

FOCUS

PAPANICOLAOU SOCIETY OF CYTOPATHOLOGY

Companion Society of the United States and Canadian Academy of Pathology

Dedicated to Clinical Practice, Clinical Education and Clinical Research



PAST PRESIDENT'S MESSAGE

AN INTERNATIONAL PERSPECTIVE COMES OF AGE: THE PSCO IN 2004-2005

CARLOS WM BEDROSSIAN, MD, PH.D (HON.), FIAC

It seems like only yesterday that a group of cytopathologists met in Toronto to plan a new companion society to meet during USCAP. After adopting as its motto "Bridging the Gap Between Cytopathology and Surgical Pathology" at its first organizational meeting in 1990, the PSC has grown and matured into an international organization that will celebrate a decade and a half in Atlanta next spring. In the new millennium, a name change: from PSC to the Papanicolaou Society of Pathology Organization (PSCO), but the same innovative, pioneering spirit has remained unscathed. Judging from the year 2004-2005, there is a lot to make the organization proud of its accomplishments.

With its membership stable near 400 members, PSCO is like the little choo choo train that could. A leader in researching and defining practice guidelines in on-gynecologic cytology, the PSCO has also become better known throughout the world as a forward thinking organization that tackles cytology issues of interest not only in industrialized nations, but also in the Third World and the developing countries. Besides sessions at its USCAP regular meetings, the PSCO now regularly co-sponsors companion sessions with a number of pathology societies, including the International Academy of Pathology (IAP), the European Society of Pathology (ESP) and the Latin American Society of Pathology (SLAP). By tackling practical and neglected issues, the PSCO always breaks new ground, ranging from extending cytologic screening to the poor, to defining international standards for the use of immunocytochemical

and molecular markers in cytologic specimens.

After Dr Abati, the current PSCO President brought back the afternoon sessions with "Cells without Borders" in Vancouver, the PSCO announced a new international prize, the Yolanda C. Oertel "Interventional Cytopathologist Award" to honor pathologists who perform and interpret their own FNA biopsies. This \$1,000 award will alternate between U.S. and international cytopathologists and honored Dr. Miguel Sanchez as its first recipients for his considerable contributions to the early diagnosis of breast cancer among underprivileged women. Then, in June, 2004, the PSCO participated in two companion sessions during the Intercontinental Congress of Pathology, in Iguacu Falls, Brazil. The, first, jointly held with the ESP, focused on "Respiratory Cytopathology: Diagnostic Challenges and Pitfalls". The second, co-sponsored by the LSAP, focused on "Malignant Mesothelioma: Cytologic Diagnosis and Ancillary Techniques."

Not be outdone, the 2005 USCAP meeting in San Antonio, saw a second successful "Cells without Borders" session with speakers from Australia, Brazil and Vietnam. There was also a thorough review of the legislative and legal history behind health issues in the aftermath of the Vietnam war, which testified to the willingness of the PSCO to tackle sensitive issues. At that time the International Relations Committee announced another international laurel, the Mathilde E. Boon "Cytopathology Investigator Award" to recognize investigators who make significant contributions to advances in the field of clinical cytology. The new \$1,000 award, will annually be given on the basis of a researcher's lifetime achievement, in the utilization of cytology for the early diagnosis of disease processes. This award, together with the L.C.Tao "Educator of the Year Award", and the aforementioned "Yolanda C.

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TREASURER'S REPORT

URSULA BEDROSSIAN, PHD

JANUARY 1, 2004 THRU DECEMBER 31, 2004

ASSETS:

CURRENT ASSETS CHECKING/SAVINGS

Bank One Savings YCO	\$1,000.00
Cash in bank	\$40,947.01
Total Checking/Savings	\$41,948.01
Total Current Assets	\$41,948.01

LIABILITIES & EQUITY

Dues and subscriptions 2004	\$31,800.00
Total Current Liabilities	\$31,800.00
Equity (Net Assets)	\$12,038.48
Net Income (Loss)	(\$1,890.47)
Total Equity	\$10,148.01

CASH RECEIPTS – LESS CASH DISBURSEMENTS

Income and Expenses	
Dues and subscriptions	\$43,441.96
Donations	\$5,000.00
Total Income	\$48,441.96

EXPENSES:

L.C. Tao Award	\$1,000.00
Plaques	\$360.00
Resident in Training Award	\$500.00
Y.C. Oertel Award	\$1,000.00
Bank & Credit Card Charges	\$1,420.49
Diagnostic Cytopathology (Wiley)	\$31,316.30
Focus (Newsletter)	\$5,753.05
Accounting	\$1,475.00
Meeting Expenses	\$5,967.40
Postal Services	\$312.35
Printing	\$260.00
Website	\$1040.00
Total Expenses	\$50,404.59

Net Ordinary Income (Loss)	(\$1,962.63)
Other Income (interest)	\$72.16
Net Income (Loss)	\$1,890.47

FOCUS

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UPDATE ON CYTOLOGY PROFICIENCY TESTING

**DIANE D. DAVEY, MD AND MEMBERS OF THE
GOVERNMENT RELATIONS TASK FORCE,
PAPANICOLAOU SOCIETY OF CYTOPATHOLOGY**



Laboratories under CLIA 1988 regulations were required to enroll all individuals interpreting gynecologic cytology in a proficiency testing (PT) program by June 30, 2005, and many laboratories had already been tested by publication of this article. The only programs approved to date have been the State of Maryland Program and Midwest Institute for Medical Education (MIME) Program, and only MIME was accepting applications from all states. Other organizations including the CAP and

ASCP were in the process of seeking approval of proficiency testing programs, but CMS had not yet granted approval of either.

In February 2005, the Clinical Laboratory Improvement Advisory committee (CLIA) unanimously passed a recommendation that the cytology PT regulation and its grading criteria be revisited to ensure that it is based on the most current science and clinical practice guidelines. CLIA stated that proficiency testing programs should not evaluate and sanction individuals based on outdated standards.

The Cytopathology Education and Technology Consortium held a series of conference calls over the past months to draft a document urging CMS to address several areas of the regulations, including the frequency of testing, the grading scheme, and slide validation methods. The Papanicolaou Society is a member of this consortium along with five other pathology and cytology organizations. This draft was still under review at the time of this writing.

