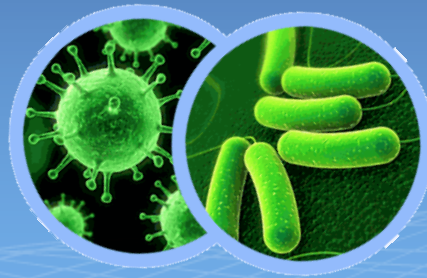




Респираторные инфекции: вирусы vs. бактерии – от мифов к поиску истины



Рузанов Дмитрий Юрьевич

Беларусь



Кто «владеет» респираторным трактом?

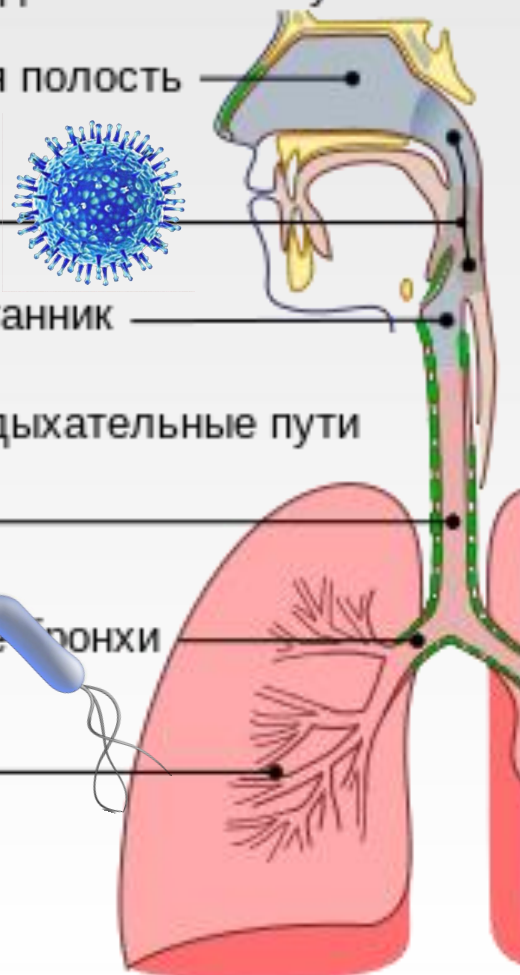


Верхние дыхательные пути

Носовая полость

Глотка

Надгортанник



Нижние дыхательные пути

Трахея

Главные бронхи

Лёгкие





Bull World Health Organ. 2008 Jun; 86(6):
494–496. doi: 10.2471/BLT.08.052753

«Кто владеет респираторным трактом – тот владеет миром» - эпидемиология ОРВИ

- Более **65%** от общей заболеваемости.
- Более **40%** от дней нетрудоспособности (в т.ч. **60%** по уходу).
- Симптомы ОРЗ у **15-45%** круглогодично.
- **9-17%** смертности.
- Реальное число заболевших в **1,5 – 3,7** раза выше.



Кривые заболеваемости ОРИ
одназначены с количеством
выписанных рецептов на АБП (в целом)

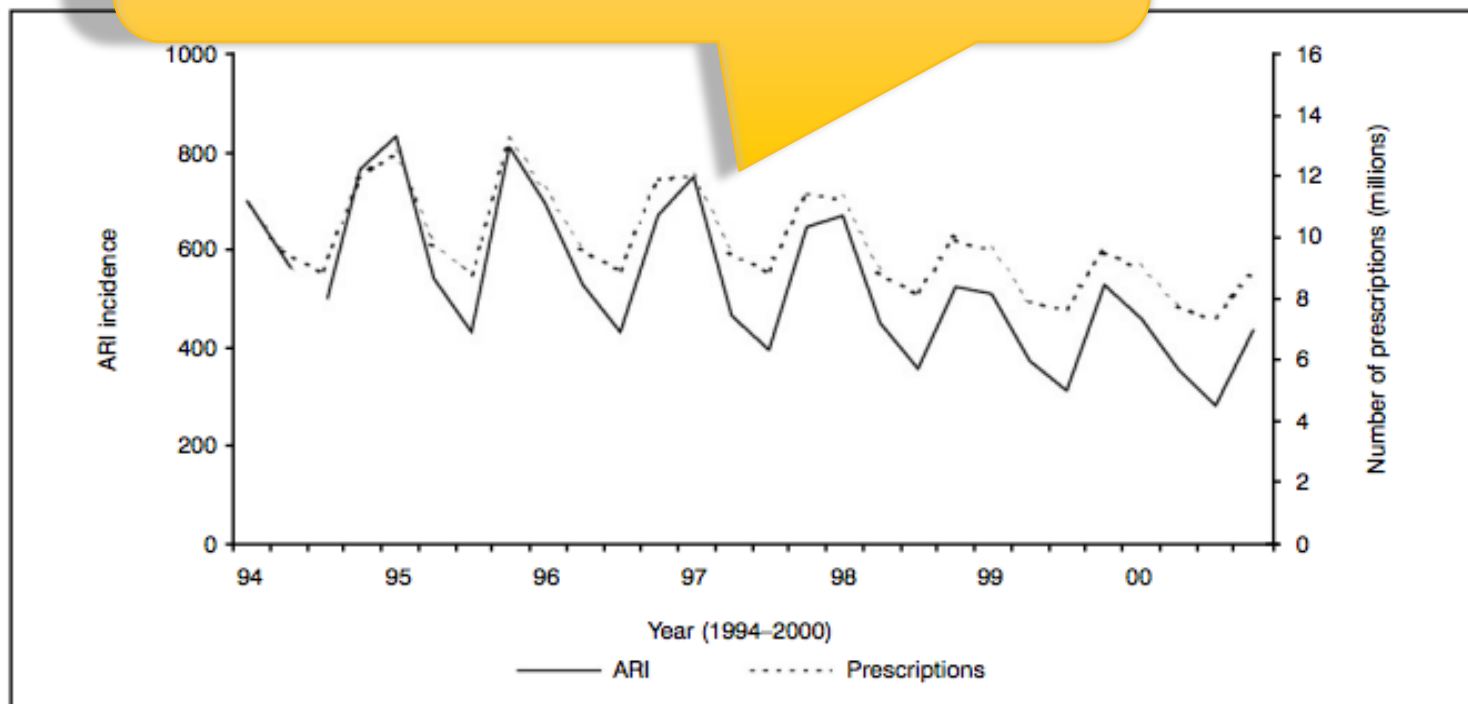


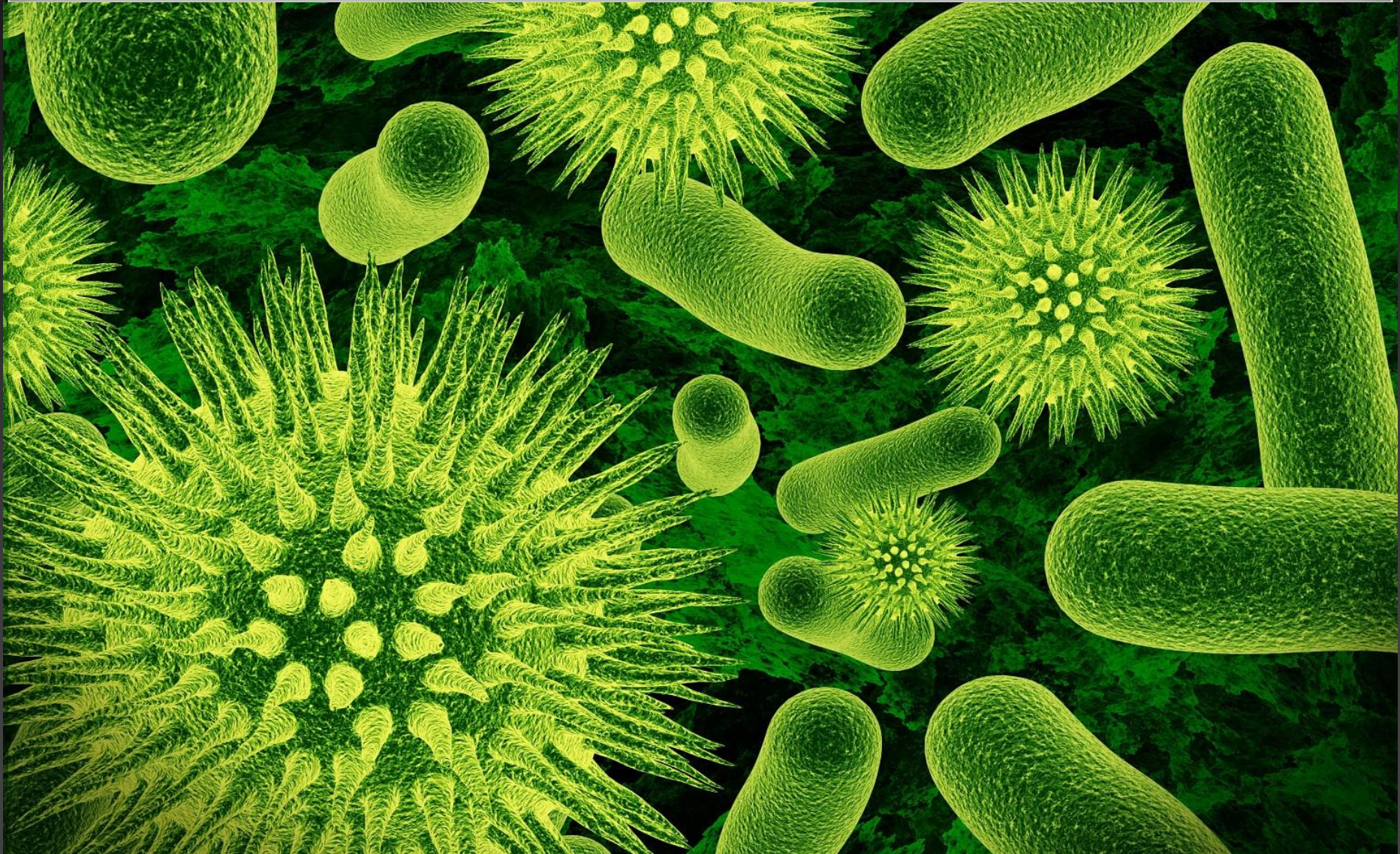
Figure 4. Mean weekly incidence of acute respiratory infections (ARI) versus number of prescriptions for antibiotics.

D M Fleming, A M Ross, K W Cross and H Kendall

The reducing incidence of respiratory tract infection and its relation to antibiotic prescribing



Размер имеет значение ?





Размер имеет значение ?



