroblast clones from normal and fibrotic lung to examine extent of and mechanistic basis for heterogeneity.
D. Regulation of mesangial cell proliferation and collagen gene expression by mediators from diseased renal tissue and cells.
E. Regulation of production of fibrogenic mediators and cytokines by pulmonary endothelial cells and fibroblasts; and keratinocytes.
F. Production of monocyte chemotactic factors by alveolar macrophages and fibroblasts and endothelial cells, and its regulation by bleomycin and cytokines.
G. Regulation of cytokine gene expression and signal transduction by fatty acids.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

A. Member, Medical Scientist Training Program Operating Committee.

REGIONAL AND NATIONAL:

A. Member, Lung Biology and Pathology Study Section, National Institutes of Health.
B. Reviewer for the following journals: American Review of Respiratory Diseases, American Journal of Pathology, Chest, Circulation Research, Experimental Lung Research, Journal of Clinical Investigation, Journal of Immunology.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Invited Seminar, "Mechanisms of fibrosis: Role of Cytokines", University of Tennessee, Memphis, Tennessee, August, 1991.
2. Invited Seminar, "Role of TGF-β in fibrosis", Graduate Hospital, University of Pennsylvania, Philadelphia, Pennsylvania, March, 1992.
3. Co-Chair for mini-symposium on "Lung Fibrosis and Cytokines", FASEB Annual Meeting, Anaheim, California, April, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Rolfe, M.W., Kunkel, S.L., Standiford, T.J., Chensue, S.W., Allen, R.M., Evanoff, H.L., Phan, S.H. and Strieter, R.M.: Pulmonary fibroblast expression of interleukin-8: A model for alveolar macrophage-derived cytokine networking. Am. J. Resp. Cell Molec. Biol. 1991;5:493-501.
2. Phan, S.H. and Kunkel, S.L.: Lung cytokine production in bleomycin-induced pulmonary fibrosis. Exp. Lung Res. 1992;18:29-43.
3. Breen, E., Shull, S., Burne, S., Absher, M., Kelley, J., Phan, S.H., Cutroneo, K.: Bleomycin regulation of TGF-β mRNA in rat lung fibroblasts. Am. J. Resp. Cell Molec. Biol. 1992;6:146-152.
4. Phan, S.H., Gannon, D.E., Ward, P.A. and Karmiol, S.: Mechanism of neutrophil-induced xanthine dehydrogenase to xanthine oxidase conversion in endothelial cells: Evidence of a role for elastase. Am. J. Resp. Cell Molec. Biol. 1992;6:270-278.
5. Brieland, J.K., Clarke, S.J., Karmiol, S., Phan, S.H. and Fantone, J.C.: Transferrin: A potential source of iron for oxygen free radical-mediated endothelial cell injury. Arch. Biochem. Biophys. 1992;294:265-270.
6. Noh, J.W., Wiggins, R. and Phan, S.H.: Urine transforming growth factor-β activity is related to the degree of scarring in crescentic nephritis in the rabbit. Nephron In Press, 1992.

7. Phan, S.H., Gharaee-Kermani, M., McGarry, B., Kunkel, S.L. and Wolber, F.W.: Regulation of endothelial cell transforming growth factor-β production by IL-1β and TNF-α. J. Immunol. In Press, 1992.

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

1. Noh, J.W., Wiggins, R.C. and Phan, S.H.: Transforming growth factor β (TGF-β) in urine predicts renal cortical scarring in rabbit anti-GMB disease. J. Am. Soc. Nephrol. 1991;2:556.
2. Phan, S.H., Wolber, F.W., and Wiggins, R.C.: Renal production of fibroblast chemotactic activity in rabbit crescentic nephritis. J. Am. Soc. Nephrol. 1991;2:557.
3. Karmiol, S. and Phan, S.H.: Fibroblasts and cytokines, in, Kunkel, S.L. and Remick, D.G. (eds.), Cytokines in Health and Disease, Marcel Dekker, New York, 1992; Chapter 16, pp 271-296.
4. Karmiol, S. and Phan, S.H.: Phenotypic changes in lung fibroblast populations in pulmonary fibrosis, in, Phipps, P. (ed.), Fibroblast heterogeneity in pulmonary fibrosis, CRC Press, Boca Raton, Florida, 1992; Chapter 1, pp 1-26.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Associate Director, Clinical Microbiology Laboratory.
B. Coordinator, Infectious Disease Laboratory Rounds.

II. TEACHING ACTIVITIES:

A. Coordinator, Pathology House Officer Microbiology Laboratory rotation.
B. Lecturer, Clinical Pathology Ground Rounds.
C. Lecturer, Microbiology 620.
D. Coordinator, Microbiology Laboratory Inservice.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. "National survey of the susceptibility of the *Bateroides fragilis* group", Merck, Sharp & Dohme and Beecham Laboratories.
B. "Prevention of antibiotic-associated colitis with *Saccharomyces boulardii* administration," Biocodex.
C. "In Vitro susceptibility of hospital isolates to meropenem", ICI Pharmaceutical.
D. "Fleroxacin Multi-Center *In Vitro* Study", Hoffmann-LaRoche.
E. "Temafloxacin *In Vitro* Study", Abbott Labs.
F. Evaluation of the *In Vitro* Susceptibility of Nosocomial Bacteria to Sparfloxacin, CI-960 and PD131628-2B, Parke-Davis Research Division.
G. Antibacterial Activity of Cefpirome against Clinical Isolates, Hoffmann LaRoche.
H. Candida Vaginosis Study, National Institute of Health.
I. Characterization of Beta-Lactamases produced by Antimicrobial Resistant *E coli* and *Klebsiella*, Merck, Sharp & Dohme.
J. Development of Resistance to Topical Mupirocin, Smith Kline Beecham.
K. EVS Endophthalmitis Vitrectomy Multi-Center Study.
L. Yellow Mercuric Oxide Ophthalmic Multi-Center Study, Del Pharmceuticals.

PROJECTS UNDER STUDY:

A. Detection of Verotoxin in Fecal Specimens.
B. Development of PCR Techniques for the Detection of Mycobacteria in Clinical Specimens.
C. Clinical Utility of Anaerobic Blood Cultures.
D. Clinical Utility of Treating Infected IV Catheters with Antimicrobics.
E. Clinical Significance of Altered Intestinal Flora.
F. Utility of Unit-Specific Susceptibility Profiles.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

A. Clinical Pathology Laboratory Director's Committee.
B. Junior Faculty Development Committee.
C. Clinical Microbiology Senior Staff Meeting (Chairperson).
D. Clinical Microbiology Inservice Program (Coordinator).

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL/NATIONAL:

A. Co-chair, TriCounty Clinical Microbiology Association.
B. Alternate, Technical Advisory Committee, Bureau of Laboratory and Epidemiological Services, Michigan Department of Public Health.
C. Coordinator, Clinical Microbiology Laboratory Directors of Michigan Group meetings.
D. Treasurer, Michigan Branch, American Society for Microbiology.
E. Board member, South Central Association for Clinical Microbiology.
F. Member of CAP Site Visit Teams.
   1. Shands Hospital, Gainsville, Florida.
   2. ARUP, Salt Lake City, Utah.

V. OTHER RELEVANT ACTIVITIES:

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

INVITED LECTURES/SEMINARS:

1. "New Enteric Pathogens" - Albion Hospital, Albion, Michigan.

IV. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Brothers, T.E., Wakefield, T.W., Schaberg, D.R., Pierson, C.L., Graham, L.M. and Stanley, J.C.: Effect of controlled hemorrhage on tissue and serum cefazolin clearance. J. Surg. Res. 1991;51;223-228.
2. Pierson, C.L. and Friedman, B.A.: Comparison of susceptibility to B-Lactam antimicrobial agents among bacteria isolated from intensive care units. Diagn. Microbiol. Infect. Dis. 1992; 15:19s-30s.
3. Cuchural, G.J., Jr., Snydman, D.R., Iannini, P.B. O'Keefe, J.P., Pierson, C.L., Rihs, J.D. and Finegold, S.M.: Antimicrobial susceptibility patterns of the *Bacteroides fragilis* group in the United States, 1989. Clinical Therapeutics 1992;14:122-136.

4. Cornick, M.A., Cuchural, G.J., Snydman, D.R., Iannini, P.B., Hill, G., Pierson, C.L. and Finegold, S.M.: Comparison of newer antimicrobial agents against the *Bacteroides fragilis* group. J. Antimicrob. Chemother. In Press, 1992.
5. Zervos, M. and Pierson, C.L.: Molecular typing of ampicillin-resistant non-B-lactamase-producing *Enterococcus faecium* from diverse geographic areas. Clin. Microbiol. In Press, 1992.
6. Reed, B.D. and Pierson, C.L.: Evaluation of a latex agglutination test for the identification of *Candida* species in vaginal discharge. J. Amer. Board Famiily Practice In Press, 1992.

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

1. Pierson, C.L. and McClatchey, K.D.: Automation, in. Encyclopedia of Microbiology 1992, Academic Press, Inc., San Diego, California, In Press.
2. Blythe, L., Hankerd, R. and Pierson, C.L.: Investigation of the pathogenicity of *Ureaplasma urealyticum* in placental membranes and amniotic fluids, Abstracts: Amer. Assoc. Clin. Microbiol. 1992; page 160.
3. Bartkowiak, D. and Pierson, C.L.: Comparison of the Primier Toxin A kit with cytotoxin B and culture for the detection of *Clostridium difficile* toxins in fecal specimens, Abstract, Amer. Assoc. Microbio. 1992; page 473.
4. Goldstein, S., Chenoweth, C., Pierson, C.L. and Bradley, S.: *Achromobacter xylosoxidans* bacteremia: Retrospecive review of the literature, Abstracts, Amer. College Physicians 1992.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Director of Autopsy Service.
B. Supervision of Autopsies (2.5 months).
C. Coordinator of Senior Staff Autopsy Call Schedule.

II. TEACHING ACTIVITIES:

A. Coordinator - Biweekly Pathology Gross Conference.
B. Lectures to Pathology House Officers in Anatomic and Clinical Pathology.
C. Morbidity and Mortality Conference.
D. Lecturer, Pathology 600 Course.
E. Mentor - Fourth Year Medical Student Clerkship - one month rotations.
F. Directed research of three postdoctoral fellows, one Visiting Scholar, two house officers (one in Pathology, one in Anesthesiology), one medical student and two undergraduate students.

III. RESEARCH ACTIVITIES:

A. Regulation of gene expression of soluble mediators of inflammation using the following models:
   1. Endotoxin-stimulated human whole blood.
   2. Endotoxin injection in mice.
   3. Cecal ligation and puncture.
B. Toxic effects of immunomodulators.
C. Pathophysiology of septic shock.
D. Quantitation of mediators in septic shock.
E. Cloning, sequencing, and expressing cytokines including mTNF, hTNF, mIL-6, hIL-8, MCP, JE.
F. Mechanisms of organ injury induced by hepatic ischemia/reperfusion.
G. Mechanisms of nosocomial pneumonia, and asociation with IL-8.
H. Directed research of Allan Olson, M.D. (Department of Pediatrics), Jorge Rodriguez, M.D. (Department of Surgery); House officers - Eric Hsi, M.D., Kyle Carr, M.D. (Pathology), and Anna Penna, M.D. (Anesthiology), Eiji Takeuchi, M.D., Visiting Scholar, Postdoctoral fellows - Laura DeForge, Ph.D., Gordon Wollenberg, D.V.M., Ph.D., Undergraduate students - Carolyn Shumas, Tony Cardillo, Connie Ngiu

SPONSORED SUPPORT:

A. Principal Investigator, "The Role of Cytokines in Sepsis and Trauma", five years, $906,182, 1990-1995.
B. Principal Investigator, Long-Term Minority Supplement for Jorge Rodriguez, M.D., 1991-1995, $200,000

C. Principal Investigator, "Cytokine Measurement in Whole Blood", Pfizer Co., one year, $50,000, 1991-1992.
D. Principal Investigator, "Hepatic Ischemia-Induced TNF and Multi-organ Injury", National Institutes of Health, four years, $924,643.
E. Principal Investigator, "Measurement of Cytokines in Sepsis Syndrome, Contracts, Cutter Biological, one year, $183,000, 1991-1992.
F. Co-Investigator, "Monokine Gene Expression/Regulation in Lung Injury", National Institutes of Health, five years, 1990-1995.
G. Co-Investigator on Core II of Program Project, "Inflammatory Cells and Lung Injury", National Institutes of Health - five years, $48,595, 1984-1994.
H. Co-Investigator, "Mechanisms of Pulmonary Fibrosis", National Institutes of Health, five years, $215,000.
I. Co-Investigator, "Myocardial Preconditioning in Conscious Dogs and Pigs", National Institutes of Health, three years, $131,792, 1990-1994.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director - Autopsy Service.
B. Member, Faculty Retreat Planning Committee, 1992.
C. Interviewer - Candidates for faculty, house officer, postdoctoral, and graduate student positions

MEDICAL SCHOOL/HOSPITAL:

A. Member, Medical School Admissions Committee.
B. Member, Michigan Cancer Center.
C. Reviewer, Biomedical Research Council grants.
D. Reviewer, Department of Surgery grants.
E. Coordinator - University of Michigan Hospital Medical Examiner On-Call.

REGIONAL AND NATIONAL:

A. Co-Chair, Michigan Department of Public Health Postmortem Examination Workgroup.
B. Member, Executive Committee, Dementia Subcommittee.
C. Member, Dementia Subcommittee, Chronic Disease Advisory Committee to the Michigan Department of Public Health.
D. Deputy Medical Examiner for Washtenaw County
E. Member, Legislative Committee, Michigan Association of Medical Examiners.
F. Member, Michigan Association of Medical Examiners, Shock Society, American Association of Immunologists, Adam James French Society, American Association of Pathologists, United States-Canadian Academy of Pathology.
G. Reviewer, NIH Teleconferences (two), 1991-1992.
H. Reviewer, National Science Foundation grants.
I. Reviewer, Veterans Administration Merit grants.
J. Reviewer, American Review of Respiratory Diseases, Laboratory Investigation, Journal of Immunology, American Journal of Applied Physiology, Journal Immunopharmacology, Journal Leukocyte Biology, American Journal of Pathology, British Journal of Pharmacology, Biochemica, Biophysica Acta, Journal of Clinical Investigations, Infection and Immunity.

INVITED LECTURES/SEMINARS:

1.. Invited Speaker, Workshop on Cytokine and Growth Factor Pathology, Basel, Switzerland, August, 1991
2. Invited Speaker, Immunopathology Series, American Society of Clinical Pathologists, New Orleans, September, 1991
3. Invited Participant, Cutter Anti-TNF Clinical Investigators Meeting, San Francisco, California, November, 1991
4. Invited Speaker, 3M Company, St. Paul, Minneapolis, March, 1992
5.. Invited Speaker, Wound Healing Society, Richmond, Virginia, April 1992
6. Invited Lecturer, House Officer Orientation, The University of Michigan, June, 1992

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Remick, D.G.: Significance of *in vivo* detection of tumor necrosis factor. Lab. Invest. (Editorial) 1991;65:259-261.
2. Kunkel, S.L., Strieter, R.M. Chensue, S.W., Campbell, D.A. Jr. and Remick, D.G.: The role of TNF in diverse pathologic processes. Biotherapy. 1991;3:135-141.
3. Van Zee, K.J., DeForge, L.E., Fischer, E., Marano, M.A., Kenney, J.S., Remick, D.G., Lowry, S.F. and Moldawer, L.: IL-8 in septic shock, endotoxemia, and after IL-1 administration. J. Immunol. 1991;146:3478-3482.
4. Ulich, T.R., Yin, S., Guo, K., Yi, E.S., Remick, D.G. and del Castillo, J.: Intratracheal injection of endotoxin and cytokines. II. Interleukin-6 and transforming growth factor beta inhibit acute inflammation. Am. J. Pathol. 1991;138:1097-1101.
5. Martin, L.F., Vary, T.C., Davis, P.K., Munger, B.L., Lynch, J.C., Spangler, S. and Remick, D.G.: Intravascular plastic catheters. How they potentiate tumor necrosis factor release and exacerbate complications associated with sepsis. Arch. Surg. 1991;126:1087-1093.
6. Guice, K.S., Oldham, K.T., Remick, D.G., Kunkel, S.L. and Ward, P.A.: Anti-tumor necrosis factor antibody augments edema formation in caerulin-induced acute pancreatitis. J. Surg. Res. 1991;51:495-499.
7. DeForge, L.E., Tracey, D.E., Kenney, J.S. and Remick, D.G.: Interleukin-1 receptor antagonist protein inhibits interleukin-8 expression in lipopolysaccharide-stimulated human whole blood. Am. J. Pathol. 1992;140:1045-1054.
8. DeForge, L.E., Kenney, J.S., Jones, M.L., Warren, J.S. and Remick, D.G.: Biphasic production of IL-8 in lipopolysaccharide (LPS)-stimulated human whole blood. Separation of LPS- and cytokine-stimulated components using anti-tumor necrosis factor and anti-IL-1 antibodies. J. Immunol. 1992;148:2133-2141.
9. Eskandari, M.K., Bolgos, G., Miller, C., Nguyen, D.T., DeForge, L.E. and Remick, D.G.: Anti-tumor necrosis factor antibody therapy fails to prevent lethality after cecal ligation and puncture or endotoxemia. J. Immunol. 1992;148:2724-2730.
10. Fischer E., Marano, M.A., Van Zee, K.J., Rock, C.S., Hawes, A.S., Thompson, W.A., DeForge, L., Kenney, J.S., Remick, D.G., Bloedow, D.C., Thompson, R.C., Lowry, S.F. and Moldawer, L.L.: Interleukin-1 receptor blockade improves survival and hemodynamic performance in *E. coli* septic shock, but fails to alter host responses to sublethal endotoxemia. J. Clin. Invest. 1992;89:1551-1557.
11. Friedland, J.S., Suputtamongkol, Y., Remick, D.G., Chaowagul, W., Strieter, R.M., Kunkel, S.L., White, N.J. and Griffin, G.E.: Prolonged elevation of interleukin-8 and interleukin-6 concentrations in plasma and of leukocyte interleukin-8 mRNA levels during septicemic and localized *Pseudomonas pseudomallei* infection. Infect. Immun. 1992;60:2402-2408.

12. Lin, H., Chensue, S.W., Strieter, R.M., Remick, D.G., Gallagher, K.P., Bolling, S.F. and Kunkel, S.L.: Antibodies against tumor necrosis factor prolong cardiac allograft survival in the rat. J. Heart Lung Transplant 1992;11:330-335.
13. Negussie, Y., Remick, D.G., DeForge, L.E., Kunkel, S.L., Eynon, A. and Griffin, G.E.: Detection of plasma tumor necrosis factor, interleukins 6, and 8 during the Jarisch-Herxheimer Reaction of relapsing fever. J. Exp. Med. 1992;175:1207-1212.
14. Sharma, R.J., Macallan, D.C., Sedgwick, P., Remick, D.G. and Griffin, G.E.: Kinetics of endotoxin-induced acute-phase protein gene expression and its modulation by TNF-alpha monoclonal antibody. Am. J. Physiol. 1992;262:R786-R793.
15. Remick, D.G., DeForge, L.E., Sullivan, J.F. and Showell, H.J.: Profile of cytokines in synovial fluid specimens from patients with arthritis. Immunol. Invest. 1992;321-327.

BOOKS/CHAPTERS IN BOOKS:

1. Editor, Cytokines in Health and Disease, Marcel Dekker Publishers, 1992.

ABSTRACTS

1. Friedland, J.S., Shattock, R., Remick, D.G. and Griffin, G.E.: Generation of mRNA for and secretion of IL-8 (neutrophil-activating peptide) after phagocytosis of *Mycobacterium tuberculosis* by human monocyte cell lines and the effect of HIV infection. 28th Annual Meeting of Society for Leukocyte Biology, 21st Leukocyte Culture Conference, 1991.
2. Remick, D.G., Kenney, J., Warren, J., Jones, M. and DeForge, L.: TNF and IL-1 account for the biphasic pattern of IL-8 production in LPS-stimulated human whole blood, Third International Congress on Cytokines, Stresa, Italy, 1991.
3. Friedland, J.S., Ho, M., Remick, D.G., Bunnag, D., White, N.J. and Griffin, G.E.: Interleukin-8 and Malaria, Third International Congress on Cytokines, Stresa, Italy, 1991.
4. Friedland, J.S., Supputtamongkol, Y., Remick, D.G., Chaowagul, W., Strieter, R.M., Kunkel, S.L., White, N.J. and Griffin, G.E.: Plasma interleukin-6, interleukin-8, and mortality in systemic and localized gram negative infection, Third International Congress on Cytokines, Stresa, Italy, 1991.
5. McCurry, K.R., Remick, D.G. and Campbell, D.A., Jr.: The role of TNF in hepatic ischemia/reperfusion injury, The Society of University Surgeons, 1991.
6. Hsi, E. and Remick, D.G.: Rapid determination of cell-associated tumor necrosis factor (TNF) by flow cytometry. United States and Canadian Academy of Pathology, 1992.
7. Remick, D.G., Negussie, Y., DeForge, L.E., Bolgos, G., Eyon, A. and Griffin, G.E.: Cytokines, pentoxifylline (PTX), and the Jarisch-Herxheimer Reaction (J-HR). United States and Canadian Academy of Pathology, 1992.
8. Carr, K.A., Ohl, D.A., Denil, J., Seager, S.W.J. and Remick, D.G.: Histopathology of implanted alloplastic spermatoceles in dogs. United States and Canadian Academy of Pathology, 1992.
9. Malak, R.A., DeForge, L.E., Tracey, D.E., Kenney, J.S. and Remick, D.G.: Interleukin-1 receptor antagonist protein (IRAP) inhibits interleukin-8 production. FASEB, 1992.
10. Remick, D.G., Nguyen, D.T., Hsi, E.D., DelBuono, E.A. and DeForge, L.E.: Cyclosporin A (CsA) inhibits release of biologically active tumor necrosis factor (TNF) from the surface of macrophages. FASEB, 1992.
11. DeForge, L.E., Bolgos, G., Fantone, J.C. and Remick, D.G.: Dimethyl sulfoxide (DMSO) inhibits interleukin-8 (IL-8) production in lipopolysaccharide (LSP)-stimulated human whole blood. FASEB, 1992.
12. Howatt, M.E., Remick, D.G., Scales, W.E. and Campbell, D.A., Jr.: Tissue associated TNF following hepatic ischemia. FASEB, 1992.
13 Takeuchi, E., Howatt, M.E., DeForge, L.E., Campbell, D.A., Jr. and Remick, D.G.: Pretreatment with TNF fails to prevent organ injury after hepatic ischemia/reperfusion (I/R). FASEB, 1992.
14. Bolgos, G., DeForge, L.E., Malak, T.A., Nguyen, D.T. and Remick, D.G.: Relative glucocorticoid potency of inhibition of cytokine synthesis. FASEB, 1992.

15. Nguyen, D.T., DeForge, L.E., Malak, T.A. and Remick, D.G.: PGE_2 suppression of TNF, IL-1, IL-6, and IL-8 in LPS-stimulated THP-1 cells. FASEB, 1992.
16. McCurry, K.R., Campbell, D.A., Jr., Tracey, D.E., Howatt, M.A. and Remick, D.G.: Interleukin-1 receptor antagonist protein (IRAP) does not prevent hepatic ischemia/reperfusion induced injury. FASEB, 1992.
17. DelBuono, E.A., DeForge, L.E., Nguyen, D.T., Bolgos, G. and Remick, D.G.: Cyclosporin A (CsA) modulation of cytokines an *ex vivo* model of human whole blood. FASEB, 1992.
18. Colletti, L., Remick, D.G., Kunkel, S. and Campbell, D.: Lipopolysaccharide (LPS) pretreatment *in vivo* decreases subsequent lung injury associated with hepatic ischemia/reperfusion. FASEB, 1992.
19. Atluru, D., Hansen, J., Remick, D.G. and Keane, W.F.: Cyclosporin A and genistein: *In vitro* effects on IL-6 and IL-8 synthesis from human mononuclear cells. FASEB, 1992.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

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

IV. ADMINISTRATIVE ACTIVITIES

DEPARTMENTAL

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

REGIONAL/NATIONAL:

Member, Southwest Oncology Group Lymphoma Review Panel.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Seminar, Surgical Pathology of the Spleen, American Society of Clinical Pathologists, National Meeting, Boston, Massachusetts, April 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hanson, C.A., Ross, C.W. and Schnitzer, B.: Anti-CD34 immunoperoxidase staining in paraffin sections of acute leukemia: comparison with flow cytometric immunophenotyping. Human Pathol. 1992;23:26-32.
2. Ross, C.W., Hanson, C.A. and Schnitzer, B.: CD30 (Ki-1)-positive, large cell lymphoma mimicking gastrointestinal carcinoma. Cancer, In Press.
3. Ross, C.W., Schlegelmilch, J.A., Grogan, T.M., Weiss, L.M., Schnitzer, B. and Hanson, C.A.: Detection of Epstein-Barr virus genome in Ki-1 (CD30)-positive, large cell anaplastic lymphomas using the polymerase chain reaction. Am. J. Pathol., In Press.
4. Perkins, P.L., Ross, C.W. and Schnitzer, B.: CD30-positive, anaplastic large cell lymphomas that express CD15 but lack CD45: a possible diagnostic pitfall. Arch. Pathol. Lab. Med., In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. Hanson, C.A., Abaza, M., Sheldon, S., Ross, C.W., Schnitzer, B. and Stoolman, L.M.: Acute biphenotypic leukemia: Immunophenotypic and cytogenetic analysis.
2. Hansen, E.R., Vejlsgaard, G.L., Cooper, K.D., Heidenheim, M., Larsen, J.L., Ho, V.C., Ross, C.W., Fox, D.A., Thomsen, K. and Baadsgaard, O.: Leukemic T-cells from patients with Sezary syndrome demonstrate enhanced activation through CDw60, CD2, and CD28 relative to activation through the T-cell antigen receptor complex.

BOOKS AND CHAPTERS IN BOOKS:

1. Hanson, C.A. and Ross, C.W.: Clinical applications of molecular biology: Hematopoietic disorders, in, McClatchey, K.D. (ed.), Clinical Laboratory Medicine, Williams & Wilkins, Baltimore, Maryland, In Press.

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

1. Ross, C.W., Hanson, C.A., Schnitzer, B. and Sheldon, S.: Chronic myeloid neoplasia associated with eosinophilia and abnormalities of chromosome 12p. Lab. Invest. 1992;66:86A.
2. Hanson, C.A., Ross, C.W., Abaza, M. and Schlegelmilch, J.A.: CD45 expression in acute leukemias and chronic lymphoproliferative disorders. Lab. Invest. 1992;66:78A.
3. Abaza, M., Ross, C.W., Sheldon, S., Stoolman, L.M., Schlegelmilch, J.A., Schnitzer, B. and Hanson, C.A.: CD7-positive acute leukemias: morphology, immunophenotype, and cytogenetics. Lab. Invest. 1992;66:73A.

NATHANIEL H. ROWE, D.D.S., M.S.D.
PROFESSOR OF PATHOLOGY, DENTISTRY
DEPARTMENT OF PATHOLOGY

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

INTRADEPARTMENTAL:

A. Oral Pathology Biopsy Service Rotation, School of Dentistry.
B. Dental Faculty Associates, School of Dentistry.

INTERDEPARTMENTAL:

A. Oral Pathology, clinical consultations on an as needed basis, The University of Michigan School of Dentistry Clinics.
B. Consultant to Veterans Administration Hospital, Ann Arbor.

II. TEACHING ACTIVITIES:

FALL TERM, 1991:

A. Oral Pathology, Course 516, to Freshmen Dental Students (course director).
B. Oral Pathology, Course 824, to Senior Dental Students.
C. Graduate Oral Pathology Seminar in Periodontics, Course 781 (course director).
D. Graduate Oral Pathology, Course 694.
E. Dental Hygiene, Course 220, to Freshmen Students.

WINTER TERM, 1992:

F. Oral Pathology Course 624, to Sophomore Dental Students.
G. Oral Pathology Laboratory, Course 625, to Sophomore Dental Students.
H. Dental Hygiene, Course 313, to Junior Students
I. Graduate Oral Pathology Core Laboratory, Course 695.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Project Director, "Oral Zovirax for the Treatment of Recurrent HSV Labialis", 3% Effort, Burroughs Wellcome Company, 09/01/89 - 08/31/91, Total Direct Costs: $56,700.00.
B. Project Director, "Determination of the Feasibility and Economy of Central Coordination of the Collection and Disposal of Medical Waste", 10% Effort, A cooperative effort: Cosponsored by Delta Dental Plan of Michigan/Michigan Department of Public Health/Michigan Dental Association/the University of Michigan, 06/91 - 07/93, Total Direct Costs: $82,192.00.

UNDER CURRENT NEGOTIATION:

A. "Oral Famciclovir in the Treatment of Experimentally Induced Herpes Simplex Labialis: A Double-Blind, Dose-Ranging, Placebo-Controlled, Multi-Center Trial", Director. 5% Effort. SmithKline Beecham Pharmaceuticals Co., 07/01/92- 06/30/94, Amount approximately $ 90,000.00 Direct Costs.

IV. ADMINISTRATIVE ACTIVITIES:

SCHOOL OF DENTISTRY COMMITTEES:

A. Infection Control Committee, School of Dentistry.
B. Hazardous Chemical Committee, School of Dentistry.

REGIONAL AND NATIONAL:

STATE OF MICHIGAN

A. Member, Council of Michigan Dental Specialty Presidents.
B. Member, Specialty Ad Hoc Committee, Michigan Board of Dentistry.
C. Member, State of Michigan Dental Specialty Task Force.
D. President, Michigan Society of Oral Pathology.
E. Member, AIDS Speaker's Bureau, Michigan State Medical Society.
F. Member, Advisory Committee, Special Office on AIDS Prevention and the Disease Surveillance Section, Michigan Department of Public Health.
G. Member, Tobacco-Free Michigan Action Coalition, Michigan Department of Public Health.
H. Member, Executive Committee, American Cancer Society, Michigan Division.
I. Member, Board of Directors, American Cancer Society , Michigan Division.
J. Area Delegate Director, American Cancer Society, Michigan Division.
K. Member, Public Issues Committee, American Cancer Society, Michigan Division.
L. Member, By-Laws Revision Committee, American Cancer Society, Michigan Division.
M. Member, Professional Education Committee, American Cancer Society, Michigan Division.
N. Consultant, Committee on Cancer and Infection Control, Michigan Dental Association.
O. Member, Special Committee on Health and Hazard Regulation, Michigan Dental Association.
P. Member, Research Screening Committee, Delta Dental Fund.
Q. Member, Michigan Coalition on Smoking or Health.
R. Member, Coalition for Access to Health Care.