The College of American Pathologists spearheaded a major effort this summer to ask the government to reconsider Cytology Proficiency Testing. A letter was mailed to the Secretary of Health and Human Services Michael Leavitt on June 3, 2005, that was co-signed by 10 national pathology and cytology organizations and nearly all of the state pathology societies. The United States and Canadian Academy of Pathology was one of the signatories to this letter. Recent scientific and technological advances to the field were described, as well as the already significant and positive impact of other CLIA 1988 regulations on the practice of cytopathology.

Specific comments made against the current regulation include the annual testing requirement and the fact that federal certification of individuals supercedes existing state licensing boards and medical specialty certification boards. (For an editorial on this topic, see Davey DD. Determining competency and proficiency in cytology: Who decides? *Diagn Cytopathol* 2005;33:1-2). Maintenance of Certification programs for certified physicians operate on 6-10 year cycles, so annual testing certainly seems excessive. The letter emphasized that general proficiency testing under CLIA regulations is directed towards measuring the entire laboratory, instead of individuals, and the current cytology PT regulations negate the team approach to laboratory specimen evaluation.

The grading scheme was criticized because it fails to recognize recent management guidelines in which both women with LSIL and HSIL are evaluated by colposcopy. Finally, this letter stressed the outdated nature of the regulation, which was written in 1992 but not implemented until recently. The 2003 Medicare Prescription Law included language that set a maximum of 3 years between the time HHS could issue a proposed rule and issue a corresponding final rule. This law does not apply to cytology PT, but it does provide support for revisiting regulations that are outdated prior to implementation.

Pathology groups also were able to get the support of House of Representatives members in sending a similar letter to the HHS Secretary. A bipartisan letter was circulated by Representatives Sue Myrick (N.C.) and Bart Gordon (Tenn) of the Energy and Commerce Subcommittee. This letter was circulating through the House over the summer, and the CAP issued calls for individuals to contact their Representatives by both e-mails and direct phone calls (see CAP Action Alert from July 13, 2005).

CMS held a series of teleconferences to explain the proficiency testing program requirements. However, there were a number of areas of misunderstanding during these conferences. For example, initially CMS claimed that pathology residents and fellows were also required to be tested. When it was pointed out that residents and fellows are in educational programs and do not independently interpret cervical cytology specimens, government officials reversed their previous comments. CMS has also failed to respond to a legal request for all written communication between CMS and MIME under the Freedom of Information Act requested several months ago.

The members of the Government Relations Task Force encourages all PSC members to keep updated on the latest cytology PT news. Some of the best areas to find the most current information include the CAP Statline and website, and the American Society of Cytopathology listserv. Please help with the advocacy efforts of pathology and cytology organizations by contacting government officials when requested.

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THE MEMBERS OF THE PAPANICOLAOU
SOCIETY THANK YOU FOR
YOUR GENEROUS SUPPORT.**

PROFILES IN CYTOPATHOLOGY: MIGUEL SANCHEZ, MD

JOAN CANGIARELLA, MD, NEW YORK UNIVERSITY SCHOOL OF MEDICINE, NEW YORK, NY

Dr. Miguel Sanchez is the first recipient of the Y.C. Oertel Award by the Papanicolaou Society of Cytopathology recognizing outstanding contributions to the practice and teaching of fine needle aspiration. Dr. Sanchez is Chief of Pathology and Medical Director of the Cytodiagnosis and Breast Care Center at Englewood Hospital and Medical Center. Dr. Sanchez holds professorial appointments at both the Mount Sinai School of Medicine and the New York University School of Medicine.

Dr. Sanchez completed his training in pathology at Temple University in Philadelphia and St. Vincents Medical Center in New York City and then pursued fellowship training in oncologic pathology at Memorial Sloan Kettering Cancer Center. He spent several months at the Karolinska Institute in Stockholm where he received specialized training in the performance and interpretation of aspiration cytology. Dr. Sanchez has authored numerous publications and book chapters. His expertise in fine needle aspiration is recognized worldwide. He has given hundreds of lectures in the United States, Europe, Latin America, China and Australia, primarily on the early detection of breast cancer, but also on studies of the humanities in medicine and on philosophy. He was instrumental in developing the concept of the multidisciplinary breast center after some observations of the Swedish system. The Cytodiagnosis and Breast Care Center run by Dr. Sanchez was designated by Congress in 1994 as a national model for breast care diagnosis and management. The center is an international training site for fine needle aspiration cytology.

Dr. Sanchez's commitment to education in diseases of the breast has been recognized both nationally and internationally. He is the recipient of the American Cancer Society Award for Physicians in the Forefront, a Zonta Award for Health Care to Women, The Gold Medal Award from The Chinese Academy of Medical Sciences, the Herbert Dardik Research and Education Award and recently was awarded a Nicaraguan Medal of Medical Merit from the Nicaraguan government for his research and teaching in breast cancer. He was named on the Castle Connolly Best Doctor and New York Magazine Best Doctor in New York list several years in a row. He is also a member of the Advisory Board of The Susan G. Komen Breast Cancer Foundation, North Jersey Affiliate, and since 1995 has served as Vice Chairman of the National Cancer Institute Subcommittee on Indications of Breast Biopsy. He is also a member of the International working group for Breast MRI from the U.S. Public Health Service

I had the opportunity to talk with Dr. Sanchez about his accomplishments in the field of cytopathology. Here are some excerpts from our conversation:

How did you decide on cytopathology as a career choice?

I started my medical career as an internist and budding cardiologist and became profoundly bored rather fast. The microscope always intrigued me. I asked a senior internist "What do you think about Pathology?". His answer "was "its okay but you will never be able to know everything". That was the best answer to encourage me to go into Pathology. As a resident in Philadelphia working with Wally Clark and Irena Koprowska, I had my first exposure to

neoplastic pathology (melanomas) and to cytology. Somehow I seemed to get the hang of cell analysis better than other fellow residents. Subsequently, in 1973, as part of my fellowship at Memorial Sloan Kettering Cancer Center I spent a month with Grace Durfee and Mike Melamed, Chief of Cytology at the time and learned two important things. One, anybody can make an observation and two, you must have the courage of your convictions.

How did you get interested in aspiration cytology?

