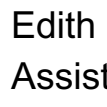
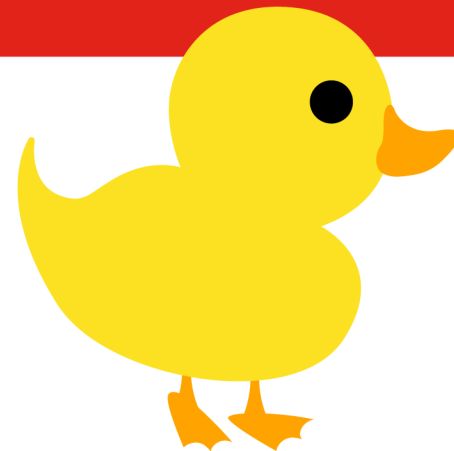


# 2020 Bloom's Syndrome Conference Immunology Overview

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# Outline

- Immune System Overview
  - Innate vs Adaptive
  - Cells and functions
  - Immunoglobulin
- What are the immune manifestations of Bloom's syndrome?
  - B cells
  - T cells
  - Immunoglobulin
- When to refer to immunology?
- Immune workup:
  - What sort of testing can be done? How are results interpreted?
- Treatment:
  - What treatments are available?
  - When should they be considered?

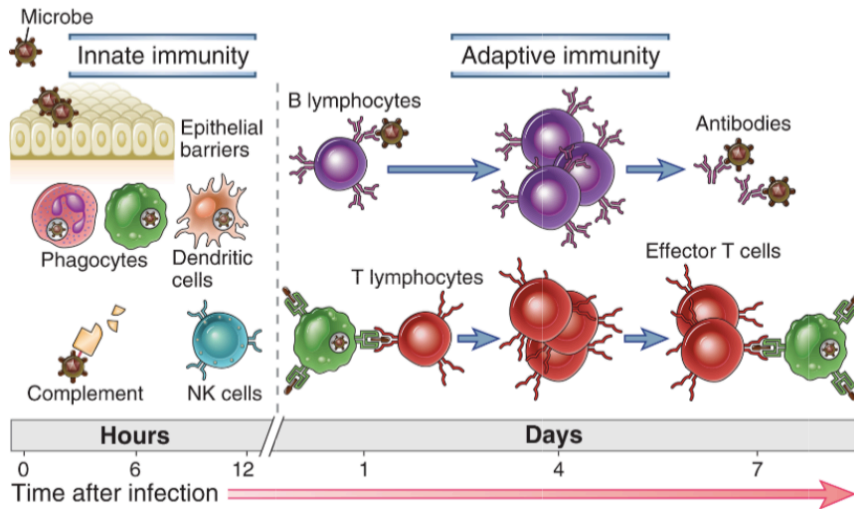
# Immune System Overview



# Functions of the immune system

- Identify threats
- Mount an attack
- Kill the invaders
- Remember that strategy for the next attack

