FORENSICS TTA PROGRAM

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Forensic Services for Medical Examiner and Coroner Offices Webinar Series

Session 2: Postmortem Testing

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Disclaimer

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Today's Agenda: Postmortem Testing

- Working with Neuropathologists, Dr. Glenn Sandberg
- Working with Cardiac Pathologists, Dr. Emily Duncanson
- Postmortem Genetic Testing: A Medical Examiner/Coroner (ME/C) Office Perspective, Dr. Laura Knight
- Q&A Segment

Working with Neuropathologists

Dr. Glenn Sandberg, MD
Forensic Neuropathology Consultants, LLC
Spearfish, SD

Dr. Glenn Sandberg

- University of California, Davis; BS, Genetics
- Uniformed Services University of the Health Sciences; MD
- Transitional Internship; Letterman Army Medical Center
- Anatomic/Clinical Pathology; Tripler Army Medical Center
- Neuropathology Fellowship; AFIP

Why Would You Need a Neuropathologist?

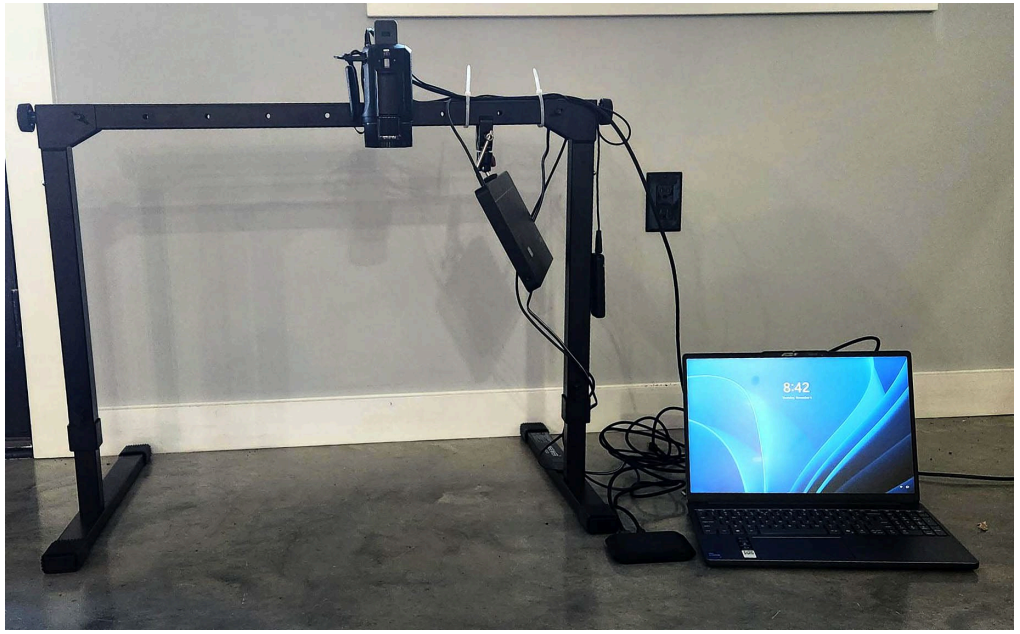
- No obvious cause of death after autopsy
- Head trauma when dating of injuries is important
- Suspected child abuse
- Sudden unexpected death in infancy
- Sudden unexpected death in epilepsy
- Developmental neurologic disorders
- Known or suspected neurodegenerative diseases

What Services are Available?

- In-person examinations at your facility
- Ship specimens to the consultant
- Slide review only
  - Virtual
- Medicolegal support
- Virtual brain cutting
  - Fully interactive/video feed only
  - Ship blocks or slides to consultant
  - Digitize slides and send consultant the link
- Trainee education

Equipment for Virtual Neuropathology

Gross Examination



Microscopic Examination

Images provided by the presenter

Additional Information/Materials Needed for Complete Examination?

- Circumstances surrounding death:
  - Date of injury
  - Date of death
  - Neurosurgical procedures
  - Organ donation
- Pertinent medical history/records:
  - Imaging studies/results
  - Ophthalmology reports
  - Presence/locations of fractures
  - Neurologic conditions:
    - Seizure history
    - Traumatic Brain Injury (TBI) history
- Neuropathology request form
- Remote access to network containing case database and autopsy photos

How Do I Find One?

