The Child with Recurrent Infections
Prof T Avenant

Blok 10, 2012

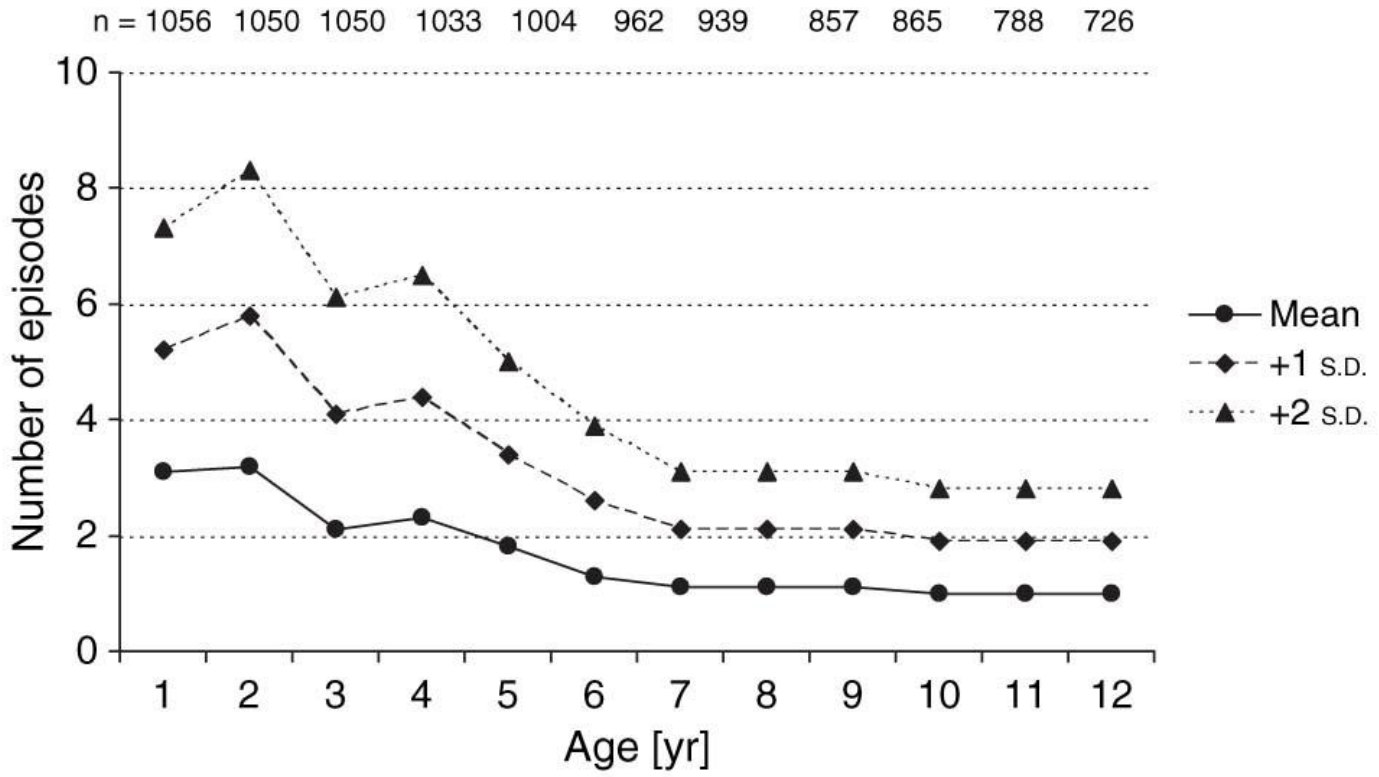
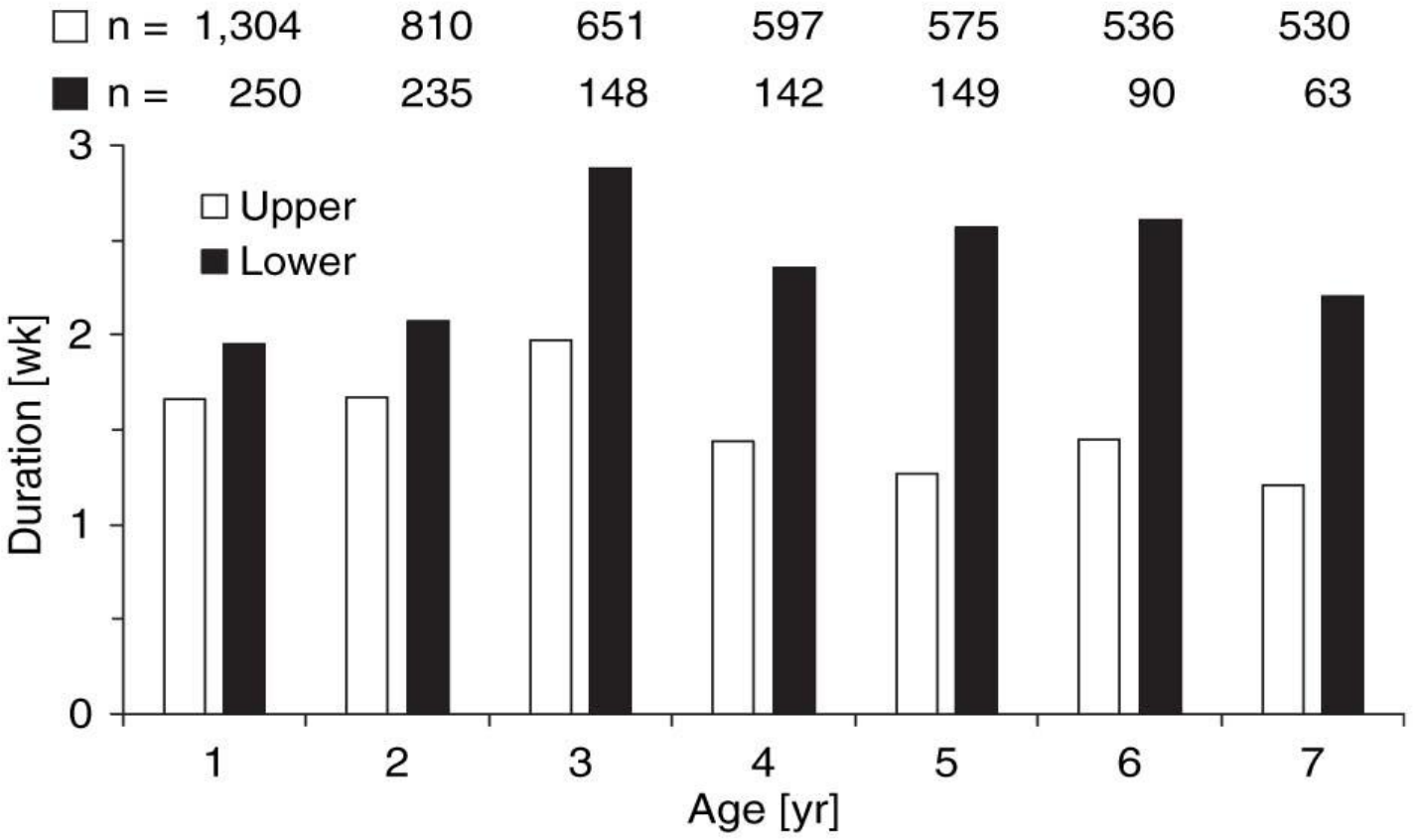


