The thymus, DiGeorge, & 22q11

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Starship

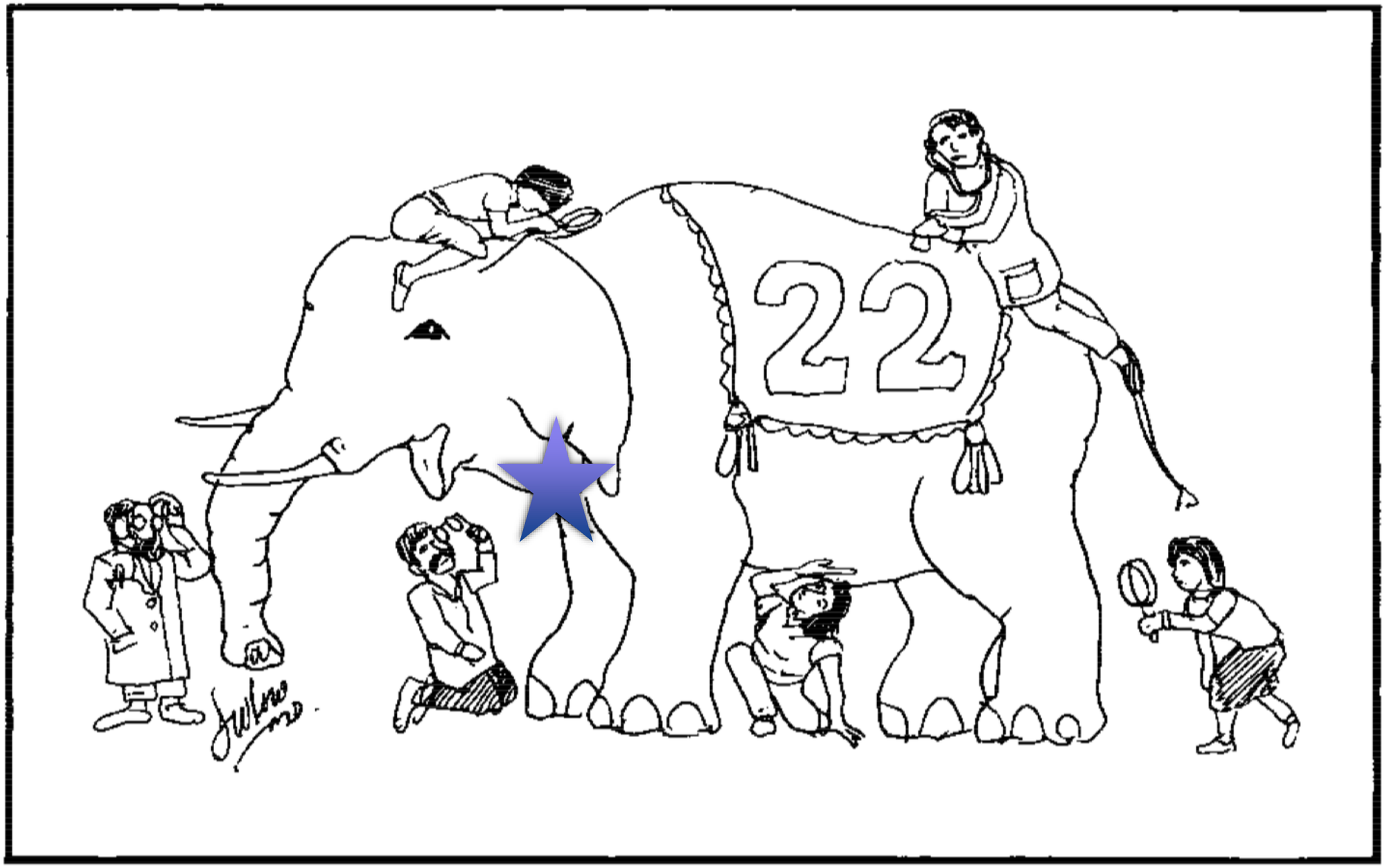
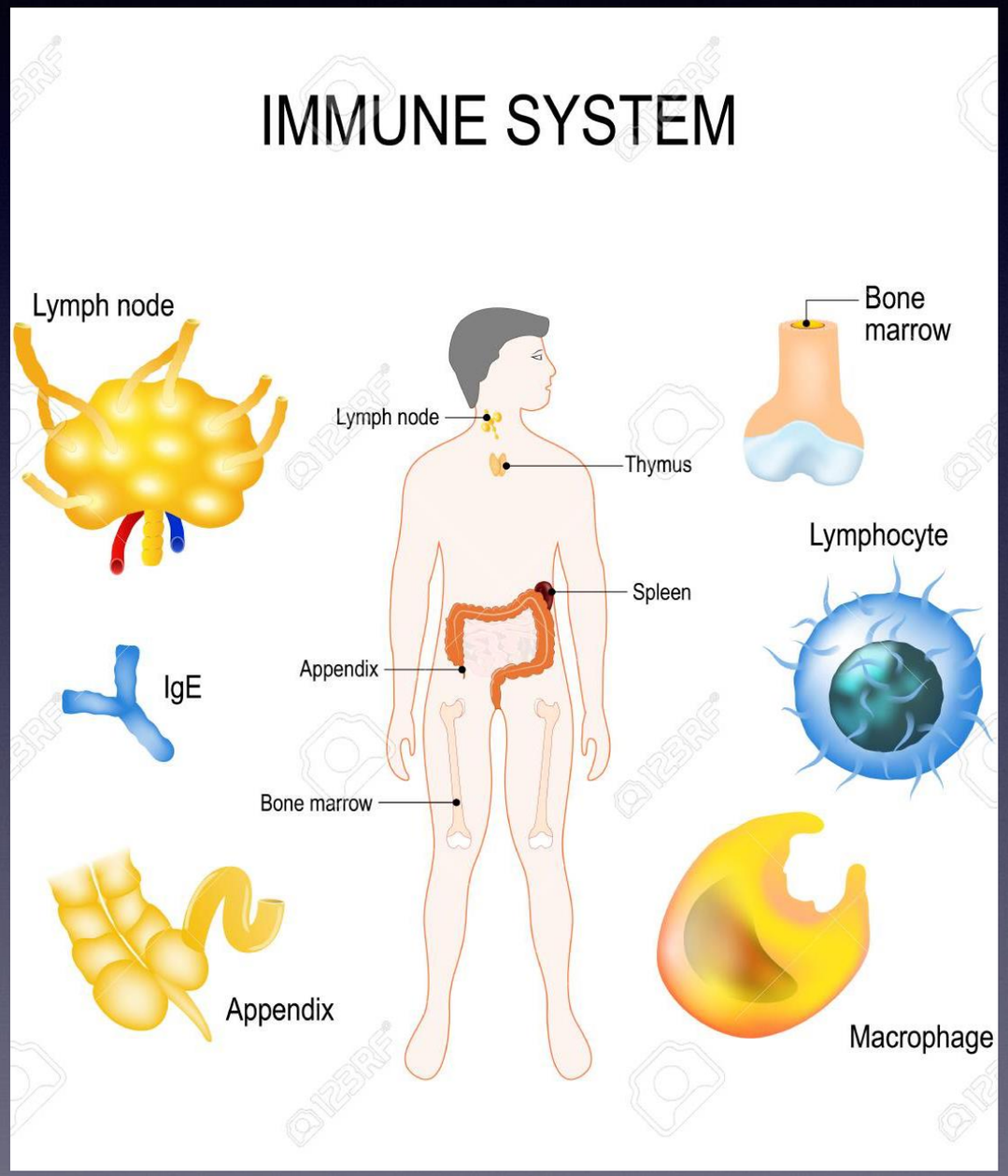


