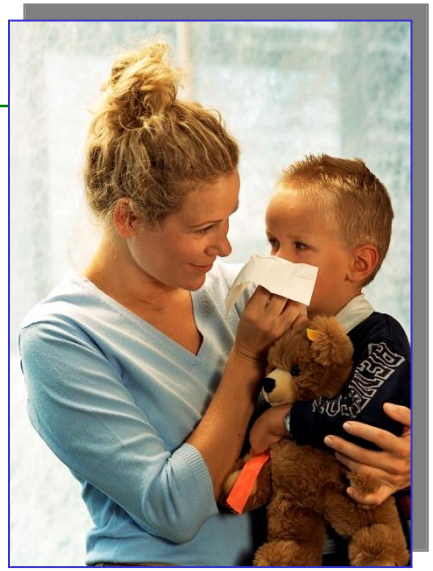
Management of respiratory tract infections – myths, facts and solutions

Andreas G. Schapowal MD, PhD, DSc (hon)

Specialist in Oto-Rhino-Laryngology
Specialist in Allergology and Clinical Immunology
Psychosomatic and Psychosocial Medicine
Medical Hypnosis, Phytotherapy

Switzerland

RTI's in children

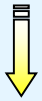


- 97%: viral infection
- Most common cause for visiting the physician
  - respiratory tract infections in children are more severe due to anatomic and physiologic factors (smaller diameter of bronchial tubes, mucosa swells faster and stronger, very viscous mucus)
  - children suffer up to 12 infections per year due to their immature immune system (maturation with 10 years)

3 common treatment options

Treatment options (I): Watchful waiting

Number of patients who continue coughing without treatment



60 % day 19*

Every third inadequately treated case of acute bronchitis develops into chronic bronchitis**

Acute complications

e.g. pneumonia/otitis media in

- Small children
- Older people
- Patients with immunodeficiencies

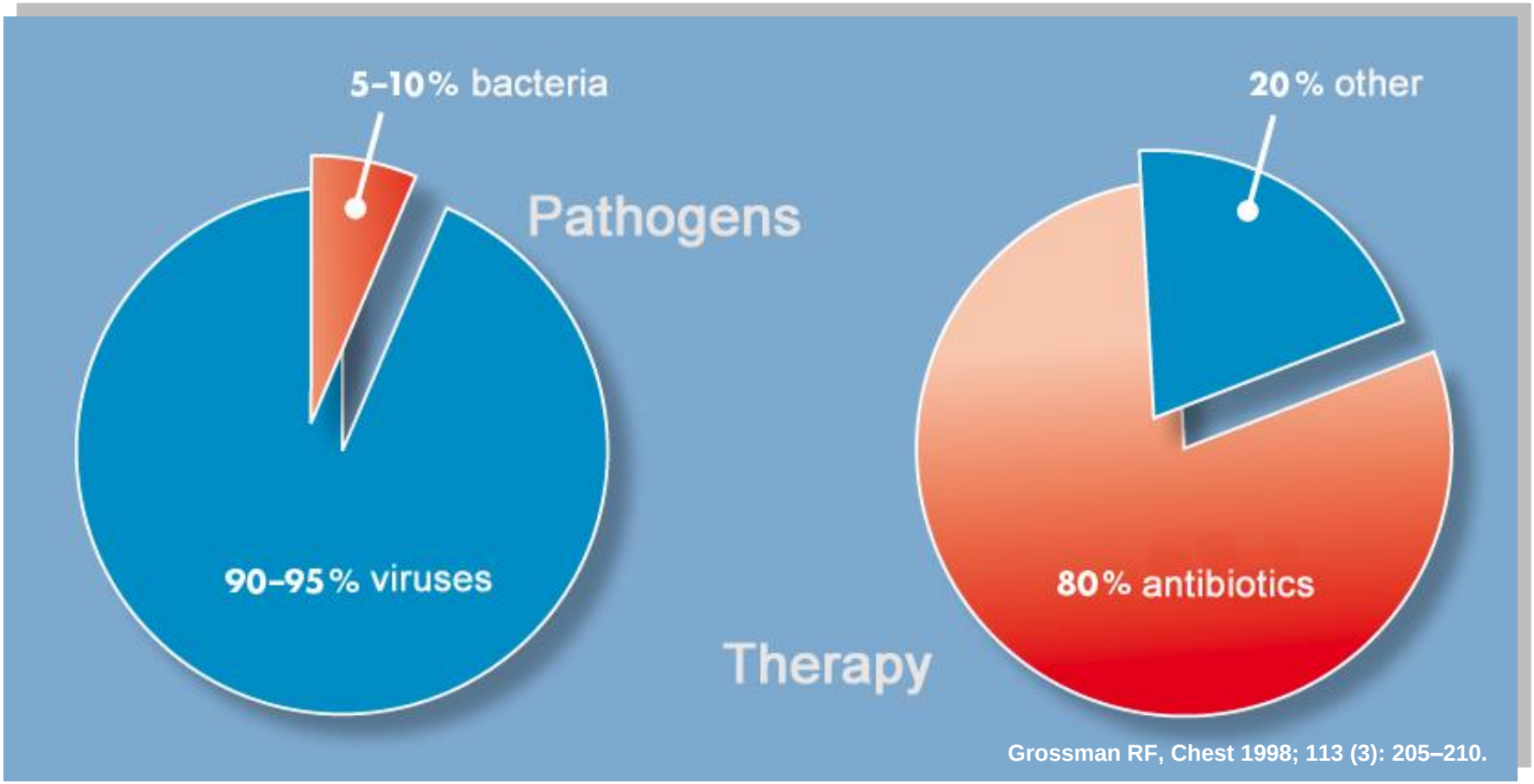
Risk of chronification

- Asthma or chronic bronchitis

***Holmes WF et al.: British Journal of General Practice, 2001, 51, 177-181**

****Jonson JS et al.: BMJ 1998; 317: 1433**

Treatment options (II): Antibiotics



Antibiotics frequently used – rarely useful

Efficacy of antibiotics in acute bronchitis

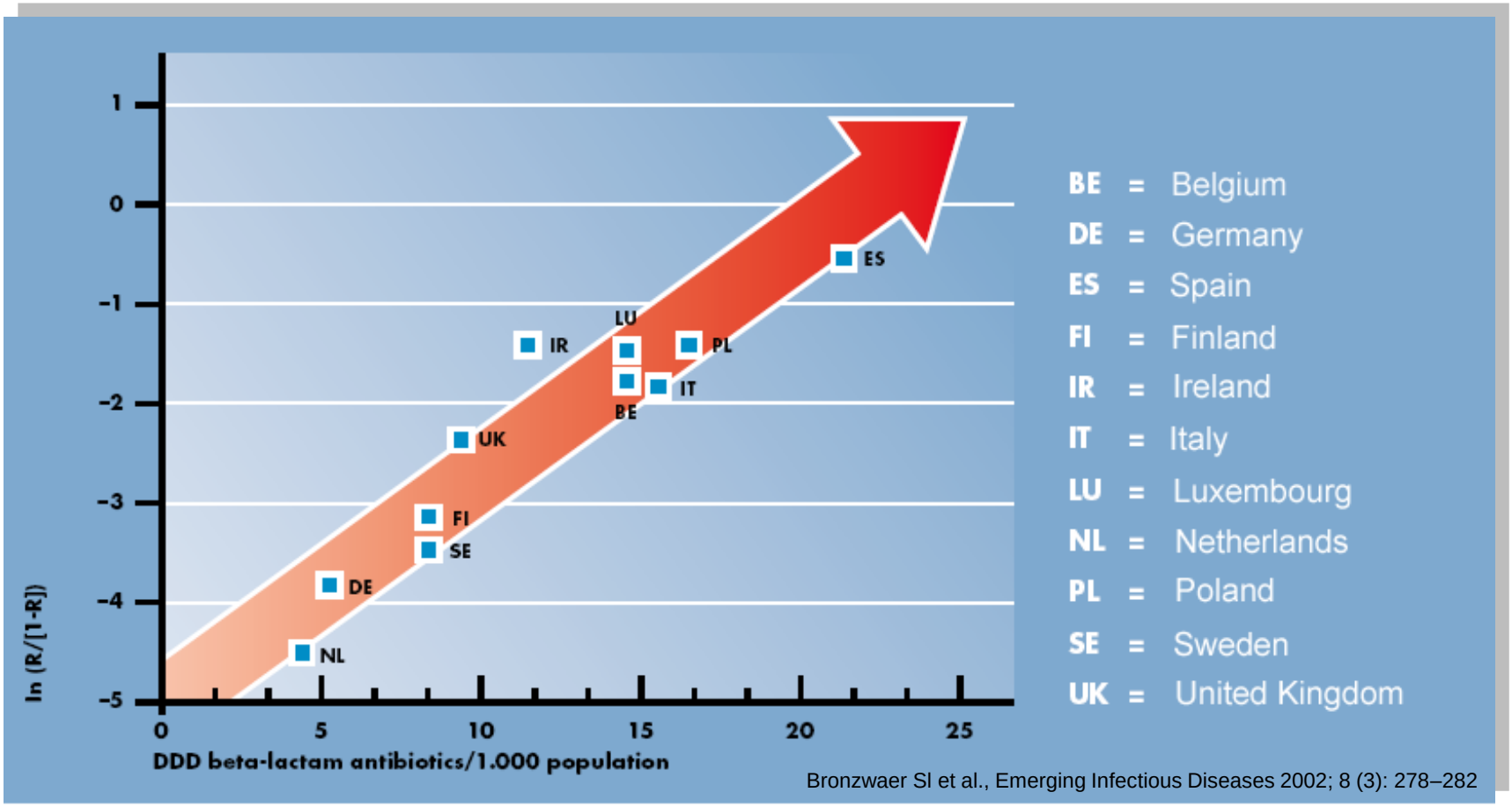
Cochrane Review

- There is no benefit in using antibiotics for acute bronchitis in otherwise healthy individuals

- Use of antibiotics needs to be considered in the context of the potential side effects…increased resistance to respiratory pathogens and cost of antibiotic treatment

Smith S. et al.: Antibiotics for acute bronchitis. The Cochrane Collaboration 2014, Issue 3

Antibiotic Resistance – a Global Challenge



Bronzwaer Sl et al., Emerging Infectious Diseases 2002; 8 (3): 278–282

… frequent use of antibiotics = increasing resistance!

Treatment options (III): Antiviral Medication

Viral resistance more often than expected

The extent of resistance development due to therapy exceeds current expectations significantly[2]

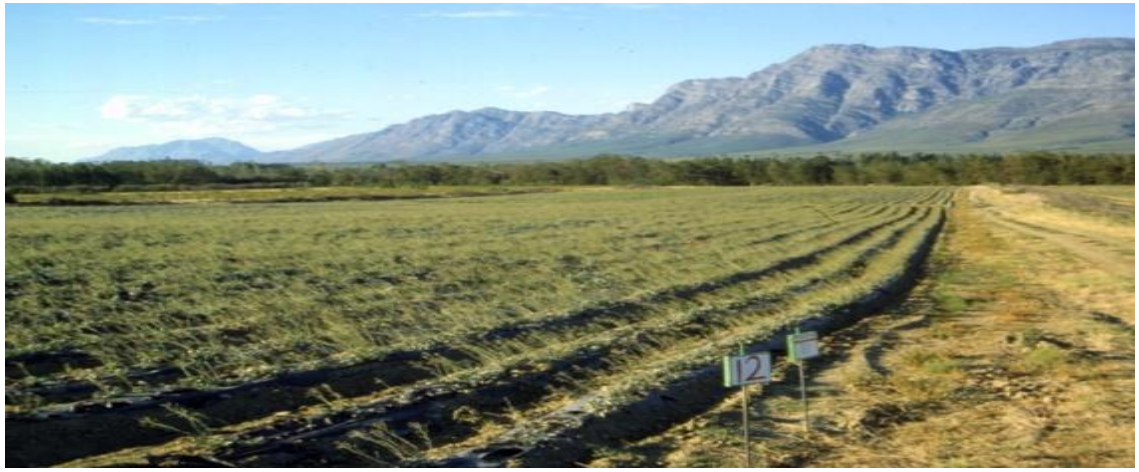
Occurrence of resistances against neuraminidase inhibitors:

- Amantadine and rimantadine up to 30 %[3]
- Oseltamivir up to 4 % of adults[4]
- Oseltamivir up to 18 % of children[1]

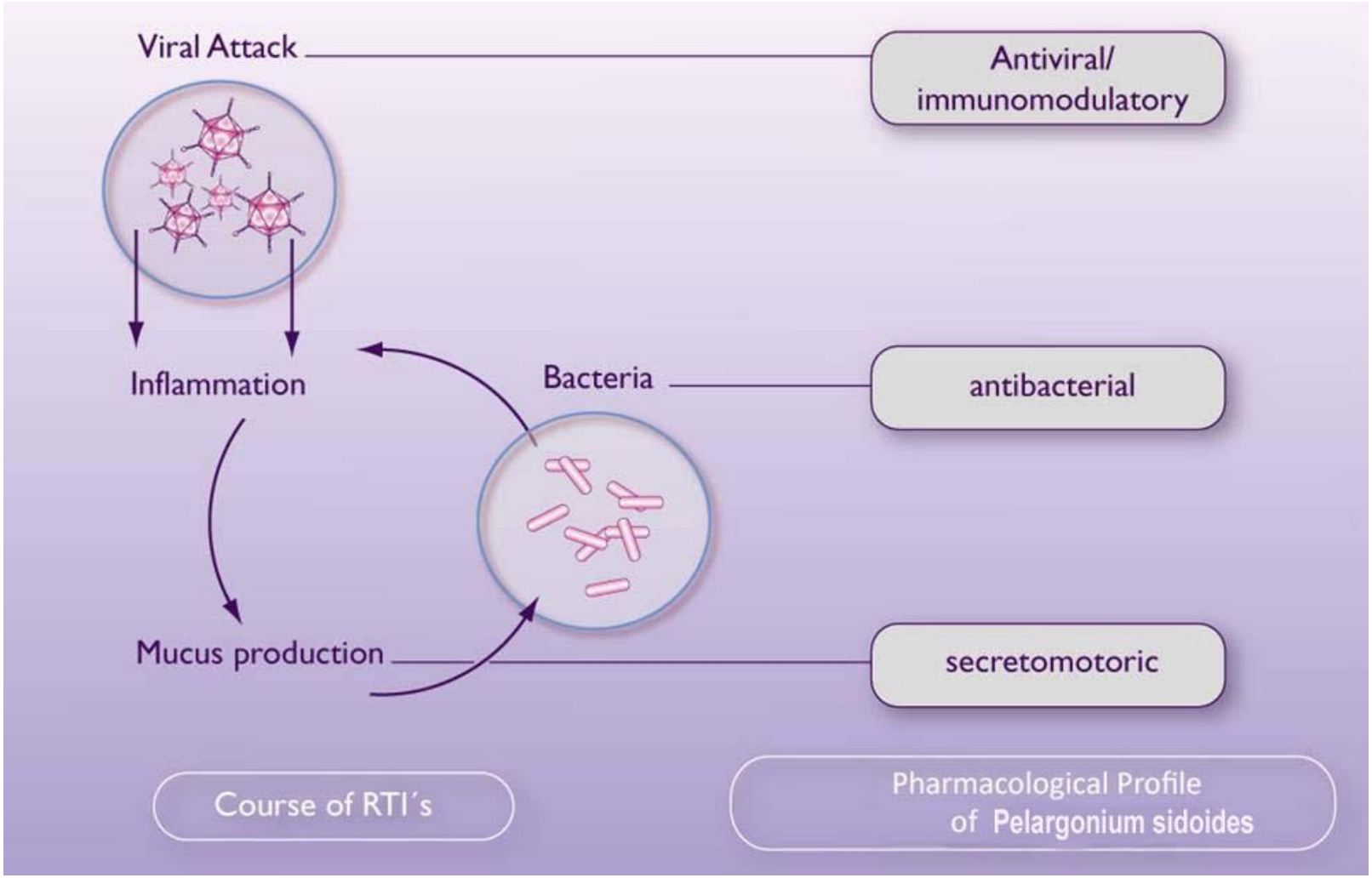
1: Moscona A, N Engl J Med 2005; 353: 25; 2: Kiso M et al., Lancet 2004; 364: 759–765; 3: Harper SA, MMWR Recomm Rep 2005; 54 (1) 4: Gubareva lV et al., J Infect Dis 2001; 183 (5): 23

