03-07-12

ALLERGY:

- **ATOPIC DERMATITIS: A CANDIDATE FOR DISEASE-MODIFYING STRATEGY** (Bieber T, Cork M, Reitamo S. Allergy 2012; 67: 969–975):
  - 30% AD have filaggrin mutation. Recently identified loci: OVOL1 and ACTL9.
  - Future: stratification of patients according to genomic profile and biomarkers.
  - **Biomarker**: a characteristic that is objectively measured and indicates normal or pathogenic processes, or response to treatment.
  - Breakdown of FLG generates natural moisturizing factor (NMF). NMF contains sodium pyrrolidone carboxylic acid (NaPCA) and urocanic acid (UcA), which are ↓ in FLG mutations and relate to AD severity.
  - **Natural history of AD**: Phase 0: postnatal preclinical phase; phase I: early skin inflammation, no evidence for IgE sensitization (non-IgE-associated infantile eczema); phase II: sensitization to food and environmental allergens, S aureus colonization; phase III: sensitization to self-proteins (autoimmune form of AD).
  - 50% of children with AD (phase II) will have complete remission at age 7 or latest at puberty. 80% will have allergic rhinitis or allergic asthma in later life. AD + allergic rhinitis → high risk (OR = 11.7) for allergic asthma in adulthood.
  - **Tacrolimus** cream until every symptom is controlled, with a subsequent extra treatment for one week. Use again if lesions reappear.

- **EVIDENCE FOR A GENETIC INTERACTION IN ALLERGY-RELATED RESPONSIVENESS TO VITAMIN D DEFICIENCY** (Vimaleswaran KS, Cavadino A, Hyppönen E. Allergy 2012; 67: 1033–1040):
  - 4 SNPs (in FCER1A, IL13, and CYP24A1) and 3 SNPs (in IL4 and CYP24A1) were associated with total IgE and specific IgE, respectively.
  - **IL4 and MS4A2** (FcεR1 beta-chain) genotypes modify the association between VDD and allergy risk. Possible ethnic differences in responsiveness to VDD.

Asthma: chronic inflammatory disorder associated with variable airflow obstruction and bronchial hyperresponsiveness. It presents with recurrent episodes of wheeze, cough, shortness of breath, and chest tightness.

Remodeling can be considered in future definitions of asthma.

Classifications of severity/persistence are recommended only for initial assessment and are being replaced by the concept of ‘control’.

Current impairment and future risk should be considered in future guidelines.

Avoidance of exposure to tobacco smoke during pregnancy and infancy: only recommended measure for the primary prevention of asthma (Evidence B).

Primary (eg. pregnancy and early life) and secondary (eg. patients with AD) prevention should improve results in asthma patients.

Spirometry in every child who can perform it (generally ≥ 5 years). At now, parameters do not differ from adults (FEV1: 80% of predicted, reversible after bronchodilation by ≥12%, 200 ml, or ≥10% of predicted). Newer tests (e.g. oscillometry) may help to diagnose asthma in young children.

NAEPP: PEF has wide normal range → better for monitoring than for diagnosis.

Sputum eos are not recommended to diagnose or monitor childhood asthma.

Diagnosis uncertain? (particularly in <5 years old) → short therapeutic trial (e.g. 3 months) with ICS. Improvement during trial supports asthma; negative response does not completely exclude diagnosis (Evidence D).

Key points for a successful treatment: 1. Education (chronic/relapsing nature of disease, need for long-term therapy and adherence, ‘controller’ and ‘reliever’ medication); 2. Partnership parents – physicians (Evidence A–B); 3. Identification (Evidence A) and avoidance (Evidence B–C) of specific (i.e. allergens) and nonspecific triggers (e.g. tobacco, exercise); 4. Asthma action plans; 5. Regular monitoring for fine-tuning treatment (Evidence A–B).

Early and prolonged use of ICS has not shown benefits in changing natural history of asthma (Evidence A).

