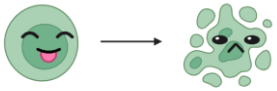
Immune Deficiencies Related to T Cells

Our immune system normally fights off things that are foreign (e.g., viruses, bacteria, fungi, etc.). **Immune deficiencies** (or immunodeficiencies) happen when the immune system is weakened. The patient may have **too many infections**, infections that are **difficult to cure**, **unusually severe** infections, or infections with **unusual organisms**.

Many individuals with 22q11.2 deletion syndrome (22q11.2DS) have T cell deficiencies. In fact, an absence of T cells was one of the features mentioned in the earliest descriptions of this syndrome. T cell deficiency is much less common in individuals with 22q11.2 duplication syndrome (22q11.2DupS).

Mild-Moderate Deficiencies of T Cells

- A newborn should have at least 2800 T cells/mm^3. 75-80% of babies with 22q11.2DS have low T cells (800 to 2000 T cells/mm^3)
- In young children with mild-moderate T cell deficiency:
  - ❑ T cells largely multiply normally in response to infections
  - ❑ There is an imbalance in the various types of T cells, which affects the way the immune system responds to pathogens
  - ❑ There is a decrease in some types of antibodies, which in turn leads to a reduced response to vaccines
- In older children and adults, the T cell counts tend to approach normal, but the T cells themselves are:
  - ❑ Not as diverse and may not respond to a wide variety of pathogens
  - ❑ Exhausted and cannot battle pathogens efficiently
  - ❑ Not able to multiply as well
  - ❑ More likely to die



Infections in Individuals with Mild-Moderate T Cell Deficiency

- Children with low T cells tend to have **an increase in infections**, e.g. viral infections that won't go away but are instead followed by bacterial infections
- Frequent infections may happen due to:
  - ❑ Eustachian tubes too horizontal – fluids cannot drain → ear infections
  - ❑ Anatomical issues – poor sinus drainage → sinus infections
  - ❑ Tracheomalacia – collapse of the airway → respiratory infections
  - ❑ Enamel hypoplasia – tooth covering is poorly formed → dental cavities
  - ❑ Stomach acid reflux – acid goes up the esophagus and goes down the airway → lung infections
  - ❑ Frequent contact with the healthcare system → encounters pathogens
- If anatomy is not a cause, infection frequency may decrease with:
  - ❑ Frequent and thorough hand washing with soap
  - ❑ Managing asthma and allergies
  - ❑ Use of gum with xylitol (to remove bacteria from teeth)
  - ❑ Antibiotic prophylaxis – taking antibiotics to prevent infections in high risk situations (e.g. before surgeries or dental procedures)

- As the children grow older, the frequency of infections usually decreases.

Counting Cells

Flow cytometry is used to count the number of T cells in a blood sample. Here is a cartoon of a flow cytometer:

Individuals with Mild-Moderate T cell deficiency should check with an immunologist before getting these live attenuated vaccines

- Rotavirus
- Smallpox
- Yellow fever
- BCG vaccine for tuberculosis
- The live attenuated, nasal mist type of flu vaccine (use the inactivated type instead)

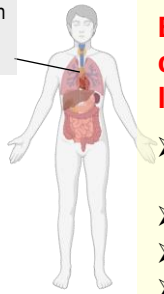
MMR (measles, mumps, rubella) and **varicella** (chicken pox) vaccines are safe and effective in children with **mild-moderate** T cell deficiency.

Immune Deficiencies Related to T Cells (continued)

Severe Deficiency of T Cells

- **Caused by having no thymus or a very small one.**
- Fewer than 0.1% of babies with 22q11.2DS have no T cells or very few of them (fewer than 200 T cells/mm^3).
- These babies are unable to protect themselves against invading viruses. They require very specific care to **avoid life-threatening infections** and **problems related to their T cells**.

Thymus: the organ where T cells form and develop



Rebuilding Immunity Related to T Cells

Babies with severe T cell deficiency (fewer than 50 T cell/mm^3) need some help to rebuild their immune system.

- Method 1: **Thymus Transplant**
  - A complex procedure; only available at 2 hospitals in the world (UK | US)
  - Small pieces of thymus from a donor is placed in the leg of the recipient.
  - The implant starts to make functional T cells in about 100 days.
  - Although the implant will eventually stop making T cells, the recipient can potentially live normally with only moderate immune deficiency.
- Method 2: **T Cell Transplant**
  - Mature T cells from a matched donor is injected into the baby.
  - These T cells do not need to spend time in the thymus to get "educated". They are ready to defend against pathogens right away.
  - However, this method does not work as well as a thymus transplant

Preventing Graft Versus Host Disease

- Babies with severe T cell deficiencies often need either a thymus transplant or donor T cells to rebuild their immune system. They may also need a blood supply during surgery. However, any immune cells that are in the incoming materials ("graft") will see the cells in the recipient ("host") as foreign and attack them, causing **graft-versus-host disease (GvHD)**.

To prevent GvHD:

- Mature T cells are removed from thymic tissues that will be transplanted into the baby. Immature immune cells are still present.
- T cells must come from a donor whose immune system characteristics match those of the recipient exactly.
- Blood for transfusion is treated with radiation to remove live immune system cells.

Babies with very low T cells should not receive live attenuated vaccines:

- MMR (measles, mumps, rubella)
- Varicella (chicken pox)
- Rotavirus
- Smallpox
- Yellow fever
- BCG vaccine for tuberculosis
- The live attenuated, nasal mist type of flu vaccine (use the inactivated type instead)

T Cell Deficiencies and 22q Differences

22q11.2DS: The T cell count is likely lower if the *TBX1* gene is deleted. This applies to deletions that span low copy repeats (LCRs) A-B, A-C, and A-D.

22q11.2DupS: The T cell count is relatively normal for most individuals.

There are no ways to predict if a baby with a 22q difference will have immune deficiencies. It is recommended that **all individuals with 22q differences get their immune system checked**.

Resources

- The immune deficiency of chromosome 22q11.2 deletion syndrome – 2017
- Variable immune deficiency related to deletion size in chromosome 22q11.2 deletion syndrome – 2018
- Immunodeficiency in 22q11.2 duplication syndrome – 2021
- Immunologic, Molecular, and Clinical Profile of Patients with Chromosome 22q11.2 Duplications – 2023
- Updated clinical practice recommendations for managing [**children** | **adults**] with 22q11.2 deletion syndrome – 2023

22q International 22q11.2 Foundation

The mission of the International 22q11.2 Foundation is to improve the quality of life for individuals affected by chromosome 22q11.2 differences through family and professional partnerships.
This information is brought to you by the Foundation for educational purposes only. It is not intended to be taken as medical advice. If you have concerns, please talk to your healthcare provider.

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