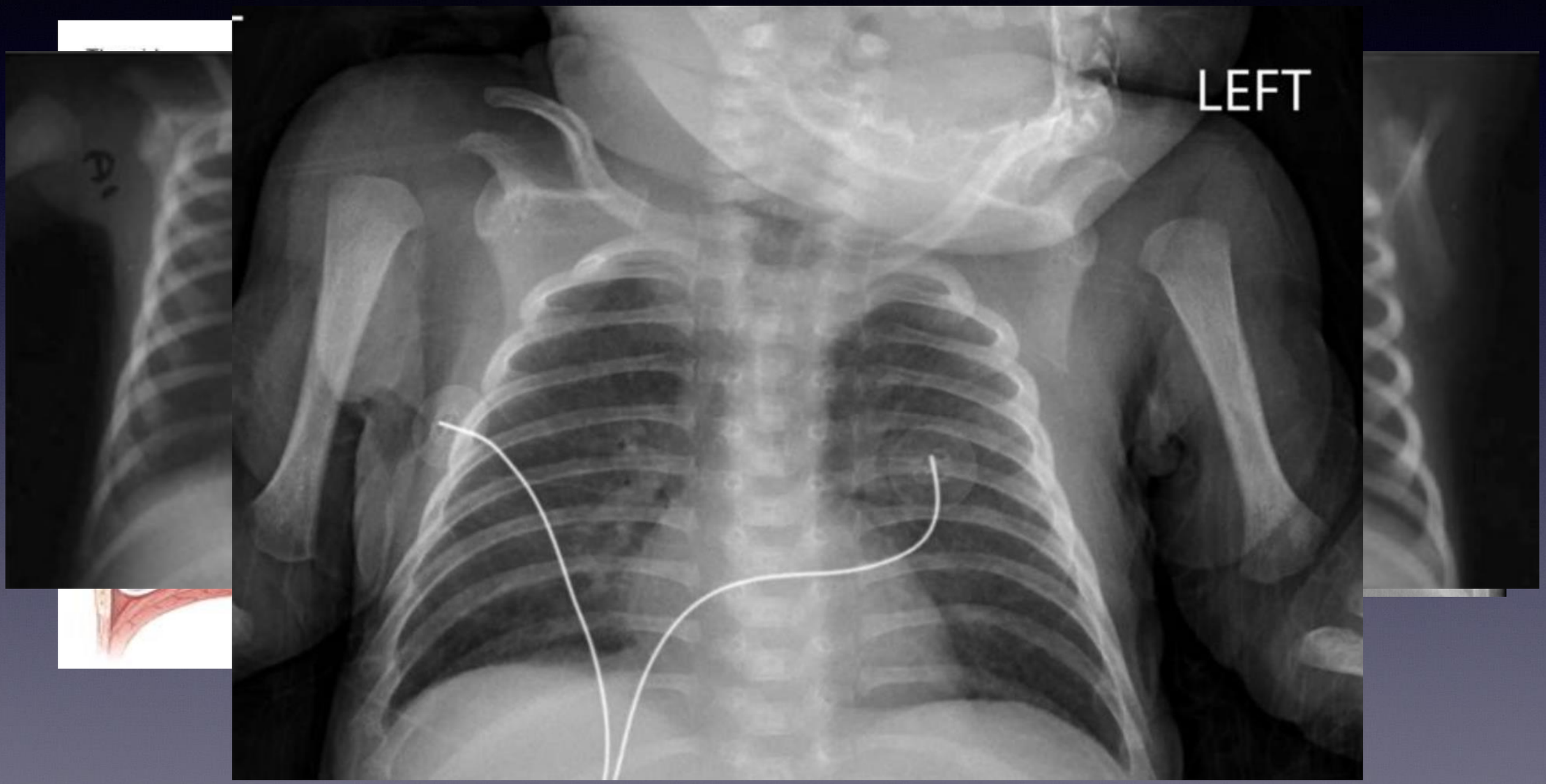
Fig. 1. The 22q.11.2 story can be likened to the old adage of a group of blind men trying to identify an elephant by each examining a separate part. Each man was accurate in describing his own area of interest, but none was able to see the big picture. Several conditions once thought to be separate are now known to be due to the 22q11.2 deletion.

