

the AFIP LETTER

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Armed Forces Institute of Pathology
Washington, D.C. 20306-6000

Vol. 154, No. 1
February 1996

Telepathology at AFIP

Reprinted from *Telemedicine Today*. 1-800-386-8632.

On January 29, 1996, Paul A. Fontelo, LTC, MC, USA, demonstrated AFIP's Telepathology Program to Wendelin Hayes, DO, Georgetown University; Russ Zajtchuk, BG, MC, USA, Commander, US Army Medical Research and Materiel Command; and Florabel G. Mullick, MD, SES, AFIP Associate Director and Director, Center for Advanced Pathology.

LAUNCHED IN 1993, AFIP's Telepathology Program has the primary objective of supporting remote medical treatment facilities within the continental United States and overseas, especially single-pathologist laboratories. According to Paul A. Fontelo, LTC, MC, USA, the major function of the Telepathology Program is to support the consultation mission. "We processed 51 cases from eight remote sites during 1995," he notes. Although originally intended to be an anatomic pathology

consultation service, recent submissions have included clinical pathology material.

Telepathology cases can be transmitted to the AFIP through a modem connection or through generic file transfer protocol (ftp) on the Internet. Contributors with the Silicon Graphics "In Person" system can link to the AFIP and hold live videoconferencing over the Internet, although bandwidth limitations require that image files be transmitted prior to the live session. "From the outset, our goal has always been to provide an expedited consultation process approximating real-time telepathology," notes LTC Fontelo, "however, synchronous telepathology consultation will likely be initiated in the future." Time zone differentials among contributors, however, restrict this modality. It would be most useful within the same time zone, although potentially valuable within the continental United States. Caseload constraints may also hinder implementation of this method. "In effect, the combination of limited manpower and time zone differences disrupts our ability to perform "real-time" consults," LTC Fontelo adds.

The telepathology consultation strategy is modeled after the standard AFIP consultation procedure, where case materials (slides, paraffin blocks, tissue) arrive by mail and are centrally accessioned and assigned to the appropriate pathology branch for review and diagnosis. AFIP faxes the final report and sends a printed copy to the contributing pathologist. In a telepathology consultation, images are transmitted electronically and viewed on a computer monitor. The remainder of the process follows the standard AFIP format.

The AFIP supports telephone modem transmissions through the Roche Image Manager system. Images selected by the contributing pathologists can be sent to the

Continued on page 4



DIRECTOR'S MESSAGE



AFIP Receives Top CAP Inspection

On January 31 and February 1, 1996, the College of American Pathologists (CAP) completed an extensive inspection of our laboratories, resulting in the finest report in our history. The team reviewed documentation and the quality of work produced in our laboratories, and held one-on-one meetings with department chairs. Their review included the consultative laboratories located here in our building and at the Armed Forces DNA Identification Laboratory in suburban Rockville, Md.

Led by Craig Dice, MD, PhD, CAP Mid-Atlantic Regional Commissioner, and a group from the Morristown, N.J., Memorial Hospital, the team provided us with an extensive review of our documentation and the quality of our product. AFIP has always been a world leader in the quality of our consultative and scientific work, and based on this latest CAP inspection, we remain world-class in all areas, including our documentation.

I'd like to congratulate the dedication, expertise, and professionalism of our staff, who worked hard to prepare for this inspection. I am proud and honored to work with such a superb group of motivated individuals.

Michael J. Dickerson
Col, USAF, MC
The Director

New publication: Tumors of the Serosal Membranes

**Tumors of the Serosal Membranes
Atlas of Tumor Pathology, Third Series, Fascicle 15**

Hector Battifora, MD, and W. T. Elliott McCaughey, MD, FRCP(C)
Armed Forces Institute of Pathology, Washington, D.C.

1995 • ISBN 1-881041-19-0

Since the appearance of the second series fascicle on this topic, there has been considerable growth in our knowledge of these neoplasms, including wider recognition of types of mesothelioma with unusual microscopic features or behavioral patterns.

Recent progress in the application of immunohistochemistry has led to more accurate histological diagnosis of mesothelioma and has made it easier to recognize those nonmesothelial tumors mimicking mesothelioma. Nonetheless, hematoxylin and eosin-stained preparations remain the mainstay of diagnosis of serous membrane tumors. Thus, due emphasis is placed on conventional histological findings in this new fascicle, while at the same time expanding the coverage of important diagnostic tests such as immunohistochemistry.

In addition to the malignant mesothe-

liomas, attention is given to other mesothelial-related tumors such as primary serous papillary carcinoma of the peritoneum, multicystic mesothelioma, intra-abdominal desmoplastic round cell tumor, adenomatoid tumor, localized fibrous tumor, and the so-called "mesothelioma" of the atrioventricular node.

Concise tables depict such features as: the differential diagnosis of diffuse malignant mesothelioma; the comparison of histologic features of mesothelial hyperplasia, mesothelioma, and carcinoma; and the immunohistochemistry of peritoneal mesothelioma and serous carcinoma.