Pelargonium sidoides extract EPs® 7630 - Umca ®

is a standardized and registered phytopharmaceutical with proven efficacy and safety in the treatment of RTI´s in children and adults



Mode of Action in RTI‘s



Mode of action (I)

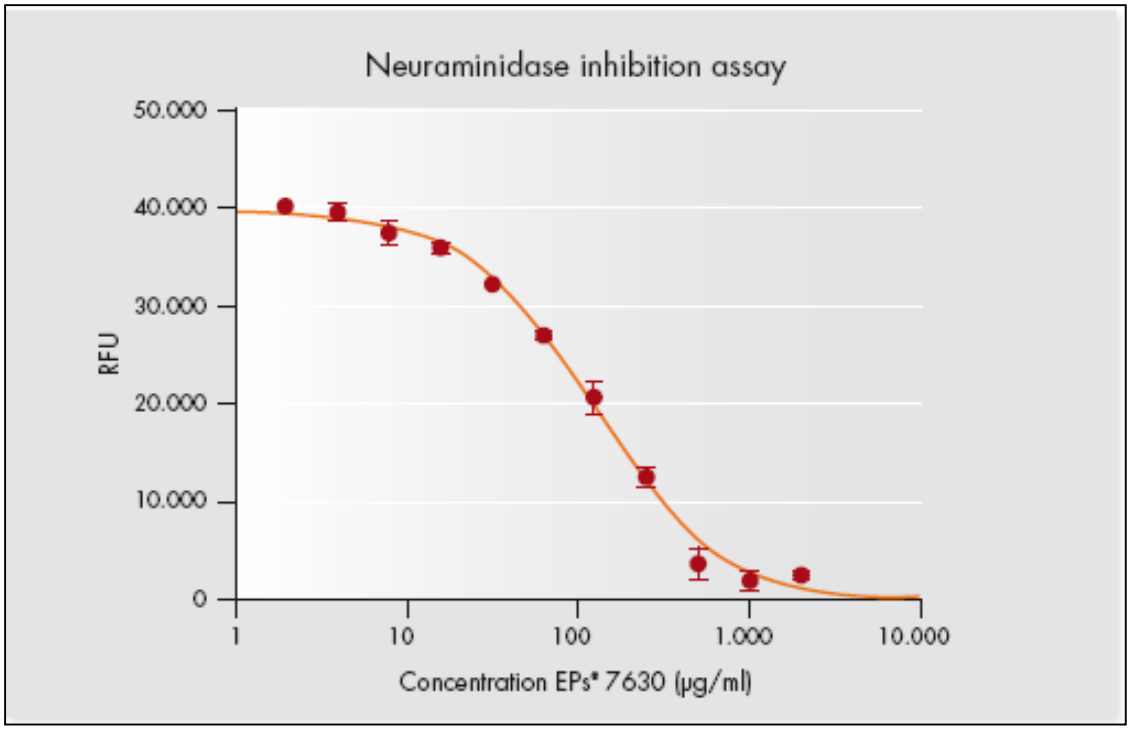
against viruses ✓

- Increases the interferon production[1]
  - → direct antiviral effect
  - → protects cells against virus-mediated destruction
  - → Activation of NK-cells

1:Kolodziej H et al.: Phytomedicine 2007; 14 (Suppl. VI): 18-26

Inhibition of Neuraminidase

Neuraminidase inhibition assay (H1N1)



RFU = rel. fluorescent units

Theisen et Muller, Antiviral Research 2012; 94: 147 - 156

Antiviral effects of EPs® 7630

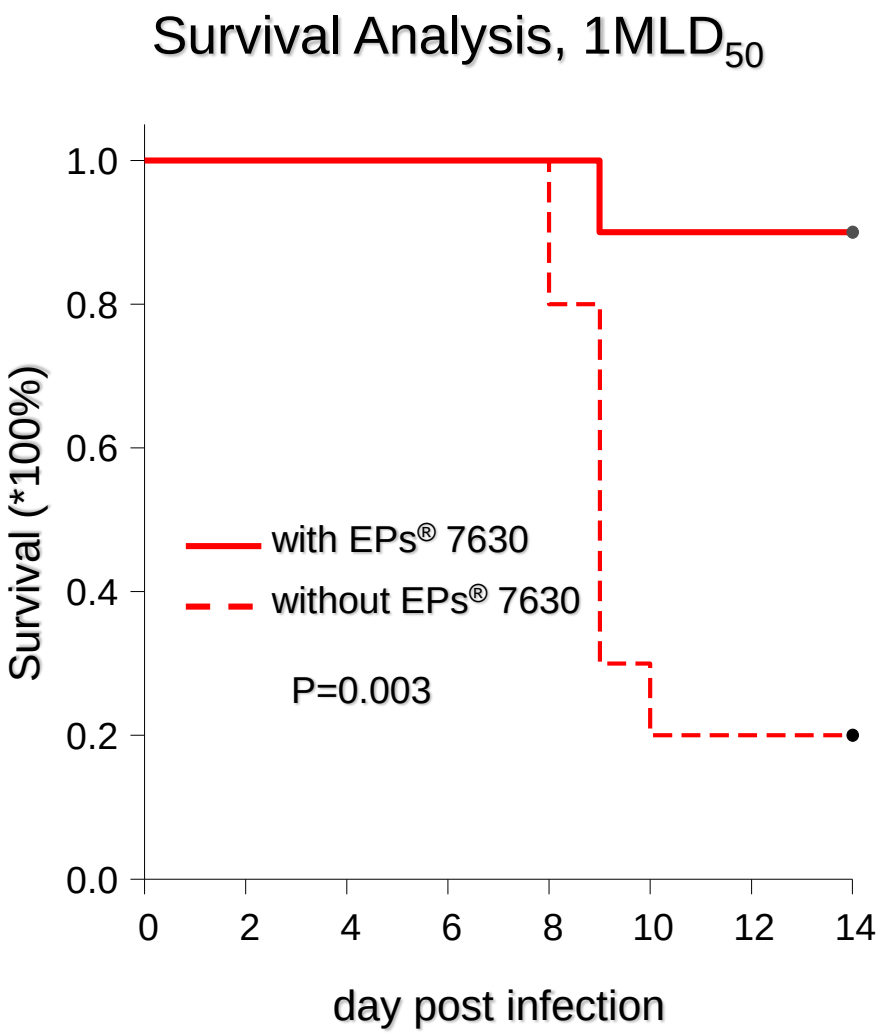
Influence of EPs® 7630 on a cytopathic effect (CPE) caused by respiratory viruses (microscopic examination) and on cell viability

Virus	IC_{50} (µg/ml)*	CC_{50} (µg/ml)**	TI***
Influenza			
H1N1	9.45 ± 2.94	>100	>10.6
H3N2	8.66 ± 1.06	>100	>11.5
H5N1 (avian)	>100	>100	n.d.
RSV	19.65 ± 1.77	>100	>5.1
Adenovirus 3 and 7	>100	>100	n.d.
Parainfluenza 3	74.35 ± 17.89	>100	>1.3
Coxsackie A9	14.80 ± 3.39	>100	>6.8
Rhinovirus	>100	>100	n.d.
Coronavirus 229E (HCo-229E)	44.50 ± 15.84	>100	>2.3

* Concentration that inhibits CPE formation by 50%
** Concentration that decreases cell viability by 50%
*** Therapeutic index = CC_{50}/IC_{50}

Michaelis M. et al., Phytomedicine 18 (2011): 384-386

Anti-influenza activity of EPs® 7630 in mice



10 female Balb/c mice,
infected with 1 LD_{50}
influenzavirus A/Puerto Rico/8/34,
treatment with EPs® 7630,
three times/day for 10 days

Theisen et Muller, Antiviral Research 2012; 94: 147 - 156

Antiviral effects of EPs® 7630

EPs® 7630

- inhibits an early step in the virus life cycle
- interferes with viral surface proteins and impaires viral hemagglutination and neuraminidase activity
- protects mice from lethal viral infection

EPs® 7630 promises to be beneficial if used as a treatment for virus infections

Theisen et Muller, Antiviral Research 2012; 94: 147 - 156

Mode of action (II)

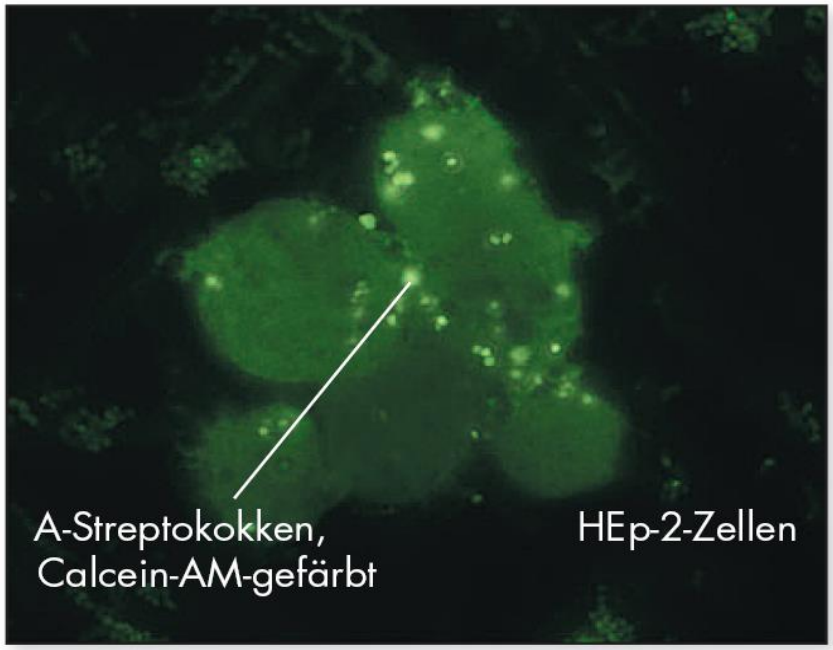
against bacteria ✓

- direct bacteriostatic effect (is inferior to that of antibiotics)[1]
- inhibits the adhesion of bacteria to healthy mucosal cells[2]
- inhibits the internalisation of bacteria in mucosal cells[2] (i.e. fewer recurrences)
- increases the adhesion of bacteria to dead epithelial cells[3]
- increases phagocytosis, oxidative burst and intracellular killing of bacteria[4]

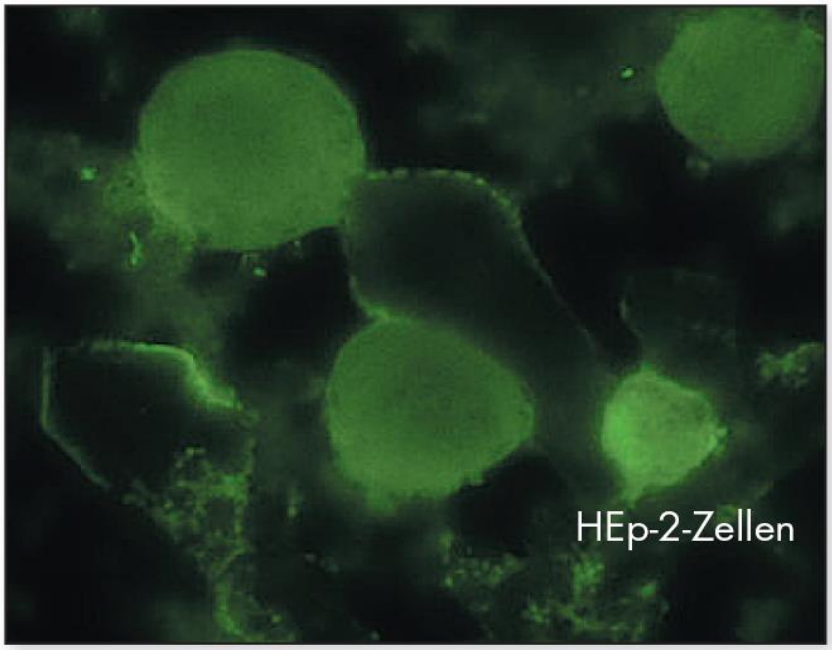
1: Kayser 1997; 2: Conrad A et al.: Phytomedicine 2007; 14 (Suppl. VI): 52-59; 3: Frank 2003;
4: Conrad A et al.: Phytomedicine 2007; 14 (Suppl. VI): 46-51

