Warning Signs of PID

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Introduction

- **Primary immunodeficiencies** are disorders in which part of the body's immune system is missing or does not function normally.
- To be considered a ***primary*** immunodeficiency (PID), the cause of the immune deficiency must not be secondary in nature (i.e., caused by other disease, drug treatment, or environmental exposure to toxins).

Primary ?

versus

Secondary?

Secondary Immunodeficiencies

- Cardiovascular diseases : CHD
- Gastro-intestinal diseases : Celiac d., CF
- Pulmonary diseases : CF
- Infectious diseases :HIV/AIDS
- Renal diseases : obstructive uropathies
- Hepatobilliary diseases : Cirrhosis
- Malignancies : Lymphoma,…
- Others : burn , surgery,

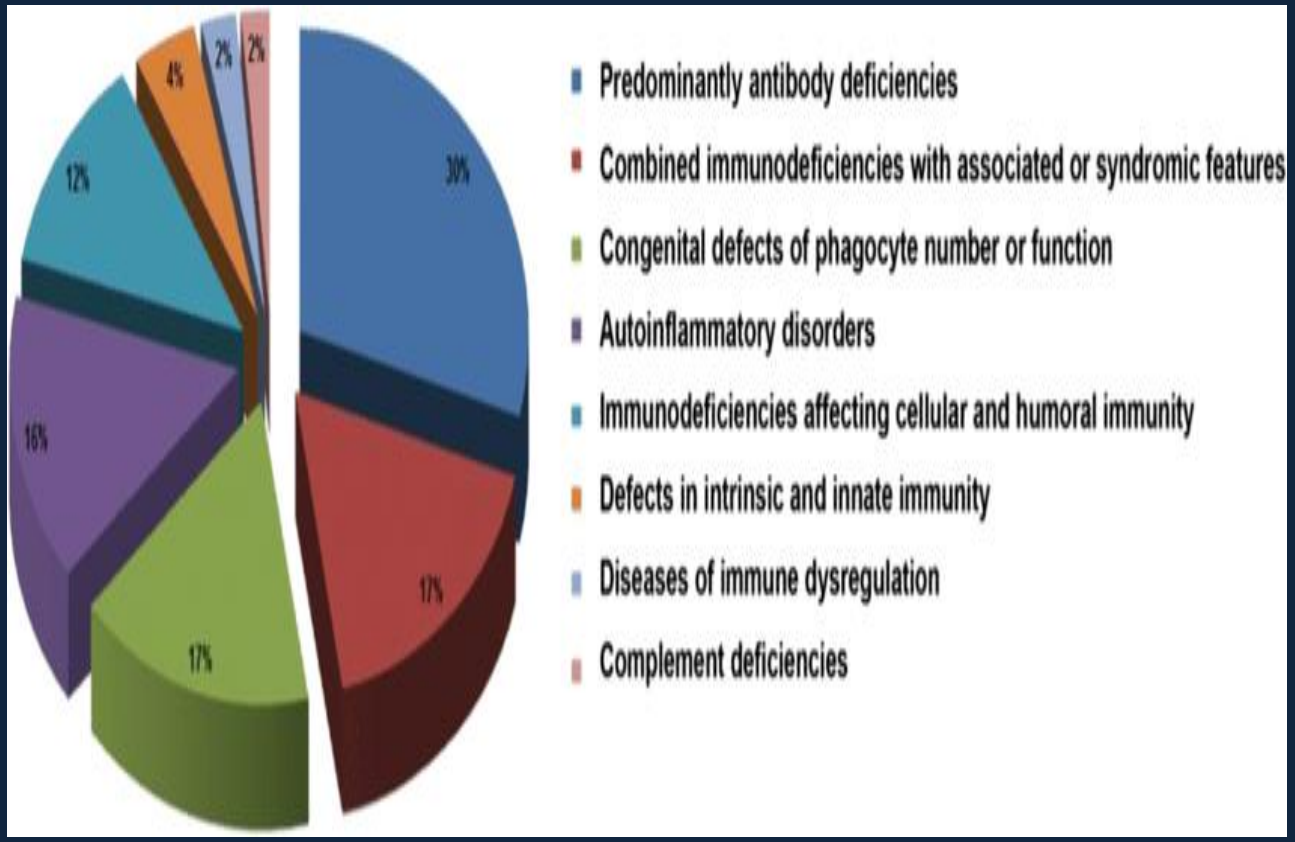
Introduction

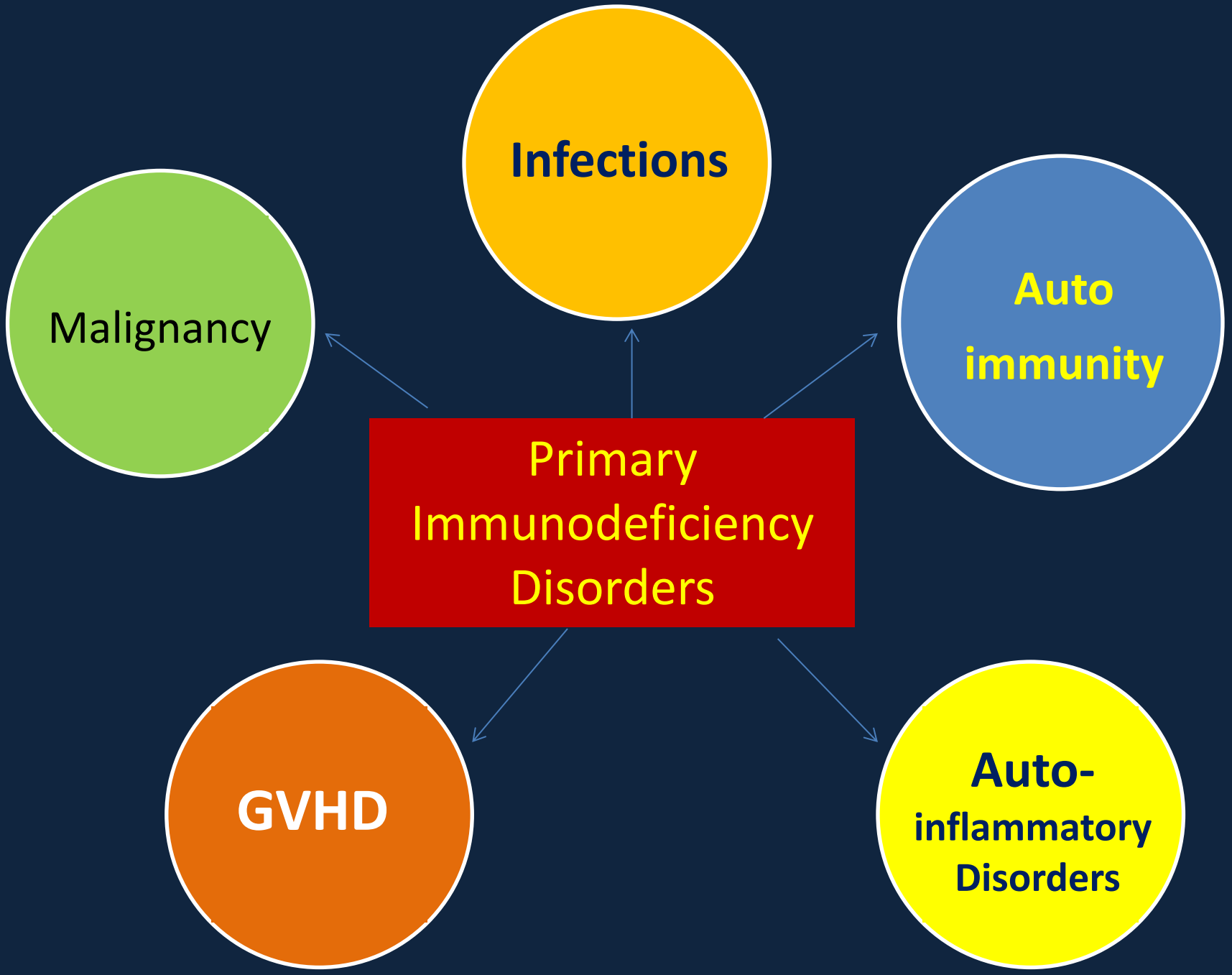
- Most primary immunodeficiencies are genetic disorders.
- The majority are diagnosed in children under the age of one, although milder forms may not be recognized until adulthood.
- While there are over 430 recognized PIDs as of 2019, most are very rare.

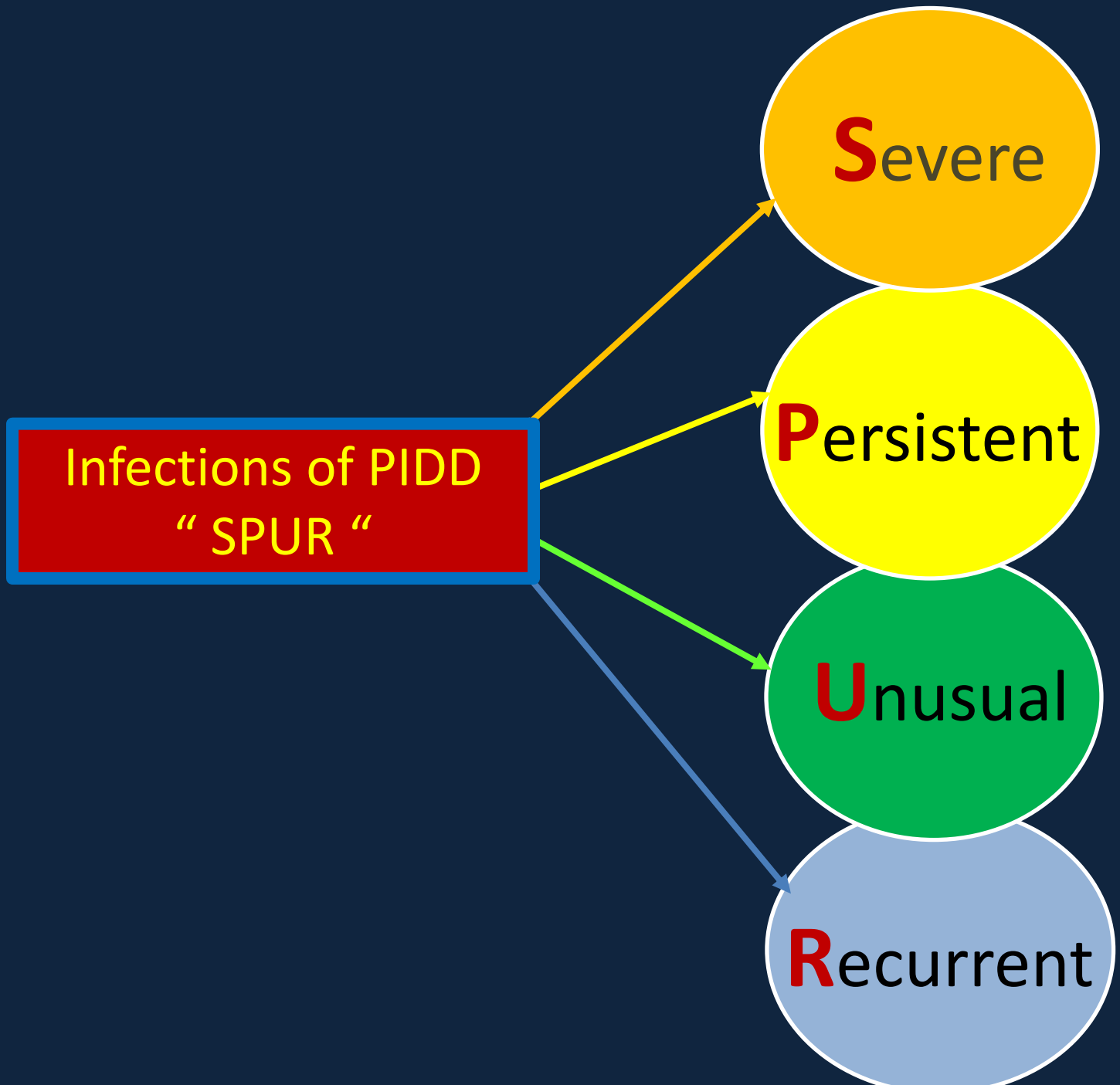
International Union of Immunological Societies (IUIS)

