GENEReviews

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X-Linked Severe Combined Immunodeficiency

[*SCID, X-Linked; SCIDX1; X-SCID*]

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Summary

Disease characteristics. X-linked severe combined immunodeficiency (X-SCID) is a combined cellular and humoral immunodeficiency resulting from lack of T and natural killer (NK) lymphocytes and nonfunctional B lymphocytes. Most males with typical X-SCID come to medical attention between three and six months of age. Nearly universal features during the first year of life are failure to thrive, oral/diaper candidiasis, absent tonsils and lymph nodes, recurrent infections, infections with opportunistic organisms such as *Pneumocystis*, and persistence of infections despite conventional treatment. Additional common features include rashes, diarrhea, cough and congestion, fevers, pneumonia, sepsis, and other severe bacterial infections. Males with atypical X-SCID may have immune dysregulation and autoimmunity associated with rashes, gastrointestinal malabsorption, other autoimmune conditions, and short stature.

Diagnosis/testing. The diagnosis of X-SCID must be made by lymphocyte counts, lymphocyte cell surface staining and enumeration by flow cytometry, lymphocyte functional tests, and molecular genetic testing. A low absolute lymphocyte count compared to age-matched normal infants is usually observed. The number of T cells is usually very low; B cells are generally present but nonfunctional. The number of NK cells is low or absent. *IL2RG* is the only gene known to be associated with X-SCID. Sequence analysis of the *IL2RG* coding region detects a mutation in more than 99% of affected individuals. Such testing is available on a clinical basis.

Management. Children with X-SCID require prompt immune reconstitution by bone marrow transplantation (BMT) for survival. BMT is usually performed using HLA-matched bone marrow from a relative or haploidentical parental bone marrow depleted of mature T cells. Interim management during immune reconstitution includes treatment of infections and use of immunoglobulin infusions and antibiotics, particularly prophylaxis against *Pneumocystis*. Long-term periodic administration of immunoglobulin may be required in those who fail to develop allogeneic, functional B lymphocytes. Gene therapy using autologous bone marrow stem/progenitor cells retrovirally transduced with a therapeutic gene has been successful for

immune reconstitution for some individuals, but is only considered for those who are not candidates for BMT or have failed BMT. Prenatal diagnosis with molecular genetic testing ensures that searches can be initiated for bone marrow donors before birth and an affected newborn can be treated immediately by BMT.

Genetic counseling. X-SCID is inherited in an X-linked manner. More than one-half of affected males have no family history of early deaths in maternal male relatives. If the mother of a proband is a carrier, the chance of transmitting the disease-causing mutation in each pregnancy is 50%. Male sibs who inherit the mutation will be affected; female sibs who inherit the mutation will be carriers and will not be affected. Males with X-SCID will pass the disease-causing mutation to all of their daughters and none of their sons. Prenatal testing is possible for pregnancies of women who are carriers for a known *IL2RG* mutation.

Diagnosis

Clinical Diagnosis

X-linked severe combined immunodeficiency (X-SCID) is a combined cellular and humoral immunodeficiency resulting from lack of T lymphocytes and nonfunctional B lymphocytes. Natural killer (NK) lymphocytes are most often absent as well. X-SCID should be considered in male infants with recurrent or persistent infections that are severe, that do not respond to ordinary treatment, that are caused by opportunistic pathogens, or that cause failure to thrive [Puck 1999, Belmont & Puck 2001].

Testing

The diagnosis of X-SCID must be made by lymphocyte counts, lymphocyte cell surface staining and enumeration by flow cytometry, lymphocyte functional tests, and molecular genetic testing [Buckley et al 1997; Puck, Middelton et al 1997; Puck 1999].

Lymphocyte count. A low absolute lymphocyte count compared to age-matched normal infants is usually observed (see Table 1) [Buckley et al 1997,Myers et al 2002].

- The number of T cells is usually very low.
- B cells are generally present, but nonfunctional.
- The number of NK cells is low or absent.
- Typical X-SCID is designated $T^{-}B^{+}NK^{-}$.

