

# The Genetics of Familial Polyposis

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# Familial Polyposis

## Familial

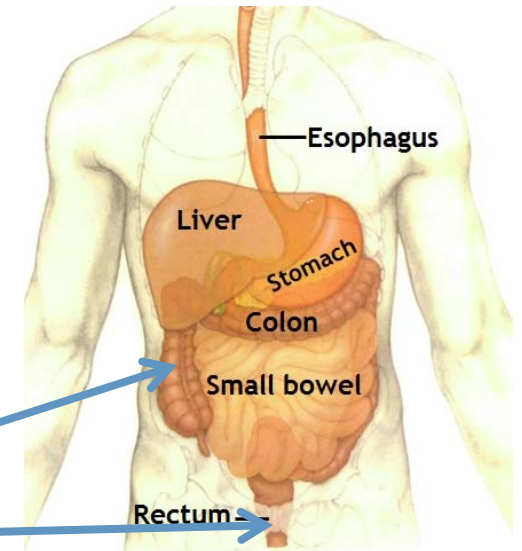
- Can run in the family – related to our “genes”

## 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

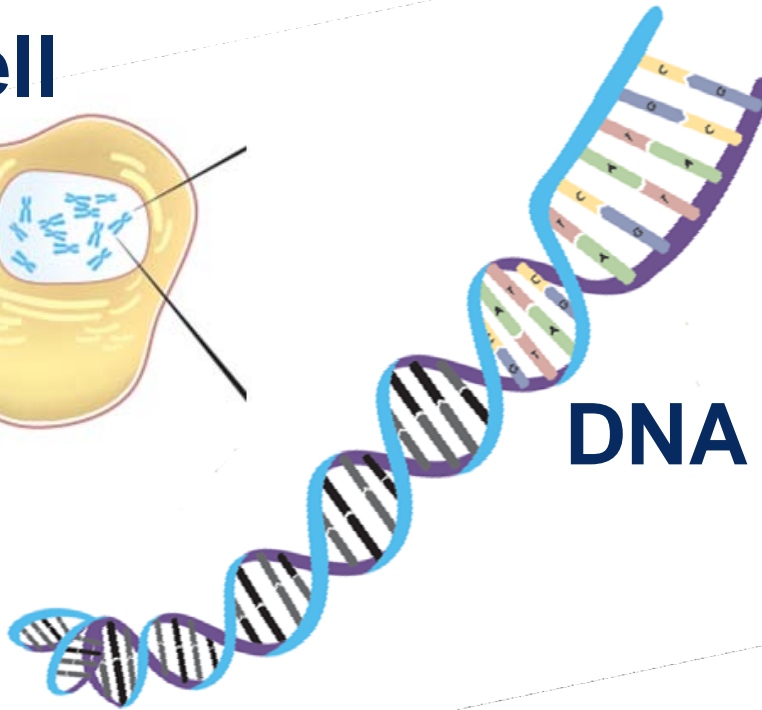
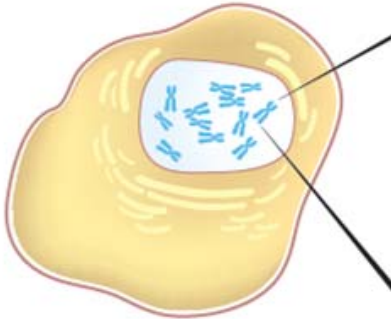
- Can also be polyps in small bowel (duodenum) &/or stomach
- Somewhat higher risk for other cancers including thyroid
- Non-cancerous features: desmoids, CHRPE, osteomas, skin cysts, extra teeth

