2017 | ACMG Annual Clinical Genetics Meeting

ACMG American College of Medical Genetics and Genomics
Translating Genes Into Health®

The Ticking Time Bomb - Adult-onset Presentations of Inborn Errors of Metabolism

Held in Phoenix, Arizona, March 21-25, 2017

Date of Release: April 3, 2017
Expiration Date: April 3, 2020 (CME, NSGC, P.A.C.E.®)
Estimate Time of Completion: 2 hours
Course must be completed by the expiration dates

COURSE DESCRIPTION

This session is geared towards genetic clinicians who evaluate adult patients but who are not necessarily specialized in managing inborn errors of metabolism. In the era of expanded newborn screening, there is an increasing appreciation of the clinical spectrum of pediatric manifestations of inborn errors when ascertainment is not based on clinical symptoms. With surveillance and appropriate interventions, it is anticipated that the clinical outcomes patients in the screened cohort can be improved. With the exception of a handful of disorders, the adult population has not had the benefit of population-based screening, setting the stage for late presentations of screenable as well as non-screenable disorders. It is important for clinicians to recognize the signs and symptoms of adult-onset forms of inborn errors of metabolism, especially those for which therapeutic options are available. This session will begin with an overview of neuropsychiatric presentations of inborn errors, as neurological presentations are a common thread in the subsequent presentations. Subsequent talks will focus on disorders which may be screenable (the recent RUSP addition X-linked adrenoleukodystrophy), non-screenable (Niemann-Pick type C, mitochondrial disorders, the porphyrias), or both (late-presenting urea cycle disorders). The final presentation will focus on mitochondrial disease as an example of a highly diverse set of adult-onset clinical phenotypes.

LEARNING OBJECTIVES

At the conclusion of this course, participants should be able to:

- Recognize cardinal signs and symptoms of inborn errors of metabolism that may present in adulthood
- Apply diagnostic algorithms for the evaluation of the conditions discussed in the session
- Describe the treatment options for the conditions discussed in the session
- Distinguish major groups of mitochondrial disorders that present in adulthood

TARGET AUDIENCE

All healthcare professionals interested in the diagnosis, management, treatment and prevention of genetic conditions and increasing their understanding of the genetic basis of common, chronic health problems affecting both children and adults will find the programming applicable to their practice. These select sessions from the ACMG Annual Meeting are targeted for the following professionals:

- Medical and clinical geneticists
- Physicians of all specialties with an interest in genetics, genomics and the genetic basis of disease
- Genetic counselors
- Laboratory geneticists, directors, technicians and technologists
- Researchers
- Pathologists
- Educators
- Nurses
- Dietitians
- Physician assistants
- Biotechnology and pharmaceutical development professionals
- Fellows, Trainees and Students
- Public health professionals
- Genetic/consumer advocates
- Others with an interest in the science and art of medical genetics and genomics

SESSIONS

- Neuropsychiatric Presentations of Inborn Errors of Metabolism in Adults- Jerry Vockley, MD, PhD, FACMG
- Mitochondrial Disorders in Adulthood- Marni Falk, MD, FACMG
- Niemann-Pick Disease, Type C - Not Just for Children- Marc Patterson, MD, FRACP, FAAN, FANA
- Urea Cycle Disorders in Adults: Better Never than Late- George Diaz, MD, PhD, FACMG
- X-linked Adrenoleukodystrophy Presentations in Adults- Gerald Raymond, MD
- Porphyrias in Adults: Diseases of Kings and Commoners- Manisha Balwani, MD, MS

Accreditation:

The American College of Medical Genetics and Genomics is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Credit Designation:

The American College of Medical Genetics and Genomics designates this activity for a maximum of 2 *AMA PRA Category 1 Credit*s™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Genetic Counselor Credit

The National Society of Genetic Counselors (NSGC) has authorized American College of Medical Genetics and Genomics to offer up to 2 Category 1 contact hours for this OnDemand course. The American Board of Genetic Counseling (ABGC) will accept CEUs earned for this course for the purposes of genetic counselor certification and recertification. Reporting of credits is sent to NSGC quarterly. Additional fee (~$25) applies for NSGC credit that is billed by NSGC.