Fig. 1. Yearly number of respiratory illness episodes in relation to age.

Gruber C, et al. Pediatr Allergy Immunol 2008: 19: 505–512.

Mean Duration per Rhinitis and Lower Respiratory Illness Episode



NB!

In young children up to 8 upper respiratory infections a year are normal. If the child attends day care even more episodes may occur. It is therefore **unnecessary** to perform extended immunologic investigations in children with minor respiratory tract ailments.

When to suspect an immunodeficiency

- The major manifestation of immunodeficiencies is increased susceptibility to infection. This includes:
  - increased frequency of infection
  - increased severity of infection
  - prolonged duration of infection
  - repeated infections without a symptom-free interval
  - increased dependency of antibiotics
  - unexpected or severe complications of infection
  - infection with a unusual organism
- A patient with a positive family history suggestive of a particular defect should also be investigated.

NB!

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.

Presented as a public service by:

Jeffrey Modell Foundation | Curing PI. Worldwide.

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National Heart, Lung, and Blood Institute (NHLBI)

National Institute of Allergy and Infectious Diseases (NIAID)

National Institute of Child Health and Human Development (NICHD)

Baxter BioScience | CSL Behring Biotherapies for Life™ | GRIFOLS | octapharma | PPTA Plasma Protein Therapeutics Association | Talecris Biotherapeutics

For information or referrals, contact the Jeffrey Modell Foundation: 866-INFO-4-PI | info4pi.org

Jeffrey Modell Foundation

OTHER DISORDERS WITH INCREASE SUSCEPTIBLITY TO INFECTION

- Circulatory disorders
  - Sickle cell disease, diabetes, nephrosis, congenital cardiac defect
- Obstructive disorders
  - Ureteral or urethral stenosis, asthma, allergic rhinitis, blocked eustachian tubes, CF, foreign body
- Integumental defects
  - Eczema, burns, skull fracture, midline sinus tract, ciliary abnormalities

OTHER DISORDERS WITH INCREASE SUSCEPTIBLITY TO INFECTION

- Unusual microbiologic factors
  - AB overgrowth, continuous reinfection e.g. contaminated inhalation equipment
  - Resistant organisms
    - Penicillin resistant pneumococcus, methicillin-resistant S. aureus, vancomycin resistant enterococcus, multidrug resistant M. tuberculosis
- Foreign bodies
  - Shunt, central catheter, artificial heart valve, urinary catheter, aspirated foreign body
- Inadequate clearance
  - Hypotonia/CNS abnormality leading to aspiration, abnormal cilia structure or function

Secondary immunodeficiencies

- Premature and newborn
- Hereditary and metabolic diseases
  - Chromosomal abnormalities, uremia, DM, malnutrition, vitamin and mineral deficiencies, protein-losing enteropathies, nephrosis, myotonic distrophy, sickle cell disease
- Immunosuppressive agents
  - Radiation, drugs, steroids, anti-lymphocyte- or thymocyte globulin
- Infectious diseases
  - Congenital rubella, measles, varicella, HIV, CMV, EBV, bacterial-, mycobacterial-, fungal- or parasitic disease
- Infiltrative and haematological diseases
  - Histocytosis, sarcoidosis, lymphoma, leukemia, myeloma, agranulatocytosis and aplastic anemia
- Surgery and trauma
  - Burns, splenectomy and anaesthesia
- Miscellaneous
  - SLE, CAH

NB!

Primary Immunodeficiencies

Definition: a group of diverse illnesses that, as a result of one of more abnormalities of the immune system, increase susceptibility to infection.