Outline

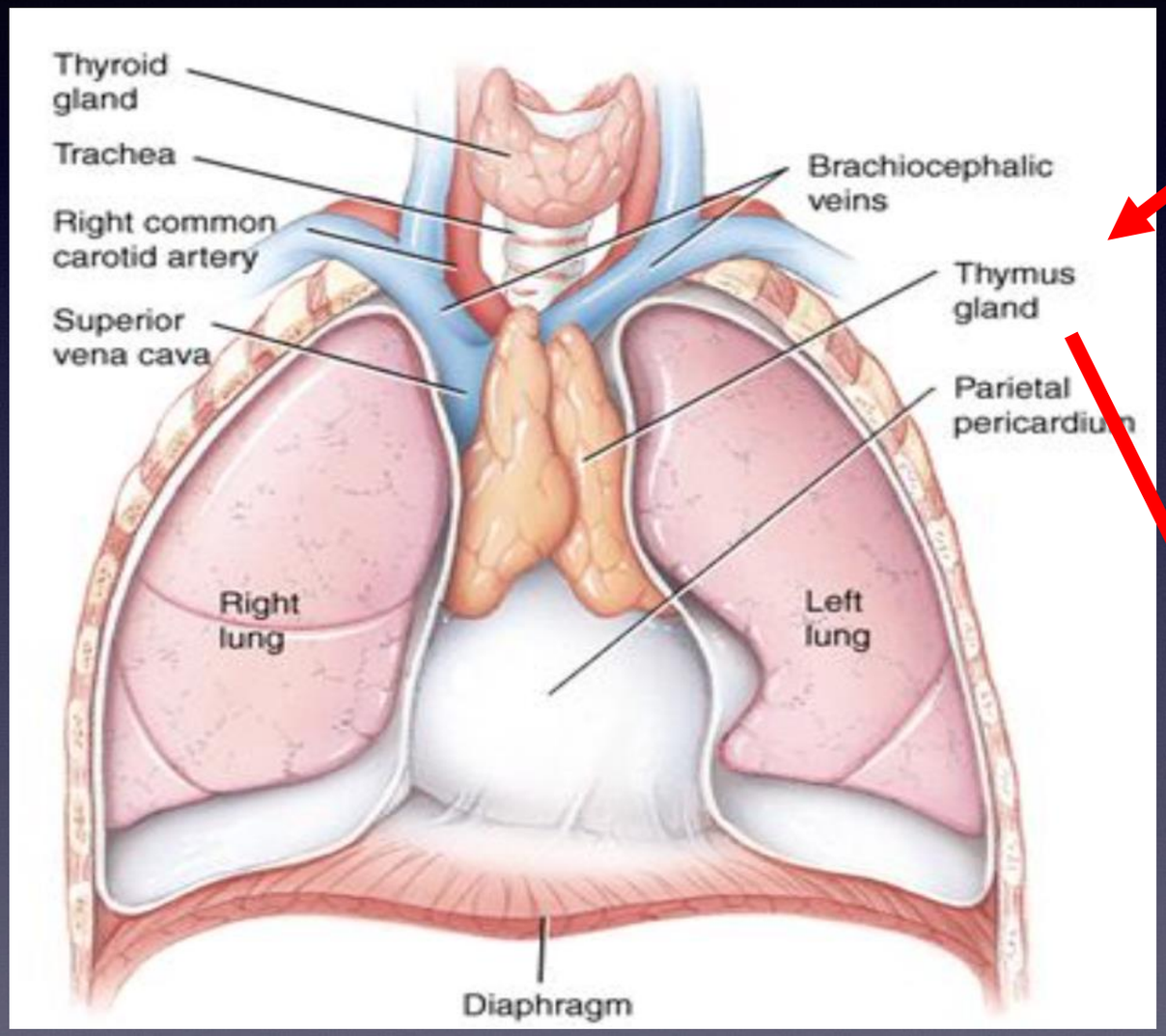
- History of the thymus
- What is the thymus
- What happens if the thymus doesn't work properly
  - Clinical consequences
  - Treatment options



Thymus



Thymus



Stem cells in the Bone marrow

Red cells

Platelets

Neutrophils

B lymphocytes

T cells

History of the thymus

- Ancient Greeks - “seat of the soul”
- 19th century - blamed for infant death “status thymolymphaticus”
- 1905 - 1st “treatment” with radiotherapy; continued until 1950s
- 1961 - recognition of thymus as source of T cell (author J Miller)

