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the AFIP LETTER

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

Vol. 151, No. 3
June 1993

Molecular pathology at AFIP

When, 40 years ago, Watson and Crick deduced the double helical structure of DNA, they set in motion a chain of events the full impact of which is yet to be realized. Understanding the molecular structure of DNA gave rise to DNA sequencing, analysis of gene structure, and the ability to precisely identify the differences between DNA of different individuals and between the nucleic acids of healthy and diseased cells. The enormous impact of this biological revolution on medicine has been reflected at the Armed Forces Institute of Pathology. Some of these changes have attracted a great deal of public attention. Panels convened by the AFIP's National Museum of Health and Medicine to discuss the ethical implications of analyzing President Abraham Lincoln's DNA for genetic alterations associated with Marfan's syndrome attracted national attention, as did the establishment of the DNA Identification Laboratory and Repository in the Office of the Armed Forces Medical Examiner.

Quietly accompanying these endeavors have been enormous changes in the approach to research and diagnosis throughout the AFIP, as well as in the background and training of the AFIP staff. The AFIP's first use of molecular biologic methods in research by Dr. Shyh-Ching Lo of the Department of Infectious Disease Pathology enabled the discovery that *Mycoplasma fermentens* and other mycoplasmas may play important roles in the clinical course of the acquired immune deficiency syndrome. Infectious disease has remained an important focus of molecular research at the AFIP. Drs. Burke, Sato, and Virmani of the Department of Cardiovascular Pathology have used in situ hybridization and polymerase chain reaction techniques to investigate the course of early human immune deficiency virus (HIV) infection as well as the cause of AIDS-associated myocarditis. Drs. Wear, Hadfield, Patel, and Meyers of the Department of Infectious and Parasitic Disease Pathology have developed rapid and effective molecular diagnostics for cryptosporidium, the cat-scratch disease bacillus, and a variety of mycobacteria.

Cynthia Wright, PhD (left), chief, Molecular Pathology Division, and Gary Bratthauer, research technician, at work in Molecular Pathology Research Laboratory

Drs. Wright, O'Leary, and Fanning of the Department of Cellular Pathology have developed methods for quantitating the extent of pulmonary *Pneumocystis carinii* infection and explored the limitations of PCR in the diagnosis of *Toxoplasma gondii* infection. These applied investigations have been accompanied by fundamental research on molecular pathogenesis, such as Dr. Wright's elegant elucidation of factors involved in vaccinia virus transcription.

Fundamental inquiries into the molecular changes involved in neoplasia are also underway. Dr. Thomas Fanning has demonstrated that a gene called LINE-1, which codes for a reverse transcriptase protein that allows the gene to "jump around" in the genome causing mutations,

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The Ash Lecture and molecular biology at AFIP

The Ash Lecture, featuring a presentation entitled "The Societal Implications of the Human Genome Project" by Dr. James Watson, was well received. He emphasized the need to spend time and resources on the ethical issues raised as genomic information is developed. He pointed out that we do not know ahead of time the nature of these ethical issues, so that the ethical effort and analysis should proceed in parallel with the development of the information. He also said that we cannot stop the genetic information from being discovered. During the afternoon prior to the Ash Lecture, Dr. Watson was briefed by the AFIP staff on the development of the Armed Forces DNA Identification Registry, which he said was a very important development which should proceed.

The establishment of a diagnostic molecular biology laboratory at the AFIP as described in our feature article is a reflection of the progress of molecular biology (especially genetic) techniques which are gradually becoming relevant and valuable in the evaluation of patient biopsies and autopsy material. These procedures are gradually being passed from basic research through clinical investigative studies, and now to more applied evaluation of diagnostic biopsies.

Finally, I would like to express my gratitude to COL John Jewell who is retiring from the Army on 30 June 1993. COL Jewell has served as Executive Officer of the AFIP for three years and has had an enormous impact on the ability of the AFIP to bring many programs, large and small, to reality. COL Jewell has a valuable combination of a scientific background (PhD in organic chemistry) and administrative experience which he brought to bear on many of these difficult and challenging problems. The AFIP has benefitted from his energetic contributions, and I speak for the entire staff when I say "thank you COL Jewell for a job well done."

Vernon W. Armbrustmacher
Col, USAF, MC
The Director

Tumors of the Parathyroid Gland

ATLAS OF TUMOR PATHOLOGY: Third Series, Fascicle 6
Ronald A. DeLellis, MD
Armed Forces Institute of Pathology, Washington, DC, 1993
ISBN 1-881041-06-9

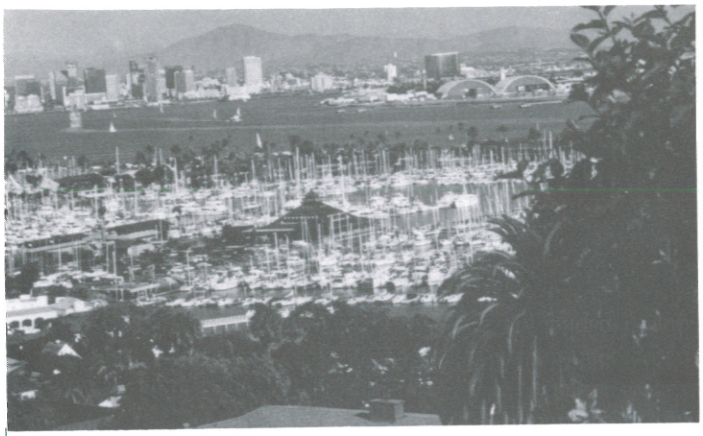
This latest AFIP atlas reflects the progress made in understanding diseases of the parathyroid since the last fascicle on this topic appeared 15 years ago.

The text begins with an overview of the embryology, anatomy, histology, and ultrastructure of the parathyroid glands. Sections on normal and abnormal physiology review current concepts of calcium homeostasis, parathyroid hormone biosynthesis and function, and mechanisms of hypercalcemia. The main body of the text provides thorough discussions of adenomas, carcinomas, and hyperplasias, with an emphasis on clinical and pathological correlations. The discussions are supplemented with recent data derived from cytogenetic and molecular analysis.