Inhibition of bacterial adhesion

Control: *Fluorescence microscopy*



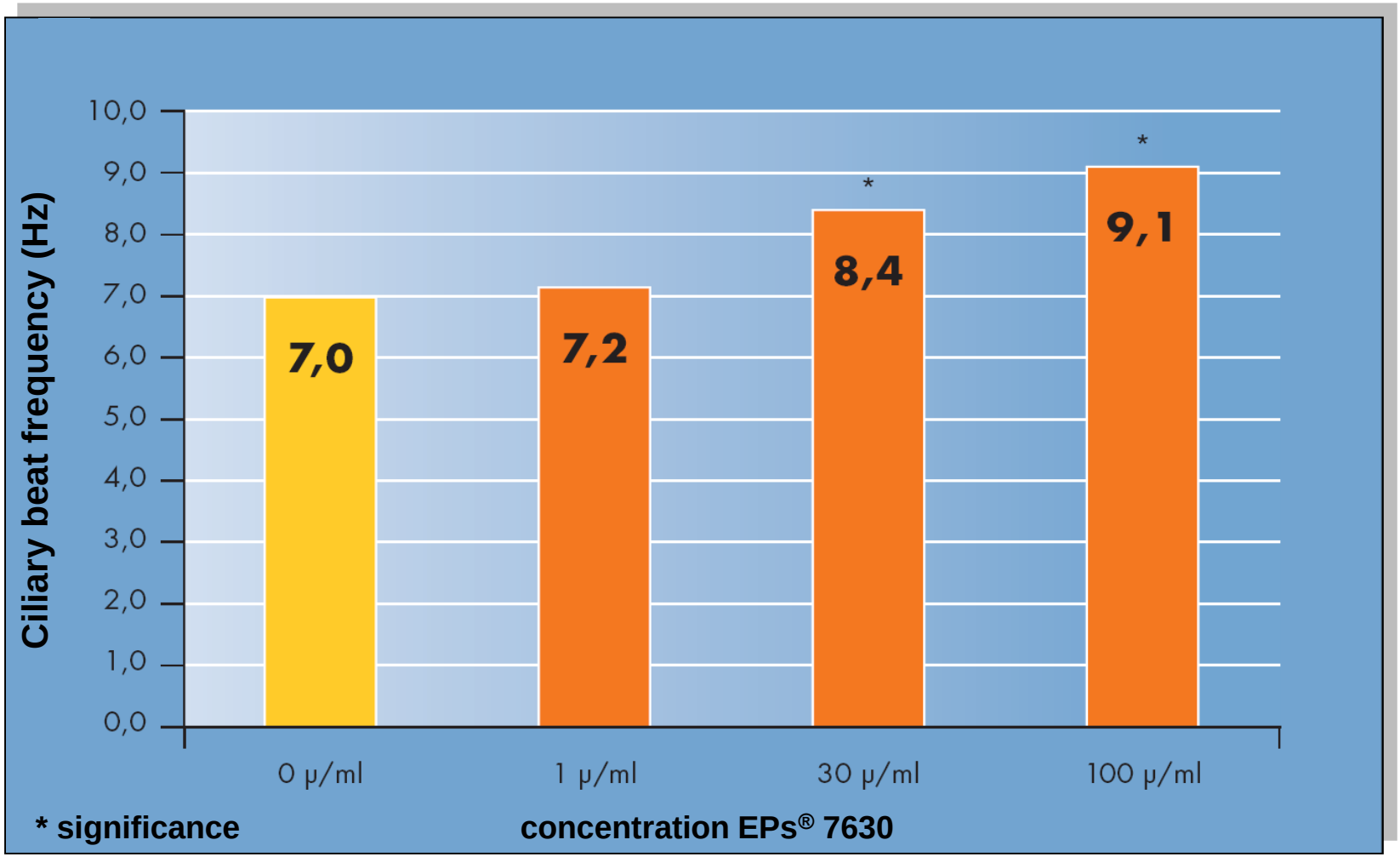
0 µg/ml EPs® 7630



30 µg/ml EPs® 7630

Conrad A et al.: Phytomedicine 2007; 14 (Suppl. VI): 52-59

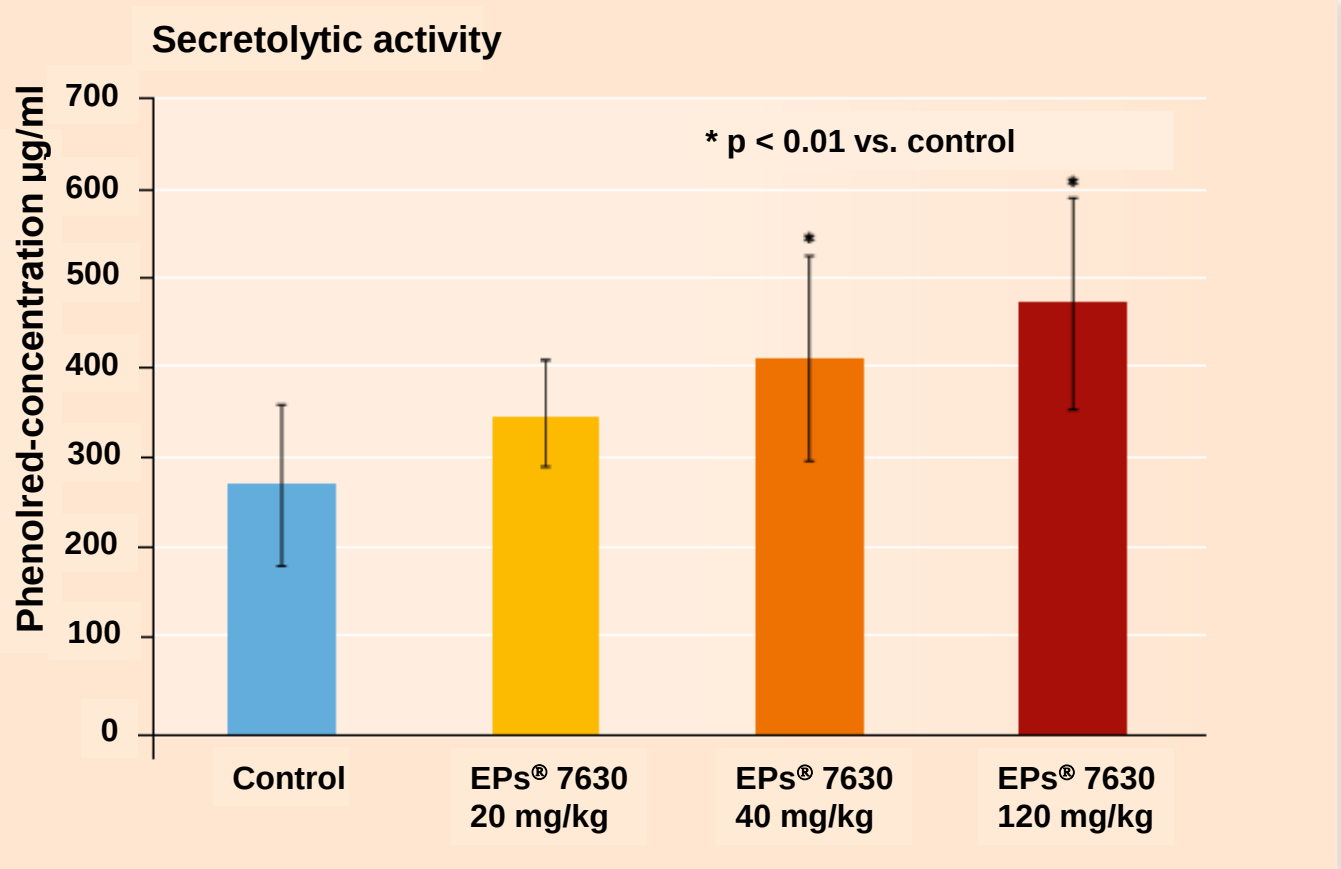
Mode of action (III): secretomotoric



Neugebauer P et al.: Phytomedicine 2005; 12: 47–52

Secretolytic action

EPs®7630 improves the secretolytic activity



Determination of tracheobronchial secretion of intraperitoneally injected phenol red in mice

Bao Y et al. (2015). Evaluation of pharmacodynamic activities of EPs® 7630, a special extract from roots of Pelargonium sidoides, in animals models of cough, secretolytic activity and acute bronchitis. Phytomedicine 22, (4), 504-509.

Mode of action - Summary

Anti-viral:

- inhibition of replication of most important respiratory viruses[1]
- inhibition of neuraminidase activity[2,3] and hemagglutination[3]
- stimulation of interferon-β-synthesis[4]

Anti-bacterial:

- inhibition of bacterial adherence[5]
- inhibition of bacterial internalization[5]

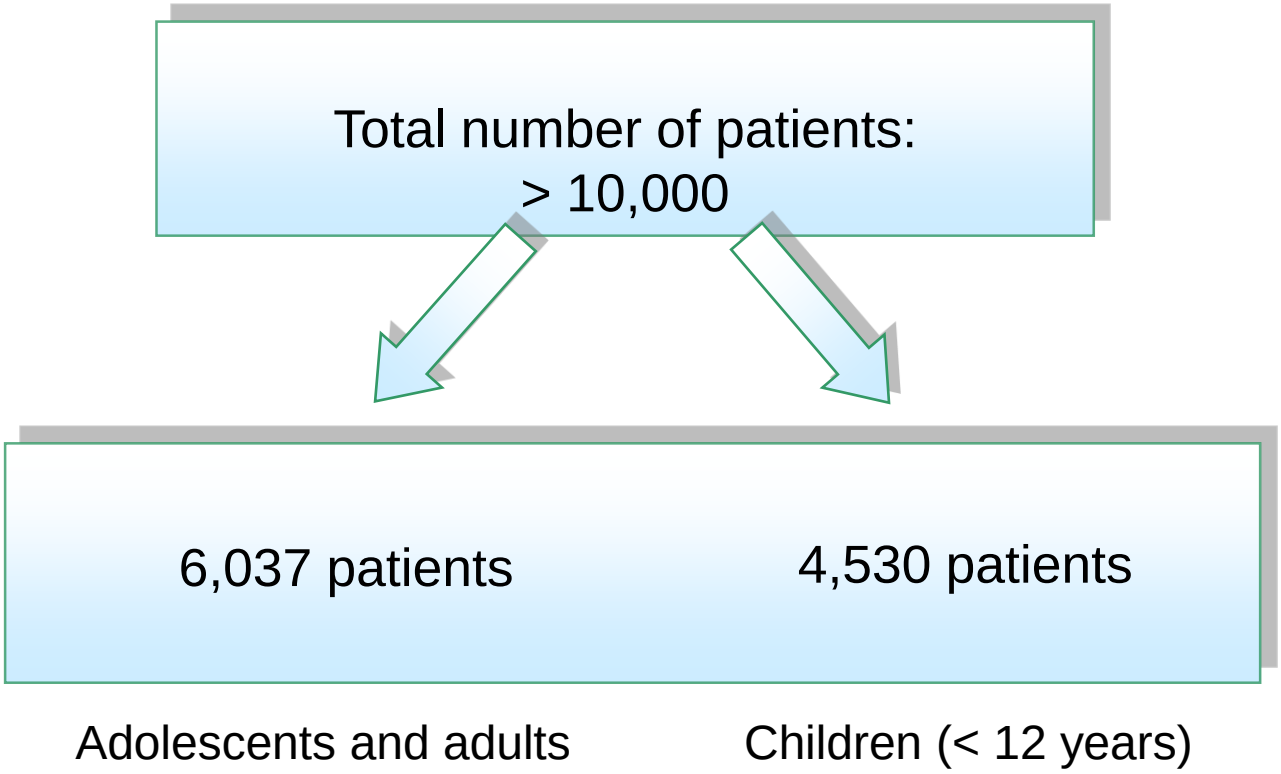
Secretomotor/-lytic:

- improvement of ciliary beat frequency[6]
- secretolytic activity[7]

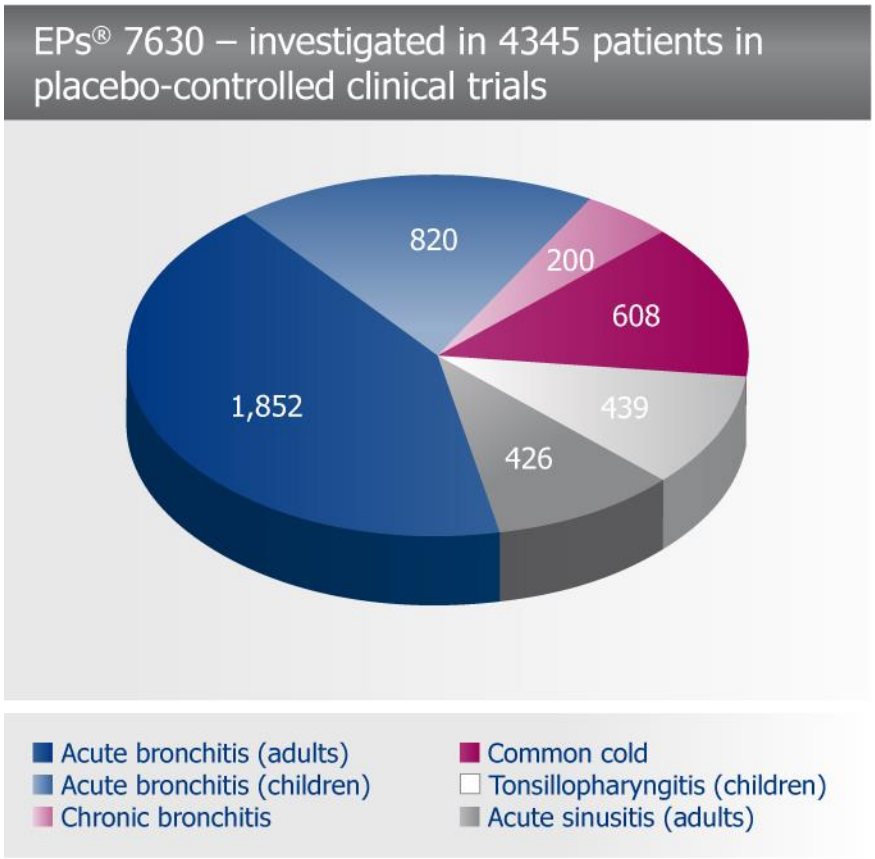
[1]Michaelis et al. Phytomedicine 2011;18:384-386. [2]Janecki et al. Planta Med 2009;75:989-989. [3]Theisen and Muller. Antiviral Res 2012;94:147-156. [4]Koch et al. Naunyn-Schmiedeberg's Arch Pharmacol 2002;365(Suppl.1):R75. [5]Conrad et al. Phytomedicine 2007;14(Suppl.VI):52-59. [6]Neugebauer et al. Phytomedicine 2005;12:46-51. [7] Bao et al. Phytomedicine 2015; 22: 504-509

Clinical trials

> 25 clinical trials: placebo-, reference-controlled, open and PMS



EPs® 7630 – clinically proven in different RTIs



19 double-blind placebo-controlled studies in different respiratory tract infections*

- **Acute bronchitis**
- **Chronic bronchitis**
- **Common cold**
- **Tonsillopharyngitis**
- **Acute sinusitis**

Matthys et al. (2013), Adv Pharmacoepidemiol Drug Saf 2: 142. doi:10.4172/2167-1052.1000142

J Compr Ped. 2016 November; 7(4):e42158. doi: 10.17795/compreped-42158.

Published online 2016 November 24. Research Article

Clinical Efficacy and Safety of Liquid *Pelargonium sidoides* Preparation (EPs 7630) in Children with Acute Non-Streptococcal Tonsillopharyngitis

Viatcheslav V. Berezhnoi,[1] Marianne Heger,[2] Walter Lehmacher,[3] and Georg Seifert[4,*]

[1]Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine
[2]ISO-Pharmaceuticals, Esslingen, Germany
[3]Universitaet zu Koeln, Institut fuer Medizinische Statistik, Informatik und Epidemiologie, Koeln, Germany
[4]Charité - Universitätsmedizin Berlin, Otto-Heubner-Center for Pediatric and Adolescent Medicine (OHC), Department of Pediatric Hematology and Oncology, Berlin, Germany

Efficacy in acute tonsillo-pharyngitis

Study setup:	Multi-center, prospective, randomized, placebo-controlled, double-blind
Patients:	124 children (6-10 years old) (duration of complaints <48h, symptom severity of 5 typical tonsillitis symptoms >8 points, negative test for ß-hemolytic streptococci)
Treatment duration:	6 days (check-up examinations after 2, 4 and 6 days)
Intervention:	3 x 20 drops EPs® 7630 solution or placebo

Berezhnoi et al. J Compr Ped 2016; 7(4):e42158.

