GENEReviews

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IPEX Syndrome

[*X-Linked Autoimmunity-Allergic Dysregulation Syndrome (XLAAD); X-Linked Syndrome of Polyendocrinopathy, Immune Dysfunction and Diarrhea (XPID); Immunodeficiency, Polyendocrinopathy, and Enteropathy, X-Linked Syndrome*]

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Summary

Disease characteristics. IPEX syndrome is characterized by the development of overwhelming systemic autoimmunity in the first year of life resulting in the commonly observed triad of watery diarrhea, eczematous dermatitis, and endocrinopathy seen most commonly as insulin-dependent diabetes mellitus. Most children have other autoimmune phenomena including Coombs positive anemia, autoimmune thrombocytopenia, autoimmune neutropenia, and tubular nephropathy The majority of affected males die within the first year of life of either metabolic derangements or sepsis; a few survive into the second or third decade.

Diagnosis/testing. Diagnosis is based on clinical findings. *FOXP3* is the only gene currently known to be associated with IPEX syndrome. Approximately 50% of males with IPEX syndrome have mutations identified in *FOXP3*. Molecular genetic testing is clinically available.

Management. *Treatment of manifestations:* immunosuppressive agents (e.g., cyclosporin A, FK506) alone or in combination with steroids; sirolimus (rapamycin) for persons in whom FK506 therapy is toxic or ineffective; granulocyte colony stimulating factor (G-CSF, filgrastim) for autoimmune neutropenia; nutritional support; standard treatment of diabetes mellitus and autoimmune thyroid disease. If performed early, bone marrow transplantation (BMT) using non-myeloablative conditioning regimens can resolve clinical symptoms. *Prevention of primary manifestations:* BMT. *Prevention of secondary complications:* prophylactic antibiotic therapy for those with autoimmune neutropenia or recurrent infections; aggressive management of the dermatitis with topical steroids and anti-inflammatory agents to prevent infection. *Surveillance:* periodic evaluation of complete blood count, glucose tolerance, thyroid function, kidney function, and liver function for evidence of autoimmune disease. *Testing of relatives at risk:* if the family-specific mutation is known, *FOXP3* sequence analysis in at-risk males immediately after birth to permit early diagnosis and BMT before significant organ damage occurs; otherwise, monitoring at-risk males for symptoms to enable early diagnosis and treatment.

Genetic counseling. IPEX syndrome is inherited in an X-linked manner. The risk to sibs of the proband depends on the carrier status of the mother. If the mother of the proband is a carrier, the chance of transmitting the disease-causing mutation in each pregnancy is 50%. Males who inherit the mutation will be affected; females who inherit the mutation are carriers and will not be affected. Affected males pass the disease-causing mutation to all of their daughters and none of their sons. Prenatal testing for pregnancies at risk is possible for families in which the disease-causing mutation has been identified.

Diagnosis

Clinical Diagnosis

The term IPEX is a mnemonic for **i**mmune dysregulation, **p**olyendocrinopathy, **e**nteropathy, **X**-linked. A clinical triad resulting from widespread autoimmunity suggests a diagnosis of IPEX syndrome:

- **Endocrinopathy,** most commonly type 1 diabetes mellitus with onset in the first months or years of life. Autoimmune thyroid disease leading to hypothyroidism or hyperthyroidism has also been observed [Wildin et al 2002, Gambineri et al 2003].
- **Enteropathy** that manifests as chronic watery diarrhea. Onset is typically in the first months of life; villous atrophy with a mononuclear cell infiltrate (activated T cells) in the lamina propria is the most common finding in biopsy.
- **Dermatitis,** most commonly eczematous. Erythroderma, exfoliative dermatitis, psoriasis-like lesions, and pemphigous nodularis have also been observed [Nieves et al 2004, McGinness et al 2006].