There are correlations between histological images and the results of immunohistochemistry, in situ hybridization, and electron microscopy. The text also provides a valuable section on procedures for pathologic examination, including information on frozen section examination, fat stains, density gradients, flow cytometry, and fine-needle aspiration biopsy.

There are 102 pages, 14 color plates, 92 black-and-white illustrations, and numerous timely references. The quality of the illustrations is outstanding. All who deal with parathyroid lesions will find it indispensable.

Book Order Form on Page 14



Left: San Diego Bay view from Point Loma. Photo: San Diego Convention and Visitors Center.

Right: Walt Disney World © at night.

Education Spotlight

Deputy Director reviews first year of courses "On the Road"

Over the last year, AFIP has "reached out" to military and civilian pathologists by providing numerous educational opportunities around the country, according to Deputy Director J. Thomas Stocker, COL, MC, USA. "We've received very positive feedback on our decision to expand traditional course offerings from beyond the Washington, D.C., area," he says, "and our attendance has remained steady across the country." COL Stocker hopes that reasonable tuition rates and courses offered near military areas will encourage even greater attendance in 1994.

AFIP began this cross-country effort when "Controversies and Recent Advances in Surgical Pathology" moved to Orlando, Florida, in February 1992. "We wanted to attract pathologists from smaller hospitals who had broad areas of diagnostic responsibility, and the 2- and 3-hour segments on different areas of pathology proved very beneficial to them," he notes.

Other AFIP courses offered out of town over the last year have included Forensic Pathology in Denver, Colo. (September 1992); Hematopathology in San Antonio, Texas (December 1992); Neuropathology in New Orleans, La. (January 1993); Controversies and Recent Advances in Surgical Pathology in Orlando, Fla. (February 1993); Hepatopathology in San Diego, Calif. (April 1993); Forensic Anthropology in Albuquerque, N.M. (June 1993); and Gastrointestinal Pathology in New York, N.Y. (June 1993).

"Upcoming courses include Infectious Diseases and AIDS in Puerto Rico (July 1993); Pulmonary Pathology in Tucson, Ariz. (November 1993); Oral Pathology in San Antonio, Texas (December 1993); another "Controversies" course set for San Diego, Calif. (February 1994); and Pediatric Pathology in Orlando, Fla. (February 1994). "In June 1994, we're planning a combined course in Gastrointestinal and Hepatic Pathology for Vail, Colorado," notes COL Stocker, "and we're also planning a course for January

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Regional Courses Planned for 1994

AFIP is designing special 2- and 3-day "regional courses" for 1994 to accommodate pathologists who might not have the flexibility to attend a full week of classes. "We hope to conduct these courses in conjunction with state pathology association meetings at a reduced tuition rate for their members," notes COL Stocker. "We're designing them especially for pathologists from smaller hospitals who may not be able to find the time to 'break away' for a more lengthy educational experience."

Classes would be offered in association with the society's annual meeting, with participants designing their own curriculum. "Participants can tell us what type of program they want to hear. For instance, we could offer half-days discussing soft tissue lesions, pediatric cases, prostatic biopsy, or whatever. Participants can, in effect, design the course for the particular interests of their society, and we'll bring AFIP experts to them," he says.

Societies or other associations interested in hosting an AFIP regional course should contact COL Stocker at AFIP- ZB, Washington, DC 20306-6000, or telephone (202) 576-2909.

Nobel Laureate, Dr. James Watson, delivers 1993 Ash Lecture

Nobel laureate James D. Watson, PhD, challenged an audience of over 500 guests to reflect on ethics issues when he spoke about "The Societal Implications of the Human Genome Project" at the Ninth Annual James Earle Ash Lecture on June 1. Watson, who is best known for his discovery of the structure of DNA, warned the audience that as genetic advances are made into the 21st century, society will have to deal with a whole new range of ethics questions. "Should prenatal testing for certain genetic diseases be compulsory, with notification that the child will be born a ward of the state and at great cost? This is a difficult issue, and choices will have to be made which will cause agony and contention," he said.

Watson accepted the invitation to speak based in large part on AFIP's development of a DNA specimen repository for military personnel. The repository will be used to identify the remains of casualties that cannot be identified by other means. "What you're doing here is very important," he noted, "...and you're doing what you should do, but where you end up may not be where you expected to, which is true of genetics."

Since 1968, he has served as director of the Cold Spring Harbor Laboratory in New York and most recently he was the director of the National Center for Human Genome Research (NCHGR) of the National Institutes of Health (NIH). Watson reflected on the historic importance of Charles Davenport, who founded Cold Spring Harbor as the center of the U.S eugenics movement in the early 20th century. Davenport and his colleagues, supported by the establishment, were proponents for breeding to eliminate "bad genes." By the time World War II ended and the horrors of Nazism had been exposed, however, the movement had been thoroughly discredited. "This was a dreadful misuse of genetic reasoning, that we should take extreme social action against people due to genes to insure that 'good' genes dominate in a society."

> "We just can't banish reality. Lots of these afflictions of mankind are due to genes, and now we have the means to do something about them. I think we would not rise to our destiny if we just did not do something about it."

Upon his appointment to head NCHGR, Watson immediately proposed using 3 percent of the budget to study ethical questions, a decision based on his knowledge of Cold Spring Harbor's involvement in the eugenics movement. NIH formed an ethics committee shortly thereafter, with members representing a cross section of the public that could be affected by genetic findings. Watson proudly noted that when he left his position in 1992, 5 percent of the budget was reserved for ethics issues.

Costs will be enormous as efforts are made to completely sequence the human genome; however, Watson noted that the resulting data will make it much easier to locate the gene that causes specific diseases. Current resources for the program are now about $200 million, and funding worldwide is about what should be needed to get the job done. Watson remains optimistic that sequencing costs will be reduced in a few years, leading to even more findings.

But ethical issues remain. How will society deal with privacy questions? What kind of testing standards will be enforced? "There can't be mistakes if you're told your child will be healthy and you've got the Huntington's disease gene," he said. In addition to reducing costs for getting this information, Watson remarked that tests should not be restricted to certain privileged population groups.