**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**

# Genetics

## Cell

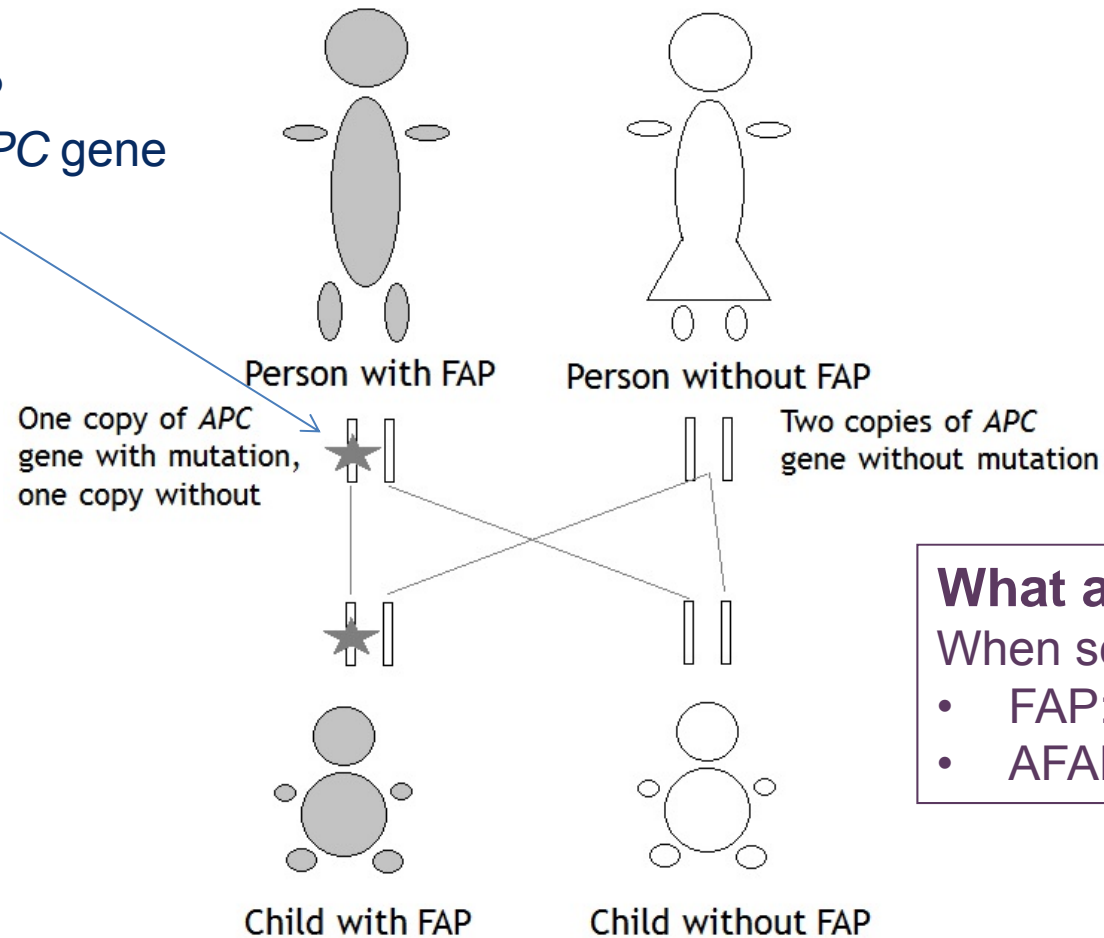


Genetic testing is usually done on DNA collected from a **blood sample**

- 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

# FAP: Dominant Inheritance

Parent with FAP  
Mutation in 1 *APC* gene



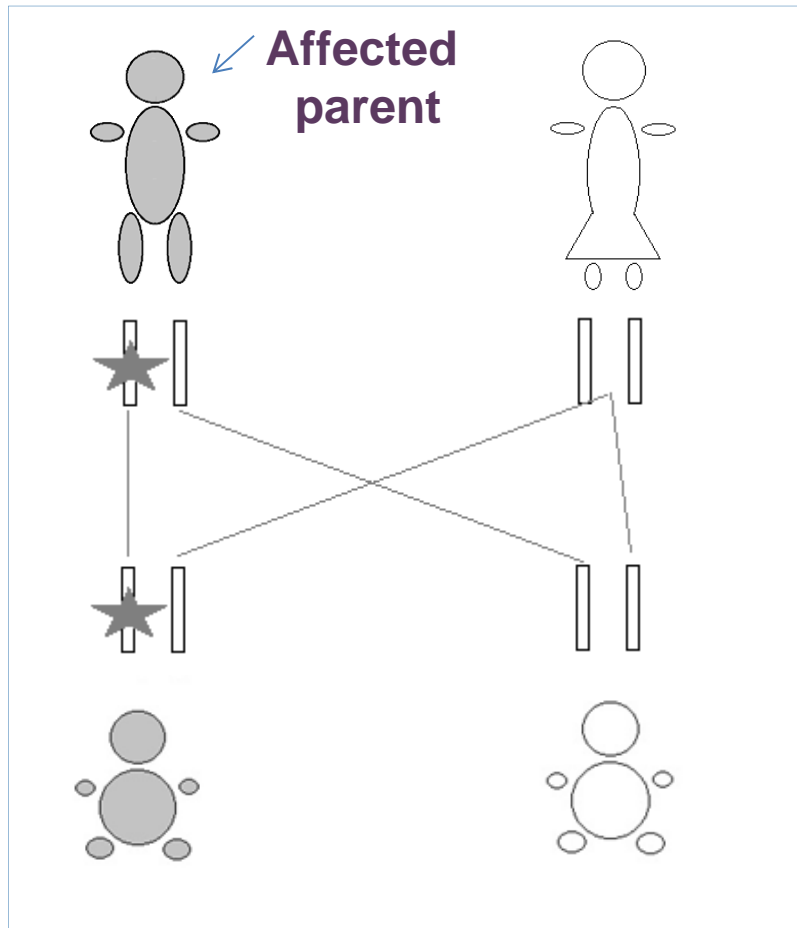
## What age to test?