I got interested in Fine needle aspiration, first because of my friend Charlie Curtin, a pathologist in Scranton and fellow with me at MSKCC. Then I met Gert Auer, in a Cytology meeting in Montreal. Gert was a researcher at the Karolinska Institute in Sweden, and after a few days of having a great time he invited me to pursue a rotation in Stockholm. There, in 1983, my Swedish period started. Sixten Franzeen, Torsten Lowhagen and Jerry Waisman, (who was in Stockholm at that time), became, with Gert Auer, lifetime friends and role models. I returned to Stockholm several times after that. The last two visits I was invited to lecture about "The Englewood model" of breast care. It was really about "what have you done with what we taught you". The last invitation was to serve as Master of Ceremony for the dinner to celebrate the memory of Torsten.



Your center for aspiration biopsy has grown remarkably over the last two decades. How difficult was it to convince your surgeons and hospital on the benefits of aspiration cytology?

The evolution of the Center was not that difficult at Englewood. You have to identify the key people and bring them to your side. Persuasion, availability, affability and ability, as you know, are the elements of success in any medical practice, in that order. Having Roz Stahl by your side is surely a plus.

What do you see as the future of cytopathology?

I think that Cytopathology is going through a transformation period. The fact that new molecular technology is adapting itself to smaller and smaller samples will be the new explosion of cytopathology.

What do you think about the future of aspiration cytology for lesions of the breast?

Breast cytopathology is also going through a difficult period. I'm convinced that with adequate training of both clinicians and pathologists, breast cytopathology will recover the position that it should never have lost. But prudent and at the same time decisive interpretations are needed. A cytopathologist that finds everything "atypical" is useless, and clinicians realize that very fast. Interpretation of breast cytopathology in a vacuum is also a mistake. I see the breast cytopathology renaissance within the context of the multidisciplinary breast center. There are so many decisions that can be made with immediate evaluation of a breast cytology sample!!

You have traveled all over the world lecturing in cytopathology. What was your most rewarding experience?

Besides being invited back to the Karolinska to show what I have done with what I have learned there, probably the most rewarding experience has been helping with setting up FNA programs in developing countries, especially Nicaragua.

What advice can you give to young cytopathologists trying to establish a Center in aspiration cytology?

To the young cytopathologist I would advise never to forget the teachings of giants like Leo Koss. To practice cytopathology you need a strong background in Surgical Pathology and Medicine in general. If not, Pathology and its branches become a form of "aesthetic morphology" instead of a unique form of practicing medicine.

What hobbies do you enjoy?

Some of my friends will tell you that I do not have "hobbies" in the traditional form. I do not believe in moderation, but passion. So I'm a dedicated, (if only mildly competent), golfer. An Opera fan that lectures in Opera analysis and travels around the world to see the latest production of Wagner's "Ring" and an amateur Egyptologist in the process of learning to read hieroglyphs from the New Kingdom. But by far my two greatest passions are my sons, Julian, a writer in Washington DC, and Thomas, a May 2004 graduate of NYIT-VIP program.

PROGRAM FOR THE PAPANICOLAOU SOCIETY OF CYTOPATHOLOGY USCAP EVENTS

MARK YOUR CALENDARS FOR ATLANTA EVENTS!!! SATURDAY, FEBRUARY 11, 2006

2 - 4 pm ***The Annual Afternoon Scientific Session of the International Relations
and Scientific Program Committees***

CYTOLOGIC SCREENING FOR CANCER IN THE REAL WORLD: SUCCESSSES, FAILURES AND CULTURAL DISTRACTIONS

Moderator: Eric Suba, MD

2:00 pm **"Early Detection of Esophageal Cancer in China"** Dr. Sandy Dawson, USA

2:25 pm **"Cervical Cancer Screening in Rural Japan"** Dr. Tadao Kobayashi, Japan

2:50 pm **"Cervical Cancer Screening in Greece"** Dr. Elena Koutselini, Greece

3:15 pm **"Cervical Cancer Screening in a Developing Country; The Nakuru Kenya Experience"** Dr. Mark Titus, Kenya

3:40 pm **"Cervical Cancer Screening in Mexico"** Dr. Matt Zarka, Mexico

4 - 5 pm ***Business Meeting of the PSC***

5 - 7 pm ***PSC Reception***

7 - 10 pm ***Evening Companion Meeting***

Guidelines for Fine Needle Aspiration of the Thyroid

GUIDELINES FOR FINE-NEEDLE ASPIRATION OF THE THYROID

LESTER LAYFIELD, MD, UNIVERSITY OF UTAH, SALT LAKE CITY, UTAH.

The Papanicolaou Society Scientific Session presented at the USCAP annual meeting offers a yearly update on issues in cytopathology important to both cytopathologists and general anatomic pathologists. This year the **Scientific Program Committee** has partnered with the **Standards of Practice & Guidelines Committee** to develop a timely and exciting review of issues and developments in aspiration cytology of the thyroid gland. Recommendations for performance, interpretation and reporting of fine-needle aspirates of the thyroid will be presented. The recommendations are patterned on those proffered at the highly successful NCI Breast Recommendations Conference held in September of 1996.

The thyroid gland represents one of the most common sites where fine-needle aspiration is performed, but no widely accepted set of guidelines exists for specimen adequacy assessment, diagnostic criteria, diagnostic terminology or report format. Significant regional and even intrainstitutional variability exists in diagnostic terminology and reporting formats. This has led to confusion among surgeons and endocrinologists in interpreting reports of thyroid aspirates written by different pathologists. The Papanicolaou Society Scientific and Recommendations Committees have assembled a panel of experts in fine-needle aspiration cytology to draft recommendations for performance and interpretation of fine-needle aspirates of the thyroid gland.

The scientific program presented during the companion societies meeting at the 2006 USCAP annual meeting will present these recommendations with a review of the histologic basis for the cytologic interpretation of thyroid nodules and important developments in ancillary studies helpful in thyroid aspiration cytology including molecular testing. Sylvia Asa, M.D., Ph.D., will give a presentation on the historical and histologic basis for the diagnosis of thyroid nodules. Zubair Baloch, M.D., Ph.D., will discuss indications for fine-needle aspiration of thyroid as well as review issues concerning FNA technique. Adequacy criteria will be discussed and reviewed by Yolanda Oertel, M.D., and Martha Pitman, M.D., will discuss proposals for report format. Tarik Elsheikh, M.D., and William C. Faquin, M.D., will discuss important issues in diagnostic terminology and criteria used in the cytologic diagnosis of thyroid lesions. Finally, William Clark, M.D., will discuss new and exciting issues in molecular diagnostics and ancillary testing useful in thyroid cytology.

