

Hereditary Leukemia

What You Should Know About Hereditary Leukemia

To date there are more than 20 cancer genes associated with hereditary leukemia. Individuals with a mutation in one of these genes have an increased lifetime risk to develop leukemia and possibly other cancers. These cancers can develop from early childhood to late adulthood.

Cancer Risks Associated with Hereditary Leukemia

There is currently limited information regarding the lifetime cancer risks for individuals with a specific hereditary leukemia gene mutation. While these genes cause an increased risk for leukemia, mutations in some of these genes are associated with increased risks for other types of cancers as well. Individuals may develop different cancers at different ages, even if they have the same gene mutation. Specific risks may depend on which specific gene is implicated.

Risks to Family Members

Some hereditary conditions that increase the risk for leukemia are caused by genes that are inherited in an <u>autosomal</u> <u>dominant</u> fashion. This means that children, brothers, sisters, and parents of individuals with a mutation have a 1 in 2 (or 50%) chance of having the mutation as well. Individuals with a mutation may develop one cancer, more than one cancer, or none at all. Both males and females can inherit a familial hereditary leukemia gene mutation and both males and females can pass it on to their children.

Other hereditary conditions that increase the risk for leukemia are caused by genes that are inherited in an <u>autosomal</u> <u>recessive</u> fashion. This means that an individual must inherit two mutations, one in each copy of the gene, in order to have higher risks for leukemia and potentially other cancers. In this case, both of the individual's parents must have had a single mutation and both parents passed that mutation on to their child. Siblings of a person affected with an autosomal recessive condition have a 1 in 4 (or 25%) chance to have inherited both mutations as well. Parents of a child affected with an autosomal recessive condition are both known to be "carriers" of the condition, meaning that they each have one copy of the mutation. Carriers may or may not have risks for cancer themselves, depending on what the mutated gene is.

Managing Cancer Risks

Currently, there are no formal management guidelines for individuals with a hereditary predisposition to leukemia. The following is suggested based on expert opinion.

At Time of Genetic Diagnosis

- Consider expert consultation at a specialized center
- Physical examination evaluating for signs of leukemia/ lymphoma and syndrome-specific findings
- Complete blood count (CBC)
- Baseline bone marrow evaluation, including aspirate and biopsy, to rule out any blood disorders or cancer. Some leukemia predisposition disorders are associated with baseline abnormalities that are not linked with impending leukemia.
- HLA typing is useful for identifying potential familial donors

At Follow-Up Appointments

Update personal and family history information

- Annual physical examination evaluating for signs of leukemia/ lymphoma and syndrome-specific findings. Visits can be considered more frequently (every 3-6 months) in patients at high-risk of developing MDS/AML.
- At least annual CBC in patients with normal blood counts or stable cytopenias (with exceptions). For those at higher risk, the American Association for Cancer Research (AACR) recommends CBC every 3-4 months.
- Annual clinical bone marrow evaluation, including aspirate and biopsy for those at higher risk of MDS/AML (even with stable blood counts). For individuals with a lower risk for MDS/AML, the frequency of bone marrow evaluation should be discussed with a specialist.
- Consider HLA typing and referral to a specialty center

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