When screening starts:

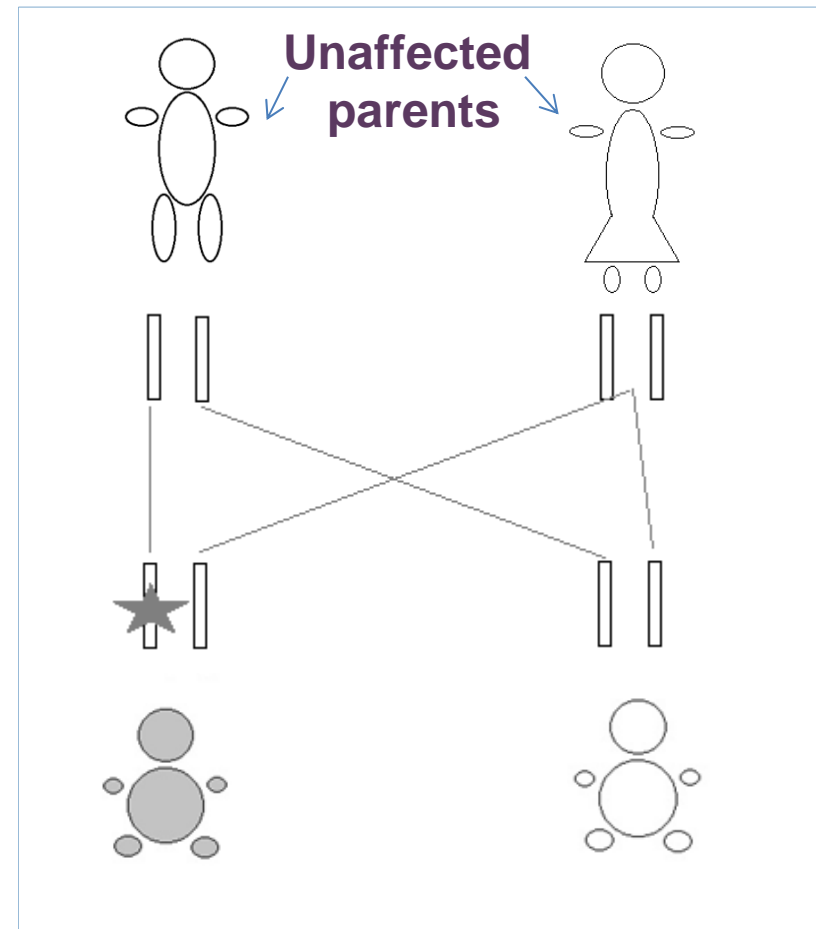
- FAP: 10-12 yr
- AFAP: 18-20 yr

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

# Inherited vs. *de novo*



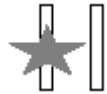
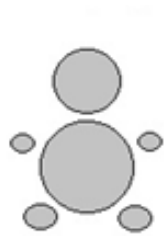
75-80% of time FAP is inherited from a parent



20-25% of time FAP starts new in a child

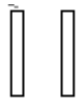
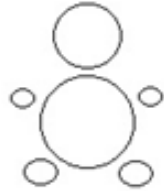