HONORS AND AWARDS:

1992 Michigan Dental Association's Public Service Award.

NATIONAL:

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

INTERNATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

A. Clinical and Patient Care.

1. Intradepartmental
   a. Oral Pathology Service Clinic, University Hospitals, Department of Dentistry and Oral Surgery.
   b. Dental Faculty Associates, School of Dentistry.
   c. Oral Pathology Biopsy Service Rotation.

2. Interdepartmental
   a. Oral Pathology, clinical consultations on an as needed basis, The University of Michigan Medical School of Dentistry Clinics.
   b. Consultant, Veterans Administration Hospital, Ann Arbor.

B. Continuing Education

1. University
   a. Continuing Education Course presented through the University of Michigan Dental School, "Testing for and recognition of diseases in the prosthodontic patient" November 14, 1991.
   b. Continuing Education Course presented through the University of Michigan Dental School, "The effect of tobacco usage and oral diseases", June 10, 1992.

EDITORIAL BOARDS:

A. Journal of the American Medical Association.
B. Journal of Oral Pathology.
C. Journal of the American Dental Association.
D. Cancer.
E. Journal of the Academy of General Dentistry.

INVITED LECTURES/SEMINARS:

1. "Sources of Infection in the Dental Office", Michigan State University, East Lansing, July 17, 1991.
2. "Infection in the Immunocompromised", Veteran's Hospital, Ann Arbor, July 31, 1991.
3. Arcan Associates: Trident Seminar (Alaska), "Strategy for Successful Practice During the Coming Decade", August 24-September 1, 1991.
4. Washtenaw District Dental Assistants Society, "Records on Intraoral Lesions", Michigan League, September 10, 1991.
5. Washtenaw District Dental Society, "Everything You Wanted To Know About AIDS and More", September 16, 1991.
6. Jackson Dental Society, "Current Topics in Oral Pathology", October 9, 1991.
7. William Wolfe Cancer Education Program, University of Louisville, Kentucky, Nov. 14, 1991.
8. Ann Arbor Civic Club, "AIDS", Michigan League, December 11, 1991.
9. "In-Office Infection Control Investigation", Jackson, December 13, 1991.
10. "AIDS", Saline Kiwanis, Saline Hospital, January 6, 1992.

11. "OSHA: Regulations and Compliance", Progressive Dental Study Club, Brighton, January 16, 1992.
12. "Infections", Continuing Dental Education, Dental Hygienists, Michigan State University Kellogg Center, Lansing, February 28, 1992.
13. Fort Sam Houston Prosthodontic Residency Program, Department of the Artmy, "Diagnosis, Treatment and Prevention of Oral Disease", Texas, March 26-27, 1992.
14. Michigan Dental Association Annual Session, "Herpes, Hepatitis, and AIDS Revisited" (A.M. Session); "Diagnosis and the Treatment or Prevention of Noninfectious Oral Health Problems" (P.M. Session), Detroit, April 3, 1992.
15. Livingston County Dental Association, "Clinical Oral Pathology", April 8, 1992.
16. "Infectious Diseases in the Dental Setting", Michigan Department of Corrections (MDOC) Dental Personnel, Lansing Community College, May 7, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Rowe, N.H.: Smokeless Tobacco, Oral Cancer and the Law. J. Mich. Dent. Assoc. 1991;73(8):44-47.
2. Rowe, N.H.: Control of Infection in Dental Practice. J. Mich. Dent. Assoc. 1991;73(9):22-23.
3. Rowe, N.H.: Glove Use In Dentistry. Part I: Preventing Glove Damage to Hands. J. Mich. Dent. Assoc. 1990;72(3):147. Reprinted in the Florida Dental Journal, 1991. Reprinted in the Pennsylvania Dental Journal, 1991.

BOOKS AND CHAPTERS IN BOOKS:

1. Rowe, N.H.: Jaw, Neuroectodermal Pigmented Tumor, in, Birth Defects Encyclopedia. #711.
2. Rowe, N.H.: Dental Caries (Revision), Chapter 17, in, Regezi, J.A. and Sciubba, J.J. (eds.), Oral Pathology, 2nd edition, W.B. Saunders Company, Philadelphia, In Press.

VII. MISCELLANEOUS:

1. Professional Meetings Attended
   A. MiOSHA Heraing, Michigan Department of Public Health, Lansing, August 15, 1992.
   B. M.D.A. Annual Session, Grand Rapids, Michigan, April, 1991.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

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

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Southwest Oncology Group (SWOG). Combination chemotherapy of unfavorable histology non-Hodgkin's lymphomas with CHOPP and CBV, with Dr. L. Dabich.
B. Southwest Oncology Group (SWOG). Combination chemotherapy of unfavorable histology non-Hodgkin's lymphomas with alternating regimens of CHOPP and CVB, with Dr. L. Dabich.
C. Pathology Coordinator, SWOG studies numbers 8515 and 8516.

SERVICE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITALS:

A. Hematology Laboratory.
B. University of Michigan Health Service Laboratories.

REGIONAL AND NATIONAL:

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARD:

A. Human Pathology. Designated reviewer.
B. Hematologic Pathology . Designated reviewer.
C. Arch. Pathol. Lab Med. Designated reviewer

INVITED LECTURES/SEMINARS:

1. "Hodgkin's Disease: Diagnosis and Differential Diagnosis", ASCP Workshop. New Orleans, Louisiana, October 1991.
2. A Practical Approach to the Diagnosis and Differential Diagnosis of Extranodal Lymphomas. ASCP Workshop, October, 1991, New Orleans, Louisiana.
3. "A Practical Approach to Diagnostic Hematological Problems", ASCP Educational Course. Lectures given included: a) Non-Hodgkin's Lymphomas; b) Hodgkin's Disease; c) A Practical Approach to the Diagnosis and Classification of Lymphomas and Leukemias by Flow Cytometry, and Electron Microscopy; d) Extranodal lymphomas; and e) Immunologic Classification of Acute Lymphoblastic Leukemias. Atlantic City, New Jersey, November, 1991.
4. Panelist, Oncodiagnosis Panel. Non-Hodgkin's Lymphomas. Plenary Session, Radiological Society of North America. December, 1991, Chicago, Illinois.
5. The Application of Modern Techniques in the Diagnosis and and Differential Diagnosis of Malignant Lymphomas: Michigan Tumor Registrars Association Annual Meeting, Midland, Michigan, May, 1992.
6. "Surgical Pathology of the Spleen. Diagnosis and Differential Diagnosis," ASCP Workshop, April, 1992, Boston, Massachusetts.

7. Hodgkin's Disease. Diagnosis and Differential Diagnosis, ASCP Workshop, April, 1992, Boston, Massachusetts.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Grossman, D.M., Hanson, C.A. and Schnitzer, B.: Simultaneous lymphocyte predominant Hodgkin's disease and large cell lymphoma. Am. J. Surg. Pathol. 1991;15:668-676.
2. Wolter, J.R., Schnitzer, B. and Wieringa, A.: Ectopic hematopoiesis in the human iris. Int. Ophthalmol. 1991;15:267.
3. Hanson, C.A., Bockenstedt, P.L., Schnitzer, B., Fox, D.A., Kueck, B. and Braun, D.K.: S-100 positive, T-cell chronic lympho-proliferative disease: An aggressive disorder of an unknown T-cell subset. Blood 1991;78:1803-1813.
4. Shah, A.R., Maeda, K., Deegan, M.J., Roth, M.A. and Schnitzer, B.: A clinicopathologic study of familial chronic lymphocytic leukemia. Am. J. Clin. Pathol. 1992;97:184-188.
5. Hanson, C.A., Ross, C.W. and Schnitzer, B.: Anti-CD34 immunoperoxidase staining in paraffin sections of acute leukemia: Comparison with flow cytometric immunophenotyping. Human Pathol. 1992;23:26-32.
6. Bittencourt, A.L., Mendonca, N., De Freitas, L.A.R. and Schnitzer, B.: Ki-1 large cell lymphoma with regressing lesions in a child. Pediat. Dermatol. 1992;9:117-122.

BOOKS AND CHAPTERS IN BOOKS:

1. Schnitzer, B.: Benign lymphoproliferative disorders, in Knowles, D.M. (ed), Neoplastic Hematopathology, Williams-Wilkins Company, 1992.
2. Schnitzer, B.: Reactive lymphoid hyperplasia, in, Jaffe E.S. (ed), Surgical Pathology of the Lymph Nodes and Related Organs, 2nd Edition, W.B. Saunders Co., In Press.

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

1. Ross, C., Hanson, C., Schnitzer, B. and Sheldon, S.: Chronic myeloid neoplasia associated with eosinophilia and abnormalities of chromosome 12p. Lab. Invest. 199266:86A, 1992; Modern Pathol. 1992;5:73A.
2. Abaza, M.A., Ross, C.W., Sheldon, S., Stoolman, L.M., Schlegelmilch, J.A., Schnitzer, B. and Hanson, C.A.: CD7-positive acute leukemias: Morphology, immunophenotype (IPH) and cytogenetics. Lab. Invest. 1992;66:73A, 1992; Modern Pathol. 1992;5:86A.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Cytopathology - 26 weeks.
B. Gynecologic Pathology (transfer cases) - 12 months.
C. Consultation service, Department of Pathology: Cytopathology and Gynecologic Pathology - 12 months.
D. Necropsy Service - One week.
E. M-Labs Surgical Pathology Service (Gyn) - As needed.

II. TEACHING ACTIVITIES:

A. Medical Students:
   1. Pathology 600 laboratory instructor, January-April.
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-OB/Gyn Pathology- one hour.
   5. One-month electives in Ob/Gyn Pathology (Cynthia Hegg, M.D., Denise Sulavik, M.D.).
   6. Instruction in Ob/Gyn Pathology and Cytopathology (Hope Haefner, M.D., Fellow, Dept. Ob/Gyn; Ralph Lelle, M.D., Fellow, Gynecologic Oncology Division.
C. Other Education Activities:
   1. Cytotechnologists-Cytopathology conferences - 3/year.
   2. Gynecologic Oncology Tumor Board Conference-weekly.
   3. Ob/Gyn Colposcopy/Pathology Conference-bi monthly.
   4. Coordinator, Histotechnologist/Cytotechnologist Conference-monthly.

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

A. Computer Applications to Cytology.
B. Cytologic Analysis of endocervical gland involvement by squamous cell carcinoma in-situ versus adenocarcinoma in-situ on cervical smears obtained with a cytobrush.
C. Cytologic features of cystic ovarian lesions.
D. Neovagina cytology following total pelvic exeneration for gynecologic malignancies.
E. The clinical significance of the degree of cellular atypia in endometrial hyperplasias (in conjunction with Dr. Hope Haefner, fellow, Dept. of Obstetrics/Gynecology).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Co-Director, Cytopathology Laboratory.

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Reviewer, Diagnostic Cytopathology.
B. Member, Cytopathology Committee, College of American Pathologists.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Cytologic features of squamous cell carcinoma in-situ involving endocervical glands in endocervical cytobrush specimens. Platform, Annual Scientific Meeting of the American Society of Cytology, Los Angeles, California, November, 1991.
2. Cytologic Diagnosis of Cystic Ovarian Lesions. Poster, Annual Scientific Meeting of the American Society of Cytology, Los Angeles, California, November, 1991.
3. Fine Needle Aspiration Cytology of Cystic Ovarian Lesions. Guest Speaker; School of Cytotechnology, Henry Ford Hospital, Detroit, Michigan, December 12, 1991.
4. The PAP Smear in 1992. Guest Speaker; Sixteenth Annual Spring Review Course: Family Practice 1992; Sponsored by The University of Michigan Medical School, Department of Family Practice and the Michigan Academy of Family Physicians. Ann Arbor, Michigan, March 17-21, 1992.
5. Cervical Cytology. Guest speaker; Grand Rounds, Department of Obstetrics and Gynecology; University of Michigan, Ann Arbor, Michigan, May 7, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFERRED JOURNALS:

1. Selvaggi, S.M. and Malviya, V.: Efficacy of the modified Ayre spatula/Zelsmyr Cytobrush versus the modified Ayre spatula/bulb aspirator in the collection of cells from the uterine cervix. Diagn. Cytopathol. 1991;7:318-322.
2. Jacques, S.M. and Selvaggi, S.M.: Multiple peritoneal cytologies collected during laparotomy for gynecologic malignancy. Diagn. Cytopathol. 7:482-486, 1991.
3. Wojcik, E.M., Selvaggi, S.M.: Comparison of smears and cell blocks in the fine needle aspiration diagnosis of recurrent gynecologic malignancies. Acta Cytol. 1991;35:773-776.
4. Wojcik, E.M. and Selvaggi, S.M.: Factors influencing fine needle aspiration cytology in the management of recurrent gynecologic malignancies. Gynecol.Oncol., In Press.
5. Selvaggi, S.M.: Cytologic features of malignant ovarian monodermal teratoma with an ependymal component in pelvic washings. Int. J. Gynecol.Pathol., In Press.

6. Wojcik, E.M. and Selvaggi, S.M.: Diagnostic accuracy of fine needle aspiration cytology in persistent or recurrent gynecologic malignancies. Diagn. Cytopathol., In Press.
7. Selvaggi, S.M.: Bronchoalveolar lavage in lung transplant patients. Acta. Cytol., In Press.
8. Selvaggi, S.M.: Cytologic features of squamous cell carcinoma-in-situ involving endocervical glands in endocervical cytobrush specimens. Acta. Cytol., In Press.

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

1. Selvaggi, S.M.: Cytologic features of squamous cell carcinoma in-situ involving endocervical glands in endocervical cytobrush specimens. Acta. Cytol. 1991;35:591.
2. Wojcik, E.M. and Selvaggi, S.M.: Cytologic diagnosis of cystic ovarian lesions. Acta Cytol. 1991;35:642-643.
3. Book Review: Comprehensive Cytopathology, Bibbo, M. (ed), W.B. Saunders Co. Am. J. Surg. Pathol. 1991,15:1209
4. Check Sample Series, American Society of Clinical Pathologists: Selvaggi, S.M.: Aspiration cytology of the ovarian follicle cyst. Cytopathology I. No. C92-4, 1992.
5. Selvaggi, S.M.: Polypoid carcinoma of the esophagus on brush cytology letter to the editor). Acta Cytol., In Press.
6. Editorial: Ovarian follicular cysts: A Potential Source of False-Positive Diagnoses in Ovarian Cytology. Nunez, C., Diaz, JI (Authors). Diagn. Cytopathol., In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Chief, Hemostasis and Coagulation Laboratory, William Beaumont Hospital, Royal Oak, Michigan.
B. Performance and diagnosis of bone marrow biopsies and aspirates.
C. Daily educational "plasma" rounds - monitoring of blood component usage on behalf of Transfusion Committee, William Beaumont Hospital.
D. Clinical Consultant - problems in bleeding, thrombosis, and anti-coagulant therapy, William Beaumont Hospital.

II. TEACHING ACTIVITIES:

A. Graduate students:

1. Seven lectures on Coagulation and Hemostasis for School of Medical Technology at William Beaumont Hospital.
2. Three discussion seminars for Pathology Residents at William Beaumont Hospital.
3. Three lectures for Intensive Care Residents on Blood Component Therapy at William Beaumont Hospital.
4. One lecture for Emergency Care Residents on Blood Component Therapy at William Beaumont Hospital.
5. Daily teaching rounds for Pathology Residents and Transfusion Fellows in Blood Component Therapy.
6. Four Clinical Pathology Grand Rounds at the University of Michigan on "Coagulation and Hemostasis".
7. Teaching rounds for Pathology Residents at the University of Michigan of Blood Component Therapy.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Production of Thrombi on Intact Endothelium In Vivo", William Beaumont Hospital Reasearch Institute, $57,667/1 year, 2/1/91-1/31-92.

OTHER RESEARCH:

A. Collaboration with Dr. Victor Yang, The University of Michigan School of Pharmacy, on development of a protamine exchange filter for removal of heparin from blood.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director of Residency Trainng Program, William Beaumont Hospital.
B. Administrator, Afternoon and Night Shifts of Clinical Laboratories, William Beaumont Hospital.

HOSPITAL:

A. Educational Committee, William Beaumont Hospital.
B. Transfusion Committee, William Beaumont Hospital.

REGIONAL AND NATIONAL:

A. Reviewer of manuscripts for:
   1. New England Journal of Medicine.
   2. Journal of American Society of Clinical Pathologist.
   3. Transfusion.
B. Member, CAP Committee to establish guidelines for blood component therapy.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "Hemostasis and Component Therapy", Grand Rounds, St. Joseph Mercy Hospital, Ann Arbor, October 10, 1992.
2. Invited Lecturer, "Anticoagulant Therapy in the Elderly", Geriatric Seminar sponsored by William Beaumont Hospital, March 7, 1992.
3. Invited Lecturer, "Setting Up a Monitoring System for Component Therapy", St. Joseph Mercy Hospital, March 12, 1992.
4. Invited Lecturer, "Platelet Thrombosis on Intact Endothelium", 1992 Penner Blood Coagulation Conference, Michigan State University, May 13, 1992.

VI. PUBLICATIONS:

ARTICLES SUBMITTED FOR PUBLICATION:

1. Shanberge, J.N. and Quatrociocchi Longe, T.: Analysis of Fresh Frozen Plasma Administration with Suggestions for Ways to Reduce Usage. Transfusion Medicine, 1992, In Press.
2. Shanberge, J.N.: Adaptor for Jamshidi Needles to Enhance Penetration of Hard Done. Blood.

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

1. Shanberge, J.N.: Re: Extracorporeal Shock Wave Lithotripsy in Patients with Bleeding Diathesis. J. Urol., Letters to the Editor. 1991;146:1618.
2. Shanberge, J.N.: Tests Used to Monitor Heparin Therapy. Clinical Pathology Newsletter, William Beaumont Hospital. 1992;1:1.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Clinical Cytogenetics Laboratory.

II. TEACHING ACTIVITIES:

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

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

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

D. Clinical Pathology Grand Rounds.

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

F. Leukemia Conference, biweekly.

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

III. RESEARCH ACTIVITIES:

PROJECTS UNDER STUDY:

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

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

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

D. Correlation of ploidy with expression of differential function.

E. Role of deletions of 12p in eosinophilia.

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

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

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Co-Director, Clinical Cytogenetics Laboratory.

MEDICAL SCHOOL/HOSPITAL:

A. Director, Clinical Research Center Cell Immortalization Facility.

REGIONAL AND NATIONAL:

A. Planning Committee, Cytogenetics Technologist Program, Eastern Michigan University.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Hanson, C.A., Abaza, M., Ross, C.W., Sheldon, S., Schnitzer, B. and Stoolman, L.M.: Acute biphenotypic leukemia (ABL): immunophenotyping, morphology, and cytogenetics. Lab. Invest. 1991;64:73A.
2. Abaza, M., Ross, C.W., Sheldon, S., Stoolman, L.M., Schlegelmilch, J.A., Schnitzer, B. and Hanson, C.A.: CD-7-positive acute leukemias: morphology, immunophenotype and cytogenetics. Lab. Invest. 1992;66:73A.
3. Ross, C.W., Hanson, C.A., Schnitzer, B. and Sheldon, S.: Chronic myeloid neoplasia associated with eosinophilia and abnormalities of chromosome 12p. Lab. Invest. 1992;66:86A.
4. Ghaziuddin, M., Sheldon, S., Tsai, L. and Alessi, N.: Abnormalities of chromosome 18 in a girl with mental retardation and autistic disorder. Welsh Journal of Personality Disorders, In Press.
5. Sheldon, S. and Hanson, C.A.: Two histologically and cytogenetically distinct populations of cells in a patient with acute promyelocyte leukemia. Amer. J. Human Genet., In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Surgical Pathology Coverage of M-Labs cases including most cases from:
   1. Albion Community Hospital, Albion, Michigan.
   2. Thorn Hospital, Hudson, Michigan.
   3. University of Michigan Health Service, Ann Arbor, Michigan.
   4. Other various institutions.

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

C. Rotation with other staff pathologists.
   1. Seven weeks coverage at the University Hospital of weekend autopsy call.

II. TEACHING ACTIVITIES:

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

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

C. In-Service teaching to laboratory staffs at Albion, Lapeer, and Thorn Hospitals.

III. RESEARCH ACTIVITIES:

A. Investigation of hepatic fatty change in exogenous obesity and following gastric exclusion surgery.

B. Investigation of malacoplakia of the endometrium.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Director, M-Labs.
   1. Participate in planning, marketing, and implementation of M-Labs programs.

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

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

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

E. Director of Laboratories, Thorn Hospital, Hudson, Michigan.

F. Chairman, Tissue/Transfusion Committee, Thorn Hospital, Hudson, Michigan.

G. Chairman, Infection Control Committee, Thorn Hospital, Hudson, Michigan.

H. Director of Laboratories, Lapeer Regional Hospital, Lapeer, Michigan.

I. Member, Tissue/Transfusion Committee, Infection Control Committee and Ethics Committee, Lapeer Regional Hospital, Lapeer, Michigan.

V. OTHER RELEVANT ACTIVITIES:

1. Poster Presentation - Regression of Hepatic Steatosis with Weight Loss After Gastric Exclusion for Morbid Obesity at ASCP/CAP Meeting, April 4-9, 1992, Boston, Massachusetts.

VI. PUBLICATIONS:

ABSTRACTS:

1. Silverman, E.M., Appelman, H.D. and Sapola, J.A.: Regression of Hepatic Steatosis with Weight Loss After Gastric Exclusion. Am. J. Clin. Pathol. 1992;97:446.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. 33% Neuropathology Service.

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Neuropathology 858 - six hours.
      b. CME accredited Conferences.
      c. Brain Conference - 40 hours.
      d. Neuromuscular Conference - 40 hours.
      e. Neuropath Conference for house staff - 16 hours.

B. Undergraduate students:
   a. Neuropathology (NSB 600) - 4 hours.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Pathology of the Node of Ranvier in Diabetic Neuropathy", RO1-I 43884-01 (40%), National Institutes of Health, with Tennekoon, G. and Rutkowski, $1,472,882/5 years, 4/1/91 - 3/31/96.

B. Principal Investigator, "The Role of Trophic Factors and Their Synthesis in Diabe Neuropathy", #1901122, Juvenile Diabetes Foundation International, $47,801.00/ year, 7/1/1 - 2/1/93.

C. Co-Investigator, "Synthesis and Responsiveness to Trophic Factor by Diabetic Nerve of the I Rat", Murphy, L.J. (PI), Medical Research Council of Canada, $141,180.00/ year, 4/1/8 3/31/93.

D. Sima A.A.F. (Co-Investigator, 5% effort), "Molecular Elements, Neurocircuits and Mei Illness", Watson, S. (PI), National Institute of Mental Health. $5,166,343.00/5 yrs, 12/1/ 11/30/96.

E. Sima, A.A.F. (Co-Investigator, 5% effort), "Luteotrophic Actions of Insulin-like Growth Fa I", Keyes, L. (PI), National Institutes of Health, $404,922, 7/1/92-6/30/95.

PENDING:

A. Sima, A.A.F (Co-Investigator, 10% effort), Michigan Diabetes Research & Training Cen Image Analysis Core, National Institutes of Health, 5 P60 DK20572-16, 12/1/92-11/30/ $1,250,000 annual

B. Sima, A.A.F. (Principal Investigator, 20% effort) Neuropathology Core, Michigan Alzheim Disease Research Center, National Institutes of Health, $225,027/yr, 10/1/94-9/30/99.

C. Sima, A.A.F. (Principal Investigator, 10% effort) Diffuse Lewy Body Disease (DLBD), Michigan Alzheimer's Disease Research Center, National Institutes of Health, $105,600/yr, 10/1/94-9/30/99.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. CERAD representative, Michigan Dementia Program.

MEDICAL SCHOOL/HOSPITAL

A. Member, Executive Committee, Michigan DRTC.
B. Director, Image Analysis core, Michigan DRTC.
C. Director, Animal Core, Michigan DRTC.
D. Director, Neuropathology Core, MADRC.
E. Member, Executive Committee, MADRC.

REGIONAL/NATIONAL.INTERNATIONAL:

A. Member, Medical Advisory Board, Juvenile Diabetes Foundation International, New York, New York.
B. Executive Committee, Lessons from Animal Diabetes, Jerusalem, Israel.
C. Member, Council on Diabetic Complications, American Diabetes Association, New York, New York.
D. Abstract Review Board, ADA, Alexandria, Virginia.
E Member, Specialty Committee Neuropathology, Royal College of Physicians and Surgeons of Canada, Ottawa, Canada.
F. Scientific Advisor, Wyeth-Ayerst Radon, Pennsylvania.
G. Scientific Advisor, Endocrinology Section FDA, Rockville, Maryland.
H. Member, Executive Committee, Wyeth Ayerst Inc.
I. Member, Executive Committee, Pfizer Pharmaceuticals.
J. Awards Committee, American Association of Neuropathologists.

OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. Diabetes Research and Clinical Practice.
B. Lessons from Animal Diabetes.
C. International Diabetes News.
D. Journal of Diabetic Complications.
E. Ad hoc Reviewer for 9 journals (Neuropathology and Diabetes).
F. Study sections:
    1. Medical Research Council of Canada.
    2. Juvenile Diabetes Foundation International.
    3. American Diabetes Association.

INVITED LECTURES/SEMINARS

1. Diabetic Neuropathy Study Group of the EASD, Cork, Ireland, 1991.
2. Miles Pharmaceutical Inc., Annapolis, Maryland, 1991.
3. Wyeth-Ayerst Mexico, Puerto Vallarto, Mexico, 1991.

4. Wyeth-Ayerst France, Malmö, Sweden, 1991.
5. US Japan Cataract Research Group, Kona, Hawaii, 1991.
6. American Diabetes Association, Washington D.C., 1991.
7. Wyeth-Ayerst, Princeton, New Jersey.
8. Investigators' Meeting, West Palm Beach, Florida, 1992.
9. Eisai Company, Tokyo, Japan, 1992.
10. University of Nagoya, Department of Medicine, Nagoya, Japan, 1992.
11. Uppsala University, Department of Medicine, Uppsala, Sweden, 1992.
12. University of Göteborg, Department of Medicine, Göteborg, Sweden, 1992.
13. German Diabetes Association, Hanover, Germany, 1992.
14. Brazilian Diabetes Association, Sao Paulo, Brazil, 1992.

IV. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Sima, A.A.F., Nathaniel, V., Prashar, A., Bril, V. and Greene, D.A.: Endoneurial microvessels human diabetic neuropathy: Endothelial cell dysjunction and lack of treatment effect by ald reductase inhibitor. Diabetes. 1991;40:1090-1099.
2. Ghahary, A., Chakrabarti, S., Murphy, L.J. and Sima, A.A.F.: Effect of insulin and statil on ald reductase expression in diabetic rats. Diabetes 1991;40:1391-1396.
3. Chakrabarti, S., Ghahary, A., Murphy, L.J. and Sima, A.A.F.: Insulin-like growth factor-I expressio not increased in the retina of diabetic BB/W-rats. Diab. Res. Clin. Prac. 1991;14:91-98.
4. Paro, M., Prosdocimi, M., Fiori, M.G. and Sima, A.A.F.: Autonomic innervation of the bladder in t models of experimental diabetes in the rat: Functional abnormalities, structural alterations and effects ganglioside administration. Urodinamica 1991;1:161-163.
5. Sima, A.A.F. and Chakrabarti, S.: Long-term suppression of post-prandial hyperglycemia with acarb retards the development of neuropathies in the BB/W-rat. Diabetologia 1992;35:325-330.
6. Chakrabarti, S. and Sima, A.A.F.: The effect of myo-inositol treatment on basement membr thickening in the BB/W-rat retina. Diab. Res. Clin. Prac. 1992;16:13-17.
7. Simmons Z. Albers J.W. and Sima A.A.F.: Case of the Month: Perineuritis presenting as mononeur multiplex. Muscle and Nerve 1992;15:630-635.
8. Sima A.A.F. and Greene D.A.: Morphologie der peripheren diabetischen Neuropathie und i Korrelation mit Funktionstesten. Diabetes und Stoffwechsel 1992;1:29-33.
9. Greene D.A. and Sima A.A.F.: Stellenwert der Aldosereduktase-Hemmer in der Therapie diabetischen Neuropathie des Menschen. Diabetes und Stoffwechsel 1992;1:45-51.
10. Sima, A.A.F.: Structural-functional interactions in the therapeutic response of diabetic neuropathy. Diabetic Complications 1992;6:40-44.
11. Sima, A.A.F., Brown M.B., Prashar, A., Chakrabarti, S., Laudadio C. and Greene, D.A.: T reproducibility and sensitivity of sural nerve morphometry in the assessment of diabetic periphe polyneuropathy. Diabetologia. 1992;35:560-569.
12. Foster, N.L., Gilman, S., Berent, S., Sima, A.A.F., D'Amato, C., Koeppe, R.A. and Hicks, S. Progressive subcortical gliosis and progressive supranuclear palsy can have similar clinical and P abnormalities. J. Neurol. Psychiatry and Neurosurg, In Press.
13. Sima, A.A.F., Zhang, W-X, Cherian, P.V. and Chakrabarti, S.: Impaired visual evoked potentials a primary axonopathy of the optic nerve in the diabetic BB/W-rat. Diabetologia, In Press.
14. Sima, A.A.F. and Greene, D.A.: Structural-functional interactions in the therapeutic response diabetic neuropathy. Diabetic Medicine, In Press.
15. Greene, D.A. and Sima, A.A.F.: Effects of aldose reductase inhibitors on the progression of ne damage. Diabetic Medicine (in press)
16. Sima, A.A.F., Stevens, M.J., Feldman, E.L., Cherian, P.V. and Greene, D.A.: Animal Models as To for the Testing of Preventive and Therapeutic Measures in Diabetic Neuropathy, in, Lessons fr Animal Diabetes IV, Smith Gordon, In Press.

17. Greene, D.A., Sima, A.A.F., Stevens, M.B., Feldman, E.L. and Lattimer, S.A.: Complications: neuropathy, pathogenetic considerations. Diabetes Care, In Press.
18. Sima, A.A.F.: Pathogenesis, progression and therapeutic intervention of diabetic neuropathy. J. Ocular Pharmacology, In Press.