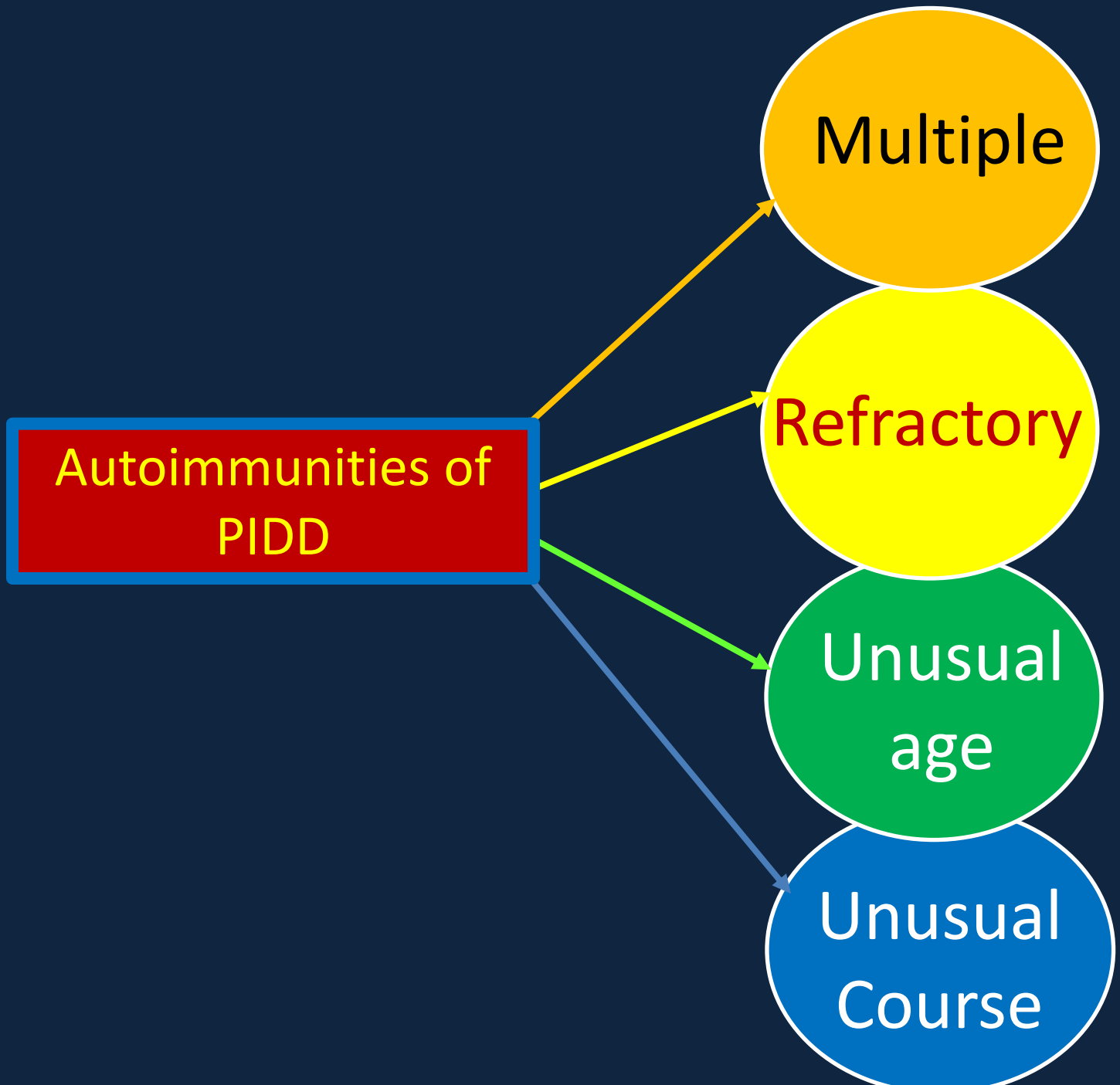
1. Immunodeficiencies affecting cellular &humoral immunity
2. CID with associated or syndromic features
3. Predominantly antibody deficiencies.
4. Diseases of immune dysregulation
5. Congenital defects of phagocyte number, function, or both
6. Defects in intrinsic and innate immunity
7. Auto-inflammatory disorders
8. Complement deficiencies
9. Bone marrow failure disorders
10. Phenocopies of PID

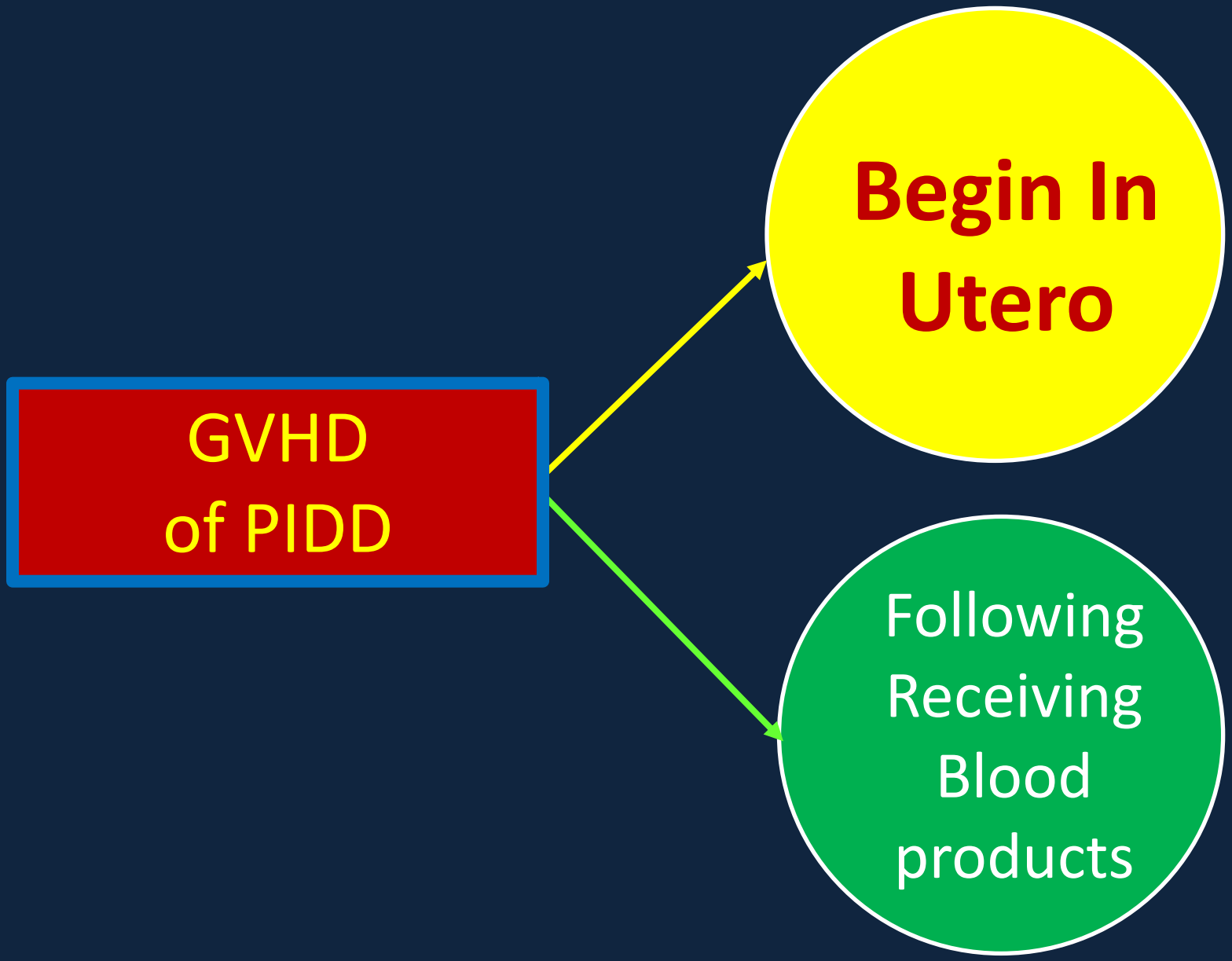
International Union of Immunological Societies (IUIS)

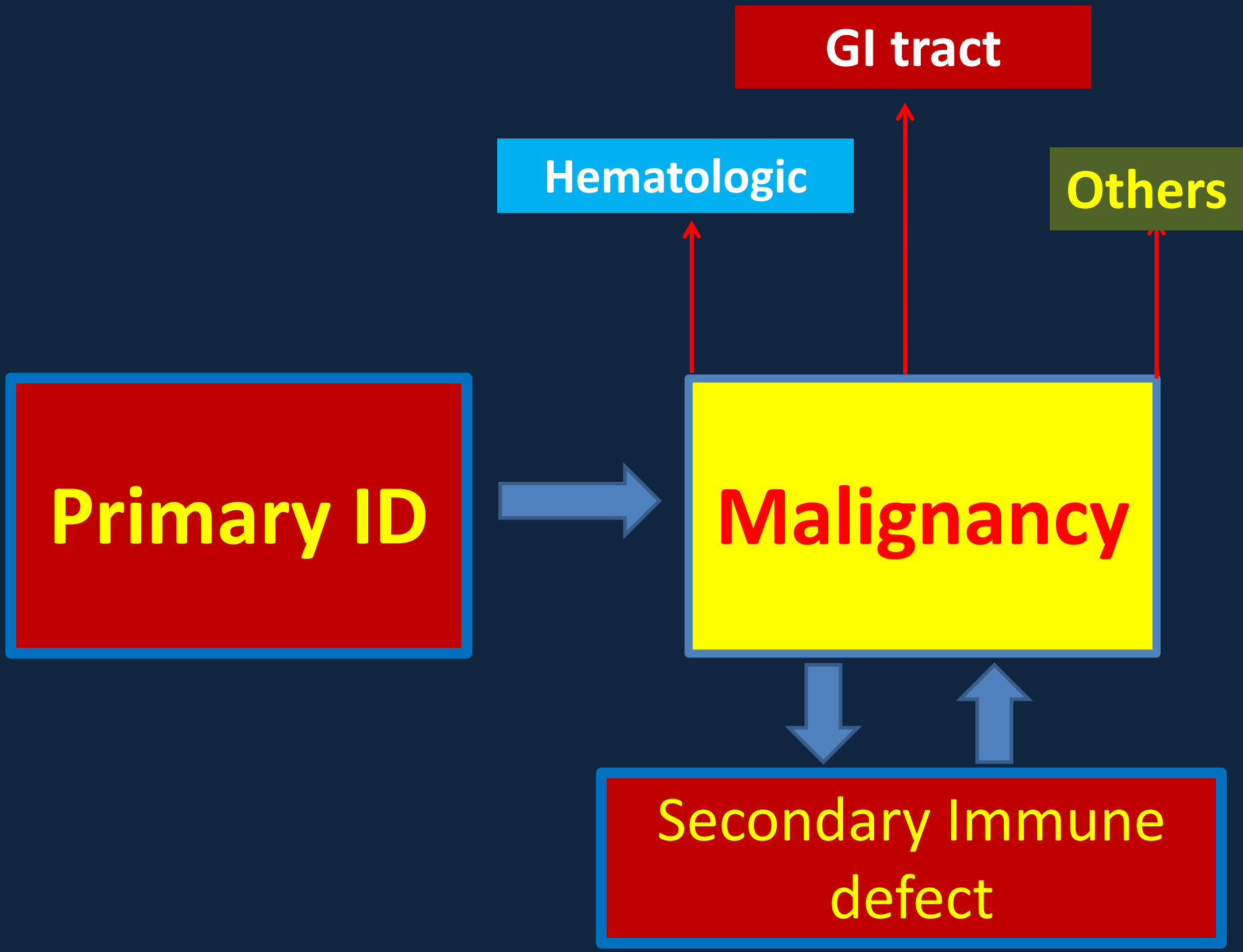



Infections
Malignancy
Auto immunity
Primary Immunodeficiency Disorders
GVHD
Auto-inflammatory Disorders


Infections of PIDD
“ SPUR “
Severe
Persistent
Unusual
Recurrent


Autoimmunities of PIDD
Multiple
Refractory
Unusual age
Unusual Course


GVHD
of PIDD
Begin In
Utero
Following
Receiving
Blood
products


GI tract
Hematologic
Others
Primary ID
Malignancy
Secondary Immune defect

Jeffrey Modell Foundation

- Vicki and Fred Modell established the Jeffrey Modell Foundation (JMF) in 1987, in memory of their son Jeffrey, who died at the age of 15, from complications of Primary Immunodeficiency (PI) .

Jeffrey Modell Foundation (JMF)

- JMF is an international, non-profit, organization dedicated to helping individuals and family members affected PID.