P.A.C.E. CEUs – Laboratory Directors and Laboratory Personnel

ACMG is approved as a provider of continuing education programs in the clinical laboratory sciences by the American Society for Clinical Laboratory Science (ASCLS) Professional Acknowledgment for Continuing Education (P.A.C.E.®) Program. The American College of Medical Genetics and Genomics designates this course for a maximum of 2 contact hours. ACMG is approved by the Florida Board of Clinical Laboratory Personnel as CE Provider. ACMG is approved by the California Department of Health Services through the ASCLS P.A.C.E.® Program as CE Provider #275.

HIPAA Compliance

The ACMG supports medical information privacy. While the ACMG is not a "covered entity" under HIPAA 1996 and therefore is not required to meet these standards, ACMG wishes to take reasonable steps to ensure that the presentation of individually identifiable health information at ACMG-sponsored events has been properly authorized. All presenters have completed a form indicating whether they intend to present any form of individually identifiable healthcare information. If so, they were asked either to attest that a HIPAA-compliant consent form is on file at their institution, or to send ACMG a copy of the ACMG HIPAA compliance form. This information is on record at the ACMG Administrative Office and will be made available on request.

Content Validation

ACMG follows the ACCME policy on Content Validation for CME activities, which requires:

Content Validation and Fair Balance

1. ACMG follows the ACCME policy on Content Validation for CME activities, which requires:
   a) All recommendations involving clinical medicine must be based on evidence that is accepted within the profession of medicine as adequate justification for their indications and contraindications in the care of patients.
   b) All scientific research referred to, reported or used in CME in support or justification of patient care recommendations must conform to the generally accepted standards of experimental design, data collection and analysis.

2. Activities that fall outside the definition of CME/CE; "Educational activities that serve to maintain, develop, or increase the knowledge, skills, and professional performance and relationships that a physician uses to provide services for patients, the public, or the profession" (source: ACCME and AMA) will not be certified for credit. CME activities that promote recommendations, treatment, or manners of practicing medicine or pharmacy that are not within the definition of CME/CE or, are known to have risks or dangers that outweigh the benefits or, are known to be ineffective in the treatment of patients.
3. Presentations and CME/CE activity materials must give a balanced view of therapeutic options; use of generic names will contribute to this impartiality. If the CME/CE educational materials or content includes trade names, where available, trade names from several companies must be used.

Off-label Uses of Products

When an off-label use of a product, or an investigational use not yet approved for any purpose, is discussed during an educational activity, the accredited sponsor shall require the speaker to disclose that the product is not labeled for the use under discussion, or that the product is still investigational. Discussions of such uses shall focus on those uses that have been subject of objective investigation.

Disclaimer: *ACMG educational programs are designed primarily as an educational tool for health care providers who wish to increase their understanding of the application of genomic technologies to patient care. The ACMG does not endorse, or recommend the use of this educational program to make patient diagnoses, particular by individuals not trained in medical genetics. Adherence to the information provided in these programs does not necessarily ensure a successful diagnostic outcome. The program should not be considered inclusive of all proper procedures and tests or*

exclusive of other procedures and tests that are reasonably directed at obtaining the same results. In determining the propriety of any specific procedure or test, a healthcare provider should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen.

2017 ACMG Program and Education Committee Members Disclosures

Members of the ACMG Staff, Education and Program Committees involved in planning the 2017 ACMG Annual Clinical Genetics Meeting are required to disclose relevant relationships which could be perceived by some as a real or apparent conflict of interest in planning. All disclosures have been reviewed and conflicts of interest resolved by the Education Committee COI sub-committee or the Executive Director and CME Associate Director and conflicts of interest are disclosed. In the cases where a conflict existed then the committee member refrained from the discussion.

Following is a list of program and education committee members who have disclosed one or more such relationships and names of companies with which those relationships exist:

EC = Education Committee; PC = Program Committee; S = ACMG Staff

1. Major stockholder/ownership interest 2. Grant/Research Support (External) 3. Salary/Employment/Royalty(ies)/Honoraria 4. Consultant/consulting fees/other remuneration 5. Speakers' bureau	6. Non-remunerative positions of influence such as officer, board member, trustee, or public spokesperson (All Committee Members Below are on ACMG Committees –Members with other affiliations are listed) 7. Receipt of intellectual property 8. Other

