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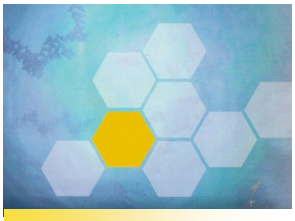
Testing of Colorectal Carcinomas for Lynch Syndrome

Approximately 1%-3% of colorectal carcinomas occur in individuals with Lynch syndrome, an autosomal dominant cancer-predisposition syndrome. Those affected are predisposed to colorectal and other carcinomas because of an inherited genetic defect in DNA mismatch repair (MMR). Recently-developed tests that identify molecular changes associated with defective DNA MMR are increasingly being used to identify Lynch syndrome related tumors. There is a growing consensus among experts that use of these tests to screen all colorectal carcinomas is the strategy most likely to identify individuals at risk for Lynch syndrome and is cost effective (depending on the number of family members who undergo screening).

Two tests are currently in use for Lynch syndrome screening: 1) Immunohistochemical stains for four Lynch syndrome-associated defective MMR proteins (MLH1, MSH2, MSH6, and PMS2) and 2) Molecular (PCR) tests for high frequency microsatellite instability (MSI-H). These screening tests are not diagnostic for Lynch syndrome, but can identify patients who may benefit from referral for genetic counseling and further testing. Less than 20% of individuals with abnormal screening tests will be found on further testing to have an inherited mutation of one of the MMR genes involved in Lynch syndrome. (Most of the remaining individuals will be found to have a sporadic tumor caused by abnormal methylation of the MLH-1 gene promoter.) The immunohistochemical and molecular tests both have sensitivities of 90-95%. However, immunohistochemistry may be considered preferable because it provides specific information that directs appropriate follow-up testing.



Screening for Lynch syndrome may also be indicated for some adenomas. Although universal testing of all colorectal adenomas is impractical due to the high incidence of sporadic adenomas of the large bowel, testing in individuals with a family history of colorectal carcinoma or other Lynch syndrome-associated tumors has a high likelihood of providing valuable information. The same is true of colorectal adenomas in young individuals and/or those with multiple adenomas. In addition, testing of all duodenal and gastric adenomas may also be warranted, as these are rare outside the settings of Lynch syndrome and familial adenomatous polyposis (FAP). In keeping with these testing recommendations, CBM supports the implementation of Lynch syndrome screening tests for colorectal carcinomas, duodenal and gastric adenomas, and colorectal adenomas in individuals with clinical and/or pathologic findings suggesting possible Lynch syndrome. Upon request, tissue from these specimens will be sent out for immunohistochemical testing to detect defective DNA mismatch repair proteins.

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Know Your GI Pathologists

Nancy Dow M.D. is head of the Gastrointestinal Pathology Department at CBM Pathology and expands our team with her expertise. Dr. Dow has many years of experience in gastrointestinal pathology at the Armed Forces Institute of Pathology (AFIP), including acting as Chief of the GI Pathology Division for two years.

Dr. Dow leads the GI program at CBM Pathology with structured GI continuing education and weekly GI conference with Cynthia Bruzzi M.D., Rachel Katz M.D. and Carla MacLeod M.D., also experts in the field.

Dr. Dow is available to consult on all cases and accessible to clinicians to discuss patients' cases. Intramural consults are integral to how patients are treated at CBM Pathology. It's as if you are getting a second opinion with the first diagnosis. Our medical team is committed to quality and truly focused on each patient's case. We want to provide the diagnosis you can feel confident treating.

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