APC AVERROES PEDIATRIC CLUB | AVERROES PHARMA

AVERROES PEDIATRIC CLUB

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When the experience meets the Egyptian modification

It gives us much pleasure to start the APC Project with the objective of transferring experience between different generations of physicians which will be reflected positively on patient health.

Averroes Works at the very center of many challenges across the broadcast base of any company in healthcare to satisfy both internal and external stakeholders especially doctors and patients with the objective of reaching an excellence in execution

Finally I am Sure that this project will have a very good impact and its results will be very beneficial with your support and help to start a success story.

Signature

Mahmoud EL Lahouny

CEO

AVERROES PHARMA

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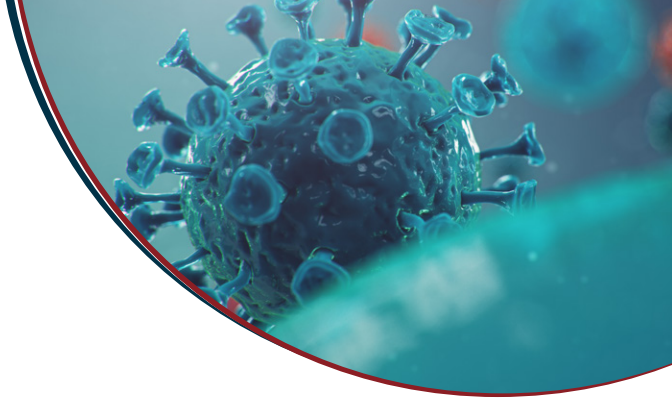

Dr.Eman Fouda
Prof. of pediatrics and head of pediatric pulmonolgy unit Ain shams university

"All you need to know about COVID-19"

1- What is the COVID 19 Suspected case?

- Acute onset of fever and cough
- Or 3 or more of the following:Fever-cough-sore-throat-coryza-fatigue-headache-myalgia-dysnea-anorexia- nausia vomiting-diarrhea-altered mental status
- Patient with acute respiratory illness. With history of fever >38° and cough, onset within last 10 days; required hospitalization.

2- What is COVID 19 Probable case?

- A case with clinical criteria AND contact with a probable or confirmed case.
- OR linked to a cluster with >1 confirmed cases
- OR A suspected case with imaging suggestive of COVID19
- OR Recent loss of smell or taste without other identified cause

3- What is COVID 19 Confirmed case?

- A person with laboratory confirmation of COVID-19, irrespective of the clinical signs and symptoms.
- Laboratory Confirmation PCR Molecular testing with deep nasal swab is the current test of choice for the diagnosis of acute COVID-19

Dr.Eman Fouda
Prof. of pediatrics and head of pediatric pulmonology unit Ain shams university

4- How you can categorize the clinical severity of COVID19?

- **Mild:** Mild symptoms and lymphopenia or leucopenia but, normal imaging.
- **Moderate:** Symptoms and/or leucopenia or lymphopenia with +ve Imaging TACHYPNEA but, SpO2 ≥92%.
- **Severe:** SpO2 <92%, PaO2/FiO2 <300, tachypnea or lung infiltrates >50% lesion or progressive lesion within 24-48 hrs.
- **Critical:**
  Respiratory failure (**SaO2 <92,** or RR>30, or PaO2/FiO2 ratio < 200 **despite oxygen therapy).**
  Chest radiology showing **more than 50% lesion** or progressive lesion within 24 to 48 hrs.
  Multiorgan dysfunction and/or **Septic shock.**

6- What are the lines of treatment for mild COVID 19 cases?

- Reassurance and Home isolation for 10 days
- Antipyratics (paracetamol)
- Maintain good hydration ,nutrition and enough sleep
- Vit C 50 mg /day 1-3 y and 100 mg /day over 3y
- Zinc 5-10 mg/day for young children and 10-15 mg/ day for older children
- Vitamin D 3 400-600 IU/day below 1 y and 600-800 IU/day for older children
- Lactoferrin sacchets once /day (if not breast feed)
- Azithromycin 10mg/kg in respiratory symptoms
- Nitazoxanide in cases of diarrhea

7- Why SARS-CoV-2 is virulent as compared to all other respiratory viruses?

- SARS-CoV-2 as compared to all other respiratory viruses:
  -upregulates cytokines and chemokines
  -while at the same time down regulating the expression of Interferon alpha (the hosts primary antiviral defense mechanism).

8- Period of infectivity and isolation after being PCR positive?

- Symptomatic patients are likely to be infectious during a narrow window starting 2–3 days before the onset of symptoms and to up to 6-8 days after the onset of symptoms

Dr.Eman Fouda
Prof. of pediatrics and head of pediatric pulmonolgy unit Ain shams university

9- Should I repeat PCR test to discontinue isolation?

- Only in severely immunocompromised patients
- **For persons who never develop symptoms,** 10 days after the date of their first positive RT-PCR test for SARS-CoV-2 RNA.
- **For symptomatic patients with COVID-19 illness,** 10 days after symptom onset and resolution of fever for at least 24 hours, without the use of fever-reducing medications, and with improvement of other symptoms.
- **Persons with severe illness** extending duration of isolation and precautions for up to 20 days after symptom onset as they may produce replication-competent virus for longer period

10- What is the magic –bullet for prevention or treatment of COVID19?

- It should be noted that there is no cure or **"Magic-bullet"** for the prevention or treatment of COVID-19.
- Furthermore, it is likely that **no single drug** will be effective in treating this complex disease and that **multiple drugs** with different mechanisms of action and used in specific phases of the disease will be required.

11- what are High-risk children for severe Corona infection?

1. **Chronic lung disease** or **moderate to severe asthma.**
2. Serious heart conditions.
3. **Immune deficiency** including cancer treatment, bone marrow or organ transplantation, and prolonged use of corticosteroids and other immune weakening medications.
4. **Severe obesity** (body mass index [BMI] ≥40)
5. **Diabetes.**
6. Chronic kidney disease undergoing **dialysis.**
7. **Liver diseases.**

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APC 7

Prof.Dr.Mortada El-Shabrawy
Prof. of Pediatrics and Pediatric Hepatology
Cairo University

"Neonatal Jaundice"

1- Is neonatal jaundice common?

Yes, 40-60% in full term and 60-80% in premature newborns

2- Is neonatal jaundice increasing?

Yes, because of better diagnosis and better survival of small and sick newborn babies

3- Is neonatal jaundice serious?

Commonly no if mild to moderate and physiologic

4- How to reassure parents/family that their baby's neonatal jaundice is physiologic?

If starts after 2 or 3 days, baby is generally well with normal urine and stools, and disappears at 10-14 days

5- How to suspect that jaundice is pathologic?

If the baby is unwell, jaundice present at birth or starts in the first 24 hours or persists after 14 days or with abnormal urine or stool color

6- How to treat neonatal jaundice?