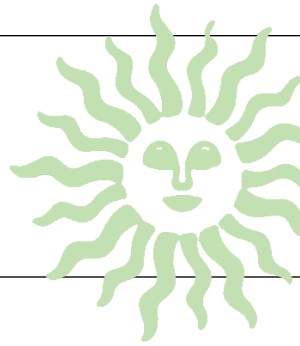
The fascicle is 128 pages long and includes over 150 illustrations, 104 of which are in color. It should be an essential reference for pathologists in practice and in training.

NOTICE

1996 Advanced Forensics Course Canceled

The 1996 Advanced Forensics Course set for the FBI Academy, Quantico, Va., has been canceled.

Questions about this course or any others should be directed to the Center for Advanced Medical Education at 202-782-5021/9280.

EDUCATION SPOTLIGHT

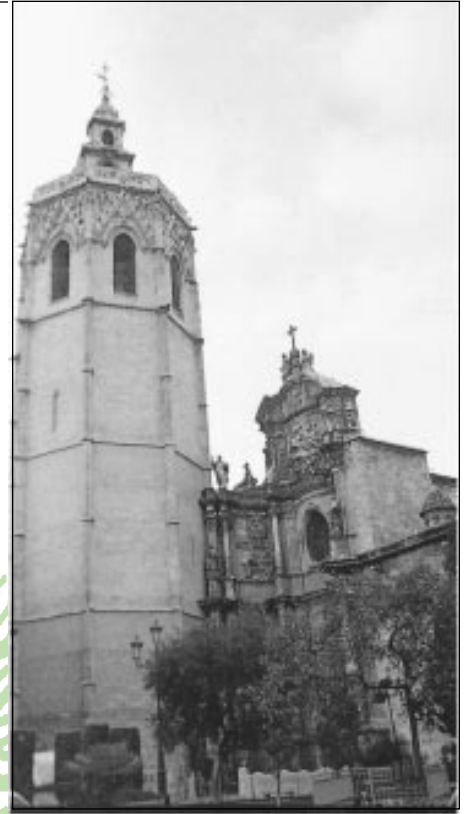
Spanish "Controversies" course set for Valencia, Spain, June 5-8

The AFIP's course "Controversias y Adelantos en Patología Quirúrgica," presented entirely in Spanish, will be held at the Expo Hotel, Valencia, Spain, from June 5-8, 1996. Directed by César A. Morán, Major, USAF, MC; Clara S. Heffess, COL, MC, USA; and Florabel G. Mullick, MD, S.E.S., Director of AFIP's Center for Advanced Pathology, the course will reach out to the Spanish-speaking community in Europe, particularly Spain, Italy, and France. AFIP's faculty of experts will be joined by representatives from such noted institutions as the National Institutes of Health, Bethesda, Md.; St. John's Hospital, St. Louis, Mo.; Baylor College of Medicine, Houston, Texas; Mt. Sinai Medical Center, Miami, Fla.; the University of Barcelona; and the University of Valencia.

A comprehensive overview will take

place on topics including cellular pathology, cytopathology, gastrointestinal pathology, gynecologic and breast pathology, soft tissue pathology, hematopathology, neuropathology, hepatic pathology, otolaryngic and endocrine pathology, and dermatopathology.

Located on the Mediterranean Sea, Valencia is beautiful in early June. Its pleasant climate and clean white sand make it the perfect setting for a variety of outdoor activities, including swimming, windsurfing, fishing, and boating. For further information about the course, contact Mr. Carlos Moran at (202) 782-2556, FAX (202) 782-7166.



*Historic Valencia, Spain.
Courtesy: Expo Hotel.*



Leslie H. Sobin, MD, SES, and Paul A. Fontelo, LTC, MC, USA, Telepathology Program director, review the images for the "Virtual GI Biopsy Course" on the Web.

Virtual Gastrointestinal Endoscopic Biopsy Course now available via the Web

The AFIP's World Wide Web server (<http://www.afip.mil>) now features the "Virtual Gastrointestinal Endoscopic Biopsy Course." This Web course consists of 20 cases selected by Leslie H. Sobin, MD, SES, chief, Division of Gastrointestinal Pathology, Department of Hepatic and Gastrointestinal Pathology. These cases were derived from the 200 cases available in the one-day course held at the AFIP in June 1995. "The cases provide limited patient histories reflecting the day-to-day practice of the surgical pathologist," Dr. Sobin points out. Thumbnail images are linked to larger representative photos typical of the disease process. A diagnosis and discussion page is linked to each case.

Continuing medical education credits through the Center for Advanced Medical Education, AFIP, are now available, and physicians can earn category 1 credits.

Other departments at the AFIP are planning similar WWW offerings in collaboration with telepathology in the near future. With more than 2 million cases and 55 million pathology slides in the repository, the AFIP is in a unique position to provide pathologists and clinicians with continuing medical education programs on the Internet.

PROFILE

SALLY-BETH BUCKNER, SCT(ASCP), IAC, is a cytotechnologist with the Division of Cytopathology, Department of Cellular Pathology. Her primary responsibility is the preliminary screening and evaluation of all consultation cases assigned to the department. Mrs. Buckner

Sally-Beth Buckner, SCT(ASCP), IAC, Division of Cytopathology

obtained her BA in the biological sciences from Mount Holyoke College and attended the cytotechnology program at the University of Virginia. She was employed as a cytotechnologist with Walter Reed Army Medical Center prior to joining the AFIP staff 17 years ago.