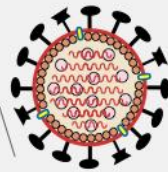
small molecules



proteins,
antibodies



ribosomes



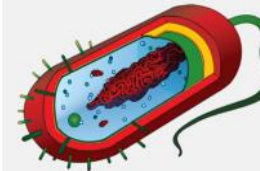
viruses



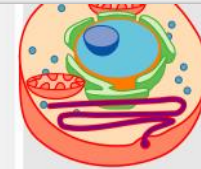
genes



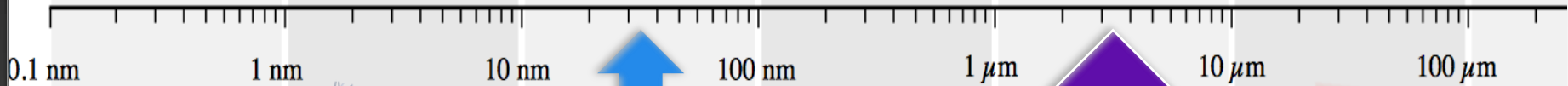
animal cells



bacteria



human hair

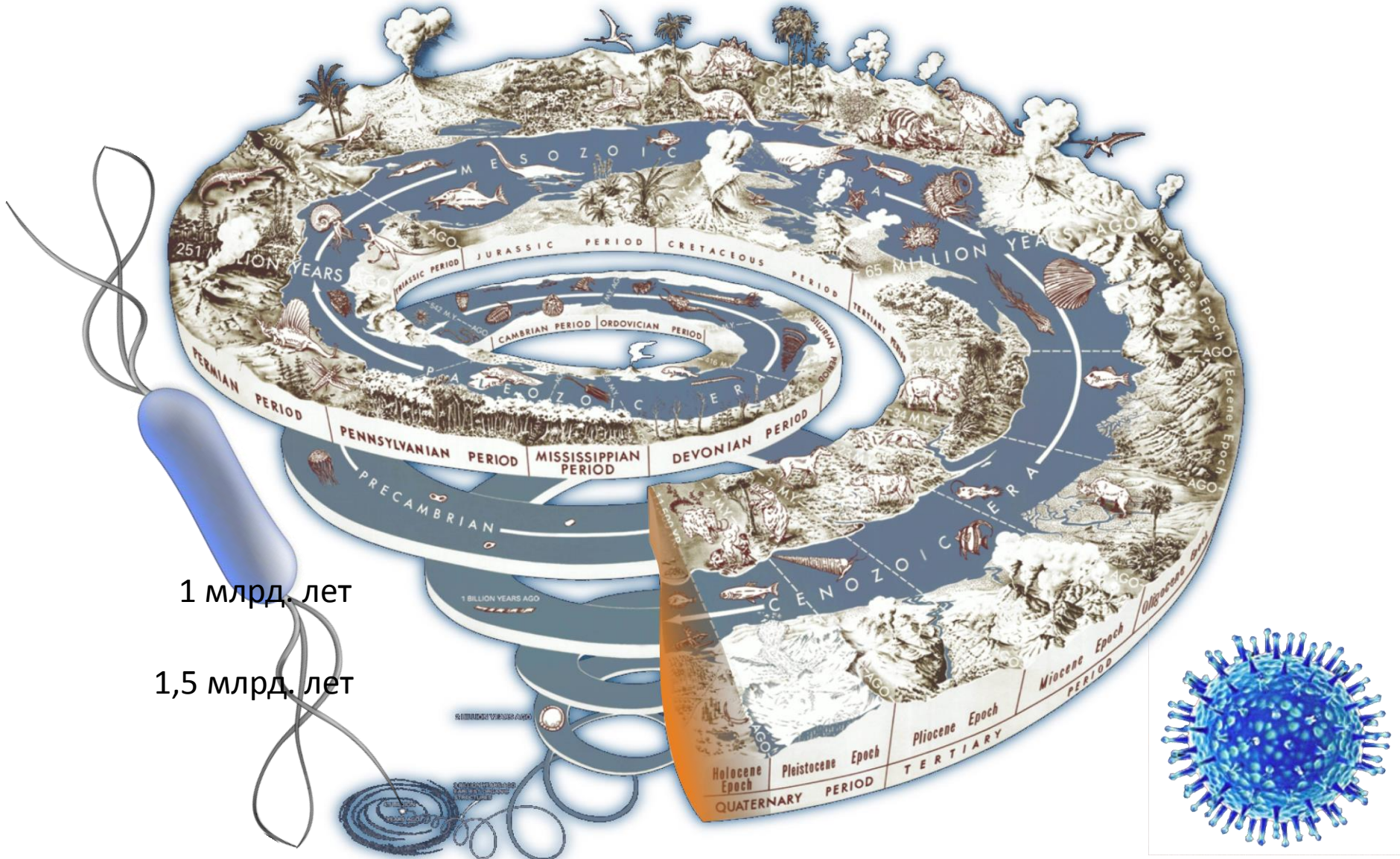


КТО КРУПНЕЕ ?



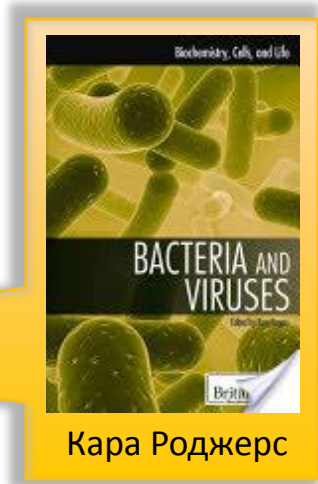
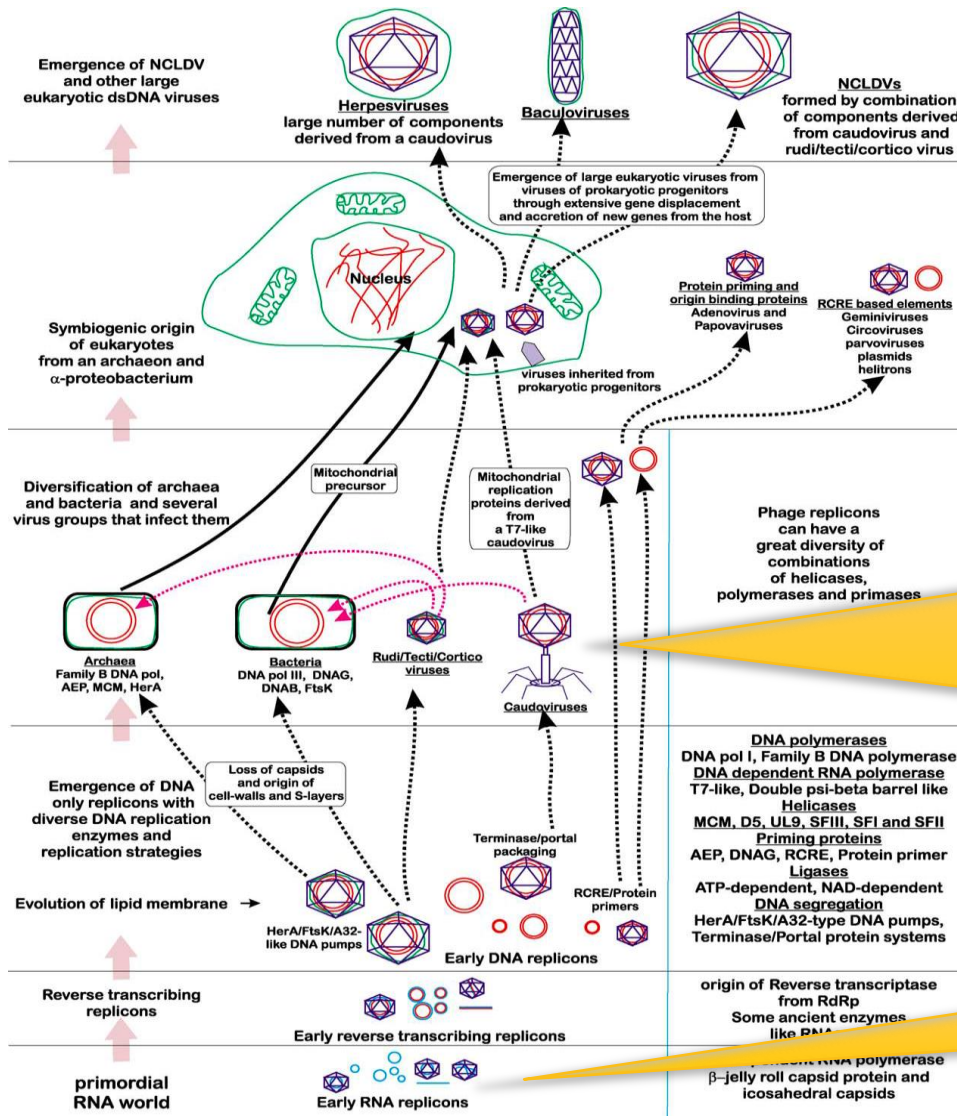


Кто старше?

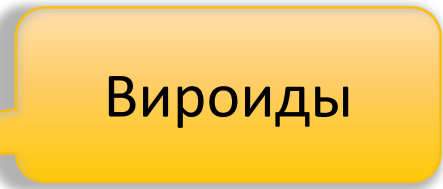




Теория коэволюции



Кара Роджерс



Вироиды



<http://www.flunewseurope.org>



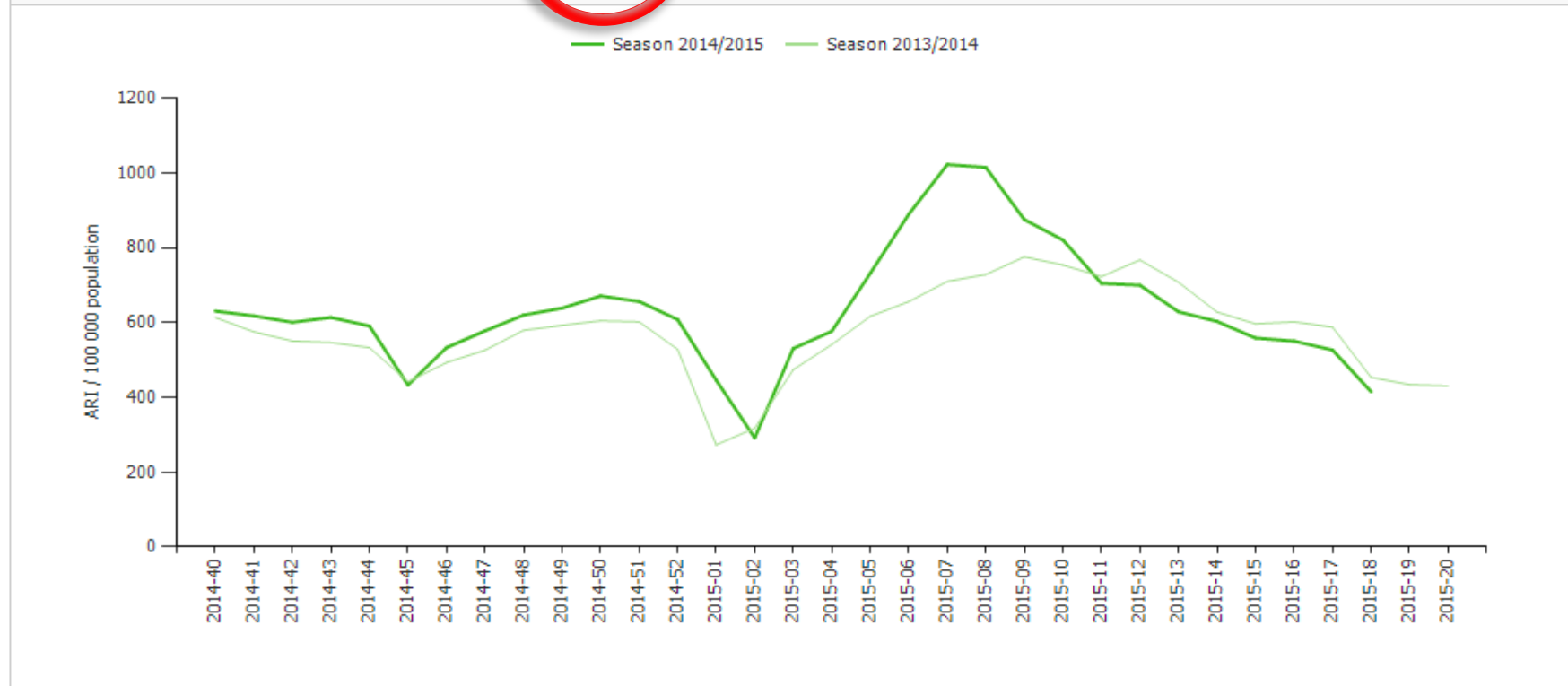
Flu News Europe

Joint ECDC–WHO/Europe weekly influenza update



Consultation rates for influenza-like illness (ILI) and acute respiratory infection (ARI) by country