If physiologic: reassurance and rarely phototherapy
If pathologic: refer to a specialized pediatric hepatologist

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APC 9

Prof.Dr.Tarek El Walili
Prof. of Pediatrics, Alexandria University

The TRIAD

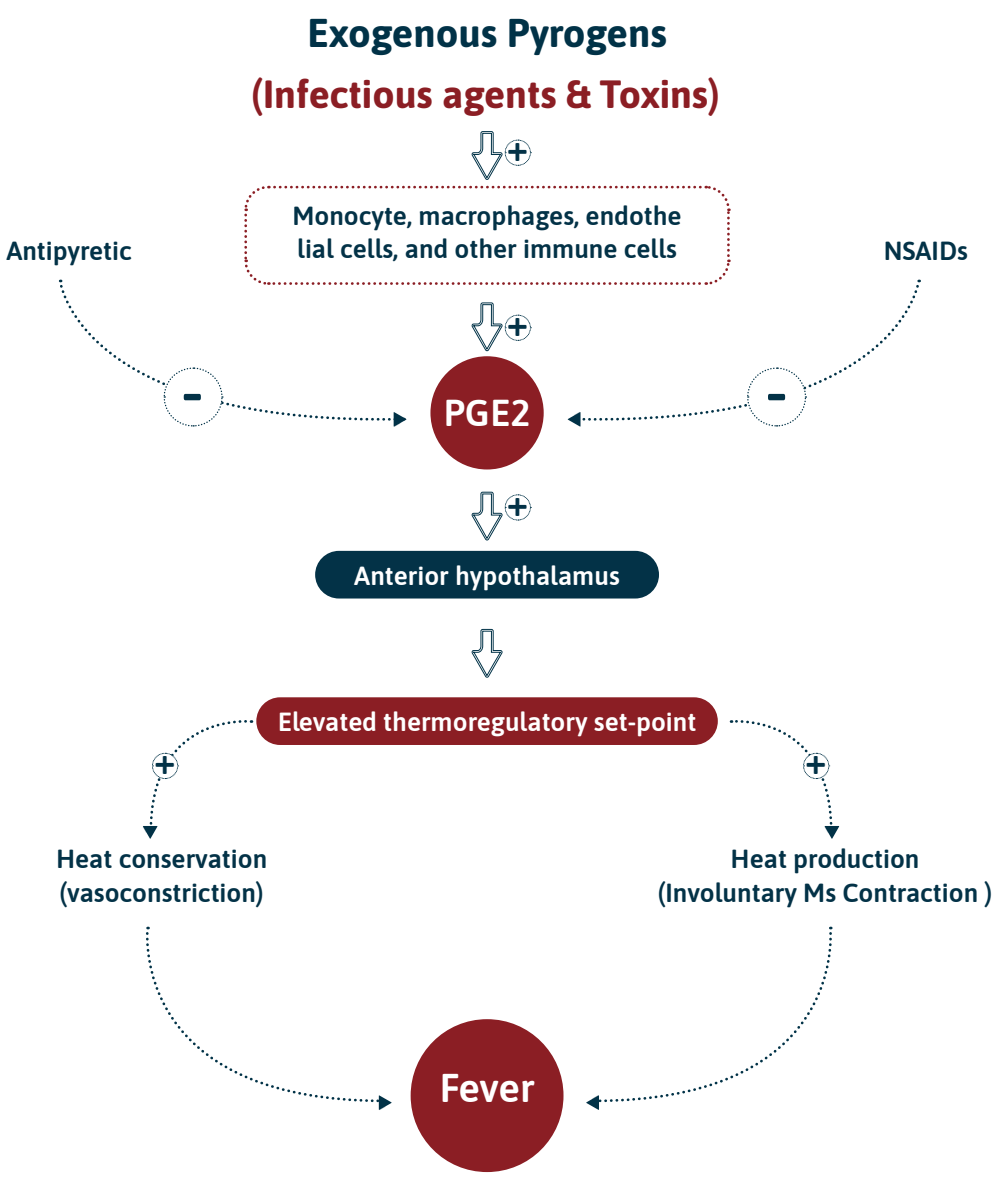
FEVER-PAIN-INFLAMMATION: THE CHALLENGE

FEVER

PAIN

INFLAMMATION

Prof.Dr.Tarek El Walili
Prof. of Pediatrics, Alexandria University



Fever Phobia!

FEVER PHOBIA

73%
of moms fear the potential of their child getting a high fever.

82%
of moms lay awake at night worrying about their child's fever.

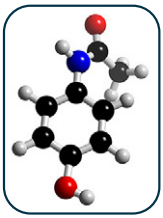
50%
of moms have missed more than one day of work because they had a feverish child.

TREATING FEVER IN CHILDREN - THE HOLISTIC APPROACH

natural Super Kids

Prof.Dr.Tarek El Walili
Prof. of Pediatrics, Alexandria University

- Acetaminophen (APAP) 10-15 mg/kg po/pr q4h
- There is no difference in effectiveness based on po or pr routes
- There is no increased effectiveness when pr dose of APAP is increased to 45mg/kg



APAP vs Ibuprofen

- There is no significant benefit to using either antipyretic preferentially
- There is no benefit in alternating the two meds but there is a significantly increased chance of dosing error and possible overdose

Prof.Dr.Tarek El Walili
Prof. of Pediatrics, Alexandria University

Paracetamol or ibuprofen for children?

Arch Pediatr Adolesc Med; 2004; 158: 521 – 526.

Items	Safety	Pain	Fever
Paracetamol	✓	✓	✓
Ibuprofen	✓	✓	Better at 2, 4 and 6 hours

Guidelines Recommendations

Feverish illness in children assessment and initial management in children younger than 5 years 2007 - Funded to produce guidelines for the NHS by NICE

Recommendations on combining pharmacological treatment to reduce temperature

Paracetamol and ibuprofen should not be administered at the same time to children with fever.

Paracetamol and ibuprofen should not routinely be given alternately to children with fever. However, use of the alternative drug may be considered if the child does not respond to the first agent.

NICE National Institute for Health and Care Excellence

Feverish illness in children assessment and initial management in children younger than 5 years, National Collaborating Centre for Women's and Children's Health, Commissioned by the National Institute for Health and Clinical Excellence, 2007.
Available from: http://www.nice.org.uk/nicemedia/pdf/CG47Guidance.pdf. Accessed 2013 October 20

Pain and inflammation

To be continued next time ...

Prof.Dr.Tarek El Walili
Prof. of Pediatrics, Alexandria University

The use of non-steroidal anti-inflammatory drugs (NSAIDs) in patients with COVID-19

Scientific brief
19 April 2020

19 April 2020

World Health Organization

Background

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used drugs, and have a wide range of uses. NSAIDs include nonselective cyclooxygenase (COX) inhibitors (such as ibuprofen, aspirin (acetylsalicylate), diclofenac, and naproxen), as well as selective COX2 inhibitors (such as celecoxib, rofecoxib, etoricoxib, lumiracoxib, and valecoxib).