Other issues arise. "At what age do you test women for the breast cancer gene? When can they handle the information?...Should people be prescreened as to their emotional well-being to be given genetic information? On the other hand, what good would knowing that you carry the Alzheimer's gene do? You may want to spend all of your money before you're

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AFIP STAFF "IN THE NEWS"

Florabel G. Mullick, MD, SES, receives Presidential Rank in Senior Executive Service

AFIP Associate Director Florabel G. Mullick, MD, SES, was presented with the Meritorious Executive Rank Award in the Senior Executive Service at a Pentagon ceremony on 15 April 1993. Dr. Mullick received the honor "for sustained superior accomplishment in the management of programs of the U. S. Government and for noteworthy achievement of quality and efficiency in the public service."

Originally from Spain, Dr. Mullick received her Doctor of Medicine degree in 1964 from the School of Medicine, Medical Sciences Campus, University of Puerto Rico. A Diplomate of the American Board of Pathology, she first joined the AFIP staff in 1970 as Assistant Chief, Division of Tissue Reaction to Drugs. A succession of progressively responsible positions followed, culminating in her current appointment as Associate Director where she oversees and coordinates the activities of the Departments of Cardiovascular Pathology, Cellular Pathology, Environmental & Toxicologic Pathology, Infectious & Parasitic Diseases Pathology, Legal Medicine, Oral Pathology, Otolaryngic & Endocrine Pathology, Pediatric Pathology, Pulmonary & Mediastinal Pathology, Radiologic Pathology, Scientific Laboratories and Veterinary Pathology.

In addition to her role as Associate Director, Dr. Mullick serves in a variety of capacities: Director of the Institute's AIDS program which includes the development of new medical research protocols which have made the AFIP part of the world's efforts in AIDS diagnosis and research; Director of the Institute's Environmental Pathology Center which serves as a nerve center on environmental issues and national environmental crises; Member of the National Research Council's Subcommittee on Permissible Exposure Levels (PEL's) for Military Jet Fuels; Coordinator for the U.S. Army Military Medicine Consortium for Applied Retroviral Research; Department of Defense representative to the National

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● James G. Smirniotopoulos, MD, chief of Neuroradiology, Department of Radiologic Pathology, returned to the birthplace of his parents to participate in the 9th Hellenic Congress of Radiology. The course was held in Athens, Greece, from 6-10 April 1993. Dr. Smirniotopoulos, in conjunction with Dr. Frances M. Murphy from the Washington, D.C., VA Medical Center, presented a categorical course on "Imaging of Neurologic Emergencies: Stroke and Trauma." Dr. Smirniotopoulos also shared the podium with Dr. Nickolas Patronas, National Institutes of Health, speaking on "Extra-axial Neoplasms." "No one there knew me," he said of Athens, "but everyone asked about my parents!"

● Kamal G. Ishak, MD, PhD, chairman, Department of Hepatic and Gastrointestinal Pathology, delivered the Eighth Annual Rosilie O. Saffos Memorial Lecture on 10 May to the University of Florida Health Science Center, Jacksonville, in cooperation with the North Florida Pathologists' Association. Dr. Ishak's topic was "Chronic Cholestasis: From the Cradle to the Grave." On 11 May, he conducted a seminar on chronic hepatitis for the same group.

● William N. Fishbein, MD, chief, Biochemistry Division, Department of Environmental and Toxicologic Pathology, received the Henry Christian Award for Excellence in Research from the American Federation for Clinical Research Foundation. Dr. Fishbein's award winning paper was entitled Detection of Chromosome 7 inversions in peripheral blood specimens dried on filter paper as a population screen for potential oncogenesis and for exposure to environmental genotoxins.

Histotechnology notes

Maintaining tinctorial quality of Mayer's hematoxylin staining method

HELPFUL HINT: This procedure is for maintaining the high tinctorial quality of the Mayer's hematoxylin staining method. The procedure for the Mayer's hematoxylin is located on page 55 in the revised AFIP Laboratory Methods in Histotechnology.

PROCEDURES:

1. To intensify the clarity of the nuclei:
   (a) Dip slides 15 to 20 times in 1% acetic water or 1% citric acid water before staining in Mayer's hematoxylin .
2. To intensify the bluing of the nuclei:
   (a) Place slides in a dish of hot tap water for two changes of 7.5 minutes each.
   (b) After staining in Mayer's hematoxylin, dip slides in 1% lithium carbonate solution or 5% solution of sodium bicarbonate.

Allen P. Burke, LtCol, USAF, MC, named 1993 Brinton Award winner

Allen P. Burke, LtCol, USAF, MC, staff pathologist in the Department of Cardiovascular Pathology, received the 1993 John Hill Brinton Award at the James Earle Ash Lecture on June 1. The Brinton Award is presented to an outstanding researcher, under the age of 41, who is not a department chairperson or equivalent and is the primary author of a scientific publication.

Dr. Burke's award winning article was entitled "Postmortem localization of HIV-1 RNA by in-situ hybridization in lymphoid tissues of intravenous drug addicts who died unexpectedly." The article appeared in the June 1993 issue of the American Journal of Pathology. Coauthors included W. Benson, J.L. Ribas, J. Smialek, D. Anderson, W.S. Chu, and R. Virmani.

Dr. Burke received his BA and MD degrees from the University of California, Los Angeles. He completed his residency in pathology at Letterman Army Medical Center in San Francisco, Calif.

From 1983 to 1984, he served as chief of pathology at the USAF Regional Hospital, Incirlik, Turkey. From 1984 to 1986, he served as a staff pathologist for AFIP's Department of Genitourinary Pathology, and from 1986 to 1989, he served as a staff pathologist for the Department of Gastrointestinal Pathology and for Walter Reed Army Medical Center. Since 1989, he has also served as a staff pathologist for the Department of Cardiovascular Pathology.

Dr. Burke is a member of the American Society of Clinical Pathologists, the International Academy of Pathologists, and the American Medical Association. He serves as adjunct professor of pathology, Uniformed Services University of the Health Sciences, Bethesda, Md.