Country: Clinical Type:





Epidemiology of Acute Lower Respiratory Disease in Children

W. Paul Glezen, M.D., and Floyd W. Denny, M.D.

N Engl J Med 1973; 288:498-505 March 8, 1973 DOI: 10.1056/NEJM197303082881005

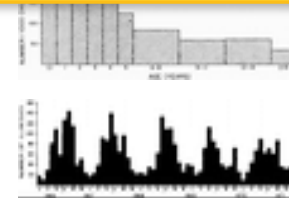
6 возбудителей;
Респираторный
микоплазмоз;
Невысокая значимость
бактериальных агентов

MEDICAL PROGRESS ARCHIVE

Epidemiology of Acute Lower Respiratory Disease in Children

W. Paul Glezen, M.D., and Floyd W. Denny, M.D.
N Engl J Med 1973; 288:498-505 | March 8, 1973 | DOI: 10.1056/NEJM197303082881005

RESPIRATORY infections are the major cause of acute illnesses in the United States.¹ Children have eight acute respiratory illnesses per year,^{2,3,4} many of which, particularly in infancy, will involve the lower respiratory tract.^{4,5} Mortality resulting from acute lower respiratory disease is a serious problem in children under five years of age.^{6,7,8} A large proportion of these illnesses have been ascribed to specific respiratory viruses and *Mycoplasma pneumoniae*.^{9,10} Despite this information and the scientific knowledge and technical advances that have led to control of diseases such as poliomyelitis and measles, little progress has been . . .





Динамика заболеваемостью ОРИ



Адаптировано по W. Paul Glezen, 1973





Динамика заболеваемостью ОРИ



Адаптировано по W. Paul Glezen, 1973





D M Fleming, A M Ross, K W Cross and H Kendall

The reducing incidence of respiratory tract infection and its relation to antibiotic prescribing

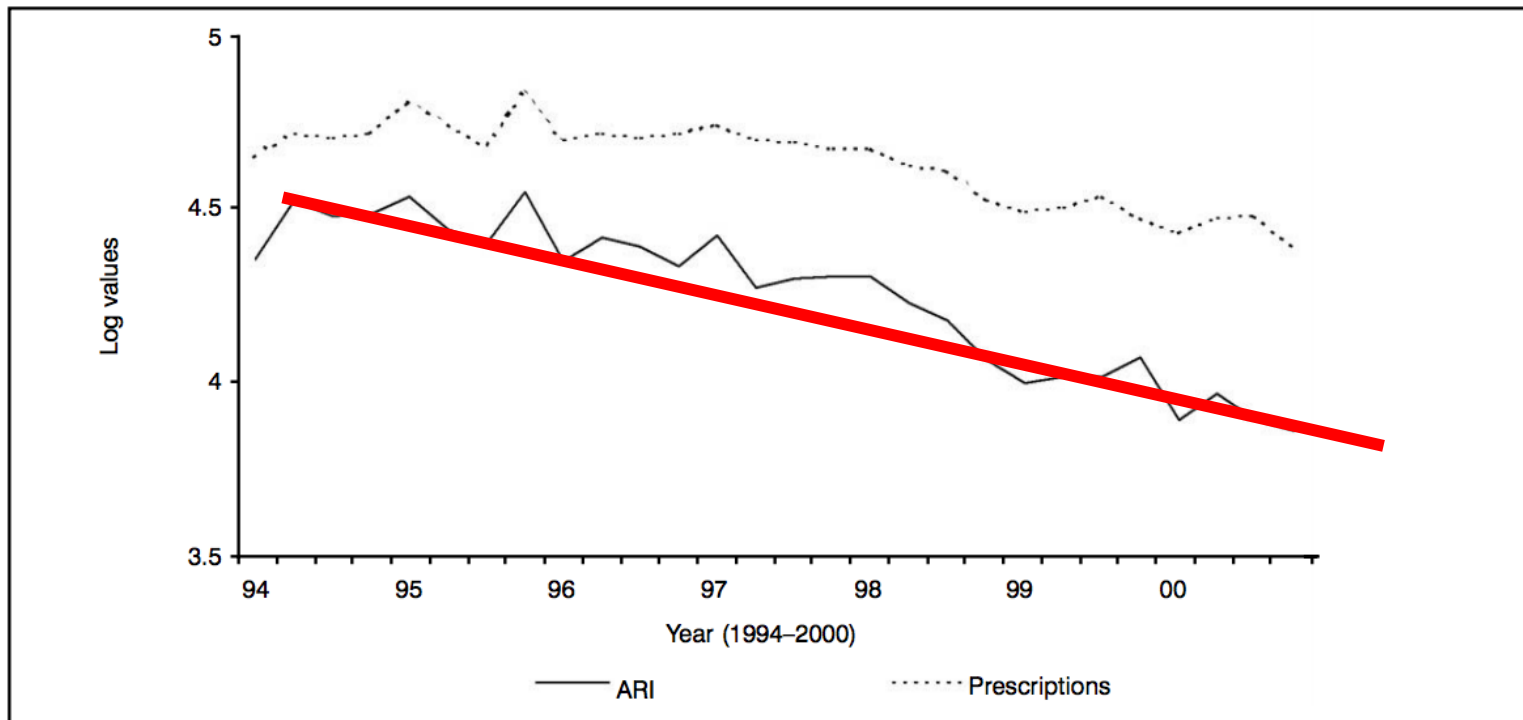


Figure 5. Seasonally adjusted trends in incidence of acute respiratory tract infections (ARI [per 1000]) and antibiotic prescriptions (per 100 000): quarterly data logged.



Новые (?) респираторные вирусы



6 **новых** вирусов, клинически связанных с респираторной инфекцией:

- метапневмовирус человека (HMPV),
- парагрипп 4,
- человеческий коронавирус NL63 и HKU1,
- вирус тяжелого острого респираторного синдрома SARSV (коронавирус)
- **boavirus**

A. Pavia **Viral Infections of the Lower Respiratory Tract: Old Viruses, New Viruses, and the Role of Diagnosis** Clin Infect Dis. 2011 May 1; 52(Suppl 4): S284–S289.



- Достоверное увеличение тяжелых вирусных пневмоний.
- «Старение» микоплазменной респираторной инфекции
- Острые бронхиолиты взрослых.
- Вирусные инфекции НДП как предшественники идиопатических заболеваний легких.
- Бронхоэктазии после инфекций с bocavirus.

Nichols WG, Peck Campbell AJ, Boeckh M. **Respiratory viruses other than influenza virus: impact and therapeutic advances.** Clin Microbiol Rev. 2008;21:274–90.



Liu WK, Liu Q, Chen DH, Liang HX, Chen XK, et al. (2014) Epidemiology of Acute Respiratory Infections in Children in Guangzhou: A Three-Year Study. PLoS ONE 9(5): e96674. doi:10.1371/journal.pone.0096674
<http://127.0.0.1:8081/plosone/article?id=info:doi/10.1371/journal.pone.0096674>



OPEN ACCESS Freely available online

PLOS ONE

Epidemiology of Acute Respiratory Infections in Children in Guangzhou: A Three-Year Study

Wen Kuan Liu^{1,2,3}, Qian Liu^{1,2,3}, De Hui Chen², Huan Xi Liang^{1,2}, Xiao Kai Chen^{1,2}, Mei Xin Chen^{1,2}, Shu Yan Qiu^{1,2}, Zi Yeng Yang^{1,2}, Rong Zhou^{1,2*}

¹ State Key Laboratory of Respiratory Diseases, National Clinical Research Center for Respiratory Disease, Guangzhou Medical University, Guangzhou, Guangdong, China, ² The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, Guangdong, China



Эпидемиология ОРИ у детей в Гуанджоу: трехлетнее наблюдение

Abstract

Acute Respiratory Infections (ARI) are some of the most common human diseases worldwide. However, they have a complex and diverse etiology, and the characteristics of the pathogens involved in respiratory infections in developing countries are not well understood. In this work, we analyzed the characteristics of 17 common respiratory pathogens in children (≤ 14 years old) with ARI in Guangzhou, southern China over a 3-year period using real-time polymerase chain reaction. Pathogens were identified in 2361/4242 (55.7%) patients, and the positivity rate varied seasonally. Ten of the 17 pathogens investigated showed positivity rates of more than 5%. The most frequently detected pathogens were respiratory syncytial virus (768/2361, 32.5%), influenza A virus (428/2361, 18.1%), enterovirus (138/2361, 13.3%), *Mycoplasma pneumoniae* (267/2361, 11.3%) and adenovirus (213/2361, 9.0%). Co-pathogens were common and found in 503 of 2361 (21.3%) positive samples. When ranked according to frequency of occurrence, the pattern of co-pathogens was similar to that of the primary pathogens, with the exception of human bocavirus, human coronavirus and human metapneumovirus. Significant differences were found in age prevalence in 10 of the 17 pathogens ($p \leq 0.009$): four basic patterns were observed, A: detection rates increased with age, B: detection rates declined with age, C: the detection rate showed distinct peaks or D: numbers of patients were too low to detect a trend or showed no significant difference among age groups ($p > 0.05$). These data will be useful for planning vaccine research and control strategies and for studies predicting pathogen prevalence.

Citation: Liu WK, Liu Q, Chen DH, Liang HX, Chen XK, et al. (2014) Epidemiology of Acute Respiratory Infections in Children in Guangzhou: A Three-Year Study. PLoS ONE 9(5): e96674. doi:10.1371/journal.pone.0096674

Editor: Cristina Costa, University Hospital San Giovanni Battista di Torino, Italy

Received: November 19, 2013; **Accepted:** April 10, 2014; **Published:** May 5, 2014

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Funding: The State Major Infectious Disease Research Program (China Central Government, 2012ZX10004-213), National Science and technology support program (2012BAI05801), The Combination Project of Guangdong Province (20108091000018), Research Project of Guangzhou Medical University (2012A04), and the project of Respiratory Medical R&D Centre of Guangdong Province (20109080100027) provided financial support for this work. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: zhourong@gjrd.cn

These authors contributed equally to this work.

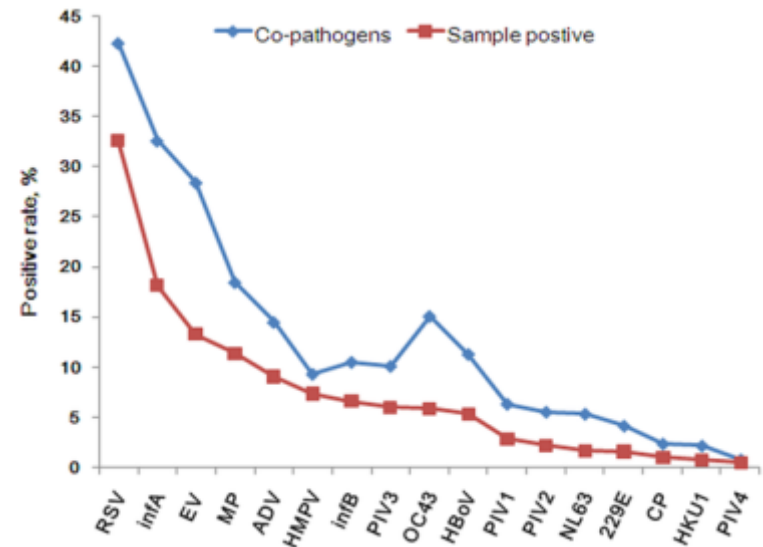


Figure 1. The rank of pathogen detection rate and co-pathogen rate in 4242 pediatric patients with ARI in Guangzhou from July 2009 to June 2012.