Efficacy in acute tonsillo-pharyngitis

Evaluation criteria

Primary outcome:

Change in total score of the 5 typical tonsillitis symptoms between baseline and day 4

- dysphagia
- sore throat
- salivation
- reddening
- fever

Secondary outcomes:

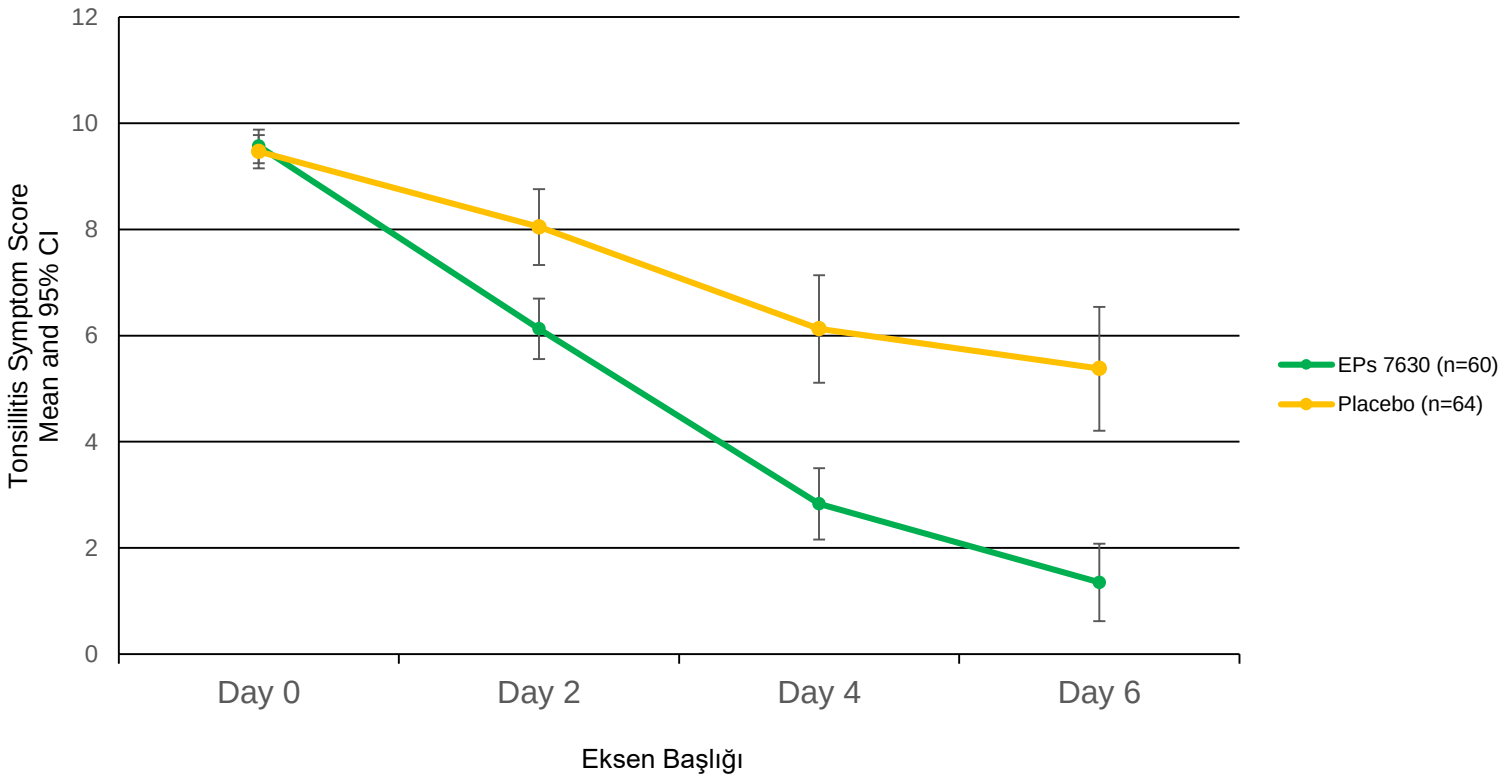
Assessment of 7 further disease symptoms: swelling of pharynx, uvula, tonsils and lymph nodes, pain on pressure on lymph nodes, headache, pain in the limbs

Global assessment of treatment success by physician and patients/legal representatives (based on a rating scale), consumption of paracetamol

Trial II: Berezhnoi et al. J Compr Ped 2016; 7(4): e42158.

Study results: acute tonsillo-pharyngitis

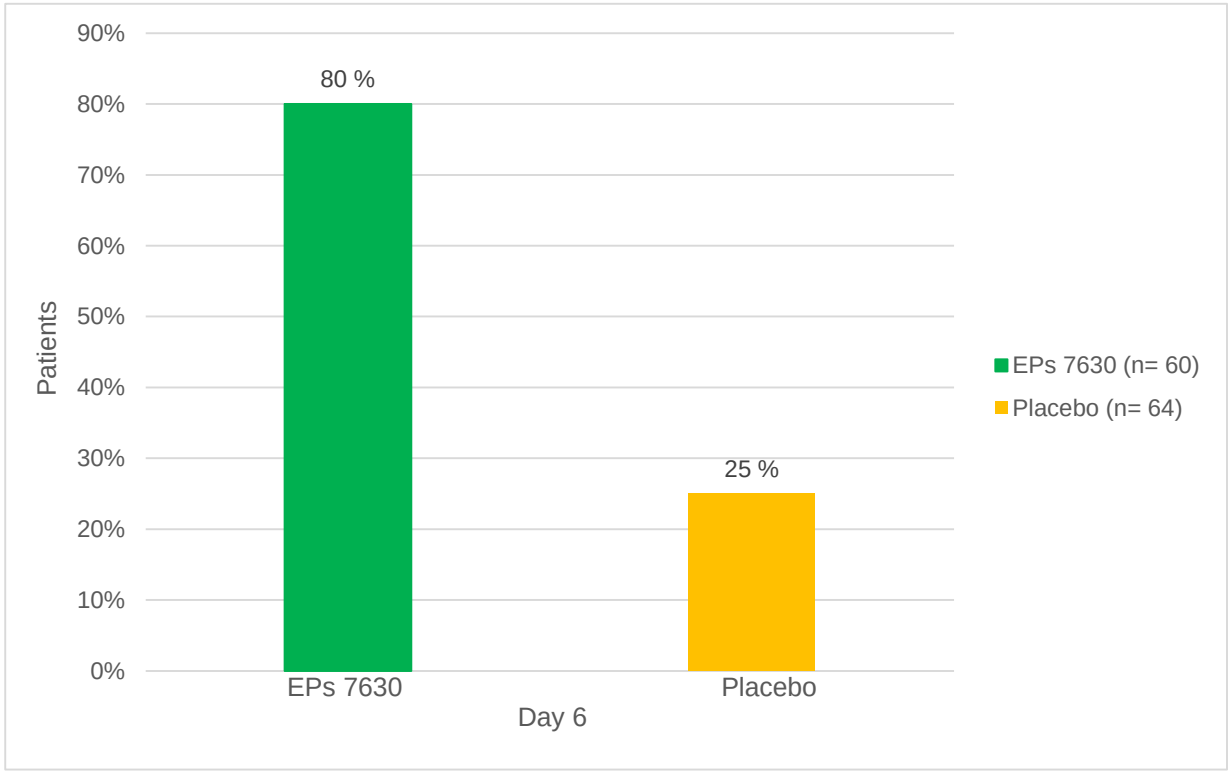
Decrease in total score of the 5 typical tonsillitis symptoms under EPs® 7630 and placebo treatment (ITT)



Berezhnoi et al. J Compr Ped 2016; 7(4): e42158.

Study results: acute tonsillo-pharyngitis

Patients fully recovered (complaint-free) by day 6 according to patient-rating (ITT)



Berezhnoi et al. J Compr Ped 2016; 7(4): e42158.

Study results: acute tonsillo-pharyngitis

EPs® 7630

- is superior to treatment with placebo (statistically significant difference)
- a more rapid onset of action with EPs® 7630 than placebo within four days of treatment (e.g. in 87% vs. 30% of patients)
- requires a less frequent application of paracetamol over a markedly shorter period of time
- shows a low incidence of adverse events
- was evaluated as well or very well tolerated by the patients

⇨ **First-line treatment of the acute non-streptococcal tonsillo-pharyngitis**

Berezhnoi et al. J Compr Ped 2016; 7(4): e42158.

Efficacy and safety of EPs® 7630 in common cold

V. G. Lizogub, D.S. Riley, M. Heger 2007

- Study design: Multi-center, prospective, randomized, double-blind, placebo-controlled
- Patients: 103 patients aged 18 to 55 years, suffering from common cold
- Duration: 10 days
- Dosage: 3 x 30 drops EPs® 7630 solution or placebo
- Primary Outcome: Sum of Symptom Intensity Differences (SSID) of the Cold Intensity Score (CIS) from day 1 to day 5

Efficacy of a Pelargonium sidoides preparation in patients with the common cold: a randomized, double blind, placebo-controlled clinical trial. Explore 2007; 3: 573-584

Efficacy and safety of EPs® 7630 in common cold

Inclusion criteria

- Presence of 2 major and at least 1 minor cold symptom
- Or presence of 1major and 3 minor cold symptoms
- Presence of cold symptoms for 24-48h

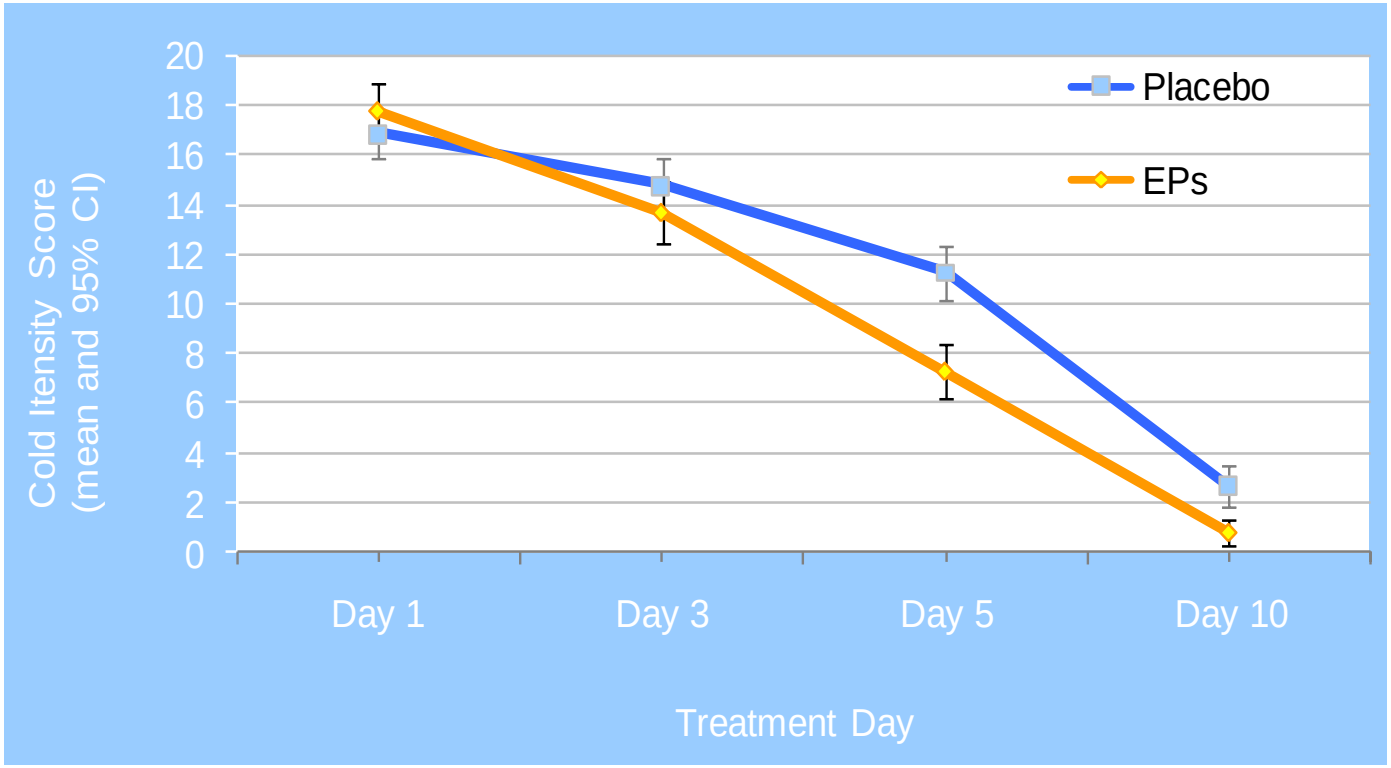
* Major symptoms: Running nose, sore throat

* Minor symptoms: Nasal congestion, cough, hoarseness, headache, aching muscles, fever

Lizogub et al. 2007

Efficacy and safety of EPs® 7630 in common cold

Changes in the CIS from day 0 till day 10



Lizogub et al. 2007

Conclusion

- EPs is an effective and safe treatment of common cold compared to placebo.
- It significantly reduces the severity of symptoms
- It significantly shortens the duration of disease

