Approach to Understanding the Genetics of VACTERL Association

Ben Solomon, MD
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Outline

• Our Research
• Genetics 301
• Progress Report
I. Our Research
Our Research: Motivations

- Variable diagnostic criteria
- No uniform plan for work-up or treatment
- Little is known about causes and long-term outcomes
- More knowledge = Better health
Our Research: Goals

- VACTERL
  - Natural History
  - Causes
Why do we want to know what causes VACTERL?

• More information for clinicians and patients
• Knowing what to look out for
• (Eventually) condition-specific treatments
Why is VACTERL so challenging to understand?
Challenges:
? “Sporadic” Inheritance
Challenges:
Many Overlapping Conditions
Challenges: Many Causes
Challenges: Many Causes
Pathways:
The "Domino" Theory
Pathways:
The “Domino” Theory
"Primary Polytopic Fields"
Our Research: What We Do

- Data Collection
- NIH Visit
- DNA Studies
Data Collection

- Phone/e-mail/mail
- Standardized questionnaire
- Medical records, images, etc.
- Initial goal = 50-100 families
NIH Visit

- Bethesda, MD (near Washington, DC)
- 3-5 days
- We pay for flights, lodging, food, etc.
- No charge for any medical tests, consultations, etc.
- Confidential (including insurance!)
NIH Visit

- History & Physical
- Genetic Counseling
- Ophthalmology (eye doctor)
- X-rays, echocardiogram, ultrasound
- Blood draw/urine collection
- Other consultations as necessary
DNA Research

- Now: only samples from people who come to the NIH
- Within a few months: samples sent to our lab from clinicians or families
- Collaborations
II. Genetics 301
Genetics 301: Seeing a Geneticist

- History
- Physical Examination
- Testing
- Genetic Counseling
Genetics 301: Definitions
Genetics 301: Tests

- Karyotype/Chromosome Analysis
- Looks under microscope at all genetic information
Genetics 301: Tests

- FISH Testing
- Looks for specific pieces of extra or missing genetic material
Genetics 301: Tests

- Microarray
- Looks for extra or missing genetic material
Genetics 301: Tests

• Specific gene testing
• Looks for tiny changes in one gene
• Labor-intensive
Genetics 301: Tests

- Research tests
- Example: Linkage analysis
III. Progress Report
Progress Report

- Data Collection: ~40 families
- NIH Visits: 12
- DNA Research: Target gene sequencing started, microarrays about to start
Progress Report

• Participants range from newborns to over 60 years old
• Huge range of testing, treatment, etc.
• ~10% with multiple family members with features of VACTERL
### NIH O8-HG-0224

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My 2 Cents…

- Everyone should meet with a clinical geneticist
- For prenatal testing, a karyotype should be offered
- For postnatal testing, specific testing can be done to test for VACTERL-like conditions
- Karyotype can be offered in “VACTERL-plus” situations
- If your questions aren’t being addressed, KEEP ASKING!!
We Need Your Help!

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Thank You!

Questions?