Mrs. Buckner has been active in local and national cytology organizations and is currently a member of the Scientific Program Committee of the American Society of Cytopathology and the Cytotechnology Examination Committee of the ASCP Board of Registry. She contributed a chapter in the *Atlas of Diagnostic Cytopathology*, edited by Barbara Atkinson, MD, and is extremely interested

in continuing education. Her proudest achievement is the annual Diagnostic Exfoliative and Fine Needle Aspiration Cytology Course that is given each June, with lectures presented by some of the finest cytopathologists and cytotechnologists in the field.

Telepathology, cont'd from page 1

AFIP via modem at (202) 782-4433. Cases can also be transmitted through the Internet by ftp. Images must be sent together with the AFIP contributor's form (preferably sent by fax), which should contain information including patient's name, social security number, contributor's surgical number, a clinical history including pertinent laboratory tests, sex, age, and site, as well as the contributor's diagnosis. The contributor must inform AFIP Telepathology that a consultation case is being sent by fax, telephone, or through e-mail (telepath@email.afip.osd.mil).

Once the images are received, the case is accessioned and the pertinent pathology department informed. After review by the AFIP pathologists, a report is faxed or telephoned. An AFIP pathologist (consultant pathologist or Telepathology pathologist) will call the referring pathologist to discuss the case if necessary. If more images are required, the AFIP will call the referring pathologist. The final diagnosis is reported before the end of the day for cases accessioned before 10:00 a.m. EST. Dr. Fontelo notes that "the AFIP strives for a turnaround

time approaching real-time consultation. In practice we have been able to fax the final diagnosis within 1 to 4 hours after the images are received."

Due to the proprietary nature of commercially available telepathology systems (both parties must possess the same hardware and software), many overseas medical treatment facilities have not been able to send cases to the AFIP. In order to serve these international sites (mostly developing countries), LTC Fontelo has instituted Internet transmission of images through regular ftp. Institutional accounts are created in Telepathology's computers for referring pathologists to upload their image files. AFIP receives images in several commonly used formats. Most cases have been transmitted as PICT, GIF, or JPEG files.

Images should be identified by the contributor's accession number only. This ensures a certain degree of confidentiality since only the referring laboratory and the AFIP will have access to the patient's surgical number. The AFIP encourages use of a dedicated fax machine at the contributor's laboratory so that access to reports is limited to authorized personnel.

"The greatest value of telepathology in present-day medical care is the speed in

obtaining expert diagnostic consultation over remote distances," says LTC Fontelo. AFIP's goal of expediting the diagnostic process approaching real-time systems offers real advantages. Its complement of internationally known pathologists provides a resource for expert opinion. Expedited diagnosis by telepathology translates into timely management and cost savings. New imperatives in the national health care system herald the value of telepathology as an indispensable diagnostic modality for the future.

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COL Michael J. Dickerson
COL, USAF, MC
The Director

Welcome to the Armed Forces Institute of Pathology's Home Page! AFIP is a world leader in pathology consultation, education, and research. Last year, we received over 45,000 consult requests, consultation reports, provided over 60,000 education training hours, and utilized sophisticated research to study the disease process.

AFIP's National Tissue Repository contains approximately 2.2 million cases, including 50 million histological slides, 42 million paraffin blocks, and 20 million frozen cryostat sections, making it a tremendous resource for the international pathology community. We are especially interested in research collaboration projects and encourage you to contact us with your ideas.

Our customers include all military services, VA Medical Centers, other Federal agencies, and the international civilian medical community. AFIP's Center for Advanced Pathology (CAP) has over 22 departments in 22 different

Center for Advanced Medical Education (CAME)
Listing of CME courses and educational programs sponsored by the AFIP and ARP. An on-line registration form is available

National Museum of Health and Medicine
Information on some of the exhibits and services

The AFIP Letter
Bimonthly publication in the PDF format

AFIP Highlights:
Featured pages of the AFIP WWW site and announcements of additions

Weekly Seminars
Presentations by Pathology Departments at the AFIP which may be of interest to pathologists in the Washington DC metropolitan area

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- ▶ Department of Virology Pathology
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- ▶ AFIP Telepathology
- ▶ Department of Orthopedic Pathology
- ▶ Department of Pulmonary Pathology
- ▶ Department of Cellular Pathology
- ▶ The AFIP Letter

National Museum of Health and Medicine

The Museum is a place to make discoveries and ponder intriguing questions. Exhibitions draw upon the Museum's collections to illuminate current health issues, the nature of medicine, and technology used in the treatment of disease. Exhibitions offer an array of health and science information, interactive computer stations, anatomical materials and fascinating photographs and illustrations.

A Place to Make Discoveries...

War Medicine
Medical practices at a time when the germ theory of disease was not known. View medical kits of both Union and Confederate doctors. See battlefield injuries, including General Daniel L. Sickles' femur, donated to the Museum in 1953. Follow the progress of individuals undergoing facial reconstruction—the beginning of surgery.

In a World with AIDS
Interactives to better understand the choices you can make to protect yourself and learn about the science of HIV transmission. Find out how people living with AIDS can live with the syndrome's challenges. Compare the historical struggle against other recurrent diseases with today's campaign to fight AIDS.

