

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
- Hepatobiliary diseases : Cirrhosis
- Malignancies : Lymphoma,...
- Others : burn , surgery,

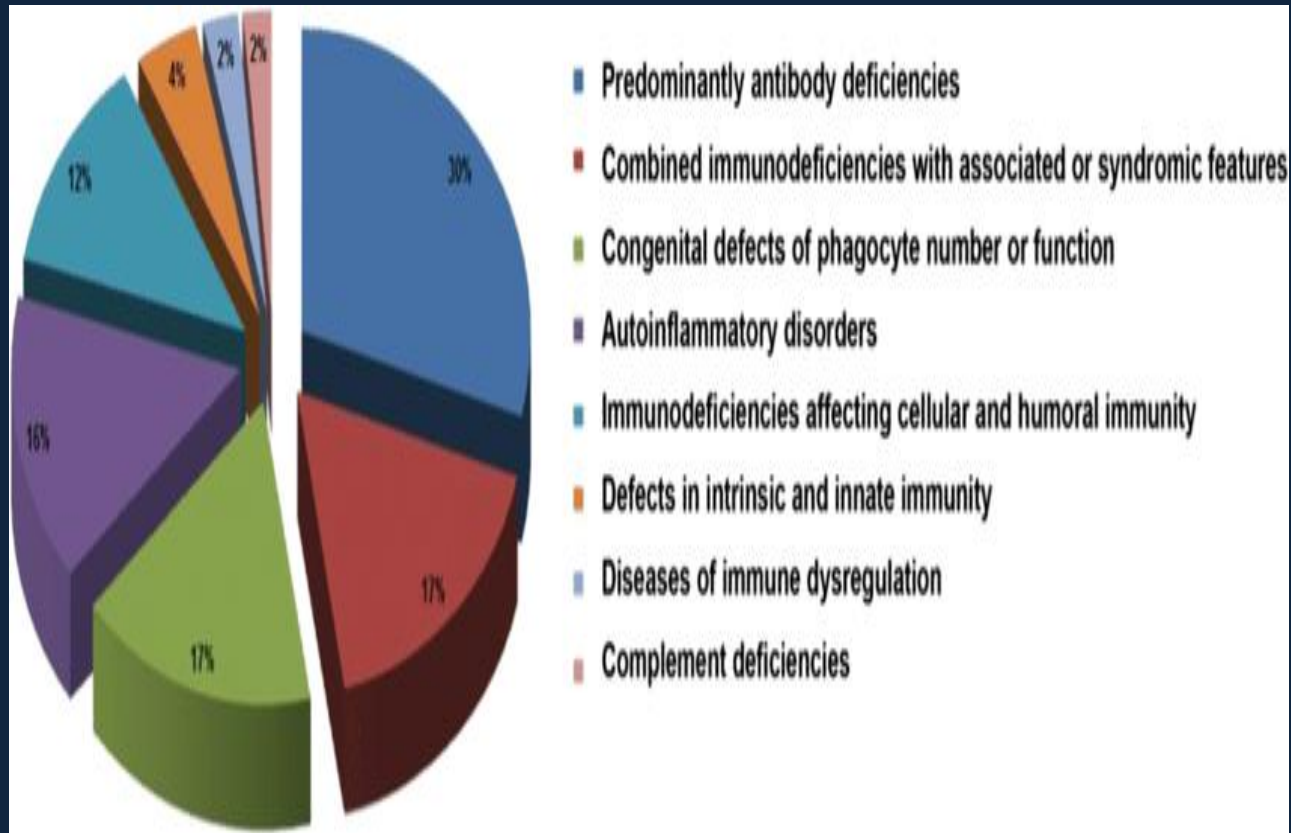
Introduction

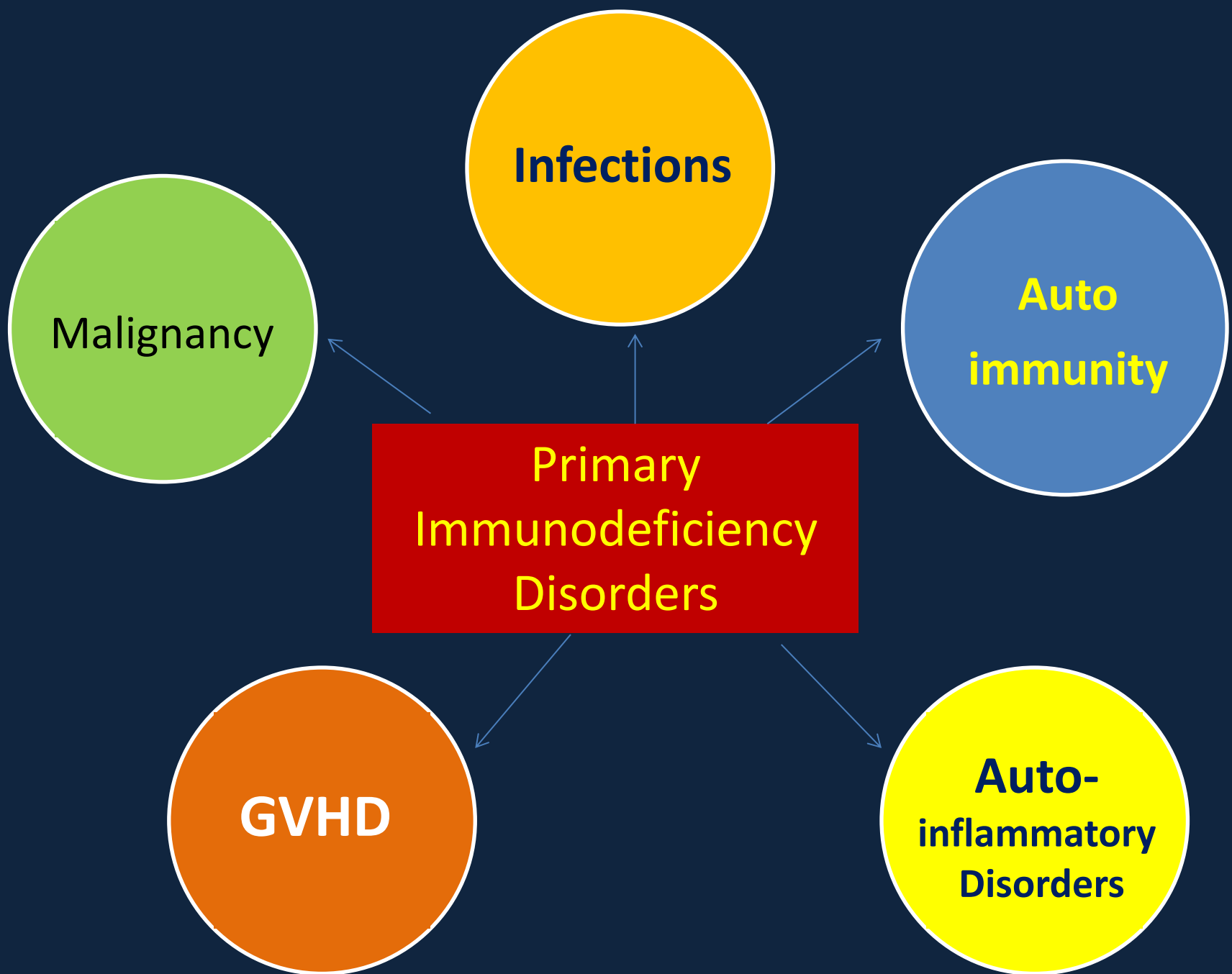
- Most primary immunodeficiencies are genetic disorders.
- The majority are diagnosed in children under the age of one, although milder forms may not be recognized until adulthood.
- While there are over 430 recognized PIDs as of 2019, most are very rare.