- Word of mouth
- Local large teaching hospitals
- American Association of Neuropathologists (AANP):
  - https://www.neuropath.org/neuropathology-fellowships

Contact Information

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Working with Cardiac Pathologists

Dr. Emily Duncanson, MD
Jesse E. Edwards Registry of Cardiovascular Disease
St. Paul, MN

Dr. Emily Duncanson

- MD degree from the University of Minnesota Medical School
- Anatomic Pathology residency at New York Presbyterian – Weill Cornell Medical Center, Manhattan
- Forensic Pathology fellowship at the New York City Office of Chief Medical Examiner (NYC OCME)
- Forensic Neuropathology/Cardiac Pathology fellowship at NYC OCME
- 17 years practicing Cardiac Pathology at the Jesse E. Edwards Registry of Cardiovascular Disease in Saint Paul, MN

Cardiac Pathology (CP) in the Forensic Setting

- Sudden unexpected death in an otherwise healthy individual will often fall under the jurisdiction of the ME/C
- Most sudden death involves the heart or the brain
- Heart is complex and specialized
- ME/C may not have the time or resources to do a complex dissection
- Most common reasons for consult:
  - No anatomic cause of death (conduction system study)
  - Suspected cardiomyopathy – important implications, sparse knowledge
  - Complex surgery or presence of cardiac devices
  - Congenital heart disease

CP is a Rare Specialty

- Non-boarded specialty
- Fewer than 300 practitioners
- Very few full-time practitioners
  - Often a secondary specialty
  - Often in an academic center, mostly biopsies and some autopsy hearts
- Very few specialized in Forensic Pathology (FP)

CP as a Full-time Specialty

- Jesse E. Edwards Registry is 2 full time FP/CP
- We accept whole or dissected hearts from ME/C offices and hospitals
- We receive heart remnants from tissue donations and issue reports
- 2,000-2,200 hearts examined per year
- Consult hearts retained indefinitely
- Donation hearts retained for 6 months
- 5-7 business day turnaround times

In-house, Outside Consultant, or Send-out

- ME/C office must decide:
  - Look for in-house doctor with Cardiovascular specialty
  - Outside person who periodically visits for in-person heart cutting
  - Send out to specialty laboratory
- Considerations for in-house:
  - Workforce
  - Salary and benefits
- Considerations for outside in-person consultant:
  - Availability
  - Workforce
  - Employee vs. 1099
  - Budget

Sending Consults Out of Agency

- Challenges to send-outs:
  - Consult budgets
  - Patient safety – shipping, confidentiality, chain of custody
  - Families may want heart returned

What to Look for in a Cardiovascular Consultant

- Turnaround times
- Transparent pricing
- Training and background
- Are they willing/able to testify on legal cases?
- Will special requests be honored?
- *Ask colleagues!*

Case Example #1

- A 38-year-old man with no past medical history
- Collapses while jogging outside
- Transported by an ambulance in ventricular fibrillation
- No return of circulation
- Heart referred for specialty consultation