Netscape: ortho.html

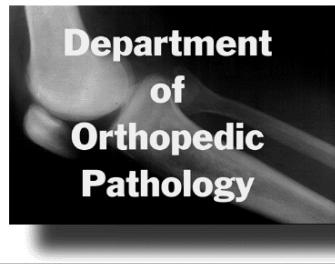
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THE AFIP

Department of Orthopedic Pathology



Donald E. Sweet, M.D.
Chairman & Registrar

Department of Orthopedic Pathology
American Registry of Orthopedic Pathology

This site under construction...Beware of falling bytes!
Last Modified 15 December 1995

- ▶ Metabolic Bone Evaluation Program & Protocol
- ▶ Modified Oil Red O Method for Demonstration of Polymeric Debris
- ▶ Orthopedic Pathology Study Cases

- What's Here:**
- CME Courses
 - Links to all AFIP departments
 - Telepathology information
 - On-line course registration
 - Electronic Fascicle page

http://www.afip.mil

REPOSITORY AND RESEARCH SERVICES

A note on case submission requirements

The most common reasons cases are delayed in the accessioning process are that insufficient material (no paraffin blocks) was sent or that the contributor requested the return of submitted slides. AFIP policy is that submitted slides are permanently retained. When contributors request slides be returned, our personnel must call and receive permission from the contributor to retain the slides. If permission is not given to keep the slides, the case is not accessioned and is returned to the contributor. This takes time and delays accessioning of the case. Paraffin blocks will be returned upon request and

are usually forwarded back to the contributor within 30 to 60 days. Contributors are encouraged to consult the AFIP Case Consultation Matrix attached to the AFIP Form 288-R, Contributor's Consultation Request, for material submission requirements for specific departments. Copies of the AFIP Contributors' Manual containing these requirements are also available and can be obtained by writing the AFIP Research Office or calling (202) 782-2500.

AFIP Letter mailing list update

The AFIP Research Office is responsible for maintaining the mailing list for the AFIP Letter Mailing List for all **civilian** organizations and individuals who want to continue receiving this publication. This list currently contains over 15,000 addresses. When submitting a change of address please include your mailing label to help us identify the correct address to be changed. If you are receiving the AFIP Letter both at your home and place of employment, please let us know which address you prefer and we will delete one. Requests for additions, deletions, or for a change of address should be forwarded to the AFIP Public Affairs Office, ATTN: AFIP-PA; Washington, DC 20306-6000.

HISTOTECHNOLOGY NOTES

Helpful Hint: Clear Leuco Fuchsin

Clear leuco fuchsin by using one filter paper when filtering activated carbon. Using one filter paper eliminates residual carbon found in the leuco fuchsin.

Procedure:

In the last step of preparing Coleman's fuchsin, add one teaspoon to 400 ml of this solution. Stir for 1 minute and pour into a coarse filter paper. Collect the first 100 ml of the filtered solution in a separate container; then transfer funnel to clean stock bottle, return filtered solution to the funnel, and continue.

Prognostic Factors in Cancer

Edited by

P. Hermanek, M.K. Gospodarowicz, D.E. Henson, R.V.P. Hutter, L.H. Sobin
With 14 figures and 60 tables

This monograph is the result of an effort by the International Union Against Cancer (UICC) to study prognostic factors related to cancer. It is an extension of the long-term work on the TNM Classification, the most widely used staging classification and the strongest prognostic tool for most cancers. The purpose of the monograph is to compile information on prognostic factors for most tumor sites and selected tumor types. Each site- or tumor-specific chapter provides a general overview of the relevant literature on prognostic factors. Where possible, the authors have attempted to assess these factors in terms

of their clinical relevance and of their strength and independence in influencing prognosis.

This monograph can be ordered directly from the publisher, Springer-Verlag (1-800-SPRINGER).

AFIP STAFF IN THE NEWS



From left: Sharda G. Sabnis, MD, Florabel G. Mullick, MD, and Brent J. Wagner, Maj, USAF, MC

● **Russell L. Corio, DDS, MSD**, director, Oral Pathology Services, School of Medicine, Johns Hopkins University, Baltimore, Md., was recently appointed the American Academy of Oral and Maxillofacial Pathology's representative to the American Registry of Pathology (ARP). Dr. Corio currently serves on the ARP Executive Committee and was the American Dental Association representative to ARP from 1991 to 1995. From 1981 to 1983, Dr. Corio served as chair, Department of Oral Pathology, AFIP.

● **Gary L. Cohen, Maj, USAF, MC**, staff pathologist, Department of Infectious and Parasitic Disease Pathology, has been named a diplomate of the American Board of Pathology. Maj Cohen has been certified by the Board in anatomic and clinical pathology. He is now a fellow of the College of American Pathologists.

● **Leslie H. Sobin, MD**, chief, Division of Gastrointestinal Pathology, Department of Hepatic and Gastrointestinal Pathology, and director, Center for Scientific Publications, gave the keynote lecture at the National Cancer Institute of Canada's workshop on "The Pathologist's Role in the Staging of Cancer," on November 29, 1995, in Toronto. Dr. Sobin is chairman of the TNM Project, International Union Against Cancer (UICC).