Concerns have been raised that NSAIDs may be associated with an increased risk of adverse effects when used in patients with acute viral respiratory infections, including COVID-19.[1,2] This review aimed to assess the effects of prior and current use of NSAIDs in patients with acute viral respiratory infections on acute severe adverse events (including mortality, the acute respiratory distress syndrome (ARDS), acute organ failure, and opportunistic infections), on acute health care utilization (including hospitalization, intensive care unit (ICU) admission, supplemental oxygen therapy, and mechanical ventilation) as well as on quality of life and long-term survival.

Methods

A rapid systematic review was carried out on 20 March 2020 on NSAIDs and viral respiratory infections using MEDLINE, EMBASE, and WHO Global Database. The review included studies conducted in humans of any age with viral respiratory infections exposed to systemic NSAIDs of any kind. All studies on COVID-19, the Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) were included irrespective of their sample size.

Conclusion

At present there is no evidence of severe adverse events, acute health care utilization, long term survival, or quality of life in patients with COVID-19, as a result of the use of NSAIDs.

References

1. Russell B, Moss C, Rigg A, Van Hemelrijck M. COVID-19 and treatment with NSAIDs and corticosteroids: should we be limiting their use in the clinical setting?. Ecancermedicalscience. 2020;14:1023. Published 2020 Mar 30. doi:10.3332/ecancer.2020.1023
2. Non-steroidal anti-inflammatory drugs and covid-19. BMJ 2020;

Conclusion

- At present there is **No Evidence** of severe adverse events, acute health care utilization, long-term survival, or quality of life in patients with COVID-19, as a result of the use of NSAIDs.

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APC 16

Prof.Dr.Mostafa Al-Saeed
Prof. of Pediatrics, Asyut University

"COUGH IN CHILDREN"

when does it matter?

What matters for the respiratory pediatrician is whether the cause of the cough will result in damage to the airways or lung.

Duration of cough

Acute: cough lasting less than 4 weeks

Chronic: cough lasting more than 4 weeks (3 to 12 weeks)

What is the etiology of cough?

Normal or expected cough: the occasional daily cough or a mild cough that has an obvious cause(after URTI) .

Specific cough: cough associated with other symptoms and signs suggestive of an underlying problem.

Prof.Dr.Mostafa Al-Saeed
Prof. of Pediatrics, Asyut University

Cough does it matter if associated with Specific cough pointers :

Chest pain	Immunodeficiency
History suggestive of inhaled foreign body	Risk factors for T B
Dyspnea, exertional dyspnea	Signs of respiratory distress
Hemoptysis	Digital clubbing
Failure to thrive	Chest wall deformity
Feeding difficulties (including choking/vomiting)	Auscultatory crackles
Cardiac or neurodevelopmental abnormalities	Chest radiographic changes
Recurrent sino-pulmonary infections	

Non-specific cough: Dry cough in the absence of an identifiable respiratory disease of known etiology. The majority of cases are due to non-serious etiology (post-viral cough and/or increased cough receptor sensitivity) and may spontaneously resolve.

The age of the child

Cough that began around the time of birth suggest a congenital [e.g. tracheomalacia, laryngeal ,TOF).

The nature of the cough

The most important quality of the cough is whether it is wet or dry.

A productive (sounding) cough is always abnormal and suppurative lung disease should be considered.

Protracted Bacterial Bronchitis

is persistent infection of the conducting airways (wet cough for more than 4 weeks, absence of symptoms or signs of other causes of wet or productive cough which resolved following a 2-week course of an appropriate oral antibiotic (usually amoxicillin-clavulanate).

Cough in asthma worsens when the child has a viral infection, occurs while your child is asleep or is triggered by exercise or cold air.

Finding out if the child sleeps through the night despite the cough can give a clue as to whether the parents are more affected by the cough but does not necessarily exclude serious pathology.

Prof.Dr.Hassan Elkenany
Professor of pediatrics, Alexandria University

"Physician's dilemma in choosing an antibiotic on an empirical basis !!!"

This is an overview " flying bird looking " presentation..

The goal of antibacterial therapy ABC

- **A**ppropriate antibacterial therapy guided by PD
- **B**acteriological eradication
  - Clinical failure
  - Recurrence or relapse
  - Selection of resistance
- **C**linical cure
  - Morbidity
  - Mortality
  - Resource utilization/cost

"Physician's dilemma in choosing an antibiotic on an empirical basis !!!"

Prof.Dr.Hassan Elkenany
Professor of pediatrics,Alexandria University

Prescription statistics in Egypt

- Total antibiotic prescriptions 23 Millions/y
- Oral antibiotic prescriptions 19 Millions/y

IMS DATA 2010

Prescribing an empirical antibiotic :

1- The first question that usually faces the doctor is :

Do I have reasonable indication(s) to give an antibiotic ?

Viral OR Bacterial infection or..a non infectious illness ..!!!

2- Please try to name the possible causative bacterial pathogen in your mind

This necessitates identifying the site and nature of the infectious illness.

3- The spectrum of activity of the antibiotic !

- **Narrow spectrum Atics are preferred.**
- **Post antibiotic effect.**

4- Is the bacterium an extracellular or an intracellular pathogen.

Question "which is more important : serum or tissue concentration of the antibiotic ?"

5. Pharmacology, PK and PD of the antibiotic.

Take care of once daily antibiotics...

The Relationship Between Pharmacokinetics/ Pharmacodynamics and Clinical Outcome

Pharmacokinetics	Pharmacodynamics
Effect in Humans	**Effect in Bacteria**
Serum concentration profile	Potency (MICs)
Penetration to site of infection	Killing mechanism
(middle ear, sinuses, skin, CSF, joints,...)	Post antibiotic effect

Clinical Efficacy

Prof.Dr.Hassan Elkenany
Professor of pediatrics,Alexandria University

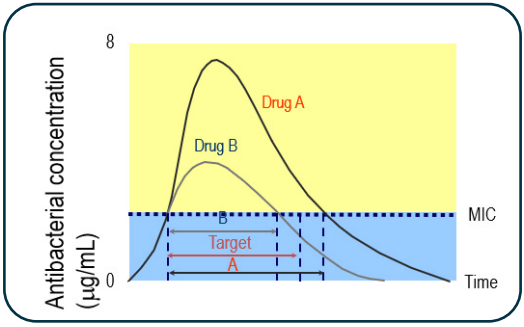
Pharmacodynamics of the antibiotic :"Therapeutic response in relation to drug concentration"

MIC

Time > MIC
in time dependent antibiotics

AUC > MIC
in concentration dependent antibiotics

PD therapeutic goals for β-lactams: "Time above MIC" > 40–50% of dosing interval



Drug A present at 2 µg/mL for 50% of dosing interval; Drug B for 30% of dosing interval.

