Lynch Syndrome (Hereditary Nonpolyposis Colorectal Cancer or HNPCC)
Information for Physicians and Other Health Care Professionals

What is Lynch syndrome?
- Lynch syndrome is an inherited genetic condition that significantly raises a person's risk of developing cancer. The cancer is most frequently in the digestive tract, particularly the colon, rectum and stomach, but also can be present in the liver, gallbladder ducts, urinary tract, brain, skin and prostate.
- Women have a higher risk of developing endometrial and ovarian cancer.
- A person with Lynch syndrome is at greater risk of developing cancer at a younger age, usually before the age of 45.
- If one parent carries the gene mutation related to Lynch syndrome, there's a 50 percent chance the mutation will be passed on to each child that person has.
- Not everyone who carries these mutations develops cancer. For people with a family history of cancer, confirming who has Lynch syndrome is important so affected individuals and carriers take the steps to prevent illness.

How common is Lynch syndrome?
Lynch syndrome is the cause of 2 percent to 7 percent of new colorectal cancers diagnosed each year.

What causes Lynch syndrome?
Lynch syndrome is caused by a mutation in DNA repair genes. The four genes, MLH1, MSH2, MSH6, and PMS2, are responsible for 32 percent, 38 percent, 14 percent and 15 percent of cases, respectively.

With Lynch syndrome, what are the lifetime risks for developing cancer and the average age of onset?
Lifetime cancer risk for those with Lynch syndrome depends on several factors, including which gene is present and prevention behaviors. The following table summarizes overall lifetime cancer risks.

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>General Population Risk</th>
<th>Lynch Syndrome</th>
<th>Mean Age of Onset in LS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>5.50%</td>
<td>Men: 54-74%; Women: 30-52%</td>
<td>42-61 years</td>
</tr>
<tr>
<td>Endometrium</td>
<td>2.70%</td>
<td>28-60%</td>
<td>47-55 years</td>
</tr>
<tr>
<td>Stomach</td>
<td>&lt;1%</td>
<td>5-8%</td>
<td>56 years</td>
</tr>
<tr>
<td>Ovary</td>
<td>1.60%</td>
<td>4-11%</td>
<td>42.5 years</td>
</tr>
<tr>
<td>Hepatobiliary tract</td>
<td>&lt;1%</td>
<td>2-18%</td>
<td>Not reported</td>
</tr>
<tr>
<td>Upper urinary tract</td>
<td>&lt;1%</td>
<td>Overall: 8.4%; up to 27% in men</td>
<td>~55 years</td>
</tr>
<tr>
<td>Small bowel</td>
<td>&lt;1%</td>
<td>3-6%</td>
<td>49 years</td>
</tr>
<tr>
<td>Brain/central nervous system</td>
<td>&lt;1%</td>
<td>4%</td>
<td>~50 years</td>
</tr>
<tr>
<td>Sebaceous neoplasms</td>
<td>&lt;1%</td>
<td>1%-9%</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

When should you suspect Lynch syndrome?
You should suspect Lynch syndrome if a patient has a family history of cancer, especially if there are:
- Three or more family members, one of whom is a first-degree relative of the other two, with HNPCC-related cancer
- Two successive affected generations
- One or more of the HNPCC-related cancers diagnosed before age 50 years
- Exclusion of familial adenomatous polyposis (FAP)
How is a person diagnosed with Lynch syndrome? What kinds of test are done?
Taking a family health history is the first step, but the fact that it may be caused by different mutations in one of several genes complicates diagnosis and testing. Genetic testing can be done to confirm if a person has a mutation, but it is not always useful to test everyone in the family for Lynch syndrome. It is best to test the person who has the cancer for Lynch syndrome before testing others in their family. Identifying Lynch syndrome also involves a combination of various genetic and immunohistochemical tests to first establish the probability of Lynch syndrome and then identify which gene is most likely causing the cancer.

If Lynch syndrome runs in a family, how can cancer be prevented?
The only proven ways to reduce cancer risk is frequent cancer screenings and preventative prophylactic surgery when appropriate. Some resources on cancer screening guidelines are below.

Resources on Lynch syndrome

General information

Screening and prevention
- The National Comprehensive Cancer Network has guidelines for colorectal screening related to Lynch syndrome at http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#detection (free registration is required to access the documents).

Testing

Management