748 SEPTEMBER 30, 1961 Lancet.

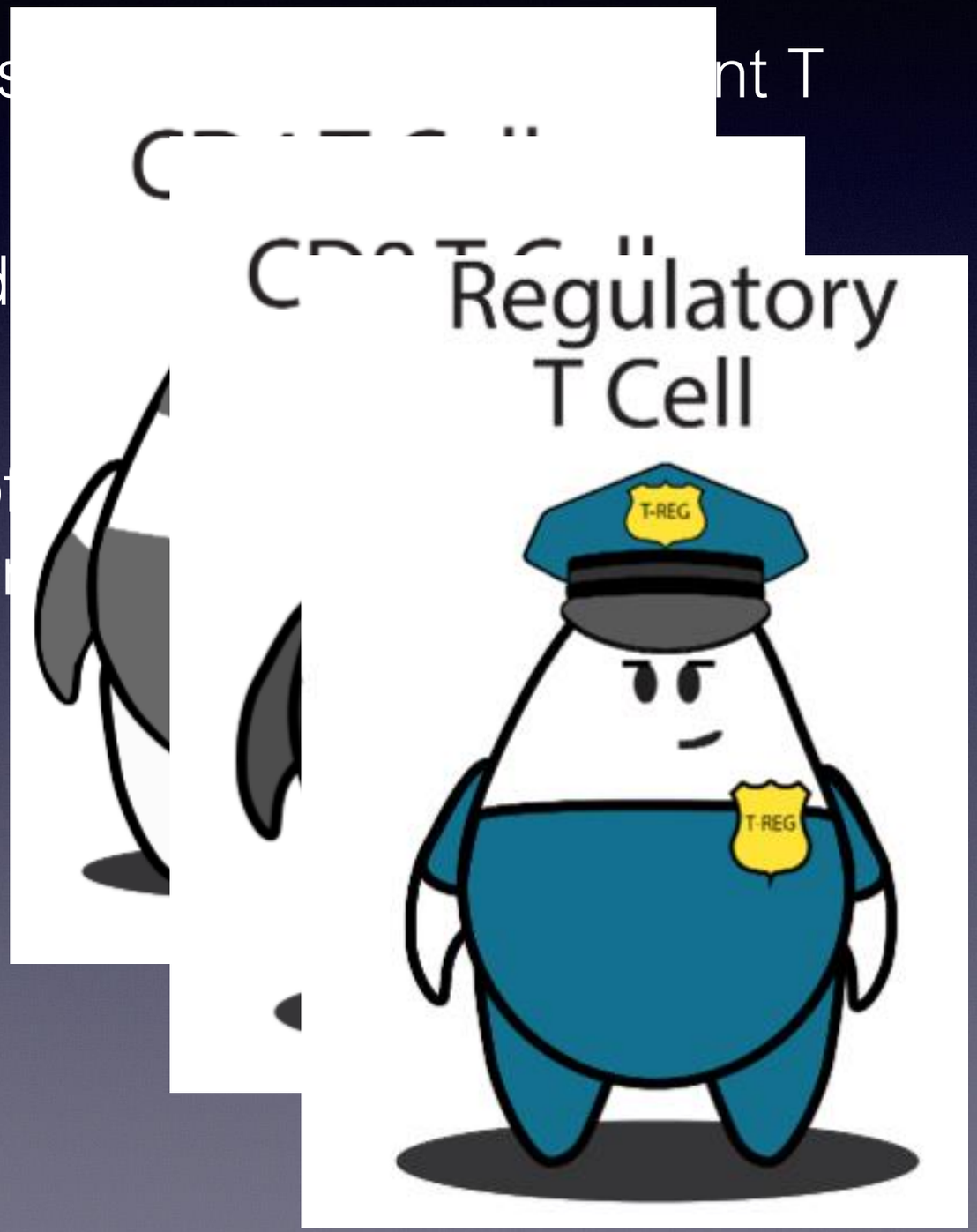
Preliminary Communications

IMMUNOLOGICAL FUNCTION OF THE THYMUS

IT has been suggested that the thymus does not participate in immune reactions. This is because antibody

T cells

- Lymphocytes learn to be T cells[illegible]nt T cells that:
  - Tolerate all the bits of “self”; d[illegible] that attacks yourself
  - Can interact with all the bits o[illegible] orchestrate an immune respo[illegible]
- T cells
  - Help B cells make antibodies
  - Kill infected cells
  - Regulate immune responses



T cell killing

CYTOTOXIC T-LYMPHOCYTE:
A specialized white blood cell
responsible for eliminating
unwanted body cells (e.g.
cancer) is killing a cell infected
with the influenza virus

The thymus in 22q11

- Most individuals with 22q11 have “partial” DiGeorge syndrome
  - Thymus generally small or in the wrong place (ectopic)
  - T cells low but not absent
  - These infants don’t have a severe immune deficiency