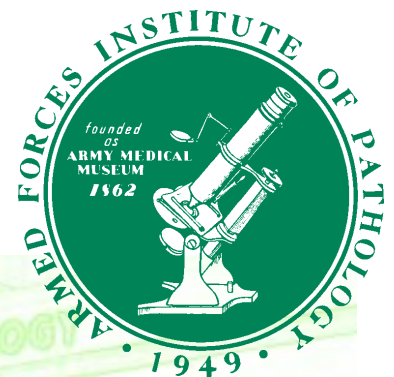
● Representing the **Department of Oral Pathology** as guest faculty members at the Naval Dental School's 39th Annual Course in Oral Pathology were Robert B. Brannon, Col, USAF, DC; Gary L. Ellis, DDS, VA; Robert K. Goode, Col, USAF, DC; Charles W. Pemble, Col (select), USAF, DC; Dale V. Watkins, LCDR, DC, USN; and Theodore Zislis, COL, DC, USA. The course was held at the National Naval Dental Center, Bethesda, Md., January 29–February 2, 1996.

● **Sharda G. Sabnis, MD**, chief, Division of Nephropathology, Department of Genitourinary Pathology, received the Distinguished Professor Award at the joint meetings of the International Conference of the Indian Society of Organ Transplantation, January 4-7 1996, in Ahmedabad, India. She also chaired two sessions and lectured on "Forms of Glomerular Injury in Adults and the Pediatric Population."

● **Florabel G. Mullick, MD**, AFIP Associate Director and Director, Center for Advanced Pathology, was recently recognized by the National Research Council for her contributions as a member of the Subcommittee on Permissible Exposure Levels for Military Jet Fuels from 1993 to 1996. As Director of AFIP's Environmental Pathology and Toxicology Center, Dr. Mullick has expanded the Institute's environmental program to include multiple national and international collaborations. Her educational activities

include participation in over 30 seminars, conferences, and courses in various aspects of environmental and drug-related diseases over the past several decades.

● **Brent J. Wagner, Maj, USAF, MC**, is serving as chief, Genitourinary Radiology, Department of Radiologic Pathology. Maj Wagner teaches the genitourinary section of the 6-week Radiologic and Pathologic Correlation course held throughout the year at AFIP. He also serves as course director for both the week-long categorical courses and the weekend review courses in genitourinary radiology. Maj Wagner serves on the Telemedicine Committee and has been involved in the assessment of digital imaging as it might apply to the AFIP. He is a member of the permanent staff of the Uniformed Services University of the Health Sciences, Department of Radiology and Nuclear Medicine.



RECENT PUBLICATIONS

Histopathology of hepatitis C virus infection

Zachary D. Goodman, M.D., Ph.D.,
and Kamal G. Ishak, M.D., Ph.D.

The advent of testing for hepatitis C virus (HCV) infection has allowed us to refine our knowledge of the diseases produced by this virus. Because HCV is the cause of over 90% of what was previously called non-A, non-B (NANB) hepatitis, most of what has been written over the past two decades about the pathology of NANB is applicable to the study of HCV. Recent investigations have generally confirmed and expanded these observations, although there are exceptions. The availability of reliable tests for the virus prompted a number of reports describing the characteristic histopathology and comparing HCV to other causes of chronic hepatitis. This review summarizes our experience and information in the literature on the morphology of the various forms of HCV infection, including acute and chronic hepatitis, cirrhosis, and precursors of hepatocellular carcinoma.

Seminars in Liver Disease. 1995;15:70-81.

Lipid cell (steroid cell) tumor of the ovary: immunophenotype with analysis of potential pitfall due to endogenous biotin-like activity

Jeffrey D. Seidman, M.D., Susan L. Abbondanzo, M.D., and Gary L. Bratthauer, M.S., M.T. (A.S.C.P.).

Summary: Twenty-eight lipid cell (steroid cell) tumors of the ovary were studied by immunohistochemistry using an avidin-biotin complex detection system; 75% of tumors were vimentin positive, 46% were positive for cytokeratin (CAM5.2 antibody), 37% were positive with the cytokeratin cocktail AE1/AE3 and CK1, and 29% were positive for smooth muscle alpha-actin. Three tumors were positive for CD68 (KP-1), a histiocyte marker, and each of the following markers was positive in two cases: desmin, epithelial membrane antigen, neuron-specific enolase, and S-100 protein. All tumors tested were negative for chromogranin A, CD15 (Leu-M1), myoglobin, neurofilament protein, alphafetoprotein, carcinoembryonic antigen, and melanoma-associated antigen (HMB-45 antibody). Immunoreactivity for cytokeratins was usually focal paranuclear, and globoid, while reactivity for actin and vimentin was

diffuse and cytoplasmic. Based on these findings, melanomas and some carcinomas should be distinguishable from lipid cell tumors. However, the immunohistochemical profiles of smooth-muscle tumors, other gonadal stromal tumors (granulosa cell tumors, thecomas), and hepatocellular, renal cell, and adrenocortical carcinomas overlap with that of lipid cell tumors, and therefore these tumors may not be distinguishable from lipid cell tumors using this technique. In 10 cases (36%), negative controls exhibited weak to moderate nonspecific cytoplasmic staining. Evidence obtained using a biotin blocking kit, and a monoclonal antibody against biotin, suggests endogenous biotin-like reactivity as the source of the nonspecific staining.