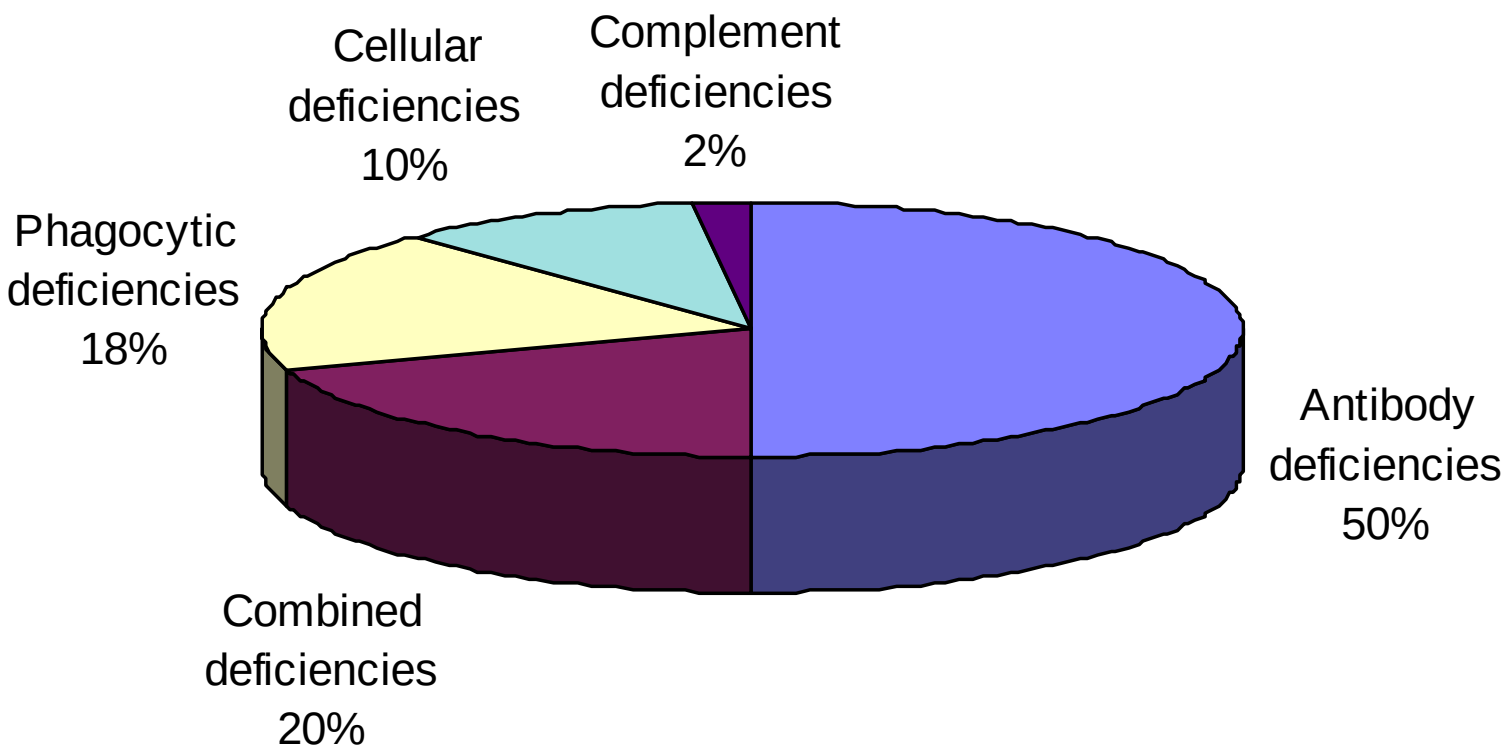
- These are relatively uncommon disorders. The incidence is estimated at 1/10 000 excluding selective IgA deficiency.

NB!

Classification and physiology

- The immune system is conventionally divided into four separate systems:
  - B-lymphocyte (antibody) system
  - T-lymphocyte (cellular immune) system
  - Phagocytic (polymorphonuclear) system
  - Complement (opsonic) system
- There is a close interaction between the B-cell and T-cell system

Relative distribution of the primary immunodeficiencies



Primary Immunodeficiencies

- Primary immunodeficiencies are usually congenital and hereditary so that the majority patients are infants or children.
- Time of diagnosis
  - 40% first year
  - 40% by age 5
  - 15% by age 6
  - 5% in adulthood
- In children: 72% of cases in males
- In adults: more females because of frequent occurrence of late onset CVID

Evaluation of possible immunodeficiencies

History

- Respiratory infections common in immunodeficiency
- Often accompanied by other severe bacterial infection
  - pneumonia, sepsis, meningitis, osteomyelitis
- One such severe infection may occur in a normal child
  - second occurrence possible immunodeficiency
- Repeated infections lead to chronic sinusitis, otitis, mastoiditis.
- Purulent nasal discharge

Evaluation of possible immunodeficiencies

History

- Bronchiectasis may occur at an early age
- Diarrhoea, malabsorption and vomiting, aggravated by antibiotics.
- Patients with severe cellular immunodeficiency particularly likely to have chronic diarrhoea.
- Failure to thrive, underweight, short, delayed milestones as result of chronic infection.