# If a child inherits a mutation in *APC*



- 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 *APC* mutation



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

**Importance of informing relatives about genetic testing:**  
FAP screening vs. general population screening

**Parents, siblings, children, others**



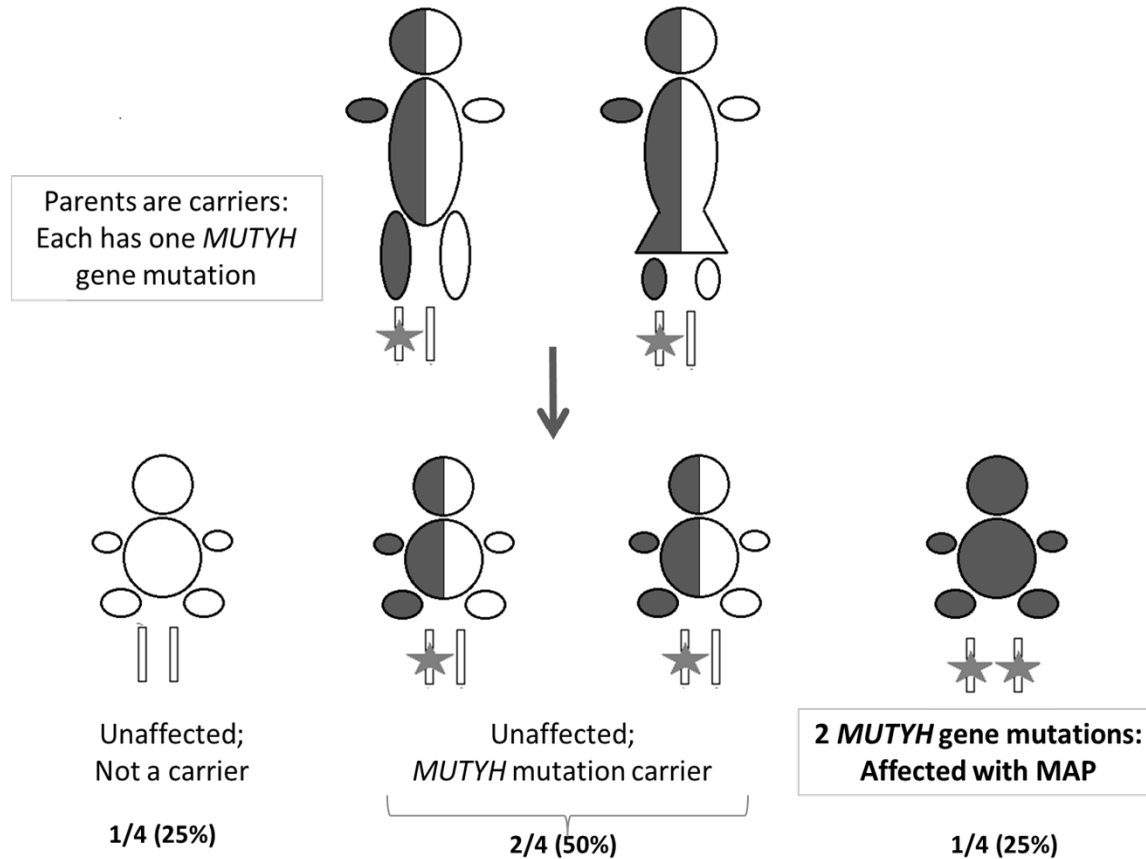


# M***UTYH***-Associated Polyposis (**MAP**)

## MAP vs. (A)FAP

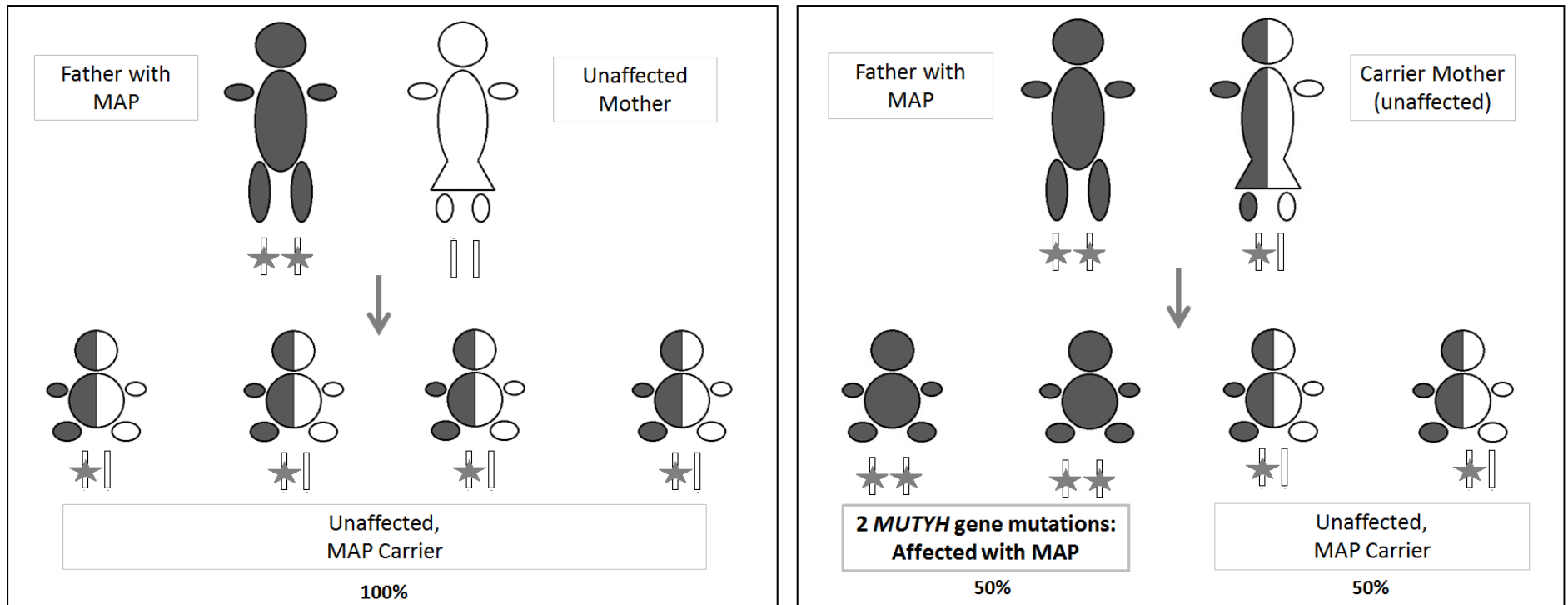