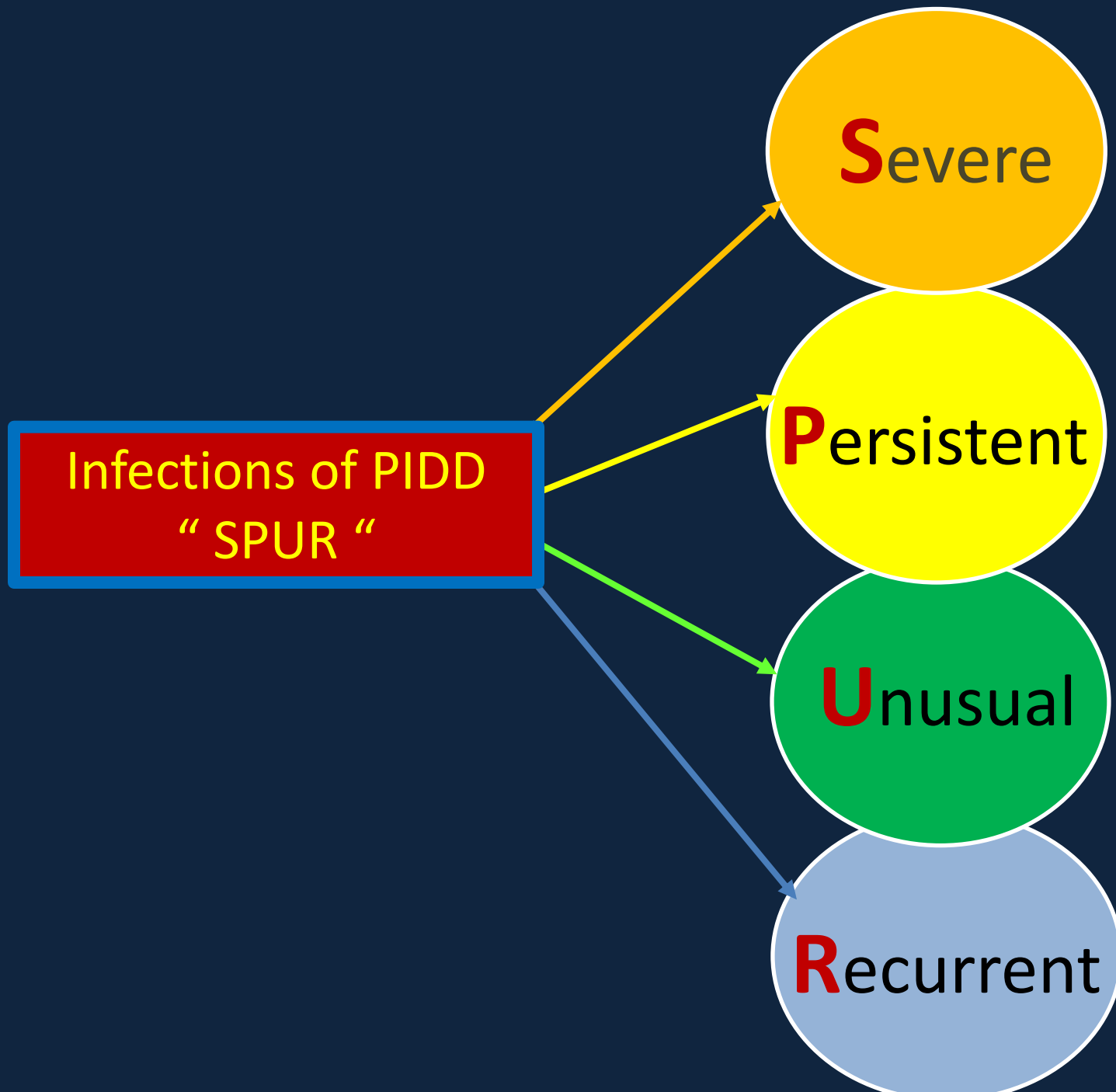
International Union of Immunological Societies (IUIS)