# What is the difference between innate and adaptive immunity?



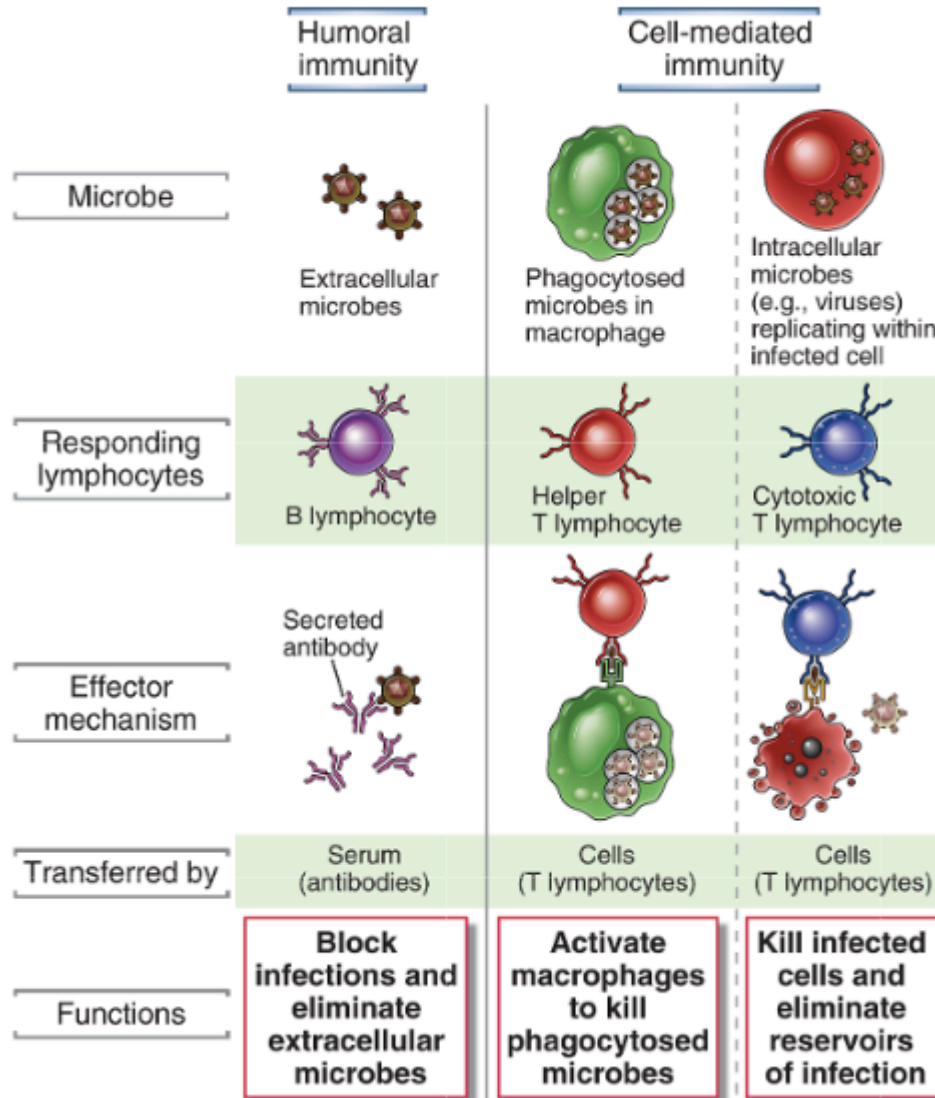
## ▪ **Innate immune response**

- Cells are non-specific
- Distinguish invader from human but not one invader from another
- Very fast (minutes to hours)
- No memory, responds the exact same way every time.

## ▪ **Adaptive immune response**

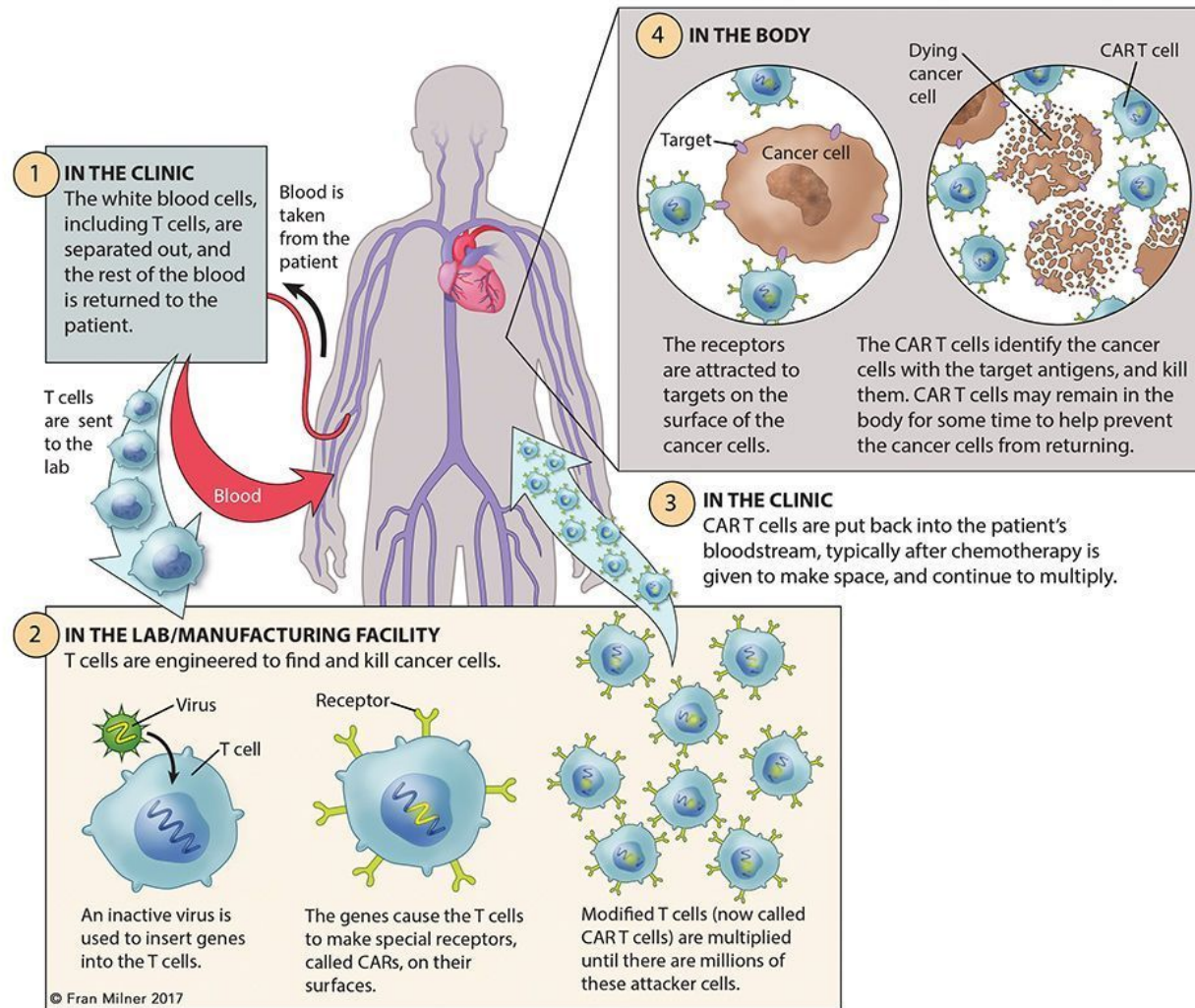
- Highly specific for each invader
- The adaptive response can tell one germ from another
- Can take weeks
- Has memory: the adaptive system responds faster and stronger each time

