Genetics in Primary Care

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Disclosures

• I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity.

• I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.
Objectives

• Role of genetics in primary care
• Current status
• Relevance
• How to improve
Genetics in Primary Care

• Genetics is the ultimate family practice—preconception to death (and even counseling beyond!)
• Genetics is not just about rare diseases
• Genetics, genomics and epigenetics—oh, my!
• Paradigm shift – “virtually all medical decisions will someday be informed at least, in part, by genomics, yet it will be impossible to have a medical geneticist involved in every decision” (Medical Genetics in Pediatric Practice, 2013; Trotter and Saul)
Genetics in Primary Care

• Order genetic testing every day
• 71% of pediatric inpatients have a genetic or genetically-related condition (McCandless et al., AJHG, 2004)
• More than 50% of the population at increased risk of common disease because of familial predisposition
• Genetics in the 21st century might be considered similar to infectious diseases in the 20th century
Genetics describes the study of genes and their role in inheritance—the way certain traits or conditions are passed down from one generation to another.
Genetics, Genomics and Epigenetics

- Genomics describes the study of all of a person's genetic material, the interactions among components of that genetic material, the interactions of that material with the environment, and the resulting phenotypic changes.

For example, genetics uses information from one or two genes to explain a disease state, whereas genomics examines all of the genetic information to determine biological factors that predispose an individual to disease. The terms represent a continuum of genetic analysis.
• **Epigenetics** refers to functionally relevant chemical modifications to the DNA and proteins in the genome that do not involve a change in the DNA nucleotide sequence.
AAP Initiatives in Genetics

- Committee on Genetics
- Section on Genetics and Birth Defects
- Division of Children with Special Needs
  - Genetics in Primary Care Institute
- Strategic Priority for Children’s Health
  - Epigenetics Strategic Initiative
Genetics in Primary Care Institute

- A cooperative agreement between the American Academy of Pediatrics (AAP) and the Health Resources & Services Administration (HRSA)/Maternal & Child Health Bureau (MCHB), Genetic Services Branch
  - June 1, 2011 - May 31, 2014
- Vision of the Genetics in Primary Care Institute (GPCI) is to improve primary care provider (PCP) knowledge and provision of genetic medicine
Overview of the GPCI

• Goal 1
  – Utilize quality improvement (QI) science to develop a change package for the improved provision of genetic-related services

• Goal 2
  – Establish a technical assistance center to address systems and policy (www.geneticsinprimarycare.org)

• Goal 3
  – Embed the practice of genetic medicine into the future PCP workforce
• Objective
  – Identify current practices and attitudes of pediatricians regarding genetic medicine

• Methods
  – 88 providers in the AAP QuINN membership (29% response rate)
  – Online, 43 item survey
  – Data analysis with Mann-Whitney two-sample statistic
Results—Attitudes

“Taking a family health history is important...” 100%

“I gather a three generation family health history...” Strongly Agree/Agree 32%
“How do you usually collect a family health history from your patients”?

- Standard Checklist
- Ask general questions
- Ask about health of specific family members
- I do not obtain FH from my patients
- Other

Eg, “Do any diseases run in your family?”

Percent
Targeted vs. Tailored vs. Comprehensive

- **Targeted**—disease focused and at point-of-service
- **Tailored**—life-stage focused
- **Comprehensive**—WCC and/or disease focused
  - 3-generation
  - Updated at WCCs
  - Evolving document over the life of a patient and pertinent to life stages
  - Multiple purposes
Results—Current Practices

• 86% order genetic-based tests ≤ 3 annually
• 13% discuss with patients risks, benefits, and limitations of test in question
• Refer a mean of 4.8 patients a year to geneticist
  – 89% have access to a genetics professional
  – 75% have genetic professionals within 30 miles
• 83% report having a system for genetics referrals
• There was moderate to low awareness of national resources but overwhelmingly they had not been utilized or perceived useful
  – Out of 12 national genetics resources, less than 50% were aware of ACT Sheets or State Genetics Program, between 4% and 30% of respondents were familiar with the others
Results—Competency

- 49% agree or strongly agree that they feel competent in providing genetic medicine
  - Agreement was not associated with more recent training \((p=0.29)\) or number of genetic tests ordered annually \((p=.84)\)
- Of the 63 respondents that have an EHR, 65% report ability to easily & efficiently capture genetics information and FH as fair or poor
Results—Incentives

What would incentivize you to more effectively integrate genetic-based medicine into your practice?