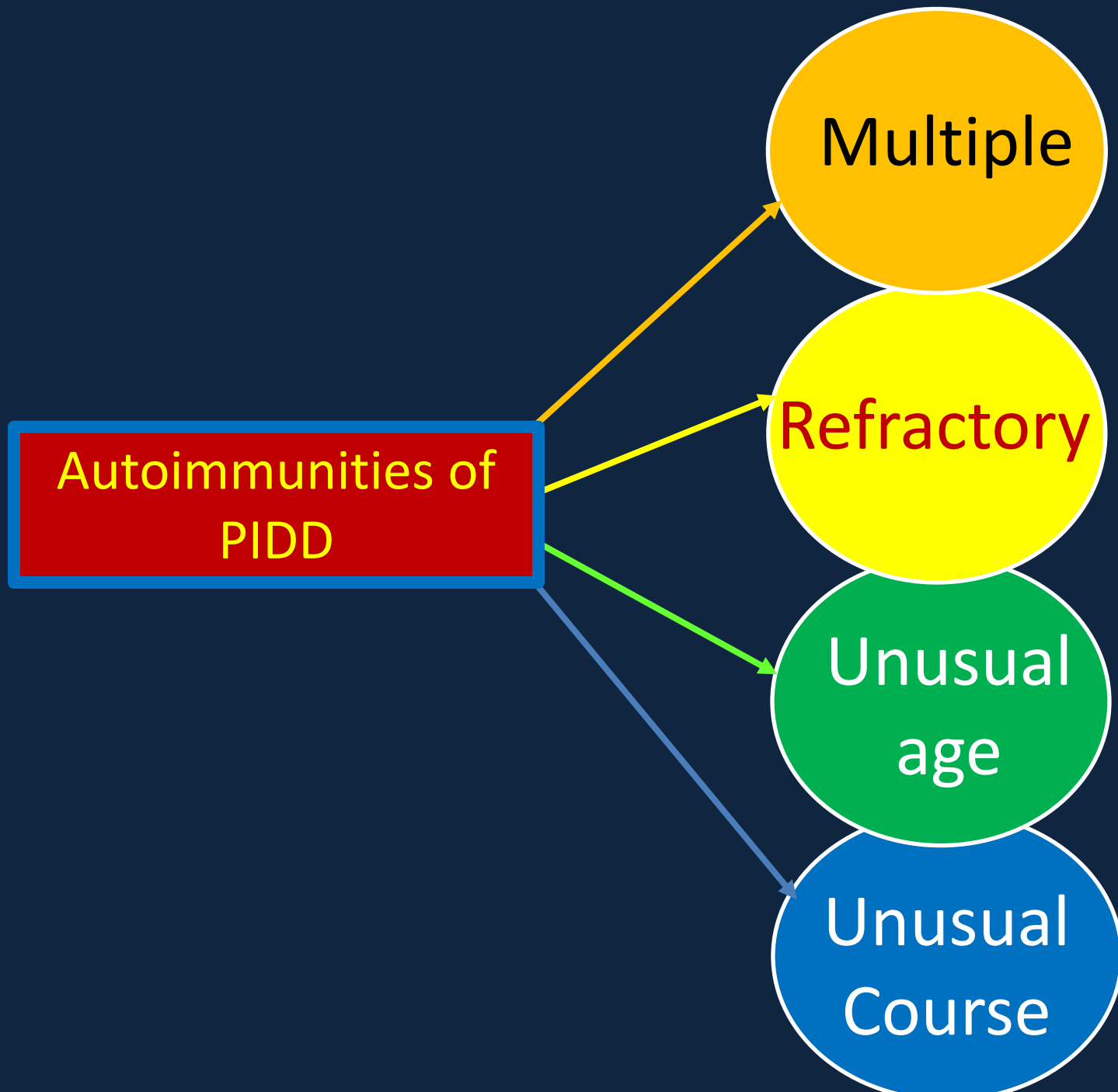
1. Immunodeficiencies affecting cellular & humoral immunity
2. CID with associated or syndromic features
3. Predominantly antibody deficiencies.
4. Diseases of immune dysregulation
5. Congenital defects of phagocyte number, function, or both
6. Defects in intrinsic and innate immunity
7. Auto-inflammatory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

International Union of Immunological Societies (IUIS)