These presentations should offer an exciting and informative review of fine-needle aspiration of the thyroid gland and offer recommendations useful to both the specialist cytopathologist and general practicing anatomic pathologist.

PAST PRESIDENT'S MESSAGE *Continued from page 1*

Oertel Award", completes the PSCO's recognition all three major aspects of the cytopathology art and science: diagnosis, research and education.

One can safely state that the PSCO progress proceeds deliberately along a well thought-out vision and a strategy. This could only help through the dedication of its hardworking members to put others ahead of one self. With amazing regularity, individuals step up to the plate, and, imbued by the true volunteer spirit, move the ball forward for the next person. Like in any other field of endeavor, there are the occasional misfires, but soon the dissonant glitch is overcome, with minimal acrimony, because a tradition has been established, by example and otherwise, that in the PSCO what matters most is dedication to the greater good. Through it all, PSCO's core value has remained the pursuit of excellence in its various scientific sessions. For those unable to attend, the Focus newsletter keeps everyone informed and Diagnostic Cytopathology strives to capture the essence of the sessions in high caliber articles. More recently, the Treasurer began developing a very popular calendar, with photos of cells that tickle the funny bone.

As exciting as these developments have been, perhaps one of the most memorable event took place during the PSCO evening session of USCAP-2005, in San Antonio, Texas, focusing on the 2001 Bethesda System. This point/counter point format drew a large audience and the session brought together for the first time during a USCAP meeting cytopathologists and attorneys who broached the thorny issue of litigation. Still controversial almost two decades after the Wall Street Journal catapulted cytology into the headlines, the topics presented captured the breadth of emotions that patients, physicians and lawyers go through, when experiencing highly charged dilemmas. To say that the session was lively, would be an understatement, but anyone leaving the session too soon missed one of the most passionate discussions of the ASCUS topic in recent memory. A testimony to the uncertainties still surrounding the

unfinished ASCUS story, the session not only shed new light upon a difficult subject in cytologic interpretation, it also pointed to new directions for future research in a still hot topic.

Based on the first half of this year, 2005-2006 promises another round of stimulating PSCO sessions. In September alone, PSCO President, Dr. Andrea Abati and Dr. Ricardo Bardales participated in another joint session with the ESP's Cytology Working Group in Paris France about advances in ultrasound guided endoscopic FNAs of the GI tract. In addition, I had the privileges to represent PSCO at the George L. Wied Memorial Symposium, in Vienna Austria, attended by over one hundred cytopathologists as well as Dr. Wied's family, but that is not all. In early October, the PSCO and the ESP's Cytology Working Group will join forces, again in Paris, in a session about "Advances in the Cytologic Diagnosis of Pleuro-Pulmonary Diseases"

What is in store for the rest of the year? The PSCO will co-sponsor with the Norwegian Radium Hospital of Oslo Norway a joint session on "Fine Needle Aspiration Biopsy: Current Practice and Future Challenges," with a number of experts from both sides of the Atlantic. This 2 day meeting will feature the latest advances in the use of ancillary techniques in the interpretation of small tissue cores and cellular samples. As a past President, I could not be more pleased with PSCO's progress over the past fifteen years. From a bridge between cytopathology and surgical pathology, the organization now has expanded its horizons and is also bridging gaps between various regions of the world. It is only fitting that in our globalization era, the PSCO would follow a path to break down barriers of language, culture and technology. Nothing like this could have happened without your active participation. It has been a privilege and a blessing to be part of these exciting times. Here is one hoping to see you in one our next endeavors wherever it happens to be!

U.S. FEDERAL AND STATE NEWS

Aylin Simsir, MD and Joan Cangiarella, MD • New York University School of Medicine, New York, NY

PATIENT SAFETY AND QUALITY IMPROVEMENT ACT OF 2005 (S. 544)

In March 2005, The Senate Health, Education, Labor and Pensions Committee (HELPC) approved a bipartisan bill referred to as “Patient Safety and Quality Improvement Act of 2005 (S. 544)”. The background of this legislation is as follows (excerpt from S.544):

In 1999, the Institute of Medicine released a report entitled “To Err is Human” that described medical errors as the eighth leading cause of death in the United States, with as many as 98,000 people dying as a result of medical errors each year. In their report, the Institute of Medicine called on Congress to provide legal protections with respect to information reported for the purposes of quality improvement and patient safety. The HELPC of the Senate held several hearings in the 106th and 107th Congresses on patient safety. The Congress acknowledged that voluntary data gathering systems are more supportive than mandatory systems in creating a learning environment as stated in the Institute of Medicine’s report. Promising patient safety reporting systems have been established throughout the United States and the best ways to structure and use these systems are currently being determined, largely through projects funded by the Agency for Healthcare Research and Quality. Many organizations currently collecting patient safety data have expressed a need for legal protections that will allow them to review protected information and collaborate in the development and implementation of patient safety improvement strategies. Currently, the State peer review protections are inadequate to allow the sharing of information to promote patient safety. It is the purpose of this Act to encourage a culture of safety and quality in the United States health care system by providing for legal protection of information reported voluntarily for the purposes of quality improvement and patient safety; and ensure accountability by raising standards and expectations for continuous quality improvements in patient safety.”

Patient Safety and Quality Improvement Act of 2005 (S. 544) will create public and private Patient Safety Organizations to collect voluntary provider reports of medical errors. The bill promises strong confidentiality and legal protections for providers. The full Senate now must vote on the measure.

TIGHTER REGULATIONS ON RESIDENT WORK HOURS EXPECTED

Senator Corzine introduced a bill in July, 2005 to tighten restrictions on residents’ work hours and for

increasing fines against hospitals violating these requirements. Any teaching hospital that violates the requirements is subject to a civil money penalty not to exceed \$100,000 for each medical residency training program operated by the hospital in any 6-month period. Residents must not work more than 80 hours a week, and must have 10 hours off in between assignments; in house calls are limited to 24-hour shifts instead of 30-hours as stated in the 2001 Patient and Physician Safety and Protection Act.