Georgianne L. Arnold, MD, FACMG - Horizon, 2; Recordati, 2; Biomarin, 2; Actelion, 2; SIMD, 6; ACGME, 6; AAP, 6; ASHG, 6 (PC)
Karen W. Gripp, MD, FACMG – Wiley Publishing Inc., 3; FDNA, 4; Novartis, 4 (PC)
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Thomas E. Mullen, PhD, MS, FACMG - Good Start Genetics Inc., 3 (EC)
Christian P. Schaaf, MD, PhD, FACMG - Springer Publishing Company, 3 (PC), (EC)
Katrina M. Dipple, MD, PhD, FACMG – ACGME, 6; AAP, 6; ASHG, 6; LA BioMed DSMB, 4; SIMD 6 (PC)

Following is a list of committee, education members and staff who have no relationships to disclose:

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Jane Radford, MHA, CHCP (PC), (EC), (S)
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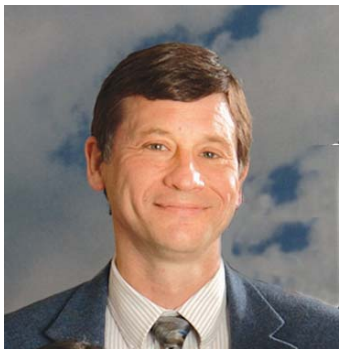
Penelope Freire, CMP (PC), (S)

SPEAKERS AND MODERATORS

Faculty Disclosures:

As a sponsor accredited by the ACCME, the American College of Medical Genetics and Genomics must ensure balance, independence, objectivity and scientific rigor in all its sponsored educational activities. All faculty participating in a CME-certified activity are expected to disclose to the audience any relevant financial interest(s) or other relationship(s) with the manufacturer(s) of any commercial product(s), provider(s) of commercial services or any commercial supporters, including diagnostic laboratories, of the activity discussed in an educational presentation. Relevant financial interest(s) or other relationship(s) can include such things as grants or research support, consultancy, major stock holder, etc. The intent of this disclosure is not to prevent a planner or speaker with a relevant financial or other relationship from course planning or making a presentation, but rather to provide learners with information on which they can make their own judgments. It remains for the audience to determine whether the speaker's interests or relationships may influence the presentation with regard to exposition or conclusion. All conflicts of interests have been reviewed and resolved by the education and CME subcommittee.

Speaker: Jerry Vockley, MD, PhD, FACMG
University of Pittsburgh
No financial relationships to disclose.

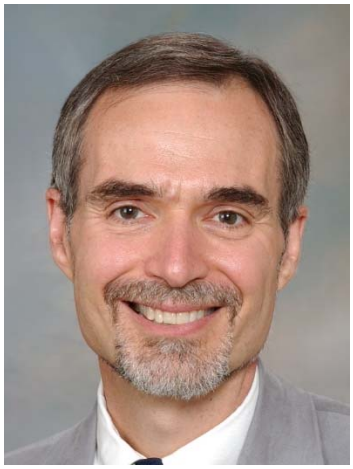


Dr. Vockley received his undergraduate degree at Carnegie-Mellon University in Pittsburgh, Pennsylvania, and received his degree in Medicine and Genetics from the University of Pennsylvania School of Medicine. He completed his pediatric residency at the University of Colorado Health Science Center, and his postdoctoral fellowship at Yale University School of Medicine. Before assuming his current position, Dr. Vockley was Chair of Medical Genetics in the Mayo Clinic School of Medicine. He is currently the Cleveland Family Professor of Pediatric Research, and Chief of Medical Genetics at the University of Pittsburgh. He is the founder of the Plain Communities Translational Medicine program at the Children's Hospital of Pittsburgh. Dr. Vockley is internationally recognized as a leader in the field of inborn errors of metabolism. His current research focuses on the molecular architecture of mitochondrial energy metabolism, in which he is breaking new ground in describing the role of dysfunction of mitochondrial energy metabolism in common conditions. Dr. Vockley has served on numerous national and international scientific boards including the Advisory Committee (to the Secretary of Health and Human Services) on Heritable Disorders in Newborns and Children where he was chair of the technology committee. He also serves as chair of the Pennsylvania State Newborn Screening Advisory Committee and the American College of Medical Genetics Therapeutics Committee. He is a past president of the Society for the Inherited Metabolic Disorders (SIMD), and is the co-founder of the North American Metabolic Academy. He is founder of the International Network on Fatty Acid Oxidation Research and Management (INFORM). He is also a volunteer medical advisor for several parent and family support groups including the Fatty Acid Oxidation Family Support Group, Save Babies through Screening, United Mitochondrial Disease Foundation, and the Organic Acidemia Support Group.