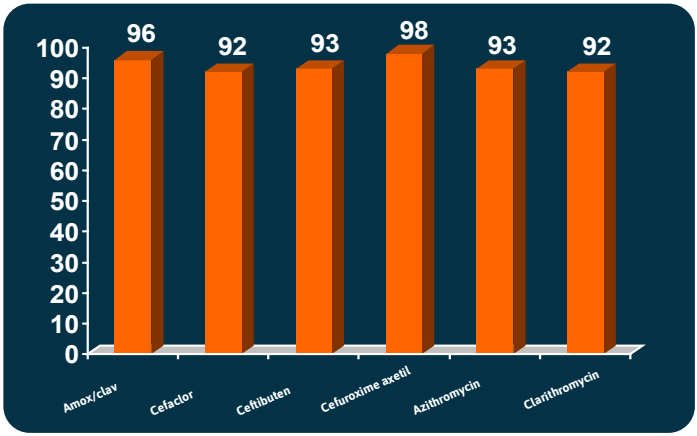
Target – drug present at 2 µg/mL for ≥ 40–50 % of dosing interval

6- Compliance to the medication
7- Culture studies ??
8- Special situations : Age, serious infection, ICU setting, post operative, renal/hepatic affection .....
9. Brand or generic ? and.....personal factors !!!!?
10. Are you concerned with the problem of pathogen eradication and antibiotic resistance ??!!

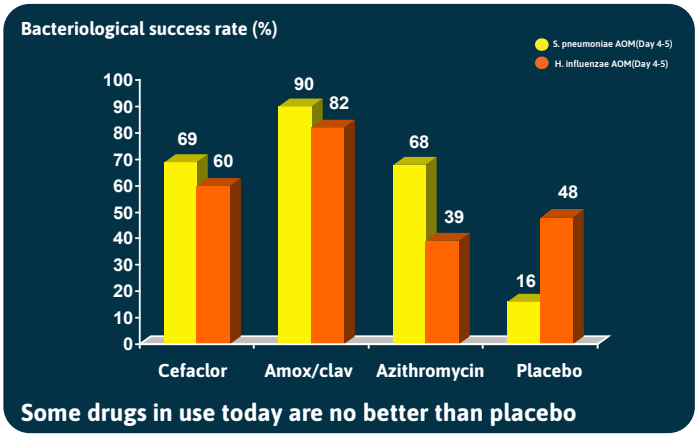
"Physician's dilemma in choosing an antibiotic on an empirical basis !!!"

Prof.Dr.Hassan Elkenany
Professor of pediatrics,Alexandria University

Many antibiotics may seem to be clinically equal for respiratory tract infections (RTIs)



But..there are differences in bacteriological success rates



Some drugs in use today are no better than placebo

Prof.Dr.Hassan Elkenany
Professor of pediatrics,Alexandria University

Main reasons for developing resistance :

1. Overuse of antibiotics.
2. Under treatment and inadequate doses and duration.

So, the question is : How to combat antibacterial resistance ?

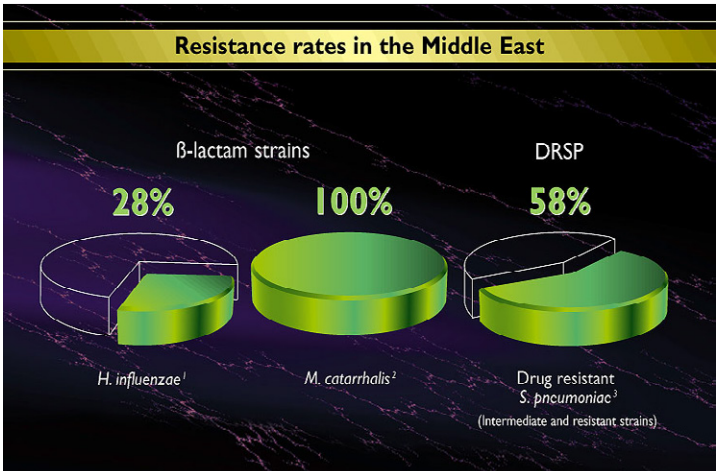
Mechanisms of resistance

I.To β Lactam antibiotics :

1. lactamase production.
2. Change in bacterial cell wall.
3. Bacterial antibiotic binding proteins.
4. Efflux mechanism.

II. To Macrolides :

1. Very effective efflux mechanisms
.2. Intracellular methylases.



AVEROBIOS

Amox 600mg - Clav 42.9mg

60ml 75ml

It is atime of high dose

APC 24

Prof.Dr. Salah El-Din Amry
Prof. of Pediatrics, Asyut University

“Streptococcal Throat Infection[1]”

What are the causes of throat infections?

Infectious Agents

Viruses	Bacteria
Adenovirus	**Streptococcus pyogenes [Group A-β hemolytic streptococcus (GAS)]**
Coronavirus	Arcanobacterium haemolyticum
Cytomegalovirus	Fusobacterium necrophorum
Epstein-Barr virus	Corynebacterium diphtheriae
Enteroviruses	Neisseria gonorrhoeae
Herpes simplex virus (1 and 2)	Group C streptococci
Human immunodeficiency virus	Group G streptococci
Human metapneumovirus	Francisella tularensis
Influenza viruses (A and B)	Yersinia pestis
Measles virus	Chlamydophila pneumoniae
Parainfluenza viruses	Chlamydia trachomatis
Respiratory syncytial virus	Mycoplasma pneumoniae
Rhinoviruses	Mixed anaerobes (Vincent angina)

Non-Infectious Agents

Prof.Dr. Salah El-Din Amry
Prof. of Pediatrics, Asyut University

Environmental Exposure	Inflammatory Conditions
• Tobacco smoke. • Air pollutants. • Allergens. • Contact with caustic substances, hot food, and liquids.	• Periodic fever, Aphthous stomatitis, Pharyngitis, Adenitis (PFAPA) syndrome. • MIS-COVID 19 • Kawasaki disease. • Inflammatory bowel disease. • Stevens-Johnson syndrome. • Systemic lupus erythematous.

What is the significance of streptococcal throat (GAS) infection?

Viral respiratory tract infections can predispose to bacterial middle ear infections. The complications of GAS pharyngitis include local suppurative complications, such as parapharyngeal abscess, and later nonsuppurative illnesses, such as acute rheumatic fever and acute postinfectious glomerulonephritis.

How to diagnose streptococcal infection?

Clinical Presentation:	Lab Tests:
• Sudden onset of sore throat • Age 5-15 yr • Fever • Headache • Nausea, vomiting, abdominal pain • Tonsillopharyngeal inflammation • Patchy tonsillopharyngeal exudates • Palatal petechiae • Anterior cervical adenitis (tender nodes) • Winter and early spring presentation • History of exposure to strep pharyngitis • Scarlatiniform rash	• The specificity of rapid tests to detect GAS antigen is high, so if a rapid test is positive, throat culture is unnecessary and appropriate treatment is indicated. • Because rapid tests are generally less sensitive than culture, confirming a negative rapid test with a throat culture has been recommended, especially if the clinical suspicion of GAS is high.

Prof.Dr. Salah El-Din Amry
Prof. of Pediatrics, Asyut University

What is the significance of the antistreptolysin O assay (ASOT)?

