The Use of Genetics and Personalized Medicine in Health Promotion and Chronic Disease Management: What the Family Health Team Needs to Know

Sean Blaine, MD, STAR Family Health Team
Jill Davies, Genetic Counsellor, Medcan Clinic

AFHTO
October 26, 2011

Introduction

In a recent survey, Canadian physicians reported:

- Genetics testing and personalized medicine can have a positive impact on their practice
- Genetic tests they have ordered have benefited their patients
- 1 in 3 physicians are being asked by their patients about genetic testing

Introduction

In a recent survey, Canadian physicians reported they:

- Are not sufficiently informed about genetic testing and how to interpret test results
- Are not comfortable discussing test results with their patients
- Have not had undergraduate or graduate training in genetic testing and personalized medicine
- Have attended lectures and engaged in self-study in genetic testing

Introduction

- Personalized medicine and genetic testing is here, and will become common practice
- Primary care practitioners must be ready to adopt these diagnostic and prognostic tools, and be ready to discuss genetic testing with their patients

Objective of this workshop

- To present interactive case studies, that reflect current and future practice
- To identify and discuss different strategies for communicating with your patients

Objective of this workshop

- Background information on Genetics/Genomics
- Case Study #1: Sudden Cardiac Death
- Case Study #2: Personal Genome Testing
- Case Study #3: Pharmacogenomics Testing (Warfarin)

Family history in Primary Care

Key Elements

- Number of affected relatives
- Sex
- Degree of relationship
- Age of Onset
- Ancestry
- Lineage (maternal vs. paternal)

Family history in Primary Care

Limitations

- 3-generation pedigree preferred – limited by time in primary care setting
- Accuracy of family history is questionable – dependent on patient recollection or knowledge
- Clinical utility is questionable – specifically for *complex diseases* where contribution of genes vs. environment should be considered
- Clinical utility proven when identifying known genetic syndromes (ie. BRCA)

When to refer to Genetics

1. Cancer
    - Family history patterns suggestive of hereditary cancer
    - Rare cancer syndrome in family
2. Cardiovascular disease
    - Sudden cardiac death
    - Strong history of MI, stroke, thrombosis, atrial fibrillation
3. Neurologic disorders
    - Personal or family history of adult neurologic conditions - neuropathy, ataxia, prion disease, early-onset dementia, ALS
4. Known genetic disorders in family
    - Family history of single gene disorder – polycystic kidney disease, cystic fibrosis, muscular dystrophy, hemophilia

When to refer to Genetics

5. Known genetic disorder in patient
    - If patient hasn't seen a geneticist in the past or would like updated information
    - Implications for children and/or other family members
6. Pregnancy and fertility concerns
    - Infertility, multiple miscarriages, pregnancy planning, reproductive options
7. Personalized Medicine / Pharmacogenomics
    - Patients in multiple medications or with a history of adverse drug reaction
8. When patients asks "IS IT GENETIC"
    - Family history of single gene disorder – polycystic kidney disease, cystic fibrosis, muscular dystrophy, hemophilia

Genetic Contribution to Disease

RARE:
Genetic variations for rare diseases

≤1% of the population affected

Predictable family inheritance

Example:

- Sickle cell anemia,
- Cystic fibrosis

COMMON:
Genetic variations for common diseases

≥1% of the population affected

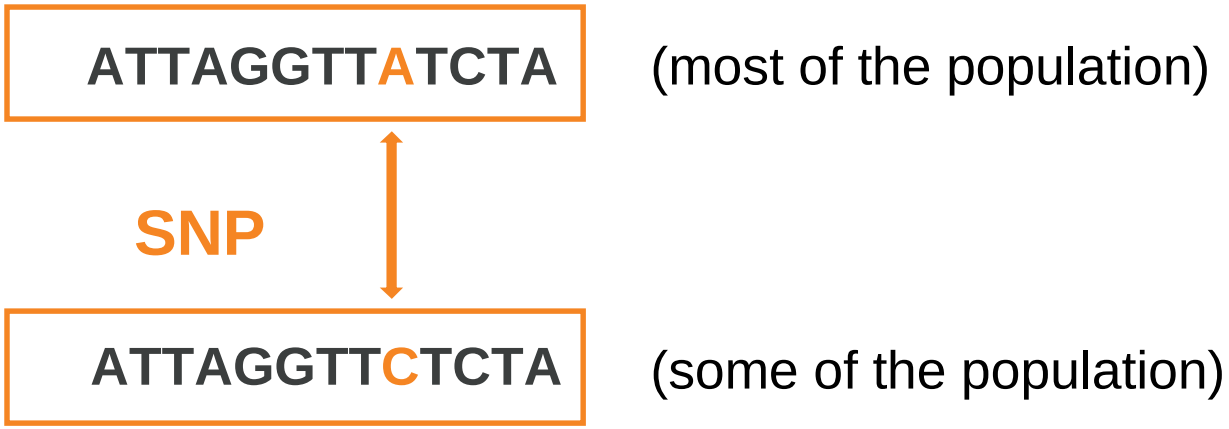
Multifactorial, polygenic inheritance

Example:

- Heart disease
- Type 2 diabetes

Genetic Variation in Common Diseases

A SNP (single nucleotide polymorphism) is a single letter change in the genetic code, that occurs frequently (>1%) in the population



Case Examples

Case Study #1: Sudden Cardiac Death

A 25 year old female patient reports that her father died at age 35 from sudden cardiac death. She is a triathlete and is concerned about her risk of sudden death.