Consider IT for children with symptoms linked to relevant allergen (Evidence B). Only treatment with long-term disease-modifying potential. Common duration: 3–5 years. No defined lower age limit; PRACTALL suggests ≥3 years old; GINA can’t recommend for <5 years old.
• **Single interventions** for indoor allergens have limited effectiveness; **multiple interventions** are a prerequisite for clinical benefit (Evidence A).

• **Triggers of asthma:** (1) indoor and outdoor pollution and allergens; (2) viral infections.

• **Drug-sensitive (e.g. NSAIDs) or food-sensitive (e.g. sulfites) children with asthma** → complete avoidance should be advised.

• **Goal of asthma treatment:** control using the least possible medications.

• Control not achieved after 1–3 months → review diagnosis, device use, compliance, environmental control, treatment for comorbid rhinitis → **step up**.

• Control achieved for at least 3 months → **step down** (Evidence A–B).

• **Side effects of SABA:** dose-dependent, self-limiting tremor and tachycardia.

• **Anticholinergic agents:** second-line relievers, less effective than SABA.

• **ICS:** first step of regular treatment (Evidence A). Most children with mild asthma can be well controlled with low-dose ICS.

• Low-dose ICS for prevention of **virus-induced wheezing** in young children? Controversial.

• Main potential **risk effect of ICS:** growth delay (an effect on adult final height cannot be excluded). Most information refers to low-medium doses, **be careful with high doses**. Consider total steroid load (for allergic rhinitis or eczema).

• **LTRA:** effective at all ages (Evidence A). Generally less efficacious than ICS; with some exceptions (younger and less atopic children). Effective as add-on therapy, but less than LABA. Particular effectiveness in **exercise-induced asthma**, possibly superior to other therapies; relatively free of adverse effects (montelukast).

• Older children and adults: **ICS–LABA** may be a better option than higher doses of ICS. Caution in children <5 years old.

• **SMART strategy:** single inhaler to ‘control’ and ‘relieve’ (fast action of formoterol). Efficacy in adults and children.

• **Omalizumab:** non responsive poorly controlled allergic asthma (Evidence B).

• **Essential asthma drugs:** SABA and ICS. SABA should be available to all patients with asthma, irrespective of age, severity, or control.

• **Spacers** should always be used with MDIs in 0- to 5-year-olds and in exacerbations; they are also preferable in older children. A 500-ml plastic bottle spacer may be adapted as an effective spacer for children of all ages.
• **Individual response to medications** is frequently responsible for therapy fail.

• Moving between medications of the same step should be considered.

• **Asthma exacerbation**: an acute or subacute episode of progressive increase in asthma symptoms, associated with airflow obstruction.

• **Bronchodilation** is the cornerstone of exacerbation treatment (Evidence A); should be started at home and as first measure in emergency department. Ipratropium may give additional improvement (Evidence A–B). Response should be seen after within first hour.

• **Systemic corticosteroids**, preferably oral, are most effective when started early in an exacerbation (Evidence A). **High-dose ICS** may be effective for exacerbations or preemptively after a common cold.

• **TRYPTOPHAN, NEOPTERIN, AND NITRITE IN ALLERGY** *(Ciprandi G, Fuchs D. Allergy 2012; 67: 1083)*:

  • IFN-γ → strongly induces indoleamine 2,3-dioxygenase (IDO) → degradation of tryptophan → immune regulation, antiproliferative strategy of cells to decrease growth of infected and malignant cells.

  • The reason for the higher tryptophan concentrations in pollinosis patients outside season remains obscure.

  • **Inducible NO synthase (iNOS) inhibitors** → decrease NO production → increased production of IDO. Candidates for anti-allergic therapy.
**ANNALS OF ALLERGY AND CLINICAL IMMUNOLOGY:**

  - Asthma patients with *C pneumoniae* or *M pneumoniae* airway infection → macrolides for 6-16 weeks → lung function and symptom improvement.
  - Macrolides effects: (1) antibiotic; (2) anti-inflammatory: ↓ NF-κB and AP-1 → ↓ TNFα and IL-8, ↑ eosinophil apoptosis.
  - Long-term macrolide therapy (LTMT) is used for: diffuse panbronchiolitis, cystic fibrosis, posttransplantation bronchiolitis obliterans, COPD.
  - Case report: 61 year-old patient, asthma controlled with clarithromycin 500 mg/day (he has been using it for 26 months), which allowed steroid sparing.
  - Eosinophilic difficult-to-treat asthma + chronic sinusitis → try LTMT.