Henry J. Norris, MD, Chairman, Department of Gynecologic and Breast Pathology, retires

Henry J. Norris, MD, chairman of the Department of Gynecologic and Breast Pathology since 1970, retired in May. Dr. Norris arrived at the AFIP in 1963 as a staff pathologist in the same department. In his distinguished career he has authored or coauthored over 175 articles and most recently coauthored the AFIP fascicle, *Tumors of the Uterine Vulva, Vagina and Uterine Cervix.*

Dr. Norris graduated from Linfield College in McMinnville, Oregon, and the University of Rochester School of Medicine. Following an internship at Boston City Hospital, he served as senior assistant resident in pathology at the Mallory Institute of Pathology, also at Boston City Hospital. He completed a residency in surgical pathology at Barnes Hospital, Washington University School of Medicine, and was a medical fellow specialist in the Department of Laboratory Medicine at the University of Minnesota Hospital prior to coming to the AFIP.

Dr. Norris currently serves as editor-in-chief for the *International Journal of Gynecological Pathology* and on the editorial board for *Gynecologic Oncology*. He has served as referee pathologist for the Gynecologic Oncology Group since 1971. He has also served as clinical professor of pathology at the Uniformed Services University of the Health Sciences and as president of the International Society of Gynecological Pathologists.

Dr. Norris was named Linfield College Alumnus of the Year in 1989 and received the Distinguished Service Award from the American College of Obstetricians and Gynecologists in 1986.

Dr. Norris will retire to Orlando, Florida, where he will serve as staff pathologist at Orlando Regional Medical Center and Arnold Palmer Hospital for Women and Children.

***Education**, continued from page 3*

1995, in Orlando, that will be similar to the 'Controversies' course, except that it will be given entirely in Spanish."

The success of AFIP's "out-of-town" courses has led to improved facilities and better organized Washington, D.C.-based programs. "We have an extremely important community of pathologists and other physicians in the greater Washington, D.C., area, stretching from New York to Ohio, and we're very cognizant of their desire to take courses here." As a result, the Institute is scheduling courses at local sites, including Georgetown, Bethesda, Alexandria, and Baltimore. "Every course that we take 'on the road' comes back to Washington for a year or two, and we think this is a great way to have attendees take advantage of the marvelous tourist opportunities offered in the Washington, D.C., area."

PROFILES

Jack H. Lichy, MD, PhD, codirector, Molecular Pathology Reference Laboratory, Department of Cellular Pathology

Jack H. Lichy, MD, PhD, has been named codirector of the Molecular Pathology Reference Laboratory, Department of Cellular Pathology.

Dr. Lichy received his BA in biochemical sciences from Harvard University and his MD and PhD degrees from the Albert Einstein College of Medicine, Bronx, N.Y. As a graduate student with Dr. Jerard Hurwitz at Einstein, he identified and characterized several proteins involved in viral DNA replication. He completed a residency in anatomic and clinical pathology at the Hospital of the University of Pennsylvania. Prior to joining the AFIP, he spent 4 years as a postdoctoral fellow for Dr. Peter Howley at the Laboratory of Tumor Virus Biology, National Cancer Institute. During this time, he cloned a novel gene assocated with tumor suppression in human cervical carcinomas. At the AFIP, in addition to clinical duties in the Department of Cellular Pathology, he plans to continue his experimental work on this gene, focusing on regulation of expression, mechanism of action, and its role in carcinogenesis.

Jeffery K. Taubenberger, MD, PhD, codirector, Molecular Pathology Reference Laboratory, Department of Cellular Pathology

Jeffery K. Taubenberger, MD, PhD, has been named codirector of the Molecular Pathology Reference Laboratory, Department of Cellular Pathology. His duties include supervising the Molecular Diagnostics Laboratory and developing molecular methodologies for diagnostic and research pathology. In addition, he conducts basic research in developmental immunology.

Dr. Taubenberger received his BS in biology from George Mason University and earned a combined MD, PhD from the Medical College of Virginia (MCV). His dissertation work in the department of anatomy at MCV involved the characterization of prethymic T lymphocytes. He taught histology to medical students at MCV for 2 years and was awarded three "best professor" awards by the first-year classes.

Prior to joining the AFIP in May 1993, he served as a staff surgical pathologist at the National Cancer Institute. He is board certified in anatomic pathology and did his internship and residency at the National Cancer Institute. While at NCI, he conducted postdoctoral research with Dr. Ada Kruisbeek and Dr. Dinah Singer.

Since 1992, Dr. Taubenberger has been conducting collaborative research with Dr. Kevin Holmes in the Laboratory of Immunopathology, National Institute of Allergy and Infectious Diseases, involving characterization of a novel antigen expressed by early hematopoietic cells and activated B lymphocytes.

WATSON & CRICK, continued from page 1

is greatly overexpressed in some types of cancer. Dr. Jack Lichy is investigating the role of suppressor gene alterations in cervical cancer. Dr. Jeffery Taubenberger is exploring the molecular alterations occurring during T-cell maturation. Dr. Isabell Sesterhenn of the Department of Genitourinary Pathology utilizes chromosomal in situ hybridization to perform interphase cytogenetic studies. Investigations of p53 mutation take place within the Departments of Genitourinary, Cellular, Pulmonary and Mediastinal, and Hepatic and Gastrointestinal Pathology. Other studies have included investigations of the role of HER2 amplification in breast cancer and of Epstein-Barr virus infection in the etiology of Hodgkin's disease and lymphoepitheliomalike carcinomas outside the nasopharynx. This fundamental research is not cheap. About $1 million a year of funding from the National Institutes of Health, the Army Medical Research and Development Command, and various private organizations allows the work to continue during a period of "belt tightening," and has resulted in the publication of scores of papers and several books.

The AFIP's fundamental research efforts have paid off in our ability to use molecular biologic methods in diagnosis. In situ hybridization has been used as an adjunct for the diagnosis of JC virus infection associated with progressive multifocal leukoencephalopathy for almost 5 years. Immunoglobulin and T-cell receptor gene rearrangement assays assist in diagnosing difficult lymph node biopsies. Infectious diseases are diagnosed with the help of a variety of molecular techniques.