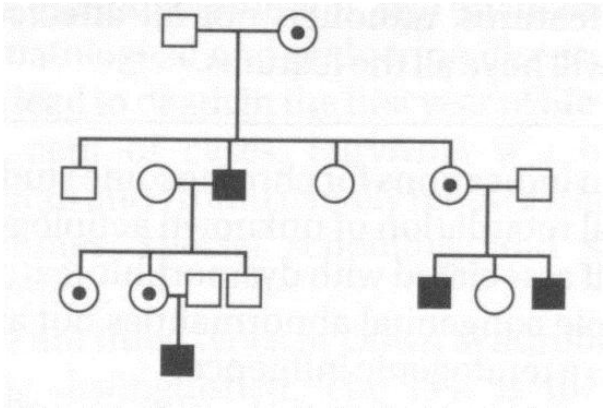
Evaluation of possible immunodeficiencies

Past history

- The birth history:
  - maternal illness, gestational length, birth weight and neonatal illness.
- Delayed umbilical cord attachment suggest chemotactic disorder
- Immunization
- Nature and severity of past infections
- Autoimmune type features
- Prior surgery
  - tonsillectomy
  - adenoidectomy
  - splenectomy

Evaluation of possible immunodeficiencies

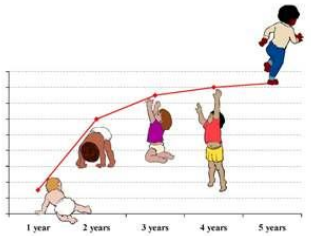
Family history



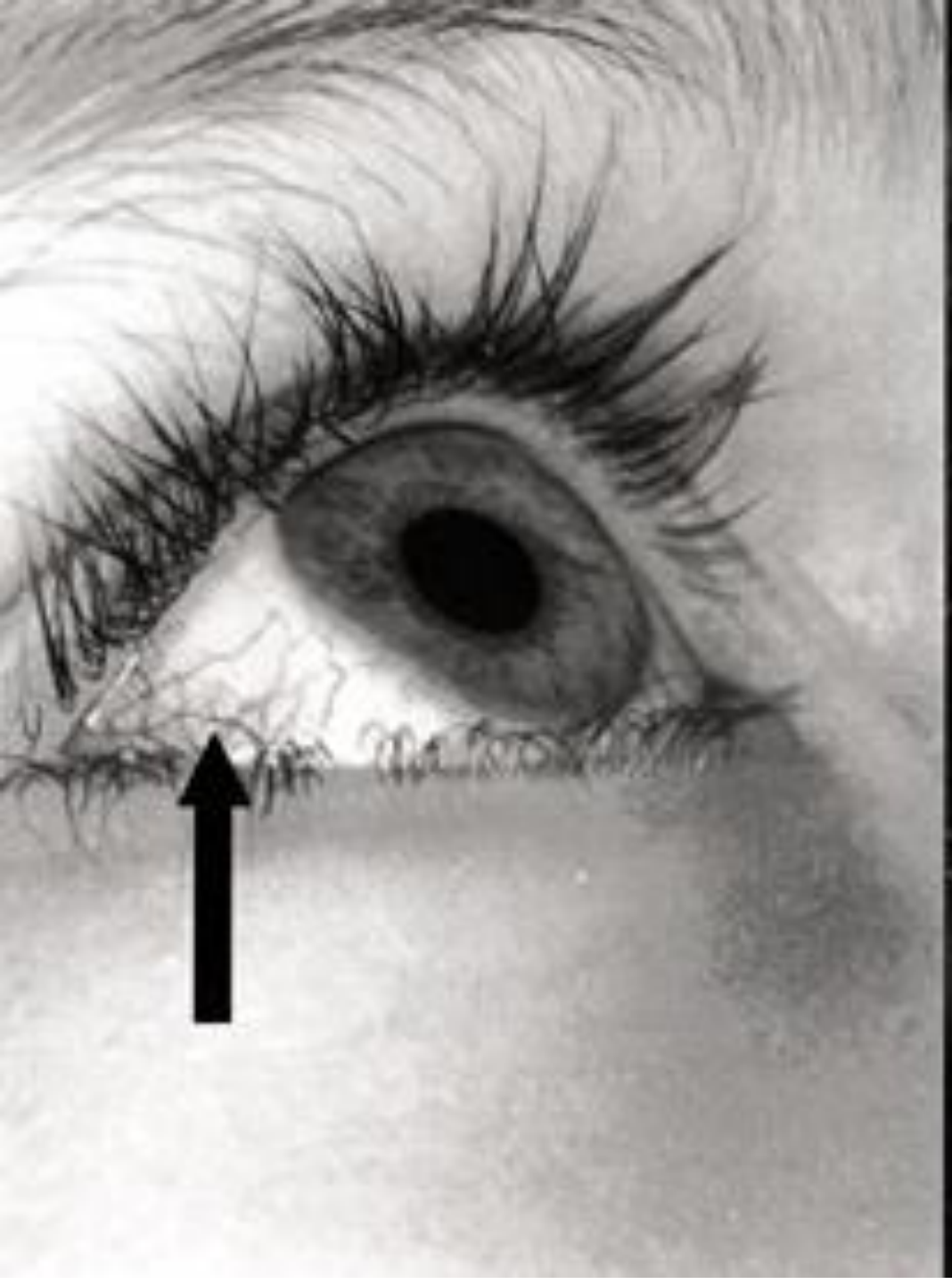
- Positive in 25% of patients
  with primary immunodeficiency
- Inquire about severe infections or early death of near and distant relatives.
- If positive, a genetic tree should be constructed.
- Other things
  - history of consanguinity, ethnicity, occurrence of arthritis, collagen disease, allergy, hypersensitivity or lymphoreticular malignancy in family members.