Одновременное выявление различных респираторных вирусов у детей с выявленным жизнеспособным респираторно-синцитиальным вирусом человека

Journal of Medical Virology 85:1852-1859 (2013)



16 JUL 2013

Concurrent Detection of Other Respiratory Viruses in Children Shedding Viable Human Respiratory Syncytial Virus

T.B. Gagliardi,¹ F.E. Paula,¹ M.A. Iwamoto,¹ J.L. Proença-Modena,¹ A.E. Santos,¹ A.A. Camara,² M.C. Cervi,³ O.A.L. Cintra,³ and E. Arruda^{1*}

¹Department of Cell and Molecular Biology, University of Sao Paulo School of Medicine, Ribeirão Preto, SP, Brazil

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³Department of Pediatrics, University of São Paulo School of Medicine, Ribeirão Preto, SP, Brazil

У 74% выявлены другие кроме HRSV вирусы, из них у 23% более двух дополнительно

Human res
important
majority o
of virus co
been base
PCR, which
tion from p
from prev
whether co
ratory virus
severity of HRSV illnesses from patients who
were shedding viable HRSV, nasopharyngeal

HRSV infection; HRSV isolation; respiratory virus co-infection; severity of HRSV disease

INTRODUCTION

Human respiratory syncytial virus (HRSV) is a major cause of acute respiratory infections (ARI), especially in children. Upper HRSV infections spread

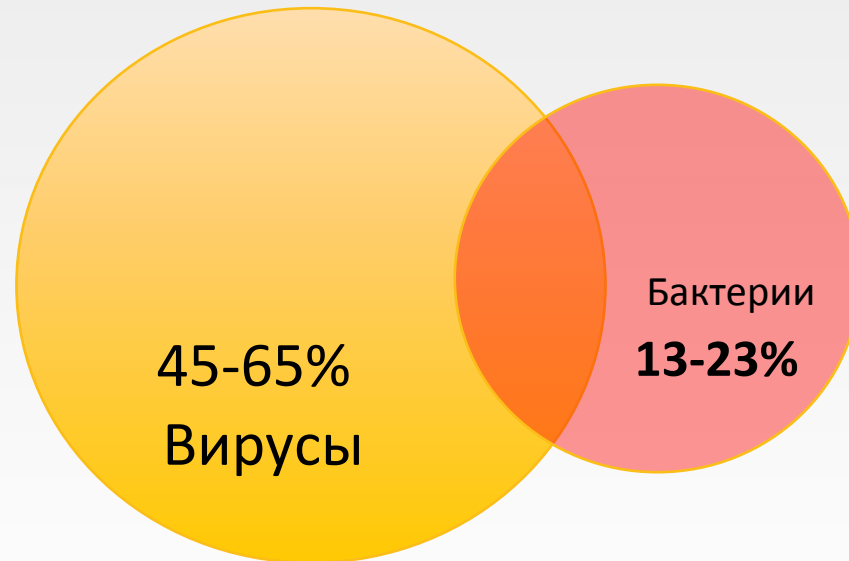


**Вирусы гриппа А и В – 10 – 35%,
парагриппозные вирусы (4 типа) – 12-15%,
респираторно-синцитиальная инфекция - 8-10%,
аденовирусы (более 30 типов) – 10-24%,
риновирусы 15-43%,**

коронавирусы - 3-5%
энтеровирусы - 5-15%,
реовирусы - 1-3%.



Profiling acute respiratory tract infections





Jartti T, Jartti L, Peltola V, Waris M, Ruuskanen O (2008) Identification of respiratory viruses in asymptomatic subjects: Asymp Infect Dis J 27(12):1103–1107.

До 68% в респираторных образцах от бессимптомных детей были обнаружены респираторные вирусы

22 исследования, 3 Кокрановских обзора

Year	Season ^a	Number ^b	Age	Risk Group	Viral P	n (%)	Picorn	HRV
2011 [67]	Autumn, winter, spring	66	6 m–3 y	Healthy	28	(42%)		
2011 [99]	All year	34	<1 y	Healthy	8	(24%)		
		51	1–4 y	Healthy	7	(14%)		
		69	5–19 y	Healthy	9	(13%)		
2011 [95]	Winter	30	<1 y	Healthy	6	(18%)	0 (0%)	1 (3%)
							3 (9%)	2 (6%)
							0 (0%)	0 (0%)
							6 (18%)	2 (6%)
							0 (0%)	0 (0%)
		23	1–2 y	Healthy	4	(16%)	0 (0%)	0 (0%)
							0 (0%)	0 (0%)
							2 (8%)	0 (0%)
		97	2–6 y	Healthy	14	(15%)	1 (1%)	0 (0%)
							2 (2%)	1 (1%)
							0 (0%)	0 (0%)
							3 (3%)	3 (3%)
2010 [68]	All year	570	<2 y	Healthy	94	(17%)	20 (3.5%)	0 (0%)
							3 (0.5%)	0 (0%)
							8 (3.6%)	3 (0.6%)
							4 (1.8%)	
		436	<2 y	At risk	103	(24%)	37 (8.5%)	2 (0.5%)
							3 (1.8%)	6 (3.5%)
							2 (0.5%)	3 (1.8%)
2010 [98]	Autumn, winter	272	<3 y	Rural				
							3 (1.1%)	1 (0.4%)
2010 [97]	All year	57	<12 y	Rural				
							2 (4%)	
2010 [100]	All year	425	<3 y	At risk	140	(33%)	68 (16%)	18 (4%)
							29 (7%)	15 (4%)
							3 (1%)	13 (3%)
2009 [101]	Autumn, winter, spring	65	<7 y	Healthy	14	(22%)	2 (3%)	0 (0%)
							0 (0%)	0 (0%)
							5 (8%)	0 (0%)
2008 [102]	All year	116	<14 y	Healthy	11	(9.5%)	5 (4.3%)	2 (1.7%)
							1 (0.8%)	1 (0.8%)
							0 (0%)	0 (0%)
							0 (0%)	0 (0%)
2008 [112]	Autumn, winter, spring	100	≤3 y	Healthy				43 (43%)
2007 [103]	Autumn, winter, spring	269	1.5–9.3 y	Healthy	29	(11%)	7 (3%)	2 (1%)
							2 (1%)	1 (0%)
							1 (0%)	1 (0%)
2006 [96]	All year	456	<1 y	High risk of atopy	52	(11%)		
2006 [104]	All year ^c	410	1–9 y	Healthy	37	(9%)		
2004 [94]	NS	70	5 m	Healthy	12	(17%)		
		64	1 y	Healthy	18	(28%)		
		38	1.5 y	Healthy	10	(26%)		
		49	2 y	Healthy	7	(14%)		

В 27% случаев от бессимптомных здоровых детей выделено несколько респираторных вирусов в носоглотке в любой момент времени

Вирусные ассоциации
RSV – bocavirus
Риновирус - аденовирус

В 94% случаев бессимптомного вирусонительства были обнаружены колонизирующие бактерии. Чаще всего *M. catarrhalis* and *H. influenzae*

^aRelated to geographical area.
^bNumber of samples tested.
^cStratified for season.
^dPicornavirus general.
M, months of age; Y, years of age; HRV, human rhinoviruses; EV, enteroviruses; AdV, adenoviruses; HBoV, human bocavirus; PIV, para-influenza viruses; NS, not specified.
doi:10.1371/journal.ppat.1003057.t002



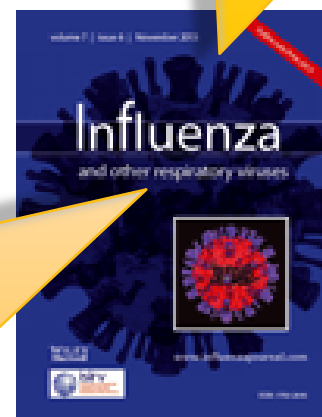
Грипп А и множественные инфекции с другими респираторными вирусами и риск госпитализации и смертности

Influenza A viruses dual and multiple infections with other respiratory viruses and risk of hospitalisation and mortality

Edward Goka¹, Pamela Vallely², Kenneth Mutton^{1,2} and Paul Klapper^{1,2}

Article first published online: 19 OCT 2012

Issue

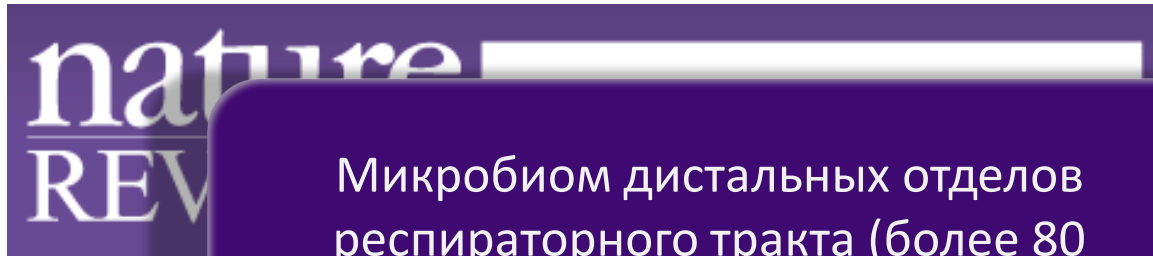


Influenza and Other Respiratory Viruses
Volume 7, Issue 6, pages 1079–1087, November 2013

**Ко-инфекция
Грипп А и
РСВ и AdV**

в 3,3 раза увеличивает
риск госпитализации с
необходимостью
интенсивной терапии

Ургентная комбинация респираторных вирусов



Микробиом дистальных отделов респираторного тракта (более 80 бактериальных геномов).

Host–microorganism interactions in lung diseases

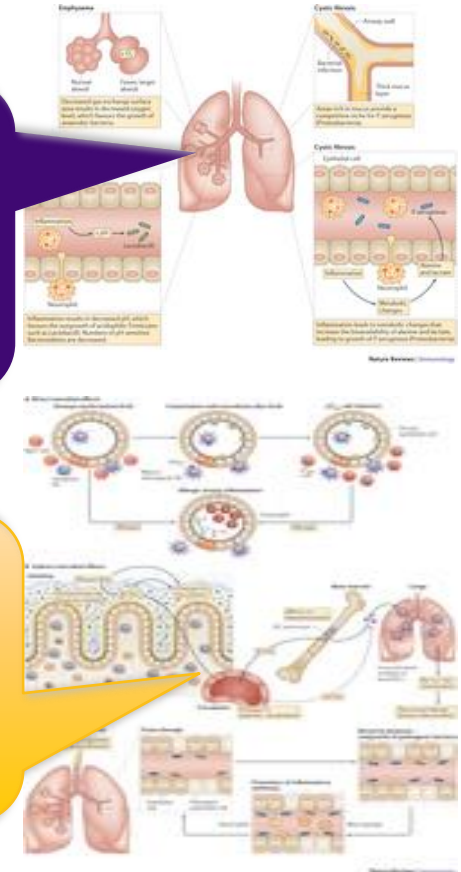
Benjamin

Affiliation

Nature Reviews

Published online 25 November 2014

...дисбактериоз микробиоты дыхательных путей может лежать в основе восприимчивости (прогрессирования) и хронизации заболеваний легких.