  - Stress may exacerbate asthma. Proposed mechanisms: (1) dysfunctional HPA; (2) less cortisol production; (3) cortisol insensitivity.
  - Stress → CRH production → mast cell activation, ↓ IL-10 production by Tregs.

  - Cold contact urticaria (CCU): wheals and/or angioedema within minutes of contact with cold air, liquids or objects. Anaphylaxis may occur during aquatic activities. Most cases are primary, but secondary CCU has been reported.
  - Case report: 68-year-old woman who acquired CCU 12 days after a large local reaction to wasp sting. Previous case reports of CCU at 24-48 hours after sting. CCU may appear after stings, and may worsen with further stings.
  - Laboratory: CBC, ESR, CRP, hepatitis set, ASO, ANA, RF, CH50, cryoglobulin, cold agglutinin, SPE, immunoglobulins, peripheral blood flow cytometry, TSH, thyroid autoantibodies: within normal limits or negative.

  - Currently, more than 1,200 allergen extracts are registered by the FDA.
• **IS NASAL SALINE IRRIGATION ALL IT IS CRACKED UP TO BE?** *(Khianey R, Oppenheimer J. Ann Allergy Asthma Immunol 2012; 109: 20–28)*:

  - **Nasal saline irrigation (NSI):** well tolerated, may provide some help in sinonasal diseases by ↓ inflammation.
  - Many techniques, devices and saline compositions; not known the best.
  - **Origins of NSI:** ancient Hindu practice of Ayurveda. Neti (or Hatha Yogi) is an important part of the yogic system of body cleansing techniques. It is intended mainly for cleaning of air passageways in the head, and it has been used for thousands of years to alleviate sinus and allergy symptoms.
  - **Contraindications for NSI:** incompletely healed facial trauma, increased risk for aspiration (such as neuromuscular disorders), not able to use.
  - Rare and generally mild **side effects:** ear fullness, burning or stinging of nasal mucosa, epistaxis, device contamination and recalcitrant infections.
  - **Microwaving** can be used to sterilize bottles used for NSI.

• **NOT ALL THAT ITCHES IS URTICARIA** *(Morris AE, Hall AG, Marshall GD. Ann Allergy Asthma Immunol 2012; 109: 10–13)*:

  - **Acute urticaria:** 20% of the population; varied causes (drug, food, infection, etc). **Chronic urticaria:** 0.5-1% of the population; often autoimmune or idiopathic, rarely allergic (frequent referral mistake).
  - **Gleich** et al (1984) described 4 patients with episodic angioedema/urticaria, eosinophilia and fever. **Differences with HES:** lack of eosinophilic infiltration of internal organs, younger age of onset, response to steroids, good prognosis.
  - **Autoimmune diseases** in patients with chronic urticaria: thyroid diseases (1st place), rheumatoid arthritis, type 1 DM, celiac disease, SLE.


  - **Behçet syndrome:** multisystemic autoimmune disease; oral and genital aphthous ulcers, skin lesions, pathergy phenomenon, ocular involvement (2006 International Criteria for Behçet’s Disease).
  - **IVIG** can be useful for ocular manifestations of the disease.
  - Behçet syndrome associated with **PID:** SCID, Nezelof syndrome, XLA, CVID, thymoma with hypogammaglobulinemia, transient hypogammaglobulinemia.
  - **Case report:** IVIG 1 g/kg controlled unresponsive Behçet syndrome complicated by CVID, and preserved remission for >2 years.
• **IVIG** have dual effect: control inflammation (for Behçet) and enhance immunity (for CVID).