The increasingly important role of molecular diagnosis in pathology is reflected in the AFIP's establishment of a Molecular Pathology Reference Laboratory, under the direction of Drs. Lichy and Taubenberger, in the Department of Cellular Pathology. The initial mission of this laboratory is to provide molecular diagnostic consultation to the AFIP staff in support of military consultation. In time, these services will also be made available for civilian cases. #

Interview

AFIP Executive Officer, John Jewell, COL, MSC, USA, retires

COL John Jewell, AFIP Executive Officer since July 1990, retired from the Army on 30 June 1993, to take a position with CIBA- Corning Diagnostics Corporation. In a wide-ranging interview, he discusses recent accomplishments and looks towards the future of the Institute.

Q. How has AFIP's role in health care changed over the last 3 years?

A. As budgets have grown tighter, we've seen the Department of Defense (DoD) emphasize preventive health care. This means keeping people healthier by diagnosing potential diseases early on, and we've really taken the lead in this area. Among other initiatives, we've improved our consultation turnaround time, developed sophisticated technologies, particularly in immunology, and encouraged cross-training in different departments. Cross-training has two benefits: first, younger staff members are exposed to more information from senior personnel, and secondly, we improve our diagnostic capabilities without increasing staff.

We've also expanded our pathology education courses, developed a telepathology pilot program, and are moving rapidly to develop a quality assurance program for military clinical laboratories.

Q. How exactly has turnaround time improved, from an administrative view?

A. When I arrived here 3 years ago, we were in the process of reducing our turnaround time to 72 hours for our consults, from an average of 2 weeks. This was a major educational process which included streamlining administrative and laboratory functions to support our pathologists. This allows our staff to focus specifically on the consultation, keeping our turnaround time low without sacrificing accuracy. In addition, more information is available to the pathologist by increasing the diagnostic test menu.

Q. What about the growth of the Armed Forces DNA Identification Laboratory (AFDIL) and the new DoD DNA Registry?

A. The DNA lab was a concept when I arrived. Today it has a $5 million annual budget and is growing, but it's extremely cost-effective. The military will always need a way to identify remains of fallen service members, and with DNA, we've found an accurate identification method that lends itself to automation. Today AFDIL is also involved in a quality assurance program for forensic DNA laboratories through the College of American Pathologists, which will ensure that these labs are testing in the appropriate manner. So you can see that AFDIL has come a long way, and fast.

The speed with which this division responds to requests for implementation of new services is especially commendable.

Q. Speaking of quality assurance, what other areas beside AFDIL are we involved with?

A. Three areas come to mind: forensic toxicology, telemedicine, and the new military Clinical Laboratory Improvement Program (CLIPO). For many years forensic toxicology has been a 'model' quality assurance program, ensuring that laboratories are performing as they are supposed to by sending "open" and "blind" samples for testing. They also evaluate and communicate between labs doing similar types of testing to prevent any systematic error. New procedures are evaluated to insure accuracy before they are implemented.

In telemedicine, we've been conducting a pilot study in telepathology by providing a tentative diagnosis, followed by the familiar written AFIP diagnosis. This will evaluate the effectiveness of the modality for consultation and education.

As far as the Clinical Laboratory Improvement Program office is concerned, AFIP will house the office (CLIPO) for implementing the program in DoD and will review QA cases and CAP inspections of military laboratories to ensure that we are meeting CLIA's standards. We're also writing new training procedures for each of the services and technicians. A major improvement in this program will enable our service members to obtain an associate's degree during their career in the military.

Q. AFIP has also been involved with helping the services to run special programs. The Air Force Cytology Program comes to mind. How would you characterize our involvement there?

A. AFIP was asked to augment the Air Force Cytology Program. We now provide them with a service at a reason-

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Jewell, continued from page 8

exposure. In DoD, families with children 6 years of age and under are the highest risk group, and that's the age group we'll test. AFIP's role will be to conduct quality assurance for the program, so that everyone who is exposed to lead poisoning will receive appropriate follow-up care and treatment. We've already purchased equipment to support this program, and I'm sure we'll have a major role in it.

Q. With all of these changes, what kind of Institute do you envision in the future?

A. I see a very bright future for the Institute. We are heavily involved in training professional and technical support staffs in order to develop expertise in laboratory medicine.

We have done very well at organizing 'fast response teams' when needed and I'm sure you'll see more of this in the future. We have coordinated people from personnel, logistics, and resources management to successfully fund and staff projects. That's very important.

As far as this building is concerned, we're constantly upgrading our laboratories and ventilation systems, purchasing new equipment, and conducting renovations. But that's not enough, especially with our new missions. We've conducted a site study to move the AFIP to Bethesda, and I think that will become a reality by the year 2000.

As I've said, the improved technologies, cross-training, and our role in quality assurance initiatives will be especially important in helping to keep people healthier in the coming years. We'll continue to be an asset to both DoD and civilian medicine. #

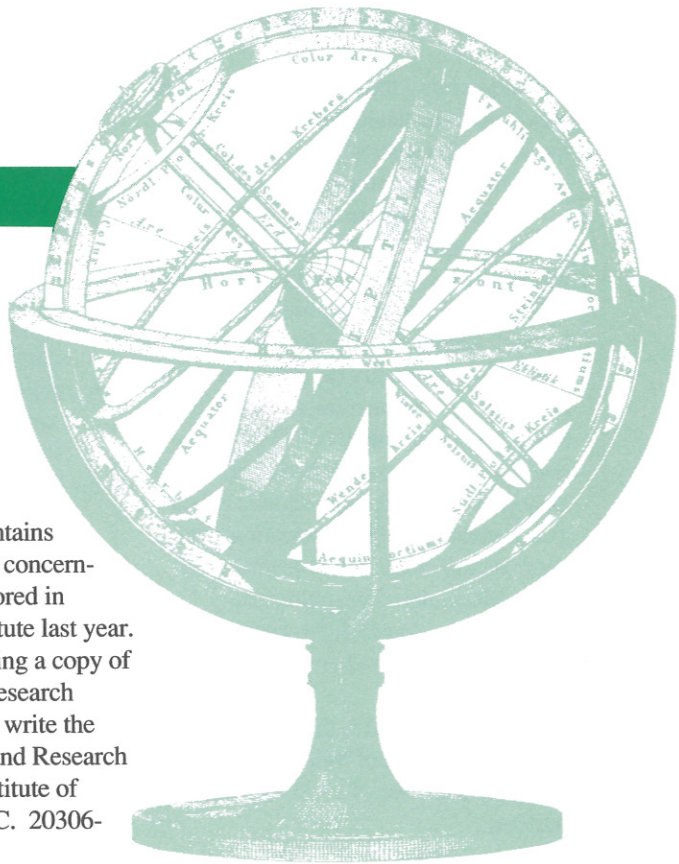
***Ash Lecture**, continued from page 4*

50 and be prepared to take a pill."