Testing

No laboratory findings specifically identify affected individuals. Evidence of **immune dysregulation** manifested by the following is suggestive of the syndrome:

- Elevated serum concentration of immunoglobulin E (IgE)
- Autoantibodies to pancreatic islet antigens, thyroid antigens, small bowel mucosa
- Autoimmune anemia, thrombocytopenia, and/or neutropenia
- Intermittent eosinophilia
- Decreased numbers of FOXP3-expressing T cells in peripheral blood determined by flow cytometry

Normal findings

- Serum concentration of IgG, IgM, and IgA
- Circulating leukocyte counts
- T- and B-cell subsets [Peake et al 1996, Ferguson et al 2000, Wildin et al 2002]. Occasionally an expanded population of cells expresses markers of T-cell activation and commitment (e.g., HLA-DR, CD45RO).
- Neutrophil function
- Serum concentration of complement
- In vitro proliferative responses of T lymphocytes to common mitogens (e.g., phytohemagglutinin, cross-linking of CD3) or activation with specific antigen (e.g., tetanus, candida). Peripheral blood mononuclear cells from individuals with IPEX syndrome show an excess production of the Th2 cytokines IL-4, IL-5, IL-10, and

IL-13 and decreased production of the Th1 cytokine interferon-γ [Chatila et al 2000, Nieves et al 2004].

Note: Caution must be exercised when interpreting data regarding the immune responses of individuals with IPEX syndrome as many are on immunosuppressants at the time of diagnosis.

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. *FOXP3* is the primary gene associated with IPEX syndrome.

Other loci. Mutations in *IL2RA* (also known as *CD25*) have been identified in two persons with an IPEX syndrome-like phenotype [Roifman 2000, Caudy et al 2007]. The mutations were inherited in an autosomal recessive manner.

Owen et al (2003) suggest the possibility of an additional autosomal locus. Among the males who lack *FOXP3* mutations, approximately half have low *FOXP3* mRNA expression levels and low numbers of FOXP3-expressing cells in peripheral blood [Torgerson, unpublished results], suggesting that defects in other genes or gene products, possibly in the same pathway as *FOXP3*, may cause a similar phenotype.

Clinical testing

- **Sequence analysis** of all exons, exon/intron boundaries, and the first polyadenylation site detects mutations in approximately 50% of males with the IPEX syndrome phenotype [Gambineri & Torgerson, unpublished results].

Table 1 summarizes molecular genetic testing for this disorder.

Table 1. Molecular Genetic Testing Used in IPEX Syndrome

Test Method	Mutations Detected	Mutation Detection Frequency [1]	Test Availability
Sequence analysis	*FOXP3* sequence variants	>50%	Clinical Testing

1. Proportion of affected individuals with a mutation(s) as classified by test method

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

Testing Strategy

Confirmation of the diagnosis in a proband requires the following:

- Assessment of general immune function including blood cell counts and white blood cell differential
- Analysis of T- and B-cell subsets
- Measurement of serum concentration of immunoglobulins including IgE
- Screening for autoimmune liver and renal disease with measurement of serum concentration of aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), and creatinine; urinalysis

- Flow cytometry to evaluate regulatory T cells for expression of both FOXP3 and CD25 (helpful as an initial screen for the disorder)
- Sequence analysis of *FOXP3* for definitive diagnosis

Carrier testing for at-risk relatives requires prior identification of the disease-causing mutations in the family.

Note: Carriers are heterozygotes for an X-linked disorder and could develop clinical findings related to the disorder.

Prenatal diagnosis for at-risk pregnancies requires prior identification of the disease-causing mutation in the family.

Genetically Related (Allelic) Disorders

No other phenotypes are associated with mutations in *FOXP3*.

No contiguous gene deletion syndromes that include deletion of *FOXP3* have been reported.

