Understanding congenital athymia

Information for healthcare providers

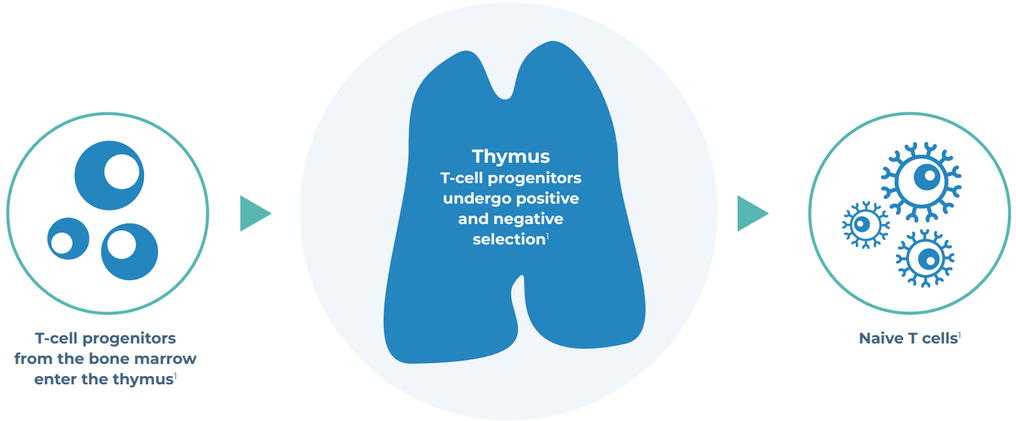
Not an actual patient.

Sumitomo Pharma

Congenital athymia is a rare immune condition that causes life-threatening immunodeficiency[1,2]

Congenital athymia is a primary immunodeficiency (PI) characterized by the lack of a functioning thymus at birth, leading to an increased susceptibility to life-threatening infections. Approximately 17 to 24 infants per year are born with congenital athymia in the US.[1,3,4]

The thymus is the only organ where T-cell progenitors can undergo positive and negative selection to become naive T cells.[1]



Congenital athymia has been associated with multiple conditions[1]

Congenital athymia has previously been referred to as complete DiGeorge anomaly, but has since been associated with other genetic conditions, congenital syndromes, and environmental exposures. These may include[1,2]:

- Complete DiGeorge syndrome (22q11.2 deletion syndrome)
- CHARGE* syndrome
- *FOXN1* deficiency
- Diabetic embryopathy

For some patients there may be no known cause.[5]

Scan the QR code to learn more about the diagnostic process for congenital athymia, or visit congenital-athymia.com/diagnosis

*Coloboma, heart defects, atresia of the nasal choanae, retardation of growth and development, genitourinary anomalies, and ear anomalies.

Early diagnosis is key to making the right supportive care decisions[1]

The sooner congenital athymia is detected, the sooner isolation and infection prevention measures can be initiated—and the less likely a patient will be treated with potentially inappropriate therapies.[1]