- Increased understanding of genetics: 94%
- CME in genetics: 88%
- Improved reimbursement: 85%
- More comprehensive medical home: 83%
- Increased relevance to PC: 79%
- Easier access to professionals: 69%
Conclusions

• Convenience sample has slightly skewed results--Sample group is more highly motivated and knowledgeable than providers nationally

• This sample reported few interactions with genetic patients, wide variability, expressed discomfort in GM

• Need for increased awareness, understanding, and access to education and resources
Personalized Medicine—Relevance

- Tarini and Saul, 2013 [Personalized Medicine 10(6), 515-517]
  - Personalized medicine must prove its relevance to the world of primary care. Failing to do so in a concrete data-driven way places personalized medicine at risk of being branded as irrelevant and overhyped
  - The biggest fear for those ... who believe in personalized medicine ... is that primary care providers have already stopped listening to us
Impact of Low Genetic Literacy

• Management of diagnostic workup of positive NBS
  – More than half of pediatricians prefer not to manage

• Advanced molecular genetic testing expand ability to diagnose and treat genetic conditions
  – Providers not aware of their role in testing or in treatment advancements
Genetic Literacy in Primary Care Colloquium

• Purpose and Overview
  – Increase the knowledge base about, and awareness of, genetic literacy in the medical home
  – October 2-3, 2012
  – Develop and present papers, formulate recommendations

• Outcomes
  – Overarching consensus statement accompanies the papers published as a supplement to Pediatrics (Pediatrics 2013; 132:s198-s237)
1. Define how pediatric primary care providers should use genetics and genomics in practice.
2. Define, develop, and provide the tools/resources that are needed to integrate genetics and genomics into primary care.
3. Integrate genetics and genomics into primary care training at all levels.
4. Provide an evidence base for optimal integration of genetics and genomics into primary care.
AAP Plans to Address Shortfalls

• Genetics in Primary Care Institute
  – Technical Assistance Center
    (www.geneticsinprimarycare.org)
  – Educational Webinars
  – Promotion of vetted tools and strategies
  – Development of Family History Tool for Pediatric Providers
  – Residency training initiatives
AAP Plans to Address Shortfalls

- Genetics in Primary Care Institute
  - Educational Webinars
    - Series of 10, one-half hour talks in 2012
    - Well-received (audience and reviews)
    - Archived on website
      (http://www.geneticsinprimarycare.org)
    - Organization from the AAP’s Genetics Handbook
    - Template for collaborative efforts for professional societies and educational efforts
AAP’s Newest Strategic Planning Priority

“Genetics, Genomics, and Epigenetics”
AAP Plans to Address Shortfalls

• Committee on Genetics
  – New AAP Manual: *Medical Genetics in Pediatric Practice*
  – 23 Chapters
  – Over 500 pages
  – Released May 2013
  – Companion mobile app released (PediaGENE) [tablets and iPhone]
AAP Plans to Address Shortfalls

• Committee on Genetics
  – Policy Statements
    (Recently Published)
    • Health Supervision for Children with Down Syndrome
    • *Health Care information for Down Syndrome parents*
    • Health Supervision for Children with Fragile X Syndrome
    • Health Supervision for Children with Prader Willi Syndrome
    • Ethical Issues with Genetic Testing in Pediatric Practice
    • Health Supervision for Children with Marfan Syndrome
AAP Plans to Address Shortfalls