Clinical Description

Natural History

Males. IPEX syndrome is generally considered to be a syndrome of neonatal polyendocrinopathy [Dotta & Vendrame 2002] and neonatal enteropathy [Ruemmele et al 2004]. The most common presentation of IPEX syndrome is severe watery diarrhea, type 1 insulin-dependent diabetes mellitus, and dermatitis in males younger than age six months. IPEX syndrome can also present with this triad in a somewhat older child, often accompanied by other autoimmune phenomena.

The enteropathy of IPEX syndrome, often the first symptom, is present in virtually all cases. Watery diarrhea, which may at times also have mucus and blood, leads to malabsorption, failure to thrive, and cachexia, often requiring the use of total parenteral nutrition (TPN). Food allergies are common [Torgerson et al 2007].

Endocrinopathy is present in most (not all) children. Type 1 diabetes mellitus with onset in the first months of life is the most common endocrine manifestation. Thyroid disease (most often hypothyroidism) is also common [Wildin et al 2002, Gambineri et al 2003].

The dermatitis is most frequently eczematous, erythroderma, psoriasiform dermatitis, and pemphigus nodularis have also been described [Nieves et al 2004, McGinness et al 2006].

The outcome of IPEX syndrome is universally poor. Most children die within the first or second year of life secondary to metabolic derangements, severe malabsorption, or sepsis, although improvements to immunosuppressive regimens and bone marrow transplantation (BMT) have improved survival to a degree [Kobayashi et al 2001, Levy-Lahad & Wildin 2001, Taddio et al 2007]. A somewhat milder course was reported in the original family described by Powell et al (1982): two affected males survived into the second and third decades.

Most affected individuals have other autoimmune phenomena including Coombs positive anemia, autoimmune thrombocytopenia, autoimmune neutropenia, and tubular nephropathy. Lymphadenopathy, splenomegaly, and alopecia have also been reported [Hattevig et al 1982, Powell et al 1982, Jonas et al 1991, Satake et al 1993, Di Rocco & Marta 1996, Peake et al 1996, Ferguson et al 2000].

In a series of more than 50 males with *FOXP3* mutations, half had serious infections including sepsis, meningitis, pneumonia, and osteomyelitis [Gambineri & Torgerson, unpublished results]. The most common pathogens were *Staphylococcus,Enterococcus,* cytomegalovirus, and *Candida.* The reason for the increased susceptibility to infections is unclear. It may be a direct function of the genetic defect or the decreased barrier function of the skin and gut. Some infections may be secondary to immunosuppressive therapy, although many occur prior to the initiation of therapy.

Female carriers of *FOXP3* mutations are generally healthy, although one female carrier had an expression level of *FOXP3* mRNA intermediate between the very low level observed in her affected son and the normal level in a control [Bennett et al 2001]. One carrier female has type I diabetes mellitus. X-chromosome inactivation studies performed on another carrier female demonstrated that normal and mutated *FOXP3* alleles are equally expressed in peripheral blood mononuclear cells [Tommasini et al 2002].

Genotype-Phenotype Correlations

As a rule, persons with mutations that abrogate expression of functional FOXP3 protein (nonsense, frameshift, or splicing mutations) have severe, early-onset IPEX syndrome.

Mutation of the first polyadenylation signal of the gene with an otherwise normal gene sequence leads to low expression levels of normal *FOXP3* mRNA and generally results in severe, early-onset disease [Bennett et al 2001; Torgerson, unpublished results]. In one of the two kindreds with this type of mutation, two brothers had mild, late-onset disease and lived into the second and third decades of life, suggesting that other modifying factors affecting mRNA stability may be the cause of the observed variability [Powell et al 1982].

A number of affected individuals have missense (point) mutations that result in expression of mutant proteins, some of which appear to be functionally hypomorphic and are associated with a milder clinical phenotype [De Benedetti et al 2006; Torgerson, unpublished results].

Prevalence

IPEX syndrome is a rare; no accurate estimates of prevalence have been published. It is, however, likely to be underreported judging by the prevalence of other syndromes (e.g., Wiskott-Aldrich syndrome) caused by mutations in similarly-sized genes located nearby on the X chromosome.