ARTICLES SUBMITTED FOR PUBLICATION

1 Sutherland, G.R., Bose, R., Pinsky, C. and Sima, A.A.F.: The variable status of the radical-scavenging systems in primary intracranial neoplasms. Neuroscience Letters. Submitted.
2. Lindström, P., Brismar, T., Sima, A.A.F. Impaired recovery after anoxic conduction block in diabetic (BB/W)-rat nerve in vivo. Ann. Neurol. Submitted.
3. Goodison, K.L, Parhad, I.M., White, C.L., Sima, A.A.F. and Clark, A.W.: Neuronal and glial gene expression in neocortex of Down's Syndrome and Alzheimer's disease. J. Neuropath. Exp. Neurol. Submitted.
4. Uccioli, L., Magnani, P., Tilli, P,, Cotroneom P,, Mantom A,, Grecom A,V,, Simam A.A.F., Greene, D.A., Menzinger, G. and Ghirlanda, G.: Abnormal agonist-stimulated cardiac parasympathetic acetylcholine release in streptozotocin diabetes. Diabetes. Submitted.
5. Chakrabarti, S., Cherian, P.V. and Sima, A.A.F.: The effect of acarbose on diabetes- and age-related basement membrane thickening in retinal capillaries of the BB/W-rat. Diabetes Research and Clinical Practice. Submitted.
6. Murray, F.T., Beyer-Mears, A., Johnson, R.D., Sima, A.A.F., Cameron, D.F., Sninsky, C.A. and Selawry, H.: Assessment of proteinuria and neuropathy in the non-immunosuppressed BB diabetic rat following abdominal, intratesticular, islet transplantation. Transplantation. Submitted.
7. Sima, A.A.F., Prashar, A., Nathaniel, V., Bril, V., Werb, M.R. and Greene, D.A.: Overt diabetic neuropathy: repair of axo-glial dysjunction and axonal atrophy by aldose reductase inhibition and its correlation to improvement in nerve conduction velocity. Diabetic Medicine. Submitted.

BOOKS/CHAPTERS IN BOOKS

1. Sima, A.A.F., Nathaniel, V. and Greene, D.A.: Peripheral nerve repair following ARI-treatment, in, Vranic, M., Efendic, S., and Hollenberg, C.H., (eds.), Fuel Homeostasis and The Nervous System, Advances in Experimental Medicine and Biology, Plenum Publishing Company, New York, Vol. 291, pp. 265-270, 1991.
2. Chakrabarti, S., Zhang, W.-X. and Sima, A.A.F.: Optic neuropathy in the diabetic BB-rat, in, Vranic M., M., Efendic, S., and Hollenberg, C.H., (eds.), Fuel Homeostasis and The Nervous System, Advances in Experimental Medicine and Biology, Plenum Publishing Company, New York, Vol. 291, pp. 257-264, 1991.
3 Sutherland, G. and Sima, A.A.F.: Incidence and clinicopathological features of meningioma, in, Schnidek H.H. (ed.), Meningeomas and Their Surgical Management, W.B. Saunders, Philadelphia, pp. 10-21, 1991.
4. Italiano, G., Paro, M., Magri, V., Fiori, M.G., Sima, A.A.F., Guillon, G.B. and Prosdocimi, M.: Ganglioside administration in experimental autonomic diabetic neuropathy, in, Proc. Int. Symp. Clin. Neuropharmacol., In Press.
5. McKeever, P.E., Sima, A.A.F. and Blaivas, M.: Neoplasms of the sellar region, in, Lloyd R.V. (ed.), Surgical Pathology of the Pituitary Gland, W.B. Saunders, Philadelphia, In Press.
6. Sima A.A.F.: The natural history of diabetic neuropathy in the BB-rat, in, Sharma A. (ed), Diabetes mellitus and its complications-an update, Elsevier Publ., Amsterdam, 1991, In Press.
7. Sima A.A.F.: Diabetic neuropathy and responses to ARI-treatment, in, Sharma A. (ed.), Diabetes mellitus and its complications-an update, Elsevier Publ., Amsterdam, 1991, In Press.
8. Chakrabarti, S. and Sima, A.A.F.: Diabetic retinopathy in experimental animal models, in, Sharma A. (ed.), Diabetes mellitus and its complications-an update, Elsevier Publ., Amsterdam, 1991, In Press.
9. Sima, A.A.F.: Somatosensory polyneuropathy, pathological-electrophysiological correlations and the role of AR in man, in, Excerpta Medica Int. Congress Series, Elsevier Publ., Amsterdam, 1991, In Press.

10. Sima, A.A.F.: Pathogenesis, natural history and therapeutic potentials. (Plenary Lecture), Proceedings of the 1991 Acarbose Preclinical Workshop, Neva Press, In Press.
11. Chakrabarti, S. and Sima, A.A.F.: Diabetic retinal microangiopathy in the BB/W rats: The effects myo-inositol supplementation, in, Proceedings of the 1991 Acarbose Preclinical Workshop, Neva Pre In Press.
12. Sima, A.A.F. and Chakrabarti, S.: Acarbose slows the progression of diabetic neuropathy in the diabe BB/W rats, in, Scriabine, A. and Vasselli, J.R. (eds.), Proceedings of the First Acarbose Preclini Workshop, October 1991, Annapolis, Maryland, Neva Press, Branford, Connecticut, In Press.
13. Sima, A.A.F.: Pathological-electrophysiological correlations and the role of A/R in man, in Excer Medica International Congress Series, Elsevier Science Pub., In Press.
14. Stevens, M.J., Feldman, E.L., Funnell, M.M., Sima, A.A.F. and Greene, D.A.: Optimal Methods Detecting Early Neuropathy and Its Progression, Karger, Basel, 1992, In Press.
15. Sima, A.A.F.: Pathogenesis of diabetic neuropathy and applications of nerve biopsy. Symposium Diabetic Neuropathy, Sao Paulo, Brazil, April, 1992.
16. Sima, A.A.F.: Treatment of diabetic neuropathy: effect on nerve morphology. Symposium on Diabe Neuropathy, Sao Paulo, Brazil, April, 1992.

ABSTRACTS

1. Caplan, M. and Sima, A.A.F.: Diffuse axonal injury in head-trauma. Michigan Neuropathology D October, 1991.
2. Simmons, Z. and Sima, A.A.F.: Perineuritis presenting as mononeuritis multiplex in a patient with m diabetes. Michigan Neuropathology Day, October, 1991.
3. Sima, A.A.F.: Optic neuropathy in diabetes. Michigan Neuropathology Day, October, 1991.
4. Sima, A.A.F., Cherian, P.V., Carson, C., Chakrabarti, S. and Greene, D.A.: Prevention of diabetic op neuropathy in the BB/W-rat with an aldose reductase inhibitor. Peripheral Neuropathy Associat Meeting, May 14-18, 1992, Rapallo, Italy.
5. Sima, A.A.F.: Morpholgie der peripheren diabetische Neuropathie und ihre Korrelation 1 Funktionstesten. Deutsche Diabetes-Gesellschaft Meeting, May 28-30, 1992, Hanover, Germany.
6. Fratkin, J.D., Jomes, M,Z., D'Amato, C.J., Foster, N., Rennick, D., Dragovic, L., Garcia, J.H., Ho K. Huang, T.E., Sima, A.A.F. and Lovell, K.L.: Michigan postmortem examination network for demer patients. J. Neuropath. Exp. Neurol. 1992;51:315.
7. d'Amato, C.J., Foster, N.L., Hicks, S.P. and Sima, A.A.F.: Swollen cortical neurons and Lewy bod accompanying progressive supranuclear palsy and Creutzfeldt-Jakob's disease. J. Neuropath. E Neurol. 1992;51:324.
8. Sima, A.A.F., Brown, M.B., Laudadio, C. and Greene, D.A.: Diabetic neuropathy: The sensitivity a reproducibility of sural nerve morphometry. J. Neuropath. Exp. Neurol. 1992;51:347.
9. Sima, A.A.F., Cherian, P.V. and Kamijo, M.: Diabetic optic neuropathy is prevented by ald reductase inhibition. Meeting of the American Association of Neuropathologist, St. Louis, Misso June 18-21, 1992. J. Neuropath. Exp. Neurol. 1992;51:357.
10. Sima, A.A.F., Cherian, P.V., Carson, C., Kamijo, M. and Chakrabarti, S.: Diabetic optic neuropathy a its prevention in the BB/W-rat with an aldose reductase inhibitor. Diabetes 1992;41(Suppl 1):139A.
11. Magnani, P., Tennekoon, G., Sima, A. and Brosius, F.: Biochemical and molecular characteristics glucose transporters (GT) in cultured Schwann cells (SwC) and peripheral nerve. Diabe 1992;41:22A.
12. Sima, A.A.F., Cherian, P.V., Albers, J.W., Greene, D.A. and the Tolrestat Study Group: Nerve fi loss in diabetic neuropathy correlates with impaired evoked potential amplitudes and nerve conducti velocity. European Association for the Study of Diabetes, 28th Annual Meeting, September 8-11, 19 Prague, Czechoslovakia.
13. Steiner, K., Sima, A.A.F., Hohman, T.C., Greene, D.A., and the Tolrestat Study Group: Use Morphometry in the assessment of biochemistry in sural nerve biopsies from diabetic neuropat patients. European Association for the Study of Diabetes, 28th Annual Meeting, September 8-11, 19 Prague, Czechoslovakia.

14. Greene, D.A., Hohman, T.C., Sima, A.A.F., Graepel, G.J., Gonen, B., Bochenek, W. and Beg M: The relationship of human sural nerve biochemistry and function in diabetic neuropathy. European Association for the Study of Diabetes, 28th Annual Meeting, September 8-11, 1992, Prague, Czechoslovakia.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

B. Autopsy service.

II. TEACHING ACTIVITIES:

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

1. Jim Grober, M.D., Rheumatology Fellow, Department of Internal Medicine, University of Michigan, School of Medicine (July, 1990-October, 1991) - recipient of NIH post-doctoral fellowship to study the adhesion molecules mediating attachment of leukocytes to the endothelium of rheumatoid synovium.
2. Eric Kaldjian, M.D., Pathology Research Fellow (July, 1991 - present)- Dr. Kaldjian's project focuses on the transcriptional regulation of the lymph node homing receptor (L-selectin) in normal and malignant lymphoid cells. An abstract covering this work was selected for a FASEB '92 minisymposium presentation.
3. Terry Behrend, B.A., Medical Student (M1), University of Michigan, School of Medicine (July, 1991-September, 1991) - recipient summer research grant focusing on the regulation of carbohydrate ligand(s) for E-selectin on leukocytes. Initial work on this project culminated in co-authorship on paper demonstrating the role of fucosyl-transferases in construction of ligands for E-selectin.
4. Francis Wolber, Ph.D. candidate in Experimental Pathology (July, 1992 - September, 1992) - project focuses on mononuclear leukocyte attachment to induced and constituently expressed adhesion molecules at physiologic levels of shear-stress.
5. Jennifer Ballew, undergraduate student (July, 1990 - present) - projects focus on development of basic and advanced laboratory skills including tissue culture, immunostaining and operation of flow cytometer.

B. Laboratory Instructor, Organ Systems Pathology (Pathology 600) - joined group of ten instructors as permanent faculty in the course. Instructors selected for interest and skill in teaching.

C. Section leader, Hematopathology Section of Pathology 600 Course.

D. Lecturer, Host Defense Section of ICS 600 Course.

E. Lecturer, Experimental Pathology (Pathology 580 and 581).

F. Member, Graduate Comprehensive Examination Committee - formulate questions, conduct and grade written and oral examinations for Ph.D. candidates in Experimental Pathology Program.

G. Daily sign-out of cases in flow cytometry and hematopathology with pathology residents and medical students (three-four months).

H. Didactic case-studies on the clinical applications of flow cytometry for the residents, fellows and medical students.

I. Attending, Autopsy Service (two weeks).

J. Preceptor, Senior medical student (M4) elective in Pathology (1 month).
K. Speaker, Rheumatology, Hematology/Oncology and Cancer Center Research Seminars.

III. RESEARCH ACTIVITIES:

SPONSORED RESEARCH:

FUNDED:

A. Principal Investigator, "Endothelial Binding Lectins of Lymphoid Malignancies", NIH, RO1 ($425,000; 30 September 1989 - 31 August 1992), 30% effort.
B. Principal Investigator, "Leukocyte-microvascular adhesive interactions in Rheumatoid Arthritis", NIH, SCOR in Rheumatoid Arthritis ($398,269; 30 September 1992 - 31 August 1995), 25% effort.
C. Co-Principal Investigator, "Mechanisms of Lymphocyte Recruitment to the Lungs", NIH, SCOR in Occupational and Immunologic Lung Diseases, ($650,000; 1 December 1991 - 31 November 1996), 15% effort.

IN PREPARATION:

A. Principal Investigator, "Regulation of selectins and their counter-receptors in normal and malignant cells", NIH, R01, competitive renewal.
B. Principle Investigator, "Selectin-mediated leukocyte recruitment in chronic inflammatory disease", NIH, P01, Peter A. Ward, Program Director.

IV. ADMINISTRATIVE ACTIVITIES:

A. Co-director Flow Cytometry Laboratory.
B. Member, Quality Assurance Committee.
C. Member, Equipment and Space Allocation Committee.
D. Member, Coordinating Committee for Elective in Laboratory Medicine.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES AND SEMINARS:

1. Chair, Minisymposium on Cell-Cell Interactions, American College of Rheumatology, Boston, Massachusetts, November, 1991.
2. "Selectin and integrin dependent monocyte adhesion in rheumatoid arthritis", 2nd International Titisee Symposium on Leukocyte Adhesion Molecules, Titisee, Germany. October, 1991.
3. "Selectins in leukocyte recruitment and recirculation", First International Workshop on CD15, Dusseldorf, Germany, December, 1991.
4. "P-selectin dependent monocyte attachment to the synovial microvasculature in rheumatoid arthritis", FASEB Major Symposium on Leukocyte-Endothelial Adhesive Interactions, Aneheim, California, May, 1992.
5. "Direct evaluation of monocyte-microvascular adhesion in human rheumatoid arthritis", IBC Conference on Cell Adhesion Molecules in Inflammation, San Francisco, California, May, 1992.
6. "Introduction to Leukocyte Recruitment and Lymphocyte Recirculation", Cytokines and Transplantation, Rush-Presbyterian-St. Luke's Medical Center, May, 1992.
7. "Adhesive interactions in leukocyte recruitment and recirculation", State-of-the-Art Presentation, 35th Annual Thomas L. Petty Aspen Lung Conference, Aspen, Colorado, June, 1992.

MANUSCRIPT REVIEWS:

A. Journal of Clinical Investigation.
B. Journal of Laboratory Investigation.
C. American Journal of Pathology.
D. Journal of Immunology.
E. Nature

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Kansas, G.S., Spertini, O., Stoolman, L.M. and Tedder, T.F.: Molecular mapping of functional domains of the leukocyte receptor for endothelium, LAM-1. J. Cell Biol. 1991;114:351.
2. Lowe, J.B., Stoolman, L.M., Nair, R.P., Larsen, R.D., Behrend, T. and Marks, R.M.: A transfected human fucosyltransferase cDNA determines biosynthesis of oligosaccharide ligand(s) for endothelial-leukocyte adhesion molecule 1. Biochem. Soc. Trans. 1991;19: 649.
3. Nickoloff, B.J., Mitra, R.S., Shimizu, Y., Barker, J.N., Karabin, G., Stoof, T. and Stoolman, L.M.: HUT 78 Cells bind to noncytokine-stimulated keratinocytes using a non-CD 18-dependent adhesion pathway. Am. J. Path. 1992;140(6): 1365.
4. Stoolman, L.M. and Kaldjian, E.: Adhesion molecules involved in the trafficking of normal and malignant leukocytes. Invasion and Metastasis, In Press.

ARTICLES SUBMITTED FOR PUBLICATION:

1. **Stoolman, L.M.**, Situ, R., Wang, L. and Varani, J.: Regulation of fibronectin and laminin binding activity in human T-lymphoblastic cell lines.
2. Grober, J.S., Bowen, B.L., Ebling, H., Athey, B., Thompson, C., Fox, D.A. and **Stoolman, L.M.** 1992. Monocyte-endothelial adhesion in chronic rheumatoid arthritis: in situ detection of selectin (LEC-CAM) and integrin-dependent interactions.
3. Ley, K., Linnemann, G., Meinen, M., **Stoolman, L.M.** and Gaehtgens, P. Fucoidin, but not the yeast polyphosphomannan PPME, inhibits leukocyte rolling in venules of the rat mesentery.

BOOK CHAPTERS:

1. Stoolman, L.M.: Selectins: lectin-like receptors involved in lymphocyte recirculation and leukocyte recruitment, Chapter 3, in, Fukuda, M. (ed.), Cell Surface Carbohydrates and Cell Development,CRC Press, Inc., New York, 1992.
2. Stoolman, L.M., Grober, J., Bowen, B., Reddy, P., Shih, J. Thompson, C., Fox, D.A. and Ebling, H.: Selectin-dependent monocyte adhesion in frozen sections of rheumatoid synovitis, Chapter 16, in, Lipsky, P. and Smith, C.W. (eds.), Structure, Function and Regulation of Molecules Involved in Leukocyte Adhesion, Springer-Verlag, New York, 1992.

ABSTRACTS:

1. Fox, D.A., Bowen, B. and Stoolman, L.M.: LEC-CAM (selectin)- mediated monocyte-endothelial adhesion in chronic rheumatoid arthritis, J.S. Grober, presented by JSG at American College of Rheumatology Annual Meeting, Boston, November, 1991..
2. Grober, J.S., Bowen, B.L., Ebling, H., Shih, S., Thompson, C., Reddy, P., Fox, D.A. and Stoolman, L.M.: Selectin and integrin dependent monocyte attachment to venules in rheumatoid

arthritis, presented by LMS at the Keystone Symposium on Glycobiology, Park City, Utah, March, 1992.

3. Kaldjian, E., Reddy, B.P. and Stoolman, L.M.: Transcriptional regulation of L-selectin expression in normal and malignant T-cells, presented by EK at FASEB '92 minisymposium on leukocyte-endothelial interactions, Anaheim, California, April, 1992.
4. Abaza, M.A., Ross, C.W., Sheldon, S., Stoolman, L.M., Schlegelmilch, J.A., Schnitzer, B. and Hanson, C.A.: CD-7-positive acute leukemias: Morphology, immunophenotype and cytogenetics, presented by MAA at the International Association of Pathology Conference, New Orleans, Louisiana, March, 1992.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

None.

II. TEACHING ACTIVITIES:

A. Lectures on inflammation and wound healing (Immunopatholoyg Course 630, for dental and graduate students.
B. Supervision of postdoctoral fellows and premedical/medical students in research.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Lung Injury Produced by Oxygen Metabolites (GM-29507). Co-Principal Investigator with Dr. P.A. Ward.
B. Role of Oxidants, Complement and Neutrophils in Ocular Ischemia-Reperfusion Injury (Michigan Eye Bank and Transplantation Center). Principal Investigator.

PROJECTS UNDER STUDY:

A. Cytokines and adhesion molecules in thermal injury.
B. Ocular ischemia-reperfusion injury.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Reviewer for the following scientific journals: American Journal of Pathology, American Journal of Physiology, Clinical Immunology and Immunopathology, International Archives of Allergy and Applied Immunology, Journal of Leukocyte Biology, Journal of Vascular Surgery, Pharmacological Research.

V. OTHER RELEVANT ACTIVITIES:

Member Editorial Advisory Board Immunobiology.

INVITED LECTURES/SEMINARS:

1. Invited Speaker and workshop chair, Annual Meeting of the American Burn Assoc., Salt Lake City, 1992.
2. Invited Speaker, 3rd International Symposium on Uveitis, Brussels, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Thomson, P.D., Till, G.O. and Smith, D.J., Jr.: Modulation of IgM antibody formation by lipid peroxidation products from burn plasma. Arch. Surg. 1991;126:973-975.
2. Yang, V.C., Port, F.K., Kim, J.S., Teng, C.L., Till, G.O. and Wakefield, T.W.: The use of immobilized protamine in removing heparin and preventing protamine-induced complications during extracorporeal blood circulation. Anesthesiology 1991;75:288-297.
3. Wakefield, T.W., Kirsh, M.M., Till, G.O., Brothers, T.E., Hantler, C.B. and Stanley, J.C.: Absence of complement-mediated events after protamine reversal of heparin anticoagulation. J. Surg. Res. 1991;51:72-76.
4. Friedl, H.P. Till, G.O. Trentz, O. and Ward, P.A.: Role of oxygen radicals in tourniquet-related ischemia-reperfusion injury of human patients. Klin. Wochenschr. 1991;69:109-112.
5. Ward, P.A., Till, G.O. and Warren, J.S.: Pathophysiology of leukocyte-mediated tissue injury. J. Critical Care 1991;6:112-116.
6. Punch, J., Rees, R., Cashmer, B., Wilkins, E., Smith, D.J. and Till, G.O.: Xanthine oxidase: its role in the no-reflow phenomenon. Surgery 1992;111:169-176.
7. Mulligan, M.S., Varani, J., Warren, J.S., Till, G.O., Smith, C.W., Anderson, D.C., Todd, R.F., 3d. and Ward, P.A.: Roles of beta 2 integrins of rat neutrophils in complement- and oxygen radical-mediated acute inflammatory injury. J. Immunol. 1992;148:1847-1857.
8. Till, G.O.: Startreaktionen des traumatischen Schocks: experimentelle Ergebnisse. Hefte Unfallheilkunde, In Press.
9. 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.
10. Wilkins, E.G., Rees, R.S., Smith, D., Cashmer, B., Punch, J., Till, G.O. and Smith D.J.: Identification of xanthine oxidase activity following reperfusion in human tissue. Surgery, In Press.
11. Murphy, H.S., Shayman, J.A., Till, G.O., Mahrougui, M., Owens, C.B., Ryan, U.S. and Ward, P.A.: Superoxide responses of endothelial cells to C5a and TNFα: divergent signal transduction pathways. Am. J. Physiol., In Press.
12. 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.
13. Garner, W.L., Rodriguez, J.L., Miller, C.G., Till, G.O., Rees, R.S., Smith, D.J. and Remick, D.G.: Acute skin injury releases neutrophil chemoattractants. J. Trauma, In Press.
14. Hultquist, D.E., Xu, F., Quandt, K.S., Shlafer, M., Mack, C.P., Till, G.O., Seekamp, A., Betz, A.L. and Ennis, S.R.: Evidence that NADPH-dependent methemoglobin reductase and administered riboflavin protect tissues from oxidative injury. Am. J. Hematol., In Press.

BOOKS AND CHAPTERS IN BOOKS:

1. 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, 1991, pp 381-401.
2. 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.
3. Till, G.O. and Ward, P.A.: Oxygen radical-mediated endothelial cell injury, in, The Immune Consequences of Trauma, Shock and Sepsis, Springer Verlag, Heidelberg, In Press.
4. 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.
5. Friedl, H.P., Trentz, O., Till, G.O. and Ward, P.A.: Role of oxygen radicals in multiple organ failure, in. The Immune Consequences of Trauma, Shock and Sepsis. Springer Verlag, Heidelberg, In Press.
6. Marak, G.E., Till, G.O. and Ward, P.A.: Endothelial cell regulation of acute uveitis, Proc. Third International Symposium on Uveitis, Kugler Publication, Amstelveen, Netherlands, In Press.
7. 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.), Proceedings on Free Radicals, Diseased States and Anti-Radical Interventions, The Richelieu Press, London, In Press..

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

1. 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. 1992;33:518A.
2. Till, G.O., Lee, S. and Monem, K.: Inflammatory mediator-induced conversion of xanthine dehydrogenase to xanthine oxidase in rat neutrophils. FASEB J. 1992;6:1339A.
3. Till, G.O., Elner, S.G., Lee, S., Elner, V.M. and Marak, G.E.: Production of toxic oxygen metabolites by retinal pigment epithelial cells, 3rd International Symposium on Uveitis, Brussels, May 24-27. Program & Abstracts 1992;42.
4. Marak, G.E., Till, G.O. and Ward, P.A.: Endothelial cell regulation of acute uveitis, 3rd International Symposium on Uveitis in Brussels, May 24-27. Program & Abstracts 1992;39.
5. Seekamp, A., Mulligan, M., Till G.O. and Ward, P.A.: Role of CD18 and ELAM-1 in hind limb ischemia reperfusion-induced lung injury. Circ. Shock. 1992;37:23.
6. Mulligan, M.S., Smith, C.W., Anderson, D.C., Till, G.O. and Ward, P.A.: Role of CD18 in lung and skin injury following thermal skin trauma. Proc. Am. Burn Assoc. 1992;24:79.
7. Rodriguez, J.L., Kelty, L., Miller, C.G., Garner, W., Smith, D., Till, G.O. and Remick, D.G.: Interleukin-8 (IL-8) and acute burn injury. Proc. Am. Burn Assoc. 1992;24:80.
8. Rodriguez, J.L., Garner, W.L., Till, G.O., Miller, C.G., Moore, N.P., Thompson, P.D., Remick, D.G. and Smith, D.J.: Correlation of local and systemic cytokine response with clinical outcome following thermal injury. AAST, In Press.
9. Seekamp, A., Mulligan, M., Till, G.O. and Ward, P.A.: Neutrophil adhesion antagonists and antioxidants provide comparable protection against acute lung injury caused by hind limb ischemia-reperfusion. Orthopaedic Trauma Assoc., In Press.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. None.

II. TEACHING ACTIVITIES:

A. Lecturer, Pathology 580.
B. Lecturer, Pathology 581.
C. Course Director, Pathology 850.
D. Member, Dissertation committee of Mr. Todd Kroll
E. Member, Dissertation committee of Mr. Zwehi Soong.
F. Mentor for students who worked in my laboratory over the past year including two post-doctoral fellows, six undergraduate students, and one graduate student.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Monocyte Recognition of Target Cells", American Cancer Society IM-432.
B. Principal Investigator, "Biochemical Control of Microcarrier Culture", NIH CA33052.
C. Co-Investigator, "Thrombospondin Receptors on Squamous Carcinoma Cells", American Cancer Society PDT-324.
D. Co-Investigator, "Protease-Oxidant Interactions in Lung Inflammation", NIH HL42607.
E. Principal Investigator on Project 10, "Retinoic Acid and Cells of the Skin", Johnson and Johnson Corporation.

PROJECTS UNDER STUDY:

A. The development of substrates for optimum growth of cells in large-scale culture.
B. Mechanisms by which monocytes recognize and interact with the endothelium and with squamous epithelial cells.
C. The role of thrombospondin in the biology of human squamous carcinoma cells.
D. Influence of retinoic acid on proliferation and matrix production by dermal fibroblasts and epidermal keratinocytes in monolayer culture and organ culture.
E. Mechanisms of vascular cell injury in lung inflammation and kidney inflammation.

IV. SERVICE ACTIVITIES:

DEPARTMENTAL:

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

MEDICAL SCHOOL/HOSPITAL:

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

REGIONAL AND NATIONAL:

A. Editorial Board of Invasion and Metastasis.
B. Manuscript reviewer for: American Journal of Pathology, Cancer Research, Clinical and Experimental Metastasis, Experimental Cell Research, International Journal of Cancer, Journal of Immunology, Journal of Investigative Dermatology, Journal of Leukocyte Biology, Laboratory Investigation, Invasion and Metastasis, Science, Proceedings of the National Academy of Sciences.
C. Grant reviewer for the Medical Research Council of Canada, Veterans Administration, and the Johns Hopkins Center for Alternatives to Animal Research. and for the Veterans Administration.
D. NIH Study Section Member: National Drug Development Cooperative Grants review panel.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. Invited Speaker, Amgen, Inc., Thousand Oaks, California, September 20, 1991.
2. Invited Speaker, American Society of Dermatopathology, Dallas, Texas, December 6, 1991.
3. Invited Participant, UCLA Symposium on Biology of Endothelial Cells, Keystone, Colorado, January 21-28, 1992.
4. Invited Speaker, Cell Culture Engineering III, Palm Coast, Florida, February 4-8, 1992.
5. Invited Speaker, Department of Pharmacology and Toxicology; Michigan State University, Lansing, Michigan, January 17, 1992.
6. Invited Speaker, Johnson and Johnson Symposium on Retinoids and Skin, Raritan, New Jersey, May 28, 1992.
7. Organizer, Meeting of the Inflammation Research Association on Oxygen Radicals in Acute and Chronic Inflammation. New York, New York, April 23, 1992.
8. Speaker, Meeting of the Inflammation Research Association on Oxygen Radicals in Acute and Chronic Inflammation. New York, New York, April 23, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Varani, J., Gibbs, D.F., Inman, D.R., Shah, B., Fligiel, S.E.G. and Voorhees, J.J.: Inhibition of epithelial cell adhesion by retinoic acid: Relationship to reduced extracellular matrix production and alteration in Ca^{2+} levels. Am. J. Path. 1991;138:887-895.
2. Castle, V., Varani, J., Fligiel, S.E.G., Prochownik, E.V. and Dixit, V.M.: Antisense-mediated reduction in thrombospondin reverses the malignant phenotype of a human squamous carcinoma. J. Clin. Invest. 1991;87:1882-1889.
3. Shayevitz, J.R., Varani, J., Ward, P.A. and Knight, P.R.: Halothane and isoflurane increase pulmonary artery endothelial cell sensitivity to oxidant-mediated injury. Anesthesiology. 1991;74:1067-1077.
4. Varani, J., Ginsburg, I., Gibbs, D.F., Mukhopadhyay, P.S., Sulavik, C., Johnson, K.J., Weinberg, J.M., Ryan, U.S. and Ward, P.A.: Hydrogen peroxide-induced cell and tissue injury: Protective effects of Mn^{2+}. Inflammation. 1991;15:291-301.
5. Schuger. L., Skubitz, A.P.N., O'Shea, K.S., Chang, J.F. and Varani, J.: Identification of laminin domains involved in branching morphogenesis: Effects of anti-laminin monoclonal antibodies on mouse embryonic lung development. Develop. Biol. 1991;146:531-541.
6. Varani, J., Stoolman, L., Wang, T.L., Schuger, L., Flippen C., Dame, M., Johnson, K.J., Todd, R.F., Ryan, U.S. and Ward, P.A.: Thrombospondin production and thrombospondin-mediated adhesion in U937 cells. Exp. Cell Res. 1991;195:177-183.
7. Rao, R.C., Varani, J. and Soong, H.K.: FGF promotes corneal stromal fibroblast motility. Invest. Ophthalmol. 1992;8:77-81.
8. Petryniak, J., Varani, J., Ervin, P.R. and Goldstein, I.J.: Differential expression of glycoproteins containing α-D-galactosyl groups on normal human breast epithelial cells and MCF-7 human breast carcinoma cells. Cancer Lett. 1991;60:59-65.
9. Yamamoto, T., Varani, J., Soong, H.K. and Lichter, P.R.: Effects of 5-fluoruracil and mitomycin-C on cultured rabbit subconjunctival fibroblasts. Ophthalmology. 1991;97:1204-1210.
10. Weinberg, J.M., Venkatachalam, M.A., Roeser, N.F., Davis, J.A., Varani, J. and Johnson, K.J.: Amino acid protection of cultured kidney tubule cells against calcium ionophore-induced lethal cell injury. Lab. Invest. 1991;65:671-678.
11. Weinberg, J.M, Varani, J., Johnson, K.J., Roeser, N.A., Dame, M.K., Davis, J.A. and Venkatachalam, M.A.: Protection of human umbilical vein endothelial cells by glycine and structurally similar amino acids against calcium and hydrogen peroxide-induced lethal cell injury. Am. J. Path. 1992;140:457-472.
12. Mulligan, M.S., Varani, J., Dame, M.K., Lane, C.L., Smith, C.W., Anderson, D.C. and Ward, P.A.: Role of ELAM-1 in neutrophil-mediated lung injury in rats. J. Clin. Invest. 1991;88:1396-1406.
13. Varani, J., Inman, D.R., Gibbs, D.F., Fligiel, S.E.G. and Voorhees, J.J.: Modulation of Ca^{2+} levels in keratinocytes by all-trans retinoic acid. Pathobiology 1992;60:93-99.
14. Varani, J., Gendimenico, G.J., Shah, B., Gibbs, D.F., Capetola, R.J., Mezick, J.A. and Voorhees, J.J.: A direct comparison of the pharmacologic effects of retinoids on skin cells in vitro and in vivo. Skin. Pharmacol. 1991;4:254-261.
15. Fligiel, S.E.G., Inman, D.R., Talwar, H.S., Fisher, G.J., Voorhees, J.J. and Varani, J.: Modulation of growth in normal and malignant melanocytic cells by all-trans retinoic acid. J. Cutan. Pathol. 1992;19:27-33.
16. Varani, J., Jones, J., Dame, M.K., Sulavik, C., Gibbs, D.F. and Johnson, K.J.: Effects of all-trans retinoic acid on neutrophil-mediated endothelial cell injury and immune complex injury in rats. Am. J. Path. 1992;139:901-909.