What would you do?

Case Study #1: Sudden Cardiac Death

What are possible causes of sudden cardiac death?

- Hypertrophic cardiomyopathy
- Arrhythmias (Long QT syndrome, Brugada syndrome)
- ARVC/D (Arrhythmogenic Right Ventricular Cardiomyopathy)
- Other ??

Case Study #1: Sudden Cardiac Death

What could you do?

- Elicit further family history information (any other cases of sudden death, accidental drownings, fainting spells, suspicious MVA's)
- Attempt to obtain medical records re: father's cause of death
- Arrange screening tests (echocardiogram, ECG)
- Referral to Cardiology
- Referral to Genetics

Case Study #1: Sudden Cardiac Death

Key considerations for discussion with your patient

- Some causes of sudden cardiac death are inherited
- Important to clarify diagnosis of affected relative
- Ongoing cardiac screening is recommended for all first-degree relatives (Echo, ECG)
- Genetic testing may help to provide information about risk and appropriate screening options
- Genetic testing may help to provide risk information for other relatives

Case Study #2: Personal Genome Testing

A 37 year old male patient who has been in your practice for 8 years, presents you with results from a Personal Genome Test and asks:

“My Grandfather recently died from colon cancer. I did some research and understand it can be hereditary, so I found an online source and submitted a sample for genetic testing. Here are my results, can you help me understand them?”

What would you do?

Case Study #2: Personal Genome Testing

What is a Personal Genome Test?

- Conducted by private healthcare organizations and Direct To Consumer companies
- Provides information on susceptibility to diseases and conditions such as:
  - Disease Risk (predisposition)
  - Carrier testing
  - Response to drugs (pharmacogenomics)
  - Nutrigenomics (diet/nutrition related)
  - Traits

Case Study #2: Personal Genome Testing

What could you do?

- Review the test results with your patient
- Discuss family history in more detail – validate the patient's concerns
- Discussion of risk (lifetime risk vs. current risk)
- Discussion of limitations of testing – should be used as a tool in risk stratification. Is not a diagnostic test.
- Discuss screening options based on level of risk
- Refer to a Genetic Counsellor

Case Study #2: Personal Genome Testing

Key considerations for discussion with your patient

- PGT markers are probablistic, not diagnostic
- PGT markers are additional tools to help stratify patient risk for disease
- Combining PGT with family history allows for risk assessment for single gene conditions
- Combining PGT with family history allows for further refinement of risk for common/complex diseases (family history on its own is limited)

Case Study #3: Pharmacogenomics

Your 56 year old female patient has atrial fibrillation and requires warfarin. She comes into your office and says:

"I understand that genetic testing is available to help determine Warfarin dosing and minimize the risk for side effects. Should I take this genetic test, and how would I do this?"

What would you do?

Case Study #3: Pharmacogenomics

What is pharmacogenomics?

- The study of the genetic basis of drug response, including eficacy and toxicity
- Can reveal individual differences in pharmacokinetics:
  - Absorption or distribution
  - Metabolism
  - Excretion
- Can be especially helpful in cases where the prescribed drug has a narrow therapeutic window

Case Study #3: Pharmacogenomics

Why is pharmacogenomics useful to patients?

- Focuses treatment by pre-identifying responders based on genetic background
- Reduces adverse events by predicting individuals at increased risk
- Tailors dosage to individual genotype
- Facilitates drug discovery for orphan drugs

Case Study #3: Pharmacogenomics

What could you do?

- Discuss current methods of Warfarin dosing with patient (INR)
- Review FDA label warning on Warfarin (as of 2007)
- Order testing (private paid) through US or Canadian companies
- Online resources – www.warfarindosing.org
- Refer to, or liaise with, Genetics

Case Study #3: Pharmacogenomics

Key considerations for discussion with your patient

- Warfarin dosing is complex and genetic factors account for about 40% of the variance in dosing
- Standard practice (INR) will still be indicated, but pharmacogenomic information can help reduce the time to stable and therapeutic dose

Resources

Canadian College of Medical Genetics

www.ccmg-ccgm.org

Canadian Association of Genetic Counsellors

www.cagc-accg.ca

CEPMED

www.cepmed.com

GenoScape

www.thegenoscape.com