- 4 main areas:
  - research
  - physician and patient education
  - patient support
  - public awareness of PID

Jeffrey Modell Foundation (JMF)

- The JMF provides:
- Funding of research fellowships and laboratory facilities
- Sponsors physician symposia in the United States, Canada, and Europe as well as grand rounds, seminars, and other educational activities for physicians
- Offers publications for both the lay and medical communities
- Provides affected individuals with access to leading medical centers with departments of clinical immunology.

Educational Posters

Posters for School Nurses & Day Care Centers

Immune System Poster

Jeffrey Modell Foundation

Educational Posters

NEW!

4 Stages of Immunologic Testing Poster

Jeffrey Modell Foundation

IPOPI

Educational Posters

China

Estonia

Finland

France

Germany

Greece

Hungary

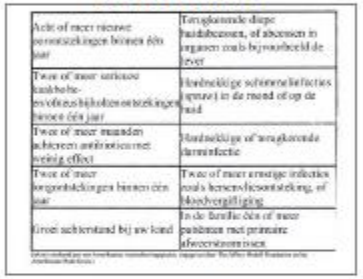
Israel

Italy

Iran

Japan

Netherlands



Poland

Portugal

Russia

Spain

Sweden

AND MANY MORE...

10 Warning Signs Posters Around the World

Jeffrey Modell Foundation

IPOPI

JMF warning signs

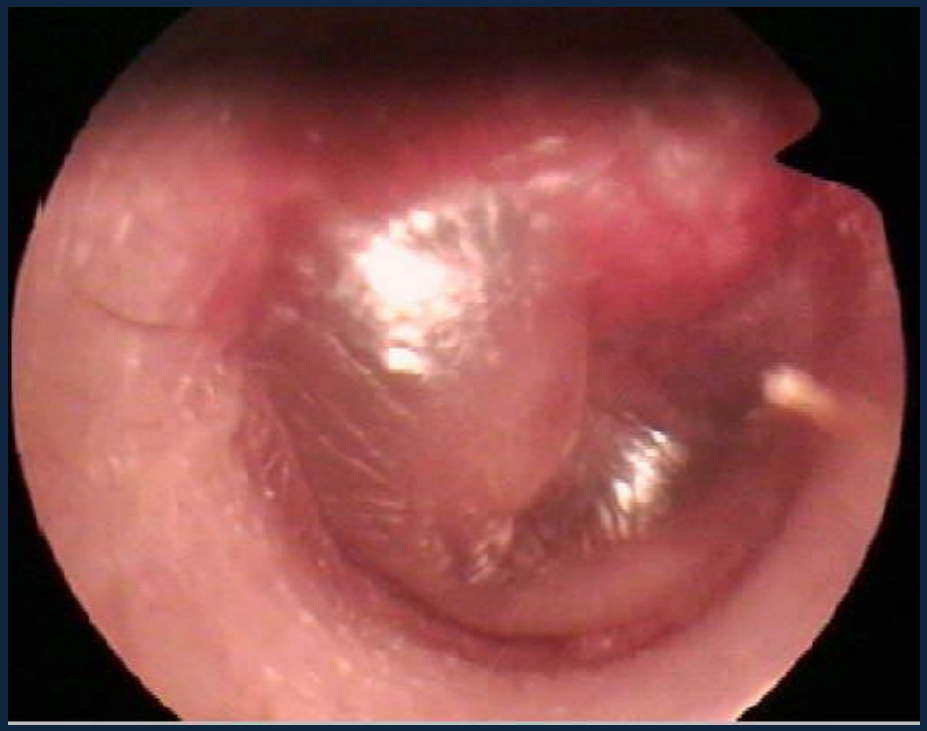
- Consultation with PID experts is strongly suggested

Warning Signs

- If a patient, child or adult,is affected by one of the following conditions, think about the possible presence of primary immunodeficiency.

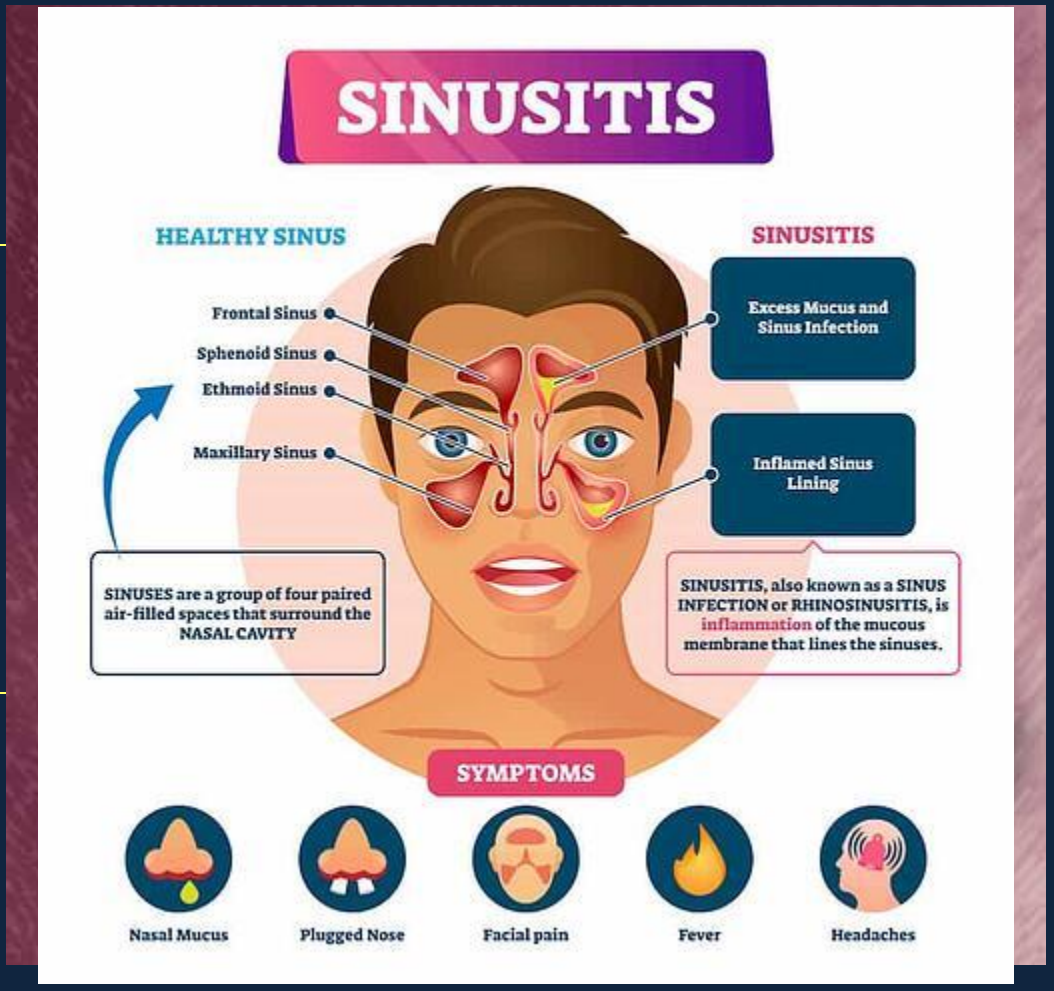
Warning Signs

- 1. 4 or more new ear infections within 1 year



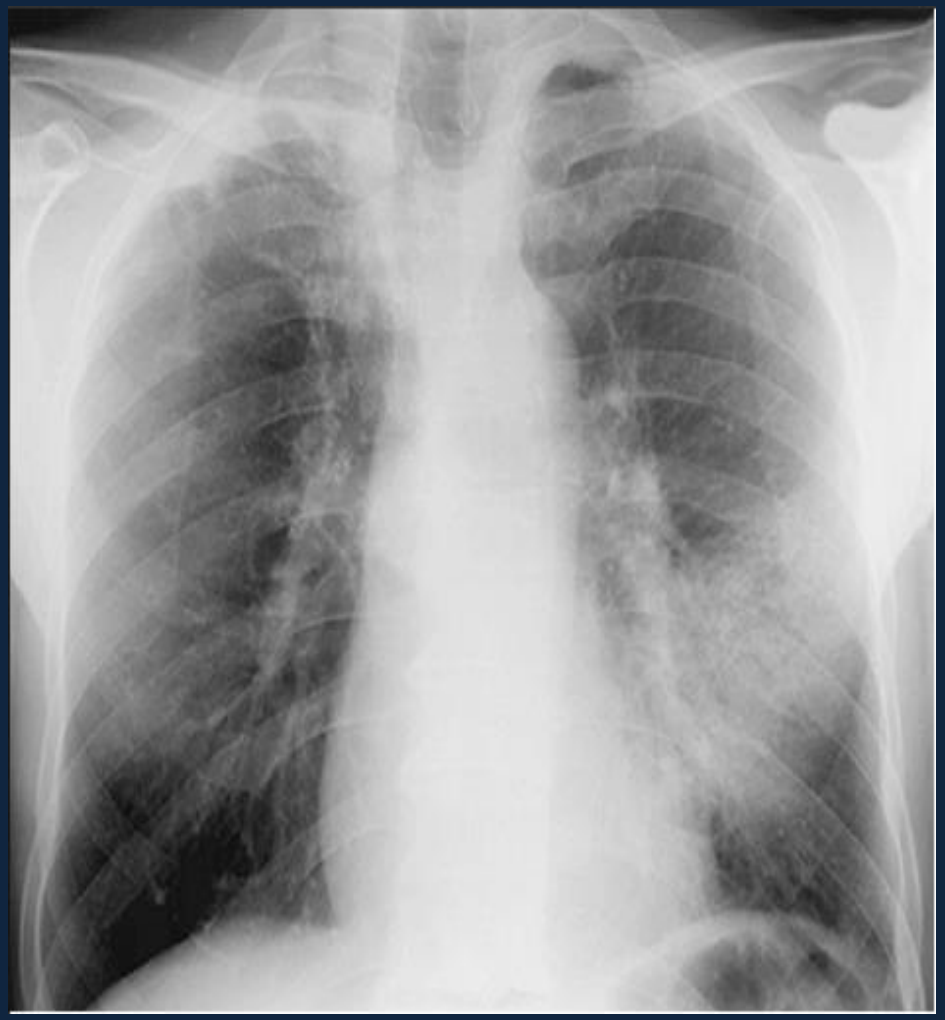
Warning Signs

- 2. **Two or more serious sinus infections within 1 year**



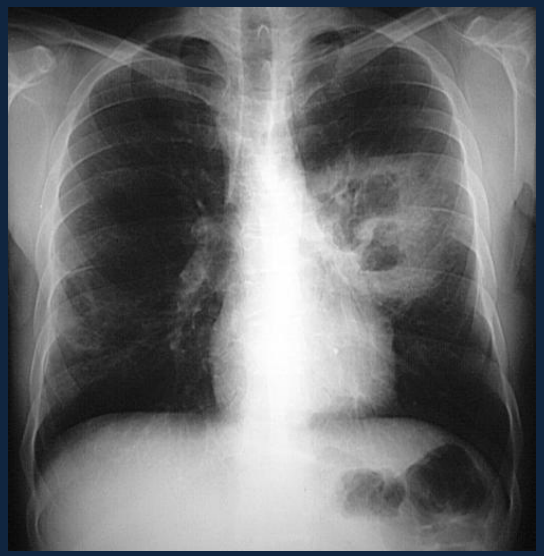
Warning Signs

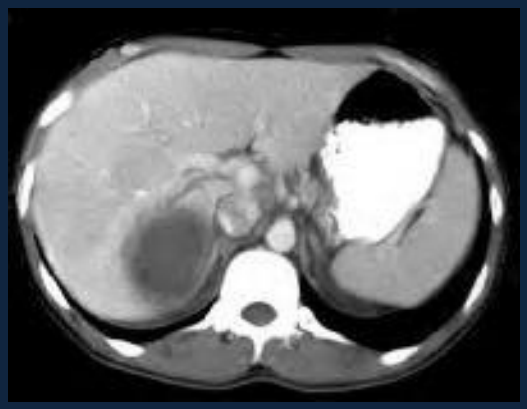
- 3.**Two or more pneumonia's within 1 year**