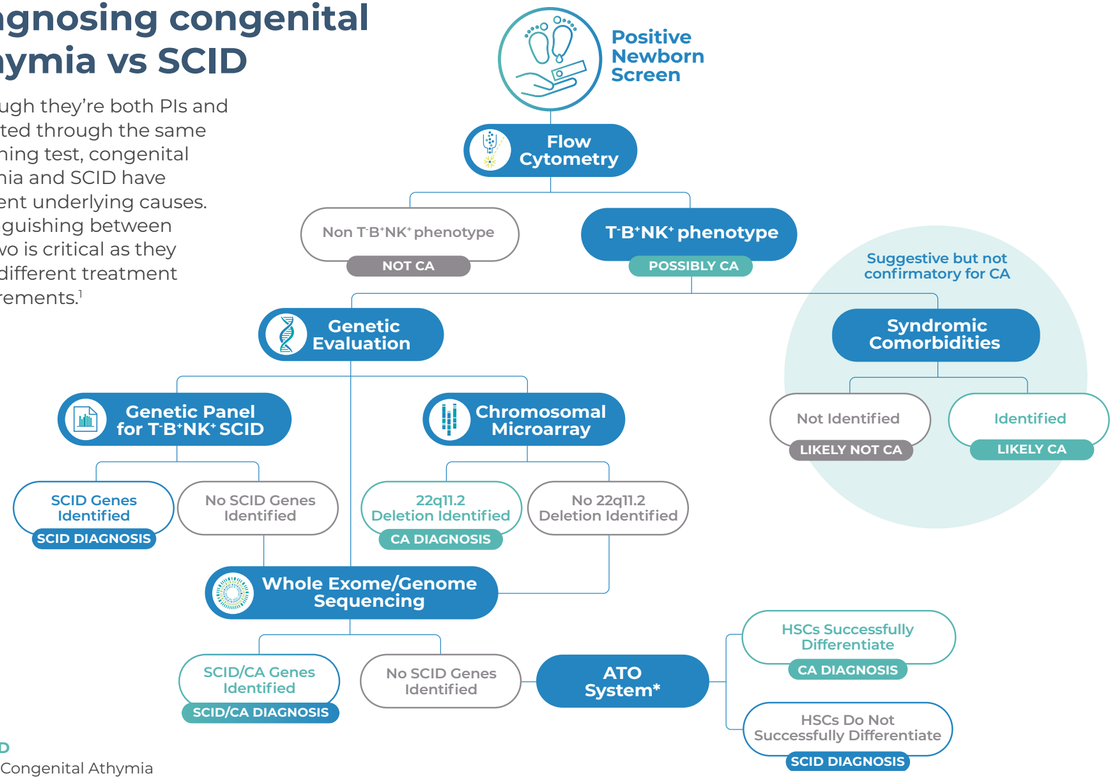
Newborn screening plays a crucial role in the early detection of congenital athymia[1]

T cell receptor excision circle (TREC) screening, a test mandated in all 50 states in the US, provides the first indication of naive T-cell deficiency, signaling a need for further testing.[1]

TREC screening may identify severe combined immunodeficiency (SCID) as well as congenital athymia.[1]

Diagnosing congenital athymia vs SCID

Although they're both PIs and detected through the same screening test, congenital athymia and SCID have different underlying causes. Distinguishing between the two is critical as they have different treatment requirements.[1]



LEGEND

CA	Congenital Athymia
SCID	Severe Combined Immunodeficiency
ATO	Artificial Thymic Organoid
HSC	Hematopoietic Stem Cell

*Investigational test available at the National Institutes of Health (NIH).

Collins C, Sharpe E, Silber A, Kulke S, Hsieh EWY. Congenital athymia: genetic etiologies, clinical manifestations, diagnosis, and treatment. *J Clin Immunol.* 2021;41(5):881-895. doi:10.1007/s10875-021-01059-7

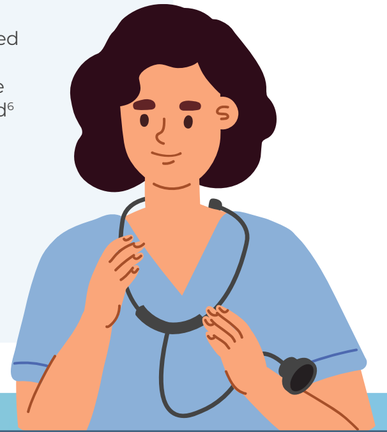
Patients with congenital athymia require vigilant care[1]

Isolation and infection prevention measures—in the hospital and at home—as well as prophylactic antimicrobials are critical to protect patients from potentially life-threatening infections.[1]

Supportive care in the hospital

Some best practices to consider for in-hospital procedure include:

- Beginning reverse isolation with laminar airflow (LAF) as soon as the patient is diagnosed. These rooms follow strict protocols that include dedicated clean spaces for staff and visitors to properly sterilize; heavily monitored ventilation; handwashing; and wearing masks, gowns, and gloves[1]
- Ensuring that all blood is irradiated before transfusions and testing that it is seronegative for cytomegalovirus (CMV)[6]
- Instructing the mother to stop breastfeeding her infant to prevent potentially transmitting CMV[1]
- Starting patients on[1,5]:
  - Prophylaxis for *Pneumocystis jirovecii*
  - Immunoglobulin replacement therapy
  - Antibiotic, antimicrobial, and antifungal prophylaxis
- Not administering any live or inactivated vaccines until the underlying immune disorder is corrected[6]



Supportive care in the home

It may be important for caregivers to understand the reasons for supportive care and to know what they can do inside and outside the home to help protect their child. Current medical literature recommends that caregivers follow strict at-home protection measures, including[1,4]:

- Limiting or restricting visitors in the home[1]
- If possible, homeschooling other children in the family[6]
- Having a “sick plan” in place for when a member of their household feels ill
- Educating those around them about the severity of the diagnosis and that special precautions and isolation are needed to protect their child[1]
- Showering and changing clothes any time they leave and return home[1]
- Washing hands frequently[1]
- Obtaining protective supplies like masks, gowns, and gloves[1]

RETHYMIC
(allogeneic processed thymus tissue-agdc)

connect is here to help

Enrolling your patients in the RETHYMIC Connect™ Patient Support Program will give their caregivers access to **educational resources** and, if eligible, **financial assistance** as they navigate the congenital athymia journey. RETHYMIC Connect is available to patients with any type of insurance—including commercial plans, Medicare, or Medicaid—as well as patients who are underinsured or have no insurance coverage.

Dedicated care team

- The Support Liaison will help your patients' caregivers understand their child's diagnosis
- The Access Specialist can help caregivers navigate insurance benefits and financial assistance

Access to exclusive resources

- Document organizer
- *Sadie's Search*, a storybook written specifically with your patient in mind
- Interactive T-cell progress tracker
- Activity book
- And more!

Co-pay program

- The RETHYMIC Connect™ Commercial Co-Pay Program can help caregivers of eligible commercially-insured patients in the US and US territories
- They may receive co-pay assistance for medication-related out-of-pocket costs for RETHYMIC

INDICATION

RETHYMIC® is indicated for immune reconstitution in pediatric patients with congenital athymia.

Limitations of Use: RETHYMIC is not indicated for the treatment of patients with severe combined immunodeficiency (SCID).

Call 877-RETHYMC (877-738-4962) today to connect your patients and their caregivers to personalized support. Support is available Monday–Friday, 8:00 AM to 8:00 PM ET.

Scan the QR code to enroll your patients, or visit RETHYMIC.com/hcp

Sumitomo Pharma America, Inc. and RETHYMIC Connect are not responsible for treatment decisions or timing for treatment.

IMPORTANT SAFETY INFORMATION

Infection Control and Immunoprophylaxis: Immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6-12 months after treatment with RETHYMIC. Follow infection control measures until the development of thymic function is established as measured by flow cytometry. Closely monitor patients for signs of infection. If fever develops, assess the patient via lab results and treat as clinically indicated. Patients should be maintained on immunoglobulin replacement therapy (IgG) and *Pneumocystis jirovecii* pneumonia prophylaxis until specified criteria are met. IgG trough level should be checked 2 months after stopping IgG to determine whether the patient may remain off IgG.

Please see full Important Safety Information and the QR code to the full Prescribing Information on pages 10 and 11, or visit RETHYMIC.com/prescribing-information.

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Graft versus Host Disease (GVHD): RETHYMIC may cause or exacerbate pre-existing GVHD, for which patients should be closely monitored and treated. Risk factors include atypical complete DiGeorge anomaly phenotype, prior hematopoietic cell transplantation (HCT), and maternal engraftment. Patients with specified elevated baseline T cell proliferative response to PHA should receive immunosuppressants to decrease this risk. GVHD may manifest as fever, rash, lymphadenopathy, elevated bilirubin and liver enzymes, enteritis, and/or diarrhea.

