UNDERSTANDING CONGENITAL ATHYMIA

INFORMATION FOR HEALTHCARE PROFESSIONALS

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Child with congenital athymia

Learn more about congenital athymia – an ultra-rare condition characterized by the absence of a thymus at birth.[1]

CONGENITAL ATHYMIA RESULTS IN **PROFOUND IMMUNODEFICIENCY[2]**

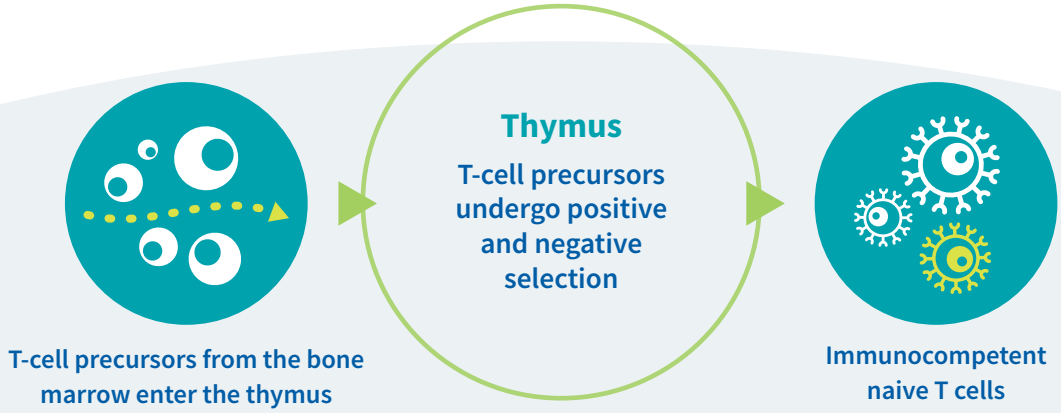
Congenital athymia is a condition in which children are born without a thymus, causing vulnerability to life-threatening infections and immune dysregulation.[2] With only supportive care, children with congenital athymia typically do not survive beyond 2 to 3 years of age.[3] The estimated incidence of congenital athymia in the United States is approximately 17 to 24 infants per ~4 million live births annually.[4]

The thymus is responsible for the development of mature T cells; it is the only organ where thymocytes can mature, be selected, and ultimately survive to become naive T cells.[1] Although T cells originate in the bone marrow as progenitor cells, the bone marrow is not equipped with the specialized tissue required for T-cell maturation.[5] T-cell progenitors emerging from the bone marrow migrate to the thymus, where they are selected to become naive T cells via positive and negative selection.[1]

Without functional thymus tissue, progenitor cells lack an immunologic epicenter for T-cell maturation.[5] Due to the absence of a functioning thymus, the inability to produce immunocompetent T cells leads to immunodeficiency, characterized by increased susceptibility to infection.[1] Children with congenital athymia may also experience immune dysregulation.[2]

Congenital athymia may be associated with other conditions, such as DiGeorge syndrome or 22q11.2 deletion syndrome; mutations in the genes *TBX1, CHD7* (CHARGE syndrome), and *FOXN1* (FOXN1 deficiency); and diabetic embryopathy.[1,2,6] These multifaceted conditions and syndromes make the already complex treatment of congenital athymia even more complex.

Role of the thymus: The thymus is crucial for development of a properly functioning immune system



Mature T cells are an essential component of the adaptive immune response. Because children with congenital athymia lack mature T cells, they lack an adaptive immune response.[7]

EARLY DETECTION IS KEY

The sooner congenital athymia is identified, the sooner isolation and infection prevention measures can be initiated and the less likely a patient is to be treated with therapies that may not be effective in congenital athymia.[1]

