Bloom syndrome

Bloom syndrome is an inherited disorder characterized by short stature, a skin rash that develops after exposure to the sun, and a greatly increased risk of cancer.

People with Bloom syndrome are usually smaller than 97 percent of the population in both height and weight from birth, and they rarely exceed 5 feet tall in adulthood.

Affected individuals have skin that is sensitive to sun exposure, and they usually develop a butterfly-shaped patch of reddened skin across the nose and cheeks. A skin rash can also appear on other areas that are typically exposed to the sun, such as the back of the hands and the forearms. Small clusters of enlarged blood vessels (telangiectases) often appear in the rash; telangiectases can also occur in the eyes. Other skin features include patches of skin that are lighter or darker than the surrounding areas (hypopigmentation or hyperpigmentation respectively). These patches appear on areas of the skin that are not exposed to the sun, and their development is not related to the rashes.

People with Bloom syndrome have an increased risk of cancer. They can develop any type of cancer, but the cancers arise earlier in life than they do in the general population, and affected individuals often develop more than one type of cancer.

Individuals with Bloom syndrome have a high-pitched voice and distinctive facial features including a long, narrow face; a small lower jaw; and prominent nose and ears. Other features can include learning disabilities, an increased risk of diabetes, chronic obstructive pulmonary disease (COPD), and mild immune system abnormalities leading to recurrent infections of the upper respiratory tract, ears, and lungs during infancy. Men with Bloom syndrome usually do not produce sperm and as a result are unable to father children (infertile). Women with the disorder generally have reduced fertility and experience menopause at an earlier age than usual.

Frequency

Bloom syndrome is a rare disorder. Only a few hundred affected individuals have been described in the medical literature, about one-third of whom are of Central and Eastern European (Ashkenazi) Jewish background.

Causes

Mutations in the \textit{BLM} gene cause Bloom syndrome. The \textit{BLM} gene provides instructions for making a member of a protein family called RecQ helicases. Helicases are enzymes that attach (bind) to DNA and unwind the two spiral strands (double helix) of the DNA molecule. This unwinding is necessary for several processes in the cell nucleus, including copying (replicating) DNA in preparation for cell division and
repairing damaged DNA. Because RecQ helicases help maintain the structure and
integrity of DNA, they are known as the "caretakers of the genome."

When a cell prepares to divide to form two cells, the DNA that makes up the
chromosomes is copied so that each new cell will have two copies of each
chromosome, one from each parent. The copied DNA from each chromosome is
arranged into two identical structures, called sister chromatids, which are attached
to one another during the early stages of cell division. Sister chromatids occasionally
exchange small sections of DNA during this time, a process known as sister chromatid
exchange. Researchers suggest that these exchanges may be a response to DNA
damage during the copying process. The BLM protein helps to prevent excess sister
chromatid exchanges and is also involved in other processes that help maintain the
stability of the DNA during the copying process.

*BLM* gene mutations result in the absence of functional BLM protein. As a result,
the frequency of sister chromatid exchange is about 10 times higher than average.
Exchange of DNA between chromosomes derived from the individual's mother and
father are also increased in people with *BLM* gene mutations. In addition, chromosome
breakage occurs more frequently in affected individuals. All of these changes are
associated with gaps and breaks in the genetic material that impair normal cell activities
and cause the health problems associated with this condition. Without the BLM protein,
the cell is less able to repair DNA damage caused by ultraviolet light, which results in
increased sun sensitivity. Genetic changes that allow cells to divide in an uncontrolled
way lead to the cancers that occur in people with Bloom syndrome.

**Inheritance Pattern**

This condition is inherited in an autosomal recessive pattern, which means both copies
of the gene in each cell have mutations. The parents of an individual with an autosomal
recessive condition each carry one copy of the mutated gene, but they typically do not
show signs and symptoms of the condition.

