MUTYH-Associated Polyposis (MAP)

What is MUTYH-Associated Polyposis (MAP)?
MUTYH-Associated Polyposis or MAP is a genetic condition that increases one’s risk of developing gastrointestinal polyps, colorectal cancer, and to a much lesser degree, other cancers (see chart below). MAP is caused by having an alteration in each of the two copies of the MUTYH gene, one inherited from each parent. Most individuals with MAP will develop ten to a few hundred polyps by the age of 50 years. Adenomas (precancerous polyps) are the most common polyp type for individuals with MAP, however there may also be other types including hyperplastic and sessile serrated polyps. It is also possible to have MAP and develop colorectal cancer with few or no polyps. MAP is a recently described syndrome, so knowledge is still unfolding.

Below are the estimated lifetime risks of cancer for people with MAP as compared to the general population. In some cases, risk appears to be increased, but studies have involved small numbers and good estimates do not yet exist. These risks are based on information that we have now and may change as more research is done.

<table>
<thead>
<tr>
<th>Cancer</th>
<th>MAP Risk</th>
<th>General Population Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>35-53%</td>
<td>5-6%</td>
</tr>
<tr>
<td>Small bowel: duodenum</td>
<td>4%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Thyroid (papillary)</td>
<td>possibly increased</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Breast (women)</td>
<td>possibly increased</td>
<td>12%</td>
</tr>
<tr>
<td>Ovary</td>
<td>possibly increased</td>
<td>1-2%</td>
</tr>
<tr>
<td>Bladder</td>
<td>possibly increased</td>
<td>1-3%</td>
</tr>
<tr>
<td>Skin (melanoma and other)</td>
<td>possibly increased</td>
<td>2%</td>
</tr>
<tr>
<td>Stomach</td>
<td>possibly increased</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Uterus (Endometrium)</td>
<td>possibly increased</td>
<td>2-3%</td>
</tr>
</tbody>
</table>


There are other non-cancerous features that have been reported with MAP, including:
- colorectal adenomas
- polyps in the stomach that are benign (fundic gland polyps)
- small bowel (duodenum) adenomas
- benign thyroid findings including multinodular goiter
- benign skin findings including sebaceous gland tumor, fibrous histiocytoma, capillary hemangioma, pilar cyst, dermatofibroma, and follicle cyst
- dental abnormalities including jaw bone cysts
- benign unusual pigment in the eye known as congenital hypertrophy of the retinal pigment epithelium or CHRPE
- soft tissue (desmoid) tumors, usually of the abdomen or abdominal wall
Carriers of one altered copy of the MUTYH gene
About 1-2% of individuals in the general population are carriers of MAP. This means that they have an alteration in one copy of the MUTYH gene, but not both. They do not have MAP or polyposis. Individuals who carry one altered MUTYH gene appear to have a small increased risk of cancer compared to the general population. The risk may include colorectal and breast cancer, however the degree of risk is still being determined. Screening in this situation is individualized and based on one’s medical and family history.

What causes MUYTH-Associated Polyposis (MAP)?
MUTYH (MutY Homolog of E. coli) is a gene that encodes an enzyme involved in DNA repair. When both copies of the gene are altered, DNA repair is impaired. This can lead to the accumulation of mutations in other genes, possibly leading to uncontrolled cell growth and tumor development. Specific MUTYH gene alterations have been found in certain populations. The two most common mutations in people of Northern European ancestry are called Y165C and G382D, and other variants have been found to be more common in other ethnic groups.

How is MAP inherited?
MAP is inherited in an “autosomal recessive” manner. Autosomal means that both men and women can have an altered MUTYH gene and both can pass it on to children. Recessive means that both copies of the MUTYH gene must be altered in order to cause MAP. In other words, both parents must pass on an altered MUTYH gene in order for the offspring to have MAP. MAP carriers are individuals who have one altered copy of the MUTYH gene and one normal copy.

If you have MAP caused by two altered MUTYH genes, there is a chance that other relatives may also have inherited one or more altered copy of the MUTYH gene.
• **Your Brothers and Sisters** – there is a 25% risk that your siblings inherited two altered copies of the MUTYH gene and have MAP. There is a 50% chance that they are MAP carriers and a 25% chance that they have two normal copies of the MUTYH gene.

• **Your children** – each child will inherit one altered MUTYH gene copy and will have a 100% chance to be at least a MAP carrier. The only way that your children would actually have MAP would be if your partner were a MAP carrier, or more rarely, if s/he actually has the condition. Carrier testing is available for MUTYH alterations for your partner.

• **Your Mother and Father** – in most cases, each of your parents is a MAP carrier with one altered copy of the MUTYH gene and would not actually have MAP due to having one functional MUTYH gene copy.

• Beyond your first degree relatives (siblings, parents, children), it becomes increasingly unlikely that relatives will have two altered copies of the MUTYH gene. As more is learned about the possible importance of having one altered copy of MUTYH, it may be appropriate to offer genetic testing and specialized screening recommendations to more extended relatives.

How is MAP managed?
There are a number of recommendations to help manage increased risks that should be considered. Although we do not currently have any perfect strategies for reducing cancer risks, we do know that close monitoring can detect pre-cancers and that colon cancer may be prevented. In most cases, with close monitoring, if colon cancer does develop it is found in its earliest stages when it is most amenable to treatment. A screening test is one that is done in an effort to identify cancer (or precancerous changes) early. Risk reduction strategies are used to try to prevent cancer. No large studies have examined the effectiveness of screening in MAP and the following recommendations for people with MAP are based on expert opinion (National Comprehensive Care Network or NCCN guidelines).

**Screening:**
- Annual physical exam
- Attention to gastrointestinal symptoms
- Polyps and gastrointestinal cancer:
  - colonoscopy (every 1-2 years beginning at age 25-30)
  - upper endoscopy (every 3-5 years beginning at age 30-35)
- Thyroid cancer: At this time, there is no consensus regarding screening intervals for thyroid abnormalities or cancers outside the gastrointestinal tract. The following may be recommended:
  - thyroid examination annually (with physical exam or ultrasound as needed)

**Risk Reduction:**
For some individuals with MAP, the number of polyps forming can become overwhelming and too difficult to remove or follow over time. In these cases, it is recommended that individuals with MAP discuss surgical options to reduce the risk of cancer.

- The type of surgery that may be recommended for individuals with MAP is called a colectomy, and involves removing the colon. This surgery can be performed in various ways and if this becomes a consideration, we recommend that you discuss the benefits and risks of these surgeries with a colorectal surgeon. Most often patients go on to live healthy, active lives and do not require a colostomy “bag”. For some individuals with MAP, the polyps are very numerous, but mostly confined to one area of the colon. In this case, a partial colectomy could be considered.
- Chemoprevention with non-steroidal anti-inflammatory drugs (NSAIDs) including a medication called sulindac, is under active study for people with MAP and other types of polyposis.

Where can I find more information?
Dana Farber Cancer Institute, Cancer Genetics & Prevention
[www.dana-farber.org/cancergenetics](http://www.dana-farber.org/cancergenetics)

Cancer.net

Collaborative Group of the Americas on Inherited Colorectal Cancer (CGA)
Colon cancer alliance
http://www.ccalliance.org/

American Cancer Society
www.cancer.org

National Cancer Institute
www.cancer.gov

References:
- Gene Reviews
  http://www.ncbi.nlm.nih.gov/books/NBK107219/
- NCCN Guidelines Version 2.2013 MUTHY-Associated Polyposis
  www.nccn.org