# The adaptive immune system : Humoral vs Cell Mediated

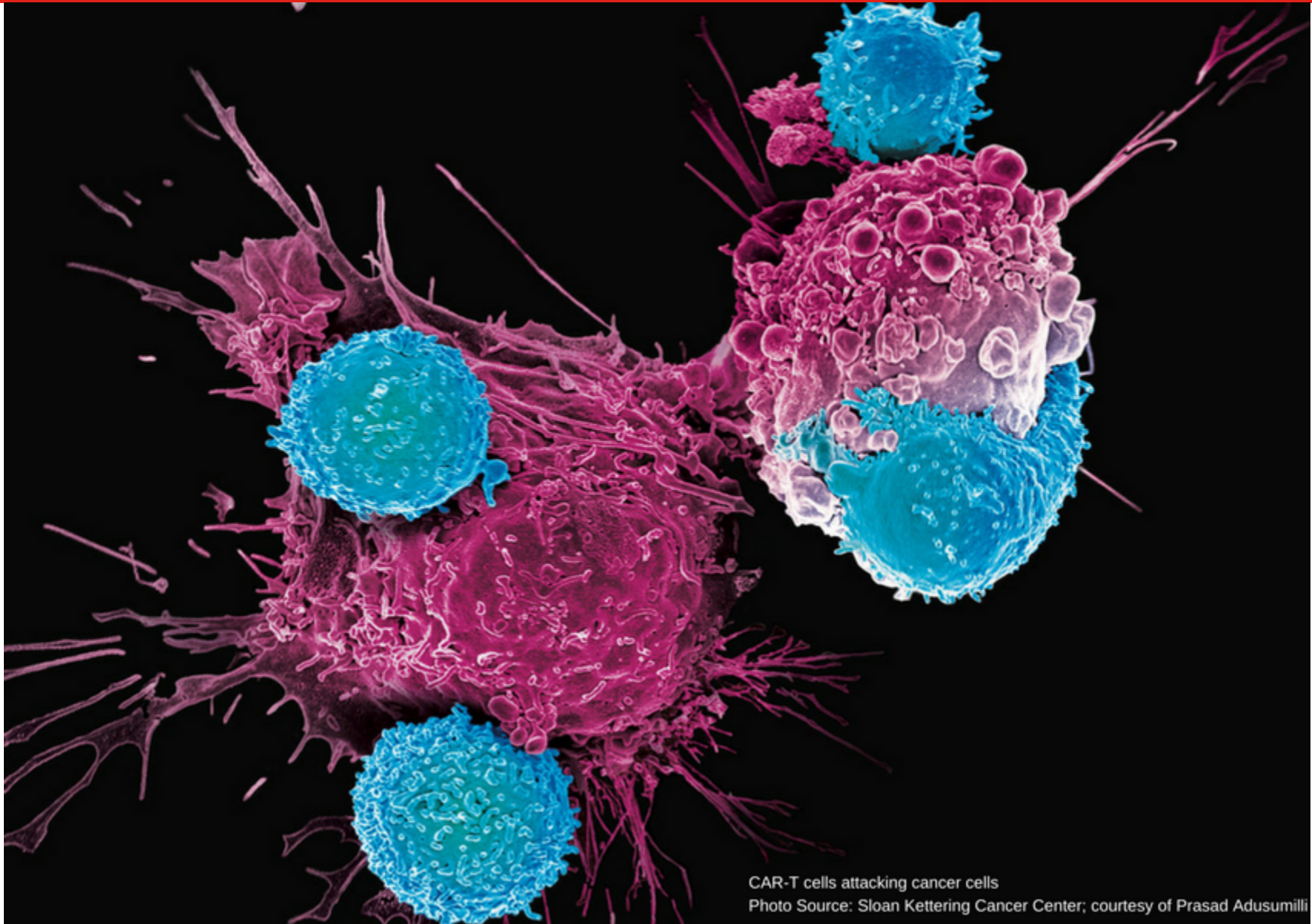




# T cells and cancer - CAR T cells



# T cells attacking cancer cells