Moderator/Speaker: Marni Falk, MD, FACMG
Associate Professor, Division of Human Genetics, Department of Pediatrics, CHOP/Penn, The Children's Hospital of Pennsylvania
Financial relationships to disclose. (Self): Member Scientific and Medical Advisory Board for United Mitochondrial Disease Foundation and Scientific Advisory Board member of Genesis Project Grant/Research Support: Raptor Pharmaceuticals, Cardero Therapeutics, Vitaflo, Stealth BioTherapeutics, RiboNova, Neurovive, Mitobridge; PI, CHOP Site, NorthAmerica Mitochondrial Disease Consortium, PI, CHOP site, RT-408 Reata Clinical Trial, PI, CHOP site, SPIMM 300/301, Stealth BioTherapeutics Clinical Trial.

Marni J. Falk, M.D., received her Bachelors of Science Degree in Biology and Medical Degree in a combined 7-year program from the George Washington University School of Medicine in Washington, D.C. She graduated Summa cum Laude, and was a member of Phi Beta Kappa and the Alpha Omega Alpha Medical Honor Society. She trained in a combined 5-year Pediatrics and Clinical Genetics residency program at Case Western Reserve University and University Hospital of Cleveland in Cleveland, Ohio. She is Associate Professor in the Division of Human Genetics within the Department of Pediatrics at The Children's Hospital of Philadelphia (CHOP) and University of Pennsylvania (UPenn) Perelman School of Medicine in Philadelphia, Pennsylvania. Board Certified in Clinical Genetics and Pediatrics, Dr. Falk established and directs the CHOP Mitochondrial Disease Clinical Center (MDCC) to aid in the evaluation and management of individuals of all ages with suspected mitochondrial disease. She organizes the global Mitochondrial Disease Sequence Data Resource (MSeqDR) consortium. Dr. Falk is PI of an NIH-funded translational research laboratory at CHOP that investigates the causes and global metabolic consequences of mitochondrial disease, as well as targeted pharmacologic therapies, in C. elegans, zebrafish, mouse, and human tissue models of genetic and pharmacologic-based respiratory chain dysfunction. She has authored 85 publications in the areas of human genetics and mitochondrial disease. Dr. Falk directs the CHOP/UPenn Mitochondria Research Affinity Group ('MITO RAG') that has 250 active participants. She is a member of the Scientific and Medical Advisory Board of The United Mitochondrial Disease Foundation, CHOP Center for Mitochondrial and Epigenomic Medicine (CMEM), North American Mitochondrial Disease Consortium, Mitochondrial Medicine Society, SPR, SIMD, ASHG, and ACMGG.

Speaker: Marc Patterson, MD, FRACP, FAAN, FANA
Professor, Depts. of Neurology, Pediatrics and Medical Genetics, Mayo Clinic Children's Center
Financial relationships to disclose. (Self): Consult for: Actelion, Alexion, Amicus, Novartis, Orphazyme, Shire, Vtesse Grant/Research Support: Actelion, Orphazyme, National MS Society, NINDS HONORARIA: Journal of Child Neurology and Child Neurology Open (Editor in Chief); journal of Inherited Metabolic Disease and JIMD Reports (Editor). ROYALTIES: Up-To-Date (Pediatric Neurology Section Editor) Off Label Disclosures: He will be discussing Miglustat