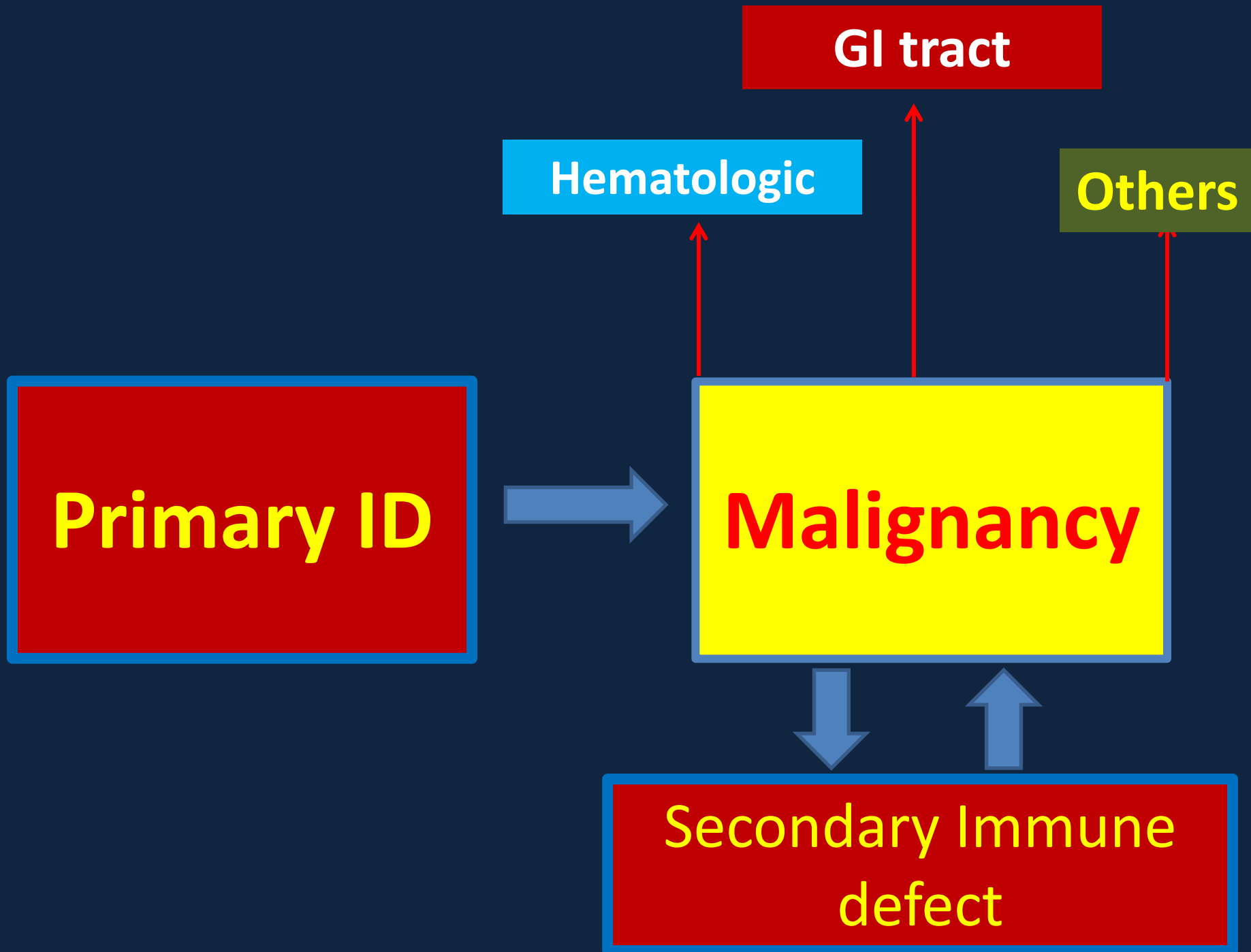


**GVHD
of PIDD**

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graph LR; A[GVHD of PIDD] -- yellow arrow --> B((Begin In Utero)); A -- green arrow --> C((Following Receiving Blood products));
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**Begin In
Utero**

Following
Receiving
Blood
products





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

Educational Posters

NEW!

4 Stages of Testing for Primary Immunodeficiency

- 1**
 - History and physical examination, height and weight
 - CBC and differential
 - Quantitative Immunoglobulin levels IgG, IgM, IgA (related to age)
- 2**
 - Specific antibody responses (tetanus, diphtheria)
 - Response to pneumococcal vaccine (pre/post) (for ages 3 and up)
 - IgG subclass analysis
- 3**
 - Candida and Tetanus skin tests
 - Lymphocyte surface markers CD3/CD4/CD8/CD19/CD16/CD56
 - Mononuclear lymphocyte proliferation studies (using mitogen and antigen stimulation)
 - Neutrophil oxidation burst (if indicated)
- 4**
 - Complement screening CH50, C3, C4
 - Enzyme measurements (adenosine deaminase, purine nucleoside phosphorylase)
 - Phagocyte studies (surface glycoproteins, mobility, phagocytosis)
 - NK cytotoxicity studies
 - Further complement studies AH50
 - Neo antigen to test antibody production
 - Other surface/cytoplasmic molecules
 - Cytokine receptor studies
 - Family/genetic studies

Presented as a public service by:



Jeffrey Modell
Foundation

Caring PI
Wardrobe

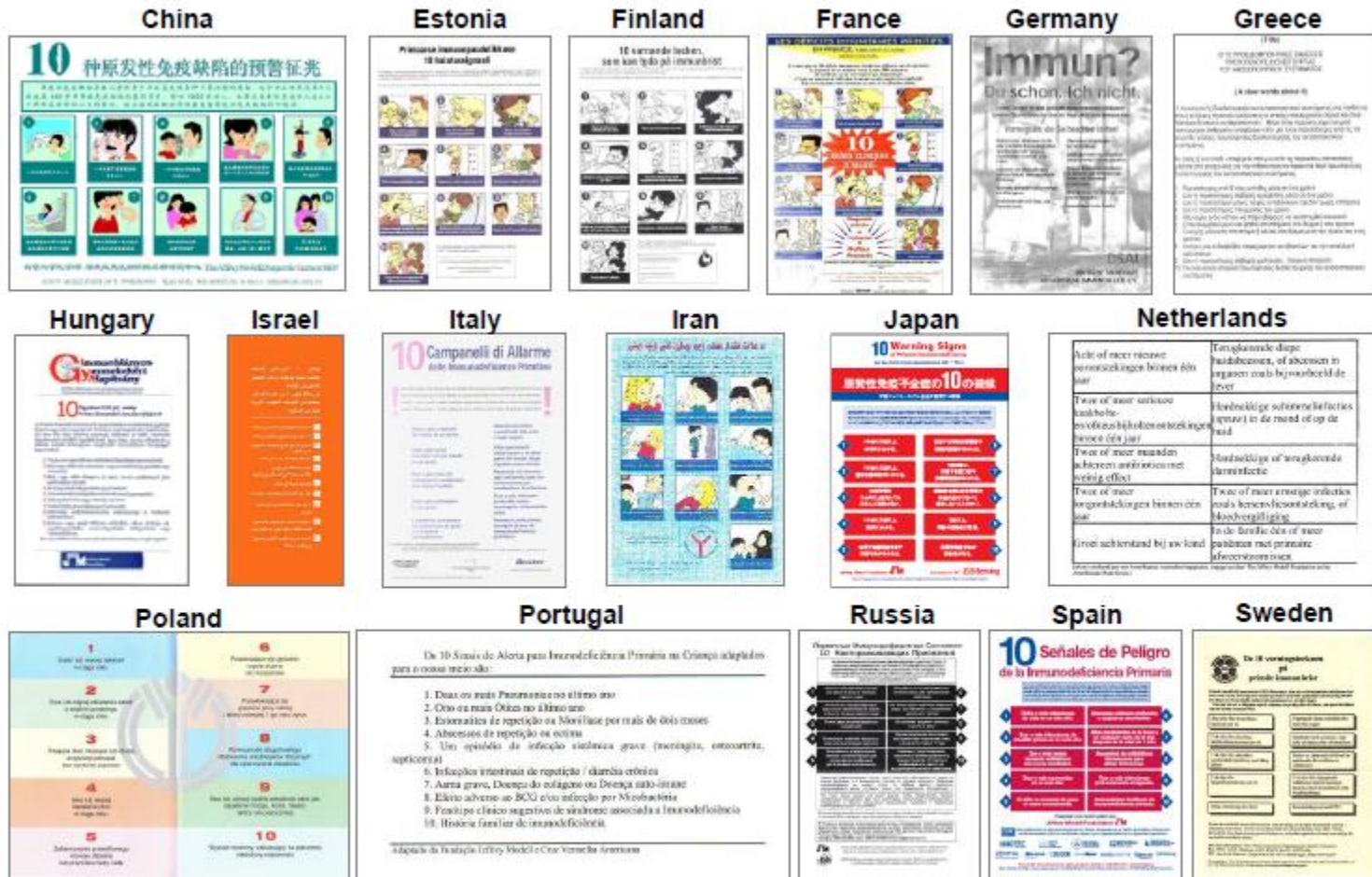


Funding was made possible in part by grant 1H75DP002048-01 from the United States Centers for Disease Control and Prevention (CDC)



These recommended immunologic tests reflect a consensus of the Jeffrey Modell Foundation Medical Advisory Board. Consultation with Primary Immunodeficiency experts is strongly suggested. © 2009 Jeffrey Modell Foundation. For information or referrals, contact the Jeffrey Modell Foundation: 866-NFC-4PI | info4pi.org

Educational Posters



AND MANY MORE...



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**.

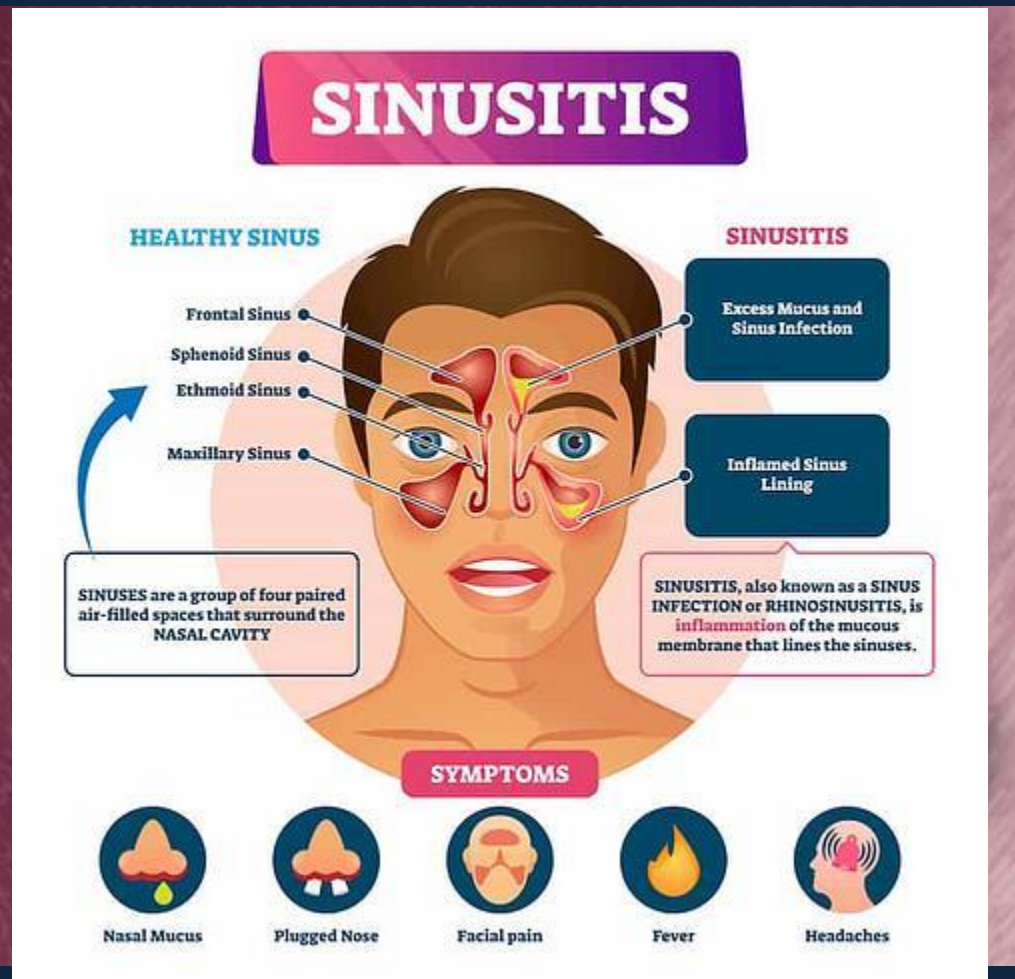
Warning Signs

- 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

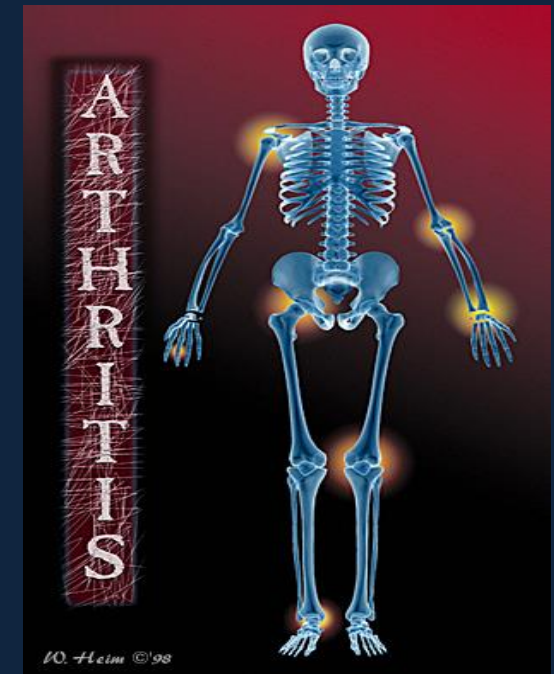
- 4. Recurrent, deep skin or organ abscesses



