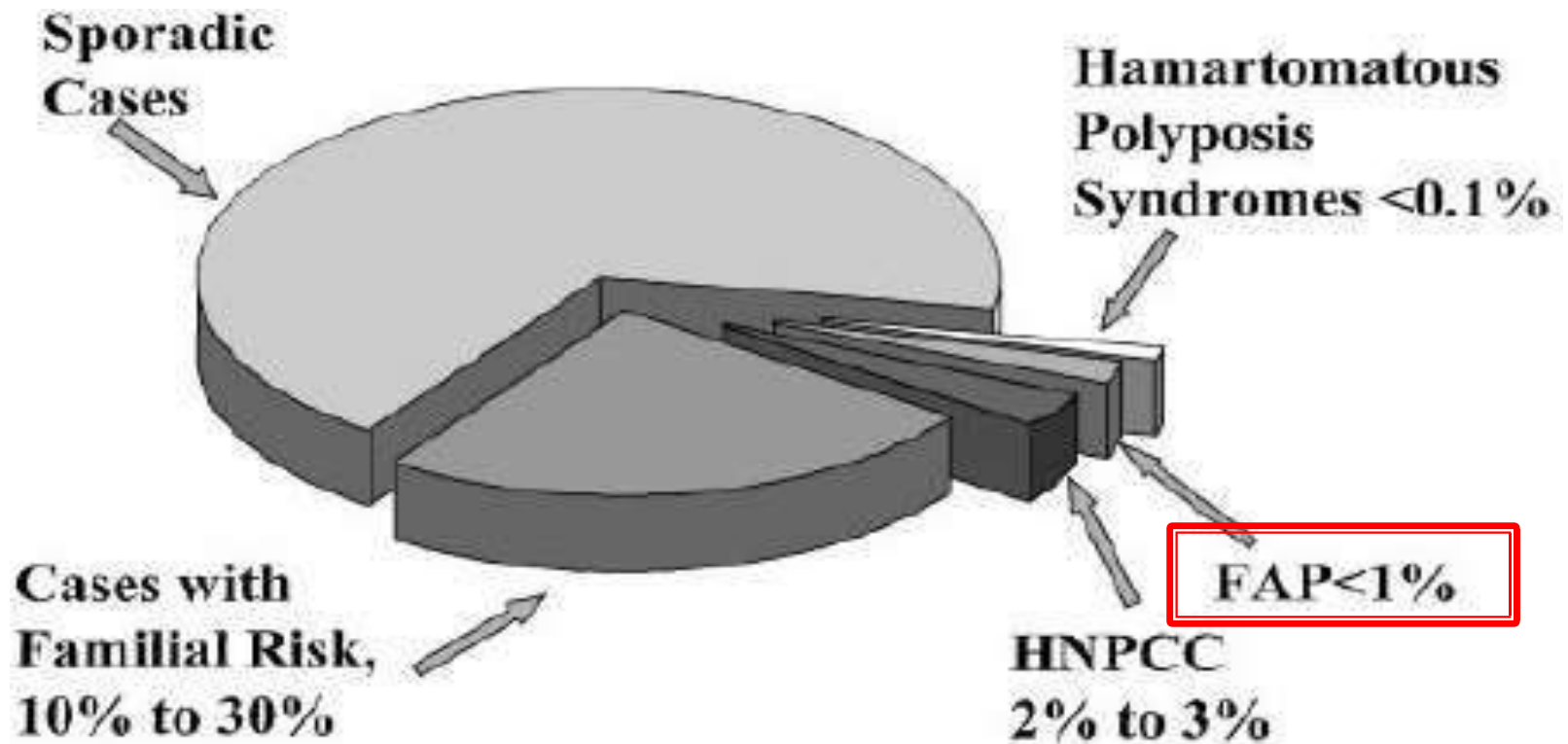


FAP

# DISCUSSION

- Introduction
  - Genetics of FAP
  - Pathogenesis of ca colon in FAP
  - Indications of surgery
  - Postop surveillance
  - Chemoprevention
  - Genetic testing
  - Family screening
  - Conclusion
- 

# Introduction



Burt RW. Colon cancer screening.  
Gastroenterology. 2000 Sep 30;119(3):837-53.

