Hereditary Nonpolyposis Colorectal Cancer Testing Algorithm

1. Identify appropriate patients for testing

2. Test tumor from affected individual using MSIHC / Microsatellite Instability (MSI)/Immunohistochemistry (IHC) Profile-Lynch/Hereditary Nonpolyposis Colorectal Cancer (HNPCC) Screen:
   - Microsatellite instability (MSI)
   - Immunohistochemistry (IHC) for MLH1, MSH2, MSH6, PMS2

3. MSI-H
   - Loss of MLH1 protein expression

   - Germline testing (DNA sequence analysis and deletion/duplication analysis) of MLH1 using MLH1Z / MLH1 Gene, Full Gene Analysis, as indicated by IHC.

4. MSI-H
   - Loss of MSH2 and/or MSH6 protein expression

   - Germline testing (DNA sequence analysis and deletion/duplication analysis) of MSH2 or MSH6 using MSH2Z / MSH2 Gene, Full Gene Analysis or MSH6Z / MSH6 Gene, Full Gene Analysis, as indicated by IHC.

5. MSI-L or MSS

   - Germline testing not recommended.

6. Consider BRMLH / MLH1 Hypermethylation and BRAF Mutation Analysis, Tumor testing to distinguish somatic vs. germline event. As indicated, testing can be considered either prior to or after germline testing of MLH1 (if germline testing was negative), depending upon the clinical and family history.

Legend

- MSI-H: MSI-high
- MSI-L: MSI-low
- MSS: Microsatellite stable