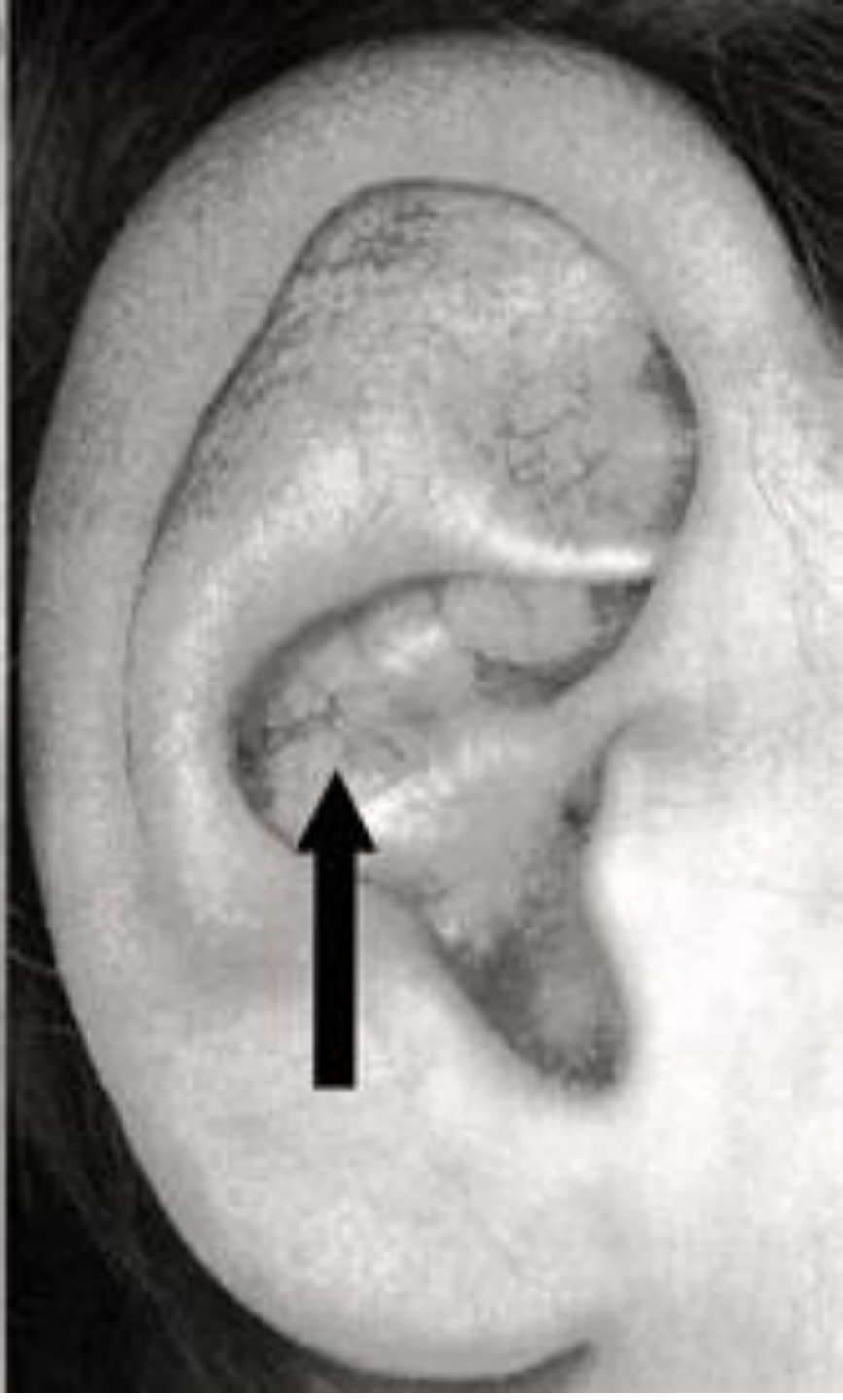
Evaluation of possible immunodeficiencies