Watson turned to the exciting progress being made in gene therapy, noting that "it would be irresponsible to tell a woman that it doesn't really matter that you give rise to a child with a serious genetic disease, because these wonderful scientists throughout the world are going to come up with gene therapy. It may not work or be very expensive."

Watson concluded that no simple answers exist because every disease is slightly different. With so many value systems existing in the U.S., making these decisions by law will be difficult. "We just can't banish reality. Lots of these afflictions of mankind are due to genes, and now we have the means to do something about them. I think we would not rise to our destiny if we just did not do something about it."

Repository and Research Services Update



It has now been a little over a year since the implementation of our optical disk imaging system for pathologic case files. As of the end of April 1993, personnel in the Records Repository Division had uploaded over 40,000 records onto our Pathology Document Storage and Retrieval System (PADSTARS). This system was recently featured in the January issue of Inform magazine. In addition, we entertained a delegation from the National Geographic Society, in March 1993, who were interested in the system. Currently, we are exploring various mechanisms for expanding our scanning capability to allow us to upload 100,000 or more records each year. We hope to be able to implement this expansion sometime in FY94.

The FY92 *Annual Research Progress Report* has been received from our printers and is available for distribution. This report contains over 200 project summaries concerning research that was sponsored in whole or in part by the Institute last year. Anyone interested in receiving a copy of this report should call the Research Office at (202) 576-2884 or write the Administrator, Repository and Research Services, Armed Forces Institute of Pathology, Washington, D.C. 20306-6000.

Museum News

Dr. Micozzi delivers commencement address at St. Louis University School of Medicine

Taking the relationship between medicine and technology as his theme, Dr. Marc S. Micozzi delivered the commencement address at the St. Louis University School of Medicine on May 14, 1993. His speech was titled "Technology Moves Medicine." Dr. Micozzi, Distinguished Scientist and Associate Director of AFIP's National Museum of Health and Medicine, was invited to speak by students at the school.

During his remarks, Dr. Micozzi noted that new medical technologies may sometimes produce profound positive effects without a huge price tag. He cited both the nicotine patch and the oral contraceptive as examples of this principle. A recent development of potential importance is the creation of new ergonomic designs for office furniture and medical equipment that reflect a more sophisticated understanding of the human body.

Addressing the twin issues of disease prevention and health promotion, he focused on the special educational and inspirational role of science museums:

"Today an informed and educated (and motivated) public must become a major factor in the prevention of disease. There are probably no more "magic bullets" against chronic diseases—like the antibiotics eventually developed to treat tuberculosis. In the modern world, in order to have an impact on disease, we must have an impact on behavior. And to impact human behavior requires education and motivation....Transformation comes not from information, but from experience. Museums offer multisensory experiences—sound, light, texture, context, memory, and emotion, all combined."

Founded in 1818, the St. Louis University School of Medicine has 600 students. The class of 1993 consists of 150 students.

***Mullick**, continued from page 5*

Advisory Environmental Health Sciences Council which meets to consider environmental issues of national import which cut across various federal departmental boundaries

Her current academic faculty appointments include: Professor of Pathology, Georgetown University Hospital Medical School; Consultant in Pathology, Oncologic Hospital, University of Puerto Rico Medical Center; Professor of Pathology, University of Puerto Rico, Medical Sciences Campus; and Professor of Pathology, Uniformed Services University of Health Sciences, Bethesda, Maryland. She holds current medical licensure from Maryland, Washington, D.C., and Puerto Rico.

Conferring on Dr. Mullick the presidential rank award certificate signed by President Bush is John P. Shannon, Secretary of the Army.

Dr. Mullick, author or coauthor of six book chapters and 45 professional journal articles, has presented lectures and papers at national and international meetings. Her activities have also included the production of numerous award-winning scientific exhibits and she has recently been appointed to the editorial board of "Modern Pathology".

Recent Publications by AFIP Staff

1. Buetow PC, Smirniotopoulos JG, Wenig BM. Pediatric sinonasal tumors. *Applied Radiology*. February 1993:21-28.
2. Conran RM, Kent SG, Wargotz ES. Oropharyngeal teratomas: a clinicopathologic study of four cases. *Am J Perinatol*. 1993:10:71-75.
3. Frisman DM, McCarthy WF, Schleiff P, Buckner SB, Nocito JD Jr, O'Leary TJ. Immunocytochemistry in the differential diagnosis of effusions: use of logistic regression to select a panel of antibodies to distinguish adenocarcinomas from mesothelial proliferations. *Mod Pathol*. 1993:6:179-184.
4. Hidayat AA, Margo CE, Mauriello JA Jr, North I. Lipofuscinosis of the cornea: a clinicopathologic study of three cases. *Ophthalmology*. 1992;99:1796-1804.
5. Jelinek JS, Kransdorf MJ. Shmookler BM, Aboulafia AJ, Malawer MM. Liposarcoma of the extremities: MR and CT findings in the histologic subtypes. *Radiology*. 1993:186:455-459.
6. Kalasinsky KS, Levine B, Smith ML, Platoff GE Jr. Comparison of infrared and mass spectroscopies for drug analysis. *Critical Reviews in Analytical Chemistry*. 1993:23:441-457.
7. Levine B. Forensic toxicology. *Anal Chem*. 1993;65:272A-276A.
8. Lipscomb TP, Harris RK, Moeller RB, Pletcher JM, Haebler RJ, Ballachey BE. Histopathologic lesions in sea otters exposed to crude oil. *Vet Pathol*. 1993;30:1-11.
9. Mikel UV, Bahr GF. A comparative study of DNA amount and nuclear dry weight in four different species (*Rana catesbeiana, Salmo gairdneri, Gallus domesticus* and *Homo sapiens*). *Comp Biochem Physiol [B]*. 1993;104:743-746.
10. Reid AH, Cunningham RE, Frizzera G, O'Leary TJ. bcl-2 rearrangement in Hodgkin's disease: results of polymerase chain reaction, flow cytometry, and sequencing on formalin-fixed, paraffin-embedded tissue. *Am J Pathol*. 1993;142:395-402.