Table 1. Lymphocyte Counts in Infants with X-linked Severe Combined Immunodeficiency

Cell Type	Lymphocyte Counts			Control Values	
	Average	Range	% of Affected Individuals	Average	Range
Total lymphocytes	<2,000		70%	7,300 [1]	4,000-13,500 [1]
				5,500 [2]	>2,000 [2]
T cells	200	0-800	90-95%	5,500	>1,800
B cells	1,300	0->3,000	5%	800	700-1,300
NK cells	<100		88%	800	

Adapted from Puck 1999, Buckley et al 1997, Buckley et al 1999, Conley et al 1990, Stephan et al 1993, and unpublished data. See also Conley & Stiehm 1996.

1. Six months [Altman 1961]
2. Cord blood [Altman 1961]

Lymphocyte functional tests

- Antibody responses to vaccines and infectious agents are absent.
- T-cell responses to mitogens are lacking.

Immunoglobulin concentrations

- Serum concentrations of IgA and IgM are low.
- IgG is generally normal at birth, but declines as maternally transferred IgG disappears by three months of age.

Thymus. The thymic shadow is absent on chest radiogram.

Molecular Genetic Testing

GeneReviews designates a molecular genetic test as clinically available only if the test is listed in the GeneTests Laboratory Directory *by either a US CLIA-licensed laboratory or a non-US clinical laboratory. GeneTests does not verify laboratory-submitted information or warrant any aspect of a laboratory's licensure or performance. Clinicians must communicate directly with the laboratories to verify information.*—ED.

Molecular Genetic Testing—Gene. *IL2RG* is the only gene known to be associated with X-SCID.

Molecular genetic testing: Clinical uses

- Diagnostic testing
- Carrier testing
- Prenatal diagnosis

Molecular genetic testing: Clinical methods

- **Diagnostic testing**
  - **Sequence analysis.** Sequence analysis of the *IL2RG* coding region is available on a clinical basis.
  - **Targeted mutation analysis.** Southern blot analysis for the detection of large deletions and complex mutations is available on a clinical basis for individuals in whom mutations are not detected by sequence analysis.

Table 2 summarizes molecular genetic testing for this disorder.

Table 2. Molecular Genetic Testing Used in X-Linked Severe Combined Immunodeficiency

Test Method	Mutations Detected	Mutation Detection Rate [1]	Test Availability
Sequence analysis	Missense and nonsense mutations, splice and regulatory regions, insertions	>99%	Clinical Testing
Targeted mutation analysis (Southern blot analysis)	Large deletions and complex mutations		

1. Noguchi et al 1993; Puck et al 1993; Puck 1996; Puck, Middelton et al 1997; Puck, Pepper et al 1997

Interpretation of test results. For issues to consider in interpretation of sequence analysis results, click here.

- **Carrier testing**
  - Testing for known family-specific *IL2RG* mutations is the optimal approach for carrier testing.

- If targeted mutation analysis for a known family-specific mutation is not possible, sequence analysis of the *IL2RG* coding region and splice regions may be used to identify carriers of *IL2RG* mutations.

  Note: Sequence analysis does not detect large deletions and complex mutations in females if direct sequence of genomic DNA is performed.

- If the family-specific mutation is not known and sequence analysis is uninformative, Southern blot analysis may be used to detect large deletions and complex mutations.

- **X-chromosome inactivation studies.** For at-risk females in whom sequence analysis and/or targeted mutation analysis are not an option for carrier testing or are not informative, X-chromosome inactivation studies performed on lymphocytes may help to assess carrier risk.

  Note: Skewed X-chromosome inactivation secondary to presence of an *IL2RG* mutation occurs only in lymphocytes; X-chromosome inactivation, even in the presence of an *IL2RG* mutation, is random in neutrophils and other tissue types [Puck et al 1987, Conley et al 1988, Wengler et al 1993]. Moreover, some females have skewed X-chromosome inactivation by chance. Thus, in order to be valid, X-chromosome inactivation testing to identify carriers of X-SCID must reveal both skewed X-chromosome inactivation in lymphocytes and non-skewed X-chromosome inactivation in another blood lineage such as granulocytes.

Genetically Related Disorders

The only phenotypes associated with mutations in *IL2RG* are X-SCID and atypical X-SCID.

Clinical Description

Natural History

Typical X-SCID. Affected males appear normal at birth. As transplacentally transferred maternal serum antibody concentrations decline, infants with X-SCID are increasingly prone to infection. Most infants come to medical attention between three and six months of age. Infections that initially appear ordinary such as oral thrush, otitis media, respiratory viral infections (e.g., RSV, parainfluenza 3, adenovirus, influenza), and gastrointestinal diseases resulting in diarrhea may only cause concern when they do not respond to usual medical management.