**Other Names for This Condition**

- Bloom-Torre-Machacek syndrome
- Bloom's syndrome
- congenital telangiectatic erythema

**Diagnosis & Management**

**Genetic Testing Information**

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Bloom syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0005859/
Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Bloom+syndrome%22

Other Diagnosis and Management Resources

- GeneReview: Bloom Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1398
- MedlinePlus Encyclopedia: Short Stature
  https://medlineplus.gov/ency/article/003271.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Short Stature
  https://medlineplus.gov/ency/article/003271.htm
- Health Topic: Cancer
  https://medlineplus.gov/cancer.html
- Health Topic: Infertility
  https://medlineplus.gov/infertility.html

Genetic and Rare Diseases Information Center

- Bloom syndrome
  https://rarediseases.info.nih.gov/diseases/915/bloom-syndrome

Educational Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Kprones/BLOID10002.html
- MalaCards: bloom syndrome
  https://www.malacards.org/card/bloom_syndrome
- Mount Sinai Center for Jewish Genetic Diseases
  https://icahn.mssm.edu/research/jewish-genetics/screening
- Orphanet: Bloom syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=125
- The Norton & Elaine Sarnoff Center for Jewish Genetics
  https://www.juf.org/cjg/Ashkenazi-Jewish-Disorders.aspx
Patient Support and Advocacy Resources

- Bloom’s Syndrome Association
  https://www.bloomssyndromeassociation.org/default.aspx
- Bloom’s Syndrome Foundation
  http://www.bloomsyndrome.eu/index.php
- MAGIC Foundation for Children's Growth
  https://www.magicfoundation.org/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/bloom-syndrome/
- Weill Cornell Medical Center: Bloom's Syndrome Registry
  https://pediatrics.weill.cornell.edu/research/bloom-syndrome-registry

Clinical Information from GeneReviews

- Bloom Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1398

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Bloom+Syndrome%5BMAJR%5D%29+AND+%28Bloom+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- BLOOM SYNDROME
  http://omim.org/entry/210900

Medical Genetics Database from MedGen

- Bloom syndrome
  https://www.ncbi.nlm.nih.gov/medgen/2685

Sources for This Summary

- Amor-Guéret M. Bloom syndrome, genomic instability and cancer: the SOS-like hypothesis. Cancer Lett. 2006 May 8;236(1):1-12. Epub 2005 Jun 13. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15950375
- Arora H, Chacon AH, Choudhary S, McLeod MP, Meshkov L, Nouri K, Izakovic J. Bloom syndrome. Int J Dermatol. 2014 Jul;53(7):798-802. doi: 10.1111/ijd.12408. Epub 2014 Mar 6. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24602044
- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Kprones/BLOID10002.html
• Cheok CF, Bachrati CZ, Chan KL, Ralf C, Wu L, Hickson ID. Roles of the Bloom's syndrome helicase in the maintenance of genome stability. Biochem Soc Trans. 2005 Dec;33(Pt 6):1456-9. Review. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16246145

• German J, Sanz MM, Ciocci S, Ye TZ, Ellis NA. Syndrome-causing mutations of the BLM gene in persons in the Bloom's Syndrome Registry. Hum Mutat. 2007 Aug;28(8):743-53. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17407155

• Guo RB, Rigolet P, Ren H, Zhang B, Zhang XD, Dou SX, Wang PY, Amor-Gueret M, Xi XG. Structural and functional analyses of disease-causing missense mutations in Bloom syndrome protein. Nucleic Acids Res. 2007;35(18):6297-310. Epub 2007 Sep 18. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17878217 
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2094094/

• Kaneko H, Kondo N. Clinical features of Bloom syndrome and function of the causative gene, BLM helicase. Expert Rev Mol Diagn. 2004 May;4(3):393-401. Review. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15137905

• Liu Y, West SC. More complexity to the Bloom's syndrome complex. Genes Dev. 2008 Oct 15;22(20):2737-42. doi: 10.1101/gad.1732808. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18923071 
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2751278/

• Ouyang KJ, Woo LL, Ellis NA. Homologous recombination and maintenance of genome integrity: cancer and aging through the prism of human RecQ helicases. Mech Ageing Dev. 2008 Jul-Aug;129(7-8):425-40. doi: 10.1016/j.mad.2008.03.003. Epub 2008 Mar 15. Review. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18430459

• Singh DK, Ahn B, Bohr VA. Roles of RECQ helicases in recombination based DNA repair, genomic stability and aging. Biogerontology. 2009 Jun;10(3):235-52. doi: 10.1007/s10522-008-9205-z. Epub 2008 Dec 15. Review. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19083132 
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2713741/

• Wu L. Role of the BLM helicase in replication fork management. DNA Repair (Amst). 2007 Jul 1;6(7):936-44. Epub 2007 Mar 23. Review. 
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17363339

Reprinted from Genetics Home Reference: 
  https://ghr.nlm.nih.gov/condition/bloom-syndrome

Reviewed: April 2015
Published: June 23, 2020

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services