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Abstracts

Pediatric sinonasal tumors

Peter C. Buetow, CAPT, MC, USA; James G. Smirniotopoulos, MD; Bruce M. Wenig, LCDR, MC, USN

The clinical histories and imaging studies of 51 pediatric patients with histologically proven tumors of the nasopharynx, nasal cavity, or paranasal sinuses were reviewed retrospectively. Radiologic evaluation included CT and plain films on all 51 cases; of these cases, 17 underwent angiography, and MR imaging was performed on 3. The majority were benign lesions (33/51), with juvenile angiofibroma (10/33) and fibroosseous lesions (9/33) accounting for almost two-thirds. Eighteen of 51 were malignant, with primary bone malignancies (5/18) being most frequent, followed by olfactory neuroblastoma (4/18), rhabdomyosarcoma (3/18), and lymphoma (3/18); there were only three cases of nasopharyngeal carcinoma. There were five inflammatory lesions, three of which included nasal polyps. The most common clinical symptoms were nasal obstruction and nasal discharge; bloody or blood-tinged discharge was seen frequently in both malignant and benign lesions. The average duration between presenting symptoms and diagnosis was nine months overall; this was slightly shorter (six months) for the malignant lesions .

Characteristic imaging features were noted in juvenile angiofibroma, nasopharyngeal teratoma, antrochoanal polyp, and odontogenic cyst. Imaging features did not serve as an indication for or against biopsy but did influence the biopsy or surgical approach. In all cases, CT imaging was paramount in determining the extent of disease and, thus, in choosing the appropriate treatment modality. Cross-sectional imaging is essential in the evaluation of pediatric sinonasal tumors.

Applied Radiology. February 1993:21-28.

Immunocytochemistry in the differential diagnosis of effusions: use of logistic regression to select a panel of antibodies to distinguish adenocarcinomas from mesothelial proliferations

Dennis M. Frisman, William F. McCarthy, Patty Schleiff, Sally-Beth Buckner, Joseph D. Nocito, Jr., and Timothy J. O'Leary

Many studies have shown immunohistochemistry to be beneficial in discriminating between adenocarcinoma and mesothelial reactions in effusions. Although many of these studies suggest using a panel of antibodies, none of them used statistical methods to optimize their choice of assays. In the current study, stepwise logistic regression was applied to our data to select an appropriate panel of antibodies to differentiate between adenocarcinoma and all types of mesothelial proliferations. One hundred effusions (64 cases of adenocarcinoma, 27 cases of benign mesothelial proliferations, and 9 cases of malignant mesothelial proliferations) were analyzed for their reactivity with anti-EMA, anti-MFG, anti-CEA, Leu-M1, B72.3, and the newly described epithelial membrane marker BER-EP4. An abbreviated panel consisting of anti-CEA, EMA, and B72.3 was shown to be sufficient in over 95% of our cases to accurately characterize a given effusion. When all three assays are negative, a diagnosis of adenocarcinoma is extremely unlikely, while when two or three of the assays are positive a diagnosis of adenocarcinoma is almost certain. The use of stepwise logistic regression has proven useful in the design of antibody panels as an adjunct to the differential diagnosis of effusions and may be applicable to the selection of panels in other diagnostic problems.

Modern Pathology. 1993;6:179-184.

Lipofuscinosis of the cornea: a clinicopathologic study of three cases

Ahmed A. Hidayat, MD, Curtis E. Margo, MD, Joseph A. Mauriello, Jr., MD, and Ian North, MD

Background: Lipofuscin pigments are the indigestible residue of lysosomal activity usually associated with normal aging. Abnormal amounts of lipofuscin also are associated with certain disease processes. The rarity of lipofuscin in the cornea and the similarities between its staining properties and those of intracellular micro-organisms caused great diagnostic problems in three cases. The correct diagnosis of corneal lipofuscinosis was made after extensive histochemical, autofluorescent, and ultrastructural studies. *Methods:* Clinical histories of three patients are correlated with morphologic and histochemical findings on five corneal buttons with lipofuscinosis. *Results:* The histopathologic features of one cornea with chronic keratitis and three corneas from two patients with bilateral opacities of undetermined origin were mostly similar. Large amounts of lipofuscin pigment were found within macrophages and stromal keratocytes. Other pathologic findings were nonspecific, including phagocytosis of degenerated collagen fibrils, scarring, and neovascularization of the stroma. *Conclusion:* The lipofuscin deposits are probably the consequence of a corneal degenerative process and not its cause, although their pathogenesis remains unclear. Familiarity with the morphologic appearance of corneal lipofuscinosis and its staining and autofluorescent properties is important because the small, 1- to 3-µm deposits may be mistaken for intracellular micro-organisms.

Ophthalmology 1992;99:1796-1804

Oropharyngeal teratomas: a clinicopathologic study of four cases

Richard M. Conran, LTC, MC, USA, Stephen G. Kent, MD, and Eric S. Wargotz, MD

Oropharyngeal teratomas (OPT) represent an uncommon congenital tumor with significant morbidity and mortality. Optimal management requires prenatal diagnosis. The clinico-pathologic features of four OPT (one stillbirth, two livebirths, and one therapeutic abortion) are reviewed and compared with cases previously reported in the literature. Diagnosis, management, clinical outcome, and the natural history of the entity are discussed.

Congenital tumors account for approximately 2.6% of childhood neoplasms. Teratomas, the largest group of congenital neoplasms, account for approximately 36% of the tumors seen in the first month of life. The oropharynx is involved in 2 to 3% of these cases. Oropharyngeal teratomas (OPT) present in most cases as a large fungating mass protruding from the oral cavity (epignathus) resulting in respiratory distress at birth. Prenatal diagnosis results in adequate management at delivery, reducing the mortality from this tumor. Four OPT cases, as well as those previously reported in the literature, were reviewed to define the natural history of this tumor in order to ensure accurate diagnosis and management.