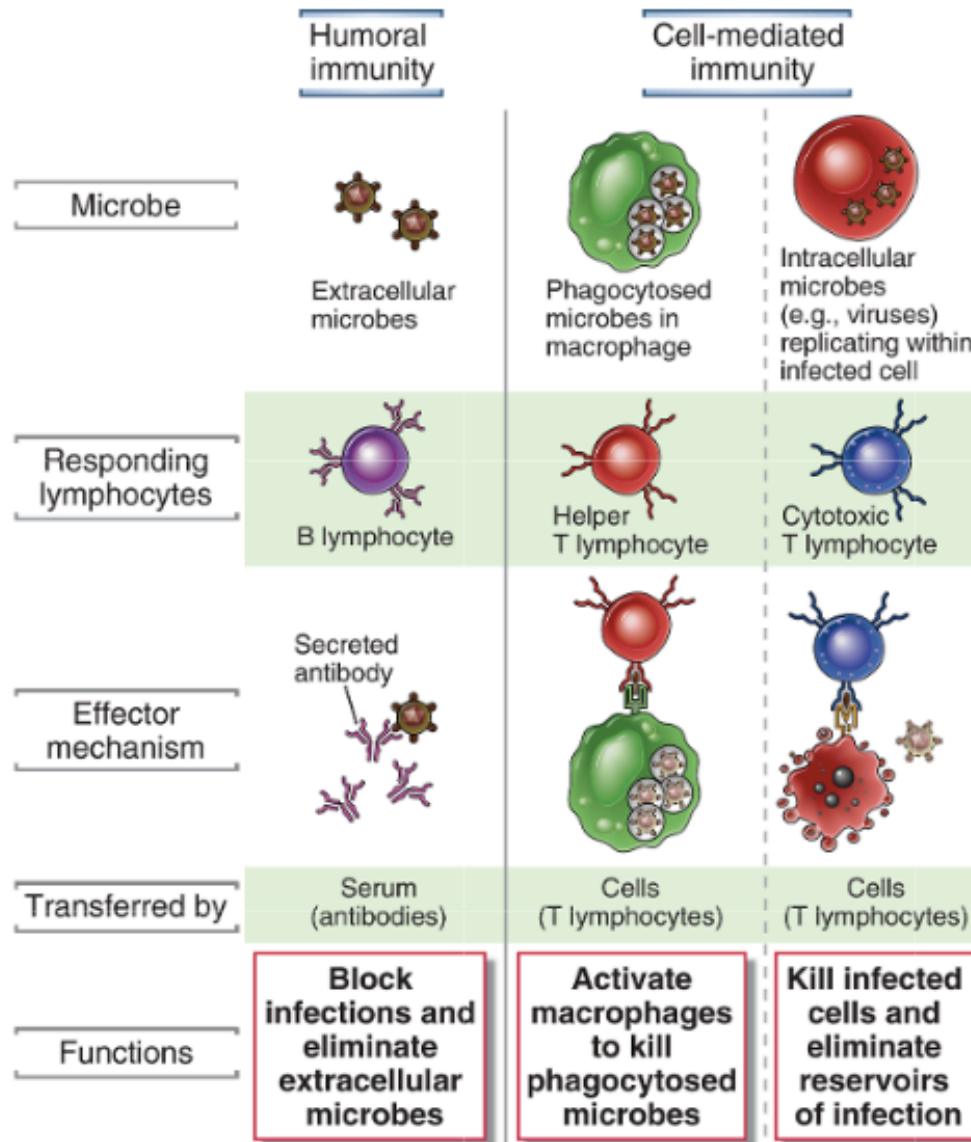


CAR-T cells attacking cancer cells

Photo Source: Sloan Kettering Cancer Center; courtesy of Prasad Adusumilli

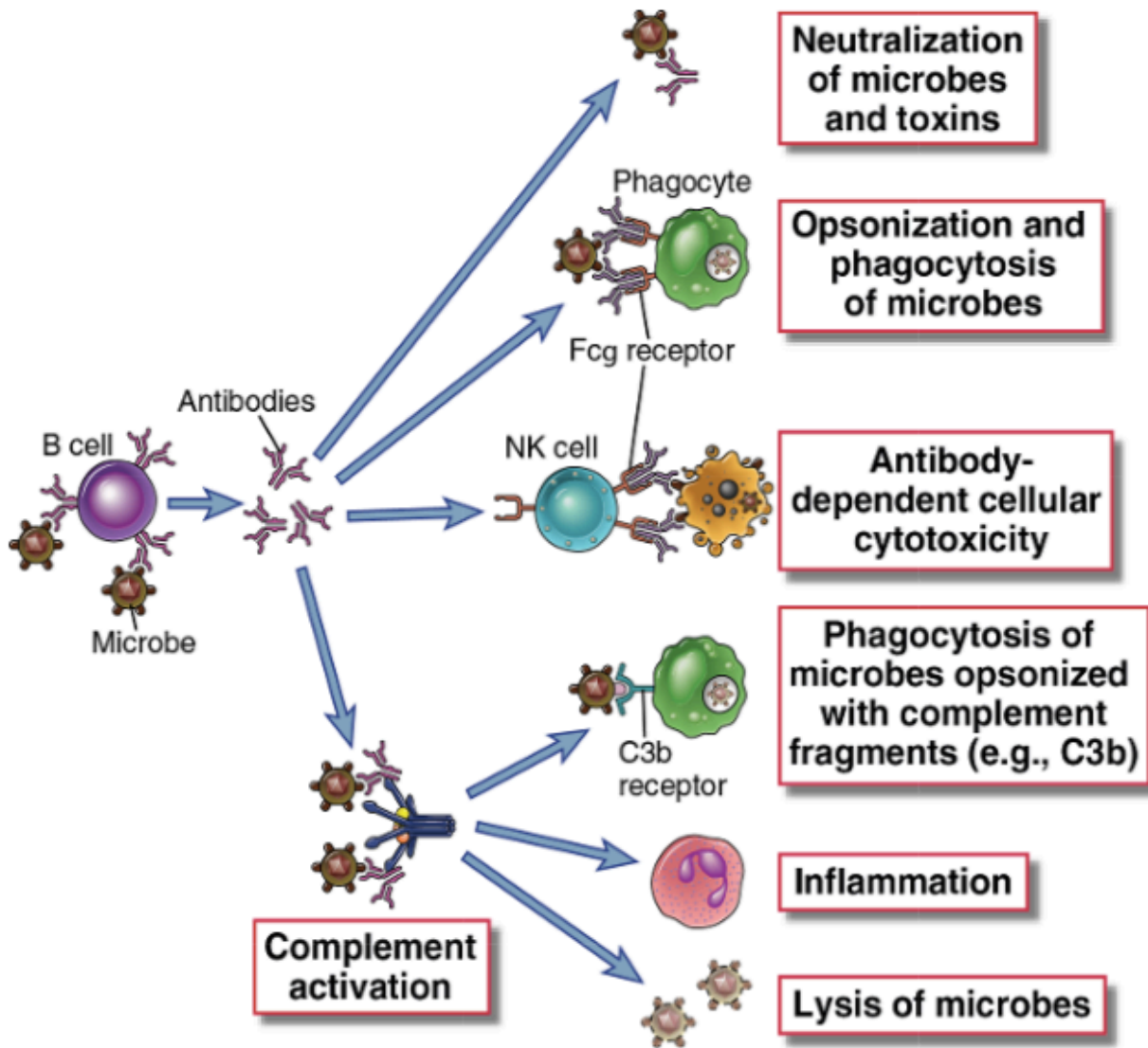