17. Varani, J., Astrom, A., Griffiths, C.E.M. and Voorhees, J.J.: Induction of proliferation of growth-inhibited keratinocytes and fibroblasts by sodium lauryl sulfate: Comparison with all-trans retinoic acid. J. Invest. Dermatol. 1991;97:917-921.
18. Mulligan, M.S., Varani, J., Warren, J.S., Till, G.O., Smith, C.W., Anderson, D.C., Todd, R.F. Ward, P.A.: Role of β2 in integrins of rat neutrophils in complement and oxygen radical-mediated acute inflammatory injury. J. Immunol. 1992;148:1847-1857.
19. Varani, J, Dame, M.K., Gibbs, D.F., Taylor, C.G., Weinberg, J.M., Shayevitz, J. and Ward, P.A.: Human umbilical vein endothelial cell killing by activated neutrophils: Loss of sensitivity to injury is accompanied by decreased iron content during in vitro culture and is restored with exogenous iron. Lab. Invest. 66:708-714, 1992.
20. Varani, J., Taylor, C.G., Riser, B., Shumaker, D.K., Yeh, K-Y, Dame, M.K., Gibbs, D.F., Todd, R.F. III, Demler, F., Bromberg, J. and Killen, P.D.: Mesangial cell killing by leukocytes: Role of leukocyte oxidants and proteolytic enzymes. Kidney International, In Press.
21. Ginsburg, I., Misgave R, Pinson, A., Varani, J., Ward, P.A. and Kohen, R.: Synergism among oxidants, proteinases, phospholipases, microbial hemolysins, cationic proteins and cytokines: A possible major cause of cell and tissue injury in inflammation. Inflammation, In Press.
22. Ginsburg, I., Varani, J: CETAB: Influence on neutrophil production of oxygen radicals and chemiluminescence. Inflammation, In Press.
23. Situ, R., Inman, D.R., Fligiel, S.E.G. and Varani, J.: Effects of all-trans retinoic acid on melanocyte adhesion and motility. Dermatology, In Press.
24. Varani, J., Inman, D.R., Perone, P., Fligiel, S.E.G. and Voorhees, J.J. Retinoid toxicity of fibroblasts and epithelial cells is separable from growth-promoting activity. J. Invest. Dermatol, In Press.
25. Varani, J., Fligiel, S.E.G., Schuger, L., Perone, P., Inman, D.R., Griffiths, C.E.M. and Voorhees, J.J.: Effects of all-trans retinoic acid and Ca^{2+} on human skin in organ culture. Am. J. Pathol., In Press.
26. Huber, A.R., Ellis, S., Johnson, K.J., Dixit, V.M. and Varani, J.: Monocyte diapedesis through an in vitro vessel wall construct: Inhibition with monoclonal antibodies to thrombospondin. J. Leuk. Biol., In Press.
27. Varani, J., Sitrin, R.G. and Hillegas, W.: Expression of heterogeneous profiles of plasminogen activator and plasminogen activator inhibitor mRNA in human fibroblasts grown on different substrates. Cytotechnology, In Press.
28. Schuger, L., Varani, J., Killen, P.D., Skubitz, A.P.N. and Gilbride, K.: Laminin expression in the mouse lung increases with development and stimulates spontaneous organotypic rearrangement of mixed lung cells. Develop. Dynamics., In Press.

BOOKS AND CHAPTERS IN BOOKS:

1. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: Cytokines, Toxic oxygen products and cell injury. Molecular Aspects of Medicine, In Press.
2. Varani, J.: Leukocyte-endothelial cell interactions, in, Catravas, J. and Ryan, U. (eds.), Vascular Endothelium: Physiological Basis of Clinical Problems, In Press.
3. Varani, J.: Extracellular matrix production and squamous cell differentiation, in, Weiss, L., Buchanan, M. and Orr, F.W. (eds.), The Microcirculation and Cancer Metastasis, CRC Press Inc., Boca Raton, Florida, pp 1-22.
4. Ward, P.A., Warren, J.S., Johnson, K.J. and Varani, J.: Inflammation, oxygen radicals and tissue injury, in, K.J. Davies (ed), Oxidative Damage and Repair: Clinical, Biological and Medical Aspects, Pergamon Press, New York, New York, 1991.
5. Varani, J., Fligiel, S.E.G. and Voorhees, J.J.: All-trans retinoic acid modulation of proliferation and adhesion in epithelial cells and fibroblasts is associated with alterations in extracellular matrix production and Ca^{2+} metabolism, **in**, Retinoids, Saurat, J.H. (ed.)., Karger, Basel, Switzerland, Karger, New York, New York, 1991..

6. Varani, J. and Johnson, K.J.: Modulation of endothelial cell injury by cell-trans retinoic acid (RA): Role in anti-inflammatory effects of RA, in, Jesaitis, A. (ed.), Molecular Basis of Oxidative Damage by Leukocytes, CRC Press, In Press.
7. Johnson, K.J., Varani, J. and Smolen, J.E.: Neutrophil activation and function in health and disease, in, Coffey, R.D. (ed.), Granulocyte Response to Cytokines: Basic and Clinical Research, Marcell Dekker, Inc., New York, In Press.
8. Varani, J. and Ward, P.A.: Neutrophil-endothelial interactions, in, Maini, R.N. and Zvaifler, N.J. (eds.), Rheumatology, Gower Medical Publishing, London, In Press.
9. Varani, J. and Voorhees, J.J.: Treatment of human skin in organ culture with all-trans retinoic acid maintains cell viability and exracellular matrix and stimulates protein synthesis, in, Retinoids: New Trends in Research and Clinical Application, Accademia Nationale Di Scienzo Lettere e Arti, Palermo, Italy, pp 78, 1991.
10. Varani, J.: Non-collagenous glycoprotein components of the extracellular matrix in pulmonary fibrosis, in, R. Thrall and S.H. Phan (eds), `Pulmonary Fibrosis', Series Title: Lung Biology in Health and Disease, Marcel Dekker, Inc., New York, N.Y., In Press.

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

1. Varani, J., Yeh, K-Y, Shumaker, D., Dame, M.K., Riser, B. and Johnson, K.J.: Mesangial cell killing by leukocytes: Involvement of adhesion factors and role of leukocyte oxidants and proteolytic enzyme. FASEB J. 1992;A1908.
2. Dame, M.K., Murphy, H. and Varani, J.: Spontaneous injury to human umbilical vein endothelial cells increases during in vitro culture and is blocked with phorbol ester. FASEB J. 1992;A1620.
3. Shayevitz, J.R., Davidson, B., Williams, B. and Varani, J.: Differential effects of hydrogen peroxide and t-butyl hydroperoxide on inosital phosphate turnover in endothelial cells. FASEB J. 1992;A1618.
4. Taylor, C.G. and Varani, J.: Comparison of antioxidant protection in rat mesangial cells and endothelial cells: A possible explanation for differences in sensitivity to oxidant injury. FASEB J. 1992;A1058.
5. Fligiel, S.E.G>, Voorhees, J.J. and Varani, J.: Effects of retinoic acid on human skin in organ culture. J. Cutaneous Pathol.
6. Nickoloff, B.J., Mitra, R.S., Varani, J., Dixit, V.M., Polverini and P.J.: Psoriatic kertinocytes induced angiogenesis is inhibited by thrombospondin. J. Invest. Dermatol. 1992;98:560.
7. Varani, J., Perone, P., Inman, D.R., Fligiel, S.E.G. and Voorhees, J.J.: Retinoic acid and Ca^{2+} stimulate proliferation of human skin cells in monolayer and organ culture. J. Invest. Dermatol. 1992:98:645.
8. Varani, J.: Resistance of human umbilical vein endothelial cells to killing by neutrophils results from a loss of intracellular iron. J. Cell. Biochem. 1992;16A:44.
9. Johnson, K.J., Varani, J. and Ward, P.A.: Role of adhesion molecules in leukocyte-mediated glomerular injury. J. Cell Biochem. 1992;16A:42.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES:

A. Graduate students:
   1. Responsible during the current academic year for teaching activities for the following:
      a. Amy Gilardi, D.V.M., Postdoctoral Fellow.
      b. Michael S. Mulligan, M.D., Postdoctoral Fellow.
      c. Hedwig Murphy, M.D., Postdoctoral Fellow.
      d. Ara Vaporciyan, M.D., Postdoctoral Fellow.
      e. Susan A. Moore, M.S., Dissertation Committee member.
   2. Indirect supervision of four Research Scientists.
   3. Gross Autopsy Conference, 25 hours.

B. Undergraduate students:
      a. Lecture, College Honors Seminar 250, "Lessons from Polio, February 5, 1991, one hour.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. Principal Investigator, "Lung Immunopathology" (Training Grant), NHLBI NIH HL-07517 (5%), $310,376/year ($1,291,531/five years), 7/1/86-5/31/91.
B. Principal Investigator, "Lung Injury by Oxygen Metabolites (Merit)", NIGMS NIH-GM-29507 (20%), $221,266/year ($1,217,378), 7/1/92-6/30/9.
C. Principal Investigator, "Inflammatory Cells and Lung Injury", NHLBI NIH-HL-31963 (30%), Section I - $93,321/year, Section V - $58,941/year, Core A - $32,826/year ($1,010,734/five years), 3/1/89-2/28/94.
F. Co-Investigator, "Mechanisms of Glomerular and Tubular Injury", NIADDK NIH-DK39255 (5%), $45,000, 8/1/92-7/31/93.

PENDING:

A. Principal Investigator, "Oligosaccharides as Inflammatory Agents", NIH AI33189-01 (10%), $449,661/year ($2,192,115).

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

A. Chief, Section of General Pathology.
B. MSP Executive Committee.
C. Pathology Associates.

MEDICAL SCHOOL/HOSPITAL:

A. Ambulatory Care Strategic Planning Steering Committee, The University Hospitals, 1991--
B. Advisory Committee for the Howard Hughes Medical Institute, 1984--
C. Board of Directors, M-Care, 1986--
D. Center Advisory Committee for The University of Michigan Multipurpose Arthritis Center, 1987---
E. Clinical Quality Improvement Lead Team, 1991--
F. Committee to Review VA FTE's, The University of Michigan Medical School, October, 1988--
G. Dean's Advisory Council, 1985--
H. Dean's Council of Clinical Chairmen, 1985-1990
I. Executive Advisory Committee for Gene Expression and Gene Transfer in the Cardiovascular System, August, 1991--
J. Executive Director's Advisory Council, 1988--
K. Feasibility Study for Multifloor Medical Research Facility Attached to Medical Science II Committee, Director
L. Geriatric Center Steering Committee, 1990--
M. Guilford Upjohn Endowed Chair in Internal Medicine and Oncology, Department of Internal Medicine, Hematology and Oncology Unit, the Universit of Michigan, 1987--
N. Hospital Advisory Group, 1988-91
O. Internal Medicine Advisory Committee for the University of Michigan George M. O'Brien Renal and Urologic Center, 1991--
P. Medical Sciences Research Building (MSRB) Task Force, Chairman
Q. Medical Science Research Building III Project, September, 1990--
R. Medical Service Plan Advisory Committee, 1987--
S. Medical Service Plan Executive Committee, 1987-91
T. Michigan Diabetes Research and Training Center Policy Committee, 1981--
U. Michigan Eye Bank Research Review Committee, 1980--
V. National Task Force on Organ Transplantation, 1985--
W. Pathology Associates, 1980--
X. Presidential Initiatives Fund, The University of Michigan, March, 1987--
Y. University of Michigan Geriatrics Center Steering Committee, 1990--
Z. University of Michigan Medical School Executive Committee, September 1, 1990--

REGIONAL AND NATIONAL:

A. American Association for Advancement of Science.
B. American Association of Immunologists.
C. American Association of Pathologists.
    1. Nominating Committee, 1985-present.
    2. Executive Committee, Intersociety Pathology Council and Universities Associated for Research and Education in Pathology, Inc.
    3. Representative to the Universities Associated for Research and Education in Pathology, 1988-89.
    4. Steering Committee for the Federal Demonstration Project, 1990-1992.
    5. Future Directions Committee, 1989--.

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

E. American Federation for Clinical Research.
F. American Heart Association, Cardiopulmonary Division.
G. American Lung Association.
H. American Society for Clinical Investigation.
I. American Pathology Foundation.
J. American Thoracic Society.
K. Association of American Physicians.
L. Association of Pathology Chairmen.
M. Center for Alternatives to Animal Testing, Johns Hopkins University.
N. Cytogen, 1983--.
O. A. James French Society of Pathologists, 1988--.
P. Health Policy Agenda for the Amerian People, Advisory Committee.
Q. Institute of Medicine, July 1, 1990.
R. United States and Canadian Academy of Pathology, Inc.
   1. Council Member, April 1, 1986-1989.
   2. Member, Finance Committee, April 1, 1986-1990.
   3. Vice-President, 1990.
   4. President-Elect, 1991.
   5. President, 1992.

S. Mallinckrodt, Inc., Advisory Board, 1984--.
T. Michigan Society of Pathologists.
U. Michigan Thoracic Society, 1988--.
V. The New York Academy of Sciences.
   1. Committee on Human Rights, Correspondent.

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

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

V. OTHER RELEVANT ACTIVITIES:

EDITORIAL BOARDS:

A. American Journal of Pathology, Editorial Board, 1982--.
B. American Review of Respiratory Diseases, Consulting Editor, 1977--.
C. Archives of Pathology and Laboratory Medicine, Reviewer, 1973--.
D. Arthritis and Rheumatism, Consulting Editor, 1975--.
E. Cancer Research, Associate Editor, 1987--.
F. Clinical Immunology and Immunopathology, Consulting Editor, 1977--.

G. CRC Critical Reviews in Free Radical Research, Advisory Board, 1986--.
H. CRC Critical Reviews in Toxicology, Advisory Board, 1986--.
I. Experimental Cell Research, Consulting Editor, 1980--.
J. Experimental Lung Research, Consulting Editor, 1980--.
K. Human Pathology, Consulting Editor, 1980--.
L. Infection and Immunity, Editorial Board, 1978--.
M. Journal of Clinical Investigation, 1982--.
N. Journal of Experimental Cell Research, Consulting Editor.
O. Journal of Experimental Lung Research, Consulting Editor.
P. Journal of Experimental Pathology, 1986--.
Q. Journal of the Reticuloendothelial Society, Consulting Editor.
R. Journal of Clinical Investigation, Consulting Editor.
S. Laboratory Investigation, Editorial Board, 1981--.
T. Nature, Consulting Editor, 1980--.
U. New England Journal of Medicine, Consulting Editor, 1980--.
V. Journal of Critical Care, Editorial Board.
W. Review Committee for new Editor-in-Chief, Human Pathology, April 1987--.
X. Toxicologic Pathology, Editorial Board, 1988--.

INVITED LECTURES/SEMINARS:

1. Invited Lecturer, "The Role of Leukocyte Adhesion Molecules in Inflammatory Injury", Smithkline Beecham P.L.C., King of Prussia, Pennsylvania, July 7-8, 1991.
2. Invited Lecturer, "Kinin System: Mechanisms of Endothelial Cell Injury", First International Congress on Xenotransplantation, The Radisson Hotel Metrodome, University of Minnesota, Minneapolis, Minnesota, August 25-26, 1991.
3. Invited Lecturer, "Mechanisms of Oxidant Mediated Endothelial Cell Injury", in session, Ractive Oxygen Metabolites: Modulators of Microvascular Functions, at the Fifth World Congress for Microcirculation, Louisville, Kentucky, August 31-September 1, 1991.
4. Session Moderator (representing the American Board of Pathology) at the College of American Pathologists Foundation Conference VI, "2001: A Profile of the Pathologist", at the Grand Hotel, Mackinac Island, Michigan, September 5-8, 1991.
5. Lecturer, "Mediation of the Inflammatory Response", The University of Michigan Medical School, Pathology 580, Ann Arbor, Michigan, September 18, 1991.
6. Invited Lecturer and Participant, "Role of Adhesion Molecules in Inflammation" and "Mechanisms of Endothelial Cell Injury", Annual Retreat, Department of Pathology, University of Washington, Seattle, Washington, September 19-22, 1991.
7. Invited Lecturer, "Lung Injury by Toxic Oxygen Metabolites", and "Role of Adhesion Molecules in Leukocyte Recruitment into the Lung", Tenth Veterinary Respiratory Symposium, Comparative Respiratory Society, Kellogg Center, Michigan State University, East Lansing, Michigan, September 23, 1991.
8. Lecture, "Mediation of the Inflammatory Response", Pathology 580 course, General Pathology or Biomedical Scientists, September 18, 1991.
9. Invited Lecturer, "Biology of Free Radical Damage" and "Role of Leukocyte Adhesion Molecules in Tissue Injury", Indiana University, Department of Physiology and Biophysics Departmental Retreat, Mooresville, Indiana, October 15-16, 1991.
10. Sophomore Course Lecturer, "Inflammation", Department of Pathology, Medical College of Wisconsin, Milwaukee, Wisconsin, November 4, 1991.
11. Invited Research Seminar Lecturer, "Leukocyte Adhesion Molecules in the Inflammatory Response", Department of Pathology, Medical College of Wisconsin, Milwaukee, Wisconsin, November 5, 1991.
12 Invited Lecturer, "Molecular Mechanisms of Pulmonary Inflammation", Keystone Symposium, Inflammation, Growth, Regulatory Molecules and Atherosclerosis, Keystone, Colorado, January 13-16, 1992.

13. Invited Lecturer, "Pathology of Injury", in the Second Conference on the Immunocompromised Surgical Patient: Mechanisms and Therapy in Trauma and Burns, Snowbird, Utah, January 26-28, 1992.
14. Review the Department of Pathology (with Dr. Ramzi Cotran), The University of Chicago, Chicago, Illinois, February 10-12, 1992.
15. Invited Discussion Leader and Participant, "Allergy and Inflammatory Reactions", Fourth Conference: Physiological and Therapeutic Effects of Cytokines Conferences on Comparative Aspects of Host Parasite and Host-Tumor Relationships, Ein Gedi, Israel, February 15-21, 1992.
16. Visiting Professor, Department of Physiology, Louisiana State University Medical Center, Shreveport, Louisiana, March 1-2, 1992.
17. Consultant, Mock Site Visit, Department of Anesthesiology, the University of Alabama, Birmingham, Alabama, March 23-24, 1992.
18. Invited Lecturer, "Adhesion Molecules and Lung Inflammation", Department of Pathology, the University of Alabama, Birmingham, Alabama, March 24, 1992.
19. Visiting Professor, "Lung Inflammation and Cellular Adhesion", US-EPA Health Effects Research Laboratory, Research Triangle Park, North Carolina, April 16-17, 1992.
20. Invited Participant, Session 2, Environmental Disease, "Control Through Molecular Research", 75th Anniversary Celebration, Johns Hopkins University, Baltimore, Maryland, April 22-23, 1992.
21. Visiting Professor, "Adhesion Molecules and Lung Inflammation", Department of Pathology, The University of Alabama at Birmingham, Birmingham, Alabama, March 24, 1992.
22. Invited Participant, "The Role of Adhesion Molecules in Lung Inflammation", First Annual Raymond P. Ahlquist Lectureship Department of Pharmacology and Toxicology. The Medical College of Georgia, Augusta, Georgia, May 6-8, 1992.
23. Invited Participant, "The Role of Cytokines and Adhesion Molecules in Lung Inflammation", Third Wiggers-Bernard Conference on Shock, Sepsis and Organ Failure, Hotel Schloff Obermayerhofen, Vienna, Austria, May 16-21, 1992.
24. Invited Participant, "Potential Role of Nitric Oxide in Tissue Injury Seen at Sites of Acute and Chronic Inflammatory Reactions", Sandoz Forschungsinstitut Workshop, The Biology of Nitric Oxide; Session I, Biochemistry of Nitric Oxide, Vienna, Austria, May 21-22, 1992.
25. Invited Lecturer, "Role of White Blood Cells in Tissue Injury", Toronto '92 Canadian Society of Clinical Chemists, Toronto, Ontario, Canada, May 24-25, 1992.
26. Invited Lecturer, "Endocrine Response in the Critically Ill", Society of Critical Care Medicine (SCCM), San Antonio Convention Center, San Antonio, Texas, May 28-29, 1992.
27. Howard Hughes Medical Institute Review Panel for Postdoctoral Research Fellowships, Howard Hughes Medical Institute, Bethesda, Maryland, June 8-10, 1992.
28. Program Project Advisory Board Meeting, Section of Pulmonary and Critical Care Medicine, New England Deaconess Hospital, Harvard Medical School, Boston, Massachusetts, June 16, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Barker, J.N.W.N., Jones, M.L., Swenson, C.L., Sarma, V., Mitra, R.S., Ward, P.A., Johnson, K.J., Fantone, J.C., Dixit, V.M. and Nickoloff, B.J.: Monocyte chemotaxis and activating factor production by keratinocytes in response to IFN-γ. J. Immunol. 1991;146:1192-1197.
2. Guice,K.S., Oldham, K.T., Remick, D.G., Kunkel, S.L. and Ward, P.A.: Anti-tumor necrosis factor antibody augments edema formation in caerulein-induced acute pancreatitis. J.Surg.Res. 1991;51:495-499.
3. Hatherill, J.R., Till, G.O. and Ward, P.A.: Mechanisms of oxidant-induced changes in erythrocytes. Agents and Actions 1991:32;351-358.

4. Mulligan, M.S., Hevel, J.M., Marletta, M.A. and Ward, P.A.: Tissue injury caused by deposition of immune complexes is L-arginine dependent. Proc. Natl. Acad. Sci. 1991;88:6338-6342.
5. Mulligan, M.S., Varani, J., Dame, M.K., Lane, C.L., Smith, C.W., Anderson, D.C. and Ward, P.A.: Role of endothelial-leukocyte adhesion moleucle 1 (ELAM-1) in neutrophil-mediated lung injury in rats. J. Clin. Invest. 1991;88;1396-1406.
6. Shayevitz, J.R., Varani, J., Ward, P.A. and Knight, P.R.: Halothane and isoflurane increase pulmonary artery endothelial cell sensitivity to oxidant-mediated injury. Anest. 1991;74:1067-1077.
7. Till, G.O., Friedl, H.P. and Ward, P.A.: Lung injury and complement activation: Role of neutrophils and xanthine oxidase. Free Rad. Biol. Med. 1991;10:379-386..
8. Varani, J., Ginsburg, I., Gibbs, D.F., Mukhopadhyay, P.S., Sulavik, C., Johnson, K.J., Weinberg, J.M., Ryan, U.S. and Ward, P.A.: Hydrogen peroxide-induced cell and tissue injury: Protective effects of Mn^{2+}. Inflammation 1991;15:291-301.
9. Varani, J., Stoolman, L., Wang, T., Schuger, L., Flippen, C., Dame, M., Johnson, K.J., Todd, R.F., III, Ryan, U.S. and Ward, P.A.: Thrombospondin production and thrombospondin-mediated adhesion in U937 cells. Exp. Cell Res. 1991;195:177-182.
10. Walker, B.A.M., Hagenlocker, B.E., Douglas, V.K., Tarapchak, S.J. and Ward, P.A.: Nucleotide responses of human neutrophils. Lab. Invest. 1991;64:105-112.
11. Walker, B.A.M., Hagenlocker, B.E., Stubbs, E.B., Jr., Sandborg, R.R., Agranoff, B.W. and Ward, P.A.: Signal transduction events and FcγR engagement in human neutrophils stimulated with immune complexes. J. Immunol. 1991;146:735-741.
12. Walker, B.A.M., Hagenlocker, B.E. and Ward, P.A.: Superoxide responses to formyl-methionyl-leucyl-phenylalanine in primed neutrophils: Role of intracellular and extracellular calcium. J. Immunol. 1991;146:3124-3131.
13. Walker,B.A.M., Seiler, A.J., Owens, C.A., Hagenlocker, B.E. and Ward, P.A.: Absence of FMLP receptors on rat macrophages. J. Leukocyte Biol. 1991;50:600-606.
14. Ward, P.A.: Mechanisms of endothelial cell killing by H_20_2 or products of activated neutrophils. Amer. J. Med. 1991;91(Suppl. 3c):89S-94S.
15. Ward, P.A.: Review Article: Mechanisms of endothelial cell injury. J. Lab. Clin. Med. 1991;118:421-426.
16. Ward, P.A. and Mulligan, M.S.: New insights into mechanisms of oxyradical and neutrophil mediated lung injury. Klin. Wochenschr. 1991;69:1009-1011.
17. Ward, P.A., Till, G.O. and Warren, J.S.: Pathophysiology of leukocyte-mediated tissue injury. J. Crit. Care 1991;6:112-116.
18. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines, toxic oxygen products and cell injury. Molec. Aspects Med. 1991;12:169-174.
19. Ward, P.A.: Overview of the process of cellular injury in interstitial lung disease. Chest 1991;100:230-235.
20. Ward, P.A., Till, G.O. and Warren, J.: Pathophysiology in leukocyte-mediated tissue injury. J. Crit. Care 1991;6:112-116.
21. Yu, G.H., Tarapchak, Walker, B.A.M. and Ward, P.A.: Adenosine-5'-0-(3-thiotriphosphate) (ATPSγS) binding to human neutrophils: Evidence for a common nucleotide receptor. Lab. Invest. 1991;65:316-323.
22. Jesaitis, A.J., Quinn, M.T., Mukherjee, G., Ward, P.A. and Dratz, E.A. Meeting Summary, The Molecular Basis of Oxidative Damage by Leukocytes, Big Sky, Montana, in Jesaitis, A.J. and Dratz, E.A. (eds), The Molecular Basis of Oxidative Damage by Leukocytes, CRC Press, Boca Raton, Florida, pp. 1-8,1992.
23. Mulligan, M.S., Varani, J., Warren, J.S., Till, G.O., Smith, C.W., Anderson, D.C., Todd, R.F.,III and Ward, P.A.: Roles of β2 inegrins of rat neutrophils in complement- and oxygen radical-mediated acute inflammatory reactions. J. Innumol. 1992;148:1847-1857.
24. Mulligan, M.S., Warren, J.S., Smith, C.W., Anderson, D.C., Yeh, C.G., Rudolph, A.R. and Ward, P.A.: Lung injury after deposition of IgA immune complexes: Requirements for CD18 and L-arginine. J. Immunol. 1992;148:3086-3092.
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31. Mulligan, M.S., Johnson, K.J., Smith, C.W., Todd, R.F., Iyasaka, 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.A.S.N., In Press.
32. Mulligan, M.S., Polley, M.J., Bayer, R.J., Nunn, M.F., Paulson, J.C. and Ward, P.A.: Neutrophil-dependent acute lung injury: Requirement for P-selection (GMP-140). J. Clin. Invest., Submitted.
33. Mulligan, M.S., Smith, C.W., Anderson, D.C. and Ward, P.A.: *In vivo* recruitment of neurtrophils: Consistent requirements for L-arginine and variable requirments for adhesion molecules. Amer. J. Pathol., In Press.
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35. Mulligan, M.S., Varani, J., Warren, J.S., Till, G.O., Smith, C.W., Anderson, D.C., Todd, R.F., III and Ward, P.A.: Roles of β2 integrins of rat neutrophils in complement- and oxygen radical-mediated acute inflammatory injury. J. Immunol., In Press.
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43. Ward, P.A.: The wound environment - Local and systemic perturbations: Inflammation and the burn wound. J. Burn Care & Rehab., In Press.
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45. Ward, P.A. and Johnson, K.J.: Lung inflammatory mechanisms. J. Human Path., In Press.
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BOOKS/CHAPTERS IN BOOKS:

1. Johnson, K.J., Chensue, S.W., Kunkel, S.L. and Ward, P.A.: Immunopathology in essential pathology, in, Rubin, E. and Farber, J.L. (eds), Essential Pathology, J.B. Lippincott, Inc., Philadelphia, 1991.

2. Ward, P.A., Morganroth, M.L., Senior, R.M., and Campbell, E.J.: Inflammatory mediators of pulmonary tissue injury, Chapter 13, in, Bray, M. and Anderson, W. (eds.), Mediators of Pulmonary Inflammation, Chapter in series, Lung Biology in Health and Disease, pp. 533-591, 1991.
3. Ward, P.A. and Warren, J.S.: Neutrophils, macrophages and cytokines, in, Baggiolini, M., Pozzi, E., and Semenzato, G. (eds.), Neutrophils, Lymphocytes and Lung, Meetings on "Pathophysiology of Pulmonary Cells", Masson, Milan, Italy, pp.31-36, 1991.
4. Ward, P.A., Warren, J.S., Johnson, K.J. and Varani, J.: Inflammation: Oxygen radicals and tissue injury, in, Davies, K.J.A. (ed.), Oxidative Damage and Repair: Clinical, Biological and Medical Aspects, The 5th Biennial meeting of the International Society for Free Radical Research, November 14-20, 1990, Pasadena, California, Pergamon Press, pp.642-646, 1991.
5. Warren, J.S., Johnson, K.J. and Ward, P.A.: 7.2.4 Consequences of oxidant injury, in, Crystal, R.G., West, J.B., Barnes, P.J., Cherniack, N.S. and Weibel, E.R. (eds.), The Lung: Scientific Foundations, Raven Press, New York, pp. 1829-1838, 1991.
6. Warren, J.S., Ward, P.A. and Johnson, K.J.: The inflammatory response, in, Williams, W.J. (ed.), Hematology, 4th Edition, McGraw-Hill, New York, New York, pp. 63-70, 1990.
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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. Kunkel, S.L. and Ward, P.A.: The complement system , in, Bellanti, J.A. (ed.), Immunology, 3rd Ed, In Press.
13. 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.
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16. Mulligan, M.S. and Ward, P.A.: Inflammatory mechanisms of cellular and tissue damage, in, Cooper, G., Duldey, 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.
17. Simon, R.H. and Ward, P.A.: Adult respiratory distress syndrome, in, Gallin, J.I., Goldstein, I.M. and Snyderman, R. (eds.), Inflammation: Basic Principles and Clinical Correlates, Raven Press, In Press.
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19. Till, G.O. and Ward, P.A.: Role of complement and neutrophils in experimental acute lung injury, in, Nuki, G. and Zvaifler, M. (eds.), The Lungs and Rheumatic Disease, Butterworths International Medical Reviews, Rheumatology 3, Butterworth and Co., England, In Press.
20. Till, G.O. and Ward, P.A.: The lung and rheumatic disease: Role of complement, in, Butterworth's International Medical Reviews, Rheumatology 3, In Press.
21. Till, G.O. and Ward, P.A.: Thermal injury and lung tissue damage, in, Critical Topics in Pulmonary Pharmacology and Toxicology, In Press.
22. 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.