• Committee on Genetics
  – Policy Statements
    (Selected Titles Under Development)
    • Clinical Genetic Evaluation of the Child with Intellectual Disability or Developmental Delay (just published)
    • Prenatal Screening and Diagnosis for Pediatricians
AAP Plans to Address Shortfalls

- **Section on Genetics and Birth Defects**
  - Educational programming at AAP’s Annual National Conference & Exhibition.
  - Articles on genetics-related topics in AAP’s monthly member news magazine *AAP News*.
  - Supports genetics-related content in *AAP Grand Rounds* and other Academy publications.
  - SOGBD-member-only online open forum discussion group.
7 Key Roles of the PCP – “thinking genetically”

1. Evaluate through screening and surveillance—use family history for prevention and need for enhanced awareness

2. Educate patients and their families—ongoing discussions

3. Explain the results—review and discuss to manage expectations
7 Key Roles of the PCP – “thinking genetically”

4. Make appropriate referrals

5. Coordinate care with sub-specialists—initiate co-management plan

6. Counsel patients and families—short- and long-term

7. Provide long-term follow-up and care—medical home
Questions for the PCP – “thinking genetically”

1. Types of genetic tests
   - Biochemical
   - Cytogenetic
   - Molecular

2. How testing used
   - Medical
     - Diagnostic
     - Predictive (for possible treatment)
Questions for the PCP – “thinking genetically”

– Personal decision-making
  • Carrier testing
  • Pre-implantation genetic dx
  • Prenatal dx
  • Predictive (no intervention)

3. Who to test
   – Neonates, infants, children
   – Family members
Questions for the PCP – “thinking genetically”

4. Why test
   – Medical management
   – Benefit family members

5. When to refer
   – Comfort level exceeded
   – Potential treatment
   – Expert opinion for family
   – Counseling re: recurrence
Genetics in Primary Care

• Joy of the practice of medicine—application of new and exciting advances to primary care of patients and their families
  – Radiology
  – Immunizations
    • Measles, Varicella, Hemophilus
  – Penicillin for Hgb SS
  – Electronic health record
Genetics in Primary Care

- Difficulty of the practice of medicine—need to continually update one’s knowledge base and skill set in primary care

- Dichotomy exists
  - Constant challenge
  - Ever-present reminder of importance of research and its application to clinical care.
Genetics in Primary Care

• Is genetics/genomics the next “revolution” in medicine?
  – Sanitation
  – Immunizations
  – Imaging
  – Transplantation

• Probably better called a milestone or the logical “evolution” of advances in medicine
  – Human Genome Project—1990 - 2003
Initial Presentation

- Allison W. presents at six years of age with a prolonged episode of coughing
- Coughing over the last week, especially after exercise
- The month is October and the beautiful fall colors are everywhere.
- She has not been febrile, and her cough is non-productive.
- She has been able to attend school but has a difficult time in gym class.
- She will wake at night to cough.
- There has not been any post-tussive emesis
Question 1. Given the history and presentation to this point, you are very suspicious of

1. asthma-like problems,
2. allergy to peanuts,
3. a lingering upper respiratory infection like a viral URI,
4. a developing ear infection.
Relevance

Question 2. Since asthma is not a typical Mendelian disorder (autosomal recessive, autosomal dominant or X-linked mode of inheritance), taking a targeted family history (asking about immediate relatives and others as indicated) will

1. Not be helpful since it will not provide any actionable information,
2. Not be helpful and will take too much time,
3. Be helpful only if there are no significant environmental triggers in the house (mold, dust, smoking exposure, etc.), or
4. Be helpful and might help guide diagnostic and therapeutic decisions.
Past Medical History