NEW YORK STATE SOCIETY OF PATHOLOGISTS (NYSSPATH) OPPOSE PATIENT NOTIFICATION BILL

A Bill that mandates laboratories to notify patients when their test results have been communicated to their physicians passed the NY State Assembly. Senator Frank Padavan of New York introduced the bill after a hospital in New York City failed to contact hundreds of women about abnormal Pap test results over an 18-month period. This incident highlighted problems with patient notification of laboratory test results. Although further investigations revealed that the failure was not due to negligence on part of the pathology laboratory but was linked to the clinical staff responsible from patient notification, the new bill shifts the responsibility of patient notification to the laboratories. The New York State Society of Pathologists (NYSSPATH) and the College of American Pathologists (CAP) asked Senator. Kemp Hannon, chair of the New York Senate’s Health Committee, to reject the Bill. The NYSSPATH and the CAP stated that this approach will not benefit patients or streamline medical care. They emphasized that ordering physicians are legally and ethically the treating physicians entrusted with the responsibility for patient care, and they must be held legally responsible for contacting patients with test results. They further commented that this legislation shifts continuity of care responsibility to the laboratory and the patient, in lieu of the treating physician, and thereby undermines conventional medical practice and escalates medical liability and health care costs for all parties.

PATHOLOGY SOCIETIES PROTEST NEW CYTOTECHNOLOGY PROFICIENCY TESTING

With the Midwest Institute of Medical Educations recent certification by the Centers for Medicare and Medicaid Services as the only nationwide provider of cytology proficiency testing the government regulations (that have been in effect since 1992 but never enforced) regarding cytology proficiency testing would be placed into

effect. These regulations are outdated and in June pathology organizations and state pathology societies wrote to Health and Human Services to request that the CMS regulations be updated. Letters have also been sent to the House of Representatives to suspend the proposed cytology proficiency testing.

CYTOLOGY PROFICIENCY TESTING REQUIREMENTS FOR RESIDENTS AND FELLOWS

Based on the information submitted by ACGME and the American Board of Pathology, Centers for Medicare and Medicaid Services (CMS) has determined the following:

- Residents are not required to participate in a CMS-approved Cytology Proficiency Testing Program. They are not board-certified and are under the constant supervision of fully licensed physicians.
- Participation in a proficiency test may be required for cytopathology fellows under certain circumstances. Fellows who render a final diagnosis on gynecologic specimens must enroll and participate in a CMS-approved proficiency test. Fellows who do not render a final diagnosis on gynecologic specimens are not required to participate in a CMS-approved proficiency test.

CAP OPPOSES PROPOSED CLOSING OF ARMED FORCES INSTITUTE OF PATHOLOGY

Daniel L. Seckinger, MD, FACP, past president of the College of American Pathology testified before the Defense Base Closure and Realignment Commission that closing the AFIP would have significant ramifications for medical research and medical care for both military personnel and veterans. The AFIP has been a source of expertise for unusual and challenging pathology cases nationally and internationally. According to Dr. Seckinger its repository contains over 50 million blocks that spans over 150 years. This source of tissue in combination with newer DNA and molecular breakthroughs has allowed treatment of incurable diseases. The closure of the Army Telepathology Program, providing expert pathology advice to military medical centers around the world would also be a serious loss for the medical community.

FEDERAL ADVISORY BOARD REPORT CALLS FOR INCREASE IN NUMBER OF PHYSICIANS TRAINED

The Federal Council on Graduate Medical Education (COGME), an advisory board to the Congress and the US Department of Health and Human Services, recently released a report predicting substantial national physician shortage. The report recommended a 15% increase in the number of students graduating from medical schools and a similar increase in the number of residency positions over the next 10 years. Three major factors causing increase in demand for physician services were noted to be population growth (18% increase between 2000 and 2020), aging population (increase in the number of Americans above age 65), and the changing age-specific per capita physician utilization rates, those over age 45 using more services, and those under age 45 using less.

DETECTION OF PROSTATE CANCER BY PSA LEVELS QUESTIONED

A recent study in the Journal of the American Medical Association (1) questions the accuracy of prostate specific antigen for monitoring healthy men for prostate cancer. The study found that there is no good cutoff value for PSA levels that has both high specificity and high sensitivity but rather there is a continuum of prostate cancer risks at all levels of PSA. The commonly used cutoff value of 4.1 ng/ml had a false positive rate of 6.2% but only detected 20.5% of the cases. Lowering the cutoff value to 1.1 ng/ml detected 83.4% of the cases but subjected 61.1% of men without cancer to a prostate biopsy.

1. Thompson IM, Ankerst DP, Chi C et al. Operating Characteristics of Prostate-Specific Antigen in men with an initial PSA level of 3.0 ng/ml or lower. JAMA 2005;294:66-70.

TOP 5 ABSTRACTS SUBMITTED BY PATHOLOGISTS-IN-TRAINING FOR THE PAPANICOLAOU RESEARCH AWARDS 2005:

FIRST PRIZE

- **Trichomonas vaginalis p16 Immunoreactivity in Cervicovaginal Pap Tests: A Diagnostic Pitfall**
L Pantanowitz, RR Florence, RA Goulart, CN Otis. Baystate Medical Center, Tufts University, Springfield, MA.

SECOND PRIZE

- **P16 and hTERT Staining as a Triage for ASCUS: Can We Forego Molecular Testing**
S Mehrotra, S Setty, A Kajdacsy-Balla, HE Gulbache, SE Pambuccian, University of Illinois at Chicago, Chicago, IL; University of Minnesota, Minneapolis, MN.

RUNNER UPS:

- Hodgkin Lymphoma Versus Reactive Lymph Node: Morphologic Clues for Diagnosis on Fine Needle Aspiration.
RY Peng, SL Hirschowitz. University of California Los Angeles, CA
- Integrated Molecular Pathology Evaluation of Pancreatic Brush Cytology. **O Lapkus**, YL Liu, M Leon, PA Swalsky, M Wilson, SD Finkelstein, JF Silverman Alleghany General Hospital, Pittsburgh, PA; RedPath Integrated Pathology, Pittsburgh, PA
- What is the Significance of a Negative FISH in Patients with Atypical Urine Cytology? **S Latif**, ML Nordberg, D Veillon, S Martin, GA Herrera, EA Turbat-Herrera. Louisiana State University Health Sciences Center, Shreveport, LA

A SPECIAL ANNOUNCEMENT

We watched with great grief and disbelief the devastation caused by one of the greatest natural disasters, Hurricane Katrina, that hit USA in the recent history. We extend our deepest sympathies to all who have lost their loved ones, homes and life long belongings in these unfortunate events that took place in parts of Louisiana, Mississippi, Alabama, and surrounding areas in late August. Dr. Fred Silva (President, USCAP) recently announced that the 2006 USCAP Annual Meeting scheduled to take place in New Orleans (February 11-17, 2006) has been moved to Atlanta. Please continue to watch the PSC and USCAP websites for updates.