Nearly universal features during the first year of life are failure to thrive, oral/diaper candidiasis, absent tonsils and lymph nodes, recurrent infections, infections with opportunistic organisms such as *Pneumocystis*, and persistence of infections. Additional common features include rashes, diarrhea, cough and congestion, fevers, pneumonia, sepsis, and other severe bacterial infections.

Less common features:

- Disseminated infections (salmonella, varicella, cytomegalovirus, Epstein-Barr virus, herpes simplex virus, BCG, and vaccine strain [live] polio virus)

- Transplacental transfer of maternal lymphocytes to the infant prenatally or during parturition that causes graft-vs-host disease (GVHD) characterized by erythematous skin rashes, hepatomegaly, and lymphadenopathy [Denianke et al 2001]
- Recurrent bacterial meningitis

Atypical X-SCID. Less frequently seen are individuals with mutations that result in production of a small amount of gene product or a protein with residual activity. These individuals may have an atypical disease characterized as $T^{+}B^{+}NK^{-}$. These individuals may have immune dysregulation and autoimmunity associated with rashes, splenomegaly, gastrointestinal malabsorption, other autoimmune conditions, and short stature [DiSanto et al 1994; Schmalstieg et al 1995; Puck, unpublished].

Genotype-Phenotype Correlations

Most disease-causing mutations are functionally null. Individuals with rare missense or regulatory mutations may have atypical X-SCID.

Nomenclature

Before the T-cell defect in X-SCID was recognized, X-SCID was included in the designation "Swiss-type agammaglobulinemia." This term is no longer used.

Prevalence

The incidence of X-SCID is unknown, but is estimated to be at least 1/50,000 -100,000 births. All ethnic groups are affected in equal frequency. Because of population structure, X-SCID may account for a larger proportion of individuals with all types of SCID in the United States than in Europe.

Differential Diagnosis

For current information on availability of genetic testing for disorders included in this section, see GeneTests Laboratory Directory. —ED.

Severe combined immunodeficiency (SCID) can be classified by the nature of T, B, and NK lymphocyte numbers and function (Table 3) [Buckley 2004]. Presence of each subclass of lymphocytes in most individuals of each genotype is indicated by (+); absence by (–). X-SCID is the most commmon form of SCID. The clinical presentation of X-SCID, *JAK3*-SCID and *IL7RA*-SCID is identical. In X-SCID, only males are affected; in *JAK3*- and *IL7R1*-SCID, both males and females are affected.

Table 3. Types of SCID

Disease Name	Gene	Lymphocyte Phenotype			Inheritance	Comments
		T	B	NK		
X-SCID	*IL2RG*	–	+	–	XLR	Majority of individuals with SCID
JAK3-SCID	*JAK3*				AR	
IL7RA-SCID	*IL7RA*	–	+	+	AR	
CD45 deficiency	*CD45*	–	+	–	AR	
ADA deficiency	*ADA*	–	–	–	AR	
RAG-deficient SCID	*RAG1*	–	–	+	AR	
	RAG2					
SCID Athabascan	*ARTEMIS*					Athabascan-speaking Native Americans (Navajo, Apache, and others) (10% carrier rate); also other ethnicities

Other X-linked immunodeficiencies includeX-linked agammaglobulinemia, Wiskott-Aldrich syndrome, X-linked hyper-IgM syndrome, X-linked lymphoproliferative disease, NEMO (X-linked ectodermal dysplasia with varying immunodeficiency) (see Incontinentia Pigmenti), IPEX (autoimmunity, polyendocrinopathy, enteropathy), chronic granulomatous disease (CGD), and properdin deficiency.

Human immunodeficiency virus (HIV). Infants with HIV may also have recurrent and opportunistic infections and failure to thrive. They have evidence of HIV virus by p24 antigen testing or PCR testing. In contrast to SCID, T cells are generally present.

Management

Evaluations at Initial Diagnosis to Establish the Extent of Disease

- History, including family history, growth and development, localized and generalized infectious processes, such as diarrhea, failure to thrive, pneumonia, sepsis, viral and fungal infections
- CBC and differential count to document absolute lymphocyte count
- Flow cytometric determination of T-cell, B-cell, NK-cell numbers
- In vitro mitogenesis assay of patient mononuclear cells stimulated with mitogens (PHA, ConA, PWM) and soluble antigens (Candida antigen, tetanus toxoid)

Treatment of Manifestations

- Diagnosis of X-SCID demands emergent treatment to provide a functional immune system (see Prevention of Primary Manifestations).
- Interim management includes treatment of infections and use of immunoglobulin infusions and antibiotics, particularly prophylaxis against *jirovecii* (formerly *Pneumocystis carinii*).