- Clinical presentation is similar:
  - Multiple adenomatous polyps
  - In MAP, other types of polyps such as hyperplastic or serrated polyps that can be seen in addition to adenomas
  - 10-100 polyps by age 50 on average
    - 100's to 1000's of polyps in some cases
- Gene is different: *MUTYH* (*MYH*)
- 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



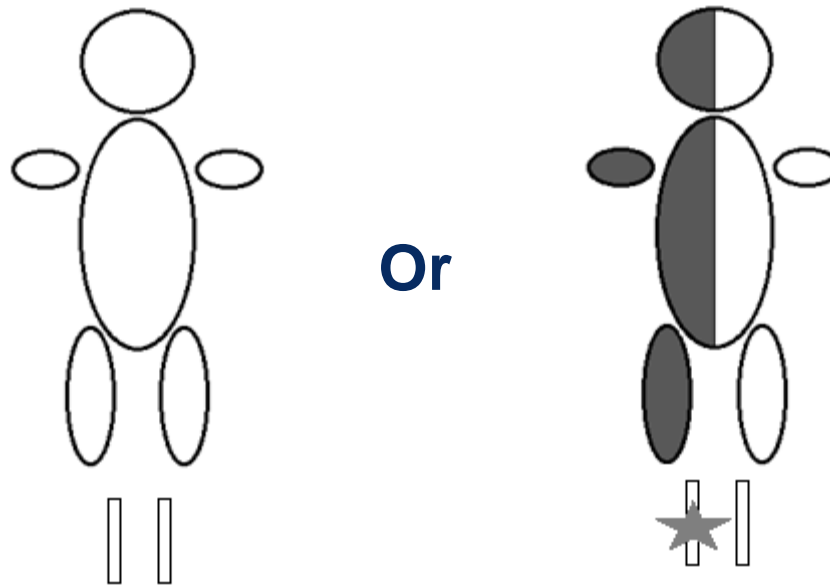
# MAP Screening



## 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