- It is not useful in the assessment of acute pharyngitis.
- It has no role in the decision of tonsillectomy.
- GAS infection is diagnosed retrospectively on the basis of an elevated or increasing streptococcal antibody titer. ASOT is the streptococcal antibody test most commonly used. Because streptolysin O also is produced by group C and G streptococcus, the test is not specific for group A infection.
- The main role of ASOT is in the diagnosis of rheumatic fever using Jones criteria. Alone, it does not diagnose active rheumatic fever.

Studies in Egypt showed that ASOT titer $\geq$ 400 indicates previous streptococcal infection?.

What is the treatment of streptococcal throat infection?

- Penicillin V: bid or tid for 10 days: 250 mg/dose for children <27 kg and 500 mg/dose for larger children and adults.
- Oral amoxicillin: once-daily dosing (750 mg fixed dose or 50 mg/kg, maximum 1 g) orally for 10 days.
- A single intramuscular dose of benzathine penicillin (600,000U for children <27 kg; 1.2 million U for larger children and adults) ensures compliance and provides adequate blood levels for more than 10 days.

Patients allergic to penicillin can be treated with a 10-day course of a first-generation cephalosporin (cephalexin or cefadroxil) if the previous reaction to penicillin was not an immediate, type I hypersensitivity reaction.

Prof.Dr. Salah El-Din Amry
Prof. of Pediatrics, Asyut University

For patients allergic to penicillin, treatment options include

- Erythromycin: 40 mg/kg/day divided bid, tid, or qid orally for 10 days
- Azithromycin: 12 mg/kg once daily for 5 days, maximum daily dose 500 mg
- Clarithromycin: 15 mg/kg/day divided bid for 10 days, maximum dose 250 mg bid
- Clindamycin: 20 mg/kg/day divided in 3 doses for 10 days, maximum daily dose 1.8 g

Proper antimicrobial treatment within 9 days of GAS infection prevents the development of rheumatic fever in susceptible children.

Continuous antimicrobial prophylaxis is recommended only for with definite history of rheumatic fever.

What are the indications of tonsillectomy?

- **Children with >7 infections in the past year, 5 infections per year in the past 2 years, or 3 infections per year in the past 3 years. Episodes should be well documented and include fever, cervical adenopathy, tonsillar exudate, or a positive test for GAS infection.**
  Tonsillectomy may lower the incidence of pharyngitis for 1-2 yr among these children.
- Tonsillectomy might be more beneficial in children who do not meet the above criteria but have resistance to multiple antibiotics, PFAPA syndrome (periodic fevers with aphthous stomatitis, pharyngitis, and adenitis), or history of peritonsillar abscess.

References:

1- Nelson Textbook of Pediatrics, 21 EDITION
2- Kotby AA, Habeeb NM and Ezz El Arab S. Antistreptolysin O titer in health and disease: levels and significance. Pediatric Reports 2012; volume 4:e8.

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Prof.Dr.Tarek Barakat
Prof. of pediatric /gastroenterology & hepaatolgy Faculty of medicine
Mansoura university

“Cow’s milk allergy: Answers for FAQs”

Frequently Asked Questions (FAQs)

(Q)[1] - What are the adverse reactions to food?
- Difference between food allergy and intolerance?

(Q)[2] - Is CMPA common?

(Q)[3] -Clinical presentation of CMPA?

- FPIES
- FPIE
- FPIAP
- CMA in Preterm

Adverse reactions to food

- In UK, about 20% of 20.000 people thought they had adverse reactions to food, but in fact this study shows that only 1.4% had a food allergy.
- Other European studies suggest that 0.3-7.5% of children have a food allergy, 2% of European adults are thought to have a food allergy.
- The prevalence of food allergy in people with an atopy is 10%.
- How many people have food intolerance is not known.
- Misunderstanding about adverse reactions to food result in unnecessary elimination of some foods.

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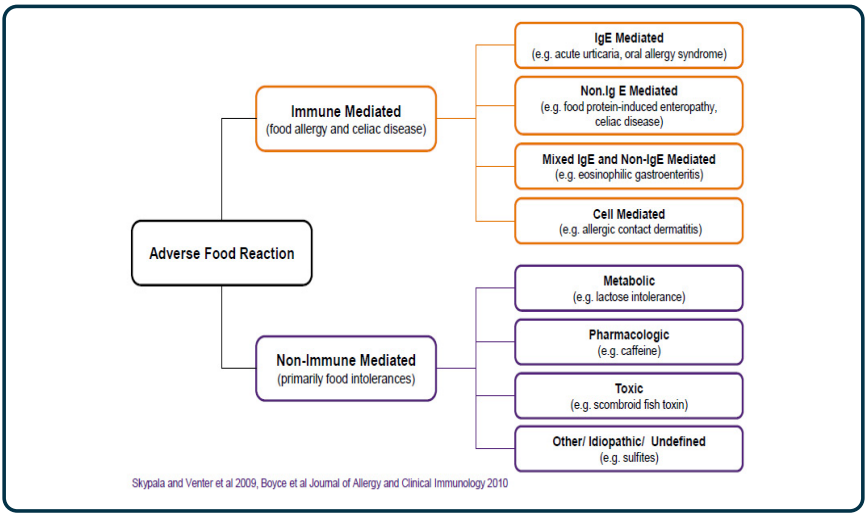


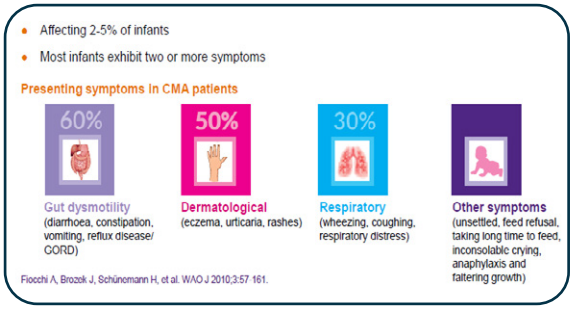
- CMP is the leading cause of food allergy in infants and children younger than 3 years; however CMPA with GI manifestation alone can be diagnosed in all age groups.
- GI manifestations of CMPA are nonspecific.
- In a small group of older children, CMPA may present with symptoms of GERD but also with dyspepsia or abdominal pain, and hence may be easily confused with FGIDs or LI.

CMPA is one of the most common food allergy

- Parents perceive CMPA in their children more often than can be proven by OFC; however, true CMPA peaks in the 1st year of life, with a prevalence ≈ 2-3%.
- This prevalence then falls to <1% in children 6 years of age and older.
- A few exclusively breast-fed infants may also develop clinically significant CMPA via dairy protein transfer into human breast milk.

Keil T, McBride D, Grimshaw K, et al. The multinational birth cohort of EuroPrevall: background, aims and methods. Allergy 2010;65:482–90.