Prevention of Primary Manifestations

Bone marrow transplantation (BMT). Prompt immune reconstitution is required for survival of children with X-SCID [Myers et al 2002]. BMT was first successful in 1968 and remains the standard means of immune reconstitution. It is estimated that over 90% of infants with X-SCID can be successfully treated with BMT [Myers et al 2002, Antoine et al 2003]. Although

many centers have expertise in performing transplantation in individuals with malignancy, the special issues arising in transplantation for X-SCID require immunodeficiency specialists to be involved for an optimal outcome.

- HLA-matched bone marrow transplantation from a relative is preferred; however, most individuals lack a matched, related donor.
- For infants who do not have a matched, related donor, haploidentical parental bone marrow that has been depleted of mature T cells can be used [Buckley et al 1999]. In this technique, the bone marrow is depleted of T cells in order to remove mismatched T cells, which would react against the baby's tissues and cause GVHD.
- Matched, unrelated donor transplantation of bone marrow or cord blood stem cells has been used in some transplantation centers, but GVHD is a significant problem.
- In addition, some centers use peripherally harvested hematopoietic stem cells for transplants.

Mismatched T cells would react against the baby's tissues and cause GVHD. Cord blood from normal infants is now being banked; frozen cells can be thawed and used as in other unrelated donor transplants.

The best timing for BMT is immediately after birth because young infants are less likely to have had serious infections or failure to thrive than older infants. Younger infants also have more rapid engraftment, fewer post-transplantation infections, less GVHD, and shorter hospitalizations than those in whom BMT is delayed [Kane et al 2001, Myers et al 2002].

Complications following BMT in some individuals include GVHD, failure to make adequate antibodies requiring long-term immunoglobulin replacement, late loss of T cells, and lymphocyte dysregulation.

The oldest surviving individuals with X-SCID received HLA-matched related BMT and are now in their 30s and healthy.

Administration of immunoglobulin. Long-term periodic administration of immunoglobulin may be required in those who fail to develop allogeneic, functional B lymphocytes.

Gene therapy. Gene therapy performed using autologous bone marrow stem/progenitor cells retrovirally transduced with a therapeutic gene has also been successful in reconstituting the immune system in individuals with X-SCID [Hacein-Bey-Abina et al 2002]; however, the youngest two plus an additional older infant of the first ten infants treated in a French study have developed leukemia as a result of retroviral insertional mutagenesis. Infants with X-SCID in England were also treated successfully with gene therapy with no occurrence of leukemia to date [Gaspar et al 2004]. Two older adolescents did not experience immune reconstitution following attempted gene transfer therapy [Thrasher et al 2005]. Gene therapy is currently only considered for those who are not candidates for BMT or have failed BMT [Gansbacher 2003].

Prevention of Secondary Complications

- Only CMV-negative, irradiated (1500 to 5000 RADS) blood products should be used.
- Immunizations should be deferred until after restoration of immunocompetence.

Surveillance

After successful bone marrow transplantation, routine evaluation of affected boys every six to 12 months is appropriate to monitor growth, immune and lung function, and gastrointestinal and dermatologic issues.

Agents/Circumstances to Avoid

- Individuals with X-SCID should not receive live vaccines.
- Transfusion of non-irradiated blood products must be avoided.

Testing of Relatives at Risk

In one study, most couples at risk of having an affected pregnancy desired prenatal testing whether or not termination of pregnancy was a consideration [Puck, Middelton et al 1997]. Prenatal testing helped families and professionals prepare for optimal treatment of an affected newborn: bone marrow transplantion centers were chosen, HLA testing of family members and the prenatal sample was carried out, and a search for a marrow donor could be initiated.

Therapies Under Investigation

Search ClinicalTrials.gov for access to information on clinical studies for a wide range of diseases and conditions.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members. This section is not meant to address all personal, cultural, or ethical issues that individuals may face or to substitute for consultation with a genetics professional. To find a genetics or prenatal diagnosis clinic, see the GeneTests Clinic Directory.