- Всего в ТБД идентифицировано более 1000 бактериальных геномов.
- Паттерны-микробиоты хроническ. респираторной патологии

Host–microorganism interactions in lung diseases

Benjamin J. Marsland & Eva S. Gollwitzer

Affiliations | Corresponding author

Nature Reviews Immunology **14**, 827–835 (2014) | doi:10.1038/nri3769

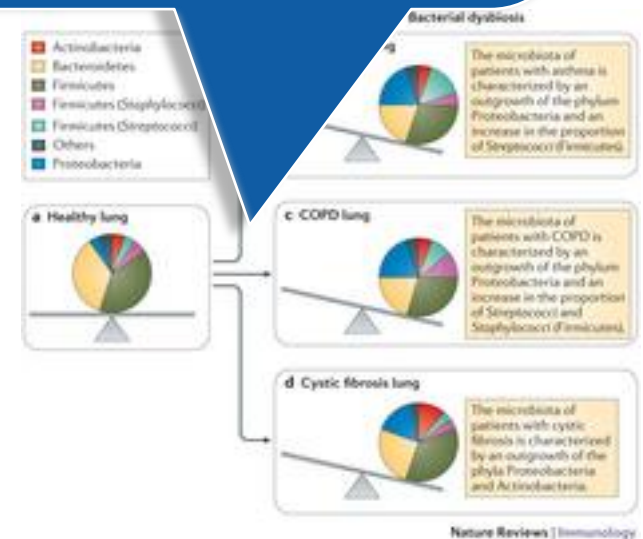
Published online 25 November 2014

Opinion article. We summarize current knowledge of the airway microbiota and outline how host–microorganism interactions in the lungs and other tissues might influence respiratory health and disease.

The respiratory tract has a surface area of approximately 75 m² and is directly exposed to the environment. In fact, topographically, the airways are external to our body, and thus are a primary site of exposure to environmental microorganisms. Until recently, however,

maturation and disease development. This is similar to the approach that has been taken for many years in intestinal research and we believe that similar principles will be shown to apply to host–microorganism relationships in the lungs as in the gut. Indeed, immu-

range from 4.5 log copy numbers per ml¹⁵ to 8.25 log copy numbers per ml¹ in the bronchoalveolar lavage fluid, whereas lung tissue samples show between 10 and 100 bacterial cells per 1,000 human cells⁴. The healthy lung microbiota is thought to be diverse, and a recent study indicated that the airway microbiota reaches a greater diversity more rapidly than the intestinal microbiota following birth¹⁶. The





«Межличностная коммуникация» вирусов и бактерий



Производство перекиси водорода H_2O_2 устраняет конкурентов

Нейтрофил (комплеммент)-опосредованные убийства «конкурентов»

«Совместное» производство компонентов наружной мембраны, инактивация комплемента C3

Конкурентное ингибирование фосфорилхолина (PhC), сиаловой кислоты (SA)



Вирусно-бактериальное взаимодействие на дыхательной поверхности респираторного эпителия

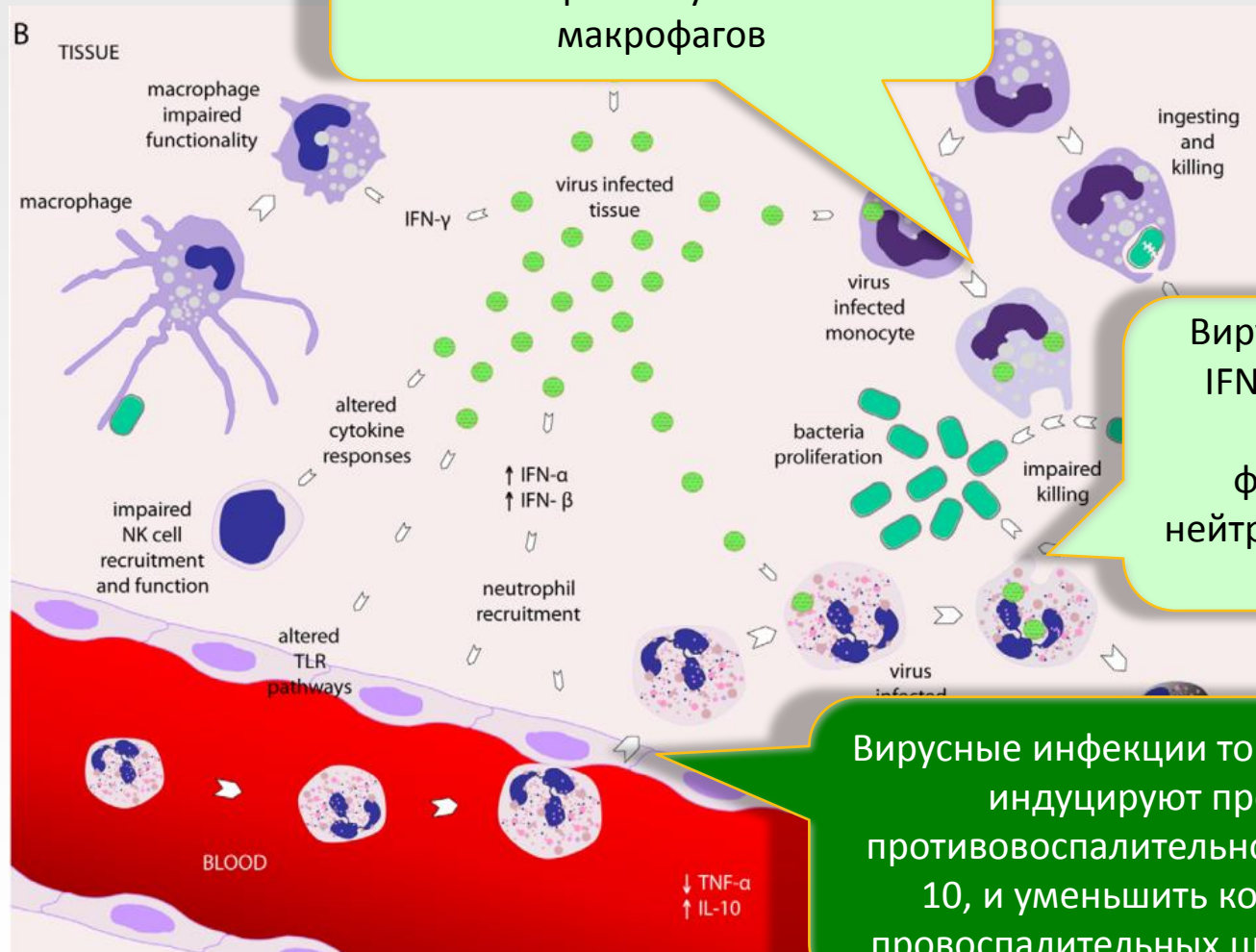


Вирусы стимулируют регуляцию рецепторов для бактериальной колонизации и повреждения поверхности

Вирусы стимулируют регуляцию различных рецепторов, необходимых для бактериальной адгезии, **КОЛОНИЗАЦИЮ** и репликацию

Вирусы стимулируют регуляцию различных рецепторов, необходимых для бактериальной адгезии, **КОЛОНИЗАЦИЮ**, **РЕПЛИКАЦИЮ** и **ТРАНСЛОКАЦИЮ** бактерий, предоставляя доступ к бактериальным рецепторам

Патогенетические механизмы вирусно-бактериальных респираторных инфекций



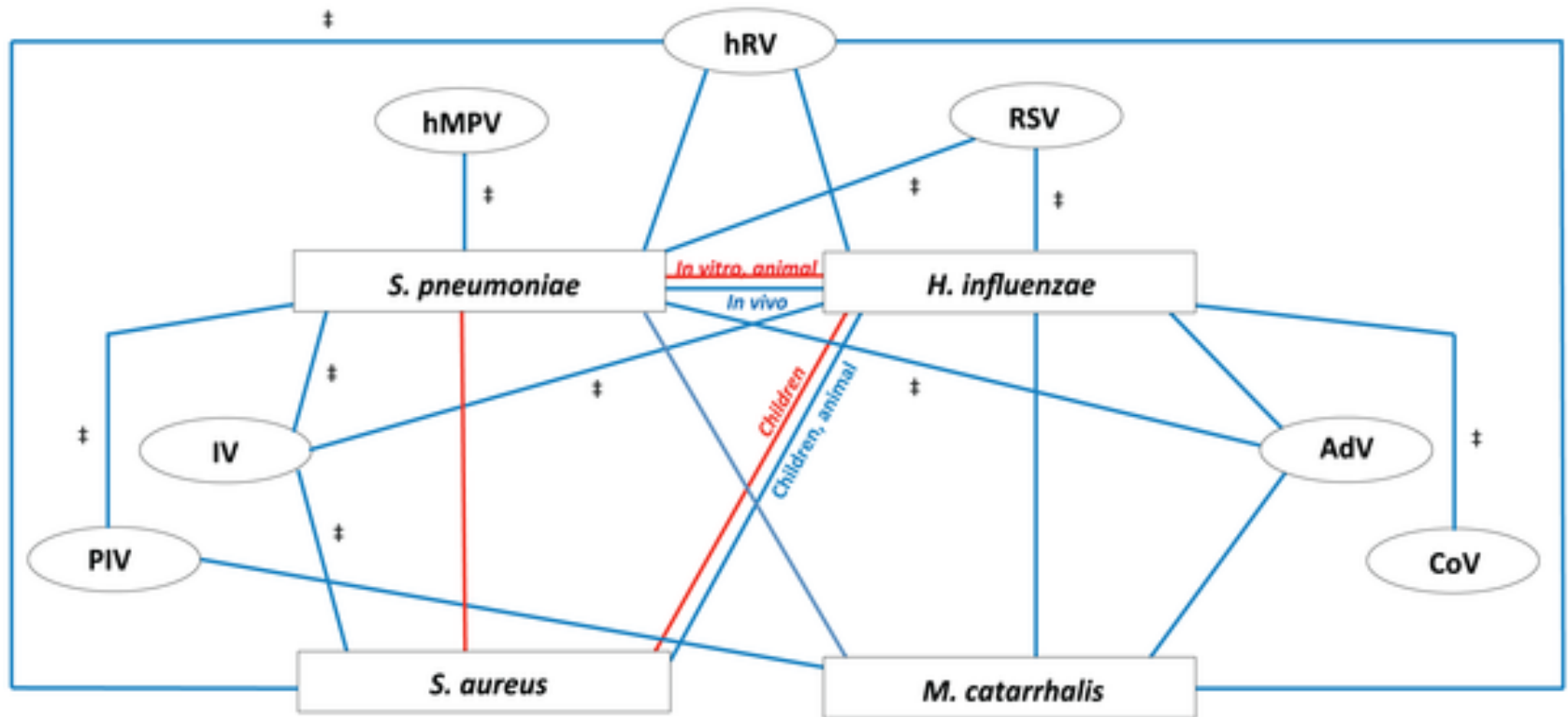
IFN- γ негативно влияет на антибактериальную активность макрофагов

Вирус-индуцированные IFN- α и IFN- β снижают активацию и функциональность нейтрофилов и приводят к их апоптозу

Вирусные инфекции тормозят TLR пути, индуцируют продукцию противовоспалительного цитокина IL-10, и уменьшить концентрацию провоспалительных цитокинов TNF- α



Модель взаимодействия вирусных и бактериальных инфекций (синергизм, антагонизм)