International Journal of Gynecological Pathology. 1995;14:331-338.

Diclofenac-associated hepatotoxicity: analysis of 180 cases reported to the Food and Drug Administration as adverse reactions

Alpha T. Banks, Hyman J. Zimmerman, Kamal G. Ishak and John G. Harter

Diclofenac is a nonsteroidal anti-inflammatory drug approved in the United States in 1988 for the treatment of patients with osteoarthritis, rheumatoid arthritis, or ankylosing spondylitis. To characterize the clinical, biochemical, and histological features and possible mechanisms of hepatic injury associated with its use, a retrospective analysis was undertaken of 180 patients whose cases were reported to the Food and Drug Administration from November 1988 through June 1991, as having had possible adverse reactions to diclofenac. Of the reported 180 cases, 79% were female, 71% were 60 years of age or older, and 77% had osteoarthritis. Sixty-seven percent of the cases were detected by symptoms and the remainder by abnormal laboratory tests. Seventy-five percent of the symptomatic patients (90 of 120) were jaundiced. Seven of the 90 icteric patients died. The biochemical pattern of injury was hepatocellular or mixed hepatocellular in 66% of cases. Only 8% had a pattern of cholestatic injury. The remainder, with modestly increased values of both transaminases and alkaline phosphatase, were considered "indeterminate," i.e., either mild hepatocellular or anicteric "cholestatic" injury. Sections of liver from 21 cases were available for study. Hepatic injury was apparent by 1 month after starting the drug in 24%, by 3 months in 63%, and by 6 months in 85% of cases. The latent period in 12% was 6 to 12 months, whereas in 3% it was greater than 12 months. A combination of rash, fever, and eosinophilia, all hallmarks of immunologi-

cal idiosyncrasy (hypersensitivity), was not reported in any case; additionally, the long latent period in most of the patients led to the inference that the mechanism is probably metabolic idiosyncrasy. The data suggest that diclofenac-related liver injury is particularly likely to involve osteoarthritic females, presenting with jaundice 1 to 6 months after starting diclofenac, with injury that is predominantly hepatocellular and presumably caused by metabolic idiosyncrasy.

Hepatology. 1995; 22:820-827.

Acetaminophen (paracetamol) hepatotoxicity with regular intake of alcohol: analysis of instances of therapeutic misadventure

Hyman J. Zimmerman and Willis C. Maddrey

Hepatic injury in alcoholics due to intake of acetaminophen (APAP or acetylparaaminophenol) with therapeutic intent has been reported, but the extent of the phenomenon is not clear, pertinent details of the association remain insufficiently clarified, and the importance of the phenomenon is not widely appreciated. The present report describes 67 patients who developed hepatic injury after ingestion of APAP with therapeutic intent. All were regular users of alcohol. Sixty-four percent of the patients were considered to be "Alcoholic" or reported intakes greater than 80 g/d, 35% took 60 g/d or less, and the remainder were vague in their reporting. Doses of APAP were in the "nontoxic" range (<6 g/d) in 60% of the group, within the recommended range (<4 g/d) in 40%, and at 4.1 to 6 g/d in 20%. Characteristic feature was the towering level reached by aspartate transaminase (AST) with figures ranging from 3,000 to 48,000 IU in more than 90 to of cases. Almost 20% of the patients died. The data on these patients were similar to 94 cases of injury from APAP taken with therapeutic intent reported in the literature. This study provides further evidence of hepatic injury in regular users of alcohol, especially chronic alcoholics, who take APAP with therapeutic intent. Susceptibility is presumably caused by induction of cytochrome P-4502E1 by ethanol and by depletion of glutathione (GSH) because of the effects of alcohol, the malnutrition often associated with alcoholism, and the depletion associated with chronic use of APAP and impaired glucuronidation caused by fasting perhaps as well. The syndrome of liver injury is distinctive, marked by uniquely elevated levels of AST, and poses a significant threat. A greater awareness of the phenomenon by the medical and lay community is essential.

Hepatology. 1995;22:767-773.

Postgraduate Short Courses in Continuing Education

Academic Year 1996

Course Title	Scheduled Dates	Location
24 th Annual Course in Orthopedic Pathology	3–8 March 96	Annapolis Marriott Waterfront, Annapolis, MD
34 th Annual Basic Science Course in Otolaryngology: Head & Neck Surgery	4–29 March 96	USUHS, Bethesda, MD
32 nd Annual Forensic Dentistry	11–16 March 96	DoubleTree Hotel, Rockville, MD
Liver Biopsy Interpretation	30–31 March 96	AFIP, Washington, DC
Abdominal & Pelvic Imaging Review	13–14 April 96	Loew's Annapolis Hotel, Annapolis, MD
6 th Annual Anatomic Pathology Review & Update	13–20 April 96	Renaissance Hotel, Arlington, VA
Emerging Infections: Clinical & Pathologic Update	27 April–1 May 96	Emory Conference Center, Atlanta, GA
Spectrum of Lymphoid Lesions in Lymph Nodes & Extranodal Sites	1–3 May 96	Bethesda Marriott, Bethesda, MD
9 th Annual Forensic Anthropology	13–17 May 96	USUHS, Bethesda, MD
2 nd Annual Musculoskeletal Radiology	18–19 May 96	Radiologic Pathology Education Center, Wash., DC
Diagnostic Exfoliative & Fine Needle Aspiration Cytology	3–7 June 96	Crystal City Marriott, Arlington, VA
Controversias y Adelantos en Patología Quirúrgica	5–8 June 96	Expo Hotel, Valencia, Spain
5 th Annual Descriptive Veterinary Pathology	11–14 June 96	AFIP, Washington, DC
Histopathology Seminar	19–21 June 96	Harvey's Resort Hotel & Casino, Lake Tahoe, NV
Hepatopathology '96	27–29 June 96	Marriott Resort, Vail, CO