Aylin Simsir, MD
Editor, Focus Newsletter

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through an unrestricted
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**The members of the Papanicolaou
Society of Cytopathology thank you
for your generous support.**

**ANNUAL MEETING AND RECEPTION
OF THE PAPANICOLAOU SOCIETY
OF CYTOPATHOLOGY,
SAN ANTONIO, TEXAS, 2005**



*Dr. Miguel Sanchez received the “2005 PSC
Interventional Cytopathologist Award” from Dr.
Andrea Abati.*



*Dr. Pambuccian accepted the PSC award for the
best research done by a resident/fellow in training
(second prize) on behalf of Dr. Mehrotra.*



*Dr. Diane Solomon receiving the “2005 PSC Educator
of the Year Award” from Dr. Kim Geisinger.*



*PSC Annual Cocktail Reception:
Colleagues catching up, getting
acquainted, and enjoying the
good company.*

BASIC SCIENCE CORNER

CELL BIOLOGY-CYTOPATHOLOGY CONNECTION

ANDREW H. FISCHER, MD, UNIVERSITY OF MASSACHUSETTS



There are exciting new findings from cell biologists in the field of histone modification with potential to take cytopathology beyond pattern recognition to a point where we can begin to phrase some of the criteria of malignancy in objective molecular terms. A specific histone methylation appears to provide the molecular basis for heterochromatin formation, and other histone modifications (detectable by immunocytochemistry) are being linked to a wide range of cell physiologies relevant to cancer.

Much of our current understanding of histone modifications can be traced back to cytologic observations. In 1928, Emil Heitz described heterochromatin as the component of chromosomes that did not completely de-condense during interphase [1]. Partly through intuition, Heitz believed that genes were not active within heterochromatin. Careful correlation of light microscopy with genetic analyses in the following decade provided direct evidence supporting this view: Genes that were translocated into, or even near, heterochromatin were silenced. The “cytologic” description of the Barr body in 1949 [2] also conformed to this model of transcriptionally inactive heterochromatin. The Cytopathologist John Frost incorporated these concepts in his book “The Cell in Health and Disease” [3]. Frost used the term “proplasia” to describe a cell that was euchromatic (i.e., a cell that expressed a large number of genes), had a prominent nucleolus (because nucleoli produced ribosomes needed for translating the gene transcripts into proteins), and had abundant cytoplasm with basophilia (because the cells had lots of mRNA and ribosomes for making a lot of cytoplasmic protein). The opposite of “proplasia” was “retroplasia”, and Frost proposed that cancer showed deregulation of these two states such that cancer cells could simultaneously show both proplastic and retroplastic features (e.g., lots of “parachromatin clearing” and large nucleoli, but scant and pale cytoplasm). While there are still few clues (and surprisingly little interest from cell biologists) as to how or why some cancer cells may show paradoxically large nucleoli and scant pale cytoplasm [4], at least a molecular basis for the distinction between heterochromatin and euchromatin is rapidly being deciphered.

The basic unit of chromatin is the nucleosome, described in 1974, consisting of eight core histones (two molecules each of histone H2A, H2B, H3 and H4) around which 147 base pairs of DNA is wrapped in 1½ turns. DNA is compacted by a factor of about 5 through its assembly into nucleosomes. Adjacent nucleosomes are joined by “linker histone” H1. The histones are highly conserved in evolution and they appeared coincidental with the emergence of eukaryotes. In an apparently highly regulated manner [5], nucleosomes can maintain a stable association with the underlying DNA strand during transcription and replication. Therefore, covalent modifications of histones can provide a stable “epigenetic” mark on a gene without a change in the underlying DNA template. Since there are dozens of acetylations, methylations, phosphorylations and other modifications of the core and linker histones, the complexity of this epigenetic “histone code” for directing DNA function is enormous [6].

Except for germ cells and immune system cells, somatic cells normally share the same DNA sequence, yet cell-type specific heterochromatin patterns are heritable. Solving the precise molecular basis for at least some of the stably inherited heterochromatin patterns was accomplished by setting up screens in *Drosophila* for genes that affected heterochromatin silencing [5] [7]. The proteins corresponding to two such genetic modifiers of heterochromatin silencing were found to be about as evolutionarily ancient as the histones themselves, and ultimately they were found to function in a similar manner from the fission yeast *S. pompe* to humans. Through analysis of the structure of the proteins, one of them (Suv39h in humans) was found to be a methyltransferase and it was ultimately determined that its substrate was histone H3 at the 9th amino acid, which is a lysine. “K” is the abbreviation for lysine, so the modification is often designated H3K9m. The other protein that modified heterochromatin silencing, called heterochromatin protein 1 (HP1), was found to bind to H3K9m [8]. HP1 dimerizes and appears to cross-link nucleosomes such that genes decorated with H3K9m nucleosomes become compacted and inaccessible to the mRNA transcriptional machinery [7]. The cross-linking effect of HP1 may also help to explain the cytologic observation that heterochromatin aggregates tend to coalesce.

Thus, much of what cytopathologists see as hematoxylin-dark heterochromatin appears to correspond to H3K9m cross linked by HP1 [9] [8]. HP1 also binds to the nuclear lamina protein LBR, which is the best available explanation for why heterochromatin is typically apposed to the nuclear envelope of cells, and why inactive genes are preferentially located peripherally [10].

An apparently reasonable extension of the histone code hypothesis relevant to cytopathologists is that cell-type specific large-scale chromatin organization derives from the patterns of specific histone modifications which in turn define how nucleosomes are packaged at higher (light microscope) levels [9]. Conforming to this hypothesis, increased di- and tri- methylation of histone H3K4 (five amino acids away from lysine 9) is associated with euchromatin and actively transcribed genes [7]. We recently observed decreased H3K4monomethylation in papillary thyroid carcinomas, presumably because the monomethylated H3K4 becomes di- or tri- methylated [11]. Euchromatin generally also has increased levels of acetylated histones [12], while heterochromatin tends to have increased DNA methylation. However, neither DNA methylation nor histone acetylation appear as closely related to cytologic chromatin features as the relation between H3K9m and (and possibly H3K4m) and chromatin morphology. For example, we observed no effect on the large-scale organization of interphase heterochromatin in a pilot study of cell lines when we demethylated their DNA (A.H. Fischer and D. Hunt, 1996, unpublished observations).