23. 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.
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25. Varani, J. and Ward, P.A.: The immonubiology of tumor cell chemotaxis, in, Waters, H. (ed.), Handbook of Cancer Immunology, Garland STPM Press, In Press.
26. Varani, J., Mulligan, M.S. and Ward, P.A.: The vascular endothelium and acute inflammation, in, Maini, R.N. and Zvaifler, N.J. (eds.), Rheumatology, Gower Medical Publishing, London, England, In Press.
27. Ward, P.A.: Inflammation, Chapter 12, in, Bellanti, J.A. (ed.), Immunology in Medicine, W.B. Saunders Company, Philadelphia, Pennsylvania, In Press.
28. 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.
29. 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.
30. 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.
31. 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.
32. 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.
33. Ward, P.A., Mulligan, M.S. and Warren, J.S.: Neutrophils, cytokines, oxygen radicals and lung injury, in, The Immune Consequences of Trauma, Shock, and Sepsis - Mechanisms and Therapeutic approaches, Proceedings of the Symposium, Munich, Germany, Springer-Verlag, In Press.
34. Ward, P.A. and Till, G.O.: The autodestructive consequences of thermal injury, Ninnemann, J. (ed.), The Immune Consequences of Thermal and Traumatic Injuries, In Press.
35. Ward, P.A., Warren, J.S. and Johnson, K.J.: Oygen radicals, inflammation and tissue injury, in, Pryor, W. and Godber, S.L. (eds.), Free Radical Biology and Medicine, In Press.
36. 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 Consequents of Trauma, Shock and Sepsis: Mechanisms and Therapeutic Approaches, In Press.
37. Ward, P.A., Warren, J.S., Till, G.O., Varani, J. and Johnson, K.J.: Modification of disease by preventing free radical formation: A new concept in pharmacologic intervention, in, Hershko, C. (ed), Iron Chelating Therapy, Bailliere Tindall Limited, Harcourt Brace Jovanovich, Publishers, London, England, In Press.
38. 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.
39. Ward, P.A., Warren, J.S., Varani, J. and Johnson, K.J.: PAF, cytokines, toxic oxygen products and cell injury, in, Molecular Aspects of Medicine, Proceedings of the VIIth Annual Inflammation Meeting, Birmingham, United Kingdom, Pergammon Press, In Press.
40. Warren, J.S., Johnson, K.J., Till, G.O. and Ward, P.A.: Mechanisms of oxygen radical-mediated acute tissue injury: *In vivo* studies, in, Proceedings of Enzyme Meeting, July, 1986, In Press.
41. 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.
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45. Warren, J.S., Ward, P.A. and Johnson, K.J.: Immune complex injury, in, Cantor, J.D. (ed.), CRC Handbook of Animal Models of Pulmonary Disease, CRC Press, Boca Raton, Florida, 1987, In Press.
46. Warren, J.S., Ward, P.A. and Johnson, K.J.: The inflammatory response, Chapter 8, in, Williams, W.J. (ed.), Hematology, 4th edition, 1991.
47. 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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ABSTRACTS, BOOK REVIEWS, PUBLISHED LETTERS TO THE EDITOR, MISCELLANEOUS PUBLICATIONS IN UNREFEREED JOURNALS:

1. Craig, R.A., Walker, B.A.M., Hagenlocker, B.E. and Ward, P.A.: FMLP-induced superoxide responses in PAF primed human neutrophils in the absence of increased intracellular Ca^{2+}. FASEB J. 1991:5;A587.
2. Dame, M.K., Varani, J., Weinberg, J.M. and Ward, P.A.: Neutrophil killing of human umbilical vein endothelial cells is oxygen radical-mediated and enhanced by TNF–α. FASEB J. 1991:5;A888.
3. Jones, M.L., Grande, J.P., Killen, P.D., Yoshimura, T. and Ward, P.A.: Regulation of monocyte chemoattractant protein (MCP-1) mRNA expression in rat mesangial cells. FASEB J. 1991:5;A975.
4. Jones, M.L., Ward, P.A. and Warren, J.S.: Cloning of rat MCP1 and its expression in a baculovirus system. Third International Workshop on Cytokines Meeting from November 10 to 14, 1991, in Stressa, Italy.100.
5 Mahrougui, M., Till, G.O. and Ward, P.A.: Diverse signal-transduction pathways in rat pulmonary artery endothelial cells. FASEB J. 1991:5;A530.
6. Murphy, H.S., Shayman, J.A. and Ward, P.A.: Signal transduction in endothelial cells stimulated by C5a. FASEB J. 1991:5;A1340.
7. Owens, C.A., Grande, J.P., Yu, G.H., Killen, P.D. and Ward, P.A.: Adenine nucleotide binding to cultured human mesangial cells. FASEB J. 1991:5;A909.
8. Varani, J., Gibbs, D.F., Mukhopadhyay, P.S., Sulavik, C., Johnson, K.J., Weinberg, J.M., Ginsburg, I. and Ward, P.A.: Hydrogen peroxide-induced cell and tissue injury: Protective effects of manganese. J. Cell Biochem. 1991;Suppl. 15c:223.
9. 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. 1991:5;A887.
10. Walker, B.A.M., Owens, C.A. and Ward, P.A.: Absence of FMLP receptors in rat macrophages. FASEB J. 1991:5;A549.
11. Mulligan, M.S., Lin, H., Ward, P.A. and Bolling, S.F.: Expression of adhesion molecules in cardiac and pulmonary allografts. International Society for Heart Transplantation, April 2-4, 1992, San Diego, California.
12. Jones, M.L., Flory, C.M., Fantone, J.C., Ward, P.A. and Warren, J.S.: Cloning and expression of functional rat monocyte chmoattractant protein I/JE in a baculovirus system. FASEB J. 1992:6;A1146.
13. Kunkel, R.G., Mulligan, M.S., Johnson, K.J., Riggs, J.K. and Ward, P.A.: Morphologic studies on inhibition of acute glomerulonephritis by anti-TNF_{α} antibody. FASEB J. 1992:6;A1606.
14. Mulligan, M.S., Johnson, K.J., Tamatani, T., Miyasaka, M., Anderson, D.C., Smith, C.W. and Ward, P.A.: Requirements for CD18 and ICAM-1 in nephrotoxic nephritis. FASEB J. 1992:6;A1689.
15. Murphy, H.S., Seiler, A. and Ward, P.A.: Protein kinase C activity in endothelial cells stimulated by C5a and TNF_{α}. FASEB J. 1992:6;A1633.

16. Vaporciyan, A.A., Jones, M.L. and Ward, P.A.: Rapid determination of neutrophil to endothelial cell adhesion *in vitro* using fluorescent labeling of cells. FASEB J. 1992:6;A1821.
17. Ward, P.A. and Mulligan, M.S. Molecular determinants of pulmonary inflammation. J. Cell Biochem. 1992:16A;2

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Director, Clinical Immunopathology Laboratory; September 1989-present.
B. Autopsy pathology, staff coverage (1 week plus one weekend)
C. Associate Director, Division of Clinical Pathology/Clinical Laboratories, January 1992-present.

II. TEACHING ACTIVITIES:

A. Pathology 631 (60 contact hours).
B. ICS 600 lectures:
   1. "Autoimmunity" (10/29/91).
   2. "Multiple myeloma" (1/27/92).
C. Clinical Pathology Grand Rounds:
   1. "Antiphospholipid antibody syndrome" (1/3/92).
   2. "Humoral immunodeficiencies" (1/10/92).
   "Monocyte chemoattractant protein 1" (1/24/92).
D. Immunopathology journal club (1 hour; biweekly).
E. Immunopathology signout: Pathology residents, M-4 medical students, EMU medical technology students (daily; every other week).
F. Microbiology/Immunology 505 (2 contact hours).
   1. "The acute inflammatory response" (2/7/92; 2/10/92).
G. Supervision of research activities for:
   1. Craig Flory, Ph.D. (postdoctoral fellow); (6/15/90-present).
   2. Peter A. Barton (M-2 medical student); (6/1/90-8/25/91) (sponsored by American Heart Association of Michigan summer fellowship).
   3. Sanjiv Ghogale (Junior undergraduate; University of Michigan); (1/15/92-present) (sponsored by Student Biomedical Research Program).
   4. Daniel Reznick; (5/15/92-present).
   5. Jeffrey Pearson, M.D. (Pathology resident); (12/2/91-present).
   6. Barbara Markey, M.D. (Pathology resident); (3/12/92-present).

III. RESEARCH ACTIVITIES:

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

SPONSORED SUPPORT:

A. Principal Investigator, NIH (R29-HL40526), (50% effort), "Monocyte-macrophage cytokines in immune complex lung injury": 4/1/89-3/31/94 ($350,000; direct costs).
B. Biomedical Research Support Grant; (5% effort), "Homozygous C5 deficiency in the endotoxin-triggered shock response": 5/1/91-7/1/92 ($8,000) (pilot study).
C. Principal Investigator, American Heart Association of Michigan Grant-in-Aid, (10% effort), "Activated endothelium influences monocyte function": 7/1/91-6/30/92 ($25,500; direct costs).
D. Prinicpal Investigator, NIH(RO1-HL48287) (40% effort), "Monocyte chemoattractant protein 1 in pulmonary granulomatosis": 4/1/92-3/31/95 ($470,623; direct costs).

IV. ADMINISTRATIVE ACTIVITIES:

MEDICAL SCHOOL:

A. Medical school admissions committee.
B. Interviewer, Medical Scientist Training Program.

DEPARTMENTAL:

A. Interviewer of Pathology Residency Candidates, 1989-present.
B. Interviewer of Pathology Graduate Program Candidates, 1990-present.
C. Selection Committee for Pathology Residents, 1991-present.
D. Task Force on Budget Reduction for the Clinical Laboratories, 1991-1992.
E. Coordinator for revised Resident Training in Clinical Pathology, 1992-present.
F. M-care/M-Labs Quality Improvement Committee, 1992.
G. Proficiency Testing Committee, 1992.

REGIONAL AND NATIONAL:

A. Ad hoc referee for American Journal of Pathology, Laboratory Investigation, Human Pathology, Journal of Applied Physiology, Lung, Blood, Journal of Laboratory and Clinical Medicine, Pediatric Research, Journal of Leukocyte Biology, American Review of Respiratory Disease, Chest, Journal of Pharmacology and Experimental Therapeutics, Circulation, Ophthalmology, American Journal of Respiratory Cell and Molecular Biology, Clinical Immunology and Immunopathology, Circulation Research, Journal of Immunology, Surgery, Reviews of Infectious Diseases, Infection and Immunity, and Experimental Lung Research.
B. Preparation of Immunopathology Subspecialty Board Exam Questions, 1990-present.
C. NIH site visit: General Clinical Research Center; Stanford University, Palo Alto, CA; August 20-21, 1991.
D. College of American Pathologists Inspection Team, Indiana University Hospitals, Indianapolis, IN, October 15-16, 1991.

V. INVITED LECTURES/SEMINARS:

1. Warren, J.S.: Monocyte chemoattractant protein 1 in the pathogenesis of monocyte/macrophage mediated pulmonary vasculitides in the rat. Cleveland Clinic Research Institute, Cleveland, Ohio, February 24, 1992.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Warren, J.S.: Intrapulmonary interleukin 1 mediates acute immune complex alveolitis in the rat. Biochem. Biophys. Res. Commun. 1991;175:604-610.
2. Barker, J.N.W.N., Jones, M.L., Mitra, R.S., Crockett-Torabe, E., Fantone, J.C., Kunkel, S. L., Warren, J.S., Dixit, V.M. and Nickoloff, B.J.: Modulation of keratinocyte-derived interleukin-8 which is chemotactic for neutrophils and T lymphocytes. Am. J. Pathol. 1991;139:869-876.
3. Warren, J.S.: Disparate roles for TNF in the pathogenesis of acute immune complex alveolitis and dermal vasculitis. Clin. Immunol. Immunopathol. 1991;61:249-259.
4. Warren, J.S., and Barton, P.A.: In vitro analysis of pulmonary inflammation using rat lung organ cultures. Exp. Lung Res. 1992;18:55-67.
5. Mulligan, M.S., Varani, J., Warren, J.S., Till, G.O., Smith, C.W., Anderson, D.C., Todd, R.F. Ward, P.A.: Roles of β2 integrins of rat neutrophils in complement-and oxygen radical-mediated acute inflammatory reactions. J. Immunol. 1992;148:1847-1857.
6. DeForge, L.E., Kenney, J.S., Jones, M.L., Warren, J.S. and Remick, D.G.: Biphasic production of IL-8 in LPS-stimulated human whole blood. Separation of LPS-cytokine-stimulated components using anti-TNF and anti-IL-1 antibodies. J. Immunol. 1992; 148:2133-2141.
7. Jones, M.L. and Warren, J.S.: Monocyte chemoattractant protein 1 in a rat model of pulmonary granulomatosis. Lab. Invest. 1992;66:498-503.
8. Mulligan, M.D., Warren, J.S., Smith, C.W., Anderson, D.C., Yeh, G., Rudolph A. and Ward, P.A.: Lung injury following deposition of IgA immune complexes: Requirements for CD18 and L-arginine. J. Immunol. 1992;148:3086-3902.
9. Warren, J.S.: Relationship between for interleukin 1b and platelet-activating factor in the pathogenesis of acute immune complex alveolitis in the rat. Am. J. Pathol., In Press.
10. Brieland, J., Jones, M., Clarke, S., Warren, J. and Fantone, J.: Effect of acute inflammatory lung injury on the expression of monocyte chemoattractant protein 1 (MCP) in rat alveolar macrophages. Am. J. Respir. Cell. Molec. Bio., In Press.
11. Jones, M.L., Mulligan, M.S., Flory, C.M., Ward, P.A. and Warren, J.S.: Monocyte chemoattractant protein 1/JE mediates monocyte/macrophage-dependent IgA immune complex alveolitis in the rat. J. Immunol., In Press.

SUBMITTED FOR PUBLICATION:

1. McCurry, K.A., Campbell, D.A.Jr., Warren, J.S., Seales, W.E. and Remick, D.S.: TNF, IL-6 and the acute phase response following hepatic ischemial reperfusion. Submitted for publication.
2. Elkins, T.E., Warren, J.S., Portz, D. and McNeeley, S.G.: The interaction of peritoneal macrophages and current adhesion-preventing solutions in the production of oxygen free radicals and the early inflammatory response. Submitted for publication.
3. Jacobs, J.C., McNeeley, S.G., Elkins, T.E., Warren, J.S. and Hoeft-Loyer, C.M.: Rabbit model for polymicrobial upper genital infections. Submitted for publication.
4. Barton, P.A. and Warren, J.S.: Terminal complement components modulate the systemic tumor necrosis factor response in murine endotoxic shock. Submitted for publication.
5. 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 chemotactic protein 1 gene expression and secretion in rat pulmonary alveolar macrophages by lipopolysaccharide, tumor necrosis factor-α, and interleukin-1b. Submitted for publication.
6. Flory, C.M., Jones, M.L., and Warren, J.S.: Monocyte chemoattractant protein 1 is required for pulmonary granuloma formation in the rat. Submitted for publication.

BOOKS/CHAPTERS IN BOOKS:

1. Keren, D.F. and Warren, J.S.: Diagnostic Immunology: Laboratory Diagnosis of Immunologic Diseases, Williams and Wilkins, Baltimore, Maryland, 1992.
2. 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.
3. 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.
4. Warren, J.S.: Role of cytokines in experimental lung injury, in, Remick, D.G. and Kunkel, S.L. (eds.), Cytokines in Health and Disease, Marcel Dekker, Inc., New York, New York, In Press.
5. 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, Proceedings of the 5th Biennial Meeting of the International Society for Free Radical Research, Pasadena, California, Pergammon Press, In Press.
6. Ward, P.A., Mulligan, M.S. and Warren, J.S.: Neutrophils, cytokines, oxygen radicals and lung injury, in, The Immune Consequences of Trauma, Shock and Sepsis - Mechanisms and Therapeutic Approaches, Proceedings of the Symposium. Munich, Germany, Springer-Verlag, In Press.
7. Warren, J.S. and Ward, P.A.: Role of cytokines in pulmonary diseases, in, Gearing, A., Rossio, J., and Oppenheim. J.J. (eds), Clinical Applications of Cytokines: Role in Pathogenesis, Diagnosis, and Therapy, Oxford University Press, Oxford, U.K., In Press.
8. Warren, J.S.., Johnson, K.J. and Ward, P.A. Consequences of oxidant injury, in, Crystal, R.G., and West, J.B. (eds,), Lung Injury, Raven Press, New York, New York, pp 69-78, 1992.

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

1. Warren, J.S.: Intrapulmonary interleukin 1 triggers endogenous platelet-activating factor in acute immune complex alveolitis. American Heart Association of Michigan, Ann Arbor, Michigan, September 12, 1991 (abstract).
2. Brieland, J., Jones, M., Clarke, S., Warren, J. and Fantone, J.: Expression of monocyte chemoattractant protein 1 (MCP1) by rat pulmonary alveolar macrophages during acute inflammatory lung injury., Soc. Leukocyte Biol., Aspen, Colorado, September 28-October 1, 1991 (abstract).
3. Barton, P.A. and Warren, J.S.: C5 or C5-dependent complement components modulate the TNF-mediated systemic response to endotoxin infusion in mice, University of Michigan Student Biomedical Research Forum, Ann Arbor, Michigan, October 8, 1991.
4. Barton, P.A. and Warren, J.S.: C5 or C5-dependent complement components modulate the TNF-mediated systemic response to endotoxin infusion in mice, Cardiovascular Research Forum, American Heart Association of Michigan, Ann Arbor, Michigan, October 25, 1991.
5. Jones, M.L., Ward, P.A. and Warren, J.S.: Cloning of rat monocyte chemoattractant protein 1 (MCP1) and its expression in a baculovirus system, Third International Workshop on Cytokines, Stresa, Italy, November 10-14, 1991 (abstract).
6. Remick, D. G., Kenney, J., Warren, J.S., Jones, M.L. and DeForge, L.: TNF and IL-1 account for the biphasic pattern of IL-8 production in LPS-stimulated human whole blood, Third International Workshop on Cytokines, Stresa, Italy, November 10-19, 1991 (abstract).
7. Warren, J.S., Jones, M.L. and Ward, P.A. Cloning of rat monocyte chemoattractant protein 1 (MCP1) and its expression in a baculovirus system: analysis of MCP 1 in rat models of human disease, Keystone Symposium on Inflammation, Growth Regulatory Molecules and Atherosclerosis, Keystone, Colorado, January 16, 1992 (abstract).

8. Jones, M.L., Flory, C.M., Fantone, J.C., Ward, P.A. and Warren, J.S.: Cloning and expression of functional rat monocyte chemoattractant protein I/JE in a baculovirus system. FASEB, 1992 (abstract).
9. Miller, B.F. and Warren, J.S.: Intrapulmonary interleukin 1 triggers endogenous platelet activating factor in acute immune complex alveolitis. FASEB, 1992 (abstract).
10. Warren, J.S. and Barton, P.A.: C5 or C5-dependent complement components modulate the TNF-mediated systemic response to endotoxin infusion in mice. FASEB, 1992 (abstract).
11. Flory, C.M., Jones, M.L. and Warren, J.S.: Analysis of MCP1 expression during glucon induced pulmonary vasculitis in the rat. FASEB, 1992 (abstract).

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

A. Chief, Laboratory Service, Department of Veterans Affairs Medical Center, Ann Arbor, Michigan and Vetrans Administration Outpatient Clinic, Toledo, Ohio.
B. Consultant for referred bone pathology cases at University of Michigan.
C. Surgical pathology, Department of Veterans Affairs Medical Center.
D. Autopsy pathology, Department of Veterans Affairs Medical Center.
E. Cytopathology - occasional coverage, Department of Veterans Affairs Medical Center.

II. TEACHING ACTIVITIES:

A. Director of program for house officers at Department of Veterans Affairs Medical Center in surgical pathology, autopsy pathology, and electives.
B. Clinicopathologic conference - monthly, Department of Veterans Affairs Medical Center.
C. Department of Veterans Affairs Medical Center Tumor Board - weekly.
D. Dental Student lectures (three) in bone pathology.
E. Medical student lectures (two) in bone pathology.
F. Medical student - second year pathology laboratory.
G. Medical student - fourth year rotation at the Department of Veterans Affairs Medical Center.
H. Gross pathology seminar for house officers at University of Michigan.

III. RESEARCH ACTIVITIES:

COOPERATIVE STUDIES:

Ongoing: With Environmental Epidemiology Service, Department of Veterans Affairs, Agent Orange and non-Hodgkin's lymphoma.

SPONSORED SUPPORT: None.

IV. ADMINISTRATIVE ACTIVITIES:

LOCAL:

A. Overall responsibility for Department of Veterans Affairs Medical Center Laboratory Service and for Laboratory at Department of Veterans Affairs Outpatient Clinic, Toledo, Ohio.
B. Executive Faculty, The University of Michigan Medical School.
C. Admissions Committee, The University of Michigan Medical School.
D. Clinical Executive Board, Department of Veterans Affairs Medical Center.
E. Dean's Committee, Department of Veterans Affairs representative.

F. Quality Assurance Board, Department of Veterans Affairs Medical Center.
G. Professional Standards Board, Department of Veterans Affairs Medical Center.
H. Radiation Safety Committee, Department of Veterans Affairs Medical Center.
I. Pharmacy and Therapeutic Committee, Department of Veterans Affairs Medical Center.
J. Resident Selection Committee, University of Michigan Department of Pathology.

REGIONAL AND NATIONAL:

A. Red Cross Medical Advisory Board, Southeastern Michigan Region.

V. OTHER RELEVANT ACTIVITIES:

A. Inspector for College of American Pathologists Inspection and Accreditation Program.
B. Deputy Medical Examiner, Washtenaw County.

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

1. Levy, D.I., Bucci, M.N., Weatherbee, L. and Changler, W.F.: Intradural extramedullary ganglioneuroma: Case report and review of the literature. Surg. Neurol. 1992;37:216-8

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES: None.

II. TEACHING ACTIVITIES:

MEDICAL SCHOOL/HOSPITALS:

A. Tutor, Microbiology small group session.
B. Lecturer, Pathology 581.
C. Organizer and discussion leader of seminar on Ethics in Science -Cellular and Molecular Biology Training Program.
D. Supervision of two postdoctoral fellows (Jie Wu and Linghua Wang).
E. Member, Program Committee - Cellular and Molecular Biology Training Program.
F. Member, Program and Examination Committees, Graduate Program in Pathology.
G. Member, dissertation committees for two graduate students.

III. RESEARCH ACTIVITIES:

SPONSORED SUPPORT:

A. American Cancer Society, Mutants for DNA Enzymes, NP770-T. Principal Investigator
B. National Science Foundation, Prevention and Repair of DNA Damage in Bacteria, DMB-8922562. Principal Investigator.

PROJECTS UNDER STUDY:

A. The consequences of replacing thymine with uracil in DNA.
B. A gene of *Escherichia coli* affecting DNA and pantothenate synthesis.
C. A superoxide response regulation of *Escherichia coli*.

IV. ADMINISTRATIVE ACTIVITIES:

DEPARTMENTAL:

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

REGIONAL AND NATIONAL:

A. Ad hoc grant reviewer for National Science Foundation
B. Referee for the following journals:
   1. Microbiological Reviews.
   2. Journal of Bacteriology.

3. Molecular and General Genetics.
4 Biochemistry.

V. OTHER RELEVANT ACTIVITIES:

INVITED LECTURES/SEMINARS:

1. University of Vermont College of Medicine, Department of Microbiology and Molecular Genetics
2. Wayne State University, Department of Chemistry.
3. Michigan State University, Genetics Program.
4. Parke-Davis Laboratories.
5. Albany Conference, "Molecular Responses to Oxygen".

VI. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS:

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

BOOKS/CHAPTERS IN BOOKS:

1. Weiss, B. and Wu, J.: Control of a superoxide response regulon of *Escherichia coli*, in, Davies, K.J.A. (e Oxidative Damage & Repair: Clinical, Biological, and Medical Aspects, Pergamon, New York, 1992, pp 191.

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

ANNUAL DEPARTMENTAL REPORT
1 JULY 1991 - 30 JUNE 1992

I. CLINICAL ACTIVITIES:

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

II. TEACHING ACTIVITIES

A. Sophomore Medical Class:
   1. Pathology 600 - lecture - two contact hours.
   2. M-4 Clerkship Rotation - twelve contact hours.
B. House Officers:
   1. Training in Surgical Pathology.
   2. Lectures - five hours.
   3. Surgical Pathology Consultation Conference - six hours.
C. Hospital Conferences:
   1. Sarcoma Conference - monthly.
   2. Correlative Radiologic/Pathologic Bone Conference - bimonthly.
D. Graduate Student:
   1. Responsible for training of Dr. Anthony Nascimento, Mayo Clinic, 7/1/91-8/1/91.

III. RESEARCH ACTIVITIES

SPONSORED SUPPORT:

A. Southwest Oncology Group, SWOG study 9055 ($3,197).

PROJECTS UNDER STUDY:

A. Expression of neurofibromatous gene product in benign and malignant soft tissue tumors.
B. Correlation of grade and flow cytometric analysis in soft tissue tumors.
C. Carpal tunnel syndrome.
D. CD-34 expression in selected soft tissue tumors.
E. Epithelioid smooth muscle tumors of soft tissue.
F. Borderline vascular tumors.

IV. SERVICE ACTIVITIES

DEPARTMENTAL:

A. Director, Division of Anatomic Pathology.
B. Chief, Surgical Pathology.
C. Member, Chairman's Advisory Committee.
D. Member, Photography Committee.
E. Member, Program Committee, Residency Training Program.
F. Co-Director, Surgical Pathology Fellowship Program.

INSTITUTIONAL

A. Vice-Chair, Ob-Gyn Chair Search Committee.
B. Member, Neurofibromatosis Center.
C. Member, University of Michigan Cancer Center and Director of Tissue Procurement Core.
D. Member, Tissue and Invasive Procedures Committee.
E. Member, Musculoskeletal Core, Year II Curriculum.

REGIONAL AND NATIONAL

A. Chairman, WHO Committee for Classification of Soft Tissue Tumors.
B. US-Canadian Academy of Pathology:
    1. Benjamin Castleman Award Committee.
    2. International Vice President - North American Division.
C. Association of Directors of Anatomic Pathology:
    1. Program Chairman.
    2. Executive Council.
D. Chairman, Sarcoma Pathology Subcommittee, Southwest Oncology Group.
E. Editorial Board, American Journal of Surgical Pathology.
F. Editorial Board, American Journal of Dermatopathology.
G. Editorial Board, American Journal of Clinical Pathology.
H. Editorial Board, Human Pathology.
I. Editorial Board, Seminars Diagnostic Pathology.
J. Editorial Board, Journal of the National Cancer Institute.
K. Editorial Board, AFIP Fascicles (3rd Series).
L. Consultant in Pathology, National Institutes of Health.
M. Member, Michigan Society of Pathologists.
N. Member, Arthur Purdy Stout Society of Surgical Pathologists.

V. INVITED LECTURES

1. Keynote Address, Pathological Society of Great Britain and Ireland, The Queen's University, Belfast, Ireland, July, 1991.
2. Site Visit, Memorial Sloan Kettering Cancer Hospital (Biology of Sarcomas, Murray Brennan, M.D., Principal Investigator), New York City, New York, July, 1991.
3. Faculty, Fourth Annual USCAP Course-Diagnostic Pathology '91, Ann Arbor, Michigan, August, 1991.
4. Faculty, "Secondo Corso Pratico di Dermatopathologia, Universita Cattolica del S. Cuore, Rome, Italy, September, 1991.
5. Faculty, Annual Diagnostic Pathology Course, Washington Hospital Center, Washington, D.C., October, 1991.

6. Program Chairman, Annual Fall Meeting, Association of Directors of Anatomic Pathology, Chicago, Illinois, November, 1991.
7. Speaker, Memphis Society of Pathologists, Memphis, Tennessee, December, 1991.
8. The Merlin L. Trumbull Lecture in Pathology, Baptist Memorial Hospital, Memphis, Tennessee, December, 1991.
9. Moderator, Bone and Soft Tissue Specialty Conference, Annual USCAP Meeting, Atlanta, Georgia, March, 1992.
10. Faculty, Soft Tissue Specialty Conference, Annual USCAP Meeting, Atlanta, Georgia, March, 1992.
11. Visiting Professor, University of Cincinnati School of Medicine, Cincinnati, Ohio, April, 1992.
12. Speaker, Cincinnati Society of Pathologists, Cincinnati, Ohio, April, 1992.
13. Visiting Professor, Penrose Cancer Hospital, Denver, Colorado, May, 1992.
14. Keynote Speaker, Colorado Society of Pathologists, Denver, Colorado, May, 1992.
15. Visiting Professor, University of Massachusetts School of Medicine, Worchester, Masachusetts, May, 1992
16. Annual Spring Speaker, New England Society of Pathologists, Boston, Massachusetts, May, 1992.
17. Visiting Professor, University of Iowa School of Medicine, Iowa City, Iowa, June, 1992.