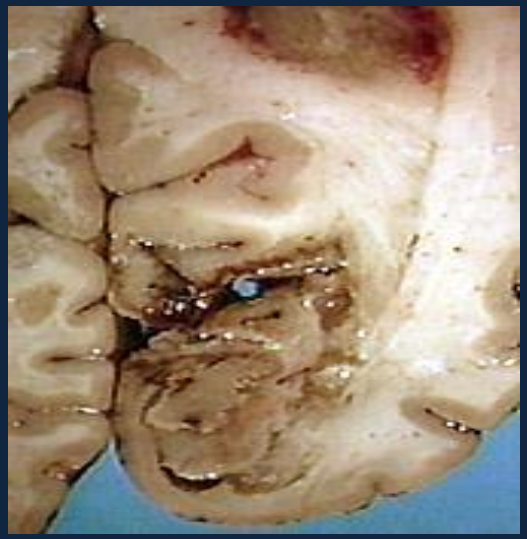


Warning Signs

- 4. **Recurrent, deep skin or organ abscesses**





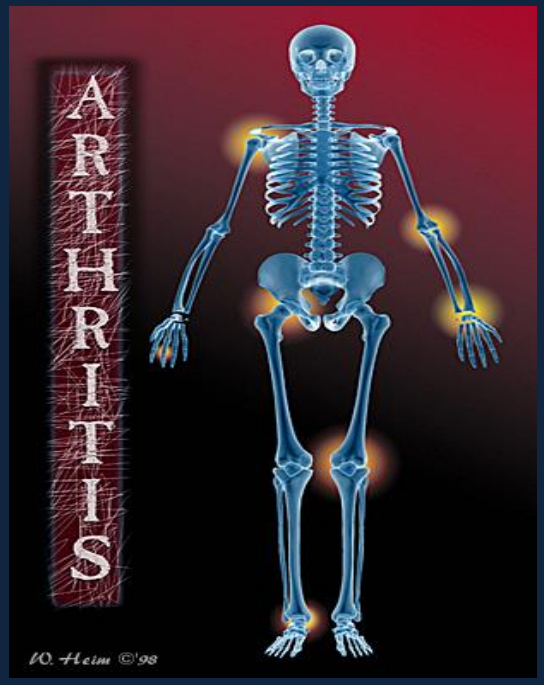


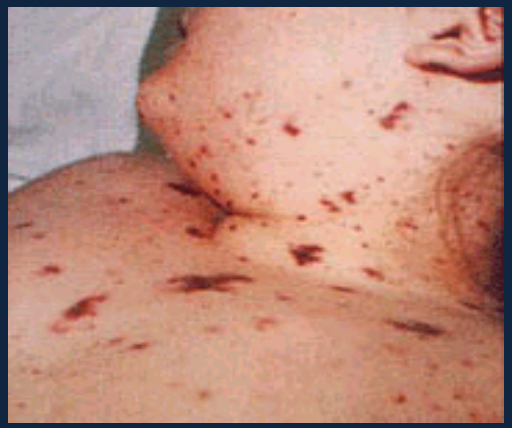
*Liver or brain abscess must be worked up at first episode.

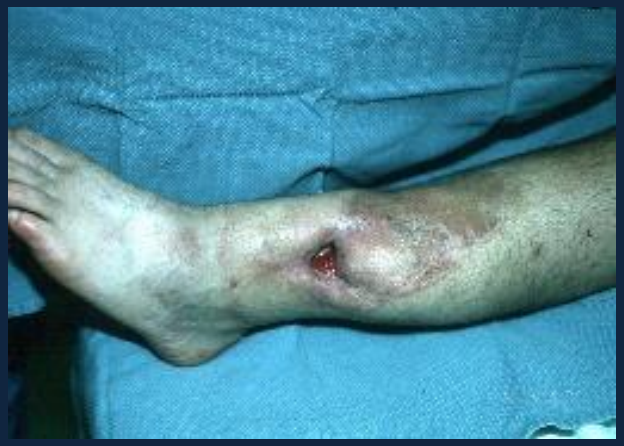
Warning Signs

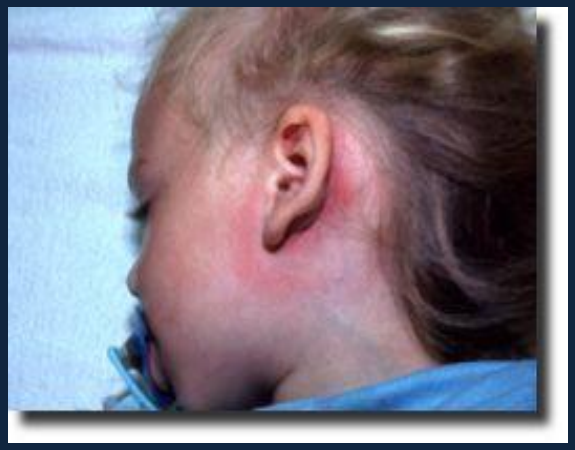
- 5. **Two or more deep-seated infections such as**
- **meningitis**
  osteomyelitis
  cellulitis
  sepsis
  arthritis

→ **during life**







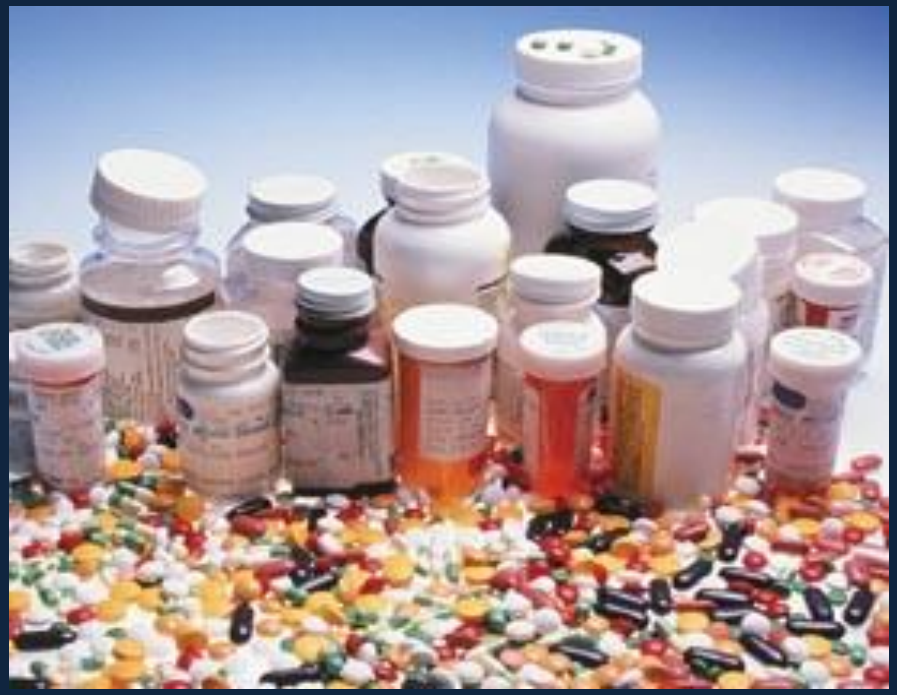


Warning Signs

6. Need for intravenous antibiotics to clear infections

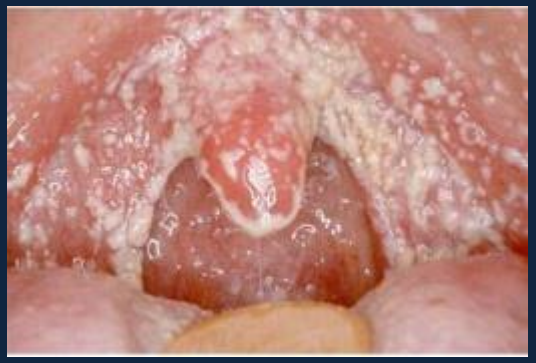
Warning Signs

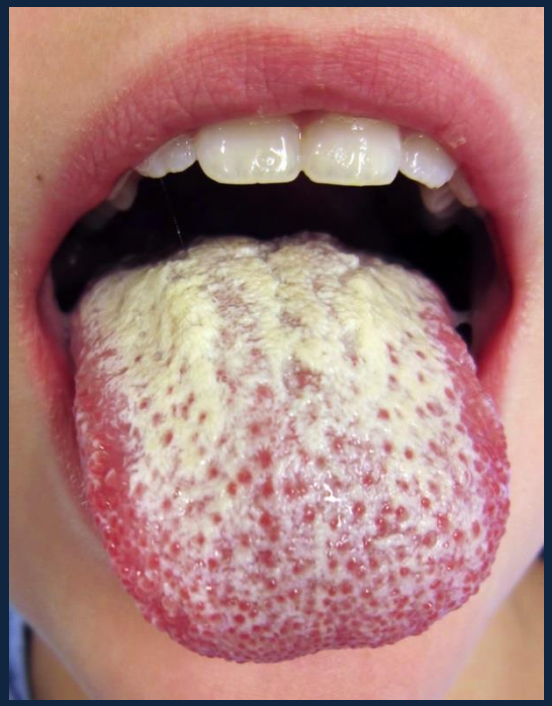
- 7. Two or more months on antibiotics with little effect

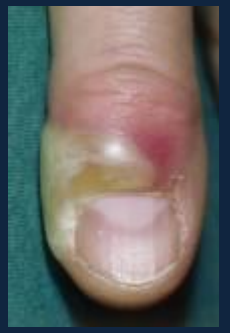


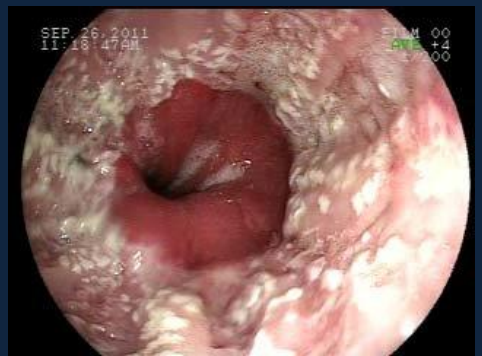
Warning Signs

- 8. **Persistent thrush in mouth or elsewhere on skin, after age 1**







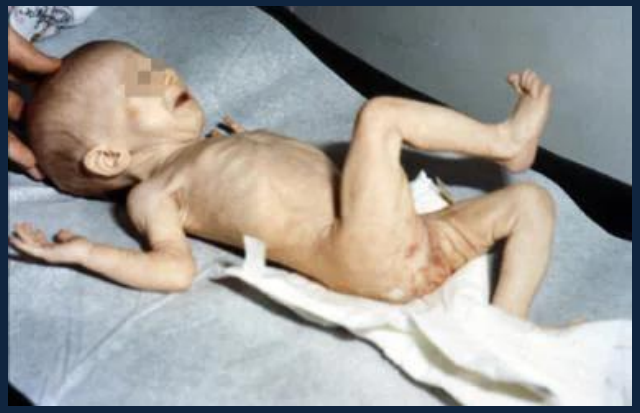


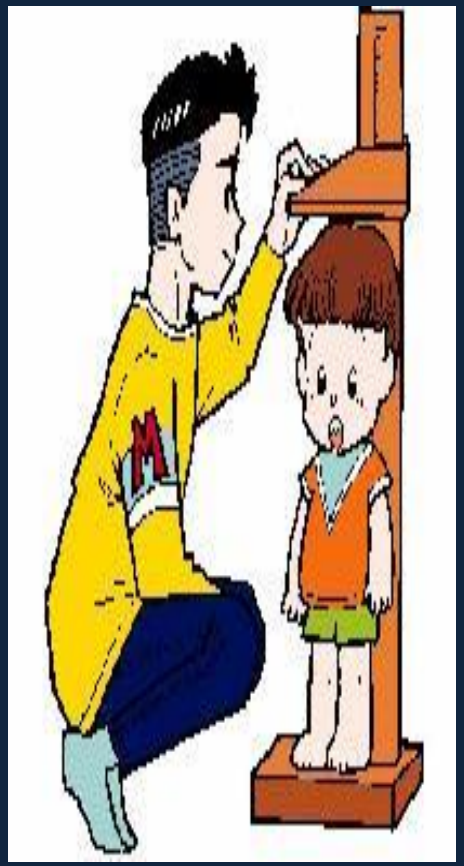
Primary immunodeficiencies with candidiasis

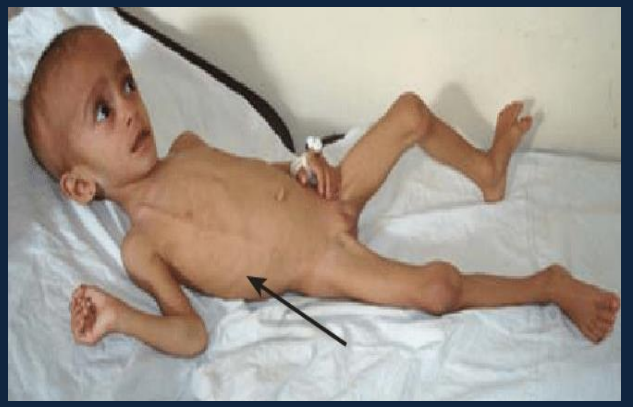
T cell/combined immunodeficiencies
Severe combined immunodeficiency
DiGeorge syndrome
Hyperimmunoglobulin-E syndrome
Autosomal dominant (STAT3 mutation)
Autosomal recessive (DOCK8 mutation)
IL-17RA & IL-17F mutation
Dectin-1 deficiency
CARD9 defect
STAT1 gain-of-function mutation
Autoimmune polyendocrinopathy–candidiasis–ectodermal dystrophy