Physical examination



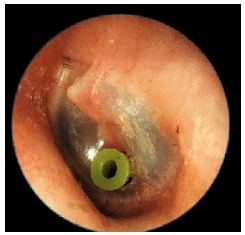
- *Important to remember that none or only a few of the findings will be present in early cases!*
- Patients characteristically appear chronically ill
  - pallor, irritability, reduced subcutaneous fat and distended abdomen.
- Skin: macular rashes, pyoderma, eczema, petechiae, allopecia, telangiectasia
- Eyes: conjunctivitis
- Lymphatic tissue: absent cervical lymph nodes despite recurrent throat infections, may also enlarged or suppurative



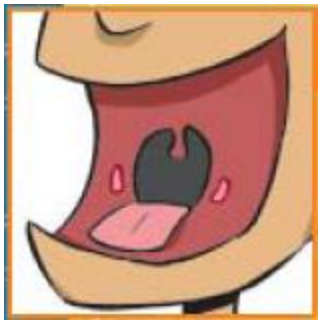


Evaluation of possible immunodeficiencies

Physical examination



- Ears
  - tympanic membranes scarred or perforated, chronic suppuration
- Nose
  - crusted and excoriated - purulent nasal discharge
- Mouth, throat and mucous membranes
  - candidiasis, periodontitis, dental decay, ulceration, atrophic tonsils
- Respiratory system
  - often deep cough, crepitations and ronchi
- Abdomen
  - hepato -and/or splenomegaly
- Musculo-skeletal
  - decreased muscle mass, joint swelling, joint motion, subcutaneous nodules
- Neurological
  - slow development or ataxia



Evaluation of possible immunodeficien

General laboratory tests

- Certain non-specific laboratory tests are often indicated
  - complete blood count, ESR, tuberculin test, chest - and sinus x-rays.
- Other tests that may be indicated to exclude other conditions include
  - a sweat test
  - tests for malabsorption, malnutrition and allergy.
  - biopsies to evaluate ciliary function.
  - autoantibodies may be present.
  - with hepatomegaly liver function tests and hepatitis studies may be indicated.
- Cultures for specific organisms