V. PUBLICATIONS:

ARTICLES PUBLISHED OR ACCEPTED FOR PUBLICATION IN REFEREED JOURNALS

1. Fetsch, J.F. and Weiss, S.W.: Observations concerning the pathogenesis of epithelioid hemangioma (angiolymphoid hyperplasia). Mod. Pathol. 1991;4:449-455.
2. Laskin, W.B., Weiss, S.W. and Bratthauer, G.L.: Epithelioid variant of peripheral nerve sheath tumor (malignant epithelioid schwannoma). Amer. J. Surg. Pathol. 1991;15:1136-1145.
3. Becker, R.L., Venzon, D., Lack, E.E., Mikel, U.V., Weiss, S.W. and O'Leary, T.J.: Cytometry and morphometry of malignant fibrous histiocytoma of the extremities: Prediction of metastasis and mortality. Amer. J. Surg. Pathol. 1991;15:957-964.
4. Smith, M.E.F., Costa, M.J. and Weiss, S.W.: Evaluation of CD68 and other histiocytic antigens in angiomatoid malignant fibrous histiocytoma. Amer. J. Surg. Pathol. 1991;15:757-763.
5. Goldblum, J.R. and Weiss, S.W.: Elastofibromatous change of the rectum; A lesion simulating amyloidosis. Amer. J. Surg. Pathol., In Press.
6. Weiss, S.W. and Rao, V.K.: Well-differentiated liposarcoma (atypical lipoma) of deep soft tissue of the extremities, retroperitoneum, and miscellaneous sites: A follow up study of 92 cases with analysis of the incidence of "dedifferentiation". Amer. J. Surg. Pathol., In Press.
7. Perosio, P.M. and Weiss, S.W.: Ischemic fasciitis: A juxta-skeletal fibroblastic proliferation with a predilection for elderly patients. Mod. Pathol., In Press.
8. Jones, M.W., Norris, H.J., Wargotz, E.S. and Weiss, S.W.: Fibrosarcoma-malignant fibrous histiocytoma of the breast. A clinicopathological study of 32 cases. Amer. J. Surg. Pathol., In Press.
9. Smith, S.H., Weiss, S.W., Jankowski, S.A., Coccia, M.A. and Meltzer, P.S.: SAS amplification in soft tissue sarcomas. Cancer Res., In Press.
10. Rao, V.K. and Weiss, S.W.: Angiomatosis of soft tissue: An analysis of the histologic features and clinical outcome in 51 cases. Amer. J. Surg. Pathol., In Press.

SUBMITTED FOR PUBLICATION

1. Zukerberg, L.R., Nickoloff, B.J. and Weiss, S.W.: Kaposiform hemangioendothelioma of infancy and childhood: An aggressive neoplasm associated with Kasabach-Merritt syndrome and lymphangiomatosis. Amer. J. Surg. Pathol.

2. Sondak, V.K., Lawrence, T.S., Robertson, J.M., Saran, P.A., Walker-Andrews, S.C., Dwarzanin, L.M., Weiss, S.W. and Chang, A.E.: Preoperative iododeoxyuridine and radiation in locally advanced sarcomas. Arch. Surg.

BOOKS AND CHAPTERS IN BOOKS

1. Laskin, W.B. and Weiss, S.W.: Benign fibrous lesions of upper limb, in, Bogumull, G.P. and Fleegerl, E.S. (ed.), Tumors of the Hand and Upper Limb, Churchill Livingstone, London, In Press.

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

1. Zukerberg, L.R. and Weiss, S.W.: Infiltrating kaposiform vascular tumor of infancy and childhood: An aggressive lesion associated with Kasabach Merritt syndrome and lymphangiomatosis, Lab. Invest. 1992;66:12A.
2. Smith, M.R. and Weiss, S.W.: Author's Reply. Amer. J. Surg. Pathol. 1992;16:427.
3. Weiss, S.W.: Pathobiology of Soft Tissue Tumors (Book Review), Mod. Pathol., In Press.
4. Sondak, V.K., Lawrence, T.S., Robertson, J.M., Saran, P.A., Walker-Andrews, S.C., Dworzanin, .L.M., Weiss, S.W. and Chang, A.E.: Preoperative iododeoxyuridine and radiation in locally advanced sarcomas. Ann. Can. Symp. of Soc. of Surg. Oncol.

SECTION REPORTS

DIVISION OF ANATOMIC PATHOLOGY

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1991 - 30 JUNE 1992

This academic year witnessed the completion of a series of academic recruitments which brings the Division to a level of full staffing. Dr. David Gordon brings to our Division an exciting level of expertise in the area of cardiovascular research. As the former director of the autopsy service at the University of Washington (Seattle), he has enhanced our autopsy service with his teaching skills and new autopsy techniques. Dr. Lisa Del Buono joined the faculty as a surgical pathologist with an area of specialization in gastrointestinal and hepatic pathology.

For our laboratories it has been a difficult and challenging year to meet the demands of the cost reduction initiative. Through a series of personnel reductions on all services we were able to reach our goal this first year. Although we have been able to offset these reductions by increasing automation in our histology laboratory, it is unlikely that we can meet subsequent goals without significant and probably unacceptable reductions in services. Continued efforts to improve our laboratory efficiency are an ongoing concern. Our departmental quality improvement team, under the capable direction of Deb Day Jansen, has initiated a splendid effort to improve the check-out and tracking of slides by means of a computer and image-assisted system.

The Division takes pride in our numerous and ongoing education activities, which range from a heavy commitment to the newly emerging curriculum for our own medical students, to national educational initiatives. Our fellowship programs have allowed our senior residents and selected outside individuals to achieve a measure of self-distinction in either surgical or cytopathology. Dr. Paul Mazarra completed the cytopathology fellowship and will be followed by Dr. Phil Perkins. Drs. Steve Mandell, Randall Shannon, and Lawrence Zukerberg (Massachusetts General Hospital), this year's departing surgical pathology fellows, will be succeeded by Drs. John Goldblum, Joe Willis (University of Rochester), and Jack Jansen (University of Kentucky). As an extension of the philosophy of the fellowship experience, the faculty has worked closely with the residents in encouraging them to find a project or area of interest in which they might excel. These efforts were amply rewarded by the presentation of eleven resident papers at the US-CAP or ASCP meetings in conjunction with the anatomic pathology faculty.

For the second year, the Division hosted the summer US-CAP Diagnostic Pathology course which, once again, earned praise for the quality of the course and facilities. As a result, we have been selected as one of the four permanent rotational sites for this course, thereby providing our own residents with the opportunity to take advantage of this course at least once during their training. Dr. Thomas Colby (Mayo Clinic) was our invited Residents' Visiting Professor this year, delivering both a lecture and seminar in pulmonary pathology. Additional visiting professors included Dr. Dale Snover (University of Minnesota) and Stanley Hamilton (Johns Hopkins) who lectured in the area of liver and gastrointestinal pathology respectively. Finally, our Division has been recognized as a collaborating center for the WHO International Committee for the Classification of Soft Tissue Tumors. This designation has been accorded to two other institutions in the country: Massachusetts General Hospital for the WHO Committee for the Classification of Gynecologic Tumors, and Memorial Sloan Kettering Hospital for the WHO Committee for Classification of Thymic Tumors.

Over the next year we look forward to the development of an image analysis facility under the direction of Dr. Flint, to the expansion of our molecular diagnostic activities supervised by Dr. Frank, and to the institution of a Staff Consensus Conference to improve the quality of diagnoses.

As we reflect on the past year, we continue to see the recruitment of young pathologists to academia as our most pressing concern. Our Division felt the annual retreat, which dealt critically and constructively with this problem, represented an important beginning to the exploration of possible solutions to this problem.

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

AUTOPSY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1991 - 30 JUNE 1992

The Autopsy Service of The University of Michigan continues to serve its central goals of resident training, performance of autopsies on University of Michigan patients, and performance of forensic autopsies for Washtenaw County.

I. Medical Examiners Cases

There continues to be difficulties related to medical examiners' cases from other counties. Legislation has been written which will allow us to either return bodies to the county of injury for autopsy, or allow us to bill these counties for our services. House Bill 4663 specifically addresses these issues, and after testimony by the University, it passed the House Judiciary Committee, as well as the full House. Its fate is currently being debated in the Senate, where it will probably have a hearing in Fall - 1992.

The University of Michigan has also instituted a policy of performing "gross only" examinations on selected medical examiners' cases and performing toxicology. A reduced fee is charged for these exams.

II. Quality Assurance:

A random review of two cases per month is now being conducted. A senior staff pathologist reviews all aspects of the case including gross description in the protocol, microscopic diagnoses, neuropathologic material and gross photographs. The results are documented, and the house officer who performed the autopsy is invited to examine the case with the pathologist who performed the review.

Turn-around time continues to be unacceptably slow, with the last analysis showing that it required an average of 80 days to complete a case. This problem is being addressed on two different fronts. First, efforts are being made to reduce the time required to complete the typing. Second, a pilot study has been initiated to determine if fewer neuropathology sections may be taken without compromising the ability to make clinically-relevant diagnoses. It is anticipated that this study will be complete in about six months, and actions will be taken based on its results.

III. Statistics:

Total U of M Cases	322
M-Labs cases	8
Medical Examiners' Cases	58
In Hospital Cases	24
Outside Cases	34
Autopsy Rate (includes tetralogy cases)	35%

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

CYTOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1991 - 30 JUNE 1992

The year began on an optimistic note, with full staffing after a period of severe depletion. By the end of 1991, however, we were down one cytotechnologist, a 25% reduction in our cytotechnologist work force, and this situation still continues. This has serious repercussions. The remaining cytotechnologists repeatedly have to work overtime on the weekends. The demands of routine diagnostic work make it difficult for the cytotechnologists to participate in Quality Assurance activity; whenever they do, the routine diagnostic work backs up. In effect, except for the screening of cytologic specimens, our cytotechnologists are unable to participate in any other kind of activity in the laboratory.

Because of the shortage of available cytotechnologists, remedying this situation has been most difficult. The few experienced cytotechnologists who have been available declined the position because the salary did not come up to their expectation. Finally, after a nine-month vacancy, we shall hire a newly trained and inexperienced cytotechnologist. These facts illustrate the difficulty in keeping a cytopathology laboratory going in today's situation.

The Cytopathology Fellowship Program is now in its sixth year. The indispensability of the Fellows is well recognized by the cytopathology staff persons. For example, in 1991 the time spent in the Medical Center away from the laboratory to participate in the procurement and/or interpretation of fine needle aspirates totalled 336 man hours (8.5 working weeks). The 596 aspirations in which our Fellows participated were mainly in the Department of Radiology, with the remainder on the patient floors or in the out-patient clinics. The total number of aspirations in which we participated is about 50% more than it was three years ago.

While the number of non-gynecologic specimens seems to have plateaued at about 7,300 per year, the number of gynecologic specimens has markedly increased. This is because the University Student Health Service has begun to send us its cervical smears, about 7,000 per year, bringing our total of gynecologic specimens to 34,000, for a total of all cytologic specimens of 41,000.

Bernard Naylor, M.D.
Director, Cytopathology Laboratory

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

DERMATOPATHOLOGY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1991 - 30 JUNE 1992

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

Work load volume is as follows:

	1990 - 1991	1991-19921
HE	822	1331
ID	NA	5651
MD	NA	NA
TD	NA	NA
Informal	350	300
Flow	NA	95
EM	NA	2

There was an estimated 10% increase in overall workload with a 100% increase in revenue from HE consultation cases.

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

Teaching included scheduled presentations to medical and dental students.

1990-1991 continued the gradual trend for an increased workload.

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

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

ELECTRON MICROSCOPY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1991 - 30 JUNE 1992

The electron microscopy continues to provide an important service to the Department of Pathology and the institution overall both in the analysis of clinical specimens as well as providing research support. For example, during this past year a total of 484 clinical biopsies were submitted for EM analysis. This is almost identical to the previous year when 482 clinical specimens were processed. The majority of cases submitted were either kidney or nerve and muscle biopsies. For example, 184 cases of the 484 total were renal biopsies, 131 were muscle biopsies and 57 nerve biopsies. Thus, the types of clinical material submitted for EM analysis continues to evolve. Previously, tumors represented a majority of samples submitted along with kidney biopsies. However, today tumors are examined much less frequently ultrastructurally because of the development of immunohistochemistry and ultrastructural evaluation of nerve and muscle biopsies is assuming increasing importance. Another change in our clinical samples is the increased use of our facility by outside hospitals. During this past year several new outside hospitals have contacted us to process EM specimens primarily in the area of renal pathology. Thus our laboratory is continuing to expand as a reference laboratory.

A major demand on the EM service continues to be the processing of research specimens. The laboratory processes well over 1000 tissue samples from experimental studies/year. Of this number 380 samples were processed completely for EM studies. In addition to routine electron microscopy more and more of these studies are requiring sophisticated morphometric and immunologic techniques as part of the evaluation process. These techniques are time consuming and because of our limited manpower have limited our ability to handle more specimens. In the future if the demand for these services continues to increase consideration will need to be made to add additional personnel.

In summary, the EM service continues to provide an important service and research function for the Department of Pathology as well as the institution as a whole. Efforts continue to decrease the turnover time particularly in regards to the handling of the clinical biopsies with our goal being a turn around time of 10 working days. In the area of research we continue to work with investigators from several departments including pathology to optimize the collection of specimens and the use of appropriate morphometric techniques. Plans are underway to develop a core facility for the researchers using various molecular probes to addition to the usual ultrastructural analysis.

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

NEUROPATHOLOGY SERVICE

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

CLINICAL ACTIVITIES:

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

1. There were 836 neurosurgical cases examined this year from Main, Mott and outside hospitals in consultation. This is a 56% increase over the previous year, a portion of which reflects better computer tracking. A portion of these were part of an interdepartmental study of PET/BUDR and neuropathology funded by NIH. 225 surgical specimens required special neurohistologic procedures. Of the 225 surgical specimens 100 were muscle, 13 were temporal lobectomies and the others required various neurohistologic procedures.
2. There were 252 brains examined out of 322 autopsies which is 78% of all autopsies at this Medical Center. An additional 27 brains were examined from other institutions and hospitals.
3. There were 183 muscle biopsies an 8% increase over the previous year, nearly all with histochemistry, some with electron microscopy. There were 60 peripheral nerve biopsies, 28 nerves referred from other institutions. There were 26 teased fiber preparations, 24 nerves had thick plastic sections only and 35 had electron microscopy performed on appropriate nerve biopsies. The combination of nerve teasing, muscle histochemistry, electron microscopy and morphometry make the service regionally competitive for diagnostic consultation.
4. Faculty interpreted 244 cases in semithin or thin section from electron microscopy. This is a 44% increase over the previous year. The majority of these cases were nerve, pediatric muscle, and neurosurgical biopsy cases.
5. The ceroid service, buffy coat division, reported six 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 120 difficult neuro-oncology cases.
7. 15 brains were examined for research purposes.
8. Autopsy neuropathology and surgical neuropathology each have monthly quality assurance meetings. Attendees have included neuropathologists from nearby institutions.

TEACHING ACTIVITIES:

1. Medical Students: This year the faculty taught the regular Neuropathology sequence to our medical students (13 hours) in the Neural and Behavioral Sciences (NBS) 600 curriculum. NBS Neuropathology consists of lectures, handouts, and posters for all second year medical students. In addition to being Director of the NBS Program for 40% of her time, Ms. D'Amato conducted 10 hours of brain cutting sessions for small groups of the second year students.

2. House Officers, Graduate Students, Postgraduate and other students and faculty: These include periodic conferences with Neurology; twice monthly Continuing Medical Education (CME) accredited conferences where all biopsies are presented and interpreted; a conference where abnormal brains are examined with all clinicians invited weekly; monthly nerve and muscle biopsy conferences accredited for CME; individual instruction on autopsies and biopsy material; Neuropathology 858, an 18 hour laboratory-lecture course; and bimonthly conferences with Neuroradiology.
3. Electives: Two neurosurgery residents and one neurology resident chose elective rotations on the Neuropathology Service. Weekly seminars with neurological and neurosurgical house staff on clinico-pathological correlations.
4. Two Neuromuscular fellows were instructed at conferences held twice a week.
5. Dr. Stephen Gebarski studied neuropathology and radiographic correlation during his sabbatical leave.

RESEARCH ACTIVITIES:

1. Dr. Hicks and Ms. D'Amato provided neuropathologic diagnostic support for Drs. Anne Young, John Penney and Roger Albin's biochemical study of Alzheimer's disease and other human dementias.
2. Dr. Blaivas and associates investigate ocular muscle (normal and abnormal). She is also investigating musculature related to cleft palates in children and mice. She is investigating pathologic changes in rat brain induced by Mk-801 with Dr. E.F. Domino.
3. Dr. Sima and collaborators are examining the regulation of all adhesive molecules and junctional molecules in diabetic nerve and retina to elucidate the etiology to defects occurring in axo-glial junctions and endothelial cell tight junctions in diabetes. Furthermore they are examining the interaction between nerve growth factors (NGF, IGF-1) and nerve regeneration in diabetes.
4. Dr. McKeever and associates are determining the extent and cause of differences in antigens in brain tumor tissue versus cells in culture. These differences may result from a separate population of cells within brain tumors or from instability of antigen expression by neoplastic cells. They are measuring DNA content and BUdR labeling indices in tumor specimens *in vivo* and *in vitro*. Dr. McKeever was on sabbatical leave from August through January.
5. Groups of the University of Michigan Cancer Center faculty and staff with clinical research interests in brain tumors, met and generated a number of project considerations from Pathology, Neurosurgery, Nuclear Medicine, Neuropathology, Neurology and Neuroradiology collaborations.
6. Collaboration with Neurology, Michigan State University, The State of Michigan Department of Public Health, the Alzheimer's Association, Henry Ford Hospital, and Beaumont Hospital has established a registry for dementias and Alzheimer's disease.

Paul E. McKeever, M.D., Ph.D.
Director
Neuropathology Service

PEDIATRIC PATHOLOGY SERVICE

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The activities of this service were carried out as in the past, primarily by Kathleen P. Heidelberger, M.D. and Mason Barr, Jr., M.D.

Necropsy figures are as follows:

M/W/H Unit Deaths (20 weeks gestation or any live born, to 18 years)	=148
Necropsies on Above	=106
Necropsy Percentage	=67%

Of the 106 posts, 33 patients' bodies, as defined above, were released to Anatomy for study and disposal. These gross posts were performed by Mason Barr, Jr., M.D., with necessary histology by Dr. Heidelberger Seventy-three patients were posted by the residents and senior staff in Pathology, primarily Dr. Heidelberger. Necropsies categorized in the adult general hospital statistics as "Medical Legal" posts included 15 posts on pediatric patients including SIDS cases, child abuse cases and trauma cases, only 10 of which were classified as inpatient deaths, because of treatment here.

A total of 355 necropsies for UMMC Hospitals patients was performed (including the 15 pediatric "Medical Legals"), 33 by Dr. Barr in the Teratology Unit and 322 by the Pathology Department Staff. Thus, 30% of the total posts at the UMMC were pediatric posts.

It should be noted that as a regional center, with a wide range of subspecialities, the total number of cases examined in the Teratology Unit was 167 - including both all referred fetuses and infants and inborn newborn fetal losses at less than 20 weeks' gestational age.

The total number of pediatric surgical specimens (including placentas) examined is almost 2,400. This represents a plateau compared to the previous academic year.

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

SURGICAL PATHOLOGY SERVICE

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During the past year, the Surgical Pathology Service experienced a growth of 5% in hospital-based accessions and nearly 30% growth in the volume of extramural (personal) consultations, bringing our total volume to 33,853 (Table 1). It is with a great deal of commitment and diligence that our laboratory has managed to deal with this volume in the face of personnel reductions associated with our cost reduction initiative. In part, we have met this challenge with a greater degree of laboratory automation in the areas of staining, cover-slipping, and labelling of slides.

In the second year of our surgical pathology fellowship, Drs. Mandell, Shannon, and Zukerberg (Massachusetts General Hospital), completed their training with distinction and will be followed by Drs. John Goldblum, Jack Jansen (University of Kentucky), and Joe Willis (University of Rochester). With this year, we expand and broaden the concept of the fellowship experience by the addition of a fourth position so as to offer a period of independent research for each fellow.

New initiatives in the Surgical Pathology Service include the applications of molecular biology techniques to our diagnostic process. Headed by Dr. Thomas Frank, our molecular diagnostic activities include pilot tests for the identification of cytomegalovirus in tissue sections, as well as two-day identification and specification of mycobacteria in surgical specimens. The latter test has proved to be of inordinate use in cases of unexpected mycobacterial infection when intraoperative cultures have not been obtained. Dr. Andrew Flint, utilizing recently upgraded image analysis equipment, is developing a rapid test for ploidy studies and quantitation of hormone receptors on tissue sections.

Plans for the upcoming academic year include expansion of our molecular diagnostic tests to determine clonality of tumors and detection of the transposition site in Ewing's sarcoma. In addition, our fellows are engaged in a research project in conjunction with the Department of Surgery to determine the patterns of utilization of intraoperative consultations.

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

TABLE I

SURGICAL PATHOLOGY ACCESSIONS
UNIVERSITY OF MICHIGAN MEDICAL CENTER

	Hospital-Based	Personal Consultations	Total
1990-91	26355	4762	31117
1991-92	27768	6085	33853

CLINICAL PATHOLOGY LABORATORIES

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The Clinical Pathology Laboratories have again undergone and endured significant changes in their operations during this past year. The laboratory directors, chief technologists, supervisors, and all laboratory personnel are to be commended for the professional and responsible manner in which they have responded to the Hospital's Cost Effectiveness Program (CEP). The first round of the CEP went into effect July 1, 1991. In spite of the loss of 26 personnel and a 7.5% reduction in the budget, the laboratories continued to operate in an efficient and professional manner. Planning for the second round of CEP began in Fall 1991 with implementation July 1, 1992. This latest effort will result in the reduction of 11 personnel and a 4.0% decrease in our overall laboratory budget.

In spite of these significant cuts into our operational budget, the laboratories saw a 0.9% increase in total test volume to 3.32 million billable tests. The laboratories have responded to the difficulties of doing more with less by continuing to enhance the efficiency of their operations. However, these operational changes that have occurred have led to increased turn-around times in some cases and decreased ability to perform the research and development needed to maintain high quality, tertiary care center laboratories. This aspect continues to be one of the biggest challenges of the Clinical Laboratories.

Several laboratory consolidation activities have occurred during this past year. The Gyn/Endocrine Laboratory was consolidated into the Ligand Laboratory in Fall 1991 and the Virology Laboratory became a part of the Pathology Laboratories also in Fall 1991. As a part of the CEP activities for the upcoming year, the Ligand, Immunology, Drug Analysis/Toxicology, and Biochemistry Laboratories will be further consolidated to enhance the overall operation of the Clinical Chemistry section. This will result in the Ligand Laboratory activities being distributed to Drug Analysis/Toxicology, as well as the Biochemistry Laboratory.

As part of the Departmental response to changes in professional reimbursement, we have reviewed and enhanced the professional billing activities of the Division. The Part B billings from Clinical Pathology faculty (Flow Cytometry, Hematology, Immunology, and Blood Bank Laboratories) accounted for 24% of the Departmental billing volume and approximately 20% of gross billings.

We have continued to support a Fellowship Program in the Hematopathology section (one per year). This program has enhanced both the service and academic needs of Hematopathology. We are also exploring opportunities for fellowships in other areas of the Clinical Pathology Division.

The academic program of the Division continues to shine. The specific academic accomplishments can be found in the faculty section but some deserve additional comment. The Clinical Pathology Faculty continue to be productive with over 100 publications published or accepted in refereed journals. Several faculty are on the Editorial Boards of prestigious and important journals. Most of the faculty have participated in national symposia, meetings, or grant study sections in their respective academic areas. Excellence in the research laboratories continue to grow with 10 Clinical Pathology faculty receiving research grants this past year. This includes our full-time clinical faculty in the Chemistry and Microbiology Laboratories who received over $200,000 for various clinical and scientific studies in recognition of their respective expertise and scientific abilities.

Several major goals of the Clinical Pathology Division will challenge us during upcoming years. These include: 1) continuing to plan for the space needs of the laboratories for the rest of the decade; 2) continue to develop the concept of decentralized laboratory testing and begin to provide more point-of-

care testing. This will likely be directed toward ambulatory care and ICU settings; 3) continue the process of evaluating and controlling utilization of laboratory resources as response to the hospital CEP; 4) continue to develop and polish the Division's QA program (under the leadership of Ms. Suzanne Butch) and continue our initiatives that will enhance quality improvement; 5) continue to expand the Molecular Diagnostic Program as applied to Clinical Pathology; 6) revise the Clinical Pathology teaching component of the Residency Training Program; and 7) offer a Laboratory Medicine Elective for senior medical students (Spring 1993). These tasks are not trivial and will demand a significant commitment and desire from the faculty and laboratory staff to effectively begin and implement these changes.

Curtis A. Hanson, M.D.
Director, Clinical Pathology Division

UNIVERSITY HOSPITALS BLOOD BANK AND TRANSFUSION SERVICE

DEPARTMENT OF PATHOLOGY
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PATIENT CARE:

Transfusion-related activity plateaued during the past year. While there was a 10 per cent decrease in the number of pretransfusion tests performed, there was a 5 per cent increase in the number of platelet concentrates transfused, a slight decrease in the number of Red Blood Cells transfused and little change in the number of units of plasma and cryoprecipitate transfused. However, the number of autologous donations for subsequent transfusion increased by approximately 30 per cent, reflecting the public's continued concern about the risk of post-transfusion infectious disease. While the moderation of blood component utilization may be attributed, at least in part, to institutional efforts to control this activity, other factors may be influential. These include a decline in length of average hospitalization, lack of increase in occupancy and pressure upon physicians to reduce use of blood because of patient concerns and fear of legal action.

Significant increases were seen in laboratory activities related to the Bone Marrow Transplantation Program. This was reflected by the advent of peripheral blood stem cell collection and the implementation of autologous bone marrow transplantation for patients with advanced carcinoma of the breast. This activity countered the slight potential reduction of apheresis activity due to the increased use of intervenous immune serum globulin for treatment of patients with Guillain-Barre syndrome.

While over-all blood utilization did not expand during the past year, it should be appreciated that there has been an increase in surgical procedures which call for large volumes of blood, often on an emergent basis. These include liver transplants and thoraco-abdominal aortic aneurysmectomies. Approximately 50 of the former procedures were performed while an average of 1 TAAA was performed each month. Blood usage for cardiac surgical procedures has remained at the level of the previous year, averaging approximately 12 donor exposures per patient. The Utilization Review Program of the Section of Thoracic Surgery, based upon data provided by the Blood Bank/Transfusion Service, has helped control inappropriate blood transfusion for these patients. A more extensive utilization review program was implemented during the past year for adult and pediatric hematology patients, and this will be expanded to include the majority of patients in University Hospital during 1992-1993.

EDUCATIONAL ACTIVITIES:

The medical, technical and nursing staff of the Blood Bank/Transfusion Service were active in education at the departmental, institutional, regional and national levels. As in past years, all first-year Clinical Pathology House Officers participated in a two-week Blood Bank orientation course. In addition, daily patient care rounds were attended by medical and technical staff and by House Officers assigned to the Blood Bank. Dr. Oberman, Dr. Davenport and Mr. Judd presented Pathology Grand Rounds during the year, and also participated in the weekly case presentation Clinical Pathology Conference. The nursing staff of the Transfusion and Apheresis Service presented regular educational services for the nursing staff of University Hospitals on topics of blood product administration, adverse transfusion reactions and use of blood component administration filters.

The nineteenth annual postgraduate course, "Current Topics in Blood Banking" was held June 3, 4 and 5, 1992. Mr. Judd was the program director. This course attracted approximately 250 attendees from throughout the United States, thereby representing one of the largest postgraduate courses held in

the Medical Center during the past year. Members of the Blood Bank and Transfusion Service staff presented workshops on pediatric immunohematology, assessment of immune hemolysis, clinical problem-solving in the blood bank, and blood bank inspections. In addition, Ms. Steiner, Mr. Judd, Dr. Davenport and Dr. Oberman participated in the lecture program of the symposium.

Members of the Blood Bank and Transfusion Service faculty and staff participated in the Annual Meeting of the American Association of Blood Banks. In addition, members of the laboratory, including Mr. Judd, Ms. Butch, Mrs. Stoe and Ms. Steiner presented invited lectures to regional organizations such as the Michigan Association of Blood Banks, Michigan Society of Medical Technologists, Toledo Red Cross, Detroit Red Cross, the Community Blood Center of Greater Kansas City (Ms. Butch) and the Pennsylvania and California Associations of Blood Banks (Mr. Judd).

PROFESSIONAL ACTIVITIES:

Blood Bank and Transfusion Service staff continued to be active at the regional and national levels. Dr. Oberman served as Associate Editor of TRANSFUSION and also chaired the Awards Committee of the American Association of Blood Banks. Mr. Judd was the North Central District representative to the Board of Directors of the American Association of Blood Banks, edited the Special Methods section for 11th edition of the Technical Manual of the American Association of Blood Banks, and chaired the "Advanced Lectures" program of the Michigan Association of Blood Banks. Ms. Butch was a member of the Standards Committee and the Informations Systems Committee of the American Association of Blood Banks and chaired the users' group on the blood donor module for the Pathnet program for Cerner. Mrs. Stoe served as an inspector for the Inspection and Accreditation Program of the American Association of Blood Banks. Ms. Steiner was a member of the Reference Laboratory and Rare Donor File Committees of the American Association of Blood Banks, is the president-elect of the Michigan Association of Blood Banks and chaired the Annual Meeting Committee of the latter organization.

RESEARCH ACTIVITIES:

The faculty and staff of the Blood Bank and Transfusion Service pursued research activities on the pathophysiology of transfusion reactions, pretransfusion testing, the genetic basis of blood group antigens, and strategies for reduction of donor exposures. The laboratory played a leading role in the national implementation of a computerized crossmatch procedure. Publications by the staff during the past year include the following (see faculty publications elsewhere in this booklet):

1. Can the reading for serologic reactivity following 37 C incubation be omitted? Judd, W.J., Steiner, E.A., Oberman, H.A. and Nance, S.J.: Transfusion 1992;32:304-308.
2. Anti-i causing acute hemolysis following a negative immediate-spin crossmatch. Judd, W.J., Steiner, E.A,, Abruzzo, L.V., Davenport, R.D., Oberman, H.A., Pehta, J.C. Nance SJ.: Transfusion, In Press.
3. Steiner, E.A.: The DAT work-up: how much is enough? A Different Vein (Michigan Association of Blood Banks) 1991.
4. Nugent, C.E., Gelinas, J.R., Judd, W.J. and Steiner, E.A.: Anti-Yta does not cause hemolytic disease of the newborn. Obstetrics and Gynecology, In Press.
5. Chenoweth, C.E., Judd, W.J., Steiner, E.A. and Kauffman, C.A.: Cefotetan-induced immune hemolytic anemia. Clin. Inf. Dis., In Press.
6. Judd, W.J., Steiner, E.A. and Nugent, C.E.: Appropriate serological teating in pregnancy. Vox Sang, In Press.

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

CHEMICAL PATHOLOGY LABORATORY

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During the past year, the workload of the Chemistry Laboratory remained constant. The lab performed approximately 2.95 million tests, a 0.2% decrease in volume from the previous year. However, due to a variety of cost cutting measures, the lab budget was decreased 3.3% over the previous year. Approximately 40% of the total testing performed by the lab was done in a STAT mode, with 1 hour turnaround time. Quality assurance monitoring studies have shown that the lab is meeting this turnaround time goal greater than 95% of the time.

The laboratory has remained active in evaluating and implementing alternate site testing options within the medical center. In January, the lab directed the standardization of all bedside blood glucose meters within the medical center. The Chemistry Lab now performs linearity checks, maintains quality control records, and supervises proficiency testing on 68 glucose meters located at nursing stations within the institution.