Of the dozens of other covalent modifications to histones besides H3K9 and H3K4 methylation, the relation with specific cellular structural changes are either not studied, or they are not apparently clear-cut. Sadly, there is very little involvement of cytopathologists in the published studies of histone modifications, and therefore there is little information about cellular level structural correlates of most findings. Histone codes affect cell physiologies other than transcription, such that an “epigenetic profiling” [13] (i.e., seeing which DNA segments have particular histone modifications in the associated nucleosomes) is expected to reveal facets of cell physiology quite different from

mRNA expression profiling. Epigenetic profiling would be feasible on scant cytologic samples, and these types of studies could be useful for disclosing the cellular-level correlates of histone modifications.

Two other histone modifications that have major potential practical value for cytopathologists include H3S10 phosphorylation and H2AX phosphorylation. H3S10 is strongly phosphorylated at the end of G2 just prior to prophase, and it is mostly dephosphorylated before the end of telophase [14]. Immunohistochemical staining for phosphorylated H3S10 therefore provides a simple and robust measure of mitotic counts. H2AX is one of 4 histone H2A subtypes that comprises from 2 to 25% of total H2A in mammalian cells. H2AX is phosphorylated at serine 139 within minutes very near regions of DNA double strand breaks [15]. The amount of immunostaining for phosphorylated H2AX-S139 therefore gives a measure of the amount of ongoing DNA damage within a cell, and a measure of cells' capacity to repair DNA damage. Cancer cells are characteristically genetically unstable, and recent studies [16, 17] showed that before gross chromosomal instability and aneuploidy have occurred, increased numbers of double strand breaks are detectable by gross immunohistochemical levels of staining for phospho-H2AX. The authors provide compelling evidence for model of continual low-level DNA damage during precancerous progression that acts as a selective pressure for mutations (e.g., p53) that bypass DNA damage checkpoints. The practical point for pathologists is that low grade or early lesions that are not grossly genetically unstable or aneuploid (and therefore may be difficult to detect by cytology) appear nevertheless to have a chromatin-based signature that is detectable by immunostaining for phosphorylated H2AX. It would certainly be great to have an objective assay for low-grade urothelial tumors. Could increase H2AX phosphorylation be the correlate for "malignancy associated change" in chromatin [18]? The amount of H2AX phosphorylation may also be useful for predicting chemo- or radiosensitivity since these anticancer treatments function in large part by inducing DNA double strand breaks.

It is almost always necessary to know how things are structured to understand how they function. Cytopathologists are in a great position to help cell biologists decipher the functional significance of diagnostic changes in cell structure.

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BULLETIN BOARD

Papanicolaou Society Committees and Task Forces

- LC TAO EDUCATOR AWARD:** The committee's charge is to select the best candidate for the Papanicolaou Society of Cytopathology Educator of the Year Award. Claire Michael, Chair, clairemi@med.umich.edu Members: Kim Geisinger, Beatrix Cochand Priollet, Susan Rollins, Rosa Davila
-
- YOLANDA OERTEL AWARD:** The committee's charge is to select the best candidate for the Papanicolaou Society of Cytopathology Interventional Cytopathologist Award. Yolanda Oertel, Chair, Yolanda.C.Oertel@Medstar.net Members: Andrea Abati, Michael Stanley, Carlos Bedrossian, Lucio Palombini
-
- BUDGET AND FINANCE:** The committee prepares a budget for the ensuing year in concert with the treasurer, to recommend a change in membership dues if and when necessary, and to recommend ways to increase the financial stability of the PSC. Martha Bishop Pitman, Chair, mpitman@partners.org Members: M Zarka, R Tambouret, M Cohen, W Faquin, U Bedrossian (ex officio)
-
- PROGRAM DEVELOPMENT:** The committee's goals are to raise funds to support the various programs and activities of the PSC. Steve Raab, Chair, raabss@upmc.edu
-
- PUBLICATION COMMITTEE:** The Publication Committee prepares and publishes the biannual PSC newsletter "Focus". Focus is published online, and also, is mailed to all PSC members through a generous donation from Cytyc Corporation. The newsletter aims to disseminate information related to the past and upcoming PSC events, society related news, new developments and timely topics associated with the practice of cytopathology. Aylin Simsir, Chair, aylin.simsir@med.nyu.edu Members: Joan Cangiarella, Oscar Lin, Isam-Eldin Eltoun, Andrew Fischer
-
- SCIENTIFIC PROGRAM:** The committee has selected and developed what we hope will be an exciting and timely program for the 2006 New Orleans annual meeting of the Society. Lester Layfield, Chair, Layfield-aruplab.com Members: Martha Pitman, Maureen Zalowski, Harvey Cramer, Tarik Elsheik, Yolanda Oertel
-
- EDUCATION & TRAINING:** The committee continues to publish interesting cases on the PSC website. David Chhieng, Chair, dchhieng@path.uab.edu Members: Alaa Afify, Joan Cangiarella, Oscar Lin, Larry Fowler, Syed Ali
-
- GOVERNMENT RELATIONS:** The Government Relations Task Force monitors legislative and regulatory issues, and proposes areas for advocacy efforts by the membership. The Task Force communicates, and partners with other medical and cytopathology organizations including the CAP, ASC, and AMA, on topics important to cytopathology. Diane Davey, Chair, e-mail: ddavey@uky.edu Members: Anna O'Grady Berry, George Birdsong, Dina Mody, R Marshall Austin.
-
- RESEARCH TASK FORCE:** The purpose of the task force is to encourage quality research and exchange of ideas relevant to Cytopathology among pathologists-in-training. Every year, members of the research committee review Cytopathology abstracts submitted to the USCAP in order to select the recipients of the Papanicolaou Society Research Awards. Applications for the awards are accepted automatically via the Stowell-Orbison award or by submitting the application form distributed via the society listserv. For details pertaining to the application and selection process please refer to the society website. Armando Filie, Chair, afilie@mail.nih.gov Members: Sue Ellen Martin, Hormoz Ehya, Robert Pu, Jan Silverman
-
- INTERNATIONAL RELATIONS:** The function of this committee is the interchange of ideas and information between members and committees of various cytology organizations at the international level. The committee facilitates joint sessions among these organizations and assists PSC in the recruitment of prospective members. Carlos Bedrossian, Chair, carlos@bedrossians.com Members: Rana Hoda
-
- CONSTITUTION & BYLAWS:** The Constitution and ByLaws Committee updates the Constitution and ByLaws as necessary. Steve Raab, Chair, raabss@upmc.edu Members: Executive Board and Officers
-
- NOMINATING COMMITTEE:** It is the charge of the nominating committee to produce a slate of nominees for all elections for the PSC. Kim Geisinger, Chair, kgeis@wfubmc.edu Members: Mary Sidawy, Michael Stanley
-
- PRACTICE GUIDELINES:** This committee's goals are to work on the proposals and guidelines regarding thyroid FNA specimens. This task is being accomplished by subcommittees (including members of guidelines and standards of practice committee) which will focus on various aspects of thyroid FNA including: indications of thyroid FNA, specimen processing, adequacy criteria, cyto-morphology of various thyroid lesions with emphasis on follicular patterned lesions and report format of thyroid FNA. Zubair Baloch, Chair, baloch@mail.med.upenn.edu Members: Douglas Clark, William Faquin, Tarik Elsheik, Sanjay Logani
-
- MEMBERSHIP COMMITTEE:** The charge of the Membership Committee is to increase membership with a particular focus on recruiting junior members. Gladwyn Leiman, Chair, Gladwyn.Leiman@vtmednet.org Members: Euphemia McGoogan, Andrew Field, Colleen Wright, David Chhieng
-
- INTERNATIONAL SCIENTIFIC PROGRAM COMMITTEE:** The charge of this committee is to make implicit connection between diagnostic cytopathology and global public health. Eric Suba, Chair, Eric.Suba@kp.org Members: David Kaminski, M. Duggan
-
- PCS WEBSITE:** The committee has been working to update the PSC webpage including the application of several new features that may be beneficial to PSC members. Rana Hoda, Chair, hodars@muscc.edu Members: Prabodh Gupta, Ricardo Bardales, Vinod Shidham, Mohammad Aktar, Volker Schneider, James Madory