Clinical presentation of CMPA



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Prof. of pediatric /gastroenterology & hepaatolgy Faculty of medicine Mansoura university

symptoms and signs related to CMPA

	Infants and toddlers	Older children	Immediate reaction (within min–2 h after ingesting CMP)
Digestive	Dysphagia Frequent regurgitation Colic, abdominal pain Vomiting Anorexia, refusal to feed Diarrhea ± intestinal protein or blood loss Constipation ± perianal rash Failure to thrive Occult blood loss Iron-deficiency anemia	Dysphagia Food impaction Regurgitation Dyspepsia Nausea, vomiting Anorexia, early satiety Diarrhea ± intestinal protein or blood loss Constipation Abdominal pain Occult blood loss Iron-deficiency anemia	Vomiting
Respiratory	Runny nose Wheezing Chronic coughing (all unrelated to infections)	Runny nose Wheezing Chronic coughing (all unrelated to infections)	Wheezing or stridor Breathing difficulties
Skin	Urticaria (unrelated to infections, drug intake, or other causes) Atopic eczema Angioedema (swelling of lips or eyelids	Urticaria (unrelated to infections, drug intake, or other causes) Atopic eczema Angioedema (swelling of lips or eyelids)	Urticaria Angioedema
General	Anaphylaxis Shock-like symptoms with severe metatobolic acidosis, vomiting, and diarrhea (FPIES)	Anaphylaxis	Anaphylaxis FPIES

Food Protein-Induced Enterocolitis Syndrome (FPIES)

- FPIES represents the acute, slightly delay-onset end of the spectrum of CMPA in the gut and is an uncommon disorder, usually presenting with repeated projectile vomiting, hypotonia, pallor, and sometimes diarrhea 1-3 hours after ingestion of CMP.
- Symptoms are severe, protracted, most commonly after ingestion of cows milk- or soy-based formula (50% of infants react to both), although solid food allergens are occasionally implicated.
- Progression to dehydration can occur and cause shock in about 20% of cases.
- Typically, FPIES occurs at the first known introduction of CMP into the diet
- It has not been reported in exclusively breast-fed infants, until cows milk or cows milk-based formulas are added to the diet.
- It may also be caused by other food proteins and may require a careful differential history.
- Despite the relatively rapid onset after ingestion, the disorder is not IgE-mediated.
- The common features; FTT, hypoalbuminemia.
- Remission usually occurs within the 1st 3 years of life.

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Cow's Milk Protein-Induced Enteropathy

- These infants may present with diarrhea, FTT, various degrees of vomiting, sometimes, hypoproteinemia and anemia.
- In younger children metabolic acidosis can develop.
- The clinical signs of 2ry LI, including perianal excoriation from acidic stools, may be present.
- Despite the acute nature of the clinical presentation, it is thought to be a non-IgE-mediated disorder.
- The implicated dietary proteins include cows milk, but also soy milk, hydrolyzed casein protein, and maternal dietary proteins transferred through breast milk.
- Lab. observations include stools that contain not only blood but also neutrophils. Mild anemia may progress to significant anemia associated with hypoproteinemia (PLE).
- An ↑ intestinal permeability was shown and ↑ inflammatory cells in the lamina propria, LNH, and ↑ eosinophilic infiltration of the crypts.
- Most infants with milk-induced entheropathy respond to eHF, although a significant number of infants require an AAF.

Dietary Protein Enterocolitis: Clinical Features

Presenting symptoms	Progressive diarrhea with bleeding Emesis, abdominal distension Protein-losing enteropathy Failure to thrive
Laboratory findings	Focal blood and leukocytes Focal elevation of α1-antitrypsin Anemia hypoalbuminemia Normal IgE Methemoglobinemia Peripheral leukocytosis on antigen challenge
Age at onset	1 day to 1 year
Implicated antigens	Frequently multiple antigens Cow's milk, soy, ovoalbumin, casein Chicken, rice, fish (older children)
Pathology	Inflammatory colitis Lymphoid nodular hyperplasia Focal vilus injury Eosinophilic infiltration of lamina propria
Treatment	80% respond to extensively hydrolyzed casein formula 15%–20% require an l–amino acid-based formula, especially if growth Rate not registered 2%–5% require transient total parenteral nutrition or steroid High rate of severe reactions to food challenge

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Food Protein Induced Procto-colitis.

- A disease of infancy usually show up by the 2nd month and represent the benign end of the spectrum of non-IgE-mediated CMPA.
- Infants with allergic proctocolitis because of CMPA can present with relatively normal stools or mild diarrhea and low-grade rectal bleeding but be otherwise well and thriving.
- If the infant is exclusively breast-fed (breast milk colitis), symptoms may be caused by protein transfer via breast milk.
- The bleeding is usually observed as stools containing mucus and flecks of blood rather than as frank rectal bleeding.
- Other features (as FTT or anemia) are usually absent.
- It can occur in the early neonatal period (in PT even after the first feed) and should be considered in the DD of any newborn with GI bleeding.
- Sometimes the condition may present with acute symptoms mimicking Hirschsprungs disease .

Manifestations of CMA in Preterm infants

- The incidence and clinical manifestations of CMPA in PT infants with comorbidities remains poorly defined.
- NEC is the most common GI emergency in PT infants, affecting 7-11% of VLBW infants.
- The "classic" presentation is the onset of abdominal distension, ↑ gastric residuals, hematochezia, and clinical instability subsequent to the initiation of enteral feeds within the first 2 weeks of life.
- The pathognomonic findings: pneumatosis intestinalis and/or portal venous gas on abd. x-ray.
- Almost 50% of affected infants who develop NEC will require emergent surgical intervention as a result of bowel necrosis and perforation.
- During routine monitoring of PT infants on PN, we observed a recurring pattern of extended duration or the requirement for multiple courses of PN because of persistent feeding intolerance, late-onset NEC, and repeat NEC-like episodes that resolved after the change of feeds to AAF.
- Reports in PT infants within 24 hr of initial exposure have been observed, suggesting the possibility of intrauterine sensitization in some patients.
- Many cases of CMPI in PT infants while receiving intact milk protein resolved with its elimination and recurred with its reintroduction.
- Several investigators have all separately presented cases of hematochezia and enterocolitis, in PT infants,
  attributed to CMPI with resolution of symptoms, without recurrence, after CMP elimination.
- CMPI and NEC are difficult to differentiate because currently no helpful distinguishing Laboratory markers.
- Therefore, NEC may be a sensitizing event for CMPI and that some forms of NEC, especially the recurring or late-onset variant, may be the manifestation of CMPI.
- Therefore, we propose that in situations when human milk is not available, clinicians should exercise a low threshold for changing feeds either to a hydrolyzed or AAF in PT or sick newborn infants presenting with symptoms of persistent feeding intolerance after NEC, intestinal perforation, recurring NEC and late-onset NEC.

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Prof.Dr. Hany Elsayed
Prof. of pediatrics and pediatric nephrology
Zagazig university

"Rickets"

1- What is the origin of the word rickets ?

Rickets was originated from the English word wrick (which means to twist)

2- What is the definition of rickets ?

Rickets is a disease of growing bone caused by defective mineralization of the matrix at the growth plates in children before fusion of the epiphyses.

3- What are types and causes of rickets ?