The lab expanded its coverage of blood gases, electrolytes, and glucose in the operating rooms with the acquisition of another analyzer. The laboratory now maintains blood gas/electrolyte analyzers and hematocrit centrifuges in the Operating Rooms of Main, Mott and Kellogg Hospitals, and a backup instrument on a cart within the Chemistry Lab. The laboratories role in these sites includes performing all quality control analysis, instrument maintenance, and supervising the training of the Department of Anesthesiology staff who perform the analysis.

In the area of quality assurance, the lab has initiated the formation of a quality improvement team with Central Distribution and Emergency Services to study methods of improving turnaround time on STAT tests to the ER. Discussions continue on expansion of the menu of tests which are performed on site in the ER. Recently, pregnancy tests were added to the menu of tests performed in the ER by phlebotomists. This should decrease the turnaround time on this frequently ordered test.

The lab director and supervisory staff have devoted a great deal of time and effort to planning for the upcoming consolidation of the Chemistry, Ligand Assay, and Immunology lab functions. This complex move and reorganization of the laboratories should occur in the fall of 1992.

Donald Giacherio, Ph.D.
Director

CLINICAL CYTOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY
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The Clinical Cytogenetics Laboratory has continued to expand, both in numbers and complexity of samples processed and in personnel. In the last year, approximately 875 amniotic fluids, 60 tissues (skin, POC, etc.), 345 peripheral blood specimens, 145 fragile-X analyses, 67 prophase analyses, 6 breakage studies and 273 bone marrows were completed for a total of 1,771. Increases were seen in all areas, particularly bone marrow and prophase analysis. It is important to note that more than half of the non-prenatal specimens required special processing and analysis. With expanded staffing, the use of the laboratory computer and daily sign-out, the turn-around time for the prenatal cases has gone from 3 to 4 weeks to 14 days or less.

The laboratory as a whole is planning to continue to decrease turn-around times and expand the extent of its analyses, as this appears to be the direction that the field of cytogenetics is taking. A collaborative effort with a group from Maternal-Fetal Medicine resulted in the institution of a program of earlier prenatal diagnoses by chorionic villus biopsy. Approximately 100 cases were done during the first year (which began in May, 1991), and these do not appear to have replaced any of the amniocenteses being performed now.

Bone marrow cytogenetic analyses continue to increase; this trend is expected to continue as the Bone Marrow Transplant program grows. A number of studies are underway to determine the value of various mitogens and growth factors for stimulation of abnormal clones for bone marrow analyses. In addition, some solid tumors, primarily sarcomas, have been analyzed and this type of analysis is now available clinically.

Some molecular cytogenetic analysis is being offered by the clinical laboratory. Using fluorescent *in situ* hybridization, chromosomes X, Y, 1, 7, 12, 13, 14, 15, 21, and 22 can now be identified, a procedure which is useful in ascertaining the origin of certain "marker" chromosomes. These studies continue to expand in the future. Additionally, molecular diagnostic techniques, such as implementation of a DNA-based test for fragile-X syndrome, are anticipated in the next year.

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

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

CLINICAL FLOW CYTOMETRY LABORATORY

DEPARTMENT OF PATHOLOGY
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Over the past year, the Clinical Flow Cytometry Laboratory processed approximately 2800 immunophenotyping specimens. This was a volume increase of 17% from the previous year. This change was attributable mainly to a 67% increase in requests for T-cell subset phenotyping in patients with acquired immunodeficiencies, inherited immunodeficiencies, and organ transplants. In addition, the laboratory analyzed approximately 400 leukemia specimens and performed about 3900 flow cytometry reticulocyte counts. Anti-platelet and anti-neutrophil antibody assays were performed on approximately 400 specimens. Direct anti-platelet antibody testing continues uninterrupted, but indirect anti-platelet antibody testing has been suspended indefinitely due to poor reproducibility of the assay. The lymphocyte mitogen assay was also discontinued; it is now performed in the HLA/Tissue Typing Laboratory. The Flow Cytometry Laboratory continues to provide support to the Hematopathology section of the Molecular Diagnostics Laboratory (see report on Molecular Diagnostics Laboratory for further description).

By year's end, the laboratory was prepared to implement two-color analysis for all leukemia profiles. Although two-color reagents are more expensive than single-color reagents, the significant reduction in preparation and analysis time has afforded compensatory savings.

As noted above, there has been a dramatic increase in the volume of specimens sent for T-cell subset analysis. This is attributable mainly to increased numbers of acquired immunodeficiency patients and the increased demands for transplant immunosuppression monitoring. As the demand for these tests is expected to continue to rise, plans are underway to purchase an upgraded flow cytometer to replace the Coulter Profile instrument. To enhance the accuracy of our lymphocyte subset enumerations, a concomitant CBC and 5-part differential is now required for all acquired and inherited immunodeficiency specimens.

The laboratory staff continued efforts to enhance our Quality Assurance Program. The hematopathologists staffing the laboratory must triage all requests for leukemia/lymphoma phenotyping; inappropriate requests are cancelled. As a result of this utilization control procedure, approximately 300 submitted specimens were not analyzed flow cytometrically.

Biweekly Quality Assurance Conferences are held for the medical staff to review all leukemia/lymphoma phenotyping cases signed-out for the preceding two-week period. These meetings entail a comprehensive review of each case to assure such things as appropriateness of the test request, technical quality of the analysis, clerical quality of the reports, and consensus regarding final diagnoses.

Teaching activities in the laboratory include the daily case sign-out with the residents and the hematopathology fellow. Continuing medical education for the technologists and house staff is also offered at the biweekly leukemia conference.

Finally, the laboratory has provided collaborative support to several investigators in other departments. These research activities include: leukocyte adhesion molecule analysis in patients with inflammatory dermatoses and inflammatory bowel disease (Depts. of Dermatology and Gastroenterology); phenotyping of lymphocytes in lymphoma patients receiving experimental anti-CD20 therapy (Division of Hematology/Oncology); bone marrow stem cell enrichment study (Adult

Bone Marrow Transplant Program). In addition, the laboratory has become a beta test site for application of a new flow cytometry data analysis program being developed by Verity Software Systems, Topsham, Maine. This collaboration is expected to enhance the efficiency of data analysis in the laboratory.

Charles W. Ross, M.D.
Director

Curtis A. Hanson, M.D.
Co-Director

CLINICAL HEMATOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
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LABORATORY ACTIVITIES:

A. The criteria for doing automated differential white blood cell counts were revised to decrease technologist time for the labor-intensive manual differentials, which is often not necessary. Implementation of this automation increased the percentage of these differential counts from 41% to 59%.

B. Criteria were revised for review of body fluids by hematopathologists. These revisions together with a 16% decrease in the number of fluids sent to the laboratory for review resulted in a 31% (from 4200 to 2900) decrease in the number of cases being reviewed by hematopathologists.

C. Reduced our number of F.T.E's by 1.2 in accordance with the budget reduction program. Eosinophil counts and L.E. preparations were discontinued.

D. There was an overall increase in billable tests of 10% due to a change in the fee code structure. There was a 15% decrease in the number of ordered tests but only an 8% decrease in actual work performed.

E. 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.

F. Daily signout of in-house and UM clients' cases of abnormal smears and body and joint fluids takes place 7 days per week.

G. A quality assurance program has continued in the area of bone marrow cytochemical stains for leukemia and other labor intensive "specialty" tests within the laboratory. This program has led to a substantial decrease in the number of special tests and cytochemical stains performed, resulting in improved utilization of resources.

TEACHING ACTIVITIES:

A. Pathology House Officers and Hematopathology Fellows participated in the following activities:
   1. Daily review of abnormal blood smears, body fluids, joint fluids for crystals, bone marrow aspirates and bone marrow biopsies.
   2. Daily review of in-house and transfer consultation cases in hematopathology (lymph node biopsies, bone marrow biopsies, aspirates, splenectomy specimens, etc.).
   3. Daily review of outside consultation cases of Drs. Schnitzer and Hanson.
   4. Correlation of morphology with special studies (cytochemistry, flow cytometry, immunoperoxidase and occasionally electron microscopy).
   5. Daily review of abnormal blood smears from M-Labs clients.
   6. A formal teaching conference for House Officers has been continued.
   7. Review of SWOG cases.
   8. Weekly Interdepartmental Lymphoma Conference.
   9. Biweekly Interdepartmental Leukemia Conference.
   10. Pediatric and adult Hematology/Oncology Fellows participate in signouts.

B. Hematopathology Fellowship Program.

C. Continuing medical education for medical technologists - monthly.

D. Senior Student Clerkship Elective.

E. Summer Clinical/Research Program for Under-represented Minority Students.

FISCAL YEAR 1992/1993 GOALS:

A. Implementation of cost-containment programs.
B. Review and development of laboratory utilization.
C. Implement limits on repetitive differential requests.
D. Continue to liberalize automated differential criteria.
E. Preliminary studies of limiting WBC requests from intensive care units.
F. Continue to enhance the overall efficiency of the laboratory operation.
G. Transfer of hemoglobin eletrophoresis from the Chemistry Laboratory to the Hematolology Laboratory.

Bertram Schnitzer, M.D.

Curtis A. Hanson, M.D.

Directors
Clinical Hematology Laboratory

CLINICAL IMMUNOPATHOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
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OVERVIEW:

With the impending chemistry "mega-lab" consolidation, implementation of some CLIA 88 regulations, and a hospital-imposed budget restructuring, fiscal year 1991-92 has been challenging. The immunopathology laboratory experienced an increase in test volume and several new assays/programs were instituted. John Lowe, M.D. has again provided an invaluable service commitment to the laboratory. Kent Johnson, M.D., and Kevin Cooper, M.D. (Dermatology) continue to signout tissue immunofluorescence studies.

CLINICAL SERVICES:

As the fiscal year approached its conclusion, the laboratory had experienced a modest increase in total volume (approximately 4%). Particularly gratifying has been the growth in several relatively new assays; these include the neutrophil cytoplasmic antibody (NCA) test, prealbumin assay, and immunoglobulin G subclass determinations. Neutrophil cytoplasmic antibody determinations have increased from approximately 20/month to more than 50/month, prealbumins have increased three-fold and immunoglobulin G subclass determinations have increased by approximately 50%. In addition, we instituted the microalbuminuria assay as a clinical test. We have recently evaluated and initiated a variety of utilization control measures in the laboratory.

RESEARCH AND DEVELOPMENT:

The laboratory has participated in an ongoing methods comparison study of microalbuminuria assays. This study is being conducted by Dr. Patricia Mueller at the Centers for Disease Control in Atlanta. Involvement in this study has been an outgrowth of our support of clinical studies of ambulatory diabetic patients that were carried out by Dr. William Herman (Department of Medicine, University of Michigan) and Dr. Mindy Smith (Department of Family Practice, University of Michigan). We continued laboratory support of a clinical study of atypical antinuclear antibodies in conjunction with Dr. Joseph McCune (Department of Medicine, University of Michigan). After conducting a method comparison study of IgG subclasses quantitated by microELISA versus radial immunodiffusion, we have recently switched to the later method. The RID method should prove to be more reliable and the laboratory should realize a significant annual cost savings. We have recently added the capability of determining specific IgG and IgM anti-cardiolipin antibody concentrations. This assay has relevance to the "anti-phospholipid antibody syndrome" which has been associated with thrombosis, thrombocytopenia, and fetal wastage. Finally, we recently completed a collaboration with Dr. Paul Watkins (Internal Medicine, University of Michigan) in an analysis of serum samples for anti-liver-kidney-microsomal antibodies from patients with Cognex-induced hepatitis.

QUALITY ASSURANCE:

The laboratory completed two QA projects. These relate to proper specimen procurement for CSF oligoclonal bands and proper screening requests for Bence Jones proteins. More recent efforts have been directed towards analyzing utilization of circulating immune complex assays.

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. Three clinical pathology grand rounds were presented by Dr. Warren. Dr. Daniel Remick presented a CP grand rounds entitled "Update on Cytokines" as part of the immunopathology series. Other professional activities of faculty and staff in the laboratory are summarized under individual faculty reports.

Jeffrey S. Warren, M.D.
Director
Clinical Immunopathology Laboratory

HISTOCOMPATIBILITY & IMMUNOGENETICS LABORATORY

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1991 - 30 JUNE 1992

The HLA laboratory has had a very successful year. The laboratory has made a number of changes that have increased both the efficiency and the function of the facility. This resulted in increased revenues for the Department. In addition, two new staff members were incorporated in the laboratory that helped increase the quality of our service.

CLINICAL ACTIVITIES:

Clinical Activities in the Histocompatibility Laboratory showed a consistent increase from last year with approximately a 17% overall increase in the number of test performed and a 21% increase in overall revenue. This was despite a decrease of approximately 22% in consumable cost. A new laboratory test, the lymphocyte proliferation assay, was added and has progressively increased its activity to approximately 2 to 3 per week.

Two personnel were added to the laboratory this year. These two individuals Debra Marantis and Mary-Lee Sharp markedly improved the efficiency of the laboratory and helped in the cost savings.

Technical improvements in the laboratory included the full implementation of Class II HLA typing by magnetic beads, which as resulted in a tremendous improvement in the ability to identify Class II antigens on samples. In addition, DNA analysis of Class II antigens was also initiated and is currently being quality controlled before its introduction into clinical use.

The automation of the laboratory was finished and this also increased efficiency. Jeff Hayward, the Data Supervisor of the Laboratory in conjuntion with Tomas Peterson and James Dignan of Pathology data services were key in achieving these gains.

TEACHING ACTIVITIES:

Every member of the laboratory was involved in the teaching activities of the laboratory and they were effective in their work. The laboratory was involved in the instruction of Pathology Residents, Allergy Fellows, Renal Fellows and Postdoctoral Candidates from the Department of Hematology. Dr. Baker, the Laboratory Director, took an active role and also served as the alternate for theUniversity for its UNOS membership. Ms. Cynthia Schall, the Laboratory Supervisor, was involved in teaching review courses at Henry Ford Hospital and the University of Michigan. She also oversaw the activities for Residents in the Laboratory and several "Women In Science" Interns.

NEW GOALS:

The goals of the laboratory in the coming year include implementing HLA Class II typing by DNA analysis as a standardized test and attempting to increase the overall efficency of the laboratory to better meet the needs of both the solid organ and bone

marrow transplant programs. In addition, the laboratory is a key to the development of a basic-science research program in Transplantation Immunology. This program will center its investigations on clarifing the role of cell surface antigen recognition in allograft transplantation and the immune response to allografts.

James R. Baker, Jr., M.D.
Director, Histocompatibility & Immunogenetics Laboratory

CLINICAL MOLECULAR DIAGNOSTICS

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1991 - 30 JUNE 1992

CLINICAL ACTIVITIES:

The Molecular Diagnostics Laboratory was relocated to a newly renovated facility in August 1991. During the past year, the laboratory has been involved in three main activities: (I) Diagnostic Hematopathology under the supervision of Drs. Hanson and Ross, (II) Research and development of new methodology for the diagnosis of infectious agents, and (III) development of genotyping techniques for the detection of cystic fibrosis mutations.

I. **Diagnostic Hematopathology.** The laboratory performed 196 immunoglobulin and T-cell receptor gene rearrangement studies. PCR of the bcr/abl fusion gene was performed in 12 cases. Finally, PCR of the EBV genome was performed in 4 diagnostic cases. The goals for the next year are (A) to develop PCR methodology for the detection of minimal residual disease in lymphoma and leukemia and, (B) to develop non-radioactive methods for the analysis of single-copy genes by Southern-blot analysis.

II. **Development of PCR-based methods for the detection of infectious agents.** Charles Ross, working with Javed Siddiqui and Carl Pierson, has developed a PCR-based technique for the specific amplification of DNA from Mycobacterium tuberculosis in sputum samples. Analysis of 140 sputum specimens has shown a perfect correlation between PCR and the standard mycobacterial cultures. We are currently assessing, with clinicians, ways to use this methodology for the diagnosis of patients admitted to the University Hospital. Tom Frank has also developed a technique of diagnosing mycobacteria in paraffin tissue sections and distinguishing between pathogenic mycobacterial species using restriction enzymes. Gabriel Nuñez and Donald Zhou in collaboration with Dr. Frank are applying hybridization with specific biotinylated oligonucleotides for the diagnosis of Mycobacterium tuberculosis vs. avium/intracellulare complex in unfixed specimens. Preliminary results are very encouraging. In addition, Dr. Frank developed a PCR-based method of detecting cytomegalovirus in formalin fixed tissue, which was recently published.

III. **Development of a Genotyping Core for CF mutations.** We were funded last October by the Cystic Fibrosis Foundation to establish a genotyping facility for the main CF mutations. The main purpose of the Core is to support CF investigators at the University of Michigan. We have developed a nonradioactive reverse dot-blot assay for the screening of the five most common CF mutations. So far we have genotyped 75 CF patients. Our plan is to extend genotyping to seven mutations during the next year.

TEACHING ACTIVITIES:

We have established a weekly conference on Molecular Diagnostics and encourage residents and interested faculty to attend. At the present time, the focus of the resident's rotation in Molecular Diagnostics is Hematopathology. Charles Ross has been coordinating this rotation. In addition, Drs. Del Buono, Cook , Goldblum, and Perosio have worked with Dr. Frank in research projects applying PCR-based methodology to paraffin-fixed tissue sections.

Gabriel Nuñez, M.D.
Director, Clinical Molecular Diagnostics

DRUG ANALYSIS AND TOXICOLOGY LABORATORY

DEPARTMENT OF PATHOLOGY
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Despite the major changes affecting the Medical Center and Clinical Laboratories, the Drug Analysis and Toxicology Laboratory has maintained its prominent role as an active, progressive, and vital contributor to the success of the Department of Pathology and the University of Michigan.

Multiple new assays were introduced in-house during the last year. A novel drug screen for newborns utilizing meconium sampling was instituted. Previously the turnaround time for this type of screening was 2 to 3 weeks, but has been shortened to under 2 days in-house. A screen for diuretics has been developed, as well as therapeutic assays for clomipramine, norclomipramine, and Cyclosporin G.

The laboratory continues to be certified by the College of American Pathologists for the forensic drug testing program. The requirements and demands to achieve this recognition escalate each year. The laboratory is currently awaiting the next accreditation inspection for recertification in this special area. Support of the M-Labs program through involvement in this added certification process places a large burden of responsibility on the staff of the laboratory, and the technologists in the laboratory deserve special recognition for their efforts. The Drug Analysis Laboratory also underwent an interim clinical laboratory inspection by the College of American Pathologists and performed very well during the accreditation review.

The laboratory has been involved in several ongoing quality assurance projects. These projects involve reviews of the utility of both therapeutic drug assays and components of the existing drug screen menus, turnaround times, accuracy of data entry, and the appropriateness of critical value assignments. Dr. Annesley is also involved in a pharmacokinetic Quality Improvement Team, headed by the Pharmacy Department, which is evaluating the appropriateness of serum drug requests.

The Drug Analysis Laboratory continues to be active in novel research and development projects. The laboratory supports a large number of institutional clinical projects through collaboration with the Departments of Surgery, Dermatology, Obstetrics and Gynecology, Pediatrics and Pharmacology. Dr. Patel is performing primary development and clinical applications studies in a project investigating novel chromatographic resins and materials for a major corporation, and is also investigating approaches for monitoring testosterone and epitestosterone under a grant from the National Collegiate Athletic Association. Dr. Annesley is a co-investigator in a major-funded project from the Sandoz Corporation which is investigating the clinical utility of a new immunosuppressant drug. Dr. Annesley is also a co-investigator in a Clinical Research Center NIH-funded project evaluating predictors of Cyclosporine A bioavailability, and also a co-investigator in a recently finished Department of Health and Human Services Innovation Research Grant evaluating the measurement of anticonvulsant drugs in saliva.

The laboratory staff were activity involved in the training of house officers and medical students. At the national level, Dr. Patel has maintained involvement in the NCAA and IOC drug testing programs, and both Drs. Annesley and Patel are members of NCAA drug testing teams. In an effort to explore ways to enhance and improve the scope of service, the Drug Analysis Laboratory has recently enrolled in a pilot project co-sponsored by the CAP and AACC to evaluate interlaboratory performance in the areas of drug and steroid testing, with the possible goal of future expanded involvement in these areas.

The laboratory has been involved in the first important stages of the consolidation of functions performed by the three major laboratories making up the Biochemistry Section. The therapeutic drug

assays for digoxin, methotrexate, amikacin, gentamicin, tobramycin, and vancomycin have been transferred to the Drug Analysis and Toxicology Laboratory. Two medical technologists have joined the laboratory as part of this change and have been a welcome addition to the staff.

Lastly, the laboratory has struggled with ways to meet the budgetary reductions imposed by the medical center, while striving to maintain the same high quality level of service. The laboratory successfully achieved its cost reduction goal for this last fiscal year, during which both personnel hours plus commodities were lost. Most of the burden in adapting to the changes were placed upon the technologists and the success of the process is a credit to these individuals. A proposed plan to comply with further cost reductions has been submitted to hospital administration. The impact of these cuts remains to be seen during the next fiscal and academic year.

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

LIGAND ASSAY LABORATORY

DEPARTMENT OF PATHOLOGY
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CLINICAL ACTIVITIES:

The Ligand Assay Laboratory continues to undergo significant changes with the goal of consolidating operation with the Immunology and Chemistry Laboratories in the Main Hospital. Much of the planning required for this change has been completed. The therapeutic drugs and two medical technologists have been transferred to the Drug Analysis Laboratory and preliminary plans for laboratory renovation to accomodate the move have been submitted to the University Hospital architect for his comments and suggestions. We are actively examining and adapting for our operation, a new microcomputer based data analysis package, that will replace the current data analysis software maintained on the DEC PDP-11/44, which is located on the second level in Medical Science I. Consolidation of the former OB/GYN laboratory with all of its assay repetoire and the transfer of 2 medical technologists into the Ligand Assay laboratory occured during the past fiscal year. Total volume of specimens processed increased to approximately 156,000/yr. during the last fiscal year. This represents an increase of approximately 4%. In addition to the changes outlined above, the laboratory is continuing to convert many of its radioisotopic procedures to semi-automated and fully automated non-radioisotopic methodologies. These changes should permit an increase in laboratory efficiency with the goal of accomodating the continuing demands on the laboratory in the face of decreasing resources.

The Ligand Laboratory has acquired two Ciba-Corning ACS:180 analyzers that will allow us to convert several of our assays to chemiluminescence methodology. At the present time TSH, total T_3, and free T_4 are being run on the ACS:180. The goal is to add all of the thyroid hormones, LH, FSH, prolactin, vitamin B_{12} and folate during the present year. This analyzer has random access capabilities with bar code reading capabilities for reagents and patient samples. This significantly reduces the potential for identification error and improves turnaround time. Utilization of these instruments will allow us to handle the ever increasing test volume and the development and evaluation of assays for the measurement of newer analytes without increasing staff levels or increasing overtime expenses. The incorporation of this new instrumentation into the laboratory will greatly increase laboratory efficiency, reduce reagent costs by avoiding the requirement for duplicate samples and reducing the number of standards and calibrators required per result. All of these changes will result in a significant reduction in our per-test cost.

Barry G. England, Ph.D.
Director

MICROBIOLOGY/VIROLOGY LABORATORY

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CLINICAL ACTIVITIES

Based on the first 11 months of activity this year, the Microbiology Laboratory has experienced an 8.1% decrease in activity. A total of 133,932 tests were performed from July 1991 to May 1992. This total includes 17,425 M-Labs tests (a decrease of 6.9% from the previous year). M-Labs represents 13.0% of the total laboratory volume. The decrease in lab test volume is strongly influenced by laboratory staff initiatives made to decrease inappropriate utilization of laboratory tests. Tests showing a decrease of 15% or more, in order of decreasing volume are: Susceptibility Test, Borrelia Antibody, Ova & Parasite Exam, Stool Culture, CSF Culture, AFB Culture and Fungus Culture. Tests showing a volume increase greater than 15% were Mycoplasma/Ureaplasma Culture and Neisseria Gene Probe Test.

Significant changes were made to meet Cost Effectiveness Program goals including: reduction of 3.5 staff positions, elimination of 4 tests, significant ordering restrictions on 6 tests, implementation of susceptibility orders, requiring physician order, procedural changes in all lab areas, reduction of weekend and holiday coverage for routine cultures and reduction in overtime.

New tests/procedures implemented this year include: routine use of gene probe analysis for Neisseria gonorrhoeae testing, gene probe analysis for confirmation of AFB identification, combined fastidious/anaerobe MIC panel, Mycoplasma/Ureaplasma culture from CSF and blood, new Mycoplasma/Ureaplasma transport and Acridine Orange for smear negative blood cultures that are instrument positive.

The laboratory achieved several other important goals during the year. Virology Laboratory was integrated into the Microbiology/Virology Laboratory. The manual blood culture system was replaced by the semi-automated BacT/Alert system. Significant effort was used to update the Chemical Hygiene Plan and to establish safe work practices to meet new OSHA regulations for Bloodbourne Pathogens. A semi-automated susceptibility inoculation instrument replaced manual methods. The Diamedix EIA system replaced 6 traditional IFA tests in the Virology section of the laboratories.

The laboratory has also actively participated in the Total Quality Program. Nine lab staff completed QI leader and team training, and the Microbiology QI team is currently in step 1 of the QI Story. All supervisors have completed the Leadership for Total Quality training program. In addition, the laboratory completed 2 CAP Q-Probe interlaboratory quality assurance studies and 4 intralaboratory QA studies.

Finally, the Microbiology/Virology laboratory has actively utilized laboratory-based information services to improve the delivery of quality laboratory data. The Virology database was completely restructured so statistical reports can be produced. Custom programs for Infection Control daily hospital surveillance for nosocomial infections and the Reportable Disease daily report were implemented. Several creative programs were written to support the CEP program for physician order of susceptibility tests. Monthly susceptibility data is now collected automatically on the computer and downloaded to a IBM-PC to produce the highly-regarded Quarterly Susceptibility Report.

RESEARCH ACTIVITIES

Investigations into the *in vitro* efficacy of four new quinoline and three new beta-lactam antimicrobics were conducted using special microtiter plates prepared in-house for this purpose. The laboratory continues to participate in the multi-center monitoring of antimicrobial resistance of the *Bacteroides fragilis* group and participated in a multi-center quinoline study. Much effort has gone into investigations to determine antimicrobic resistance profiles that were found to be unique among various intensive care units. This may lead to more specific empiric therapy recommendations for these units. Strains of *Escherichia coli* and *Klebsiella spp.* were noted to have unusual resistance to third generation cephalosporins and we are currently investigating these strains for atypical beta lactamases. Numerous cooperative investigations were carried out with other members of the department or with members of other departments. *Mycobacterium tuberculosis* can now be detected in tissue and fluid specimens directly by the polymerase chain reaction conducted in the Molecular Diagnostic Unit. Plans are underway to expand this service. Several innovative computer programs have been developed in cooperation with Pathology Data Systems personnel to investigate changes in antimicrobic susceptibility and to monitor the ordering of potentially ineffective antimicrobics for patient therapy. The laboratory continues to cooperate with members of the Infectious Disease Service in the use of biological inhibitors to control *Clostridium difficile* enterocolitis. We are participating in two projects with the Department of Ophthalmology, one involving vitrectomy fluids and the other involves testing the efficacy of a topically-applied dye to control blepharitis. We continue to monitor the susceptibility of Gram-positive bacteria to topical mupirocin that are recovered from dermatology patients. In addition, we conducted two investigations for other departments as part of the Cost Containment Program. We showed that vials of Magnevist can safely be used twice/day rather than only once with consequent savings to the hospital. We also showed that Fentanyl/Bupivacaine preparations in the Pharmacy Department were unlikely to support the growth of contaminants. We initiated a program with Pediatrics to study the rate of mycoplasma isolation from neonates and maternal/fetal membranes. Preliminary data showed this to be an interesting area to pursue and the investigation has been expanded. These investigations contributed to the six publications and to the four presentations (abstracts) at national scientific meetings this year.

PUBLICATIONS

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2. Cuchural, G.J., Jr., Snydman, D.R., Iannini, P.B., O'Keefe, J.P., Pierson, C.L., Rihs, J.D. and Finegold, S.M.: Antimicrobial susceptibility patterns of the Bacteroides fragilis group in the United States, 1989. Clinical Therapeutics 1992;14:122-136.
3. Cornick, N.A., Cuchural, G.J., Snydman, D.R., Iannini, P., Hill, G., Pierson, C.L. and Finegold, S.M.: Comparison of newer antimicrobial agents against the Bacteroides fragilis group. J Antimicrob. Chemother., 1992, In Press.
4. Zervos, M. and Pierson, C.L.: Molecular typing of ampicillin-resistant non-B-lactamase-producing Enterococcus faecium from diverse geographic areas. J. Clin. Microbiol., 1992, In Press.
5. Reed, B.D. and Pierson, C.L.: Evaluation of a latex agglutination test for the identification of Candida species in vaginal discharge. J Amer. Board Family Practice, 1992, In Press.

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1. Pierson, C.L. and McClatchey, K.D.: Automation, in, Encyclopedia of Microbiology 1992, Academic Press, Inc., San Diego, California, In Press.
2. Blythe, L., Hankerd, R. and Pierson, C.L.: Investigation of the pathogenicity of Ureaplasma urealyticum in placental membranes and amniotic fluids. Abstracts: Amer. Assoc. Clin. Microbiol. 1992; page 160.

3. Bartkowiak, D. and Pierson, C.L.: Comparison of the Premier Toxin A kit with cytotoxin B and culture for the detection of Clostridium difficile toxins in fecal specimens. Abstracts: Amer. Assoc. Microbiol. 1992; page 473.
4. Goldstein, S., Chenoweth, C., Pierson, C.L. and Bradley, S.: Achromobacter xylosoxidans bacteremia: retrospective review of the literature. Abstracts: Amer College of Physicians, 1992.

Kenneth D. McClatchey, M.D., D.D.S.
Director
Clinical Microbiology Laboratory

Carl L Pierson, Ph.D.
Associate Director
Clinical Microbiology Laboratory

PATHOLOGY DATA SYSTEMS

DEPARTMENT OF PATHOLOGY
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The activities of Pathology Data Systems for the past year can be divided into three separate categories: (1) PathNet software modifications and enhancements; (2) new hardware and software applications to support the data processing needs of users; (3) information support and educational activities.

PATHNET SOFTWARE MODIFICATIONS AND ENHANCEMENTS:

1. Deployed "rules" in hematology, chemistry, and immunology, achieving personnel time savings by shifting previously manual activities to computer-automated tasks.
2. Installation of Version 305 of the Cerner PathNet software.
3. Deployed WP-Link in Anatomic Pathology, allowing faculty members to generate customized reports for personal consultation cases and then upload the report into the departmental database.
4. Deployed automatic SNOMED coding for personal consultation cases in Surgical Pathology with WP-Link as well as for non-gynecologic cytology reports.
5. Implemented bar-code labeling on all specimen collection labels.
6. Activated Cernermail (i.e., the Cerner proprietary electronic mail products) in all laboratories to facilitate communication.
7. Introduced computer-generated slide labels for histology slides.
8. Implemented a pilot project whereby "future" test orders can be entered into the PathNet System and activated when the patient arrives in the future at any blood drawing site for test performance.
9. Upgraded and installed several new instrument interfaces to improve the productivity of the laboratories.