*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

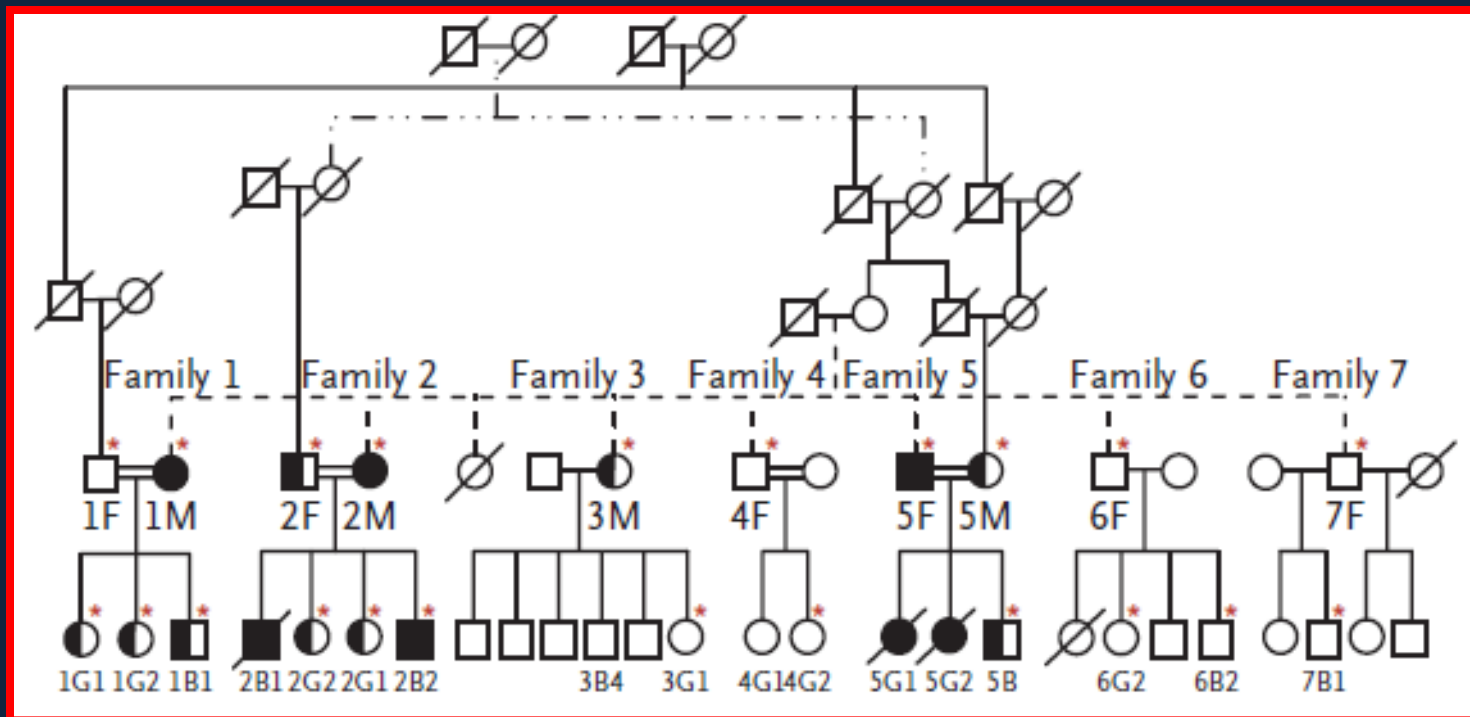
Warning Signs

- 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

10 Warning Signs of Primary Immunodeficiency

Primary Immunodeficiency (PI) causes children and adults to have infections that come back frequently or are unusually hard to cure. 1:500 persons are affected by one of the known Primary Immunodeficiencies. **If you or someone you know is affected by two or more of the following Warning Signs, speak to a physician about the possible presence of an underlying Primary Immunodeficiency.**

- 1** Four or more new ear infections within 1 year.
- 2** Two or more serious sinus infections within 1 year.
- 3** Two or more months on antibiotics with little effect.
- 4** Two or more pneumonias within 1 year.
- 5** Failure of an infant to gain weight or grow normally.
- 6** Recurrent, deep skin or organ abscesses.
- 7** Persistent thrush in mouth or fungal infection on skin.
- 8** Need for intravenous antibiotics to clear infections.
- 9** Two or more deep-seated infections including septicemia.
- 10** A family history of PI.

Jeffery Modell Criteria for PID

ADULTS

10 FOR ADULTS Warning Signs of Primary Immunodeficiency

Primary Immunodeficiency (PI) causes children and adults to have infections that come back frequently or are unusually hard to cure. 1:500 persons are affected by one of the known Primary Immunodeficiencies. **If you or someone you know is affected by two or more of the following Warning Signs, speak to a physician about the possible presence of an underlying Primary Immunodeficiency.**

- 1** Two or more new ear infections within 1 year.
- 2** Two or more new sinus infections within 1 year, in the absence of allergy.
- 3** One pneumonia per year for more than 1 year.
- 4** Chronic diarrhea with weight loss.
- 5** Recurrent viral infections (colds, herpes, warts, condyloma).
- 6** Recurrent need for intravenous antibiotics to clear infections.
- 7** Recurrent, deep abscesses of the skin or internal organs.
- 8** Persistent thrush or fungal infection on skin or elsewhere.
- 9** Infection with normally harmless tuberculosis-like bacteria.
- 10** A family history of PI.

