Dear Colleagues in Women’s Health,

Greetings to all! We hope you are enjoying another beautiful fall season in East Tennessee. This edition of Gyn Oncology Update focuses on Lynch Syndrome, a common and important hereditary mutation that places women at increased risk for uterine, colon and ovarian cancer. We continue our efforts to raise awareness and educate providers, resident physicians and patients about this syndrome.

Each time we see a new or existing patient in our office we ask them to update their personal and family history of cancer at the same time they update their medications. We have included the form we use in this update for your review and we encourage you to use this form or something similar in your practice. We will be happy to fax or email this form to your office or you may download it from our website listed below. We modified this form to be limited to one page for quick reference and ease of completion for patients.

Lynch Syndrome is inherited as an autosomal dominant mutation and the genes involved are deficient in their ability to repair DNA damage. Surprisingly, Lynch Syndrome is just as common as the well-recognized mutations in BRCA 1 and BRCA 2. Both syndromes occur in about 1 in 400 patients, however, we have identified fewer than 10% of patients with these mutations.

Please contact us if we can be of assistance to you or your patients. Please note our mailing and office addresses, as well as, phone and electronic contacts. This and other Gyn Oncology Updates are available to you at www.universitygynoncology.org under the referring physicians tab. We wish you continued health and happiness in 2014.

Best Regards,

Larry C. Kilgore, MD
Kristopher J. Kimball, MD
Amanda W. Berry, NP
Shelly B. Foust, NP
Amanda O. Cameron, NP
Lynch Syndrome

Lynch Syndrome is the most common cause of hereditary gynecologic malignancy and the most common cause of hereditary colon cancer. It is also known as Hereditary Non-polyposis Colorectal Cancer (HNPCC) with an incidence in the general population of approximately 1 in 400 patients. It is as common as Hereditary Breast and Ovary Cancer (HBOC) but grossly underappreciated by most clinicians. It is inherited as an autosomal dominant trait. It is caused by genetic mutations in MLH1, MSH2, MSH6, PMS2 or EPCAM; genes important in DNA mismatch repair. The most common Lynch Syndrome cancers and the lifetime risks are uterine (up to 60%), colon (70%) and ovary (12%). In women, a gynecologic cancer (uterine or ovary) is often the sentinel cancer in Lynch Syndrome instead of colorectal. Uterine and colorectal cancer in Lynch Syndrome often occurs at younger ages (<50 y/o). Colon cancers are frequently right sided. Additional Lynch cancers may include gastric, small bowel, renal pelvis, ureter, biliary and others. Uterine and colorectal tumors may be tested for evidence of microsatellite instability (MSI) or immunohistochemical (IHC) analysis by pathology. This may lead to formal genetic testing. It is imperative that a patient’s personal and family history of cancer be updated annually and reviewed for identification of hereditary traits for increased screening, risk reduction strategies and identification of family members at risk. Once suspected, Lynch Syndrome can be confirmed by genetic testing for the mutation.

Red Flags for Lynch Syndrome:

- Personal history of uterine or colon cancer before age 50
- Personal history of ≥ 2 Lynch Syndrome cancers at any age
- Positive MSI tumor test results
- Personal history of Lynch cancer with ≥ 1 relative with Lynch cancer
- ≥2 relatives with Lynch cancer if one occurred before age 50
- ≥3 relatives with a Lynch cancer at any age
- Known Lynch mutation in the family

How is Lynch Syndrome managed?

Gynecologic Cancer Screening (uterine and ovary) – begins at age 30-35
- Annual pelvic exam, vaginal ultrasound, endometrial biopsy, CA-125
- Removal of uterus, tubes, ovaries at age 40 and older

Colorectal Cancer Screening – begins at age 20-25
- Screening colonoscopy +/- chromoendoscopy dye spray every 1-2 years
- Remove entire or right colon if cancer occurs

Renal pelvis/ureter Screening
- Annual urinalysis for cytology (value not proven)

Gastric/Small intestine Screening
- Periodic upper endoscopy screening (value not proven)

Kilgore and Kimball Take Home Message:

Lynch Syndrome is as common as HBOC or BRCA but is often overlooked and under-valued. Clinicians should update annually the personal and family history of cancer to identify those patients at risk for hereditary syndromes including Lynch and HBOC. (Form attached) Lynch Syndrome is the most common hereditary cause of a gynecologic malignancy accounting for increased risks of uterine AND ovary cancer. Multiple family members with colon or uterine cancer, as well as, uterine or colon cancer in a patient under the age of 50 should alert one to a possible Lynch Syndrome mutation. Screening for the female Lynch patient includes annual colonoscopy, pelvic exam, endometrial biopsy, vaginal ultrasound and CA-125. Risk reduction for Lynch Syndrome includes complete hysterectomy with removal of tubes and ovaries. Once suspected, the patient should be counseled and offered genetic testing for the mutation.

References:
Hereditary Cancer Risk Assessment

Name: __________________________ Date: __________________________

Most cancer happens by chance and is not passed down generation to generation. In a small number of families however, cancers may be due to specific genetic factors that can be passed from parent to child. A careful review of your family history is necessary, to help determine your risk.

**Have YOU been diagnosed with:**

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Age at diagnosis</th>
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<tbody>
<tr>
<td>Ovarian Cancer</td>
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<tr>
<td>Breast Cancer</td>
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<td>Pancreatic Cancer</td>
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<td>Endometrial/Uterine Cancer</td>
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<td>Colon Cancer</td>
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<td>Sebaceous adenomas</td>
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<tr>
<td>Other</td>
<td></td>
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</tbody>
</table>

**Age at diagnosis:**

**List ALL members of your family diagnosed with any of the following:**

Include parents, grandparents, great-grandparents, children, grandchildren, siblings, half-siblings, aunts, uncles, great-aunts, great-uncles, nieces, nephews and cousins.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Relationship</th>
<th>Age at diagnosis</th>
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<tbody>
<tr>
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<td>Prostate Cancer</td>
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<td>Urinary Tract/Kidney Cancer</td>
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<td>Stomach/Intestine/Biliary tract Cancer</td>
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<tr>
<td>Sebaceous adenomas</td>
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<tr>
<td>Other</td>
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</tbody>
</table>

**Have you or anyone in your family had genetic testing for hereditary cancers?**

- [ ]

**Do you have Jewish Ancestry (Central & Eastern European)?**

- [ ]

**Patient Signature**

Date: __________________________

For office use only:

Does not meet current criteria for testing: [ ]

Patient meets criteria for: COLARIS: [ ] HBOC: [ ] Patient offered genetic testing: Accepted [ ] Denied [ ]

Patient counseled that family member is the appropriate candidate for genetic testing: [ ]

Patient would like results reported: by Phone [ ] In-Office Consultation [ ]

Specimens collected: Yes [ ] No [ ], Reason:

Notes: ____________________________

Healthcare Providers Signature: ____________________________