Lizogub et al. 2007

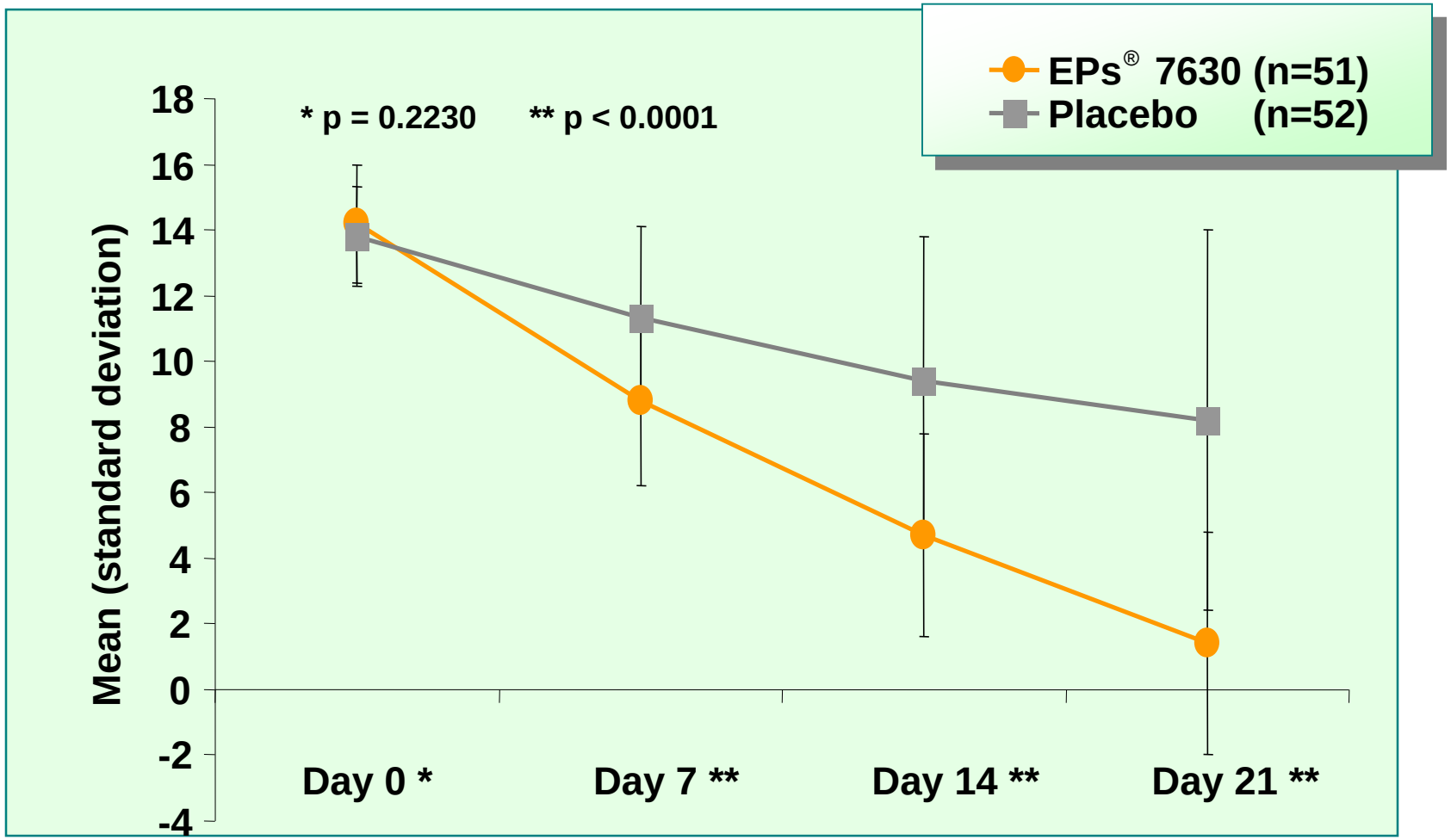
EPs® 7630 in acute rhinosinusitis

Study design:	multi-center, prospective, randomized, placebo-controlled, double-blind
Patients:	103 adults (18-60 years old) (confirmed by sinus radiography, severity of symptoms ≥ 12 points)
Duration:	22 days (check-up examinations after 7, 14, and 21 days)
Dosage:	EPs® 7630 solution: 3 x 60 drops or placebo
Primary outcome:	Change of the 6 typical sinusitis symptoms on day 7: - headache - maxillary pain - maxillary pain worsening when bending forward, percussion or pressure - nasal obstruction - purulent nasal secretion - purulent nasal discharge visualized in the middle meatus or purulent postnasal discharge

C. Bachert, A. Schapowal, P. Funk, M. Kieser:
Treatment of acute rhinosinusitis with the preparation from Pelargonium sidoides EPs ® 7630: A randomized, double-blind, placebo-controlled trial. Rhinology 2009; 47: 51 - 58

EPs® 7630 in acute rhinosinusitis

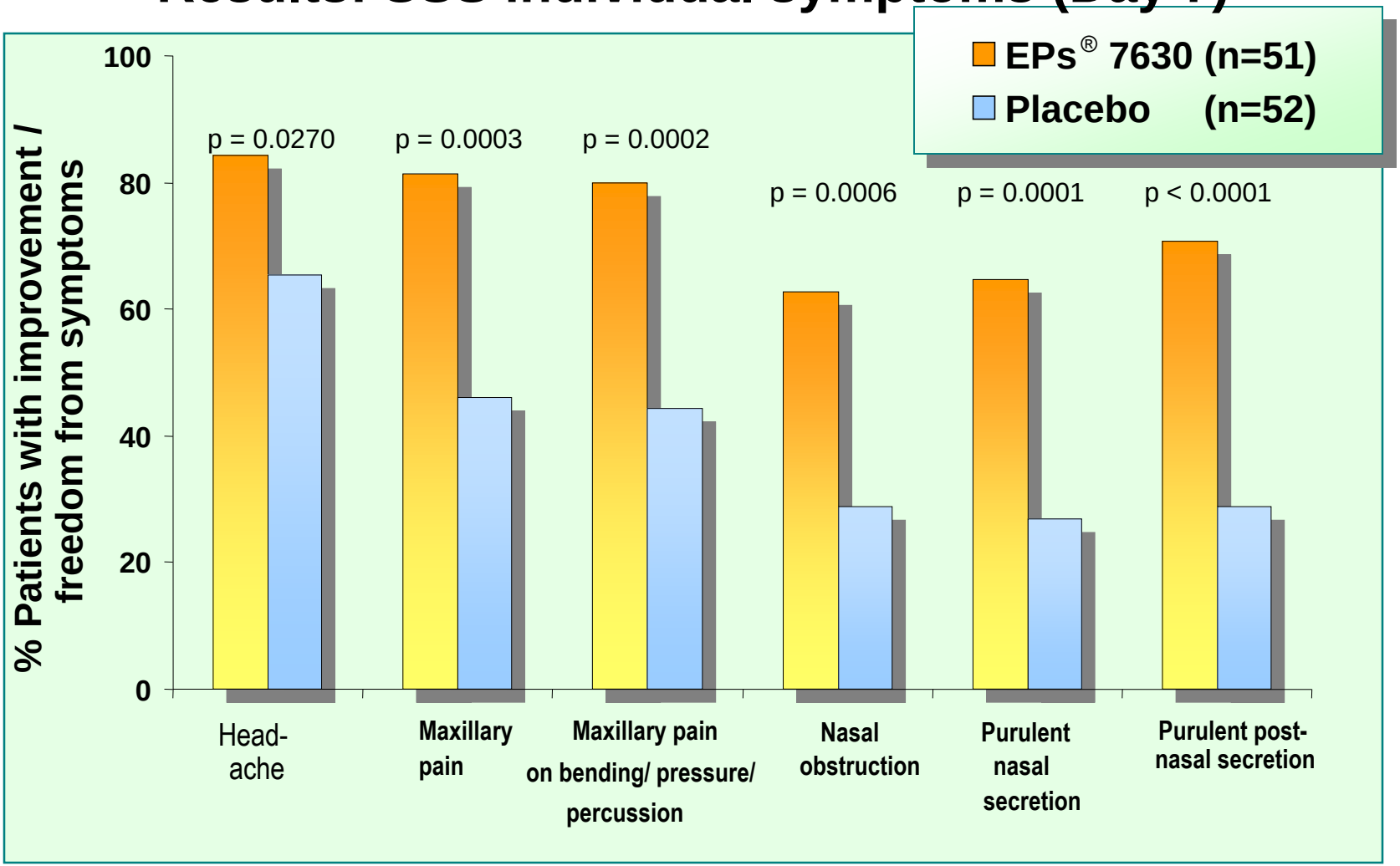
Results: Sinusitis Severity Score (SSS)



Bachert et al. 2009

EPs® 7630 in acute rhinosinusitis

Results: SSS individual symptoms (Day 7)



Bachert et al. 2009

Conclusion

- **Statistically significant and clinically relevant improvement in SSS**
- **Relevant improvement in state of health (IMOS)**
- **Shortened period of disability (Ability to work on day 7: EPs® 7630 (62.7% patients) vs. placebo (36.5% patients)**
- **Good tolerability**

EPs® 7630 compared to placebo is an effective and well tolerated therapeutic option for the treatment of acute maxillary sinusitis

Bachert et al. 2009

Case report: Bela, 12.5 year old school boy

Anamnesis:

Persistent allergic rhinitis and asthma for 10 years, especially March – September

Sore and itchy throat when eating apples and carrots

Recurrent respiratory tract infections with rhinitis, pharyngitis, tonsillitis, bronchitis, asthma exacerbations

Current therapy:

Cetirizine 10 mg on demand, Seretide 120 inhaler once daily during asthma exacerbation, antibiotics in RTIs 6 times in the last 12 months

Family doctor proposed tonsillectomy

Case report: examination findings

ENT status: reddened palatine arches, reddened and slightly swollen nasal mucosa, reddened conjunctiva, auscultation: no wheezing

Skin prick test positive to pollens (grass, barley, oats, rye, wheat, dandelion, alder, hazel, birch, european beech, oak, robinia, ash-tree) and house dust mites

Total IgE 460 kU/l, specific IgE dermatophagoides farinae >100.00 kU/l, dermatophagoides pteronyssinus 68.90 kU/l, apple 2.44 kU/l, carrot 1.07 kU/l

Eosinophils 6.6 %, antistreptolysine titer 456 kU/l

Nasal provocation test positive to dermatophagoides pteronyssinus and dermatophagoides farinae

Spirometry: Mild obstruction

Metacholine challenge: moderate hyperreactivity, PD 20: 387.5 µg

Case report: diagnosis and treatment

Chronic tonsillitis - **tonsillectomy**

Recurrent RTIs – **EPs® 7630** 3 x 30 drops from the very beginning for at least 7 days, 3 RTIs and no need for antibiotics in the last 12 months

Persistent allergic rhinitis, persistent allergic asthma, food allergy

Mometasone nasal spray 2 x 1, **Seretide 250 diskhaler** 2 x 1

Specific subcutaneous immunotherapy with dermatophagoides pteronyssinus and dermatophagoides farinae 50 : 50, and with grass and birch pollen extract 50 : 50 for three years

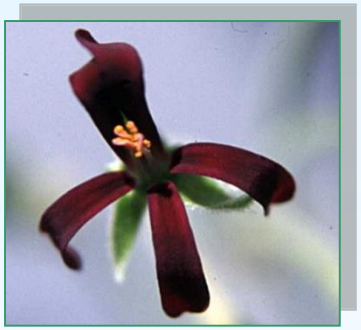
Allergen avoidance: Encasing of mattress, bedcover, pillow; no apples, no carrots

Take-Home-Messages

Umca®

Comprehensive therapy with threefold mechanism of action:

- **antiviral effects**
- **antibacterial effects**
- **secretomotoric/secretolytic**



Take-Home-Messages

- Unique product
- Intensively researched
- Clinically proven in RTI‘s in a high patient number (>10,000)
- Extensive clinical research data and experience in children
- Shortens the duration of the disease
- Fast onset of action
- Significant symptom relief
- Treats the cause of infection
- No antimicrobial resistance
- Excellent safety profile

İlginize çok teşekkür ederim!

andreas@schapowal.ch

Akut bronşit

- Akut bronşit; trakeobronşiyal ağacın akut inflamasyonudur.
- Bu inflamasyon sonucunda havayolu mukozasında ödem ve sekresyon artışı olur.
- Sıklıkla bir üst solunum yolu enfeksiyonu ile birlikte veya onu takiben ortaya çıkar.

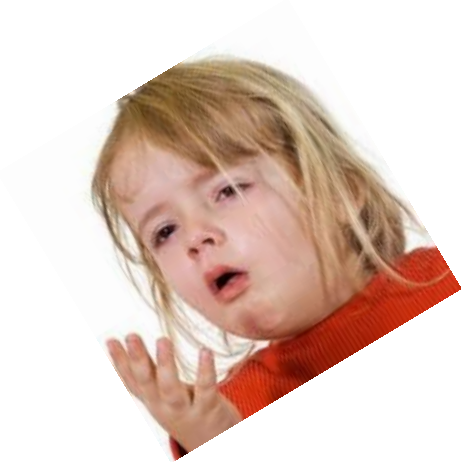
Akut bronşitte olguların %85-95'i viral kökenli

- Basit akut bronşit ile ilişkilendirilmiş en yaygın patojenler, influenza A ve B virüsleridir
- Diğer yaygın viral patojenler:
  - Parainfluenza virüsü
  - Rinovirüs
  - Koronavirüs
- Respiratuvar sinsityal virüs (RSV), sıklıkla 1 yaşından küçük çocuklar ve yaşlılarla ilişkilendirilmektedir
- Olguların %30'unda, hastalarda birden fazla viral enfeksiyon saptanabilir

Adapted from Worrall G, 2008[1]

Akut bronşitte bulgular

- Hastaların %50'sinde 3 haftadan kısa süren, %25'inde 1 aydan uzun süren öksürük
- Hırıltılı soluma
- Balgam oluşumu
- Göğüs ağrısı
- Yorgunluk



Akut bronşitte komplikasyonlar

Tedavi eksikliği veya uygunsuz bir tedavi, istenmeyen sonuçlara sebep olabilir:

- Sekonder bakteriyel enfeksiyon
- Yaşamı tehdit edici enfeksiyonlar (örn: pnömoni)
- Kronikleşme
- Kronik bronşit
- Alerjik astım

Semptomatik tedavi: Avantaj/Risk

- **Semptom giderici ilaçlar**
  - Mukolitik /ekspektoranlar
  - Antipiretikler
  - Dekonjestanlar ve antihistaminikler
  - Bronkodilatatörler

- **Semptom gidericilerin sorunları:**
  - Sadece semptomlara etki etmektedir
  - Hastalığın nedenini tedavi etmemektedir
  - Yan etkilere neden olabilmektedir
    - örn. Dekstrometorfan, nörodavranışsal değişikliklere yol açabilir.

Akut bronşitte Umca, iki benzer çalışma!