# The adaptive immune system : Humoral vs Cell Mediated



Abbas, Cellular and Molecular Immunology 2014

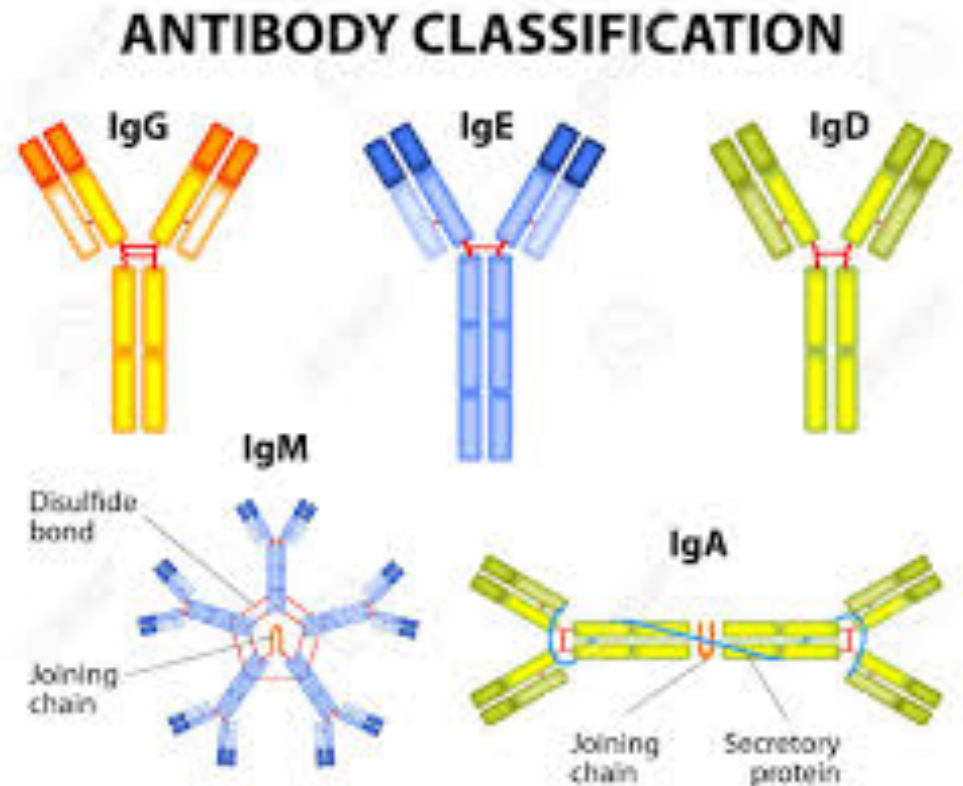
# What are immunoglobulins?