Types of Rickets

Nutritional	Resistant Rickets		Renal Rickets
Vit D-deficient	Vit D-resistant	Vit D-dependent	Renal osteodystrophy
Decreased dietary intake of Vit D or ***absorption***	XL-Hypophosphatemic rickets. (PHEX mutation → FGF23)→ - 1α & Phosphaturia	Type I >>>> defective renal hydroxylase activity	Early RF >>> hyperphosphatemia >>> Hypocalcemia >>> Hyperparathyroidism
Hypoparathyroidism >>> decreased calcium control >>> Hypocalcemia & No Rickets		Type II >>> defective 1,25 D3 receptors (Huge Doses)	Advanced RF >>> decreased renal activation of Vitamin D >>> Hypocalcemia

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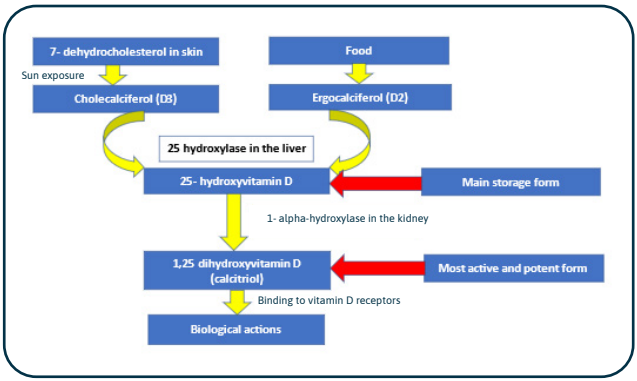
4- What are the dietary sources of vitamin D ? rickets ?

1- Plant source **-ergot-** like commercial preparation
2- Animal source like fatty fish, fish liver oil, egg yolk...etc.
3- Milk is a moderate source .

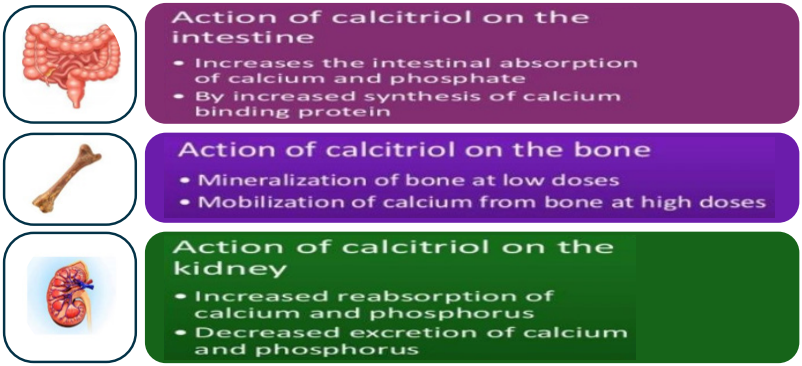
5- Why is vitamin D considered as a hormone ?

1- Synthesis and target organs are different
2- Different target organs
3- Synthesis is feedback regulated
4- Structure and mechanism of action similar to steroid hormones
5- Acts in conjunction with other hormones like PTH and calcitonin.

6- How is vitamin D activated inside the body ?



7- what are the main actions of vitamin D ?



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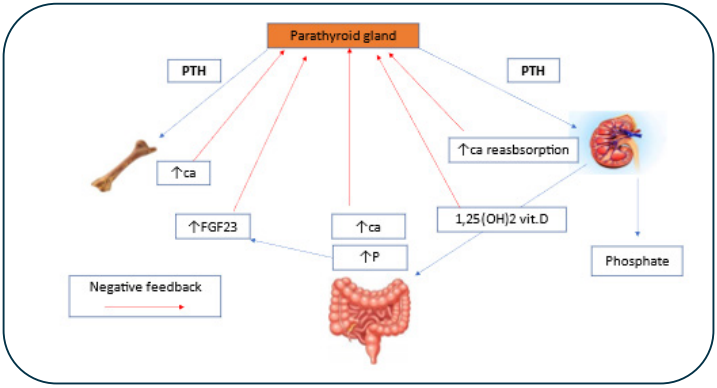
8- Are there other actions of vitamin D ?

1- Increase insulin secretion (good control of blood glucose)
2- Decrease renin synthesis (good control of blood pressure)
3- Increase skeletal muscle strength
4- Decrease tumor cell proliferation and angiogenesis (antineoplastic)
5- Increase macrophage antimicrobial activity (against infection)

9- What is the feedback relationship between vitamin D and PTH ?



To be continued next time ...

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Prof.Dr. Ayman Hammad

Prof. Of pediatric nephrology Faculty of medicine, Mansoura university

"Nocturnal enuresis (NE)"

Significant involuntary wetting during sleep (≥ two wet nights/week for ≥three consecutive months) in a child who has a developmental age of at least 5 years; not caused by a general medical problem, drugs, polyuria. Depending on its frequency; enuresis can be classified as frequent if ≥4 wet nights/week or infrequent if <4 wet nights/week.

Ty pes of NE:

- Primary NE: child was never consistently dry at night before.
- Secondary NE: Child was previously dry at night for ≥6 months before having nocturnal bedwetting again.
- Monosymptomatic nocturnal enuresis: enuresis without manifestations of lower urinary tract symptoms or bladder dysfunction.
- Non monosymptomatic nocturnal enuresis: enuresis with manifestations of lower urinary tract symptoms.

Pathophysiology:

Complex interaction of variable combination of possible diminished nocturnal bladder capacity; nocturnal polyuria and sleep arousal problems.

Red Flags:

It is an important task for the general paediatrician to diagnose properly primary uncomplicated nocturnal enuresis and to refer non monosymptomatic cases to paediatric nephrologist / urologist for proper assessment and management

1- recent secondary nocturnal enuresis could be the presenting symptom of major medical problem as type 1 diabetes mellitus (polyuria polydipsia, weight loss) or urinary tract infections (dysuria, urinary frequency; daytime urinary symptoms).

2- primary nocturnal enuresis associated with longstanding daytime symptoms need urologic assessment to exclude bladder dysfunction. When it is associated with abnormal neurologic examination findings in the legs or sacral anomalies it requires referral to exclude spinal dysraphism.

3- Recent onset nocturnal enuresis may be the presenting manifestation of child abuse or family problems at home.