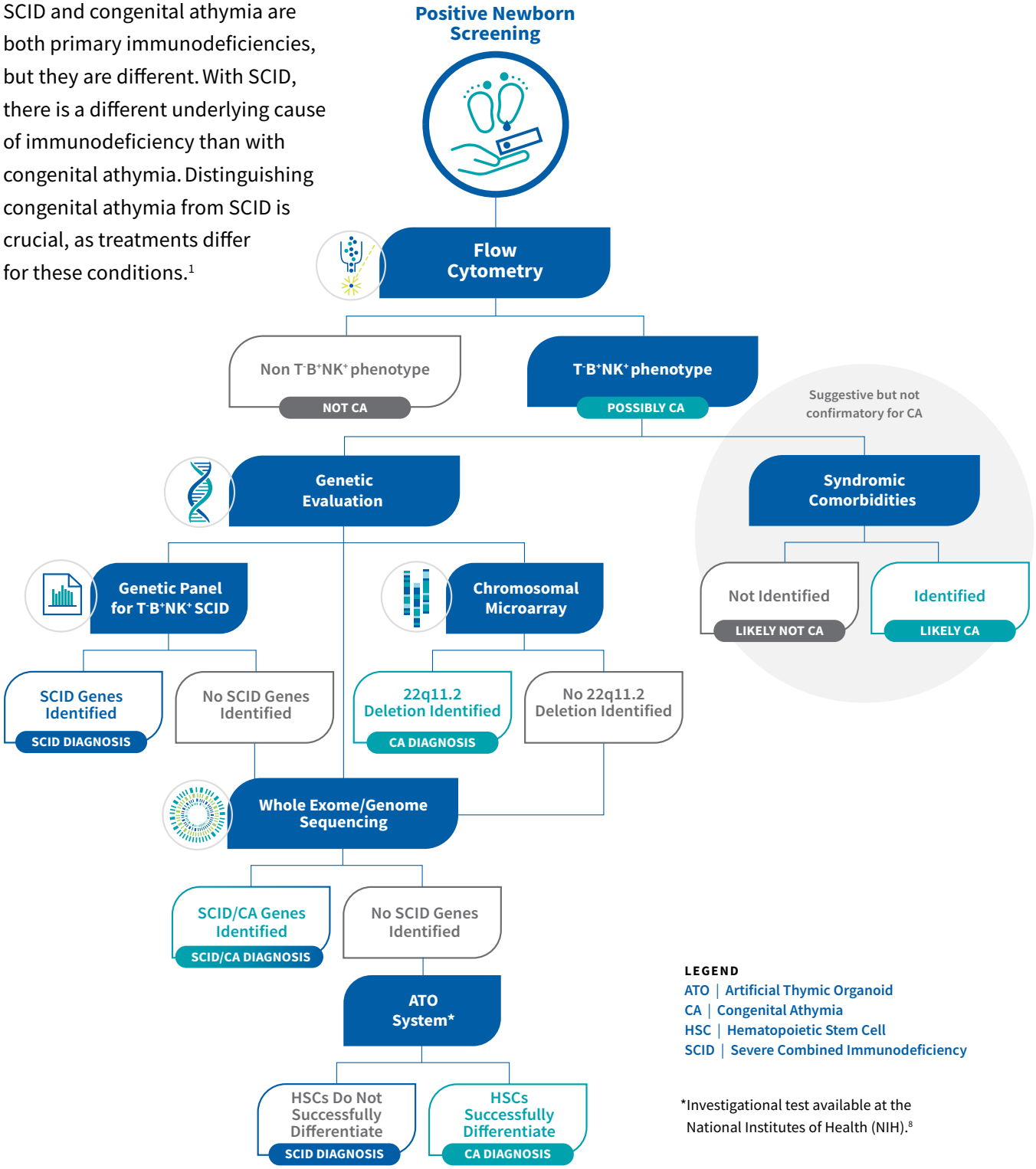
Newborn screening plays a crucial role in the early detection of congenital athymia.[6]

Congenital athymia is initially detected through T-cell receptor rearrangement excision circle (TREC) screening, also known as severe combined immunodeficiency (SCID) screening.[1] TREC screening is critical, as it provides the first indication of an immunologic issue in an infant's T-cell development.[6] Low TREC levels indicate the need for further testing.[6] This test is now a standard part of the newborn screening panel, required in all 50 US states.[1]

Isolation, infection prevention measures, and prophylactic antimicrobials are critical for children with congenital athymia. Immunosuppression may also be necessary for these children.[1] However, with only supportive care, they typically do not survive beyond 2 to 3 years of age.[3]