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



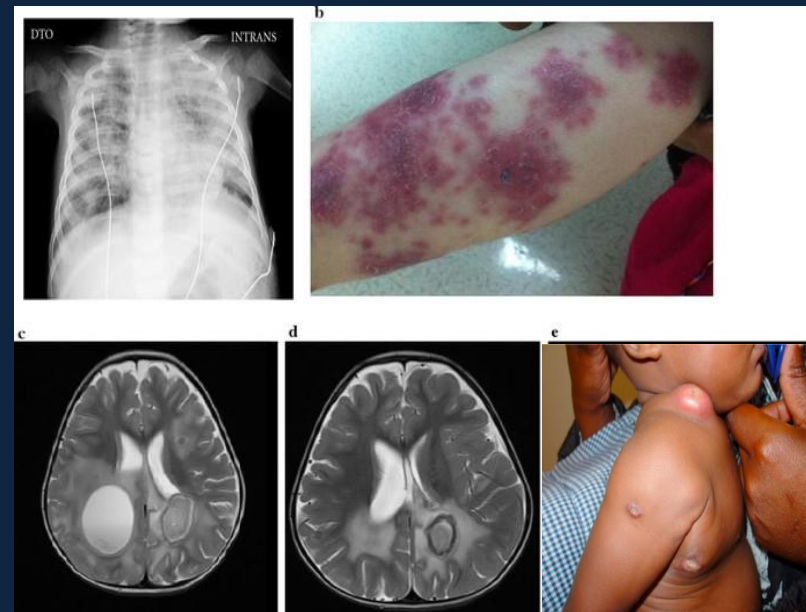
Other Warning Signs

Adverse reactions 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

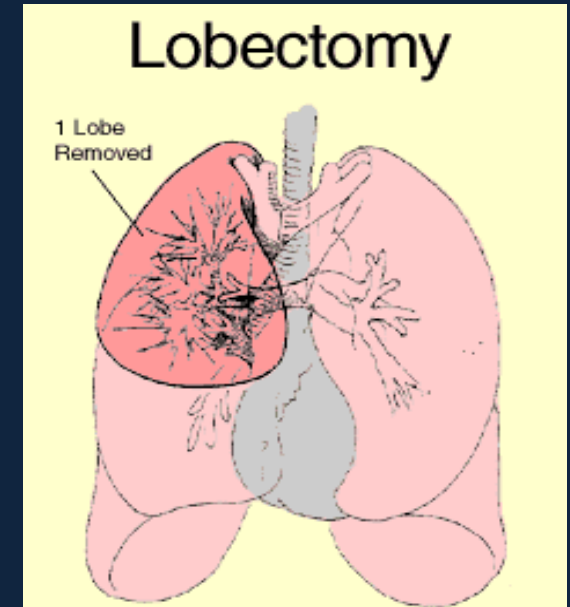


- Recurrent severe conjunctivitis

Other Warning Signs

Surgical intervention for chronic infection

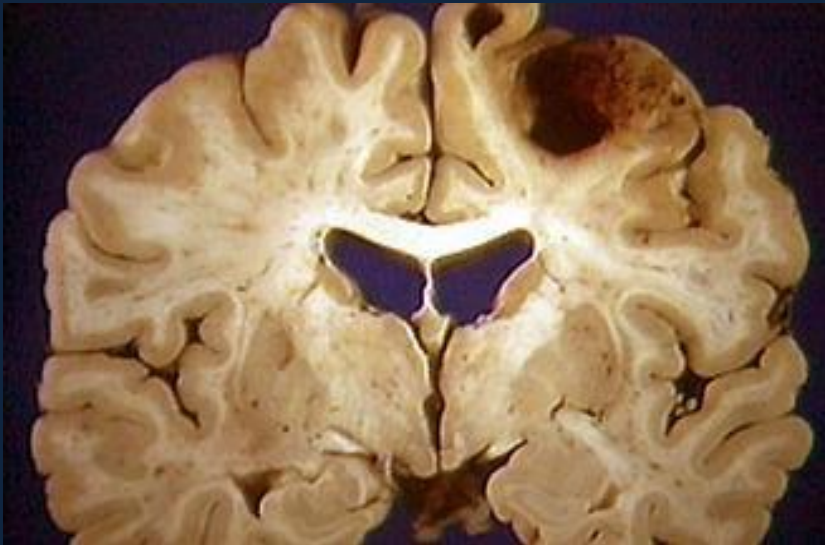
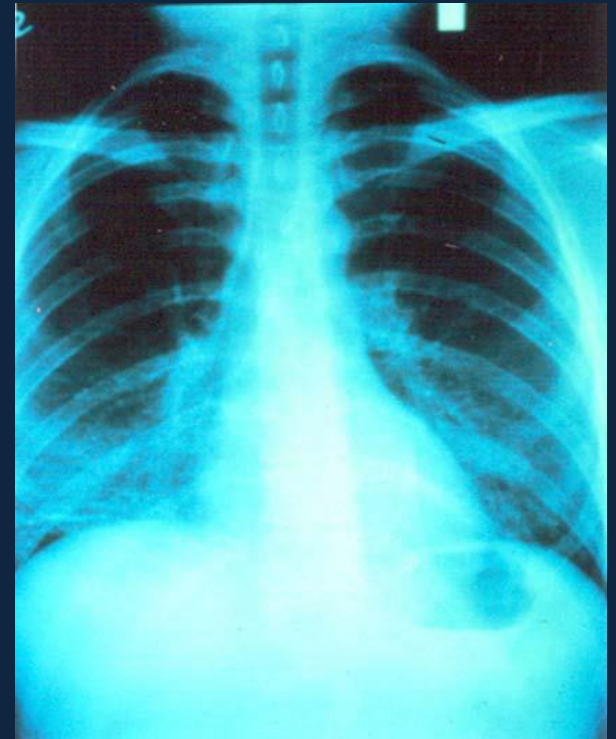
- lobectomy for bronchiectasis
- tonsillectomy*
- adenoidectomy*
- recurrent grommet insertion
- recurrent incision of boils



Other Warning Signs

Unusual pathogens

Nocardiosis
Aspergillosis
P. carinii Pn.