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APC 41

Prof.Dr. Rasha El Ashry
Prof. Of pediatric hematology
Faculty of medicine, Mansoura university

"Iron deficiency anemia in children consensus recommendations"

Epidemiology

- Most widespread nutritional deficency affecting > 2 billion people (WHO)
- IDWA in - 7% of infants 1-2ys
  - 6 % of preschool child
  - 20 % of female adolescent

Symptoms

ID/IDA/IDWA = same symptoms

- Hair loss
- Angular cheilitis
- Dry, rough skin
- Loss of appetite
- PICA
- Fatigue
- Tennitis
- Heart failure
- Syncope
- Stroke

“Iron deficiency anemia in children consensus recommendations„

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Psychomotor and developmental signs

- Iron play a role in cognitive development
- ID before birth Interferes with neurotransmission and neurometabolism
- So, In children, ID lead to delayed cognitive, motor, memory deficits, visual and auditory diseases
- Age of onset, duration, severity and presence of anemia affect the outcome

Attention-deficit/hyperactivity disorder

Most common behavioral disorder in children

- Poor attention, distractibility, hyperactivity,
- Impulsiveness, impaired academic performance, or behavioral problems at home or at school.
- Lower serum ferritin
- In children with ADHD when iron substitution
- Leads to an improvement of ADHD symptoms, a dysregulation of central dopa
- Dopaminergic neurotransmission
- Pathophysiology of ADHD

Restless legs syndrome

in school-aged children

- Urge to move the legs that occurs during inactivity or sleep
- Disturbance of dopaminergic neurotransmission in the striatum and iron metabolism is affected,, Decreased brain iron has been documented

Breath-holding spells

- A benign paroxysmal non-epileptic disorder an association between BHS and anemia
- Iron substitution could lead to a decrease in the frequency and intensity of seizures
- ID could be attributed to increased activity of serotonin and/or increased availability of sympathomimetic neurotransmitters due to a reduction of degrading enzymes

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Pica

- The desire for ingestion of non-food materials
- Differentiated from pagophagia (craving for ice)
- Pagophagia is considered quite specific to ID and responds quickly to iron substitution Pica can also contribute to ID by reducing gut iron absorption

Iron and physical performance

- regular aerobic exercise can lead to ID through
- increase of iron losses via sweating, the gastrointestinal system, and the urinary tract (mainly related to hypoxia, increased blood pressure, acidosis, etc.)
- Second, exercise-induced hemolysis can typically be observed in runners,
- Third, exercise-induced inflammation has also recently been pointed out as potential cause of reduced iron absorption, an increase in hepcidin secretion induced by physical activity exercise-related nutritional needs is present in athletes
- a decrease in physical performance has been reported in adolescents with IDA or IDWA

Iron and the immune system

- ID leads in vitro to an inhibition of maturation, proliferation,
- And activation of lymphocytes with impairment of cell mediated immunity, and iron is a known co-factor in the synthesis of myeloperoxidase and nitric oxide synthase, which are implicated in the eradication of infectious pathogens

“Red flags” for iron deficiency with anemia

- Mosty Asymptomatic
- Dyspnea, palpitations, vertigo, tachycardia, syncope leading potentially to hemodynamic instability, myocardial infarction,heart failure, or stroke
- Differential diagnosis
- Jaundice ± splenomegaly suggesting (hemolytic anemia) Bleeding signs (ecchymoses and/or petechiae, hematuria, suggesting a (bone marrow in volvement, coagulopathy, or auto-immune condition) Fever of unknown origin, recent weight loss (oncological condition)

"Iron deficiency anemia in children consensus recommendations"

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Treatment of ID (IDWA and IDA)

- Asymptomatic child with ID alone, improving the dietary iron intake, by educating the family and providing nutritional recommendations.
- Non-heme iron is available from most food sources
- introduction of solid nutrition is advised at the age of 6 months (iron and vitamin content of breast milk > 4 months is by then decreasing). In adolescents, we recommend reducing the intake of

Oral iron therapy

- legumes such as lentils, chickpeas or white or soya beans, wheat bran, or nuts. Iron absorption can be improved by adding different forms of acid to food, e.g., ascorbic acid in orange, lemon or grapefruit juice, or non-ascorbic acid sources such as apples, grapes or gooseberries, lemons, pears, or raspberries. Tannins in coffee, tea or wine, oxalate in spinach,rhubarb or cacao, and phosphate in soda drinks have been described as inhibitors of non-heme iron absorption. Most importantly, proteins in milk or egg white also inhibit intestinal iron absorption. In addition, macroglobulins in cows'
- Tea, soft drinks/sodas or supplements of phytates, oxalates,

Items	Fe2+ supplementation	Fe3+ supplementation
DOSE	2–3 mg/kg of elemental Fe2+	3–5 mg/kg of elemental Fe3+
Time (related to meals)	half an hour before or half an hour after the meal.	with meals
Using juice or water	to improve taste.	to be dissolved in the gastric fluid

Intravenous iron therapy

- iron dextran was removed from the markets in 1991
- patients affected by renal failure requiring dialysis
- the advent of recombinant human erythropoietin
- (ferric gluconate and iron sucrose)
- Iron sucrose, authorized from the age of 3 years
- Iron carboxymaltose (ferric carboxymaltose, FCM), authorized from the age of 18 years

Safety of IV iron in children

- that IV iron is contraindicated in the course of infections, in the first trimester of pregnancy, and in patients with a history of iron or of another significant

Safety precautions for the IV administration of iron to children

- Antianaphylaxis medications (i.e., antihistamines, steroids and epinephrine) should be available and ready to use without delay when IV

Pediatric areas with clear indications for intravenous iron use

- IBD in whom oral iron worsens bowel symptoms,
- Second, children undergoing dialysis for chronic kidney disorders benefit from IV iron,

Areas in which IV iron use is debated

- The role of IV iron administration in children with IDA

IV iron use in IRIDA versus URIDA

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45 mg elemental iron/5ml syrup

120ml

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Oral Suspension
Ibuprofen 200 mg / 5ml

Anschlarin
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45 mg elemental iron/5ml syrup

Salfoverose
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AVEROZOLID
Linezolid 100 mg
(60ml/150ml)

ZITHRODOSE
Azithromycin 500mg

ZITHRODOSE
Azithromycin 100mg/5 ml
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Prof.Dr. Ahmed ELbeleidy
Prof. of pediatrics and pediatric pulmonolgy
Cairo University

Linezolid (10mg/kg /8 or 12 hours) as an add-on therapy

- Persistent sinusitis
- Persistent otitis media
- Staph. tonsillopharyngitis
- Necrotizing pneumonia
- Poor response in Strep. pneumoniae or staph. aureus meningitis

- 1st Line: High dose Amoxicillin-Clavulanic (90mg/kg/d)
  (3rd Generation Cephalosporin if vomiting or poor compliance)
- 2nd line: 3rd Generation Cephalosporin or respiratory quinolone

Organism is not known in AOM and Acute Bacterial Rhinosinusitis
(? ß-Lactamase Producing Gram-Negative Bacteria: H. influenzae/M. catarrhalis, ? S. pneumonia) Particularly with high-risk of resistant organisms ***(Antibiotic treatment in the preceding 3 months - Age 2-5yr & Daycare attendance and Age <2 yr)***

ß-Lactamase Producing Gram-Negative Bacteria	Penicillin-sensitive S. pneumoniae	Penicillin-Intermediate S. pneumoniae	Penicillin-resistant S. pneumoniae
1st Line Treatment Standard or high Dose Amox-Clavulanic(45mg/kg/d)	1st Line Treatment standard Dose Amoxicillin (45mg/kg/d)	1st Line Treatment high Dose Amoxicillin (90mg/kg/d)	1st Line Treatment Linezolid (10mg/kg/8 or 12 hours)

by: A. Elbeleidy