Mode of Inheritance

X-SCID is inherited in an X-linked manner.

Risk to Family Members

Parents of a proband

- The father of an affected male will not have the disease or be a carrier of the mutation.
- In a family with more than one affected individual, the mother of an affected male is an obligate carrier.
- If a woman has more than one affected son and the disease-causing mutation cannot be detected in her DNA extracted from her leukocytes, she has germline mosaicism. Female germline mosaicism has been documented in X-SCID [O'Marcaigh et al 1997].
- If pedigree analysis reveals that the proband is the only affected family member, the mother may be a carrier or the affected male may have a *de novo* gene mutation, in which case the mother is not a carrier. New mutations follow Haldane's rule, accounting for one-third of cases.
- More than one-half of affected males have no family history of early deaths in maternally related affected males [Puck, Pepper et al 1997]. If an affected male

represents a single case in the family, several possibilities regarding his mother's carrier status and carrier risks of extended family members need to be considered:

- He has a *de novo* disease-causing mutation in the *IL2RG* gene and his mother is not a carrier.
- His mother has a *de novo* disease-causing mutation in the *IL2RG* gene, either (a) as a "germline mutation" (i.e., occurring at the time of her conception and thus present in every cell of her body); or (b) as "germline mosaicism" (i.e., occurring in a certain percentage of her germ cells only).
- His maternal grandmother or grandfather has a *de novo* disease-causing mutation in the *IL2RG* gene, which may have been present only in the germline.

Direct DNA testing can often determine the family member in whom the mutation initially arose. Determining the family member in whom a *de novo* mutation arose is important for determining which branches of the family are at risk for X-SCID.

Sibs of a proband

- The risk to sibs depends upon the carrier status of the mother.
- If the mother is a carrier, the chance of transmitting the disease-causing mutation in each pregnancy is 50%. Male sibs who inherit the mutation will be affected; female sibs who inherit the mutation will be carriers and will not be affected.
- Germline mosaicism has been demonstrated in this condition [O'Marcaigh et al 1997]. Thus, even if the disease-causing mutation has not been identified in the mother's leukocytes, the sibs are still at increased risk.

Offspring of a proband. Males with X-SCID will pass the disease-causing mutation to all of their daughters and none of their sons.

Other family members of the proband. The proband's maternal female relatives may be at risk of being carriers, and their offspring, depending upon their gender, may be at risk of being carriers or of being affected.

Carrier Detection

Carrier testing of at-risk female relatives is available on a clinical basis. See Molecular Genetic Testing section.

Related Genetic Counseling Issues

Family planning. The optimal time for determination of genetic risk, clarification of carrier status, and discussion of the availability of prenatal testing is before pregnancy.

DNA banking. DNA banking is the storage of DNA (typically extracted from white blood cells) for possible future use. While DNA banking may not be necessary if a disease-causing mutation in the *IL2RG* gene is identified as causing X-SCID in a family, it may be helpful for other types of SCID. Because it is likely that testing methodology and our understanding of genes, mutations, and diseases will improve in the future, consideration should be given to banking DNA of affected individuals. DNA banking is particularly relevant in situations in which the sensitivity of currently available testing is less than 100%. See DNA Banking for a list of laboratories offering this service.

Carrier testing of minors. Carrier testing of at-risk female relatives under the age of 18 years warrants consideration of specific issues, including the minor's experience (or lack of experience) with the disorder, the implications of the test results, the significance that she attributes to them, and the likelihood of her becoming a mother in the near future. The possible benefits of early testing and disclosure must be weighed against the potential harm of loss of autonomy [Fanos, Davis et al 2001; Fanos & Puck 2001]. It is important to assess the minor's ability to understand options and consequences. A minor who can project into the future and has a stable set of values with which to weigh options is the best candidate to participate in determining whether or not to undergo X-SCID carrier testing. A current NIH study is investigating the effects of learning carrier status in females between the ages of 12 and 18 years who decide to undergo X-SCID carrier testing.

Prenatal Testing

Molecular genetic testing. Prenatal testing is possible for pregnancies of women who are carriers for X-SCID [Puck, Middelton et al 1997]. The usual procedure is to perform chromosome analysis for sex determination on fetal cells obtained by chorionic villus sampling (CVS) at about 10-12 weeks' gestation or by amniocentesis at about 15-18 weeks' gestation. If the karyotype is 46,XY and if the disease-causing *IL2RG* mutation has been identified in a family member, DNA from fetal cells can be analyzed for the known disease-causing mutation.