Other Warning Signs

Multiple Warts



Multiple warts in patient with PID



Erythroderma in PIDDs

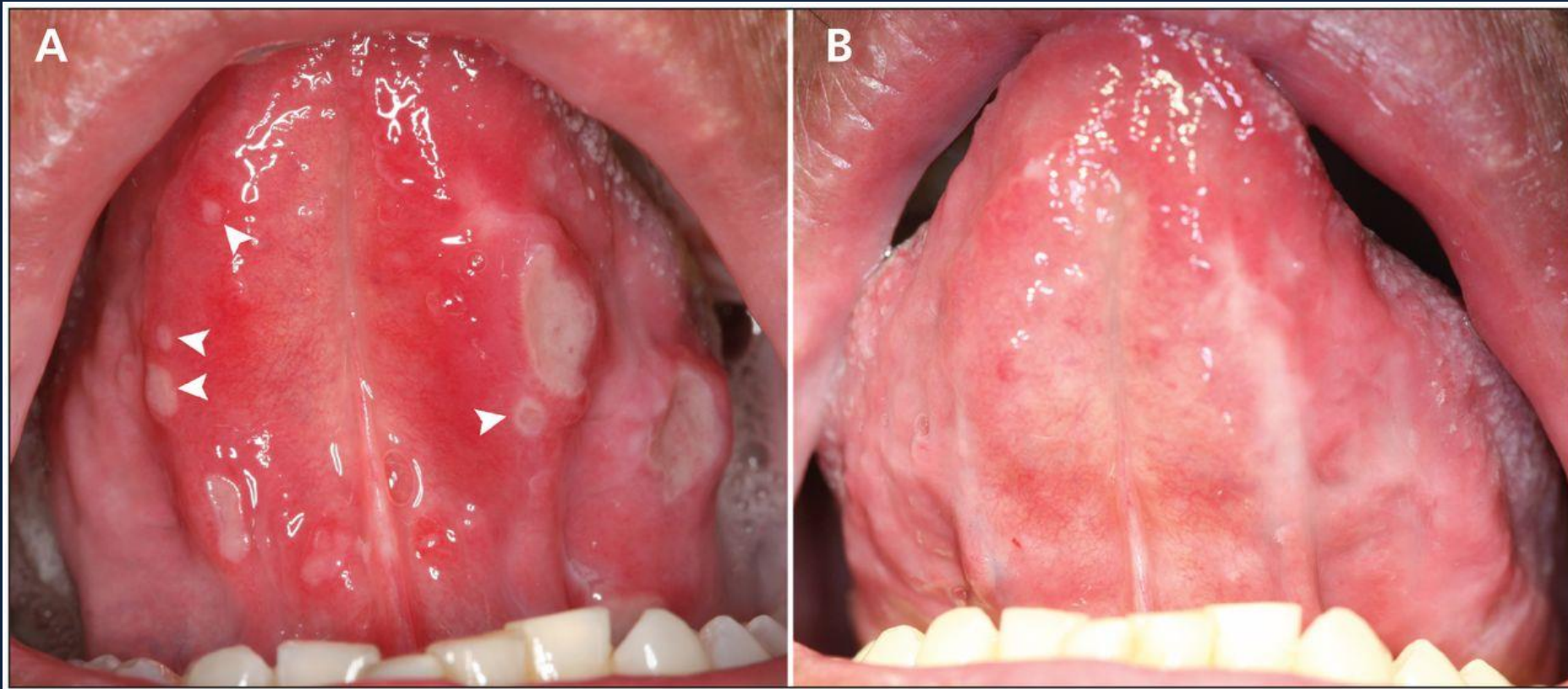
- Erythroderma is defined as the involvement of greater than 90 % of the total body surface area with erythema and/or scaling.
- A survey of erythroderma in infancy found 48 % of cases to be due to primary immunodeficiency.



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 Aphthous 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 (*AP3B1* mutation)
- 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

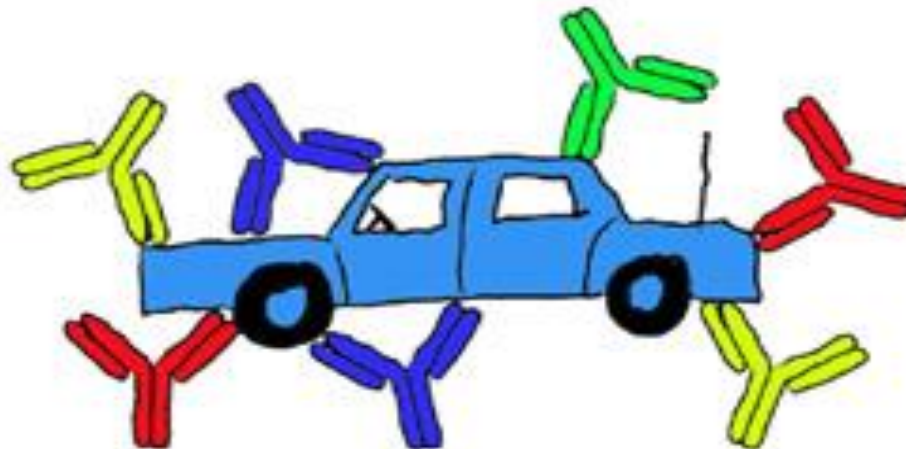
- Evaluate if the patient has:
- Rotavirus
- Enteroviruses
- Campylobacter
- Cryptosporidium
- Persistent Salmonella
- Clostridium difficile
- Recurrent giardiasis

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)



Autoimmunity

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Cancer