Warning Signs

- 9. **Failure of an infant to gain weight or grow normally (FTT)**

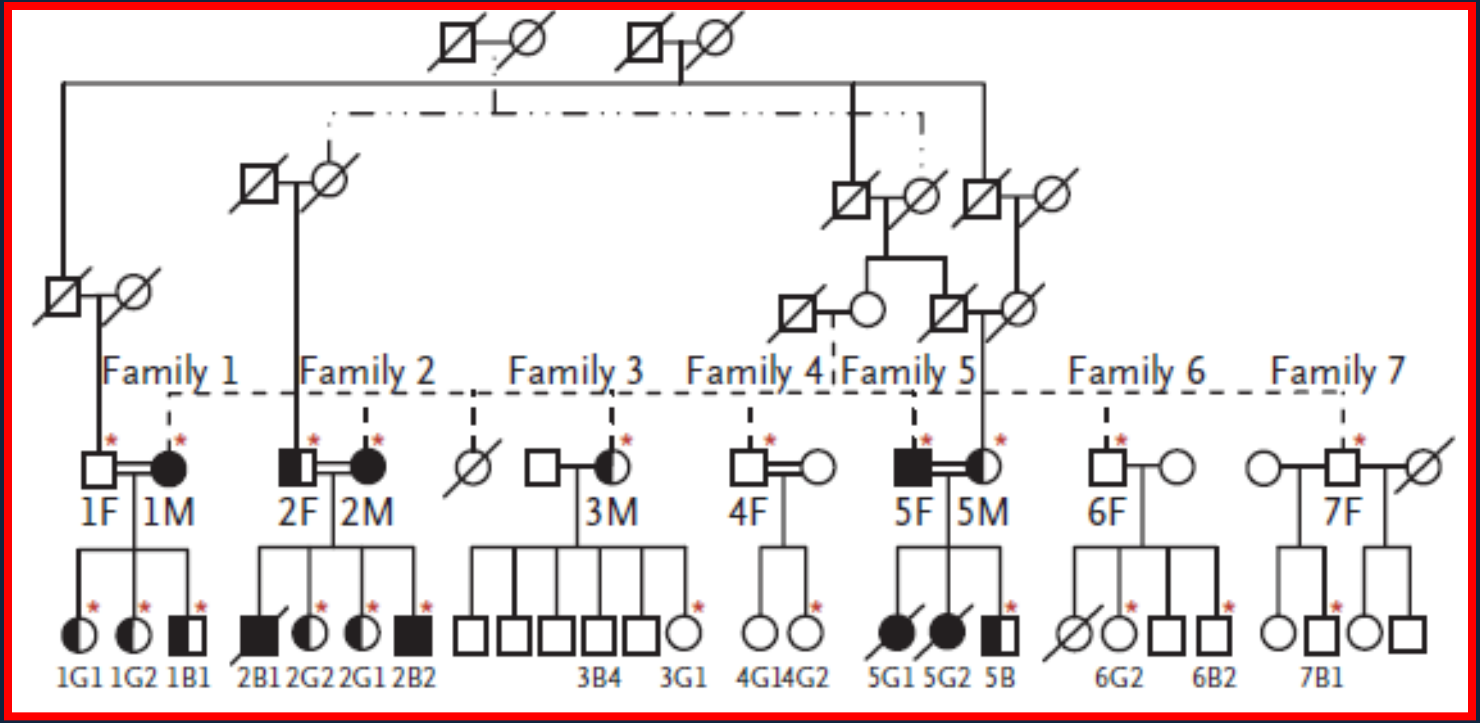






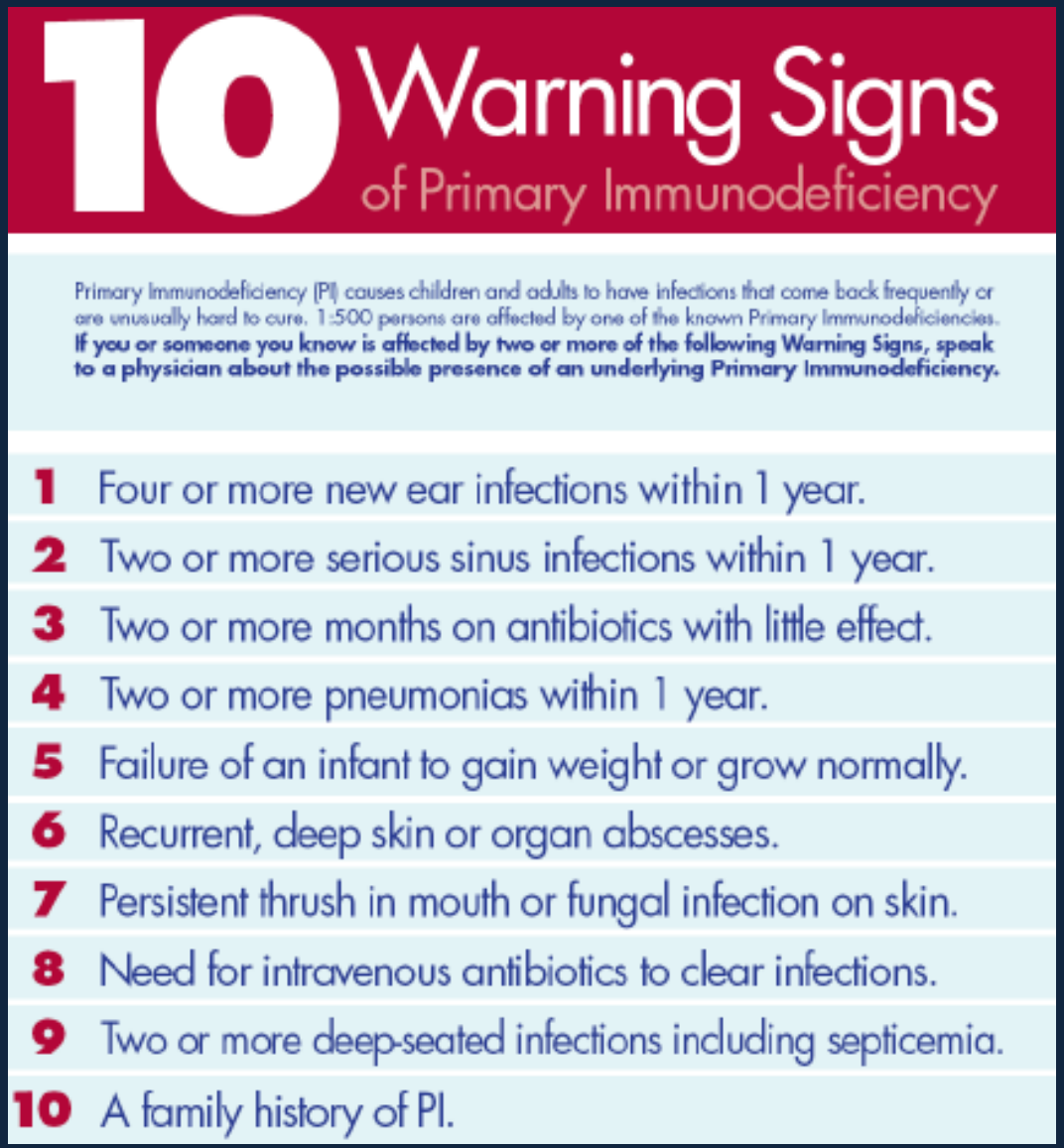
Warning Signs

- 10. **A family history of primary immunodeficiency**

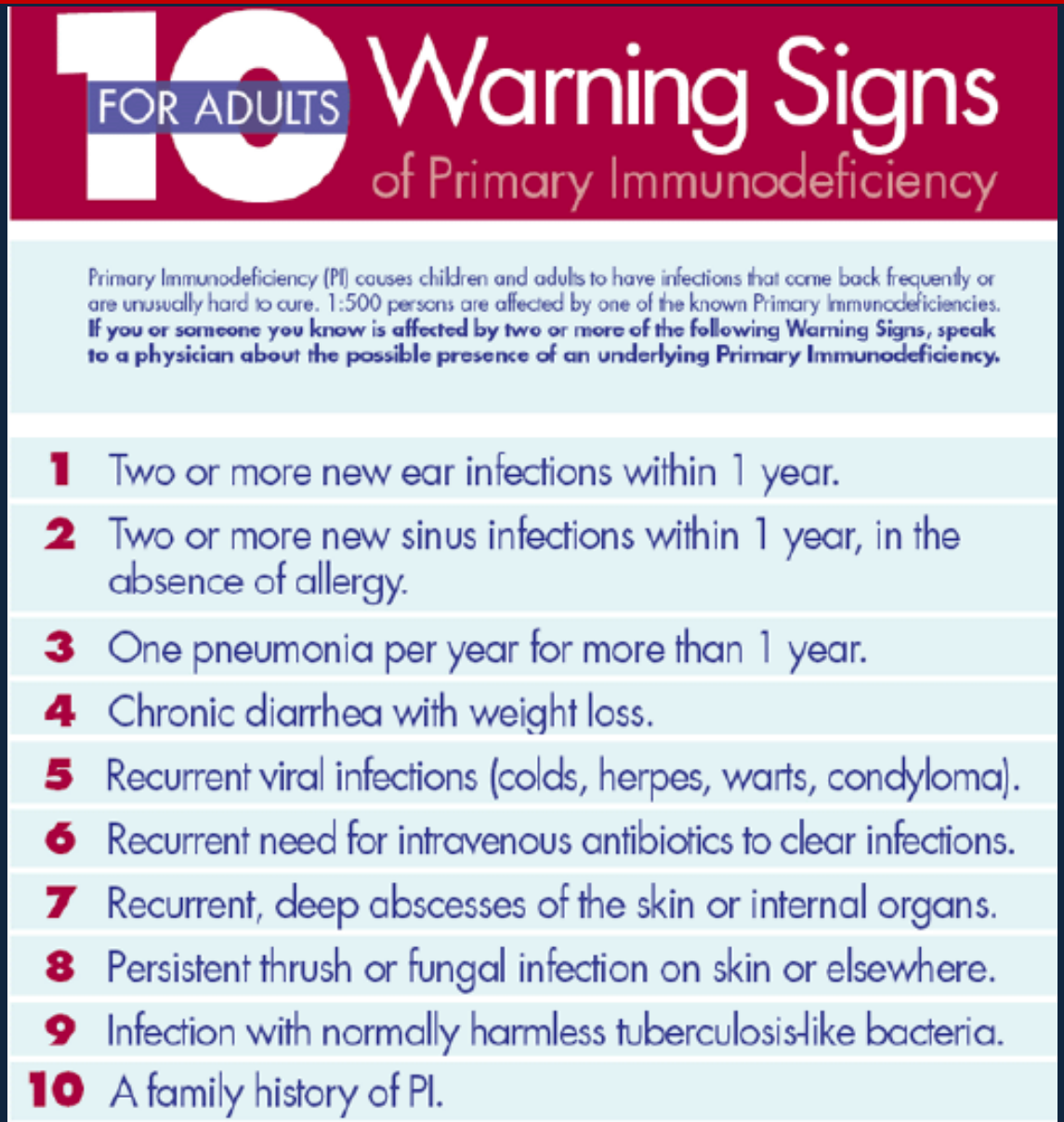


Jeffery Modell Criteria for PID

CHILDREN



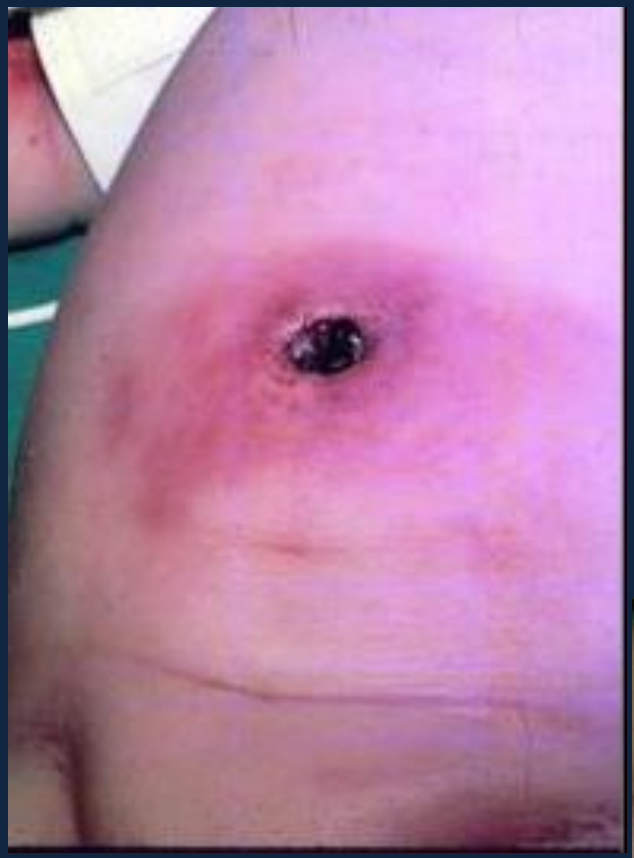
Jeffery Modell Criteria for PID ADULTS

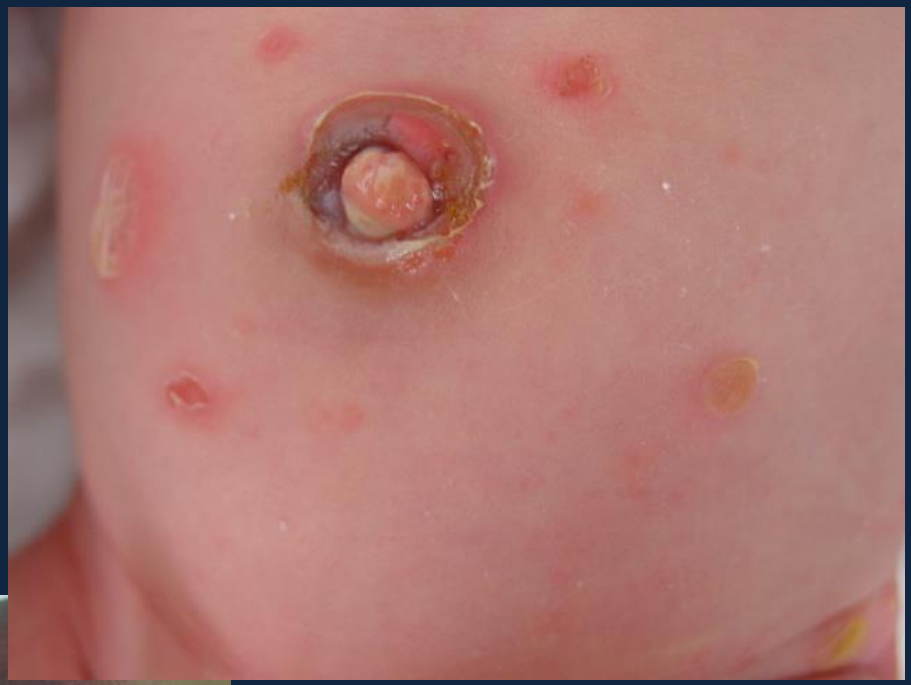


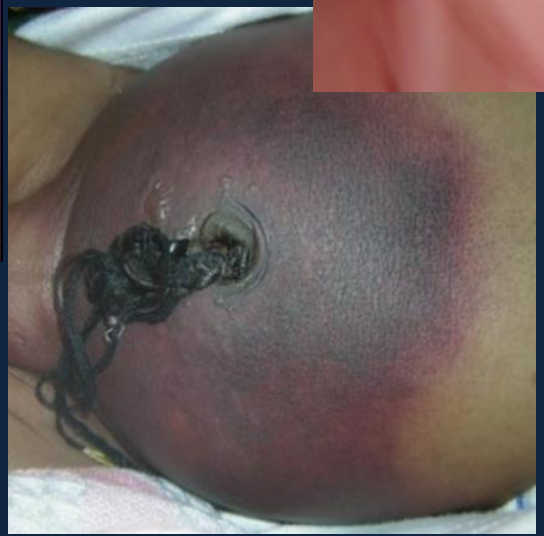
Other Warning Signs
Delayed separation of umbilical cord