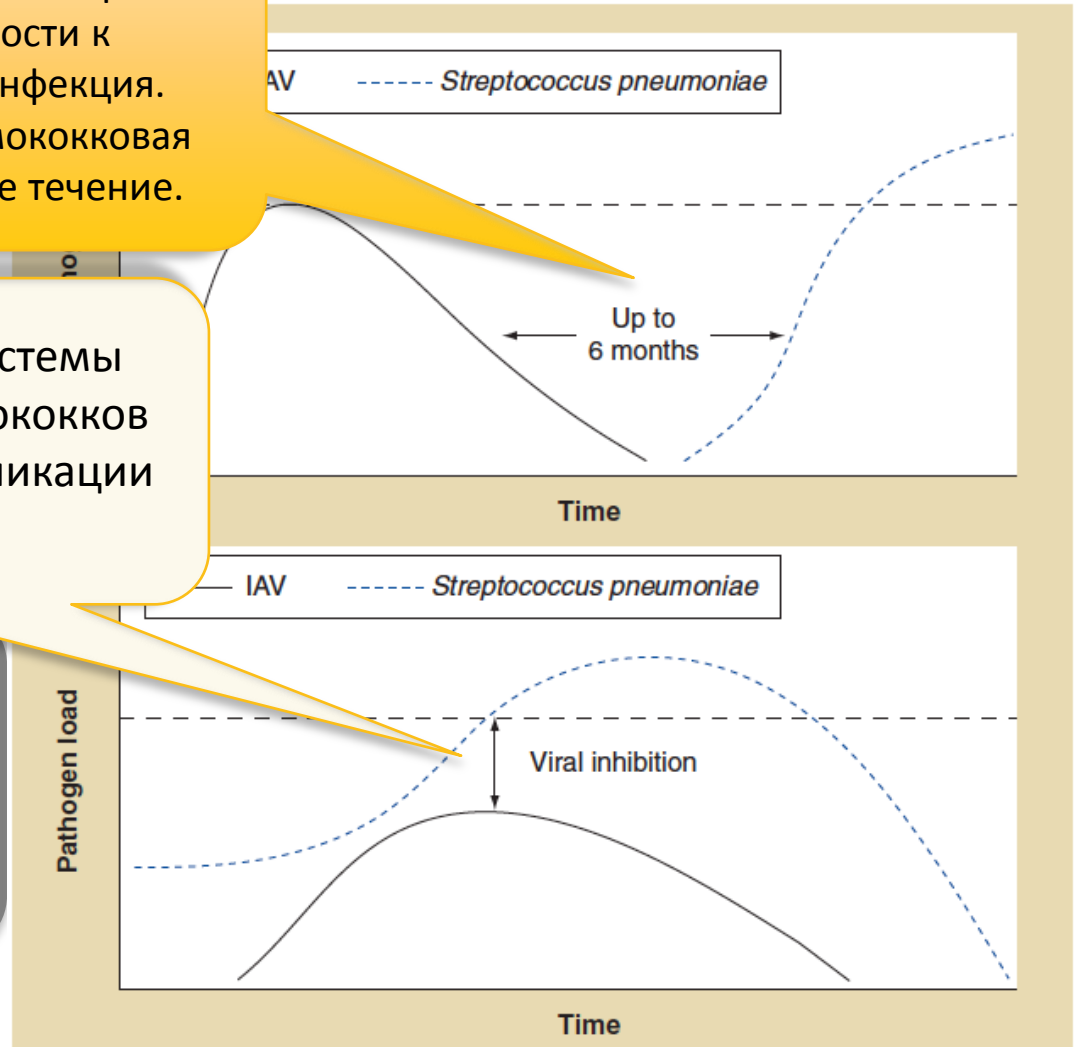




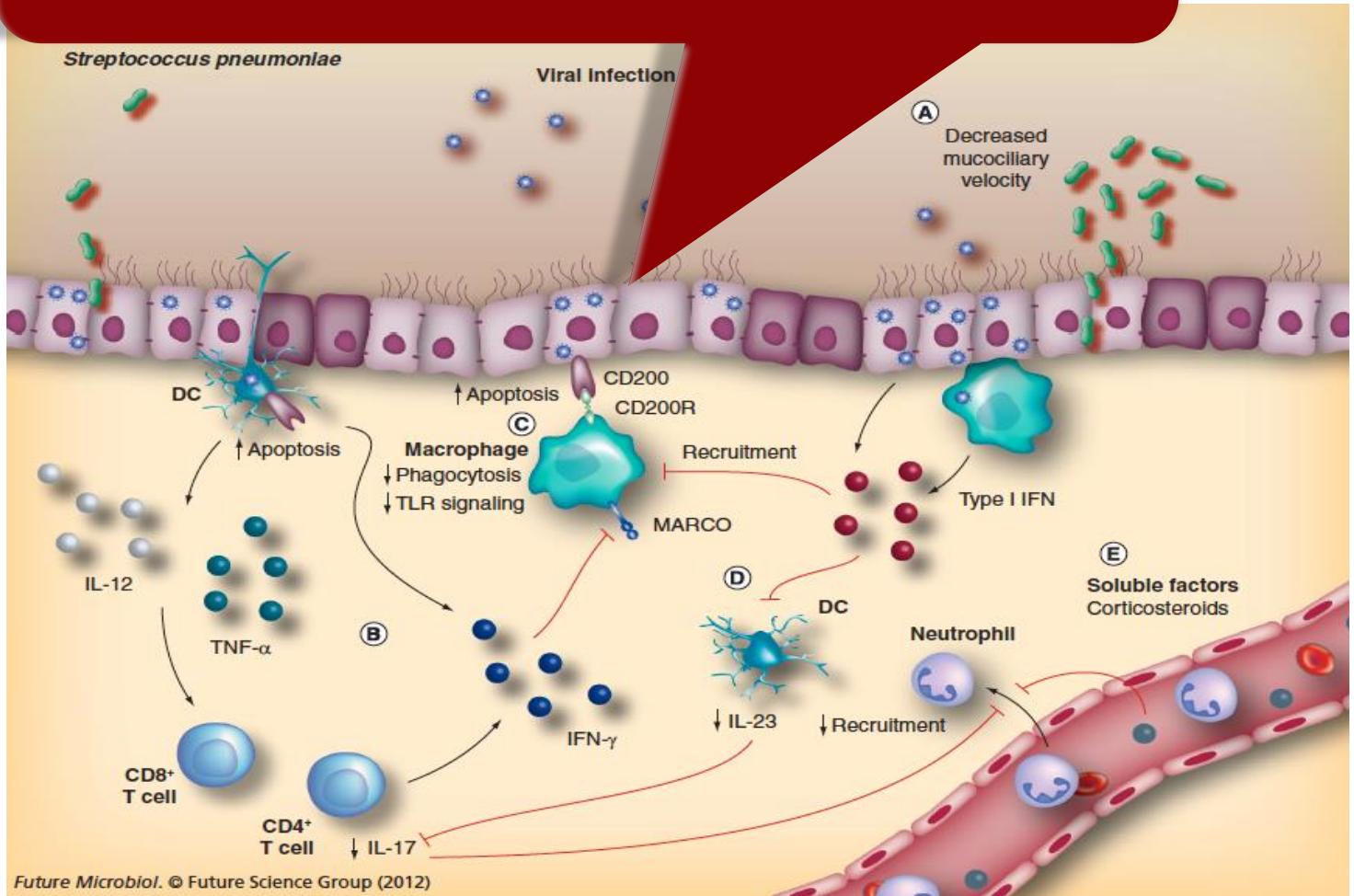
Первичное инфицирование вирусом гриппа создает окно восприимчивости к вторичной пневмококковой инфекции. **У детей** пост-гриппозная пневмококковая инфекция приобретает тяжелое течение.

Стимуляция иммунной системы путем колонизации пневмококков может препятствовать репликации вируса.

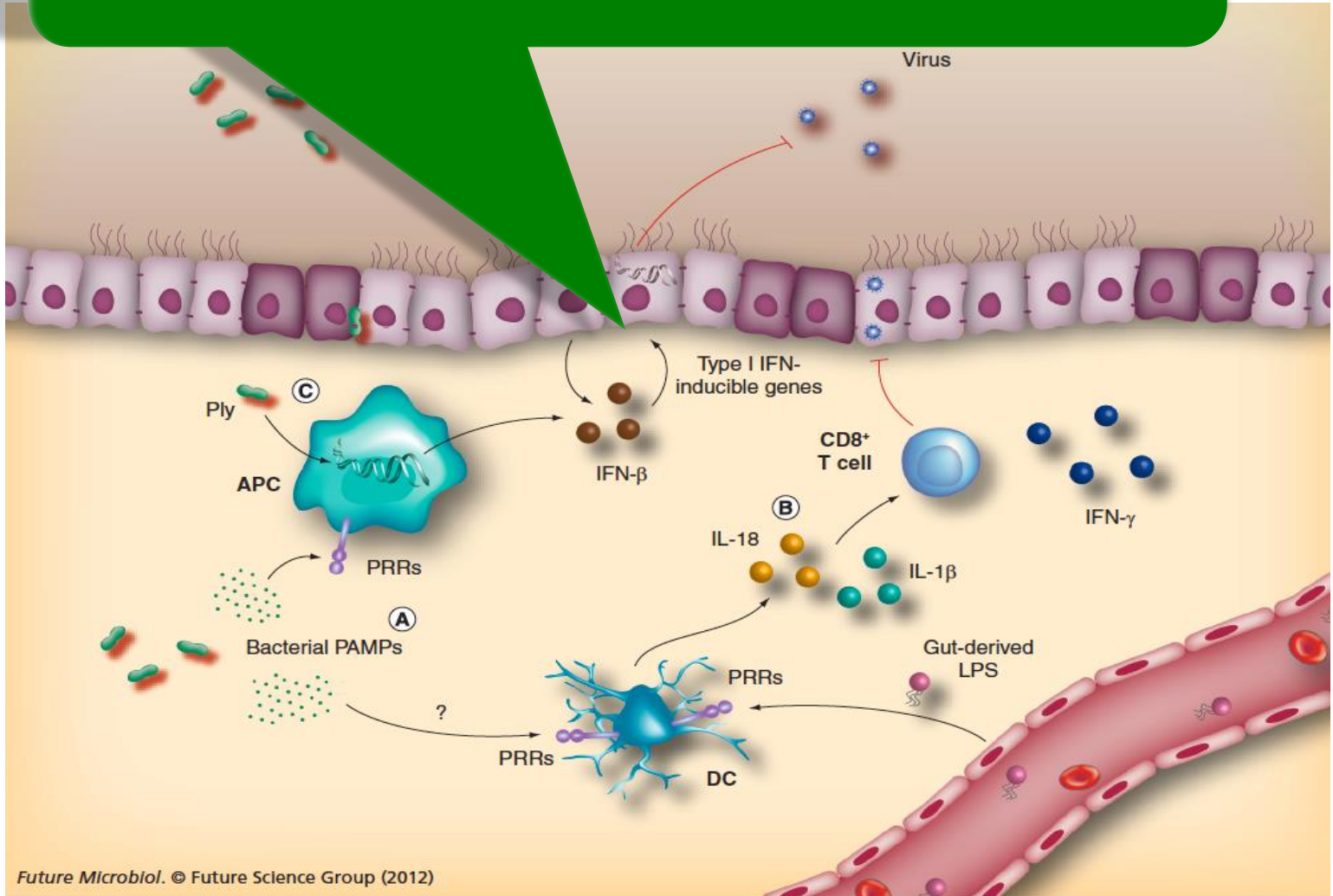
Взаимодействие между пневмококком и вирусом гриппа: взаимовыгодные отношения?