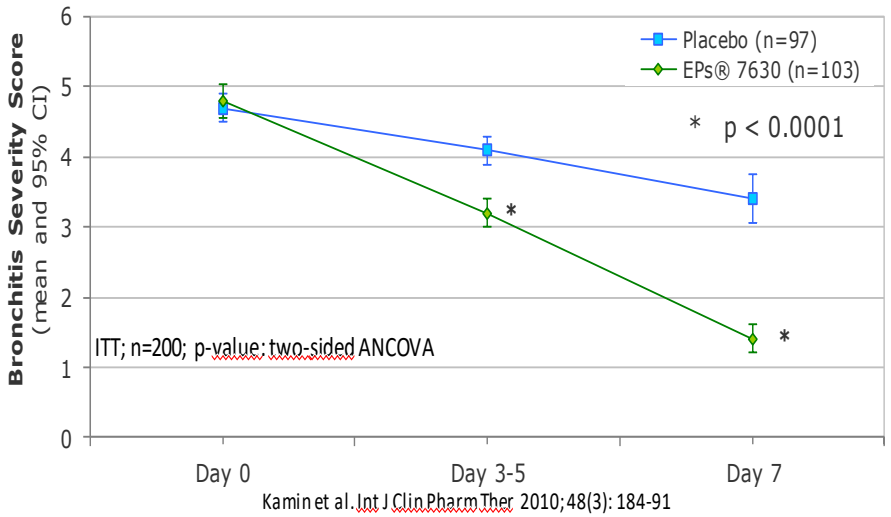
Primer amaç:	**Akut bronşiti olan 1-18 yaş arası hastalarda EPs® 7630 solüsyonunun etkinliği ve güvenliği**
Çalışmaların tasarımı:	Randomize, çift-kör, plasebo-kontrollü klinik çalışmalar
Doz:	1 - 5 yaş, 3x10 damla, 6 - 12 yaş, 3x20 damla, >12 - 18 yaş, 3x30 damla, 7 gün boyunca EPs® 7630 veya aynı şekilde plasebo
Primer kazanım kriteri:	0 ile 7. günler arasında BSS (Bronşit semptom skorlaması) değişimi
BSS (Bronşit semptom skorlaması) semptomları	• Öksürük • Dinlemekle pulmoner raller • Dispnea

Kamin W et al. Int J Clin Pharmacol Ther. 2010;48:184-91
Kamin W et al. Pediatr Int. 2012;54:219-26

Akut bronşitte Umca

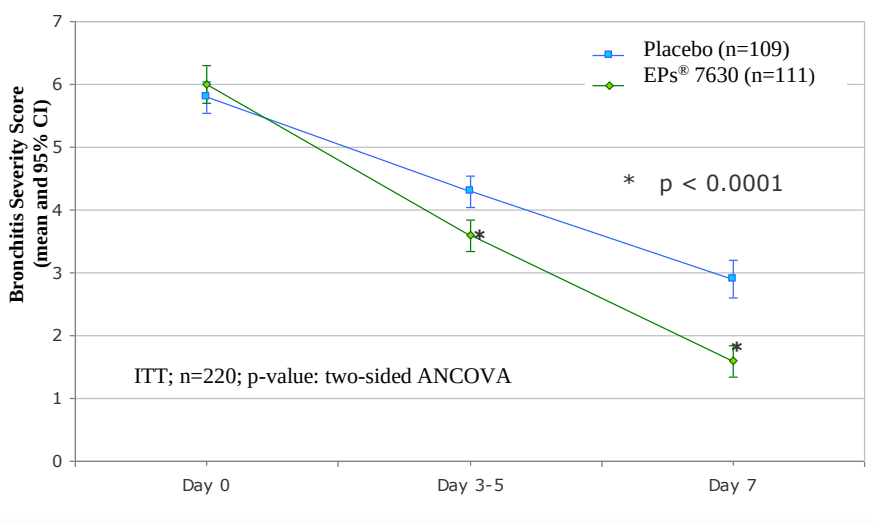
BSS'nin zaman ile değişimi:

Çalışma I (ITT analizi; n=200)



Kamin et al. Int J Clin Pharm Ther 2010;48(3): 184-91

Çalışma II (ITT analizi; n=220)

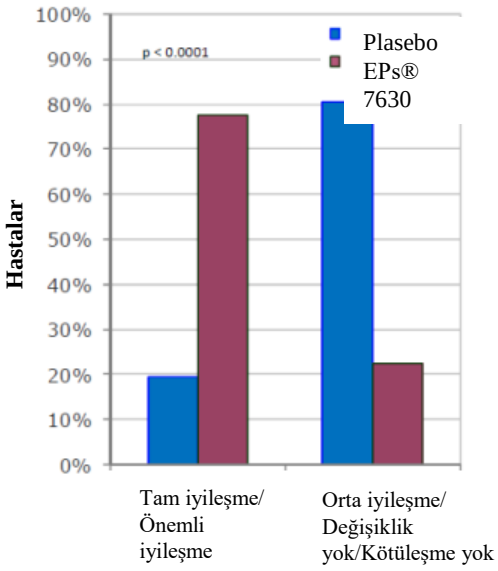


Kamin W et al. Int J Clin Pharmacol Ther. 2010;48:184-91
Kamin W et al. Pediatr Int. 2012;54:219-26

Akut bronşitte Umca

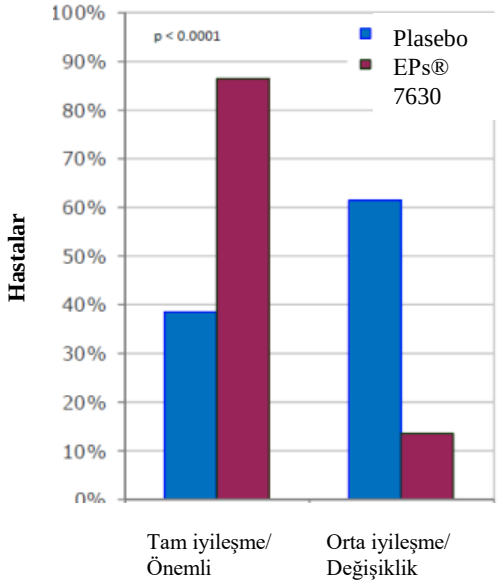
Hekim değerlendirmesine göre, 7. gün tedaviden kazanım:

Çalışma I (ITT analizi; n=200)



Kamin et al. Int. J. Clin. Pharmacol. Ther. 2010;48:184-191

Çalışma II (ITT analizi; n=220)

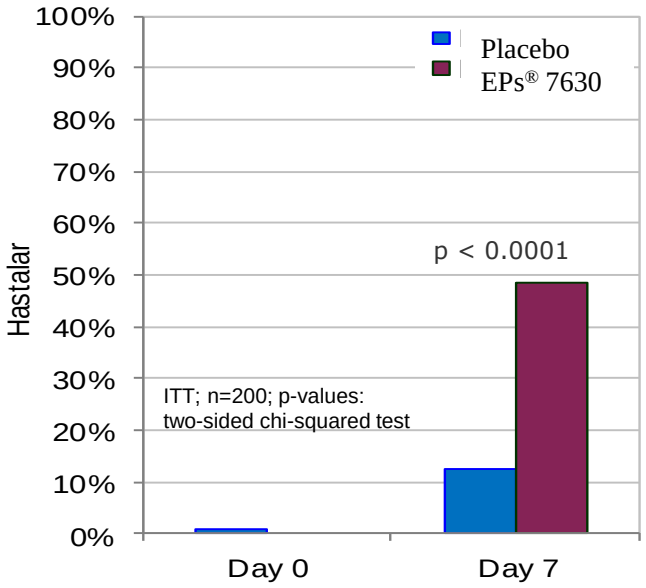


Kamin et al. Pediatr Int 2012;54:219-26

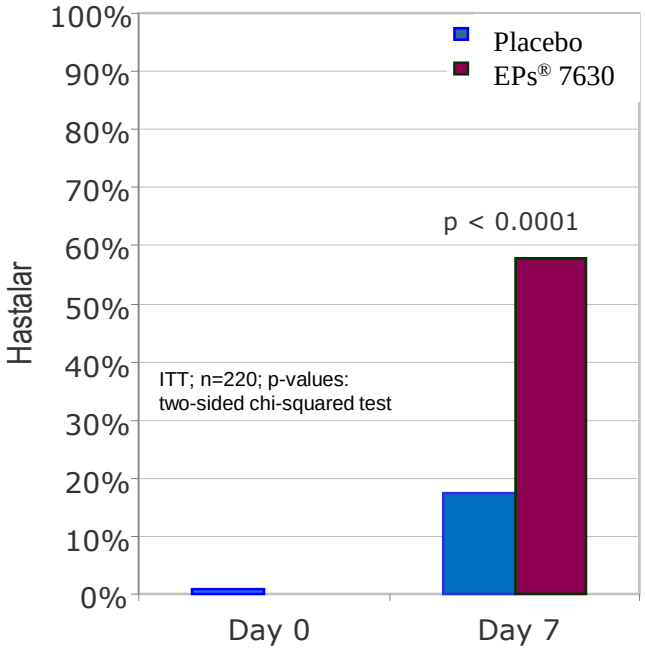
P değerleri:
iki yönlü Cochran-Mantel- Haenszel testi

Akut bronşitte Umca

7. Gün kreşe, anaokuluna, okula dönebilen hastalar:



Kamin W et al. Int J Clin Pharm Ther 2010;48:184-91



Kamin W et al. Pediatr Int 2012;54:219-26.

Her iki çalışmanın sonucu

- Hızla ortaya çıkan etki
- Bulgularda erken düzelme
- Öksürük ve ral sıklık ve şiddetinde belirgin azalma
- Tüm yaş gruplarında benzer etkinlik
- 7. günde tüm bronşit bulgularında anlamlı azalma
- 7. günde tedaviye yanıt oranı iki kat daha fazla
- 7. günde okula gidebilme oranında belirgin fark

Original Article

Treatment of acute bronchitis with EPs 7630: Randomized, controlled trial in children and adolescents

Kamin 2010 ve 2012

UMCA, Akut Bronşitte, Amerika Aile Hekimleri Akademisi Kılavuzunda önerilmektedir.

Diagnosis and Treatment of Acute Bronchitis

ROSS H. ALBERT, MD, PhD, *Hartford Hospital, Hartford, Connecticut*

Cough is the most common symptom bringing patients to the primary care physician's office, and acute bronchitis is usually the diagnosis in these patients. Acute bronchitis should be differentiated from other common diagnoses, such as pneumonia and asthma, because these conditions may need specific therapies not indicated for bronchitis. Symptoms of bronchitis typically last about three weeks. The presence or absence of colored (e.g., green) sputum does not reliably differentiate between bacterial and viral lower respiratory tract infections. Viruses are responsible for more than 90 percent of acute bronchitis infections. Antibiotics are generally not indicated for bronchitis, and should be used only if pertussis is suspected to reduce transmission or if the patient is at increased risk of developing pneumonia (e.g., patients 65 years or older). The typical therapies for managing acute bronchitis symptoms have been shown to be ineffective, and the U.S. Food and Drug Administration recommends against using cough and cold preparations in children younger than six years. The supplement pelargonium may help reduce symptom severity in adults. As patient expectations for antibiotics and therapies for symptom management differ from evidence-based recommendations, effective communication strategies are necessary to provide the safest therapies available while maintaining patient satisfaction. (*Am Fam Physician*. 2010;82(11):1345-1350. Copyright © 2010 American Academy of Family Physicians.)

▶ Patient information: A handout on treatment of bronchitis, written by the author of this article, is provided on page 1352.

Cough is the most common symptom for which patients present to their primary care physicians, and acute bronchitis is the most common diagnosis in these patients.[1] However, studies show that most patients with acute bronchitis are treated with inappropriate or ineffective therapies.[2] Although some physicians cite patient expectations and time constraints for using these therapies, recent warnings from the U.S. Food and Drug Administration (FDA) about the dangers of certain commonly used agents underscore the importance of using only evidence-based, effective therapies for bronchitis.

Diagnosis

Acute bronchitis is a self-limited infection with cough as the primary symptom. This infection can be difficult to distinguish from other illnesses that commonly cause cough (Table 1).

The common cold often causes coughing; however, nasal congestion and rhinorrhea are also usually present, and a cold typically lasts only seven to 10 days. Symptoms of acute bronchitis typically persist for approximately three weeks.[3]

Pneumonia can usually be ruled out in patients without fever, tachypnea, tachycardia, or clinical lung findings suggestive of pneumonia on examination.[4] However, cough may be the only initial presenting symptom of pneumonia in older adults; a lower threshold for using chest radiography should be maintained in these patients. The presence or absence of colored (e.g., green) sputum does not reliably differentiate between bacterial and viral lower respiratory tract infections.[5]

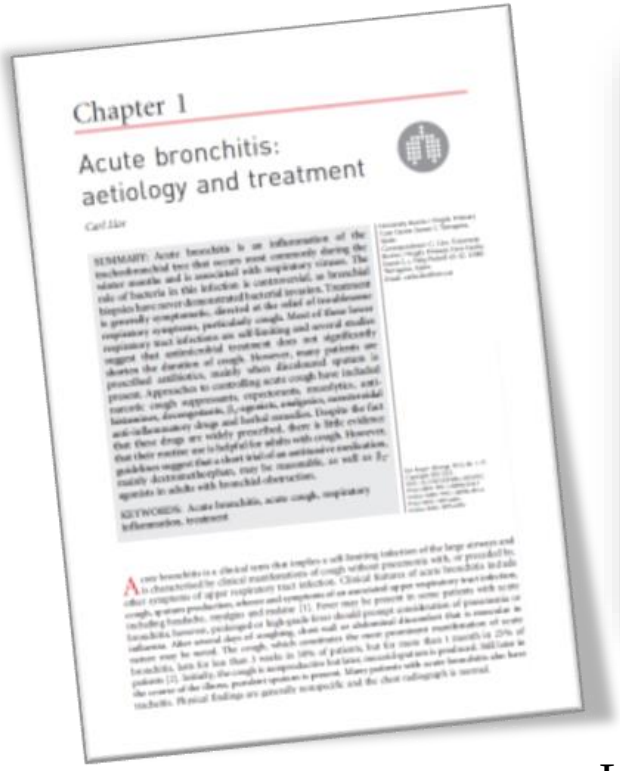
The causative pathogen for bronchitis is rarely identified (Table 2[6]). In clinical studies, identification of the causative pathogen occurs in less than 30 percent of cases.[7] Approximately 90 percent of acute bronchitis infections are caused by viruses.[7] Because the yield of viral cultures is typically low and results rarely affect clinical planning, routine serologic testing is not recommended for bronchitis. Testing may be considered for influenza when risk is thought to be

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Antibiotics should not be used routinely for the treatment of acute bronchitis	B	10, 12, 13
The following therapies may be considered to manage bronchitis-related symptoms:		
Antitussives (dextromethorphan, codeine, hydrocodone) in patients six years and older	C	12, 19
Beta-agonist inhalers in patients with wheezing	B	23
High-dose episodic inhaled corticosteroids	B	24
Echinacea	B	25
Pelargonium	B	26-28
Dark honey in children	B	28
The following medicines should not be used to manage bronchitis-related symptoms:		
Expectorants	B	22
Beta-agonist inhalers in patients without wheezing	B	23
Antitussives in children younger than six years	C	20, 21

Ross, Diagnosis and treatment of acute bronchitis, Am Fam Physician, 2010

UMCA, Akut bronşitte, Avrupa Solunum Topluluğu Kılavuzunda önerilmektedir



Chapter 1

Acute bronchitis: aetiology and treatment

Carl Llor

SUMMARY: Acute bronchitis is an inflammation of the tracheobronchial tree that occurs most commonly during the winter months and is associated with respiratory viruses. The role of bacteria in this infection is controversial, as bronchial biopsies have never demonstrated bacterial invasion. Treatment is generally symptomatic, directed at the relief of troublesome respiratory symptoms, particularly cough. Most of these lower respiratory tract infections are self-limiting and several studies suggest that antimicrobial treatment does not significantly shorten the duration of cough. However, many patients are prescribed antibiotics, notably when discoloured sputum is present. Approaches to controlling acute cough have included narcotic cough suppressants, expectorants, mucolytics, antihistamines, decongestants, β_2-agonists, antimicrobial and anti-inflammatory drugs and herbal remedies. Despite the fact that these drugs are widely prescribed, there is little evidence that their routine use is helpful for adults with cough. However, guidelines suggest that a short trial of an antitussive medication, mainly dextromethorphan, may be reasonable, as well as β_2-agonists in adults with bronchial obstruction.