Autoimmune Disorders: Autoimmune-related adverse events occurred in patients treated with RETHYMIC. These events included thrombocytopenia, neutropenia, proteinuria, hemolytic anemia, alopecia, hypothyroidism, autoimmune hepatitis, autoimmune arthritis, transverse myelitis, albinism, hyperthyroidism, and ovarian failure. Monitor complete blood counts with differential, liver enzymes, serum creatinine, urinalysis, and thyroid function.

Renal Impairment: Pre-existing renal impairment is a risk factor for death.

Cytomegalovirus Infection (CMV): In the clinical studies, 4 out of 4 patients with pre-existing CMV infection died.

IMPORTANT SAFETY INFORMATION (cont'd)

Malignancy: Due to underlying immune deficiency, patients who receive RETHYMIC may be at risk of developing post-treatment lymphoproliferative disorder. Patients should be tested for Epstein-Barr virus and CMV prior to and 3 months after treatment or after any suspected exposure.

Transmission of Serious Infections and Transmissible Infectious Diseases: Transmission of infectious disease may occur because RETHYMIC is derived from human tissue, and product manufacturing includes porcine- and bovine-derived reagents.

Vaccine Administration: Immunizations should not be given in patients treated with RETHYMIC until immune-function criteria have been met. Live virus vaccines should not be given until patients have met the criteria for and received inactivated vaccines.

Anti-HLA Antibodies: All patients should be screened for anti-HLA antibodies prior to receiving RETHYMIC. Patients testing positive should receive RETHYMIC from a donor who does not express those HLA alleles.

HLA Typing: HLA matching is required in patients who have received a prior HCT or a solid organ transplant. Patients who have received a HCT are at increased risk of developing GVHD after RETHYMIC if the HCT donor does not fully match with RETHYMIC.

Deaths: Of the 105 patients in clinical studies, 29 patients died, including 23 deaths in the first year (<365 days) after implantation.

Adverse Reactions: The most common (>10%) adverse events included hypertension, cytokine release syndrome, rash, hypomagnesemia, renal impairment/failure, thrombocytopenia, and GVHD.

Please see full Prescribing Information.

Please scan the QR code to see the full Prescribing Information, or visit RETHYMIC.com/prescribing-information

References: 1. Collins C, Sharpe E, Silber A, Kulke S, Hsieh EWY. Congenital athymia: genetic etiologies, clinical manifestations, diagnosis, and treatment. *J Clin Immunol.* 2021;41(5):881-895. doi:10.1007/s10875-021-01059-7 **2.** Markert ML, Gupton SE, McCarthy EA. Experience with cultured thymus tissue in 105 children. *J Allergy Clin Immunol.* 2022;149(2):747-757. doi:10.1016/j.jaci.2021.06.028 **3.** Immune Deficiency Foundation. *Patient & Family Handbook for Primary Immunodeficiency Diseases.* 6th ed. 2019. **4.** Hsieh EWY, Kim-Chang JJ, Kulke S, Silber A, O'Hara M, Collins C. Defining the clinical, emotional, social, and financial burden of congenital athymia. *Adv Ther.* 2021;38(8):4271-4288. doi:10.1007/s12325-021-01820-9 **5.** Markert ML. Defects in thymic development. In: Sullivan KE, Stiehm ER, eds. *Stiehm's Immune Deficiencies: Inborn Errors of Immunity.* 2nd ed. Elsevier; 2020:357-379. **6.** Gupton SE, McCarthy EA, Markert ML. Care of children with DiGeorge before and after cultured thymus tissue implantation. *J Clin Immunol.* 2021;41(5):896-905. doi:10.1007/s10875-021-01044-0

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