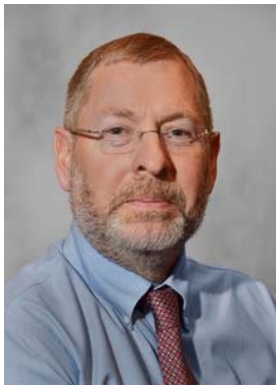


Marc Patterson was born and educated in Australia, and trained in neurology, child neurology and neurometabolic disease at the University of Queensland, at Mayo Clinic, and at NINDS/NIH, the last mentioned under the guidance of Roscoe Brady, MD. He is currently Professor of Neurology, Pediatrics and Medical Genetics, and Chair of the Division of Child and Adolescent Neurology at Mayo Clinic, He was Director of the Child Neurology Training program at Mayo 2008-2016), and had previously served as Professor and Director of Pediatric Neurology at Columbia University in New York (2001-2007). He has served as a member of the Neurology topic advisory group for revision of the ICD-10 of the World Health Organization, and leads the Education Core of the NIH-funded Lysosomal Disease Network. He has served in a number of positions in the Child Neurology Society, American Academy of Neurology, American Board of Psychiatry and Neurology and American Neurological Association. Professor Patterson has served on the editorial board of Neurology, on the oversight committee of Annals of Neurology and is currently an Editor for the Journal of Inherited Metabolic Disease. He became Editor-in Chief of the Journal of Child Neurology on January 1st, 2014, and subsequently Editor-in-Chief of its open-access sister journal, Child Neurology Open. His research and practice has focused on rare diseases in children, including multiple sclerosis and neurometabolic disorders in general, with special interests in Niemann-Pick disease, type C, other lysosomal diseases (including glycoproteinoses), mitochondrial cytopathies and congenital disorders of glycosylation, areas in which he has published more than 200 peer-reviewed papers and book chapters. He has presented widely through the United States and internationally, both to professional and lay organizations. Dr Patterson has received funding support from NIH, industry and private foundations.

Moderator/Speaker: George Diaz, MD, PhD, FACMG
Professor, Dept. of Genetics & Genomic Sciences, Icahn School of Medicine at Mount Sinai
No financial relationships to disclose.

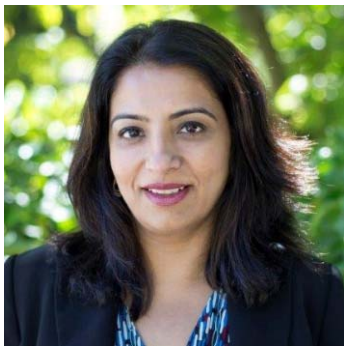
George Diaz, M.D, Ph.D. is Board Certified in Pediatrics and Medical Genetics after completing a Lucy Moses Research Residency Fellowship at the Icahn School of Medicine at Mount Sinai in 1999. He is currently Chief of the Division of Medical Genetics in the Department of Genetics and Genomic Sciences of the Icahn School of Medicine at Mount Sinai. As the Director of Mount Sinai's Program for Inherited Metabolic Diseases, one of the largest metabolic disease treatment programs in the country, his clinical focus is on inborn errors of metabolism with a special focus on urea cycle disorders (UCDs). In addition to his clinical research efforts focused on UCDs, Dr. Diaz's laboratory research efforts have resulted in the identification of the genetic basis of a number of single gene disorders including thiamin-responsive megaloblastic anemia syndrome, autosomal recessive Kenny-Caffey syndrome, WHIM syndrome, autosomal recessive myelokathexis, and choanal atresia-lymphedema syndrome. Dr. Diaz is involved in training the next generation of medical geneticists as Program Director of Medical Genetics training programs at Mount Sinai.

Speaker: Gerald Raymond, MD
Professor, Dept. of Neurology, University of Minnesota
Financial relationships to disclose. (Self): Served as an advisor or consultant for: Minoryx, Blubird Bio



Dr. Raymond received his medical degree from the University of Connecticut. He trained in pediatrics at Johns Hopkins Hospital and then Neurology at Massachusetts General Hospital. He completed training in Clinical Genetics at Harvard. Dr. Raymond is a pediatrician, a geneticist, and a neurologist with a special interest in developmental and neurogenetic disorders affecting children and adults. Currently, he works at University of Minnesota Masonic Children's Hospital. Dr. Raymond's work has focused on X-linked adrenoleukodystrophy (ALD) and other peroxisomal disorders. His efforts in this field have been in the diagnosis, care and treatment of all aspects of ALD and other peroxisomal disorders. Recently, he has advanced newborn screening of ALD and clinical trials of the natural history and treatment of all aspects of ALD.

Speaker: Manisha Balwani, MD, MS
Icahn School of Medicine at Mount Sinai
Financial relationships to disclose. (Self): Honoraria for advisory board participation at Recordati Rare Diseases and Alnylam; Clinical Trial Support from Alnylam Pharmaceuticals