KEYWORDS: Acute bronchitis, acute cough, respiratory inflammation, treatment

Acute bronchitis is a clinical term that implies a self-limiting infection of the large airways and is characterised by clinical manifestations of cough without pneumonia with, or preceded by, other symptoms of upper respiratory tract infection. Clinical features of acute bronchitis include cough, sputum production, wheeze and symptoms of an associated upper respiratory tract infection, including headache, prolonged or high-grade fever should prompt consideration of pneumonia or influenza. After several days of coughing, chest wall or abdominal discomfort that is muscular in nature may be noted. The cough, which constitutes the most prominent manifestation of acute bronchitis, lasts for less than 3 weeks in 50% of patients, but for more than 1 month in 25% of patients [2]. Initially, the cough is nonproductive but later, mucoid sputum is produced. Still later in the course of the illness, purulent sputum is present. Many patients with acute bronchitis also have rhinitis. Physical findings are generally nonspecific and the chest radiograph is normal.

Table 1. Clinical recommendations for acute bronchitis and evidence rating

Recommendation	Evidence rating
Increased fluid intake, heated and humidified air, and avoidance of smoking and second-hand tobacco smoke	C
Antibiotics should not be routinely used	A
Antivirals should not be routinely used	B
Antitussives (dextromethorphan, codeine and hydrocodone) are recommended in adults	B
Antitussives are not recommended in children	C
β_2-agonist inhalers are recommended in patients with wheezing	B
β_2-agonist inhalers are not recommended in patients without wheezing	B
Expectorants are not recommended in adults	B
High-dose episodic inhaled corticosteroids are recommended	B
Analgesics and NSAIDs are recommended	B
Echinacea is recommended	B
Pelargonium is recommended	B
Chinese herbs are recommended	B
Honey is recommended in children	B

Llor, Acute Bronchitis, Eur Respir Monogr, 2013

Yerel ve Uluslarası kılavuzlarda Umca

Uluslararası Kılavuzlar

Avrupa Solunum Monografı
ERS, Llor C., 2013

Akut bronşitte önerilmiştir.
B kanıt düzeyi

Avrupa Rinosinüzit Kılavuzu
EPOS, Fokkens, 2012

Akut rinosinuzitte önerilmiştir.
A öneri düzeyi

Lokal Kılavuzlar

Almanya: S3 **Öksürük** rehberi
German College of General Practitioners and Family Physicians:
Akut bronşitte önerilmiştir.

Almanya: S3 **Rinosinüzit** rehberi
Akut rinosinuzitte önerilmiştir.

ABD: Amerikan Aile Hekimleri Kılavuzu
American Family Physicians (Ross 2010):
Akut bronşitte önerilmiştir. **B kanıt düzeyi**

American Family Physicians (Fashner 2012):
Soğuk algınlığında önerilmiştir.

Dikkat!

Yan etkiler :

Nadiren :

- Gastro-intestinal bulgular (karın ağrısı, yanma, bulantı, diare)

Çok nadiren:

- Hafif diş eti veya burun kanaması
- Hipersensitivite reaksiyonları (fasiyal ödem, dispne, KB düşmesi)

Kontrendikasyonlar:

- UMCA'nın içinde bulunan maddelerden herhangi birine karşı aşırı duyarlılık,
- Kanama eğiliminde artışın bulunduğu hallerde ve antikoagülan ilaçlar uygulanırken,
- Yeterli deneyim bulunmadığı için, şiddetli böbrek ve/veya karaciğer yetmezliği olanlarda

Etkileşim:

- Plasebo kontrollü, çift-kör çalışmada, UMCA ve penisilin V arasında hiçbir etkileşim görülmemiştir.

Güvenlik ve tolerabilite profili

Günlük doz*
990,000,000

vs

Advers olay insidansı
1.24
tanımlanan milyon dozda

Buna göre, ortalama 7 günlük tedavi döneminde **115,000** hastadan yalnızca **1 hastada** yan etki görülecektir.

*Schwabe verisi: 1992-2016 yılları arasında satılan günlük doza göre

Klinik çalışmalarda Umca'nın güvenliği

Advances in Pharmacoepidemiology & Drug Safety

Matthys et al., Adv Pharmacoepidemiol Drug Saf 2013, 2:4
http://dx.doi.org/10.4172/2167-1052.1000142

Review Article Open Access

Safety and Tolerability of EPs 7630 in Clinical Trials

Heinrich Matthys[1]*, Stephan Köhler[2] and Wolfgang Kamin[3]
[1]*Department of Pneumology, University Hospital Freiburg, Freiburg, Germany*
[2]*Clinical Research Department, Dr Willmar Schwabe Pharmaceuticals, 76227 Karlsruhe, Germany*
[3]*Clinic for Paediatrics, Evangelic Hospital Hamm, Hamm, Germany*

In 19 double-blind, placebo-controlled trials, the type and incidence rate of adverse events under EPs 7630 were similar to those in patients treated with placebo. For gastrointestinal complaints and epistaxis, event rate differences

19 çift-kör, plasebo kontrollü klinik çalışmada EPs 7630 ile görülen advers etkilerin tipleri ve İnsidansları, plasebo ile tedavi edilen hastalarla aynıdır.

Matthsy, Adv Pharmacoepidemiol Drug Saf, 2013

Ürün profili ve pozoloji

Aktif etkin madde:	Pelargonium sidoides kökü ekstresi (1:8-10) (EPs® 7630) Ekstraksiyon ajanı: etanol 11 % (m/m)
Doz:	Doz korelasyonu: **1 tablet (20 mg) = 30 damla solüsyon = 7.5 ml şurup** Relapsı önlemek için, tedavi semptomların kesilmesinden sonra **2 gün** daha devam ettirilmelidir.
Endikasyon:	Akut solunum yolu enfeksiyonlarının tedavisi

GÜNLÜK DOZ	 12 yaş üzeri çocuklar ve yetişkinler	 6-12 yaş arası çocuklar	 1-5 yaş arası çocuklar
Solüsyon	3 x 30 damla	3 x 20 damla	3 x 10 damla
Tablet	3 x 1 tablet	2 x 1 tablet	-
Şurup	3 x 7.5 ml	3 x 5.0 ml	3 x 2.5 ml

Umca, özetle...

- Çok yoğun olarak araştırılmış, **etki mekanizması ortaya konmuş**
- Etkililiği çok sayıda hastada kanıtlanmış **(10.000),**
- Çocuklarda da yoğun klinik çalışma ve deneyim **(> 4000),**
- **Hızlı ortaya çıkan etki,**
- Semptomlarda belirgin düzelme/azalma,
- Hastalığın süresinde en az **2 gün kısalma,** kazanım...
- Enfeksiyonun nedenine etkili,
- **Direnç söz konusu değil,**
- Çok iyi bir güvenlik profili

Akut solunum yolu enfeksiyonlarında komplikasyonları önlemede

antibiyotiğin yeri yoktur!

Cochrane Library

Cochrane Database of Systematic Reviews

Antibiotics for preventing suppurative complications from undifferentiated acute respiratory infections in children under five years of age

New search | Review | Intervention

Márcia G Alves Galvão, Marilene Augusta Rocha Crispino Santos, Antonio JL Alves da Cunha

First published: 29 February 2016

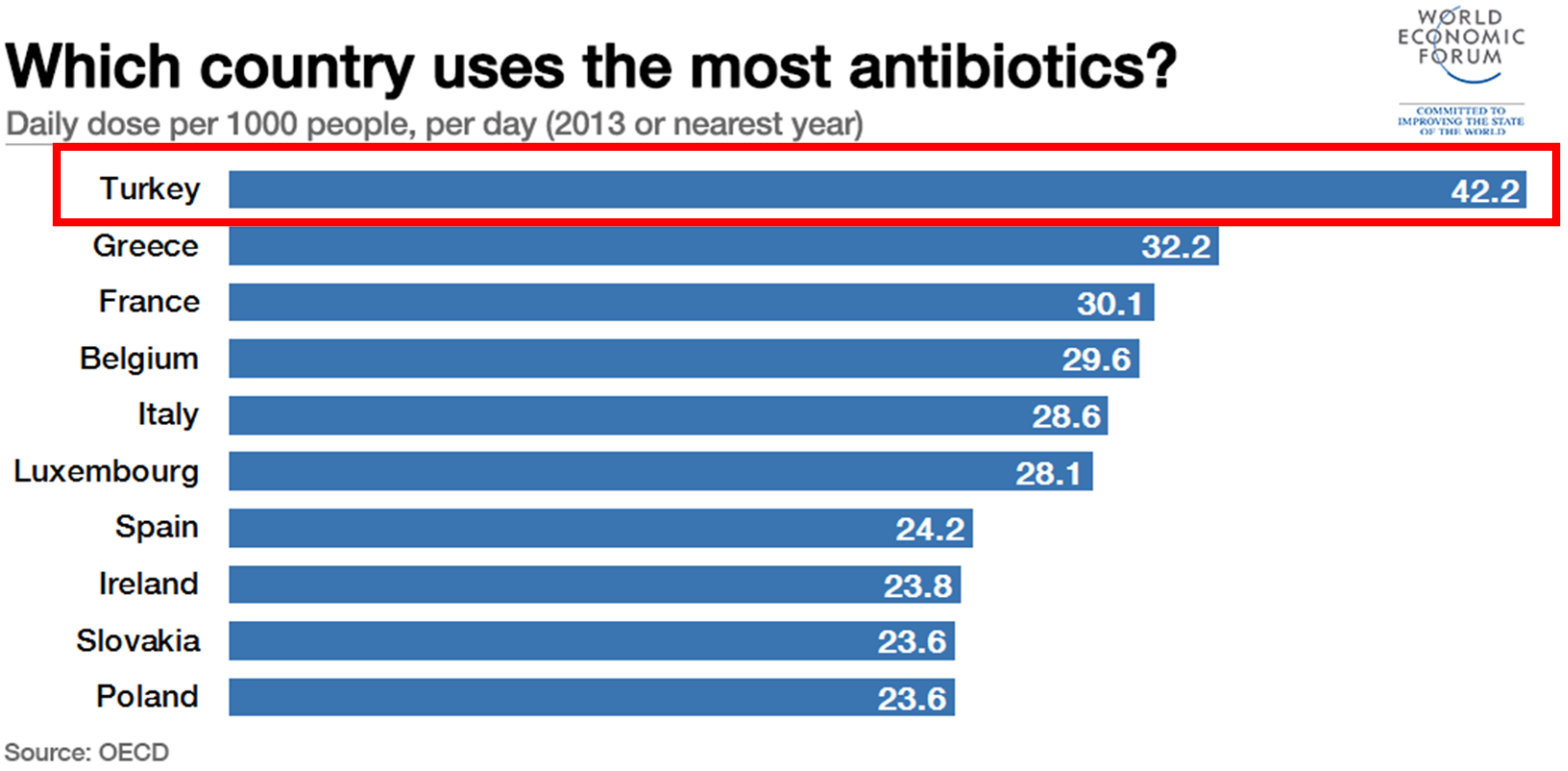
Editorial Group: Cochrane Acute Respiratory Infections Group

DOI: 10.1002/14651858.CD007880.pub3 View/save citation

Cited by (CrossRef): 1 article Check for updates | Citation tools

Cochrane Database Syst Rev. 2016 Feb 29;2:

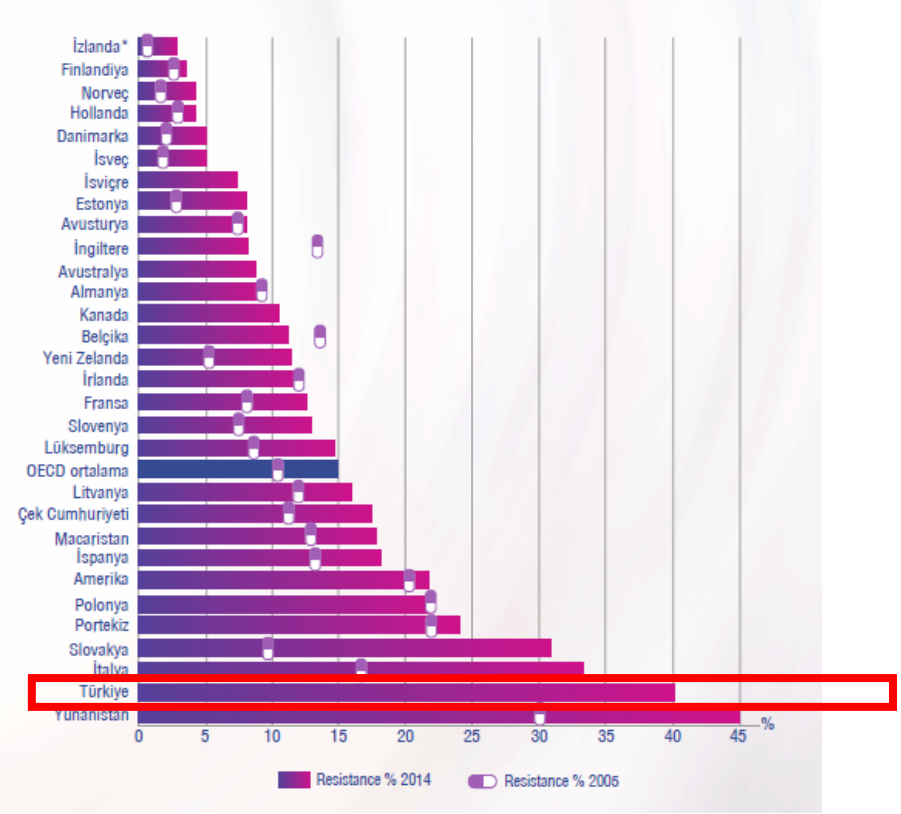
Buna karşı, Antibiyotik tüketiminde (maalesef) birinciyiz...