A Memorial Symposium

GEORGE L. WIED, MD, FIAC (1921-2004)



Drs. Koss, Bibbo, Schneider and Bedrossian at George L. Wied Symposium in Vienna, Austria.

George Wied, born in Slovakia only a few years after the demise of the Austrian-Hungarian Empire, cut an imperial figure in the world of clinical cytology. It was befitting that he was honored in Vienna, Austria, September 10-11, 2005, in an event full of memories, fun and serious science. There were no CMEs to be earned, nobody received a diploma, and it was the height of a hot summer in central Europe. Yet over 100 faithful friends came from as far west as California, and as far East as Siberia. If someone's impact is measured by to which extent he is remembered, George was a lucky man. The participants strived hard to share their fondest recollection; they actually revealed new facets of a true gentleman and a personable human being behind a long and distinguished career as the organizer par excellence in the cytology field.

In a profession blessed with truly accomplished individuals, George stood out as the quintessential renaissance man. When I first met George, in Vienna more than thirty years ago, I had just completed my cytology fellowship and would be attending his famous tutorials for the first time. Yet, "Dr. Wied" did not stand on a pedestal. He greeted me personally, chatted with me in his inimitable Viennese accent and tried to steer me into gynecologic research. So remarkable was his personality, to this day, I still remember what we discussed: the Feulgen reaction, something I learned in medical school from professors Valeri and Brandão, in Brazil. In no time, George turned on his charm and I became a subscriber to *Acta Cytologica*, joined the IAC and even began preparations to take the fabled FIAC exam. At the Vienna tribute, Dr. Leopold Koss, another giant of his own accord, probably made the most heartfelt impression with the mastery that only Leo could pull it off. He projected side-by-side photographs of George and Pope John Paul II. "They were born a few months apart and a few kilometers apart. . . The Pope preached the gospel of religion, George preached the gospel of cytology. . . The Pope saved souls, George saved lives, by popularizing the Pap smear." I don't know how George would have reacted to Leo's baritone and impeccable delivery. I can only imagine he would have chuckled and uttered some apropos repartee. Karen Lindholm related how Nils Stornby called George from Stockholm, to brag about one of the earliest car phones, "George, I'm calling you from my automobile." A short silence followed, then George replied: Wait a minute, Nils, I'm caught in Chicago traffic, let me hang up my other phone." Dr. Matias Ayala told a story he heard from Peter Bartels of how George confused a cricket's sound with the noise of a rattlesnake while camping in Arizona. During this same rafting trip in the Grand Canyon, George showed up in a suit and tie, but in a day's time, he became the "captain of the ship." As it should be expected, Dr. Leo Koss had the best closing for his oration. "I just heard from George. Upon his arrival, in heaven, he started the international academy of angels, with admission only by examinations." And, Leo added, "When I get there, I hope to join the faculty."

The most poignant moment came later in the evening. Exactly at the moment George's son stood up to remember his father, a perfect sunny evening turned dark. There was a sudden rain as his son said, "I am sure dad's longing to be here with his friends. . . He was my best friend. I can tell these are his tears, longing to join us, in these wonderful festivities." It was hard to find any dry eyes in the audience. For this moment alone, I am glad I could be in Vienna and say goodbye, to an unforgettable member of our cytology world.

Carlos W.M. Bedrossian, MD, PhD(hon), FIAC
Vienna, Austria
September 11, 2005



The Montebello Conference 2006

Fine Needle Aspiration: The Next Frontier



The Montebello Centre, Mesnali, Lillehammer, Norway
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Don't miss next year's Montebello Conference on Fine Needle Aspiration, co-sponsored by the Norwegian Radium Hospital and the Papanicolaou Society of Cytopathology. For more information contact co-moderators:

Aasmund Berner Aasmund.Berner@radiumhospitalet.no
or Carlos Bedrossian Carlos@Bedrossians.com

A partial list of confirmed speakers includes:

Carlos Bedrossian
Ben Davidson
Lester Layfield
Yolanda Oertel
Bjorn Risberg
Fernando Schmitt

Aasmund Berner
Helen Koutselini
Claire Michael
Lucio Palombini
Miguel Sanchez
Jan Silverman