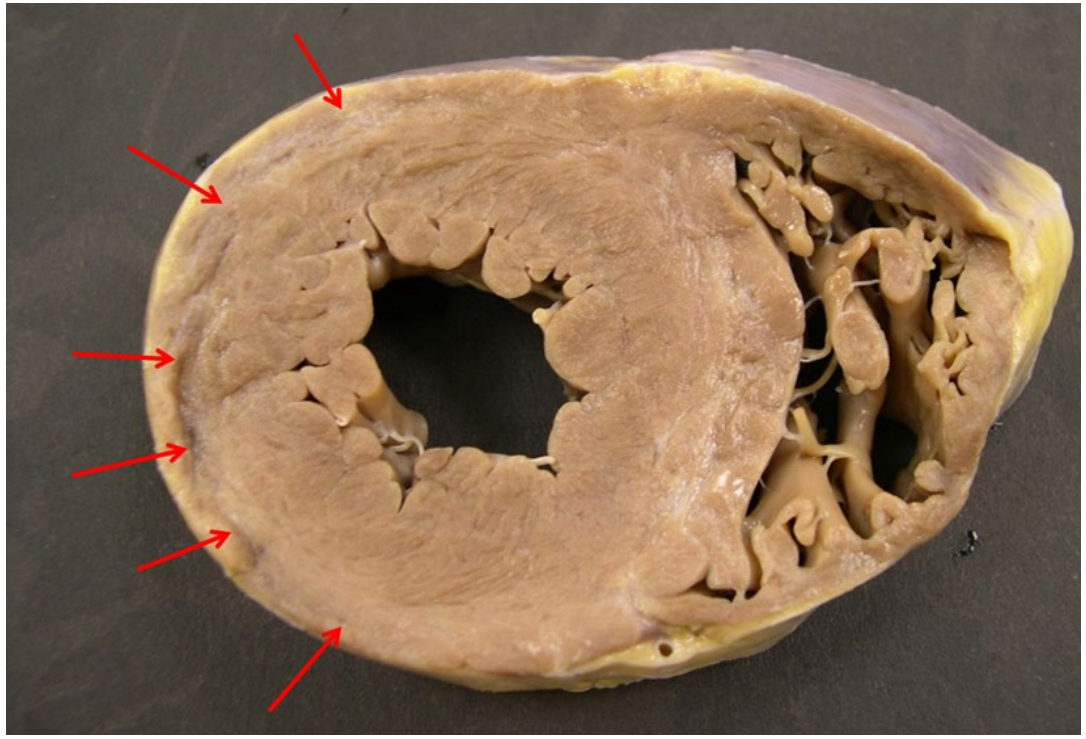


Image provided by the presenter

Case Example #1 – CP Findings

- Arrhythmogenic cardiomyopathy
  - Decedent has three children, a sister, and living parents
  - Disease is found in father on imaging
  - Father receives an Implantable Cardioverter-Defibrillator (ICD)
- Cardiomyopathy diagnoses have health implications for family members