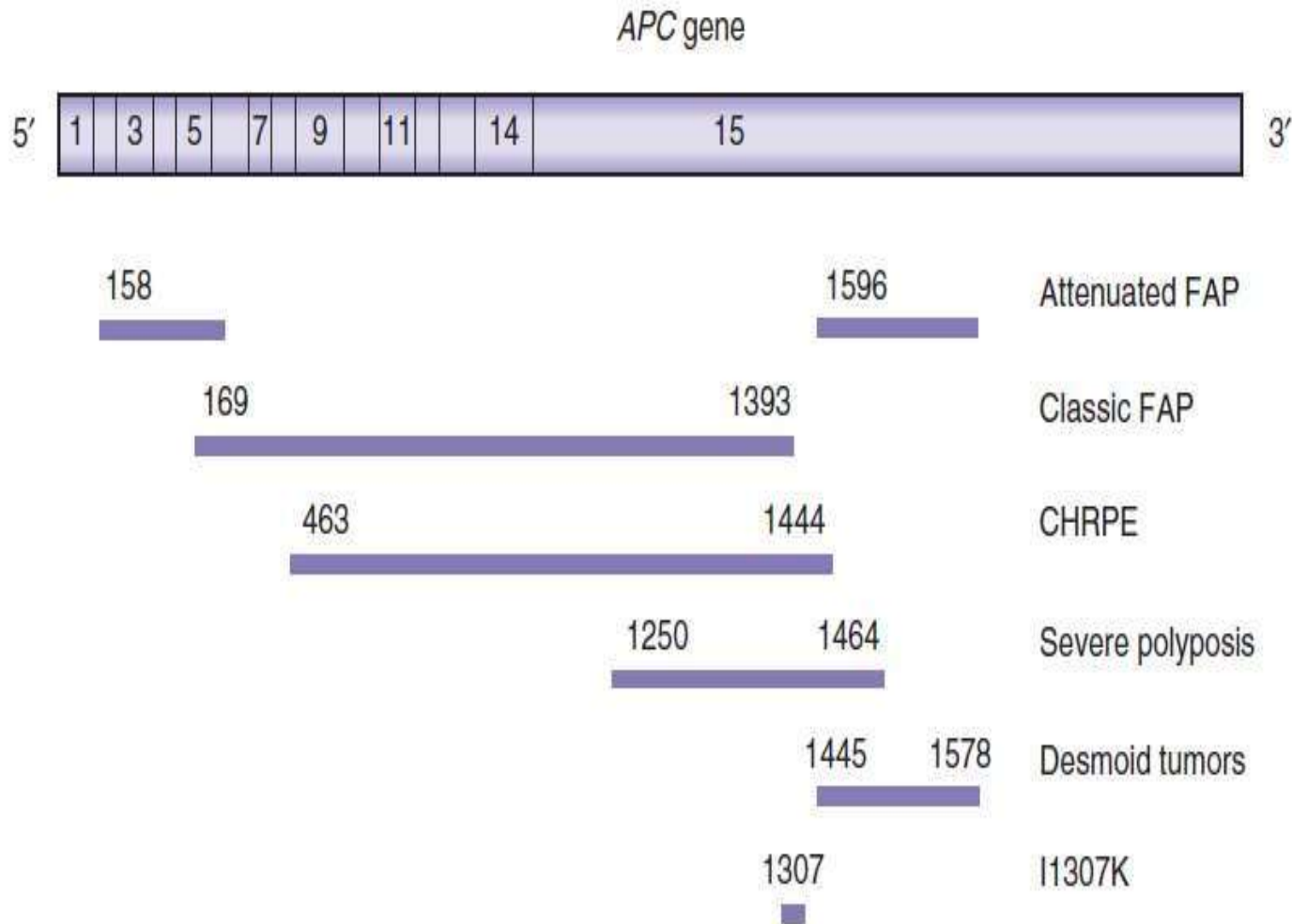
# Familial Adenomatous Polyposis(FAP)

