The Genetics of Familial Polyposis

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Familial Polyposis

Familial
• Can run in the family – related to our “genes”

Polyposis
• Multiple polyps
  – Polyp: non-cancerous growth, inside the GI system
  – Different types of polyps
    – Adenoma: Risk to become cancer if not removed

TODAY: FAP & MAP
**FAP: Familial Adenomatous Polyposis**

**Classic FAP:** 100s-1000s of colorectal adenomas, onset as early as childhood/adolescence
- Can also be polyps in small bowel (duodenum) &/or stomach
- Somewhat higher risk for other cancers including thyroid
- Non-cancerous features: desmoids, CHRPE, osteomas, skin cysts, extra teeth

**Attenuated FAP (AFAP):** less severe, fewer polyps (< 100), later onset

Both FAP and AFAP are rare – seen in only 3 per 100,000 people
Both are caused by changes in the same gene called **APC**
Many genes

Genes written in code

Mutation: change in the code

APC gene
  - ONE Mutation → affected
  - Autosomal dominant inheritance
  - Affects males & females in equal numbers
  - Location of mutation in gene associated with classic FAP vs. AFAP

Two copies of each gene

One copy inherited from mom, one from dad

Genetic testing is usually done on DNA collected from a blood sample
FAP: Dominant Inheritance

- Parent with FAP Mutation in 1 APC gene

- 50% (1 in 2) chance for each child to inherit FAP/AFAP

What age to test?
When screening starts:
- FAP: 10-12 yr
- AFAP: 18-20 yr

Child with FAP
Child without FAP

Person with FAP
Person without FAP

One copy of APC gene with mutation, one copy without
Two copies of APC gene without mutation
Inherited vs. de novo

75-80% of time FAP is inherited from a parent

20-25% of time FAP starts new in a child
If a child inherits a mutation in *APC*

- They have FAP / AFAP
- Screening for colorectal polyps
  - Classic FAP: age 10-12
  - AFAP: age 18-20
  - Surgery if too many polyps to manage by colonoscopy
  - Screening of remaining colon/rectum/pouch
- Upper GI screening from ~age 25
- Annual thyroid palpation by GP
If a child did not inherit \textit{APC} mutation

- They do not have FAP/AFAP
- They cannot pass it down to children
- Population cancer screening (unless other family history)

\textbf{Importance of informing relatives about genetic testing:}

FAP screening vs. general population screening

Parents, siblings, children, others
MUTYH-Associated Polyposis (MAP)

MAP vs. (A)FAP

• Clinical presentation is similar:
  – Multiple adenomatous polyps
  – In MAP, other types of polyps such as hyperplastic or serrated polyps that can be seen in addition to adenomas
  – 10-100 polyps by age 50 on average
    • 100’s to 1000’s of polyps in some cases

• Gene is different: MUTYH (MYH)

• Inheritance is different:
  – Autosomal RECESSIVE inheritance
Recessive Inheritance

If both parents are carriers (unaffected), each child has a 25% (1 in 4) chance of having MAP. Brothers and sisters of someone with MAP have a 25% (1 in 4) chance of also having MAP.
For Someone With MAP...

- Very small chance for children to have MAP
  - Only possible if spouse/partner is a carrier (or has MAP) - very unlikely

- Who should get tested in the family:
  - Spouse/partner
    - If negative, children don’t need testing
  - Children, if spouse/partner not available
  - Brothers & sisters
MAP Screening

2 mutations (MAP)

• Colonoscopy every 2-3 years beginning at 18-20
  – Every year once polyps detected
• Side-viewing upper endoscopy every 5 years or more often depending on findings, beginning at 25-30
Population Screening

No mutation or 1 mutation (carrier): BOTH UNAFFECTED

- Not at significantly increased risk for polyps/cancer
- Follow population cancer screening
  - unless other family history of polyps or cancer
Summary

• FAP and MAP both cause multiple polyps, BUT:
  – Different genes (APC vs. MUTYH)
  – Different inheritance (Dominant vs. Recessive)
  – Different screening recommendations

• Genetic testing has improved over the years
• You may be eligible for further testing if:
  – Your genetic testing was many years ago or you never had genetic testing
  – You have multiple polyps and had genetic testing where nothing was found
Genetic Questions?

*** Speak to your genetic counsellor ***

Dr. Zane Cohen (centre), with genetic counsellors (L to R) Melyssa Aronson, Spring Holter, Kara Semotiuk & Laura Winter