INTERNET Updates on Courses Available at *CAME@EMAIL.AFIP.OSD.MIL*

Visit our new Website at <http://www.afip.mil>

24th Annual Course in Orthopedic Pathology

This course introduces both experienced pathologists and senior pathology trainees to the basic biological principles underlying orthopedic pathology through a conceptual approach. The course will consist of lectures, unknown discussions, and laboratory experience in orthopedic pathology and will emphasize radiographic-pathologic correlation and morphologic analysis. Orthopedic-related specialists and radiologists should find this course of interest and benefit in the diagnosis of bone and joint disorders.

34th Annual Basic Science Course in Otolaryngology Head & Neck Surgery

This four-week intensive course in otorhinolaryngic anatomy, embryology, and pathology integrates basic science and clinical practice. Lectures are given by leaders in their field, giving course participants a firm foundation in the specialty. The core lectures are supplemented by a thorough review of the AFIP head and neck histology slide set, and anatomic cadaver dissections. A fresh cadaver flap demonstration with microvascular applications is also included. The course will include mini workshops in endoscopic sinus surgery and craniofacial plating. Participants will also attend the MG Paul H. Streit Memorial Seminar which will focus on facial plastic surgery.

32nd Annual Forensic Dentistry

Presented by specialists in the fields of forensic dentistry, criminal investigation, and law. This six-day course will consist of lectures, a mock trial, illustrative situations, and student participation in two laboratory exercises involving the identification of human remains by dental means. Topics to be covered include: AFIP experience with recent forensic missions; recording and use of dental data in human identification and criminal detection procedures; new developments in forensic procedures; mass disaster management; and bite mark evidence and analysis (including a limited attendance bite mark analysis exercise).

Abdominal & Pelvic Imaging Review Course

This two-day course will present a comprehensive review of radiologic imaging of the abdomen and pelvis to include the gastrointestinal tract and genitourinary tract and solid organs. Emphasis will be placed on current issues and radiologic-pathologic correlation. The faculty, which will include current and former members of the AFIP staff as well as experts in the field, will lecture on both traditional and evolving imaging techniques.

6th Annual Anatomic Pathology Review & Update

This one-week intensive review of anatomic pathology (64 hours CME) focuses on current concepts and diagnostic problems. The course materials are directed toward pathology residents in their final two years of training and individuals from the community of practicing pathologists seeking a short intense updated overview. Representative staff from each of the AFIP departments listed in the program will provide didactic lectures. The lectures will be complemented by an extensive syllabus and "hands-on" microscopic study sessions. In addition to daily sessions of 7–8 hours, there will be four evening sessions. A CD-ROM (PC) set of 2 disks containing selected digitized kodachromes of the study slides will be provided to participants.

Emerging Infections: Clinical & Pathologic Update

This year the AFIP course on infectious disease will be held in collaboration with Emory University School of Medicine and the Centers for Disease Control and Prevention (CDC). The course will focus on newly emerging and re-emerging pathogens including such conditions or pathogens as plague, Lyme disease, Kaposi sarcoma, Microsporidiosis, Buruli ulcer, Ehrlichiosis, Hantavirus, and Ebola virus. Issues of emerging drug resistance in pneumococcal and other streptococcal infections will also be discussed. Experts currently working on these diseases will present the epidemiology and clinical features paired with lectures by other experts on the pathology and pathogenesis of each disease. The role of zoonotic infections will also be covered.

Instructions for Filling Out Application Form

- 1. Accreditation:** The Armed Forces Institute of Pathology is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.
- 2. Course Fee:** Checks for all courses are to be made payable to the American Registry of Pathology (ARP). We can only register an applicant when full payment is received.
- 3. Registration Procedures for International Applicants:**

Civilians:

Mail letter of application to:

Chief, Program Resources Branch
E/VCP, Rm 266
United States Information Agency
301 4th Street, S. W.
Washington, D.C. 20547
FAX: (202) 619-4655

Letter of application should include:

1. Title of course
2. Inclusive dates of course
3. Your present position
4. Your home and office mailing address
5. Your date and place of birth
6. Your country of citizenship
7. Your financial arrangements for stay at this course

(U.S. Government cannot be responsible for any expenses incurred while you are in the U.S.)

With letter of application, attach a copy of course application form, a check drawn on a U.S. bank or international money order, payable to the American Registry of Pathology, in U.S. dollars in the amount required.