- Immunoglobulins are antibodies
  - They help identify pathogens to other cells and complement
  - flag for destruction

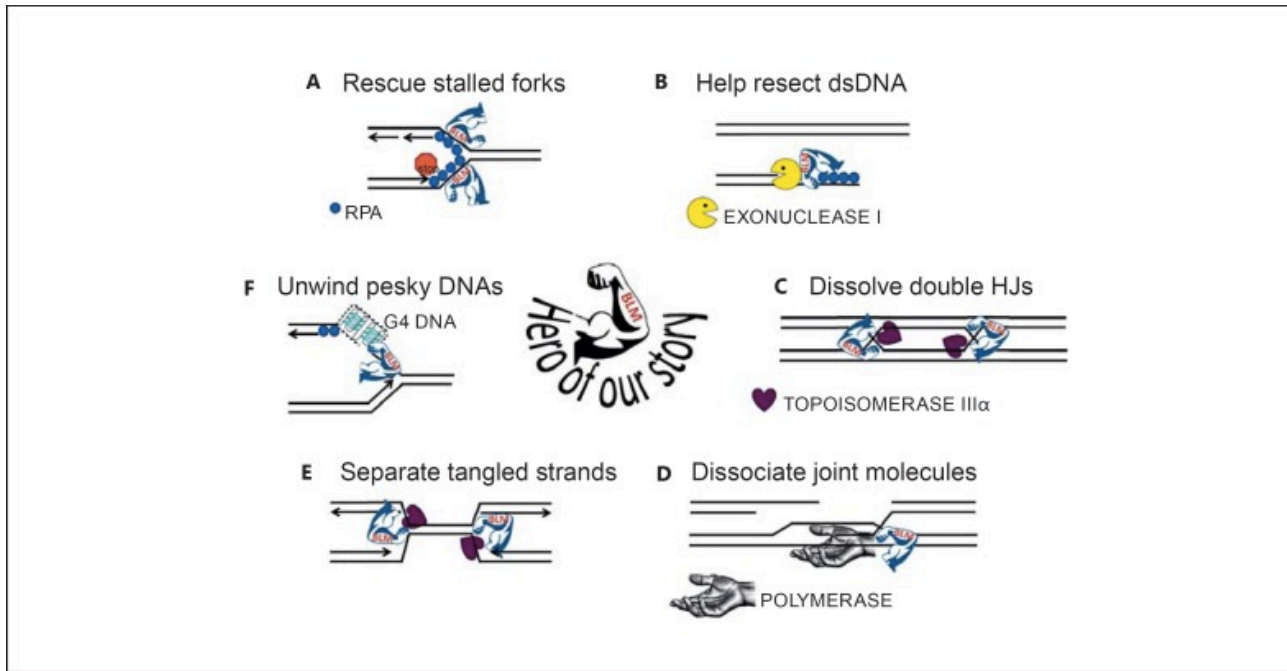
# What are immunoglobulins?

- There are 4 major types of immunoglobulin
  - IgM, IgA, IgG, IgE
    - IgM is the initial antibody found on B cells
    - Once activated by T cells B cells can switch to IgA, IgG and IgE
    - IgA is mostly on GI and Respiratory Tract
    - **IgG is the primary circulating antibody**
    - IgE circulates and sits on mast cells



# What is the immune defect in Bloom's Syndrome?

- The BLM gene is important in maintaining genomic stability

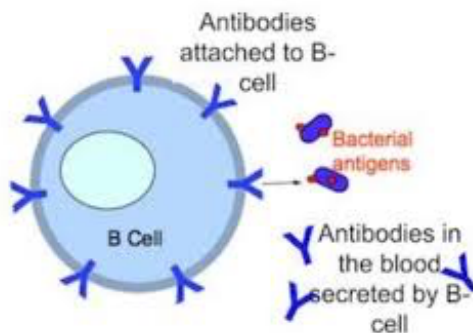


- B and T cells undergo a higher rate of gene rearrangement and replication than most cells of the body
  - DNA repair is essential for the development of the antigen receptors on B and T cells
  - also needed for cell proliferation
  - B cell class switching