Dr. Manisha Balwani is currently an Associate Professor in the Department of Genetics and Genomic Sciences and Medicine of the Icahn School of Medicine at Mount Sinai. Her clinical focus is the Porphyrias and Lysosomal Storage Diseases. She is the Director of the Lysosomal Diseases Program and Co-Director of the Porphyria Center and Mount Sinai. She is an investigator for NIH supported Rare Diseases Clinical Research Network's Porphyrias consortium and is the principal investigator on natural history studies and interventional clinical trials. Dr. Balwani began completed her medical training from the University of Bombay, followed by a Master's in Genetics at the University of Pittsburgh's Graduate School of Public Health. She completed her training in Internal Medicine followed by a fellowship in Medical Genetics and Clinical Biochemical Genetics. She joined the faculty of the Department of Genetics and Genomic Sciences at the Mount Sinai School of Medicine in 2006. Her initial research efforts were focused on the natural history of Gaucher disease and genotype-phenotype correlations. She was the Principal Investigator for therapeutic clinical trials for new therapies for Gaucher disease and Lysosomal Acid Lipase deficiency. Her current research efforts have been focused on the acute and cutaneous porphyrias and she serves as the Associate Administrative Director of the Porphyrias Consortium. She has published over 40 peer-reviewed articles and book chapters, and has presented her work at scientific conferences nationally and internationally. She is a member of the scientific advisory board of the North American International Collaborative Gaucher Group, LAL-D registry and the Genetic Disease Foundation. She has participated in the American College of Medical Genetics/Newborn Screening Translational Research Network's Lysosomal Storage Disease Workgroup and has served on the expert panel for the FDA's Scientific Workshop for Erythropoietic Protoporphyria.

Participation Instructions

1. Participant logs into ondemand.acmg.net
2. Once logged in the participant will access the session they would like to view. They will be asked if they would like to claim credit for the meeting, or if they will not claim credit for the meeting. Then, this information (Course description) will appear, and participant will have to attest that they have read the information. They will then click Continue.
3. After that, the participant will be able to select the credit types to claim.
4. For each session with a post-test, the participant will need to mark and complete the matching pre-test.
5. Then the participant will watch the session presentations.
6. Participant will complete viewing all session content. "Check marks" indicate which presentations have been viewed.
7. After viewing all presentations within a session, participant will click the "Claim Credit for Session" button under the CME dropdown at the top of the page.
8. Participant should take and then successfully pass the post-test. If they do not pass with a score of 80% or higher, they will have unlimited tries to pass the post-test.

9. Participant will continue the steps above to earn credits for additional sessions.
10. If a session does not have a test attached, the participant will not need to take a pre- or posttest, but will have to complete a Concurrent or Plenary session-specific evaluation to claim credit.
11. To print their certificate, the participant will click the "Print Certificate" button under the CME dropdown at the top of the page. Participant must complete the meeting evaluation (one time only) before they can access their certificate. Participant will then choose their certificate(s). The certificate(s) will be automatically updated as they earn new credits.

Stream Requirements	
Network	For best results, use a hardwired network connection instead of wireless
Full Screen Viewing	If you would like to view the webcast full screen, display the tool bar at the bottom and click the double arrow in the far right corner. The screen will enlarge to the full screen of you system. To restore the size, press the "ESC" key
Refresh Browser Window	If the webcast freezes and does not recover in 3-4 seconds, refresh browser window
Freezing or Stuttering Issues	Adjust the amount of bandwidth needed by putting your mouse anywhere over the video window. A tool bar will appear at the bottom. On the right side you will see a "HD" button, click on that button and you will see a list of options. The top is "auto", with decreasing numbers below. Select a lower bandwidth (such as 360p) to see if your webcast improves
For Technical Support call	1-800-504-5379

Mobile Viewing Requirements	
Android Devices	Android 2.3+ with Adobe Flash Player 10.2 or better installed Install Flash Player
Apple Devices	iOS 4+

Online Viewing Requirements	
Bandwidth	512kbps
Required Hardware and Software	Screen resolution of 1024X768 or larger Sound card and speakers/headphones
Browser	Microsoft Internet Explorer 7.0 or better Mozilla Firefox 4 or better Safari 5 or better
Windows	Operating System: Windows 8 desktop mode, Windows 7; Windows Vista; Windows XP Service Pack 2 or 3 x86 or x64 (Browsers must be in 32-bit mode) 1.6-gigahertz (GHz) or higher processor 512MB of RAM
Mac OS	Operating System: Apple Mac OS X 10.4.8 or above Intel Core™ Duo 1.83GHz or faster processor 512MB of RAM

Registration and Fees

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ACMG Members and ACMG Trainees: ($50)
Non-members ($60)
Additional fee (~$25) applies for NSGC credit that is billed by NSGC.

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