Differential Diagnosis

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

Other syndromes with neonatal diabetes mellitus:

- Transient neonatal diabetes mellitus [OMIM 601410] caused by an imprinting disorder involving chromosome region 6q24
- Pancreatic hypoplasia or agenesis caused by recessive insulin promoter factor-1 mutations [OMIM 260370, 600733]
- Dominant pancreatic hypoplasia associated with congenital heart disease [OMIM 600001]
- A presumed recessive disorder or imprinting defect causing an islet cell developmental defect [OMIM 600089]

Other syndromes of polyendocrinopathy

- Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) (APS I) [OMIM 240300, 607358] (autoimmune polyglandular failure)
- Schmidt syndrome (APS II/III) [OMIM 269200]
- Autoimmune lymphoproliferative syndrome (ALPS) [OMIM 134637, 134638, 601762, 601859, 603909, 607271] characterized by hemolytic anemia, thrombocytopenia, and splenomegaly; type 1 diabetes mellitus; and thyroid disease.

Other syndromes with immunodeficiency

- Wiskott-Aldrich syndrome [OMIM 300392, 301000] (thrombocytopenia and eczema)
- Omenn syndrome (also known as familial reticuloendotheliosis with eosinophilia or severe combined immunodeficiency [SCID] with hypereosinophilia, caused by mutations in the genes *DCLRE1C,RAG1, RAG2*) [OMIM 179615, 179616, 603554]

Other syndromes with protracted diarrhea in infancy [Sherman et al 2004]

- Microvillus inclusion disease
- Tufting enteropathy
- Autoimmune enteropathy

Management

Evaluations Following Initial Diagnosis

To establish the extent of disease in an individual diagnosed with IPEX syndrome, the following evaluations are recommended:

- **Endocrine.** Glucose tolerance test, thyroid function tests, and autoantibodies to pancreatic islet antigens and thyroid antigens
- **Hematologic.** Coombs test
- **Immunologic.** Serum IgG, IgM, IgA, and IgE concentrations
- **Renal**
- **Nutrition assessment**

Treatment of Manifestations

Monitor fluid intake to assure adequate intravascular volume.

Use of nutritional support, including TPN or elemental or low-carbohydrate-containing formula if necessary, can be beneficial [Sherman et al 2004].

Follow the standard treatment protocols for diabetes mellitus and autoimmune thyroid disease.

The most effective treatment for the autoimmune enteropathy is immunosuppressive agents (i.e., cyclosporin A and FK506) that primarily target T-cell activation either alone or in combination with steroids [Di Rocco & Marta 1996]. Toxicity and increased susceptibility to infection related to these calcineurin inhibitors reduce the potential for long-term amelioration of symptoms for most individuals. Sirolimus (rapamycin) has been successfully used in patients for whom FK506 was either uneffective or toxic [Bindl et al 2005]. The efficacy of sirolimus for the enteropathy and mechanism of action make it an excellent choice for first-line therapy of IPEX syndrome.

In persons with autoimmune neutropenia, granulocyte colony stimulating factor (G-CSF, filgrastim) is usually beneficial.

In one person who developed pemphigus nodularis, use of rituximab improved pemphigus and other IPEX syndrome-associated symptoms [McGinness et al 2006].

In severe cases in which other therapies fail, cytotoxic drugs or biologic agents that target T cells may be beneficial, as demonstrated by the patient who had complete symptomatic remission during his conditioning regimen of anti-thymocyte globulin, busulfan, and cyclophosphamide for BMT [Baud et al 2001].

