Appendix A: Hereditary Colorectal Cancer (CRC) Syndromes

Hereditary CRC implies a strong predisposition to an inherited CRC due to a genetic mutation. The hallmarks of hereditary CRC syndromes are pre-cancerous lesions and CRC diagnosed at a younger age, metachronous and synchronous CRC, multiple affected relatives, and, often, other associated cancer diagnoses.[21,22]

Genetic counselling and testing are available through the Hereditary Cancer Program at BC Cancer. Individuals affected with hereditary cancer predispositions to colon cancer, and their family members, should be followed by a gastroenterologist who, in conjunction with the Hereditary Cancer Program at the BC Cancer Agency will determine ongoing medical care.

1. **Lynch Syndrome**

   Lynch syndrome (LS) is an autosomal dominant condition caused by a germline mutation in a mismatch repair gene (MLH1, MSH2, MSH6, PMS2) or by deletions in the EPCAM gene. LS is characterized by an increased risk for cancers of the colon, endometrium, ovary, stomach, small intestine, hepatobiliary tract, urinary tract, brain, and skin. LS accounts for 2-4% of all CRCs. While usually associated with CRC, it is important to understand that endometrial cancer is often the first cancer diagnosed in women with LS.

   Muir-Torre syndrome is a subset of LS with an associated predisposition to sebaceous neoplasms and is primarily associated with MSH2 gene mutations.

   Confirmation of LS is important both for people with cancer, because of the associated risk for another LS cancer, and to inform appropriate cancer risk management for their adult family members.

2. **Polyposis syndromes**

   Inherited risk for CRC is associated with a number of polyposis syndromes (genes), some of which are well-defined and others are less common. Identification of an unusual number of polyps and/or unusual polyps should prompt consideration of Hereditary Cancer Program referral for polyposis assessment.

   Polyposis syndromes/genes include: Familial Adenomatous Polyposis/Attenuated Familial Adenomatous Polyposis (APC), Juvenile Polyposis (*SMAD4*, *BRMP1A*), MUTYH-Associated Polyposis (*MUTYH*), Polymerase Proofreading-associated syndrome (*POLE/POLD1*), Serrated Polyposis syndrome (formerly Hyperplastic Polyposis), and Mixed Polyposis. Peutz-Jeghers syndrome (*STK11*) and Cowden syndrome (*PTEN*) are also associated with specific types of polyps.

3. **Other Hereditary Cancer Syndromes**

   A number of other hereditary cancer syndromes are associated with an increased risk for CRC. These may be associated with a moderate to high risk for CRC and require increased CRC screening recommendations.