**Lynch Syndrome Testing (HNPCC)**

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**All colorectal cancer (CRC) and endometrial tumors**

- Screen for mismatch repair deficiency
  - ORDER
    - Mismatch Repair by Immunohistochemistry*

- Abnormal per IHC (positive for MMR deficiency)
  - It is usually most effective to first evaluate suspected Lynch syndrome (LS) with IHC or PCR testing, as only 2-4% of CRCs are LS. However, if strong suspicion exists (eg, family history, cancer at a young age), it is reasonable to proceed to genetic testing.

  - ORDER
    - Gastrointestinal Hereditary Cancer Panel, Sequencing and Deletion/Duplication, 16 Genes

- Normal per IHC (negative for mismatch repair [MMR] deficiency)
  - Probably not LS
    - If high clinical suspicion for LS exists
      - ORDER
        - Microsatellite Instability (MSI), HNPCC/Lynch Syndrome, by PCR

- Abnormal staining for MLH1 and PMS2
  - Test for BRAF V600E mutation
    - ORDER
      - BRAF Codon 600 Mutation Detection with Reflex to MLH1 Promoter Methylation
      - For endometrial tumors, proceed directly to MLH1 Promoter Methylation

- Abnormal staining for MSH2 and MSH6
  - Genetic mutation testing for Lynch syndrome
    - RECOMMEND
      - HNPCC/Lynch Syndrome (MSH2) Sequencing and Deletion/Duplication as first test*

- Abnormal staining for MSH6
  - Genetic mutation testing for Lynch syndrome
    - RECOMMEND
      - HNPCC/Lynch Syndrome (MSH6) Sequencing and Deletion/Duplication as first test*

- Abnormal staining for PMS2
  - Genetic mutation testing for Lynch syndrome
    - RECOMMEND
      - HNPCC/Lynch Syndrome (PMS2) Sequencing and Deletion/Duplication as first test*

  * Note
    - Targeted testing for a mutation previously identified in a family member is available (Familial Mutation, Targeted Sequencing)
    - Multi-gene panel testing is available (Gastrointestinal Hereditary Cancer Panel, Sequencing and Deletion/Duplication, 16 Genes)

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