BMT offers the only potential cure for IPEX syndrome. Early attempts at BMT using myeloablative conditioning regimens met with only limited success because of transplant-related mortality and other complications related to the underlying disease [Baud et al 2001]. Recent approaches using non-myeloablative conditioning regimens have markedly improved outcomes and survival [Burroughs et al 2007, Lucas et al 2007, Rao et al 2007]. While generally less toxic, these reduced-intensity conditioning regimens still appear to generate long-term, stable engraftment of a regulatory T-cell population and, if performed early, can resolve clinical symptoms [Torgerson, unpublished data].

Prevention of Primary Manifestations

BMT is currently the only cure for IPEX syndrome; the degree of symptomatic remission may depend on use of BMT prior to irreversible damage to target organs such as pancreatic islet cells and thyroid.

Prevention of Secondary Complications

Patients with autoimmune neutropenia or recurrent infections resulting from severe eczema may benefit from prophylactic antibiotic therapy to decrease the risk of severe infectious complications.

Aggressive management of dermatitis with topical steroids and anti-inflammatory agents can help to prevent infections from pathogens that enter as a result of the poor barrier function of the skin.

Surveillance

Appropriate surveillance includes periodic evaluation of complete blood count, thyroid function, glucose tolerance, kidney function (measurement of serum concentration of BUN, creatinine), and liver function (measurement of serum concentration of AST, ALT) for evidence of autoimmune disease.

Testing of Relatives at Risk

FOXP3 sequence analysis in at-risk males in a family with a known disease-causing mutation immediately after birth enables early diagnosis and BMT in affected males before significant organ damage occurs. If the disease-causing mutation is not known, monitoring at-risk males for early-onset diarrhea, diabetes mellitus, thyroid dysfunction, and autoimmune hematologic manifestations can allow early diagnosis of affected males.

See Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.

Therapies Under Investigation

Search ClinicalTrials.gov for access to information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

Other

There is no evidence that initiation of immunosuppressive therapy prior to the onset of symptoms prevents the primary manifestations of IPEX syndrome.

Genetics clinics are a source of information for individuals and families regarding the natural history, treatment, mode of inheritance, and genetic risks to other family members as well as information about available consumer-oriented resources. See the GeneTests Clinic Directory.

Support groups have been established for individuals and families to provide information, support, and contact with other affected individuals. The Resources section (below) may include disease-specific and/or umbrella support organizations.

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

IPEX syndrome 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 nor will he be a carrier of the disease-causing mutation.
- In a family with more than one affected individual, the mother of an affected male is an obligate carrier.
- The percentage of affected males who have no family history of IPEX syndrome is not known. If an affected male represents a simplex case, the following possibilities regarding his mother's carrier status and carrier risks of extended family members need to be considered:
  - The mother is not a carrier and the affected male has a *de novo* disease-causing mutation.
  - The mother is a carrier of a disease-causing mutation.
- Female carriers of IPEX syndrome are asymptomatic.

Sibs of a proband

- The risk to the sibs depends on the carrier status of the mother.

- If the mother of the proband has a disease-causing mutation, the chance of transmitting it in each pregnancy is 50%. Male sibs who inherit the mutation will be affected; female sibs who inherit the mutation are carriers and will not be affected.
- If the proband presents a simplex case and if his mother's carrier status is unknown, her risk of being a carrier is unknown.
- Germline mosaicism has not been observed.

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

Other family members. The proband's maternal aunts and their offspring may be at risk of being carriers or of being affected (depending their gender, family relationship, and the carrier status of the proband's mother.

Carrier Detection

- Carrier testing of at-risk female relatives is available on a clinical basis if the mutation has been identified in the proband.
- X-chromosome inactivation is random [Tommasini et al 2002] and therefore not useful in carrier detection.

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. 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 Testing for a list of laboratories offering DNA banking.

Prenatal Testing

Prenatal testing is possible for pregnancies of women who are carriers if the *FOXP3* mutation has been identified in a family member. The usual procedure is to determine the fetal sex by performing chromosome analysis on fetal cells obtained by chorionic villus sampling (CVS) at approximately ten to 12 weeks' gestation or by amniocentesis usually performed at approximately 15-18 weeks' gestation. If the karyotype is 46,XY, 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.