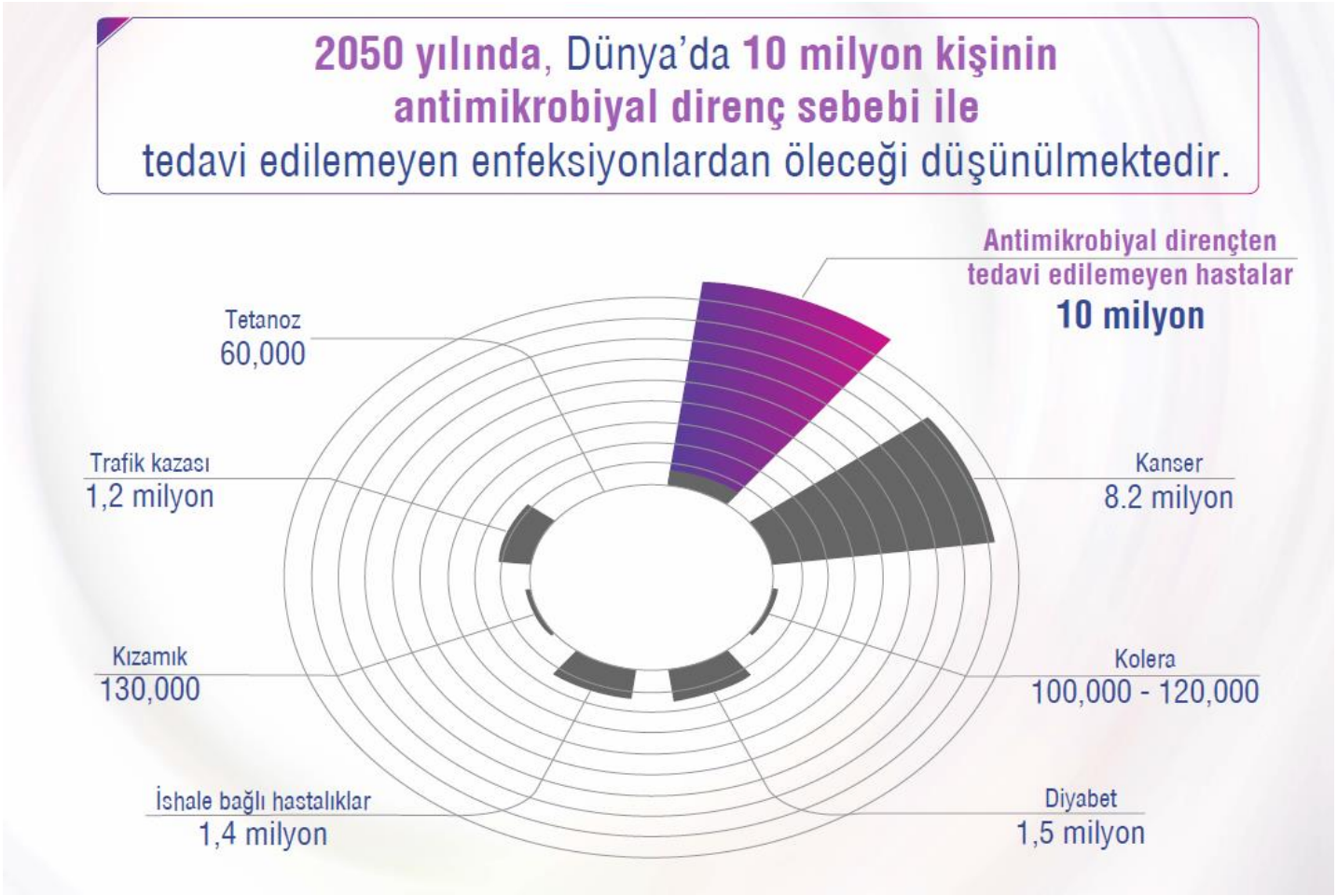
www.oecd.org/health/

Türkiye'de antibiyotik direnci yıllar boyunca artmaktadır

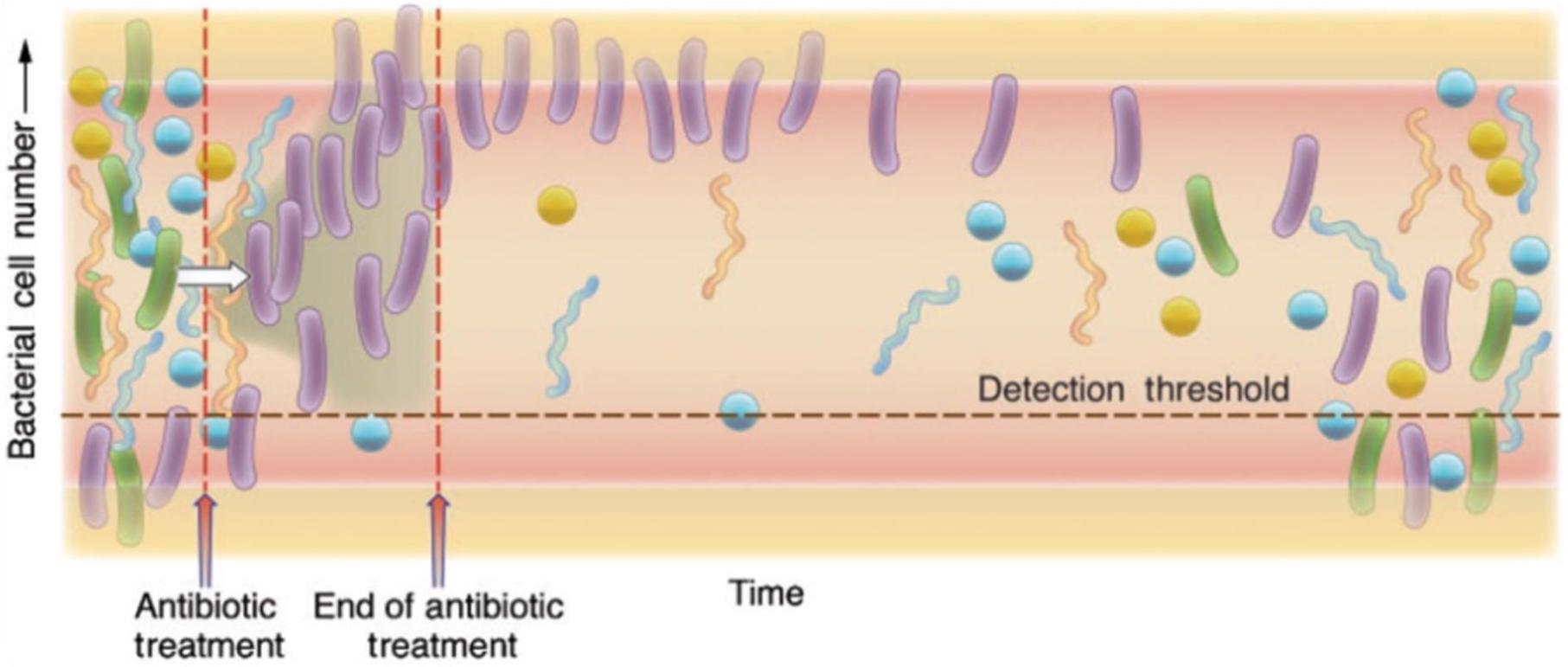
Direnç Gelişimi



www.oecd.org/health/antimicrobial-resistance.htm



https://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations_1.pdf


Bacterial cell number
Detection threshold
Antibiotic treatment
End of antibiotic treatment
Time

International Journal of Obesity

Yaşamın ilk 6 ayında

Original Article

International Journal of Obesity , (21 August 2012) | doi:10.1038/ijo.2012.

Infant antibiotic exposures and early-life body mass

L Trasande, J Blustein, M Liu, E Corwin, L M Cox and M J Blaser

Objectives:

To examine the associations of antibiotic exposures during the first 2 years of life and the development of body mass over the first 7 years of life.

Design:

Longitudinal birth cohort study.

Subjects:

A total of 11 532 children born at ⩾2500 g in the Avon Longitudinal Study of Parents and Children (ALSPAC), a population-based study of children born in Avon, UK in 1991–1992.

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Pediatrics 2012;130;e794; originally published online September 24, 2012;
DOI: 10.1542/peds.2011-3886

PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Antibiotic Exposure and IBD Development Among Children: A Population-Based Cohort Study

WHAT'S KNOWN ON THIS SUBJECT: Inflammatory bowel disease pathogenesis is incompletely understood. Previous pediatric studies suggested associations between antibiotic use and inflammatory bowel disease development but were limited by recall bias, lack of controls, incomplete antibiotic capture, or included exposures between symptom onset and diagnosis.

WHAT THIS STUDY ADDS: Our population-based cohort study suggests that certain childhood antibiotic exposures are associated with an increased risk of developing inflammatory bowel disease. Our findings have implications for understanding the condition's pathogenesis and provide additional stimulus for reducing unnecessary childhood antibiotic use.

AUTHORS: Matthew P. Kronman, MD, MSCE,[a] Theoklis E. Zaoutis, MD, MSCE,[b,c] Kevin Haynes, PharmD, MSCE,[c] Rui Feng, PhD,[c] and Susan E. Coffin, MD, MPH[b,c]

[a]Division of Infectious Diseases, Seattle Children's Hospital, University of Washington, Seattle, Washington; [b]Division of Infectious Diseases, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; and [c]Department of Biostatistics and Epidemiology, the Center for Clinical Epidemiology and Biostatistics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania

KEY WORDS

antimicrobials, epidemiology, inflammatory bowel disease, pediatric, population-based studies

ABBREVIATIONS

aHR—adjusted hazard ratio

CI—confidence interval

DOI: 10.1542/peds.2011-3880

PEDIATRICS®

WHAT'S KNOWN ON THIS SUBJECT: Inflammatory bowel disease pathogenesis is incompletely understood. Previous pediatric studies suggested associations between antibiotic use and inflammatory bowel disease development but were limited by recall bias, lack of controls, incomplete antibiotic capture, or included exposures between symptom onset and diagnosis.

WHAT THIS STUDY ADDS: Our population-based cohort study suggests that certain childhood antibiotic exposures are associated with an increased risk of developing inflammatory bowel disease. Our findings have implications for understanding the condition's pathogenesis and provide additional stimulus for reducing unnecessary childhood antibiotic use.

Pediatrics
March 2009, VOLUME 123 / ISSUE 3

Antibiotic Use in Children Is Associated With Increased Risk of Asthma

Fawziah Marra, Carlo A. Marra, Kathryn Richardson, Larry D. Lynd, Anita Kozyrskyj, David M. Patrick, William R. Bowie, J. Mark FitzGerald

Pediatrics
March 2009, VOLUME 123 / ISSUE 3

Antibiotic Use in Children Is Associated With Increased Risk of Asthma

Fawziah Marra, Carlo A. Marra, Kathryn Richardson, Larry D. Lynd, Anita Kozyrskyj, David M. Patrick, William R. Bowie, J. Mark FitzGerald

Young children's antibiotic exposure associated with higher food allergy risk

Date: September 1, 2016

Source: University of South Carolina

Summary: Antibiotic treatment within the first year of life may wipe out more than an unwanted infection: exposure to the drugs is associated with an increase in food allergy diagnosis, new research suggests.

Antibiotic treatment increased risk for type 1 diabetes in animal study

Date: August 22, 2016

Source: NYU Langone Medical Center / New York University School of Medicine

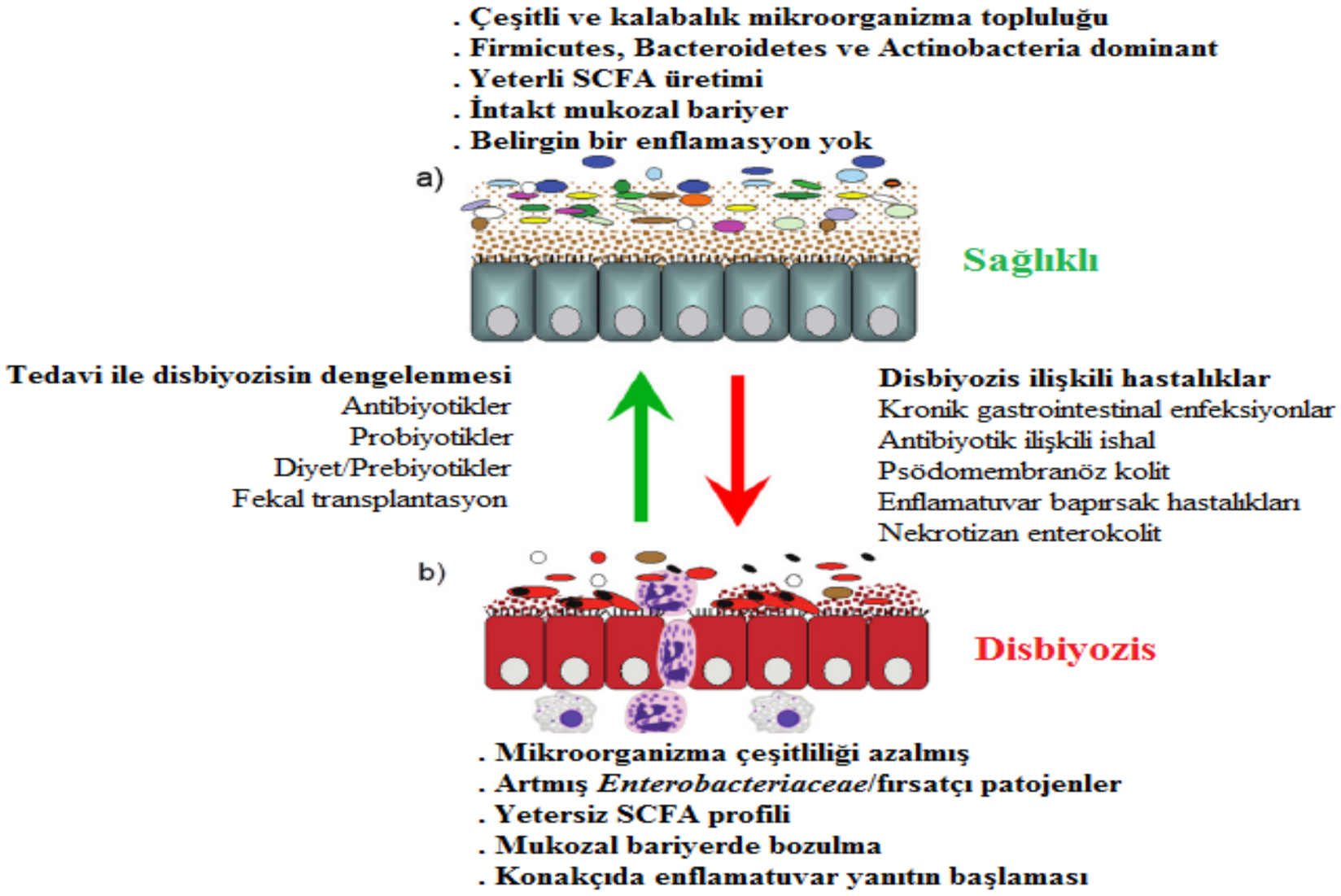
Summary: In doses equivalent to those used regularly in human children, antibiotics changed the mix of gut microbes in young mice to dramatically increase their risk for type 1 diabetes.

"This is the first study of its kind suggesting that antibiotic use can alter the microbiota and have lasting effects on immunological and metabolic development, resulting in autoimmunity.

We're eager to see how these findings may impact the discovery of type 1 diabetes preventive treatments in the future and continued research in the area of vaccines."

Jessica Dunne, director of Discovery Research at Juvenile Diabetes Research Foundation

Walker AW, Lawley TD. Pharmacological Research 2012



Sağlıklı bir intestinal sistem – disbiyozis ilişkisi

12-18 Kasım Antibiyotik Farkındalık Haftası