  - PPAR-γ agonists ↓ airway inflammation via direct effects on epithelium, smooth muscle, eosinophils and lymphocytes.

  - Airway hyperreactivity ↓ after 12 weeks of rosiglitazone therapy.

• **TYPE I VARIANT OF KOUNIS SYNDROME SECONDARY TO WASP STING** *(Ridolo E, Olivieri E, Montagni M, Rolli A, Senna GE. Ann Allergy Asthma Immunol 2012; 109: 79-81):**

  - Anaphylaxis can be complicated with acute coronary syndromes. Heart mast cells are involved.

  - Kounis syndrome: “coincidental occurrence of chest pain, allergic reactions, and laboratory findings of classic angina pectoris”. Type 1 appears in patients with normal coronary arteries; type 2 occurs in patients with a preexisting atheromatous disease; type 3 occurs in patients with stent thrombosis.

  - Allergic reactions to *Hymenoptera sting* → perform EKG even if the patient does not present with preexisting coronary artery disease. The evidence is that Kounis syndrome is not a rare disease but a rarely diagnosed disease.
JOURNAL ALLERGY AND CLINICAL IMMUNOLOGY:

  - OFC: gold standard in diagnostic workup of suspected food-related symptoms.
  - Single day OFC can induce a short-term clinical nonreactivity, which can wean off after 1 night. We propose the inclusion of a second day with a cumulative dose to ensure a correct outcome of OFC, avoiding false-negative results.

- **CORRELATION BETWEEN A POLLEN CHALLENGE CHAMBER (PCC) AND A NATURAL ALLERGEN EXPOSURE STUDY DESIGN FOR ELICITING NASAL SYMPTOMS** (Bernstein JA. J Allergy Clin Immunol 2012; 130: 128-129):
  - Environmental exposure units (EEUs) are used to investigate occupational and allergic rhinitis. Potential use: nonallergic rhinitis (cold dry air or T° change).
  - Strong correlation between PCC and natural allergen exposure → EEUs can be used as a surrogate for natural exposure. Not yet approved by FDA.

- **DOES DIVERSITY OF ENVIRONMENTAL MICROBIAL EXPOSURE MATTER FOR THE OCCURRENCE OF ALLERGY AND ASTHMA?** (Heederik D, von Mutius E. J Allergy Clin Immunol 2012; 130: 44-50):
  - Thirteen TLRs (TLR1-TLR13) have been identified in human subjects.
  - Several PAMP from bacteria and molds might have protective effects in asthma (e.g. endotoxins from gram-negative bacteria; β(1/3)glucans from molds; extracellular polysaccharides and muramic acid from gram-positive bacteria).
  - Diversity of fungal and bacterial exposure may protect from allergies.

  - Immunity to helminths: innate and adaptive TH2 responses, IgE to parasite antigens.
  - One side: helminth infections can protect from allergic disease.
  - Other side: IgE cross-reactivity between helminth antigens and allergens (e.g. filarial tropomyosin and HDM; Ascaris tropomyosins and cockroach allergens).

  - Air pollution has severe adverse effects for respiratory health.
• *Improvements in air quality* in preparation for the 1996 Atlanta Olympics lead to reduced ED visits and hospitalizations for childhood asthma.

• The US Congress is currently engaged in a debate regarding restriction of Environmental Protection Agency (EPA) authority under the Clean Air Act.

• EPA projects that by 2020, the *Clean Air Act* standard will prevent 230,000 premature deaths, 75,000 cases of chronic bronchitis, 200,000 heart attacks, 2.4 million asthma exacerbations, and 120,000 ED visits. Economic value >$2 trillion. The public and private industry costs of complying with the Clean Air Act standards are estimated to be $65 billion.

• Benefits of the Clean Air Act far outweigh the costs in the long run. For our nation’s future, as health care professionals, we urge Congress to stop the debate about the EPA’s authority and protect Americans’ health.