Preimplantation genetic diagnosis (PGD) may be available for families in which the disease-causing mutation has been identified in an affected family member. For laboratories offering PGD, see Testing.

Molecular Genetics

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

Table A. Molecular Genetics of IPEX Syndrome

Gene Symbol	Chromosomal Locus	Protein Name
FOXP3	Xp11.2-q13.3	Forkhead box protein P3

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 IPEX Syndrome

300292	FORKHEAD BOX P3; FOXP3
304790	IMMUNODYSREGULATION, POLYENDOCRINOPATHY, AND ENTEROPATHY, X-LINKED; IPEX

Table C. Genomic Databases for IPEX Syndrome

Gene Symbol	Locus Specific	HGMD
FOXP3	FOXP3	FOXP3

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

Note: HGMD requires registration.

Normal allelic variants: 11 translated exons

Pathologic allelic variants: The majority of disease-causing mutations in *FOXP3* are either frameshift mutations that lead to a foreshortened protein product or missense mutations within the C-terminal forkhead DNA-binding domain. Some mutations also affect the leucine zipper and a transrepression domain located within the N-terminal proline-rich region of the protein, demonstrating the essential role for these domains in FOXP3 function [Chatila et al 2000, Lopes et al 2006].

Normal gene product: The *FOXP3* gene encodes forkhead box protein P3 (FOXP3), a forkhead DNA-binding protein that is expressed primarily in CD4+CD25+ regulatory T cells. The protein comprises 431 amino acids and has important functional domains including an N-terminal proline-rich domain that contains sequences essential for the gene regulatory function of FOXP3, a C2H2 zinc finger and leucine zipper (both conserved structural motifs involved in protein-protein interactions) in the central portion, and a forkhead DNA-binding domain at the C terminus from which it derives its name (forkhead box) [Ochs et al 2005, Lopes et al 2006]. A putative nuclear localization signal is located at the C-terminal portion of the forkhead domain [Lopes et al 2006].

Proteins bearing forkhead DNA-binding motifs comprise a large family of related molecules that play diverse roles in enhancing or suppressing transcription from specific binding sites. Several members of this protein family are involved in patterning and development [Gajiwala & Burley 2000]. FOXP3 is expressed primarily in lymphoid tissues (thymus, spleen, and lymph nodes), particularly in CD4+ CD25+ regulatory T lymphocytes. In mice, it is required for the development and suppressive function of this important regulatory T-cell population [Fontenot et al 2003, Hori et al 2003, Khattri et al 2003, Sakaguchi 2003]. In humans, it is not expressed at baseline in CD4+ CD25- or CD8+ T cells but is expressed upon T-cell activation [Gavin et al 2006, Allan et al 2007]. The significance of this inducible expression in effector T cells is unknown.

Abnormal gene product: The FOXP3 protein is absent in individuals with IPEX syndrome; some individuals with *FOXP3* point mutations express a protein that appears to have decreased function, thereby leading to a milder form of the disease [De Benedetti et al 2006; Gambineri & Torgerson, unpublished observations].

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.

American Diabetes Association
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Alexandria VA 22311
Phone: 800-DIABETES (800-342-2382); 703-549-1500
Fax: 703-549-6995
Email: AskADA@diabetes.org
www.diabetes.org

Diabetes UK
10 Parkway
London NW1 7AA
United Kingdom
Phone: 020 7424 1000
Fax: 020 7424 1001
Email: info@diabetes.org.uk
www.diabetes.org

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
Phone: 44 01503 250 668
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

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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

Revision History

- 12 December 2007 (me) Comprehensive update posted to live Web site
- 27 April 2006 (cd) Revision: *FOXP3* testing available clinically
- 19 October 2004 (me) Review posted to live Web site
- 11 February 2004 (mh) Original submission