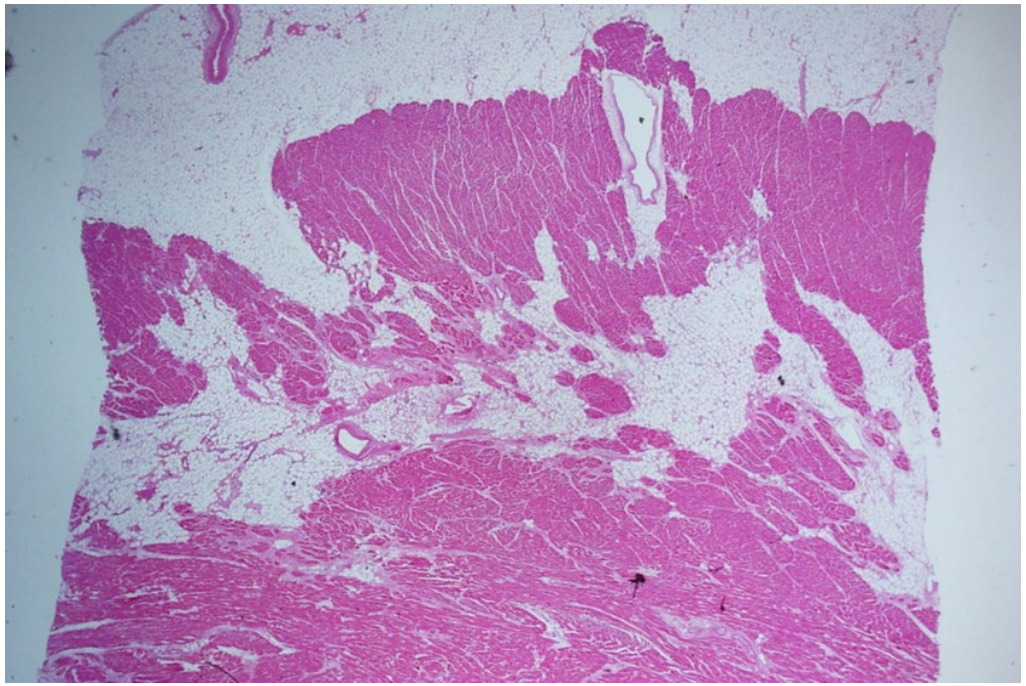


Image provided by the presenter

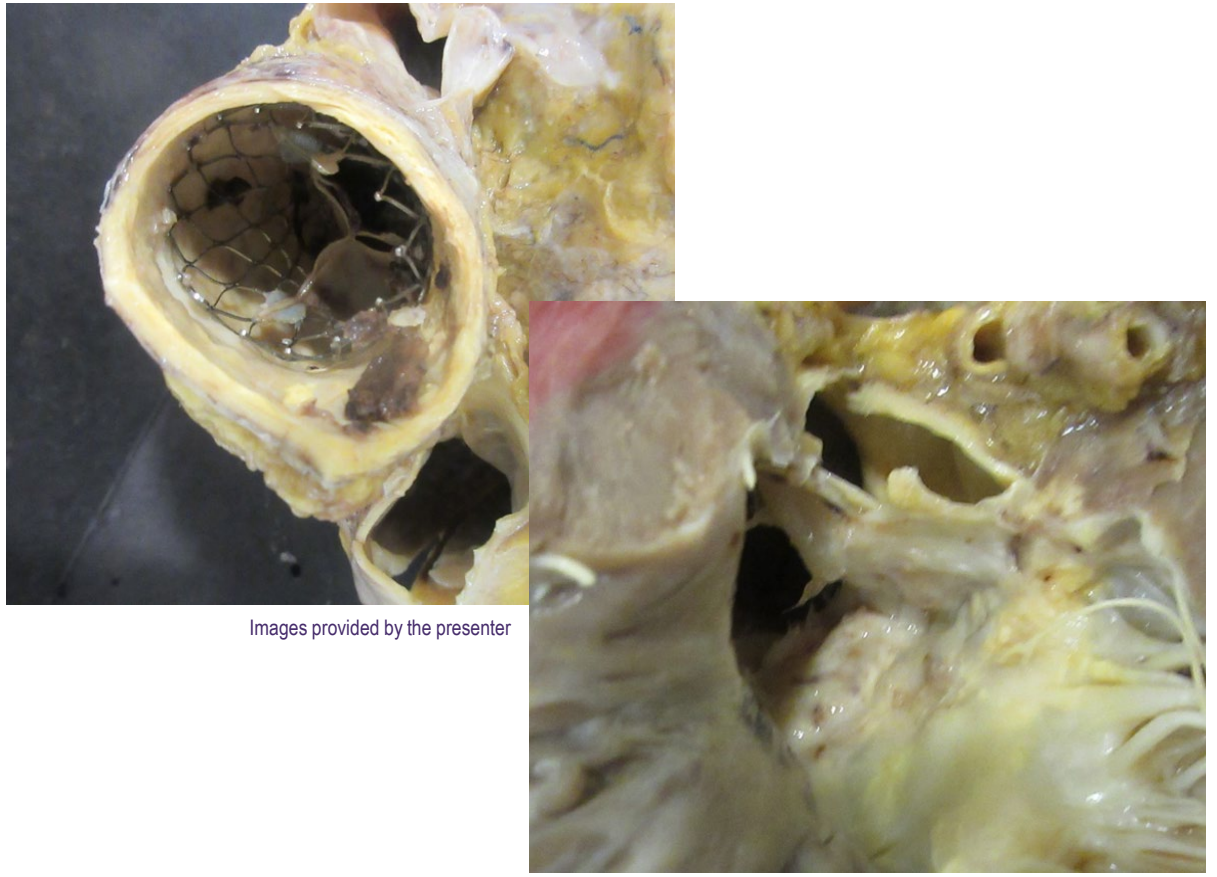
Case Example #2

- 28-year-old man found dead in jail cell
- Had been seen doing push-ups and calisthenics
- Toxicology negative
- Heart sent for expert consultation
- Undetected congenital anomaly

Image provided by the presenter

Case Example #2 – CP Findings

- Patient died suddenly the day after a Transcatheter Aortic Valve Replacement (TAVR)
- TAVR valve dislodged
- Medical device adverse events



Images provided by the presenter

Key Takeaways

- CP consultation is a rare specialty
- It is an essential service in the forensic setting
- Common reasons for consults include sudden death with no anatomic cause, cardiomyopathy, complex surgery, and congenital heart disease
- Diagnosis of cardiomyopathy has major ramifications for family members
- CP consultants should be compatible with your agency's processes including turnaround times and possible legal obligations

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Postmortem Genetic Testing: An ME/C Office Perspective

Dr. Laura Knight, MD
Washoe County Regional Medical Examiner's Office
Reno, NV

Dr. Laura Knight

- MD degree from University of Louisville School of Medicine
- Anatomic & Clinical Pathology Residency, Medical University of South Carolina
- Forensic Pathology Fellowship, University of New Mexico, Office of the Medical Investigator
- 18 years as a full-time Medical Examiner
- Chief Medical Examiner & Coroner for the past 8 years, Washoe County Regional Medical Examiner's Office in Reno, NV
- Associate Professor, University of Nevada – Reno School of Medicine, Pathology & Pediatrics Departments

Postmortem Genetic Testing (PMGT) in the Forensic Setting

- A necessity, not a luxury!
- May seem “new” but has been the gold standard for a decade or more in many ME/C offices
- Many cases called “Sudden Infant Death Syndrome (SIDS)”, or “undetermined”, in the past may have had undiagnosed genetic disease such as genetic arrhythmia syndromes (channelopathies)
- Pricing has improved significantly – postmortem cardiac panels, for example, that were $4-5K when they first came on the market are now around $350
- Participation in programs such as the Centers for Disease Control and Prevention (CDC) Sudden Death in the Young (if your state is a grant recipient) may provide free testing in certain cases