NEW HARDWARE AND SOFTWARE APPLICATIONS:

1. Defined standards and specifications for the new interface between PathNet and the patient management and patient accounting modules (HealthQuest) to be brought up on the INS mainframe computer.
2. Defined functionality requirements for the order entry-results reporting system to be deployed in the future on the hospital mainframe computer.
3. Achieved network connectivity of all Macintosh computers in the department via the Novell network.
4. Developed a series of customized, key-word-driven, utilities for extracting selected surgical pathology reports for faculty members in Anatomic Pathology.
5. Implemented improvements to the professional component billing software.
6. Developed CCL applications to support the review by anesthesiologist of laboratory test results as part of the criteria-map review of blood utilization in the hospital.
7. Deployed the Eagle Innovations software for the development of inexpensive interfaces between heterogeneous host computers.
8. Brought up a new application in cooperation with the Department of Radiology for copying radiology test results from the Radiology Information System to the VAX cluster in PDS, allowing clinicians the opportunity to review such results in an integrated fashion with laboratory results.
9. Continued to improve the performance of the VAX 4200 server whereby transplantation surgeons through the Organ Transplantation Information System (OTIS) and surgeons through

the information system in the Department of Surgery can download and manipulate laboratory information in near-real-time.

INFORMATION SUPPORT AND EDUCATIONAL ACTIVITIES:

1. Served as a host for multiple site-visit teams from other hospitals reviewing Cerner PathNet software.
2. Active participation in the Anatomic Pathology Quality Improvement Team.
3. Database support and statistical analysis for ongoing consolidation and cost-savings efforts in Pathology as well as in the hospital as a whole.
4. Multiple workshop presentation by PDS personnel at the Cerner Annual Meeting, ASCP national meetings, and local continuing education conferences at the Towsley Center.
5. Host for the tenth annual Laboratory Information System Symposium in June at the Power Center which attracted 175 registrants from thirty states and Canada, as well as 34 information system vendors and consultants.
6. Participated in initial efforts to avoid copyright infringement on software running on PCs by such efforts as monitoring software use and making software utilities available on departmental servers.

Bruce A. Friedman, M.D.
Director,
Pathology Data Systems

PHLEBOTOMY SERVICES AND CENTRAL DISTRIBUTION

DEPARTMENT OF PATHOLOGY
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1 JULY 1991 - 30 JUNE 1992

1. As part of the 1992 Cost Efficiency Program, Blood Drawing Station I in the Taubman Health Center was closed, and patients were routed to Stations II and III. This change necessitated major personnel and equipment shifts, and was completed by June 29, 1992. Economies of scale were achieved as a result of the change, but some patients have to travel further for services.

2. Changes mandated by new OSHA requirements were instituted, including gloving during all venipunctures. This change was difficult to implement because of the loss of tactile sensitivity during blood drawing, particularly with pediatric patients.

3. The Briarwood Medical Group facilities were activated in mid-November, 1991. Adult and pediatric blood drawing services were initiated at this time, as well as the option of centrifuging and freezing specimens for subsequent analysis. A considerable effort was expended in designing the laboratory area, ordering equipment, hiring and training new employees, and activating the new facility.

4. A major undertaking during the year was the sponsorship of a two-day post-graduate educational conference at the Towsley Center on phlebotomy team management and techniques. The meeting was very successful, attracting 155 registrants. Supervisory staff from Central Distribution also participated in the conference as faculty members.

5. The following new tests have been added to the menus performed by phlebotomists at the Briarwood facility and the Emergency Department: mono spot test, sedimentation rate, and pregnancy testing.

6. Barcoding of all specimens processed through Central Distribution was initiated, resulting in faster and more accurate processing of specimens through all of the laboratories,.

7. A pilot project was initiated involving Pediatric Nephrology and outpatient phlebotomy whereby physicians can order laboratory tests which are performed at some future time. Patients can thus report directly to an outpatient blood drawing station where the pending order is called up on the computer and activated.

8. Questionnaires were developed and implemented to survey both outpatients and inpatients about their degree of satisfaction with phlebotomy services. These in-depth surveys will allow supervisory personnel to better understand results from patient telephone surveys.

9. As part of the Cost Efficiency Program, personnel reductions in Phlebotomy and Central Distribution were as follows: 4.3 FTEs in Central Distribution and 1.5 FTEs in Phlebotomy during 1991; 1.5 FTEs in Central Distribution and 3.0 FTEs in Phlebotomy during 1992. As the result of this downsizing, an increased burden has been placed on the shoulders of current personnel. In addition, timed draws and stat draws are no longer performed by phlebotomists during their inpatients sweeps. Patients lacking identification bracelets are also not being drawn until the bracelets are replaced.

10. Planning activities for the Cancer and Geriatric Center were undertaken with special emphasis on phlebotomy and specimen handling services.

11. Four employees participated in Quality Improvement Teams during the year.

12. Considerable effort has been directed toward making the Central Distribution and Phlebotomy areas more ergonomically structured in an attempt to avoid carpal tunnel syndrome among employees. This is are areas where intensive "production" keyboard entry takes place for test order entry.

13. Linda Darrow visited the Mayo Clinic to learn more efficient ways to handle our large volume of specimens and to avoid tendonitis and carpal tunnel syndrome.

Bruce A. Friedman, M.D.
Director,
Pathology Data Systems

ADMINISTRATIVE/FINANCIAL AFFAIRS DIVISION

DEPARTMENT OF PATHOLOGY
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The Administrative and Financial Affairs Division, which is under the auspices of the Office of the Chairman and his designee, includes five sections which are organized 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

Surgical Pathology Transcription:

- Paulette Dozier, Office Manager
- June M. Possley, Office Supervisor

B. CLINICAL FACULTY OFFICES, UNIVERSITY HOSPITALS:

- Holly A. Wagner, Office Supervisor

C. MEDICAL SERVICE PLAN BILLING OFFICE:

- Douglas M. Kennedy, Manager
- John J. Gilbert, Financial Analyst

D. OFFICE OF RESEARCH AND EDUCATION ADMINISTRATION:

- Maydis Caldwell Skeete, Grants Administrator
- Kathleen L. Atkins, Student Services Assistant

E. OFFICE OF THE CHAIRMAN:

- Laura D. Blythe, Staff Assistant
- Mary Anne Tishma, Staff Assistant

In addition to the management of daily activities, each of the units completed major projects.

ADMINISTRATIVE SUPPORT CENTER:

1. The M-Labs Program has gained several new clients including Knollwood Clinic, Toledo General Hospital and Lyn Hadley Memorial Clinic. In addition, negotiations are underway with Mt. Clemens General Hospital and Addison Community Hospital.
2. Coordinated the interim inspection of the Laboratories by the College of American Pathologists.
3. Completed information required by CLIA `88. We are awaiting the CLIA `88 application and will coordinate implementation of these regulations for all Pathology and Hospital Laboratories.

4. Several staff are participating on Quality Improvement Teams as part of the Hospitals' Total Quality Program.
5. Participated in the planning for the renovation and remodeling of the Chemistry Laboratory to accommodate the new Chemistry Division which will integrate the General Chemistry, Immunology and Ligand Assay Laboratories.
6. Developed a plan for implementation of the second year of the cost Reduction Program for the University Hospitals and Medical School, reducing budgeted funds by approximately 3% or $700,000 which included a staff reduction of 6 FTEs. This was accomplished primarily through consolidation, reorganization and relocation of the Chemical Pathology Section.

CLINICAL FACULTY OFFICES:

1. Completed a re-organization of secretarial support staff to accommodate the needs of the faculty located in the Hospitals.
2. Participated on a Quality Improvement Team to review slide/block storage, tracking and retrieval.

MEDICAL SERVICE PLAN OFFICE:

1. Developed procedures and methodologies necessary for the implementation of the Resource Based Relative Value System (RBRVS) in January 1992. This preparation resulted in a smooth transition to RBRVS and minimal negative financial impact.
2. With staff from the Department Administration and Pathology Data Systems, implemented improvements to the automated charge entry process and interface resulted in a) ability to audit charges on the front end limiting the number of edits; b) direct charge file transfer to the IDX Billing System allowing professional fees to be posted to accounts one day after physician verification and; c) the ability to process MLabs charges through the interface rather than manually into the IDX System.
3. Automated Immunology service reporting on the charge summary report reducing paper handling by all staff.
4. Initiated direct printing capabilities for Billing Office staff to print pathology reports which enhances statusing and cash flow.
7. Participated in the presentation of the All Funds Budget for Fiscal Year 1992 as requested by the Medical School.

OFFICE OF RESEARCH AND EDUCATION ADMINISTRATION:

1. Processed two NIH grant transfers for new faculty member from the University of Washington at Seattle.
2. Participated in the revision of the Pathology Telephone Directory including placing information on-line for access by all Pathology staff.
3. Participated in the development of the annual departmental rotation for the House Officer Training Program.
4. Processed appropriate documentation to obtain Visas for three research fellows.

GENERAL:

1. Participated with the Chairman to initiate expense reduction associated with all Departmental budgets.
2. Assisted in the development of contracts for new MLabs Clients including Knollwood Clinic and the Toledo Hospital.
3. Served as a member of the A. James French Endowment Campaign Committee to endow a Chair in Dr. French's name as part of the University's Momentum Campaign.

4. Developed a proposal which was submitted to Hospital Administration for the implementation of the CLIA `88 Regulations for all Pathology and Hospital Laboratories.
5. Selected as a member of the Hospitals Division Lead Team for the Total Quality Program. Selected as member of the Purchasing/Accounts Payable "cross over" Quality Improvement Team. Selected as member of the Medical School's Total Quality Team.
6. Served as a member of the Gainsharing Committee including the development of guidelines used for implementing the Hospital's profit sharing program.

SUMMARY OF FINANCIAL DATA:

1. Grants and contracts:

114 active grants, contracts and other accounts		
Total Direct Expenditures	$4,711,414	
Indirect Research Expenditures	$2,014,751	
Total Sponsored Projects		$6,726,165

2. Medical Service Plan:

Average number of active accounts	13,718
Number of charge entries	226,361
Gross Billings - Anatomic & Clinical Pathology	$12,226,361
Net Collections - Anatomic & Clinical Pathology	$4,955,243
Part A Payment	$2,572,000

3. Pathology Laboratories:

Number of fee code procedures	3,324,655
Number of reportable laboratory test results (est.)	14,200,000
Total Gross Revenue Pathology Laboratories	$103,659,465
Total Direct Expenses Pathology Laboratories	$23,373,475

Respectfully submitted

Eugene J. Napolitan
Administrator

EDUCATIONAL ACTIVITIES

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1990 - 30 JUNE 1991

The Department of Pathology has continued 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, as well as providing for senior medical and undergraduate student pathology elective clerkships. Many faculty continue to serve on graduate student thesis committees and supervise medical student research experiences. Within the Medical Center, Departmental teaching activities extend not only to medical students, but also house officers and the staff of many clinical departments in the form of regularly scheduled formal conferences. Departmental teaching also extends to practitioners in the region and nation through courses given through Continuing Medical Education Programs of The University of Michigan and the United States and Canada Association of Pathologists (USCAP).

MEDICAL AND DENTAL STUDENT PROGRAMS:

This was the second year the Department of Pathology offered a summer clinical program for underrepresented minority medical students. The goal of this program is to provide medical students, who have completed their first year, the opportunity to participate in Departmental clinical activities and promote the integration of Basic Science studies with patient-oriented clinical problems. In addition, it is hoped that the early exposure to the multiple opportunities available in Pathology will encourage students to consider careers in the specialty. Ten students participated in the program and formal evaluations indicate that the program is viewed very positively by the students.

The Sophomore Pathology Course (Path 600) continues to be the primary focus of faculty teaching of medical students. The structure of the course is predicated on the students' acceptance of a significant responsibility for their own education, under faculty guidance. Formal evaluation indicated that the course continues to function smoothly and is well accepted by the students. Efforts to closely correlate the Introduction to Clinical Sciences Course (ICS-601) with the Sophomore Pathology Course continues to function to enhance the students' educational experience and reinforce "core material". Revision of the laboratory experience resulted in greater faculty-student interaction and promoted more active learning by students. This is viewed as a positive change by both students and faculty. During the past year a new clinical rotation in Laboratory Medicine was developed and will be offered to fourth year medical students. This rotation will complement our current fourth year Pathology clerkship and medical student research rotations. Department faculty have taken an active role in the development of the new medical student curriculum with faculty serving as Director of Component 2 (2nd year courses), Assistant Director of Component 1 (1st year courses), and individual course directors.

The Department of Pathology continues to have primary responsibilities for the teaching of general and systemic pathology to dental students. This includes the presentation of formal lectures (Pathology 630) and preceptors of laboratory sessions (Pathology 631). Formal student evaluation indicates that the course functions smoothly and is well received by the students.

DOCTORAL PROGRAM:

The graduate program in Pathology was initiated three years ago and currently has nine students enrolled. The primary goal of the Doctoral in Pathology Program is to train individuals for careers as independent scientific investigators with a focus on the study of the cellular and molecular basis of

disease processes. Five graduate level courses are offered by the Department, including a new course on the Genetics and Cell Biology of Aging. Three students are enrolled in combined M.D./Ph.D. programs and three students have achieved candidacy status.

Graduate Medical Education

The Department of Pathology provides formal advance training to M.D.s and Ph.D.s through the Residency Training Program, clinical fellowships and postdoctoral research fellowships. These programs are integrated to provide trainees the greatest opportunity for clinical and research training in their chosen discipline and to foster academic excellence.

Clinical Fellowships

The Department provides advanced training in surgical pathology, cytopathology, hematology, and transfusion medicine through formal fellowship programs. Five positions are currently supported and the clinical fellowships are closely integrated with the Residency Training Programs (see Anatomic and Clinical Pathology Sections).

Postdoctoral Research Training

The Department of Pathology provides advanced research training for approximately 33 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) and externally-funded faculty research grants. This past year 5 fellows completed their training and have assumed the following positions:

1. Mohamed Abaza, Mb,Bcm, Assistant Professor and Head of Hematopathology, University of Southern Alabama, Mobile, Alabama.
2. Robert Larsen, Ph.D., Research Scientist, Glycomed, Inc. Alameda, California.
3. Michael Mulligan, M.D., General Surgery House Officer II, Department of Surgery, Milstein Hospital, Columbia University, New York, New York.
4. Hedwig Murphy, M.D., Ph.D., House Officer, Department of Pathology, The University of Michigan Medical School, Ann Arbor, Michingan.
5. Lawrence Zukerberg, M.D., Boston General Hospital, Boston, Massachusetts

RESIDENCY TRAINING

The Department of Pathology offers high quality resident training in both anatomic and clinical pathology with opportunities to pursue basic research training in experimental pathology. The program continues to be exceedingly competitive with over 110 completed applications received, and 24 candidates invited to interview in the Department this past year. Five outstanding residents were recruited to the Department: Vonda Douglas, M.D., Lois Arend, M.D., Ph.D., Lyndon Su, M.D., Joseph Tworek, M.D. and Hedwig Murphy, M.D., Ph.D.

Currently, there are 25 residents in the Department, 23 of whom are receiving training in both anatomic and clinical pathology and 2 receiving training in anatomic pathology alone. Six residents graduated from the program this past year. Four graduates assumed positions as staff pathologists at The Toledo Hospital, Toledo, Ohio, St. Joseph's Hospital, Flint, Michigan, Mt. Sinai Hospital, Detroit, Michigan, and Swedish Medical Group, Denver, Colorado. Two residents are continuing training, one in Forensic Pathology at the New York Medical Examiners Office in New York City, New York and in the Department of Pathology, University of Wisconsin, Madison, Wisconsin.

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. The residents again completed the American Society of Clinical Pathologists' in-service examination and performed well above the national average.

Formal courses given within the Department include:

I. COURSES IN THE MEDICAL CURRICULUM

A. ICS 500:
   1. Introductory Lectures on General Pathology (15 contact hours).

B. ICS 600/601:
   1. Immunopathology Sequence (15 contact hours).
   2. Clinicopathologic Conferences (10 contact hours).
   3. Selected Topics in Surgical Pathology.

C. NBS 600:
   1. Neuropathology (13 contact hours).

D. Pathology 600:
   1. 83 hours of whole-class lecture (includes self-study, review and examinations), 71 hours of laboratory (includes self-study, review and examinations in each of six sections) (154 contact hours).

E. Pathology Clerkships:
   1. Clinical rotations elected by 49 students at University Hospitals.

F. Summer Clinical Program in Pathology for Underrepresented Minority Students
   1. Elected by nine first year students and one second year student

II. COURSES IN THE DENTAL CURRICULUM

A. Pathology 630:
   1. General Pathology Lectures (45 contact hours).

B. Pathology 631:
   1. Pathology Laboratory (60 contact hours) each of two sections (assisted by Oral Pathology staff).

III. GRADUATE COURSES IN PATHOLOGY

A. Pathology 580: General Pathology for Biologic Scientists
B. Pathology 581: Cellular and Molecular Basis of Disease
C. Pathology 583: General Pathology Laboratory - Histopathology
D. Pathology 620: Genetics and Cell Biology of Aging
E. Pathology 650: Laboratory Techniques in Experimental Pathology
F. Pathology 850: Special Topics in Pathology
G. Pathology 599: Non-Dissertation Research
H. Pathology 990: Pre-Candidate Dissertation Reseach
I. Pathology 995: Candidate Dissertation Research

IV. POSTGRADUATE MEDICINE/CONTINUING MEDICAL EDUCATION:

A. Current Topics in Blood Banking Symposium, June 3 - June 5, 1992.
B. Clinical Laboratory Computers Symposium, June 10 - June 12, 1992.
C. Pathology 858:
   1. Neuropathology (18 contact hours).

V. CLINICAL CONFERENCES:

The Department of Pathology provides an important educational service to many other clinical departments through regular participation in interdepartmental working/teaching conference. The Department is involved in many such conferences on a weekly, bi-weekly, and monthly basis. The units served include:

Internal Medicine

- Gastroenterology
- Nephrology
- Hematology/Oncology
- Nuclear Medicine
- Pulmonary Medicine
- Arthritis
- Cardiology
- General (Necropsy Review, CPC)

Dermatology

Thoracic Surgery

Urology

Pediatrics

- Cardiology
- Oncology
- Gastroenterology
- General (Death Conference, CPC)

Obstetrics and Gynecology

- Oncology

Oral Surgery

General Surgery (Breast, GI)

Otorhinolaryngology

Joseph C. Fantone, M.D.
Coordinator,
Educational Activities

THE UNIVERSITY OF MICHIGAN MEDICAL SCHOOL DEPARTMENT OF PATHOLOGY HOUSE OFFICERS AND FELLOWS 1992 - 1993



Charles J. Hunter, M.D.
House Officer V
(3rd Year)



Patricia M. Perosio, M.D.
House Officer IV
(4th Year)



Barbara A. Mackey, M.D.
House Officer V
(5th Year)



Philip L. Perkins, M.D.
Co-Chief Resident
House Officer VI
(5th Year)



John R. Goldblum, M.D.
Co Chief Resident
House Officer IV
(4th Year)



Priscilla R. Lindley, M.D
Assistant Chief Resident
House Officer IV
(4th Year)



Cheryl A. Utiger, M.D.
House Officer V
(5th Year)



Margaret M. Moll, M.D
House Officer IV
(2nd Year)



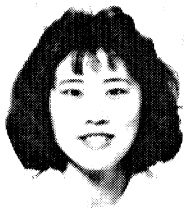
Suzanne M. Cook, M.D.
House Officer IV
(4th Year)



Kyle A. Carr, M.D.
House Officer IV
(4th Year)



Eric P. Kaldjian, M.D.
House Officer IV
(4th Year)



Jane C. Huang, M.D.
House Officer III
(3rd Year)



David A. Start, M.D.
House Officer III
(3rd Year)



Sonya K. Brown, M.D.
House Officer III
(3rd Year)



Philip J. Boyer, Ph.D., M.D.
House Officer II
(2nd Year)



Walter H. Henricks, M.D.
House Officer II
(2nd Year)



Scott G. Silverman, M.D.
House Officer II
(2nd Year)



Robert A. Stern, M.D.
House Officer II
(2nd Year)



Jeffrey P. Pearson, M.D.
House Officer III
(3rd Year)



Eric D. Hsi, M.D.
House Officer III
(3rd Year)



Hedwig S. Murphy, Ph.D., M.D.
House Officer III
(3rd Year)



Lois J. Arend, Ph.D., M.D.
House Officer I
(1st Year)



Vonda K. Douglas, M.D
House Officer I
(1st Year)



Lyndon D. Su, M.D.
House Officer I
(1st Year)



Joseph A. Tworek, M.D.
House Officer I
(1st Year)



John F. Jansen, M.D.
Surgical Pathology Fellow
(5th Year)



Joseph E. Willis, F.R.C.S.I.
Surgical Pathology Fellow
(6th Year)



Seyhan Alkan, M.D.
Hematopathology Fellow
(6th Year)

M-LABS

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1991 - 30 JUNE 1992

The M-Labs program has seen several changes in this last year. I have become the Director, Susan Sadler has become our Client Services Representative, and Rodolfo Rasche, M.D., has joined our staff part-time.

In the recent past, the M-Labs program had suffered the loss of two major clients, one an independent laboratory, the other a hospital. Although there was some increased revenue from growth of services to current clients and from the addition of a few physicians accounts, the net result has been a reduction in services delivered and in revenue generated.

M-Labs is currently beginning a marketing survey to be sent to selected pathologists within our service range of 100 miles. We are also looking forward to a reveiw by Chi Laboratory Systems, a consulting firm which has been engaged to evaluate the program and assist in the strategic planning for M-Labs.

We have meanwhile been marketing more actively and we look forward to providing Clinical Pathology Services to a major new hospital client this fall. Proposals have also been submitted to several other potential clients for Clinical Pathology and Cytopathology services.

M-Labs goals for the forthcoming year are to assess the needs of our potential clients, to see where our strengths can be utilized to meet these needs, perhaps to increase our strengths where needs are strong, and to resume the net growth in M-Labs activities that was present in earlier years.

Eugene M. Silverman, M.D.,
Director,
M-Labs Program

RESIDENT TRAINING PROGRAM

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1991 - 30 JUNE 1992

The Department of Pathology offers high quality resident training in both anatomic and clinical pathology with opportunities to pursue basic research training in experimental pathology. The program continues to be exceedingly competitive with over 110 completed applications received, and 24 candidates invited to interview in the Department this past year. Five outstanding residents were recruited to the Department: Vonda Douglas, M.D., Lois Arend, M.D., Ph.D., Lyndon Su, M.D., Joseph Tworek, M.D. and Hedwig Murphy, M.D., Ph.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 alone. Six residents graduated from the program this past year. Four graduates assumed positions as staff pathologists at The Toledo Hospital, Toledo, Ohio, St. Joseph's Hospital, Flint, Michigan, Mt. Sinai Hospital, Detroit, Michigan, and Swedish Medical Group, Denver, Colorado. Two residents are continuing training, one in Forensic Pathology at the New York Medical Examiners Office in New York City, New York and in the Department of Pathology, University of Wisconsin, Madison, Wisconsin.

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. The residents again completed the American Society of Clinical Pathologists' in-service examination and performed well above the national average.

Publications and Presentations:

1. Oberman, H.A. and Markey, B.A.: Noninvasive carcinoma of the breast presenting in adenosis. Modern Path. 1991;4:31-35.
2. Mazarra, P.: Evaluation of the rapid trehalose broth test for the identification of *Torulopsis glabrata*. Poster presentation - ASCP, New Orleans, Louisiana, 1991.
3. Carr, K.: Histopathology of alloplastic spermatoceles in dogs. Poster presentation - USCAP, Atlanta, Georgia, 1992.
4. Cook, S.: Cytomegalovirus is not associated with recurrent spontaneous abortion. Poster presentation - USCAP, Atlanta, Georgia, 1992.
5. Hegg, C.: Relationship of antigen and messenger RNA expression to biological behavior in sporadic and familial medullary thyrocarcinoma. Platform presentation - USCAP, Atlanta, Georgia, 1992.
6. Hsi, E.: Rapid determination of cell-associated tumor necrosis factor by flow cytometry. Paper presentation - USCAP, Atlanta, Georgia, 1992.
7. Kaldjian, E.: Immunohistochemical analysis of breast carcinomas: Correlation of hormone receptors prolifer. activ. tumor vascular and lymph node. Platform presentation - USCAP, Atlanta, Georgia, 1992.
8. Perosio, P.: Detection of mycobacteria in paraffin sections of lung biopsies by the polymerase chain reaction. Paper presentation - USCAP, Atlanta, Georgia, 1992.
9. Perkins, P., Jin, L, McLeod, M., Fukuuchi, A., Cho, K, Thompson, N. and Lloyd, R.V.: Analysis of gastrinomas by immunohistochemistry and *in situ* hybridization histochemistry. Paper presentation - USCAP, Atlanta, Georgia, 1992.

Joseph C. Fantone, M.D.
Director
Resident Training Program

DEPARTMENT OF VETERANS AFFAIRS MEDICAL CENTER
LABORATORY SERVICE

DEPARTMENT OF PATHOLOGY
ANNUAL REPORT
1 JULY 1991 - 30 JUNE 1992

INTRODUCTION:

The Department of Veterans Affairs Medical Center (VAMC) is a Dean's Committee institution affiliated with the University of Michigan. The VAMC Laboratory Service maintains a close relationship with the University Department of Pathology at every level. The pathologists in the Laboratory Service have academic appointments and participate in University departmental activities in a manner similar to other sections. Recruitment efforts for pathologists are combined and candidates are selected on the basis of academic performance and potential as well as professional competence similar to any departmental candidate. There are four full-time pathology staff positions and although one vacancy has existed for some time a candidate for the position has been identified and is expected to be on the staff by September 1992. Three resident training positions have been maintained at the VAMC for university pathology residents who serve monthly rotations in Surgical Pathology, Autopsy Pathology, and a number of arranged electives including Electron Microscopy and special study programs in Surgical Pathology. The Chief, Laboratory Service is a voting Member of the Dean's Committee.

ANATOMIC PATHOLOGY:

A. Surgical Pathology: 4,983 surgical cases have been accessioned and reported during this period of time. This is an increase of approximately 100 cases over the past year. The resident assigned to surgical pathology, usually a first year resident, acts as coordinator of the section and in that capacity has the opportunity to examine all of the specimens grossly and microscopically under close one-to-one supervision by the staff pathologist. The resident interacts with the clinical staff, the medical students and the other sections of the Laboratory Service as appropriate to obtain a broad educational experience and to aid in providing high quality medical care. There is an extensive quality improvement program within Surgical Pathology including regular consultations with the Armed Forces Institute of Pathology, University of Michigan, and other outside consultants. There is extensive review and analysis of frozen sections, amended diagnoses and surgical appropriateness within the medical center.

B. Autopsy Pathology: 67 autopsies were performed during this year. Assigned residents perform the autopsies, prepare the pathologic diagnosis, and present the case in conference to the staff pathologists and other residents. The resident cuts and otherwise prepares the tissue or the preparation of slides and then reviews them and makes a microscopic diagnosis. These steps are supervised by staff pathologists who permit a gradual increase in independence for the resident with increased experience. During the year the residents presented the findings of selected autopsies at the Medicine Morbidity and Mortality Conference with a total of 23 cases presented. Several autopsies performed at the VAMC were also presented at the extended Gross Conference at the University.

C. Cytology: 2,702 cases were examined and diagnosed during this period. Although there is not a mandated rotation in cytology within the VAMC the cytologic material is readily available and is used as correlative information for surgical and autopsy pathology.

D. Electron Microscopy: 412 electron microscopy cases were reported. An elective rotation is available for pathology residents in_electron microscopy. In other rotations the electron microscope findings are used to complement surgical or cytopathology

diagnoses. During the academic year Dr. Beals presents biweekly electron microscopy seminars at the University of Michigan. This VAMC is a "Center of Excellence" in electron microscopy and serves as consultant to other VA Medical Centers, to the University of Michigan Hospital, and to other hospitals by contract.

CLINICAL PATHOLOGY:

During the last fiscal year (Fiscal Year 1991) 1,511,885 clinical pathology procedures were done in the laboratory. In chemistry there were 875,454; in hematology 135,474; in microbiology 200,900; and in blood bank 200,180 tests were done. This represents raw data rather than weighted test numbers. There is not a formal clinical pathology rotation available for pathology residents at this time although the residents may participate or observe clinical pathology procedures when this activity is appropriate in relation to their other rotations. Dr. Chensue is director of clinical pathology and makes available interesting and pertinent clinical laboratory information to the residents as desired.

EDUCATION AND TEACHING:

In surgical pathology the staff pathologists provide one-to-one teaching during the surgical sign out time. In addition, there is a surgical pathology conference approximately every other week and an autopsy conference with the entire staff following each autopsy. Because of the closeness of various sections of the laboratory there is frequent consultation among the pathologists and the residents are involved throughout. Since the VAMC is relatively close to the University the residents are permitted and expected to attend the appropriate teaching conferences at the university as well. The entire staff participates in the laboratory and lecture portions of the second year medical students at the University of Michigan. Lectures in bone pathology are also given to the dental students. The VA staff also participate in other ad hoc lectures and in a moderate number of seminars for the resident staff, most often given at the University of Michigan.

RESEARCH:

The specific efforts of the pathology staff are included on individual reports. Dr. Chensue served as a member of the VA Research and Development Committee for most of the time period covered by this report. At the present time his term on that committee is complete. He does have a strong funded research program and cooperates with other investigators at the University of Michigan. Other staff participate in various clinical studies and collaborate with a variety of investigators. The laboratory in general serves the VAMC research program by providing considerable technical support for clinical research and in some cases for more basic research in both anatomic and clinical pathology. The staff serve as consultants and advisors for a number of research programs.

ADMINISTRATION:

The staff pathologists at the VAMC serve in various capacities involving administrative tasks for the University of Michigan, such as the Resident Selection Committee, the Medical Student Admissions Committee, and the teaching faculty of the second year medical students.

SUMMARY:

The Department of Veterans Affairs Medical Center Laboratory Service considers the practice of high quality medicine and the appropriate care of patients as its first and highest responsibility. Within the service there is an extensive quality improvement program that integrates with that of the hospital as a whole. The laboratory service has been accredited by the College of American Pathologists since the early 1960's. The Blood Bank is certified by the American Association of Blood Banks and is approved

by the Federal Drug Administration. The association with the University of Michigan serves to strengthen and improve the quality of patient care. The teaching effort involving both residents and medical students is of mutual benefit to the two institutions. The physical plant of the VAMC Laboratory Service is short of space but there continues to be progress toward the VA Clinical addition that will double the present space.

Lee Weatherbee, M.D.
Chief, Laboratory Service
Ann Arbor VA Medical Center