Dr. Advice: “The Geneticist Is In”
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Overview
- Introduce the Department of Genetics and Regional Genetic Services
- Discuss basic concepts in cell biology
- Review modes of inheritance and basic genetic concepts
- Introduce approach to genetic testing
- Recommend who and when to refer to genetics

Learning Objectives
- Quickly assess patient and family history to refer patients with or at risk for genetic conditions
- Briefly counsel patients on benefits and what to expect with genetic risk assessment
- Implement correct protocols for genetic testing, considering patient’s age, ethnicity and gender
- Provide appropriate after-care based on information identified by genetic risk

Question #1
What is your clinical practice?
1) Internal medicine
2) Internal medicine subspecialty
3) Family medicine
4) Hospitalist
5) Other
Question #2

Have you sent your local geneticist a Dr. Advice question in the past 3 months?

1) Yes
2) No

Question #3

Can you name or recognize your local geneticist or a genetic counselor?

1) Yes
2) No

Regional Genetic Services

- 9 clinical geneticists (MD)
- 32 genetic counselors (MS)
- Screening programs staff
- Admin/support staff

Who We Are
Where We Serve

What We Do

- Preconceptional & prenatal counseling
- Genetic screening: prenatal & newborn
- Clinical genetic services for patients of all ages
- Cytogenetic, biochemical & molecular diagnostic testing
- Educate members & health care providers on genetic issues

What We Really Do

Easy Stuff
- Reassure
- Solve puzzles
- Explain why
- Offer options
- Order right lab test
- Influence treatment
- Embrace innovation

Hard Stuff
- Give out bad news
- Can’t solve the puzzle
- Can’t explain why
- Accept patient’s choices
- Explain lab results
- Realize no treatment
- Convince KP to buy in

What Are Our Tools?

- Patient’s medical history
- Family medical history (“it’s the pedigree, stupid!”)
- Thorough PE (as required)
- Pp-to-date web resources
- Cytogenetic tests
- Biochemical tests
- Molecular tests
- Personal experience
- Effective counseling
The Human Genome

- 3 billion base pairs of DNA (6 ft)
- ~20,000 genes
- 46 chromosomes

Genes Are Recipes for Proteins

Gene

transcription

translation

Gene

Protein

Cell

Nucleus

Chromosomes

E1 E2 E3 E4 E5 E6
Sites We Serve

Gene Expression

Function of Human Genes

Types of Genetic Disorders

- Chromosomal disorders: trisomies, monosomy X, deletions, duplications, translocations
- Single gene disorders: autosomal dominant, autosomal recessive, X-linked, mitochondrial inherited
- Multifactorial disorders: combination of genetic and environmental factors

Chromosomal Disorders

47,XY+21

47,XXY

46,XY del22q11.2
## Autosomal Dominant

- Each child has a 50% chance of inheriting the mutation
- No “skipped generations”
- Equally transmitted by men and women

### Autosomal Recessive

- Two germline mutations (one from each parent) to develop disease
- Equally transmitted by men and women
X-linked Recessive

- Mutant genes are on the X (sex) chromosome
- Women typically need to inherit two mutated copies to be affected
- All men who inherit the mutation are affected (only one X chromosome)

Genetic Heterogeneity

- Frequency: 1/25,000
- Inheritance: autosomal dominant
- Features: ash-leaf spots, shagreen patches, adenoma sebaceum; epilepsy, mental retardation, intracranial calcifications; cardiac rhabdomyoma; renal anomalies
- 1<sup>o</sup> defect: “tuberin” (chromosome 16), or “hamartin” (chromosome 9) mutations

Tuberous Sclerosis

- Tuberous sclerosis
Allelic Heterogeneity

- Different mutations in the same gene can cause disease of varied severity
- Different mutations in the same gene can cause different clinically distinct diseases

Penetrance

- Likelihood of developing disease due to a particular genetic mutation
- High: huntington’s disease (100%)
- Moderate: breast/ovarian cancer sx (60%)
- Low: hemochromatosis (5%)
Genetic Testing In SCAL

What Good Is Genetic Testing?
- Establishing, confirming (or excluding!) a clinical diagnosis
- Refining risk for an inherited disorder
- Determining best treatment option (“personalized medicine”)

Choices in Testing
- Targeted vs general
- Predictive vs diagnostic
- Degree of resolution

Challenges in Testing
- Evolving technologies
- Variability among vendors
- Difficulty with interpretation
Genetic Counseling and Testing

- Primary Care Provider
- Patient
- Genetics Professional
- Other Subspecialists

Challenges in 1° Care

- Recognizing genetic disease in your patient panel
- Knowing when to refer to genetics (and what to expect!)
- Utilizing molecular technology appropriately and recognizing its limitations

Where Can We Improve?

- Accurately diagnose all members with genetic disease (refer)
- Improve management of members with genetic disease (integrate)
- Identify members at risk for genetic disease (family hx)
- Educate members and mds about genetic diseases
- Decrease morbidity and mortality
When to Refer?

- OB: AMA, ≥3 miscarriages, (+) family hx
- Neo: birth defects, dysmorphic, abnormal newborn screens
- Peds: dysmorphic, developmental delay, short stature, (+) family hx
- IntMed/FamMed: affected with or (+) family hx of genetic disease

When NOT to Refer?

- Who’s yo’ daddy?
- What’s my ancestry?
- Molecular confirmation of clinical dx
- Isolated cancer ≥50 yr old (neg fam hx)

When You’re Not Sure?