- Delayed separation of umbilical cord beyond **3 weeks** of age

Other Warning Signs
Omphalitis



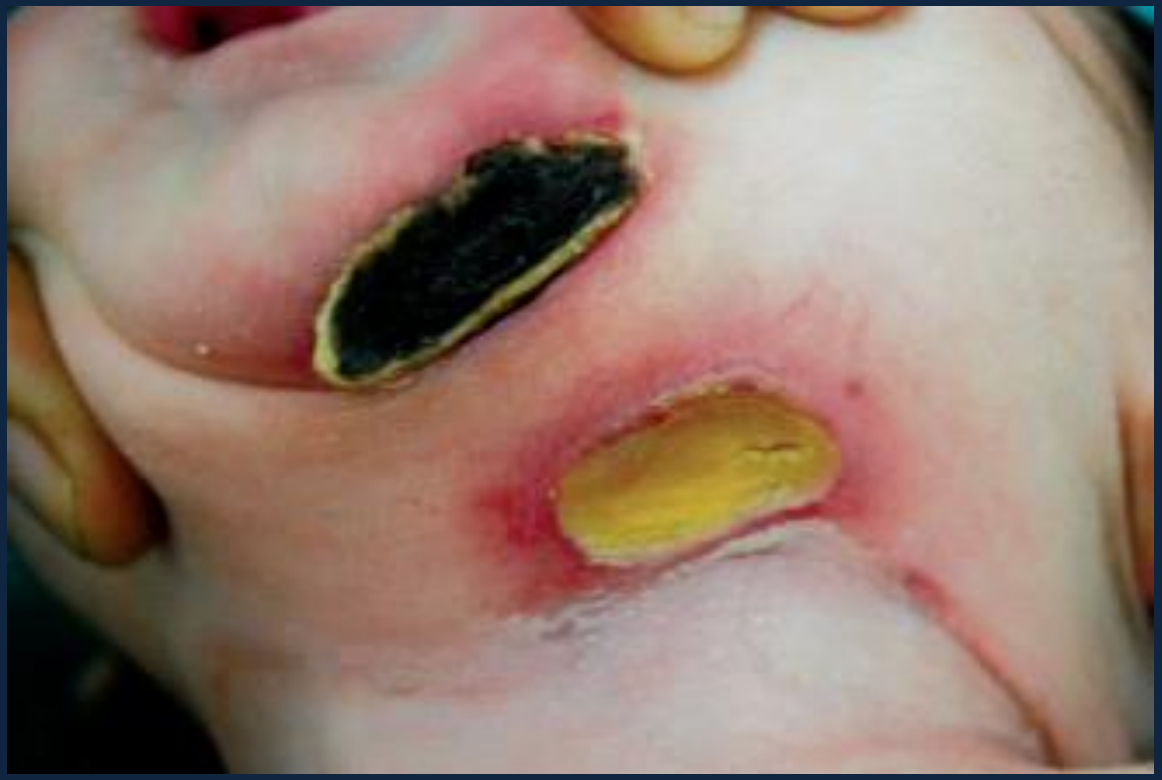




Periomphalitis with ulcer over chest wall in a 13 day old male neonate

Other Warning Signs

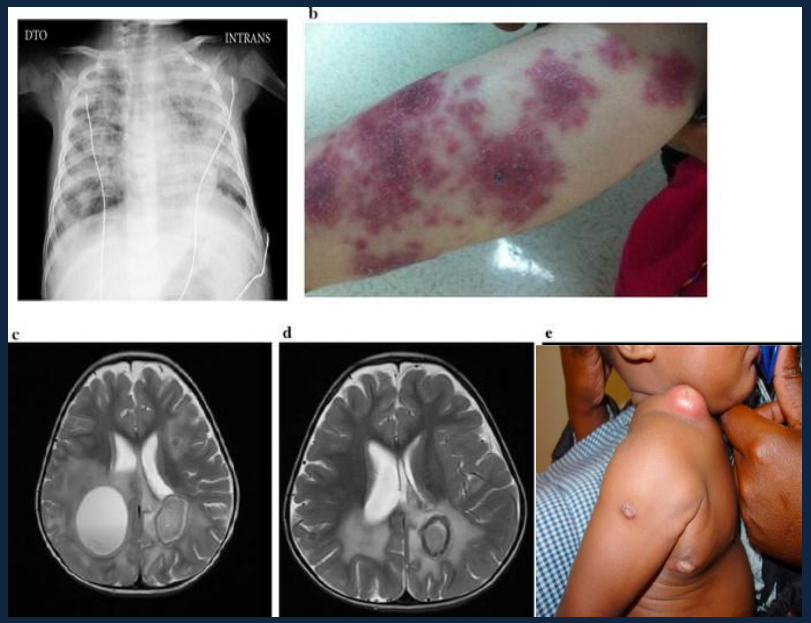
Persisting ulcer with no pus formation in a 13 day old male neonate



Other Warning Signs
Adverse ractions to Vaccines :

Polio-vaccine associated paralysis

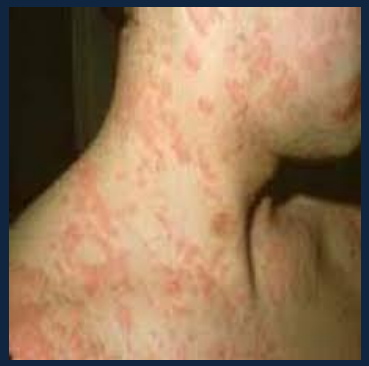
Disseminated BCG



Other Warning Signs
Adverse reactions to transfusions :