# How does Bloom syndrome affect the cells?

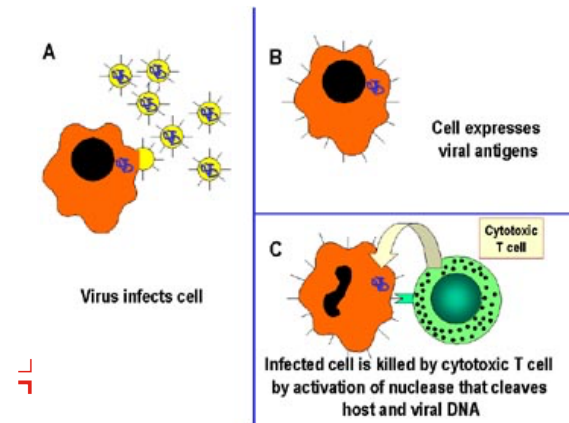
## ▪ B cells – antibody producing cells

- Typically total number of B cells is normal
- Decreased mature B cells with normal or increased naïve mature and transitional B cells decreased (suggests impaired maturation)
- Immunoglobulins may be low
  - Possibly due to impaired maturation
  - Or due to defective stimulation by T helper cells
- Class switch may be impaired



## ▪ T cells – two types killer cells and helper cells

- Total T cell number is significantly lower in children and low in adults
- CD4+ helper T cells are decreased in all patients
- CD8+ killer T cells low normal
- Absolute CD4 CD8 naïve, effector and memory T cell populations are reduced but have a normal distribution

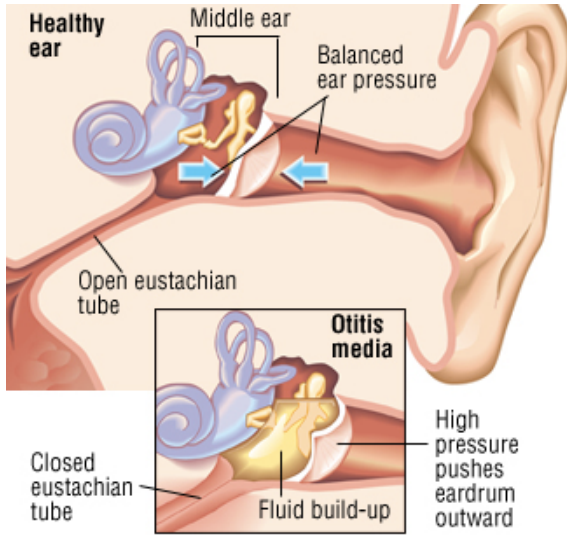




# How does this manifest itself?

## Infections in Bloom's Disease

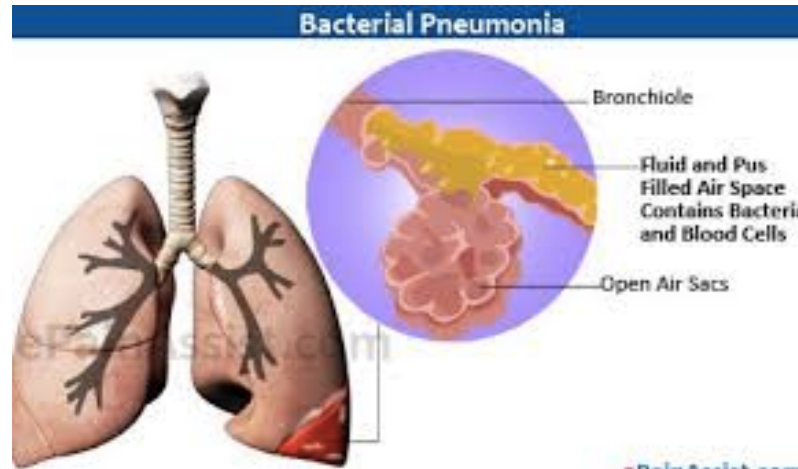
### Children -Ear Infections



### Adults- Sinusitis



### Pneumonia



# When to refer to immunology?

- **Frequent or recurrent infections**
  - chronic or recurrent sinusitis despite anatomically corrective surgery,
  - more than one pneumonia in a 10-year period
  - multiple episodes of bronchitis per year
  - bronchiectasis, severe pneumonia with empyema or blood-borne infection
- **Infections that are hard to treat**
  - Require a longer course of antibiotics or IV antibiotics
- **Particularly severe infections**
  - infection requiring ICU stay
- **Opportunistic infections**
  - infections not commonly seen in healthy people and commonly seen in people with immune abnormalities

# What lab tests should be done?

- Immunoglobulin levels (LOW)
- Immunoglobulin function (NO OR POOR RESPONSE TO VACCINES)
  - Vaccine titers
- Lymphocyte screen
  - Total lymphocytes – MAY BE NORMAL
  - Total T and B cells – MAY BE NORMAL
  - Total subsets of T helper, T killer and mature memory B cells  
DECREASES MAY INDICATE DEFICIENCY

# My recommendation. - Yearly Immune Surveillance

**Monitoring yearly rather than once there is significant infection may enable earlier identification of trends and allow intervention prior to significant infection**

- Consider immunology scan yearly
- Lymphocyte subsets
  - B memory cells
- IgG IgA and IgM levels