• **TOWARD A DEFINITION OF ASTHMA PHENOTYPES IN CHILDHOOD: MAKING A LONG WAY SHORTER?** *(Wahn U, Matricardi PM. J Allergy Clin Immunol 2012; 130: 111-112):*

  • Just et al use cluster analysis for 551 wheezing 3-year-old infants to characterize the heterogeneity of wheeze in early childhood.

  • On the basis of 19 variables, they describe 3 independent groups of wheezing children: early viral wheezers, multitigger wheezers (MTWs), and nonatopic uncontrolled wheezers (NAUWs).

• **TRICHURIS SUIS OVA: TESTING A HELMINTH-BASED THERAPY AS AN EXTENSION OF THE HYGIENE HYPOTHESIS** *(Jouvin MH, Kinet JP. J Allergy Clin Immunol 2012; 130: 3-10):*

  • Ova (eggs) of *Trichuris suis* (*TSO*) are safe. *Trichuris suis* has been chosen because doesn’t cause human pathology.

  • There is preliminary evidence of the efficacy of TSO in patients with IBD and pecan allergy.

  • Components from helminths have effects on mast cells, Treg cells, and DCs.

• **WHY DOES RESPIRATORY SYNCYTIAL VIRUS APPEAR TO CAUSE ASTHMA?** *(Adamko DJ, Friesen M. J Allergy Clin Immunol 2012; 130: 101-102):*

  • Being admitted to the hospital during infancy for RSV–induced bronchiolitis predicts an increased risk of asthma-like disease in later life.

  • 90% of children have an RSV infection by 2 years old, with 40% having lower respiratory tract involvement. If RSV were truly a causal agent for asthma, it seems unclear why association occurs only with hospitalized cases.
• It is *unclear* if RSV is a causal agent of asthma or if severe RSV-induced bronchiolitis represents a first exacerbation of asthma in susceptible subjects.

• **Rhinoviruses** are by far the most frequently detected type of virus in patients with asthma exacerbations.

• Increased CCL5 (**RANTES**) expression in nasal epithelial cells during RSV infection carried an odds ratio of 3.8 for the subsequent development of physician-diagnosed asthma. Rhinovirus also increases CCL5 release.
**DESTRUCTIVE INTERFERENCE OF PRRs** (Kåhrström CT. Nature Rev Immunol 2012; 12):

- Host challenged by multiple pathogens → different PRR pathways are induced simultaneously → alters outcome of infection.
- The RIG-I-like receptors (RLR)-mediated response is a first line of defence against viral infections.
- Virus invasion → RLR activation → interfering with TLR signalling, ↓ of IL-12 production → less Th1 and Th17 responses → inhibition of bacterial clearance.

**DISTINGUISHING CLASSICAL DENDRITIC CELLS (cDCs):** (Nature Rev Immunol 2012; 12):

- The zinc-finger transcription factor ZBTB46 (or BTBD4) is selectively expressed by cDCs and their committed progenitors. ZBTB46 enforces cDC lineage restriction by ↓ expression of alternative myeloid growth factor receptors.


- The term ‘intestinal microbiota’ has become synonymous with ‘intestinal bacteria’. Commensal fungi in the gut can alter the severity of IBD.
- Dectin 1 deficiency impairs immunity to commensal fungi in the gut, thereby promoting inflammatory responses in ulcerative colitis.


- In humans, the intestinal epithelium encompasses ~200 m² of surface area, with the skin contributing an additional ~2 m² surface.

**EPITHELIAL CELLS ACT UP IN WORM EXPULSION** (Bird L. Nature Rev Immunol 2012; 12):

- IL-25 → IL-25R in gut epithelial cells → activation of epithelial cell-specific Act1 adaptor → production of IL-25, IL-33 and T(reg) cell-attracting chemokines → expansion of type 2 LIN–KIT+ innate effector cell population → worm expulsion.


- IgM: secreted as pentamers or hexamers; high avidity for antigens with repetitive motifs (most microbial pathogens), activate complement, can’t pass into the extravascular space owing to large size.
In humans, IgG1 and IgG3 are effective against viruses; IgG2 against encapsulated bacteria; IgG4 and IgE against large extracellular parasites; IgA1 and IgA2 against pathogenic bacteria at the mucosae.