Foreign Military:

Request the desired training through your military training channels to the Security Assistance Office of the U.S. Mission in your country.

International Applicants Employed by an Agency of the U.S. Government

Attach to letter of application (see above) a letter certifying employment from your servicing personnel office and mail to:
International Training Program Manager
U.S. Army Health Professional Support Agency
Attn: SGPS-EDI; International Training Officer
5109 Leesburg Pike
Falls Church, VA 22041-3258
FAX: (703) 756-7535

APPLICATION FORM - AFIP COURSES

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I understand that I have 14 days in which to return unwanted books to the American Registry of Pathology, with subsequent credit to my account. I also understand that I may withdraw, with written notice, from the "AFIP ATLAS SUBSCRIBERS" program at any time. **Prices subject to change at any time.**

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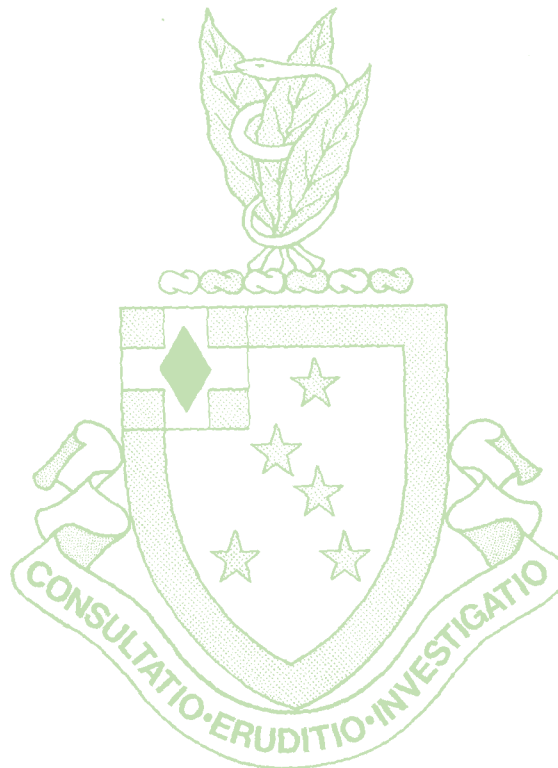
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Recent Publications by AFIP Staff

1. Banks AT, Zimmerman HJ, Ishak KG, Harter JG. Diclofenac-associated hepatotoxicity: analysis of 180 cases reported to the Food and Drug Administration as adverse reactions. *Hepatology*. 1995;22:820-827.
2. Goodman ZD, Ishak KG. Histopathology of hepatitis C virus infection. *Semin Liver Dis*. 1995;15:70-81.
3. Goodman ZD, McNally PR, Davis DR, Ishak KG. Autoimmune cholangitis: a variant of primary biliary cirrhosis: clinicopathologic and serologic correlations in 200 cases. *Dig Dis Sci*. 1995;40:1232-1242.
4. Hermanek P, Sobin LH, Hayat M. Staging classification. In: *Oxford Textbook of Oncology*. Oxford, England: Oxford University Press; 1995:880-887.
5. Ishak KG. Granulomas of the liver. *Adv Pathol Lab Med*. 1995;8:247-361.
6. Ishak KG, Markin RS. Liver. In: Damjanov I, Linder J, eds. *Anderson's Pathology*. 10th ed. St. Louis, Mo: Mosby-Year Book, Inc; 1996:1779-1858.
7. Ishak KG, Zimmerman HJ. Morphologic spectrum of drug-induced hepatic disease. *Gastroenterol Clin North Am*. 1995;24:759-786.
8. Morgan AM. Localized reactions to injected therapeutic materials. Part I. medical agents. *J Cutan Pathol*. 1995;22:193-214.
9. Morgan AM. Localized reactions to injected therapeutic materials. Part II. surgical agents. *J Cutan Pathol*. 1995;22:289-303.
10. Pantongrag-Brown L, Nelson AM, Brown AE, Buetow PC, Buck JL. Gastrointestinal manifestations of acquired immunodeficiency syndrome: radiologic-pathologic correlation. *Radiographics*. 1995;15:1155-1178.
11. Seidman JD, Abbondanzo SL, Bratthauer GL. Lipid cell (steroid cell) tumor of the ovary: immunophenotype with analysis of potential pitfall due to endogenous biotin-like activity. *Int J Gynecol Pathol*. 1995;14:331-338.
12. Sherman KE, Lewey SM, Goodman ZD. Talc in the liver of patients with chronic hepatitis C infection. *Am J Gastroenterol*. 1995;90:2164-2166.
13. Soini Y, Welsh JA, Ishak KG, Bennett WP. p53 mutations in primary hepatic angiosarcomas not associated with vinyl chloride exposure. *Carcinogenesis*. 1995;16:2879-2881.
14. Zimmerman HJ, Ishak KG. General aspects of drug-induced liver disease. *Gastroenterol Clin North Am*. 1995;24:739-757.
15. Zimmerman HJ, Maddrey WC. Acetaminophen (paracetamol) hepatotoxicity with regular intake of alcohol: analysis of instances of therapeutic misadventure. *Hepatology*. 1995;22:767-773.