Key Case Types for PMGT in the ME/C Setting

- Sudden deaths in infants, children, or adults <40 with no explanation (“autopsy negative”)
- Autopsy or history reveals a disease with potential genetic basis, such as:
  - Thoracic aortic aneurysm, aortic dissection <60 years
  - Hypertrophic cardiomyopathy
  - Thrombotic disorder (like unprovoked pulmonary thromboembolism)
  - Epilepsy / Sudden Unexpected Death in Epilepsy (SUDEP)
- Premature atherosclerotic disease (<60 women, <55 men)
- Families with multiple sudden deaths
- Congenital anatomic abnormalities suggest a genetic disorder
- Screening of fetal demise cases (especially livebirth vs. stillbirth delivered outside of hospital)

PMGT in the Forensic Setting

Different Types / Levels of Testing	Example Diseases Detected
Cytogenetics: **Karyotyping or Chromosomal Microarray** – chromosomal number and appearance	Down syndrome – Trisomy 21, Edward syndrome – Trisomy 18, Patau syndrome – Trisomy 13, etc.
Panel Testing – sequence a targeted set of genes for specific conditions; such as Cardiac, Metabolic, and Neurologic	Cardiac panel: Hypertrophic cardiomyopathy; arrhythmogenic right ventricular dysplasia; long QT syndrome; Brugada syndrome; etc.
Whole Exome Sequencing (WES) – sequencing of entire protein-coding region of DNA	Many genetic diseases; can identify both primary "cause of death" findings and secondary non-lethal diseases
Whole Genome Sequencing (WGS) – sequencing of entire coding and non-coding DNA	Unlikely to uncover disease/cause of death not detected by WES; valuable on a research basis to identify new disease-causing variants

Specimen Type Needed

- Lavender top (EDTA) tube of blood
  - Hold a frozen (-20 or -80 °C) lavender top tube of blood on **EVERY** autopsy/examination case, in case genetic testing is later determined to be necessary*
- Some laboratories accept blood spot cards
  - Blood spot cards are already held on every autopsy/examination case in most ME/C offices
- Tissue (such as heart muscle) testing may be possible for some tests
  - Recommend consulting with your specific laboratory

*2013 National Association of Medical Examiners (NAME) position paper on PMGT

Examples of laboratories offering PMGT that my office has worked with:

- Invitae through LabCorp – various panels for Cardiac, Neurologic, Metabolic Disease, etc.
- Neuberg Center for Genomic Medicine (NCGM) – targeted Orion WES on blood spot card
- Ambry Genetics – panels, WES
- GeneDx – panels, WES

- *Not an exhaustive list of all laboratories available*
- *Check with your local/regional academic medical center*
- *Check with nearby colleagues/peers about what their office does*
- ***Establish a relationship/contract with the laboratory before you have a case and need it, and to get best pricing***

Case Example – PMGT Identifies Cause of Death

- 5-year-old child with sudden death
- No cause of death identified after complete autopsy and ancillary testing; structurally normal heart; no genetic testing done (>10 years ago)
- Surviving younger sibling with subsequent syncopal episodes

- PMGT pursued after pediatric cardiologist for sibling reached out
- Channelopathy panel revealed: **Catecholaminergic Polymorphic Ventricular Tachycardia syndrome (CPVT)**

  1) Death certificate corrected from "undetermined"

  2) Huge impact for surviving sibling/family: treatments like beta blocker meds, avoiding strenuous exercise, and an ICD increase chance of survival

Special Considerations in PMGT

- Specimen failure can occur if the Postmortem (PM) interval is long
- Interpretation challenges – Variants of Unknown Significance (VUS)
- Consent – usually not needed in ME/C setting, but check your statutes
- Notification of family members of results
  - Risk of disease for surviving siblings, others
  - Consider referral to a genetic counselor
    - Often affiliated with major pediatric hospitals and pediatric cardiac disease centers, depending on your location
    - Telemedicine may be an option for remote/rural locations
    - May also be available directly through programs offered by some laboratories performing PMGT

Key Takeaways

- PMGT has become more affordable, with cost comparable to toxicology and other routine tests
- PMGT is critical in sudden unexplained deaths with negative autopsy, and may identify cause of death
- Hold a lavender blood tube on every autopsy
- Establish a laboratory contract preemptively
- Create policy around handling of genetic results, notification of families of results

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Q&A Segment

Microsoft 365 Stock Photo

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