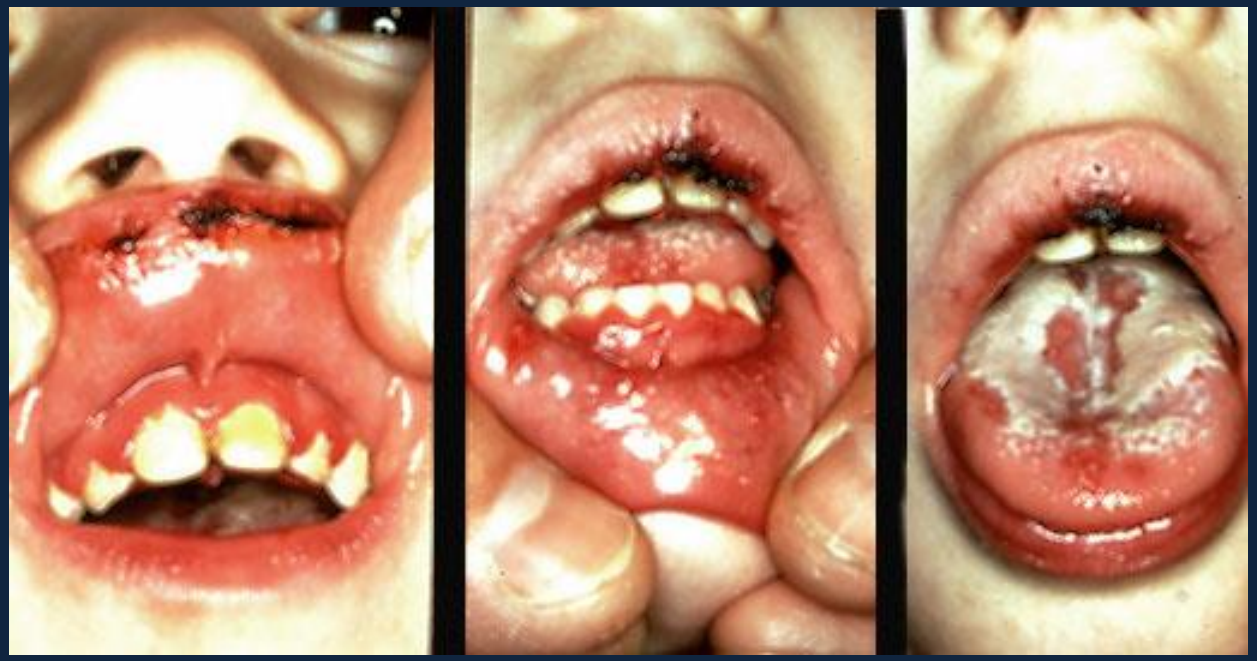
GVHD in cellular immunodeficiency

Anaphylactic reactions in IgA def

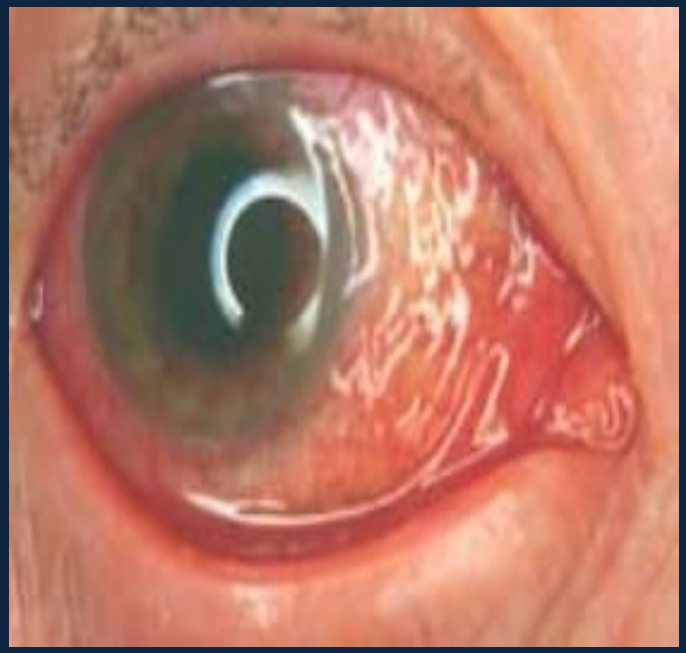


Other Warning Signs
gingivo-stomatitis & periodontitis

Persistent or recurrent gingivo-stomatitis & periodontitis



Other Warning Signs
Recurrent severe conjunctivitis

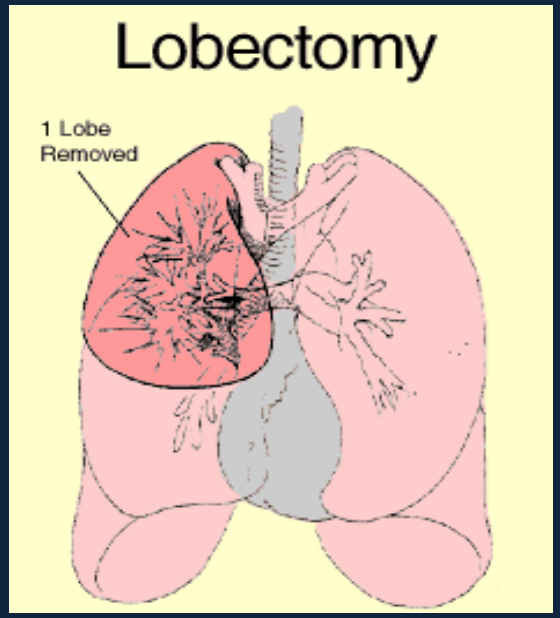


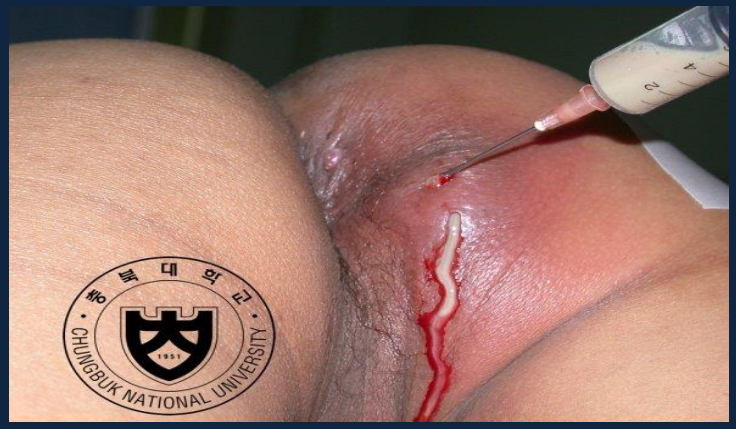
- Recurrent severe conjunctivitis

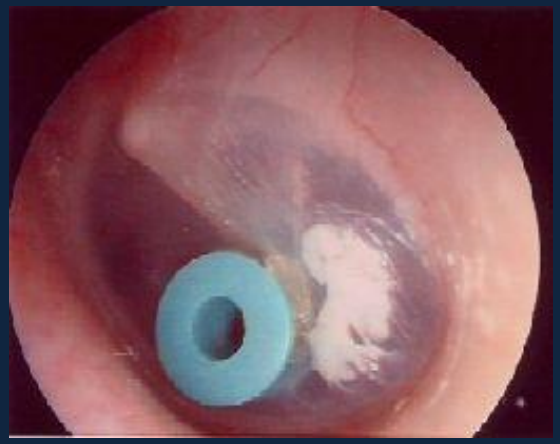
Other Warning Signs

Surgical intervention for chronic infection

- lobectomy for bronchiectasis
- tonsillectomy*
- adenoidectomy*
- recurrent grommet insertion
- recurrent incision of boils





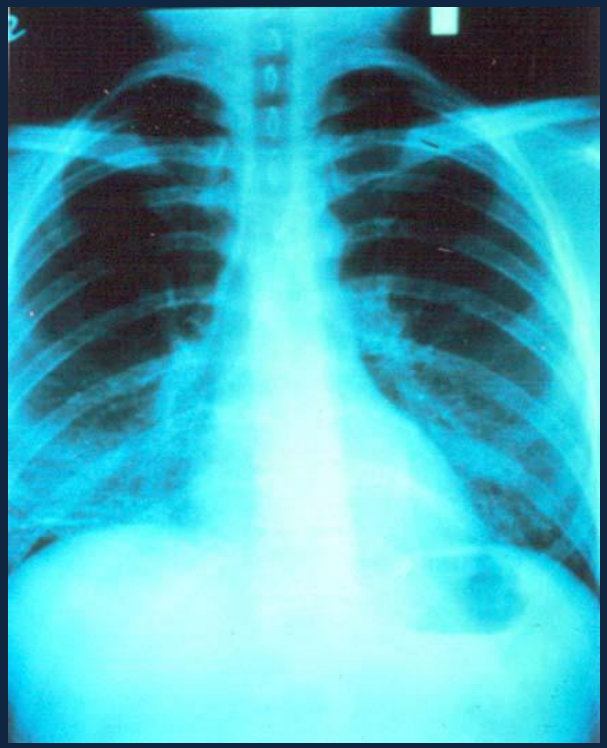


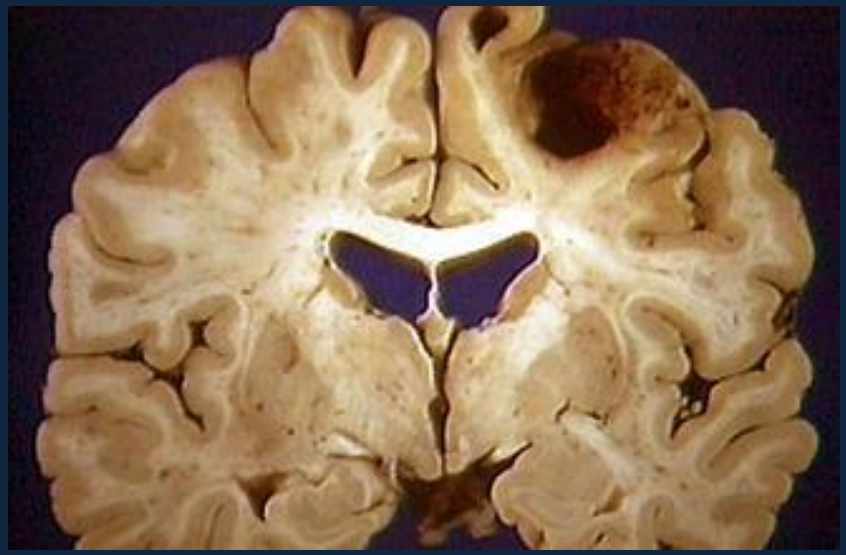
Other Warning Signs
Unusual pathogens

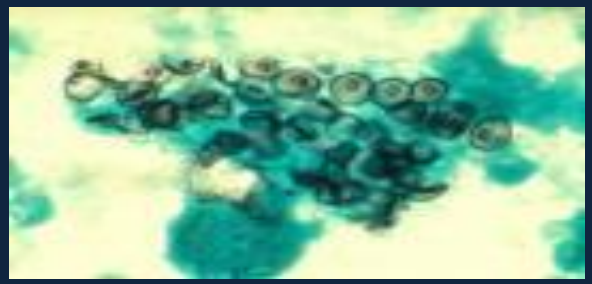
Nocardiosis

Aspergillosis

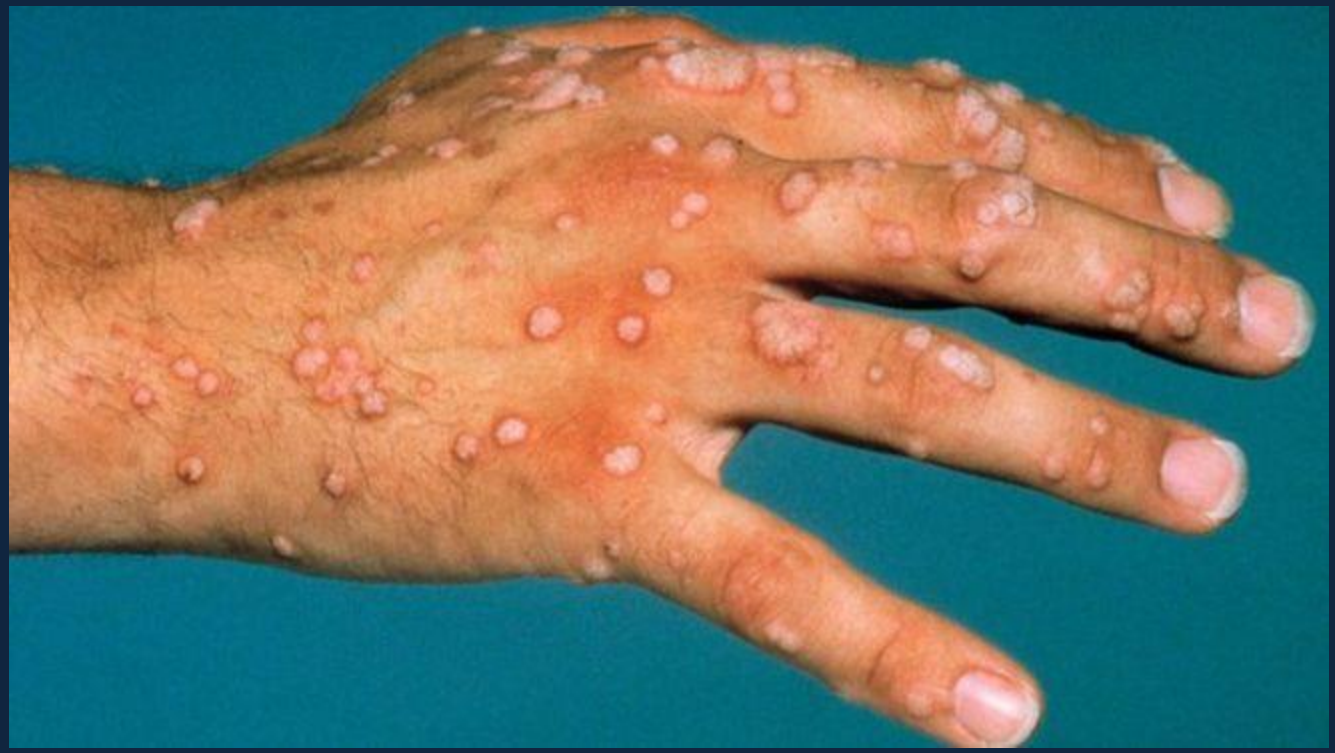
P. carinii Pn.