**Primary CSR-inducing stimuli:** Stimuli that induce expression of AID, 14-3-3 adaptors and other CSR factors. They can be: (1) Engagement of CD40 (T cell-dependent stimulus); (2) Dual TLR–BCR, TACI–BCR or TLR–TACI engagement (T cell-independent stimuli).

- **CD40 → NF-κB → AID → CSR.**
- **IL-4 → IL-4R → STAT6 → binding to Iγ1 and Iε promoters → germline transcription that proceeds through Sγ1 and Sε → CSR to IgG1 and IgE.**
- **TGFβ → SMAD3, SMAD4 and/or RUNX proteins → transcription proceeding through Sy2b and Sα → CSR to IgG2b and IgA, respectively.**
- **IFNγ → T-bet, STAT1 and/or STAT2 → germline transcription that proceeds through Sy2a for class switching to IgG2a.**


- Although TLR2 detects lipopeptides that are found in the cell walls of Gram-positive bacteria and thus can recognize intact bacteria, optimal activation of TLR2 by *S aureus* in macrophages requires phagocytosis. Part of this enhanced activity associated with phagocytosis might be due to the recruitment of TLR2 to the phagosomes and the resulting increase in sensitivity.


- **B and T cell function** (including cytokine production, differentiation and cytotoxicity) is regulated by ion channels and transporters in the plasma membrane, which modulate cytoplasmic concentrations of diverse cations, such as calcium, magnesium and zinc.

- **Ion-conducting proteins** include: calcium release-activated calcium (CRAC) channels, P2X receptors, transient receptor potential (TRP) channels, potassium channels, chloride channels and magnesium and zinc transporters.


- Decidual stromal cells (DSCs), which encapsulate the fetus and placenta, express very low levels of T cell chemoattractants CCL5, CXCL9 and CXCL10 under inflammatory conditions → prevention of T cell accumulation in the decidua → additional mechanism of feto-maternal tolerance.

**MILK FAT CAN INFLAME THE GUT** ([Nature Rev Immunol 2012; 12]):
• Diet high in saturated (milk-derived) fat → conjugation of bile acids with taurine → specific outgrowth of *Bilophila wadsworthia* in the gut → Th1-type immune response → increase in disease in colitis-susceptible (*Il10–/–*) mice.

• Dietary fats can result in microbiota dysbiosis and intestinal inflammation in genetically susceptible individuals.


  • Except TLR3, all nucleic acid-sensing TLRs depend on the adaptor protein myeloid differentiation primary-response protein 88 (*MYD88*) for signalling.

• **STEROIDS IMPROVE T CELL FITNESS** *(Bird L. Nature Rev Immunol 2012; 12):*

  • Endogenous glucocorticoids ↑ avidity threshold for thymocyte selection → generation of a T cell repertoire with immunological fitness.

• **VISUALIZING DC DYNAMICS IN THE LUNG** *(Leavy O. Nature Rev Immunol 2012; 12):*

  • There is a spatiotemporal distinction between antigen uptake in the alveoli and antigen retention and presentation in the airway regions adjacent to alveoli.
PEDIATRIC ALLERGY AND IMMUNOLOGY:

  - Prevalence of CRS in Europe: **10%**.
  - **Nasal polyps**: lack of TGF-β, surplus of MMPs over TIMPs → edema formation. **CRS without polyps**: fibrotic disease, ↑ TGF-β, high deposition of collagen.
  - 85% of polyp tissues in Europe are Th2-biased and eosinophilic. IL-4, IL-5 and IL-13 are major drivers. 85% of polyp tissues in Asia are Th2 negative and neutrophilic. IFN-γ and/or IL-17 are major drivers.
  - 30% of nasal polyps are **S aureus enterotoxins (SE) - IgE positive**: ↑ ECP and IL-5, local mucosal polyclonal IgE production, ↑ risk of comorbid asthma.
  - **Staphylococcal superantigens** activate T and B cells, and induce a significant increase in total IgE concentrations in the tissue and eventually in serum.