– Your review of Allison’s chart reveals that she was the 3.5 kg product of a term gestation to a G4P4 28 yo mother
– The pregnancy was uncomplicated as was the neonatal period
– She was breastfed (the other children were not)
– She has not had any hospitalizations, operations, or major illnesses. She is up-to-date on her immunizations and is not on any medications
– Her early and current development has been normal. She is active and doing well in first grade
– Her mother is a 10th grade math teacher and feels that Allison is the healthiest of all of her children.
Question 3. Allison’s past medical history appears to be remarkably normal. Which of the following from the PMH is most suggestive of a family history factor that needs further definition—

1) Allison was breastfed and her sibs were not,
2) Allison is the “healthiest of all of her children”,
3) Allison was born at term to a 28 yo mother,
4) Allison’s development has been normal.
Relevance

Family History—strong family history of allergies on maternal side of the family

• Mother had asthma as a child in addition to multiple “allergies”
• The mother’s sister and brother had multiple allergies and bad eczema as children. The sister had to move to Arizona as an adult to help her allergies.
• The maternal grandmother has bad “hay fever”
• Her children have the following problems—
  – Jacob, age 10, has ongoing asthma problems and has been hospitalized 3-4 times for asthma in the past. He sees a pulmonologist to manage his asthma.
  – Sara, age 9, also has allergy problems—periodic wheezing and chronic nasal congestion
  – Ethan, age 7, has had several hospitalizations for asthma like Jacob. His PCP is able to manage his asthma with inhalers.
• You construct the pedigree below.
wheezing

- asthma
- allergic rhinitis
- eczema
Question 4. Based on the family history obtained so far, you note that
1) it appears that there is a significant familial component to the asthma in Allison’s family,
2) the severity of the asthma in Allison’s siblings suggest the need for aggressive management of her problem (if asthma is diagnosed),
3) the fact that the father’s side of the family is “allergy-free” won’t affect your management,
4) it might be useful to obtain more information about the allergy problems in the affected individuals since the genetic component seems even more severe than you anticipated,
5) all of the above are applicable.
Question 5. Given the family history and Allison’s acute presentation, you decide that

1) genetic testing might be worthwhile and order a microarray test,

2) genetic susceptibility testing by direct-to-consumer (DTC) testing will help the family and ask them to collect buccal swabs and send the specimens to a DTC lab,

3) no genetic testing is indicated at this time but you will consider it in the future if it will be relevant to management,

4) genetic referral is indicated based on the family history.
Relevance

Question 6. This case has been instructive in that it has demonstrated that family history information is important in the diagnosis, treatment and potential prevention of common complex diseases. Which of the following can be said for disorders similar to asthma?

1) We know that obesity tends to “run in families.” If young adults have weight problems, counseling about recurrence risks for their potential offspring might be helpful,

2) The diagnosis of hypertension in the family would indicate the need to obtain more family history information and to consider how that information is pertinent to the child seen in the clinic,

3) Family history information in a family with cancer predisposition might help with the monitoring or anticipatory guidance that PCPs give patients and their families,

4) Family history information is important for children because it could guide their care and the care of their parents,

5) all of the above.
Personal experience

- Fragile X syndrome
  - Discovery
  - Humility
  - Learning
  - Joint journey with the family
  - “Ups and downs”
  - Life cycle
  - Serendipity and primary care
Fragile X syndrome
Genetics in Primary Care

Personal experience

• Otitis media, atopic disease, obesity
  – Siblings
  – Parents
  – Constant reminders of multiple factors—genetics and environmental
  – Psychosocial support
Results—Family History

Targeted vs. Tailored vs. Comprehensive

- **Targeted**—disease focused and at point-of-service
- **Tailored**—life-stage focused
- **Comprehensive**—WCC and/or disease focused
  - 3-generation
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Genetics in Primary Care

Genetics/genomics/epigenetics

• Integral part of the medical home
• Provides excitement and challenge
• As medicine changes, so must practitioners
• Would I do anything different (pediatrics genetics pediatrics)?
  No! Great platform to advance pediatric advocacy for all children