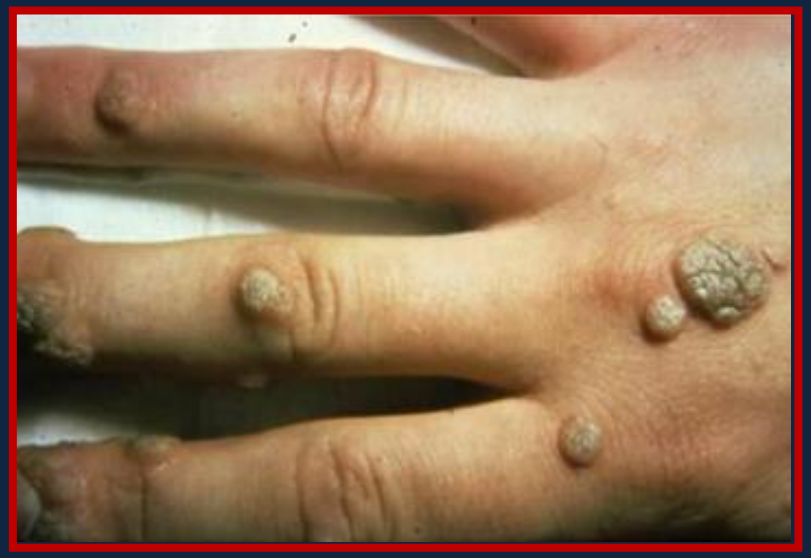


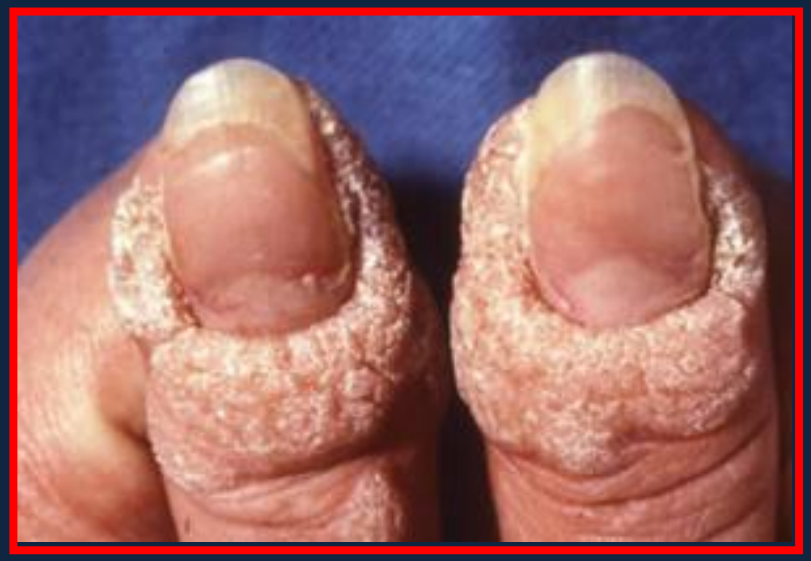


Other Warning Signs
Multiple Warts



Multiple warts in patient with PID

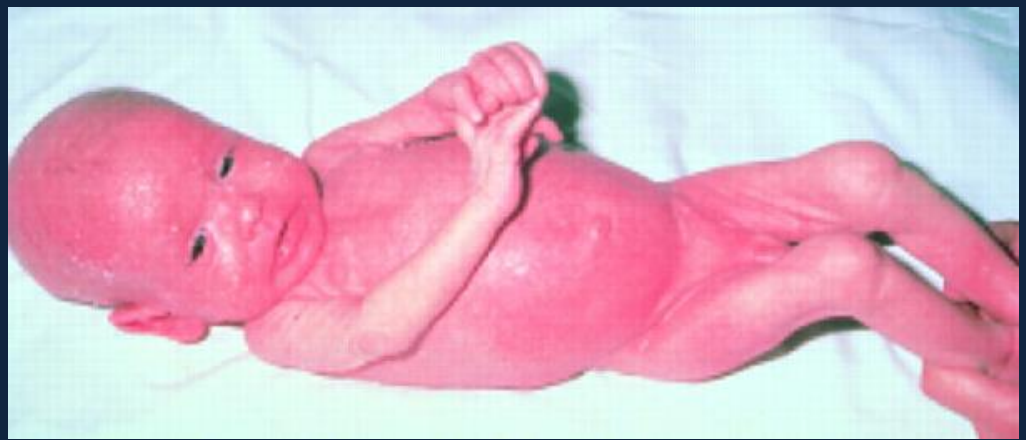




Erythroderma in PIDDs

- Erythroderma is defined as the involvement of greater than 90 % of the total body surface area with erythema and/or scaling.

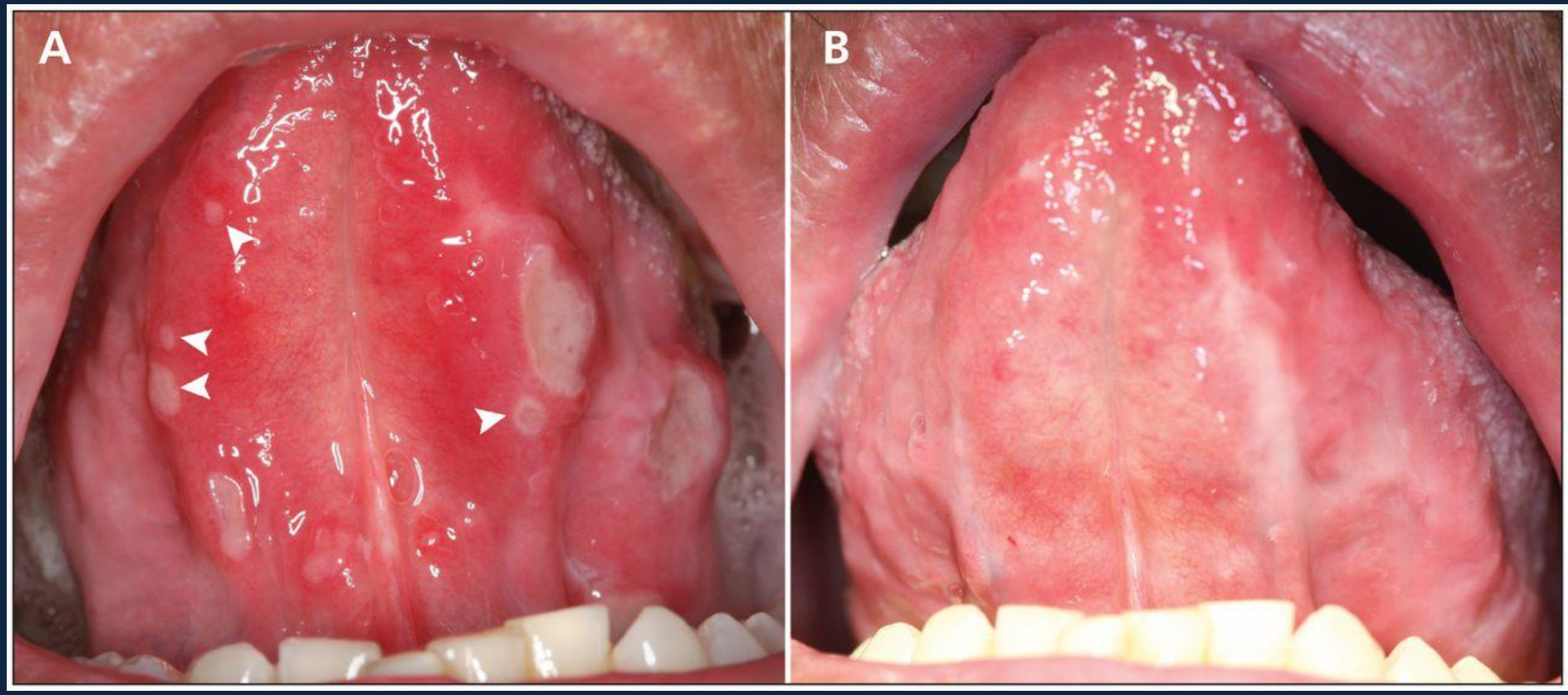
- A survey of erythroderma in infancy found 48 % of cases to be due to primary immunodeficiency.



Erythroderma in PIDDs

- Erythroderma has been associated with a relatively short list of specific PID:
- Comèl–Netherton
- Omenn Syndrome
- GVHD
- Leiner's disease (Leiner erythroderma)

Recurrent Aphtous Ulcers



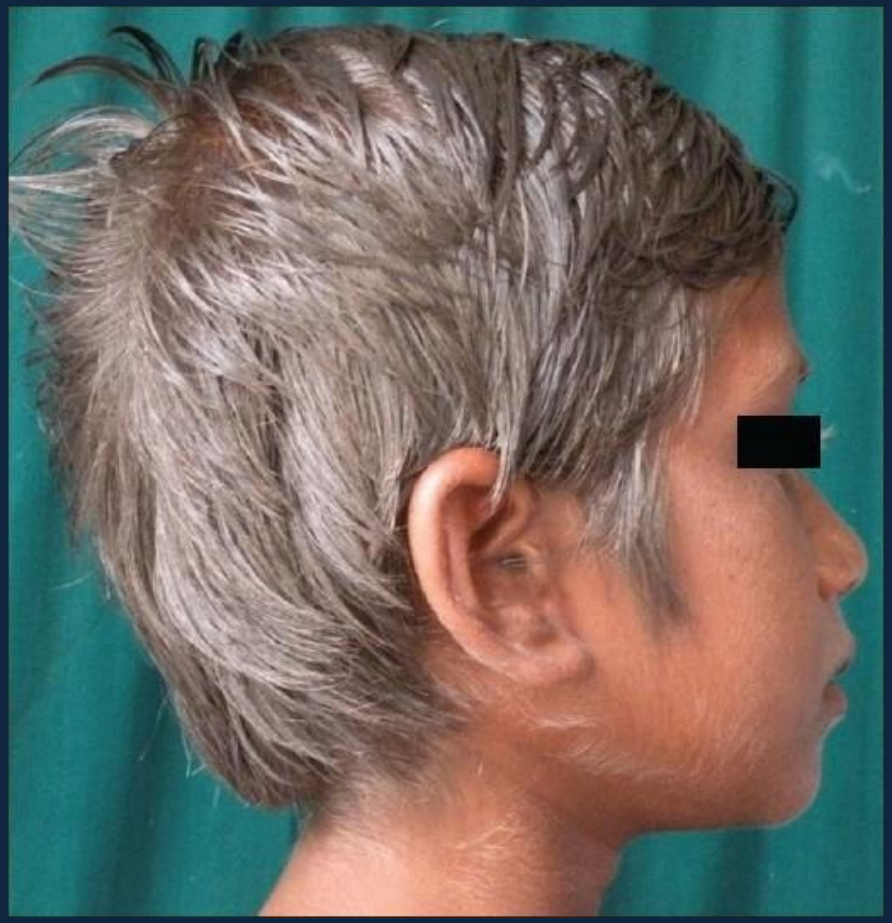
partial albinism

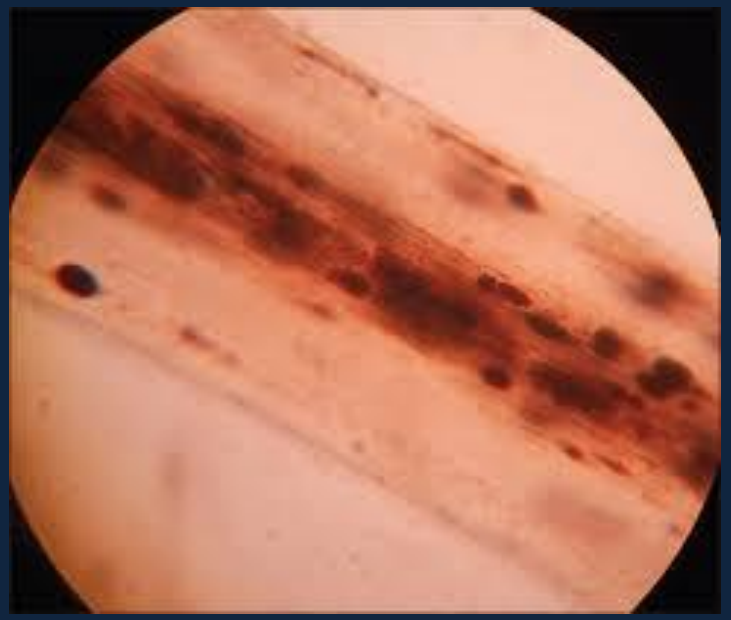
PIDs with partial albinism

- These include:
  - Griscelli syndrome type 2 (RAB27A mutation)
  - Chediak-Higashi syndrome (LYST mutation)
  - Hermansky-Pudlak syndrome type 2 (AP3B1mutation)

- These patients exhibit skin hypopigmentation and have a **silvery-grey hair**

silvery hair syndrome





general warning signs of PIDD for all clinicians

Chronic diarrhea or colitis

- Evaluate if the patient has:
- Rotavirus
- Enteroviruses
- Campylobacter
- Cryptosporidium
- Persistent Salmonella
- Clostridium difficile
- Recurrent giardiasis

PID with epidermal dysplasia

- Ectodermal dysplasia with immunodeficiency
  - X-linked (NEMO deficiency)
  - Autosomal dominant
- Cartilage hair hypoplasia
- Dyskeratosis congenita
  - X-linked (Hoyeraal-Hreidarsson syndrome)
  - Autosomal recessive
  - Autosomal dominant
- Papillon–Lefèvre syndrome

Auto-immune Disorders
(Especially when multiple)

Cancer