Complete vs partial

22q11
Est 1:4,000

Complete DiGeorge

VCFS

Infection in partial DiGeorge

- Particularly ear, sinus, chest
- Affects significant proportion (maybe 1:3)
- Consider contributing factors
  - Immunoglobulin problem
    - Low immunoglobulin levels
    - Poor specific responses
  - Swallowing problems

Autoimmunity in partial DiGeorge, n = 130

Patient no.	Sex	Disease	Age at disease (y)
1	F	Hypothyroidism	8
2	M	Hypothyroidism	7
3	F	Hypothyroidism, vitiligo	11
4	M	ITP	4
5	F	ITP	6
6	F	ITP, autoimmune neutropenia, AIHA	7
7	F	ITP, AIHA	5
8	M	Autoimmune neutropenia	0.7
9	F	Monoarticular arthritis, ANA^+	4
10	F	Polyarticular JIA	3
11	F	Psoriasis	5

Complete DiGeorge

- Makes up <1% of DiG patients
- No thymus
  - No T cells
- Severe immune deficiency
  - Fatal without treatment to replace the immune system

Complete DiG treatment

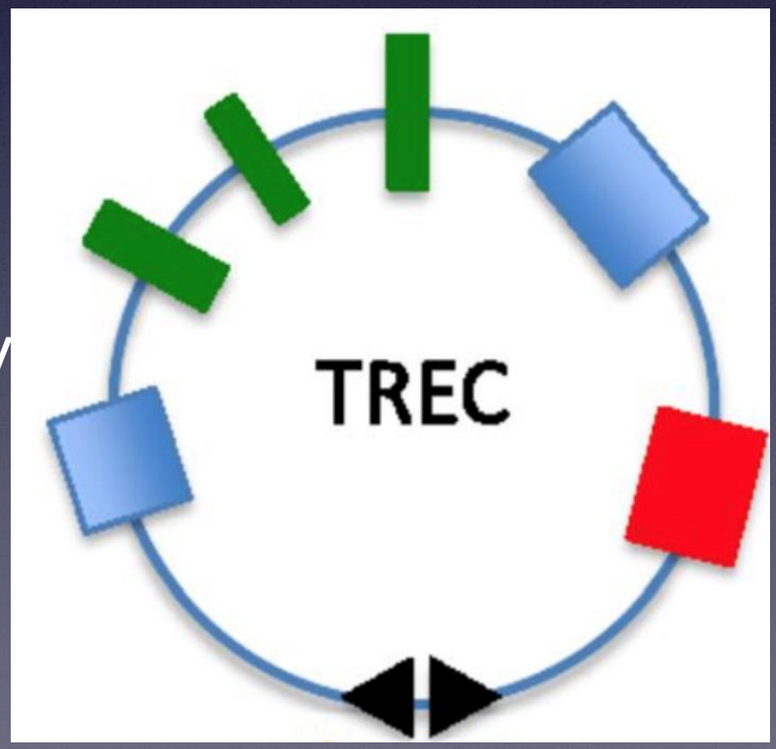
- Bone marrow transplant
  - Only an option if there is a “matched sibling”
    - Each sibling would have a 1:4 chance of being a match
- Transplant will transfer fully functional T cells to take over in the affected infant

Complete DiG treatment

- Thymus transplant
  - Thymus often removed at surgery for babies with heart defects
  - Transplanted in to the thigh muscle
  - Gives the baby's stem cells somewhere to go to learn be T cells

Newborn screening

- Dec 2017 NZ started screening for severe immune deficiency (SCID)
  - SCID babies also have no T cells
  - Screening test with TREC
  - Babies with severe immune deficiency due to DiG will also hav no TREC so can be diagnosed on the new born screening test



Approach to immune system in DiG

Abnormal new born screen

Normal new born screen

Complete DiG

- Bone marrow or thymus transplant
- Vaccines
- Antibiotics
- Immunoglobulin
- Protect

Low but not absent T cells

→ "wait and see"

- Vaccines
- Antibiotics
- Immunoglobulin
- Protect

No routine investigations

Normal vaccines

Investigate if infection or autoimmunity a problem

- Antibiotics
- Immunoglobulin