  - RS may occur in very young children (maxillary and ethmoidal sinuses are present from birth). Sphenoid sinuses are pneumatized at 5 years old; frontal sinuses appear between 7 and 8 years old.
  - RS is almost always a complication of an upper respiratory viral infection. Children have 6–8 viral infections/year in the first years of life; 5–13% of these evolve into acute bacterial RS. Most viral infections recover within 5–10 days.
  - Common cold → nasal phlogosis and ostia obliteration → accumulation of exudates → RS.
  - Acute RS: 10–30 days; subacute RS: 30–90 days; chronic RS: >90 days; recurrent acute RS: >4 episodes/year.
  - Acute and subacute bacterial RS in children are most frequently caused by **S pneumoniae, H influenzae and M catarrhalis**, which are usually present in the nasopharynx of healthy children.
  - CT and MRI of paranasal sinuses should be reserved for children reasonably considered to be candidates for surgery.
  - **ATB (10-14 days)** should be used for mild acute bacterial RS to resolve symptoms quicker. **ATB (14-21 days)** must be used in severe acute bacterial RS to avoid severe complications. ATB prophylaxis is not recommended for prevention of RS.
• Infection in acute RS can extend to orbits and endocranial structures as a result of contiguity (3% complicated with orbital cellulitis). Orbital complications are the most frequent (90% of the total).

  • Suspicion of CRS in young children: chronic cough, malodorous breath, vomiting, poor appetite, impaired sleep, decreased weight gain.
  • In some patients with CRS, nasal discharge is absent. A purulent discharge may drip only posteriorly into the oropharynx, leading to cough or throat clearing.
  • Cough: presenting symptom of CRS in 60% of children; may be wet or dry; occurs in day; often worsens at night. Suggested mechanism: post-nasal drip.
  • The adenoid infected tissue may be a bacterial reservoir that favors chronic infection of paranasal sinuses, even without obstruction.
  • Plain sinus X-rays are insensitive and of limited usefulness to diagnose CRS.
  • CT is the first choice to evaluate CRS and middle ear disorders.
  • MRI should be done when there is suspicion of orbits and brain complications; chronic fungal sinusitis; or neoplasms.
  • CRS → always look for asthma, recurrent or persistent otitis media, OSAS.
  • Ear disease (recurrent acute otitis media or otitis media with effusion) occurs in 50% of children with CRS. Sinusitis is present in 50% of children with OME.
  • About 50% of children <3 years old with suspected AOM had no fever; there was no individual symptom reliably predicting AOM.

  • Diagnosis of ARS is mainly clinical.
  • ARS should recover spontaneously within 4 weeks. ATB accelerate resolution of symptoms. Topical treatments (saline irrigation, decongestants, antiH1 and fungicides) have poor evidence of efficacy, except for topical steroids.
  • Pneumococcal and influenza vaccination can decrease frequency of infections in children with upper respiratory diseases.

• CRS is difficult to treat. Available medical treatments: ATB, topical steroids, saline irrigation.

• Balloon sinuplasty restores ventilation to the sinuses with minimal risk and tissue trauma. Functional endoscopic sinus surgery restores ostia patency and re-establishes ventilation and drainage with minimal invasion.

• Efficacy of adenoidectomy for CRS is controversial.


  • Respiratory mucosa is a pseudostratified epithelium with hair cells, muciparous cells, strial cells, and basal cells. Hair cells and muciparous cells (5:1 ratio) are the first defensive line of the upper airways (mucociliary system).

  • Normal turnover time for hair cells is 3 weeks → recurrent inflammation does not allow recovering → more muciparous cells than hair cells (?).

  • Chronic non-allergic rhinopathies (NARES, NARMA, NARNE and NARESMA) can occur at any age.

  • AOM is the most common disease in infants and children: almost all children experience at least one episode in their first 3 years of life, 30% experience ≥2.