Апоптоз иммунных клеток увеличивает экспрессию CD200, что приводит к устойчивой десенсибилизации к бактериальным раздражителям, активации интерферонов эпителиальных клеток и ингибированию PMNs и макрофагов через Ил-23-Ил-17

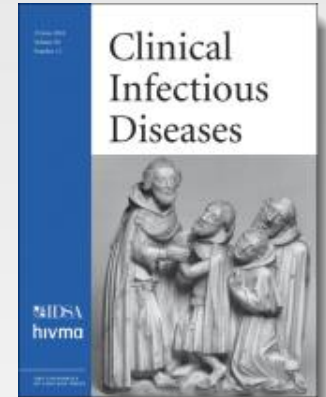


Во время колонизации, аутолиза пневмококка происходит активация IL-1 β и IL-18, стимуляция Т-клеточных ответов и производство IFN





Dynamic viral upper respiratory infection



ВИРУСНАЯ
ИНФЕКЦИЯ

ГР+ ИНФЕКЦИЯ

ГР- бактерии

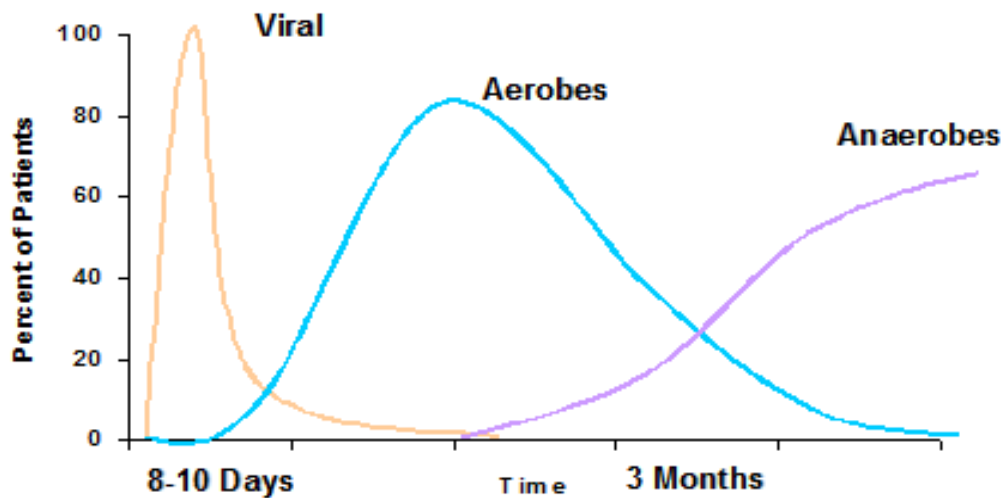
Микотическая инфекция,
колонизация ?

БАКТЕРИАЛЬНЫЙ МАРШ



Эволюция инфекционного синусита

Viral and Bacterial Causes of Sinusitis





Expert Rev. Anti Infect. Ther. 10(8), (2012)

Table 1. Studies reporting pulmonary bacterial coinfection in infants and children.

Study (year)	Study period/ study design	Study group (country)	Patients studied for coinfection ^a	Coinfection incidence (bacteriology method)	Viral pathogen(s) (in entire study group)	Coinfection bacteria	Ref.
Michelow et al. (2004)	1999–2000/ prospective	Hospitalized for community-acquired pneumonia (USA)	154	23% (sputum – bacterial culture or serology – direct fluorescent antibody)	Viruses in mixed coinfection group: influenza A 16, influenza B 6, parainfluenza 1–3 12, RSV 11, adenovirus 9, rhinovirus 2, enterovirus 1	<i>Streptococcus pneumoniae</i> 12, <i>Streptococcus pyogenes</i> 2, <i>Staphylococcus aureus</i> 2, <i>Staphylococcus milleri</i> 1, <i>Chlamydia pneumoniae</i> 7, <i>Mycoplasma pneumoniae</i> 6, <i>Mycobacterium tuberculosis</i> 1	[11]
Resch et al. (2007)	2001–2005/ retrospective	Hospitalized with RSV bronchiolitis (Austria)	428	1% (tracheal smears – bacterial culture)	RSV 428	<i>Haemophilus influenzae</i> 1, <i>S. aureus</i> 1, <i>Streptococcus</i> spp. 1, <i>Haemophilus hemolyticus</i> 1	[15]
Nascimento- Carvalho et al. (2008)	2003–2005/ prospective	Hospitalized for community-acquired pneumonia (Brazil)	184	28% (serology – direct fluorescent antibody or PCR)	Rhinovirus 21%, parainfluenza 1–3 17%, RSV 15%, influenza A + B 9%, enterovirus 5%, adenovirus 3%	Bacteria in whole study group: <i>S. pneumoniae</i> 21%, <i>H. influenzae</i> 8%, <i>M. pneumoniae</i> 8%, <i>Chlamydia trachomatis</i> 4%, <i>Moraxella catarrhalis</i> 3%, <i>C. pneumoniae</i> 1%	[19]
Hishiki et al. (2011)	2005–2007/ prospective	Hospitalized with RSV bronchiolitis (Japan)	188	44% (sputum – bacterial culture)	RSV 188	<i>H. influenzae</i> 36, <i>S. pneumoniae</i> 30, <i>M. catarrhalis</i> 24, two bacteria 10	[12]
Reed et al. (2009)	2006–2007/ retrospective	Hospitalized with influenza infection (USA)	67	30% (respiratory 70% + 20% – bacterial)	Influenza A 25, influenza B 29, influenza not typed 11	<i>S. aureus</i> 7 (MRSA 4 of 7), <i>Pseudomonas</i> 2, <i>H. influenzae</i> 1, <i>S. pyogenes</i> 1, <i>Klebsiella</i> 1, <i>Alicycobacillus xylosoxidans</i> 1	[13]
Randolph et al. (2004)	1990–2002/ retrospective	'Previously healthy' infants admitted to PICU with RSV infection (USA)	47		RSV 47	<i>M. catarrhalis</i> , <i>H. influenzae</i> , <i>S. pneumoniae</i>	[7]
van Woensel et al. (2001)	1992–2000/ retrospective	Admitted to PICU with RSV bronchiolitis (The Netherlands)					
Kneyber et al. (2005)	1996–2001/ retrospective	Ventilated with bronchiolitis (The Netherlands)					

^aNumber of patients in the study in whom pulmonary bacterial coinfection was identified.
BAL: Bronchoalveolar lavage sample; CONS: Coagulase-negative staphylococci.

Бактериальная ко-инфекция у госпитализированных наблюдалась в 17-39% и характерна для гриппа и РСВ.

Значимы вопросы инфекционного контроля

Nature Reviews Microbiology **7**, 887-894 (December 2009)

What are the consequences of the disappearing human microbiota?

Martin J. Blaser & Stanley Falkow

Каковы последствия нарушения микрофлоры человека?

Microbial Interactions in the Respiratory Tract

Murphy, Timothy F. MD*†; Bakaletz, Lauren O. MD, PhD‡§; Smeesters

Pediatric Infectious Disease Journal:
October 2009 - Volume 28 - Issue 10 - pp S121-S126
doi: 10.1097/INF.0b013e3181b6d7ec
Supplement

Микробные взаимодействия в респираторном тракте

«Индукцированный дисбаланс в респираторном микробиоме способствует появлению нового бактериального или вирусного возбудителя, трансмиссии нескольких потенциальных патогенных бактерий или вирусной ко-инфекции...»



Двунаправленный Синергизм



Sajjan US, Jia Y, Newcomb DC, Bentley JK, Lukacs NW, et al. (2006) potentiates airway epithelial cell responses to rhinovirus by increasing expression. FASEB J 20(12):2121–2123

И. Influenzae стимулирует экспрессию ICAM-1 и TLR3 на респираторном эпителии, способствуя развитию риновирусной инфекции

Microbiol Infect 17(12):1840–1844

Пневмококк существенно повышает восприимчивость респираторного эпителия к человеческому метапневмовирусу

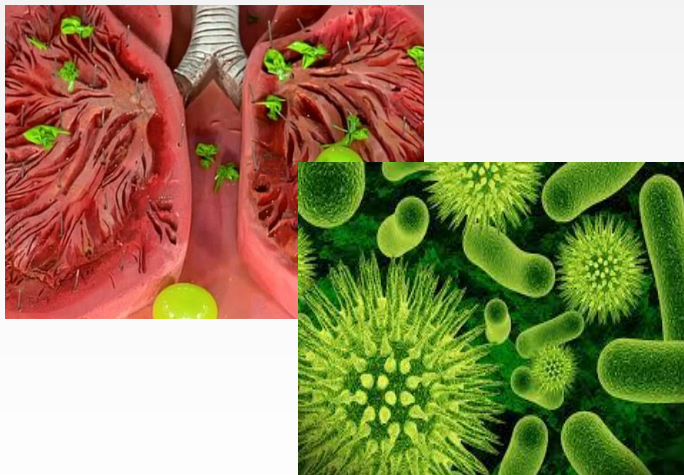
554(8855):245–252.

Трансмиссия вирусом на 54% эффективнее если микробиота разбалансирована антибиотиками.



«ОТ ВИРУСА К БАКТЕРИИ»

«Вирусы «вспахивают» и истощают клеточный иммунитет приводя к бактериальной контаминации и бактериальной патологии...» *



*V. Palladie

«ВИРУС + АБП = БАКТЕРИИ»

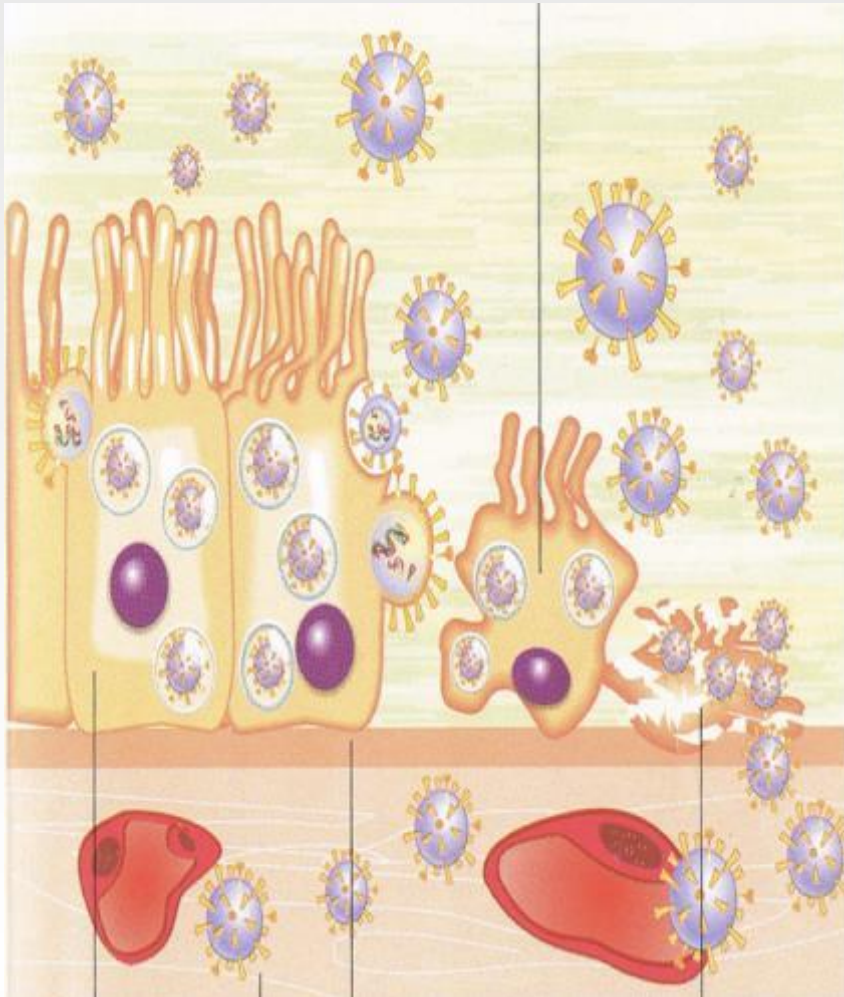
Теория дисмикробизма. Развитие дисбиоза на фоне антибиотикотерапии с последующим развитием бактериальной патологии **



**T. F. Murphy



* Клинические проявления ОРИ зависят от:



- Вирулентности вируса.
- Тропности к определенным участкам слизистой, морфологическим элементам.
- Ко-инфекции
- Места внедрения.
- Реактивности организма.
- Скорости элиминации.
- Лечения.
- Вакцинации.