# What are the available treatments?

- Prophylactic antibiotics
  - Targeted to recurrent infection





# What are the available treatments?

- Sinus infections
  - Daily nasal lavage
  - Prophylactic antibiotics



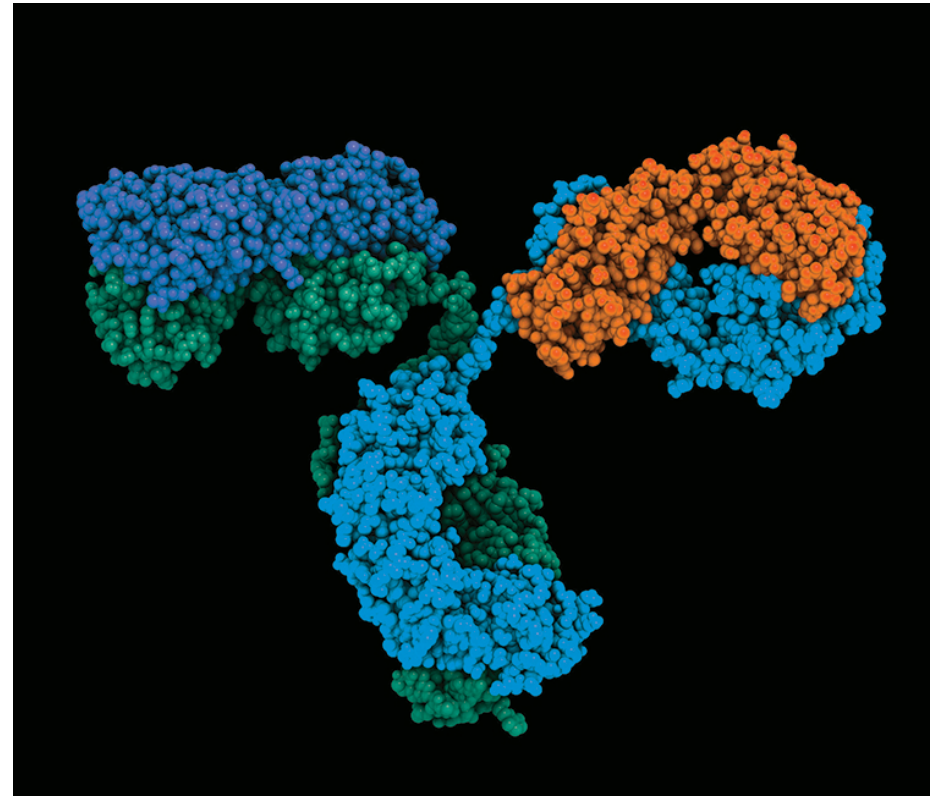
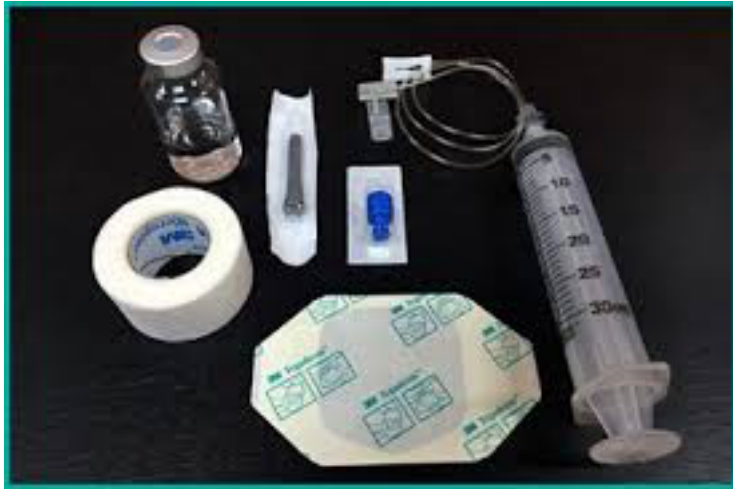
# Treatments

- Bronchiectasis (permanent enlargement of lung airways)
  - Cough assist devices
  - Vibration vests



# Treatments?

- Replacement immunoglobulin
  - If levels and vaccine titers low



# What is IVIG or SCIG?

- What is immunoglobulin replacement and how does it work?
  - Immunoglobulin replacement is a blood product.
  - It contains the IgG antibodies of the community or group from which the blood was sourced.
  - It is a pooled product, reflects the antibody of the population as a whole
  - It is not IgA or IgM - it only replaces IgG
  - High doses are used to suppress the antibody response in people with autoimmune disease – is not for everyone.



# Summary:

- No issues? – watchful surveillance including lymphocytes and IgG levels
- Recurrent infection?
  - Immune workup
    - Immunoglobulin + vaccine titers normal but recurrent infection
    - Consider prophylactic antibiotics
- Immunoglobulin levels (LOW)
  - Immunoglobulin function (NO OR POOR RESPONSE TO VACCINES)
    - consider immunoglobulin replacement



# Questions?



Thank You