DIAGNOSING CONGENITAL ATHYMIA VS SCID IS **VITAL TO SUCCESSFUL TREATMENT**

SCID and congenital athymia are both primary immunodeficiencies, but they are different. With SCID, there is a different underlying cause of immunodeficiency than with congenital athymia. Distinguishing congenital athymia from SCID is crucial, as treatments differ for these conditions.[1]



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

*Investigational test available at the National Institutes of Health (NIH).[8]

A DEFINITIVE DIAGNOSIS IS NEEDED FOR CONFIRMATION

After a positive screening result, confirmatory flow cytometry testing may help to differentiate between SCID and congenital athymia. There is no consensus on the level of naive T cells defining congenital athymia.[1]

This is followed by genetic testing, which will determine the presence of associated conditions such as 22q11.2 deletion syndrome or CHARGE syndrome.[1] Mutations in genes that cause congenital athymia support identification.[1] Additionally, the ATO system may help to distinguish between hematopoietic or thymic abnormalities to identify SCID or congenital athymia.[8] Once congenital athymia is confirmed, it is important to establish whether the phenotype is typical or atypical so that the appropriate treatment can be initiated.[6]

A diagnosis of congenital athymia calls for the specialized care of a pediatric immunologist and an extended care team.[3]

COMPLEXITY OF CARE

While treatment options continue to evolve, approaches to supportive care for patients with congenital athymia are already established. Supportive care for children diagnosed with congenital athymia has relied primarily on established isolation protocols to limit exposure to infectious pathogens, any one of which could prove fatal.[1] When congenital athymia is suspected, the following recommended in-hospital protective measures are adopted and all testing for this condition should be urgently ordered and reviewed.[1,9]

The published literature suggests the following best practices:

- **Begin reverse isolation with laminar air flow (LAF) in the hospital as soon as the patient is diagnosed with congenital athymia. LAF rooms follow a strict protocol that includes dedicated clean spaces for staff and visitors to properly sterilize; heavily monitored ventilation; hand washing; masks, gowns, and gloves[1]**
- **Ensure that all blood is irradiated before infusions and test that it is seronegative for cytomegalovirus (CMV)[1,9]**
- **Instruct the mother to stop breastfeeding her infant until she has been tested and confirmed seronegative for CMV[1]**
- **Begin prophylaxis for *Pneumocystis* and start the patient on replacement immunoglobulin therapy[1,9]**
- **Begin antibiotic, antimycobacterial, and antifungal prophylaxis[1,9]**
- **Do not administer any live or inactivated vaccines until the underlying immune disorder is corrected[1,9]**

Parents and caregivers should be advised to follow strict at-home protection measures, including isolation, hand washing, and sanitizing surfaces.

GUIDANCE FOR **AT-HOME CARE**

Parents and caregivers should be advised to follow strict at-home protection measures. Published literature suggests the following best practices[1,9]:

- **Limit the child's contact with visitors (especially young children) to reduce the possibility of illness**
- **Clean and sanitize household surfaces and items that are touched routinely, such as doorknobs, cell phones, tablets, car keys, and remote controls**
- **Wipe down any items coming into the home with disinfectant products**
- **Make a habit of frequent hand washing with antibacterial products for everyone in the family**
- **Have family members and visitors use masks, gowns, and gloves; establish a sanitation station at the entrance to the home to allow visitors to disinfect with hand sanitizer, remove shoes, and put on masks, gowns, and gloves**
- **Ask to be kept informed about any illnesses at school that siblings might bring home and request that the schools take the necessary steps to keep the surrounding environment as germ free as possible**
- **Plan for an alternative location for household members to stay should they become ill, such as staying with a friend or family member**

SUPPORT FOR **YOUR PATIENTS**

Due to the extreme isolation and stress placed on families and caregivers, support groups and resources that may help them cope with the ongoing challenges of this condition should be recommended. Although no organizations are dedicated specifically to congenital athymia, several patient advocacy organizations support patients and families dealing with the effects of immunodeficiency disorders:

Jeffrey Modell Foundation | **info4pi.org**

Immune Deficiency Foundation | **primaryimmune.org**

National Organization for Rare Disorders | **rarediseases.org**

Global Genes | **globalgenes.org**

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