- Incidence: 1 in 10000 live births
  - M:F=1:1
  - Classic FAP is characterised by
    1. Multiple colonic adenomatous polyps (>100)
    2. Early age of onset
    3. Inevitable development of colon cancer unless the colon is removed
- 

# Genetics

- Inheritance: Autosomal dominant
  - Penetrance: 100%
  - Family h/o FAP: upto 70%
  - De novo mutation: upto 30%
  - Genotype: APC gene, TSG, 5q21
  - Mutation: Truncated germline mutation
- 

# APC gene and FAP



Jo WS, Chung DC. Genetics of hereditary colorectal cancer.  
In Seminars in oncology 2005 Feb 28 (Vol. 32, No. 1, pp. 11-23).

# Extra-intestinal features in FAP

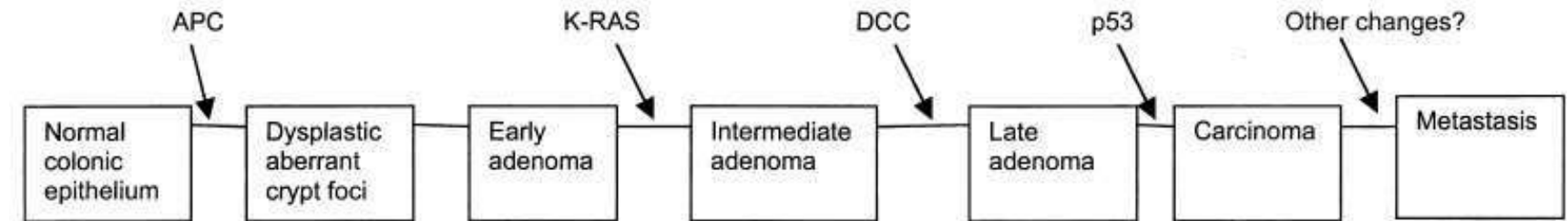
| S.No | Benign Lesions                                                    | Malignant lesions                      |
|------|-------------------------------------------------------------------|----------------------------------------|
| 1.   | Congenital hypertrophy of the retinal pigment epithelium (70–80%) | Duodenal tumors (3–5%)                 |
| 2.   | Epidermoid cyst (50%)                                             | Brain tumors (2%)<br>(Turcot syndrome) |
| 3.   | Osteoma (50–90%)<br>(Gardener syndrome)                           | Thyroid cancer (2%)                    |
| 4.   | Desmoid tumour (10–15%)                                           | Pancreatic cancer (1.7%)               |
| 5.   | Supernumery teeth (11–27%)                                        | Ampullary carcinoma(1.7%)              |
| 6.   | Adrenal gland adenomas (7–13%)                                    | Hepatoblastoma (1.6%)                  |
| 7.   |                                                                   | Gastric cancer (0.6%)                  |

Galiatsatos P, Foulkes WD. Familial adenomatous polyposis.  
The American journal of gastroenterology. 2006 Feb 1;101(2):385.

# Variants of FAP

- Attenuated familial adenomatous polyposis (AFAP)
  - Mutations close to the 5' end of the APC gene
  - Autosomal dominant
- MUTYH–Associated Polyposis (MAP)
  - Caused by mutation in the MutY homolog (MYH) gene, a base excision repair gene, 1p34
  - Autosomal recessive

# Adenoma–carcinoma sequence



**Normal tissue → Tumor initiation →**

**Tumor progression →**

**Neoplasia**

**Familial  
adenomatous  
polyposis**

**Accelerated**  
(due to germline APC  
mutation)

Normal  
(5-10 years)

Nearly 100% risk for  
colorectal cancer

**Hereditary  
nonpolyposis  
colorectal cancer**

Normal

**Accelerated**  
(due to germline mutation in  
mismatch repair gene)

70-80% lifetime risk of  
colorectal cancer

(May be 1-3 years)

Ivanovich JL, Read TE. A practical approach to familial and hereditary colorectal cancer. *The American journal of medicine*. 1999 Jul 31;107(1):68–77.