American Journal of Perinatology. 1993;10:71-75.

Postgraduate Short Courses in Continuing Education Academic Year 1993–94

Course Title	Scheduled Dates	Location
Histopathology Techniques	4–6 August 93	AFIP, Washington, DC
Pathology of Laboratory Animals	9–13 August 93	Hyatt Regency, Bethesda, MD
Tissue Culture & Mutagenesis Lab	9–27 August 93	AFIP, Washington, DC
Anatomy, Histology, & Electron Microscopy of the Eye, Orbit, and Ocular Adnexa	28–29 August 93	Georgetown University Conference Center Washington, DC
Ophthalmic Pathology for Ophthalmologists	30 Aug–3 September 93	Georgetown University Conference Center Washington, DC
Hepatic Pathology–'93	8–10 September 93	Holiday Inn, Bethesda, MD
Asia-Pacific Conference on Recent Advances in Surgical Pathology	13–16 September 93	**Friendship Hotel, Beijing, China**
Pathology of Congenital Heart Disease	13–17 September 93	AFIP, Washington, DC
Pulmonary & Mediastinal Radiology	18–19 September 93	Washington Marriott, Washington, DC
Future Technologies for DNA Analysis	4–5 October 93	Holiday Inn Crowne Plaza, Rockville, MD
Ancient Human DNA	11–12 October 93	Old Towne Holiday Inn, Alexandria, VA
3rd Annual Radiologic-Pathologic Correlation	11–15 October 93	**Colonial Williamsburg, Williamsburg, VA**
Essentials of Forensics	11–15 October 93	Holiday Inn Crowne Plaza, Rockville, MD
Interpretation of Prostatic Biopsy	6–7 November 93	Holiday Inn Crowne Plaza Metro, Washington, DC
Respiratory Tract & Mediastinum	6–8 November 93	**Tucson National Resort, Tucson, AZ**
Gynecologic Pathology	7–9 November 93	Holiday Inn, Bethesda, MD
Oral Pathology Review	15–17 December 93	**Hilton Palacio del Rio, San Antonio, TX**
Genitourinary Pathology Review	10–14 January 94	Holiday Inn, Bethesda, MD
Neuropathology Review	16–21 January 94	**Hyatt Regency, San Antonio, TX**
Pediatric Pathology	6–9 February 94	**Contemporary Hotel, Lake Buena Vista, FL**
Controversies and Recent Advances in Surgical Pathology	14–18 February 94	**Doubletree Hotel, San Diego, CA**
Neuroradiology Review	26–27 February 94	Hyatt Regency, Bethesda, MD
Paleopathology	10–12 March 94	AFIP, Washington, DC
Forensic Dentistry	14–18 March 94	Hyatt Regency, Bethesda, MD
Abdominal & Gastrointestinal Imaging Review	8–10 April 94	AFIP, Washington, DC
Descriptive Veterinary Pathology	30 May–2 June 94	AFIP, Washington, DC
Exfoliative & Fine-Needle Aspiration Cytology	6–10 June 94	Hyatt Regency, Bethesda, MD
Forensic Anthropology	20–24 June 94	USUHS, Bethesda, MD

Histopathology Techniques: Seminar and Workshops

This program offers a wide variety of scientific topics in the field of histotechnology, electron microscopy, and immunohistology. This seminar is designed to cover selected methodologies with a comprehensive discussion of potential problems, corrective measures, and desired results. Technique and equipment demonstrations will give participants a greater understanding of a variety of issues as well as methods of fixation, processing, embedding, sectioning, and staining on standard and non-standard tissue specimens.

Pathology of Laboratory Animals

This course is designed primarily for professional officers and civilians who are responsible for the recognition and interpretation of lesions in laboratory animals. Lectures will be presented by experts in the diseases of laboratory animals. Electives include opportunities for attendees to review AFIP histology study sets and to view VCR tapes of speakers from previous POLA courses.

Anatomy, Histology, and Electron Microscopy of the Eye, Orbit, and Ocular Adnexa

This two-day course is designed for physicians or veterinarians who are ophthalmologists, pathologists, or ophthalmic researchers as a review of the anatomy, histology, embryology, and ultrastructure of the normal eye and ocular adnexa.

Ophthalmic Pathology for Ophthalmologists

Designed for ophthalmology residents and clinical ophthalmologists, this five-day course consists of a basic and comprehensive survey of pathologic conditions affecting the eye and ocular adnexa. Additionally, the course will enable chief residents to develop a general background in ophthalmic pathology. Participants will gain insight into clinicopathologic correlations and electron microscopy of normal and pathologic conditions of the eye. Applicants should be board qualified or certified or well advanced in pathologic anatomy or ophthalmology. Vision scientists with training in histology and pathology equivalent to medical school instruction are welcomed. Topics will include: a review of general information; acute, chronic, and granulomatous lesions and their sequelae; injuries, cataract, glaucoma; vascular diseases; intraocular tumors; and optic nerve pathology.

Hepatic Pathology

This course provides a comprehensive review of the methodology of hepatic histopathology, chronic cholestatic disorders (e.g. primary biliary cirrhosis and primary sclerosing cholangitis), developmental and metabolic disorders, neonatal cholestasis, acute and chronic necroinflammatory diseases, selected infectious diseases, alcoholic-liver disease and differential diagnosis, hepatic transplant pathology, benign and malignant neoplasms in children and adults, and 12 case presentations. Microscopic slide sets of interesting medical and surgical diseases, as well as of the 12 cases, will be available for review by participants during the day and for two hours in the evening.

Congenital Heart Disease

This five-day course is an in-depth study of the structure, clinical manifestations, and surgical corrections of congenital cardiac malformations. It is specifically aimed for thoracic surgery and cardiology fellows who wish to familiarize themselves with pediatric cardiology and cardiovascular surgery. In addition, pathologists and radiologists who wish to increase their knowledge of congenital heart disease will greatly benefit from this course, which hosts a diverse faculty from the AFIP, National Children's Medical Center, Mayo Clinic, and Georgetown University. There will be hands-on examination of a large number of specimens, collected over decades at the AFIP and CNMC in Washington D.C., supplemented by lectures and hand-out material.

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