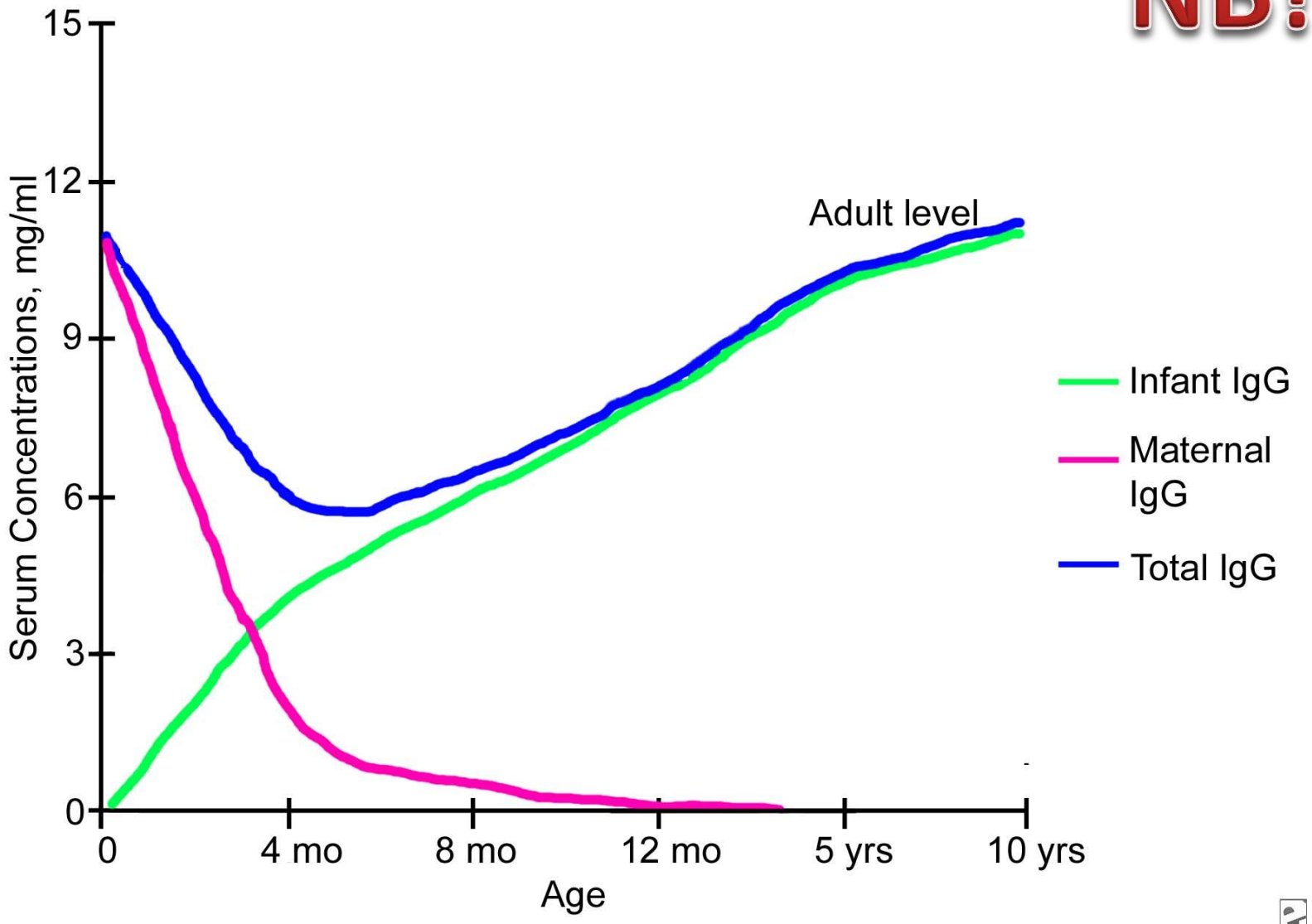
NB!

Evaluation of possible immunodeficier

Laboratory diagnosis

- Physician and laboratory should be familiar with normal values for children
  - Values vary significantly from one age group to the other.
- Evaluation of hypogammaglobulinemia in the first few months difficult because of maternal antibodies in circulation.
- Delayed hypersensitivity skin tests not reliable in young infant
  - lack of skin reactivity to antigens

NB!



emedicine.medscape.com/article/136897-media

NB!

Evaluation of possible immunodeficier

Initial screening evaluation

- Complete blood count with differential cell analysis paying attention to white blood cell morphology and granules, platelet count and estimation of platelet size
- IgG, IgM, IgA
- Isohemagglutinins
- CH50
- Delayed hypersensitivity skin test

- Over 95% of primary immunodeficiencies will be excluded by these tests

NB!

Take Home Message

- Most common causes of recurrent pneumonia
  - HIV
  - PTB
  - Foreign body aspiration
  - Misdiagnosed or inappropriately treated asthma
  - Bronchiectasis
- Refer after basic investigations have been done

Resources

Immunologic Disorders in Infants and Children. Ochs, HD, Stiehm, ER, Winkelstein, JA

The Immune Deficiency Foundation www.primaryimmune.org

The Jeffrey Modell Foundation www.info4pi.org

Immunopaedia

http://immunopaedia.org.za/

Approach to the child with recurrent infections Douglas J Barrett, MD, UpToDate ONLINE 15.3