# Management of large bowel

- Once FAP has been diagnosed, the aim is to perform prophylactic surgery
- Timing of surgery: late teens to early twenties
- Indications of early surgery
  1. Documented or suspected cancer
  2. Significant symptoms
  3. Polyps  $>10$  mm diameter
  4. Polyps with high grade dysplasia
  5. Marked increase in polyp number on consecutive examinations

Syngal S et al. ACG clinical guideline. The American journal of gastroenterology. 2015 Feb;110(2):223.

# Choice of operation

- Surgical options available
  1. Total proctocolectomy with permanent end ileostomy
  2. Total proctocolectomy with continent ileostomy (Kock)
  3. Total colectomy with IRA
    - ✓ Pros–Superior functional results
    - ✓ Cons–Leaves the rectum intact
  4. Total proctocolectomy with IPAA ± covering loop ileostomy

# Postsurgical surveillance

- Includes:
    1. Annual endoscopy of rectum or ileal pouch
    2. Examination of an ileostomy every 2 years
- 

# Chemoprevention

- The goal is to reduce the appearance of new polyps and possibly induce regression of existing ones.
- However they don't prevent cancer.
- These are:
  - NSAID: Sulindac
  - Selective COX-2 inhibitor: Celecoxib
  - Omega-3 PUFA: Eicosapentaenoic acid (EPA)

West N et al: Eicosapentaenoic acid reduces rectal polyp number and size in familial adenomatous polyposis. *Gut* 59:918, 2010

# Genetic Testing

- **Genetic counselling**
  - Integral part of genetic testing
- **Genetic testing**
  - APC gene mutation can be found in 80-90% of FAP families with present technology
  - Laboratory method available
    - ❑ Protein truncation testing
    - ❑ Gene sequencing
    - ❑ Linkage testing

# Family risk

| S.No | Family Setting                                                       | Approximate lifetime risk of colon cancer |
|------|----------------------------------------------------------------------|-------------------------------------------|
| 1.   | General population risk in the US                                    | 6%                                        |
| 2.   | One first-degree relative with colon cancer                          | 2-3 fold increased                        |
| 3.   | Two first-degree relatives with colon cancer                         | 3-4 fold increased                        |
| 4.   | First-degree relative with colon cancer diagnosed at $\leq 50$ years | 3-4 fold increased                        |
| 5.   | One second- or third-degree relative with colon cancer               | About 1.5 fold increased                  |
| 6.   | Two second-degree relatives with colon cancer                        | About 2-3 fold increased                  |
| 7.   | One first-degree relative with an adenomatous polyp                  | About 2-fold increased                    |

Winawer S et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale—update based on new evidence. *Gastroenterology*. 2003 Feb 1;124(2):544–60.

# Family screening

| S.No | Site                   | Age to begin surveillance (years) | Surveillance interval (years) | Surveillance procedures and comments           |
|------|------------------------|-----------------------------------|-------------------------------|------------------------------------------------|
| 1.   | Colon                  | 10–15                             | 1–2                           | Flexible sigmoidoscopy or colonoscopy          |
| 2.   | Upper gastrointestinal | 25–30                             | 1–5                           | EGD                                            |
| 3.   | Thyroid                | Late teenage years                | 1                             | Annual thyroid examination; annual thyroid USG |
| 4.   | Intrabdominal desmoids |                                   | 1                             | Annual abdominal palpation.                    |

Syngal S et al. ACG clinical guideline. The American journal of gastroenterology. 2015 Feb;110(2):223.

# Conclusion

- Hereditary component to be evaluated and ruled out in young patients with CRC
  - Family members– counselling
  - Correct and effective screening– reduces mortality and morbidity due to syndromic malignancy
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THANK  
YOU!!!