Note: Gestational age is expressed as menstrual weeks calculated either from the first day of the last normal menstrual period or by ultrasound measurements.

Percutaneous umbilical blood sampling (PUBS). When the family-specific mutation is not known, fetal blood sampling is considered in some centers. Fetal blood is analyzed for lymphoctyopenia, low numbers of T cells, and poor T-cell blastogenic responses to mitogens, all of which can be definitively demonstrated in affected fetuses by 17 weeks of gestation; however, caution is necessary as maternal blood contamination can make test results look falsely normal. Involvement of experienced high-risk perinatologists, genetics experts, and immunologists is advised.

Molecular Genetics

Information in the Molecular Genetics tables is current as of initial posting or most recent update. —ED.

Table A. Molecular Genetics of X-Linked Severe Combined Immunodeficiency

Gene Symbol	Chromosomal Locus	Protein Name
IL2RG	Xq13	Cytokine receptor common gamma chain

Data are compiled from the following standard references: Gene symbol from HUGO; chromosomal locus, locus name, critical region, complementation group from OMIM; protein name from Swiss-Prot.

Table B. OMIM Entries for X-Linked Severe Combined Immunodeficiency

300400	SEVERE COMBINED IMMUNODEFICIENCY, X-LINKED; SCIDX1
308380	INTERLEUKIN 2 RECEPTOR, GAMMA; IL2RG

Table C. Genomic Databases for X-Linked Severe Combined Immunodeficiency

Gene Symbol	Locus Specific	Entrez Gene	HGMD
IL2RG	IL2RG	3561 (MIM No. 308380)	IL2RG

For a description of the genomic databases listed, click here.

Normal allelic variants: The gene spans 4.5 kb of genomic DNA. The coding sequence of 1,124 nucleotides is divided into eight exons. There are no common normal allelic variants.

Pathologic allelic variants: Over 300 mutations have been identified spanning all eight exons of the gene. They are primarily single-nucleotide changes or changes of a few nucleotides, small insertions, deletions, and splice defects. Mutation hot spots in the *IL2RG* are reported [Puck 1996; Puck, Pepper et al 1997; Puck 1997]. (For more information, see Genomic Databases table above.)

Normal gene product: The normal gene product is the common gamma chain, or gamma-c, which is a transmembrane protein in the cytokine receptor gene superfamily. It is a component of multiple cytokine receptors on the surface of lymphocytes and other hematopoietic cells, including the receptors for IL-2, -4, -7, -9, -15, and 21.

Abnormal gene product: Although over two-thirds of mutations result in lack of protein expression, truncated gamma-c proteins or gamma-c proteins bearing amino acid substitutions, insertions, or deletions have been described and are nonfunctional.

Resources

GeneReviews provides information about selected national organizations and resources for the benefit of the reader. GeneReviews is not responsible for information provided by other organizations. Information that appears in the Resources section of a GeneReview is current as of initial posting or most recent update of the GeneReview. Search GeneTests*for this disorder and select* Resources *for the most up-to-date Resources information.*—ED.

National Library of Medicine Genetics Home Reference
X-linked severe combined immunodeficiency

Immune Deficiency Foundation
40 W Chesapeake Ave; Suite 308
Towson, MD 21204
Phone: 800-296-4433; 410-321-6647
Fax: 410-321-9165
Email: idf@primaryimmune.org
www.primaryimmune.org

International Patient Organisation for Patients with Primary Immunodeficiencies
Firside Main Road
Downderry
Cornwall PL11 3LE
United Kingdom
Email: david@pia.org.uk
http://ipopi.org/

Jeffrey Modell Foundation/National Primary Immunodeficiency Resource Center
747 Third Avenue, 34A
New York, NY 10017
Phone: 800-533-3844; 212-819-0200
Fax: 212-764-4180
Email: info@jmfworld.org
www.info4pi.org

Primary Immunodeficiency Diseases Registry (PIDR)
Phone: 800-296-4433
Primary Immunodeficiency Registry

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Medical Genetic Searches: A specialized PubMed search designed for clinicians that is located on the PubMed Clinical Queries page. PubMed

Published Statements and Policies Regarding Genetic Testing

No specific guidelines regarding genetic testing for this disorder have been developed.

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Chapter Notes

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