Floyd W. Denny, Jr. "**The Clinical Impact of Human Respiratory Virus Infections**", American Journal of Respiratory and Critical Care Medicine, Vol. 152, No. 42 (5), pp. S4-S12.

Jeffrey J VanWormer, Maria E Sundaram, Jennifer K Meece and Edward A Belong «**A cross-sectional analysis of symptom severity in adults with influenza and other acute respiratory illness in the outpatient setting**». BMC Infectious Diseases 14, 231/Jan-2014

Heikkinen T, Jarvinen A: **The common cold**. Lancet 2003, 361:51-59

Widmer K, Zhu Y, Williams JV, Griffin MR, Edwards KM, Talbot HK: **Rates of hospitalizations for respiratory syncytial virus, human metapneumovirus, and influenza virus in older adults**. J Infect Dis 2012, 206(1):56-62

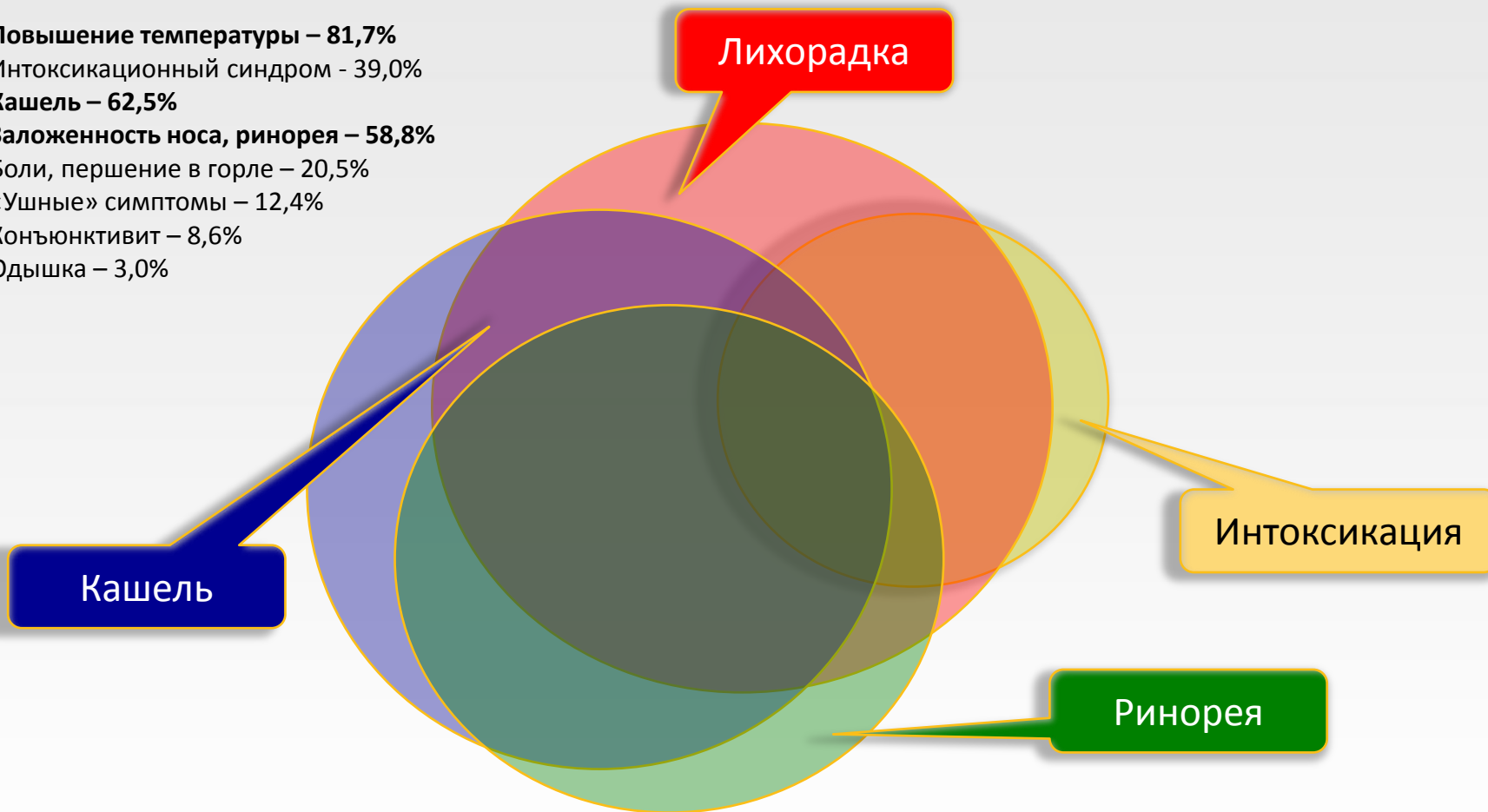
Turner RB: **Epidemiology, pathogenesis, and treatment of the common cold**. Ann Allergy Asthma Immunol 2007, 78:531-539.



Клинические паттерны ОРИ



- Повышение температуры – 81,7%
- Интоксикационный синдром - 39,0%
- Кашель – 62,5%
- Заложенность носа, ринорея – 58,8%
- Боли, першение в горле – 20,5%
- «Ушные» симптомы – 12,4%
- Конъюнктивит – 8,6%
- Одышка – 3,0%



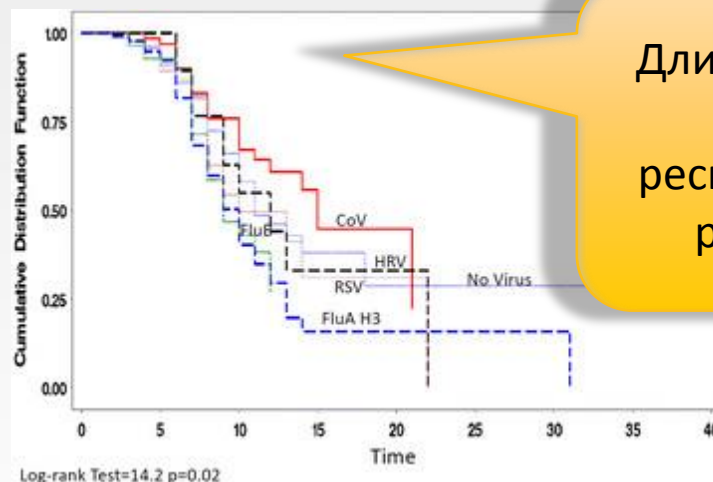


Zimmerman et al. BMC Infectious Diseases (2015) 15:87.

Influenza and other respiratory virus infections in outpatients with medically attended ARI

Table 3. Relationship of demographic characteristics and symptoms of patients presenting with medically attended acute respiratory infections to viral etiology in multinomial regression analyses, controlling for age and self-reported health status.

	Virus type				Adjusted P value
	CoV (n = 65)	HRV (n = 33)	RSV (n = 102)	FluA (n = 36)	
Categorical variables, odds ratio (95% confidence interval)					
Sex, white versus other	0.84 (0.63-1.12)	1.12 (0.77-1.62)	1.28 (0.95-1.72)	0.80 (0.54-1.17)	1.03 (0.79-1.46)
Age group*					
1-9 years†	1.37 (0.90-2.06)	1.60 (1.05-2.40)	1.39 (0.98-1.96)	1.44 (0.97-2.36)	1.91 (1.26-2.90)
10-49 years versus ≥50 years	1.12 (0.78-1.60)	0.92 (0.53-0.88)	0.99 (0.73-1.35)	0.60 (0.36-1.00)	0.63 (0.41-0.97)
Household members <18 years, %†					
1 versus 0‡	0.73 (0.42-1.28)	0.88 (0.54-1.43)	1.16 (0.74-1.82)	1.46 (0.77-2.79)	1.32 (0.74-2.33)
2 versus 0‡	0.96 (0.54-1.68)	0.88 (0.54-1.42)	0.97 (0.61-1.42)	0.64 (0.35-1.18)	1.06 (0.60-1.74)
3 versus 0‡	0.86 (0.47-1.55)	0.73 (0.37-1.40)	0.74 (0.43-1.28)	1.13 (0.54-2.36)	0.70 (0.34-1.48)
Household members ≥18 years, %†					
0 versus 0‡	0.92 (0.61-1.39)	1.00 (0.63-1.60)	0.85 (0.59-1.22)	0.71 (0.40-1.27)	0.87 (0.54-1.41)
1 versus 0‡	1.06 (0.63-1.72)	0.79 (0.43-1.43)	1.09 (0.71-1.68)	1.09 (0.59-2.01)	2.07 (1.23-3.50)
2 versus 0‡	1.20 (0.72-1.97)	1.03 (0.60-1.83)	1.43 (0.95-2.17)	0.81 (0.40-1.64)	1.08 (0.61-1.92)
Subjective nasal status (range, 1 = low to 9 = high)					
1 versus 0‡	0.71 (0.39-1.28)	1.13 (0.69-1.90)	0.75 (0.45-1.23)	1.69 (0.80-3.00)	0.95 (0.50-1.82)
2 versus 0‡	0.94 (0.59-1.47)	1.14 (0.68-1.90)	0.97 (0.66-1.43)	0.68 (0.35-1.33)	1.00 (0.60-1.68)
3 versus 0‡	1.60 (1.08-2.40)	0.61 (0.31-1.20)	1.36 (0.82-2.16)	0.75 (0.35-1.63)	1.33 (0.77-2.28)
Health indicators					
Smoker versus non-smoker	0.94 (0.43-2.08)	0.90 (0.28-2.89)	1.03 (0.53-2.02)	0.93 (0.30-2.62)	0.60 (0.19-1.90)
Household smoking versus no household smoking	1.16 (0.62-2.20)	0.78 (0.34-1.79)	1.15 (0.66-2.02)	0.64 (0.23-1.70)	0.92 (0.43-1.93)
Asthma diagnosis versus no asthma diagnosis	1.28 (0.72-2.30)	0.75 (0.33-1.63)	0.94 (0.53-1.69)	0.81 (0.35-1.86)	0.94 (0.48-1.86)
Received 2011-12 influenza vaccine	0.89 (0.51-1.55)	0.96 (0.52-1.76)	1.00 (0.62-1.61)	0.99 (0.48-2.00)	2.53 (1.22-5.26)
Self-rated health status,** reference = excellent					
Fair/poor	1.08 (0.60-2.00)	0.23 (0.03-1.90)	1.06 (0.63-1.78)	0.31 (0.07-1.43)	0.69 (0.30-1.57)
Good	1.30 (0.84-2.00)	0.91 (0.42-1.97)	1.26 (0.86-1.84)	1.24 (0.58-2.63)	1.16 (0.69-1.93)
Very good	0.87 (0.43-1.80)	1.62 (0.84-3.07)	0.68 (0.45-0.97)	1.79 (0.91-3.53)	0.94 (0.38-2.32)
Symptoms of ARI					
Cough††	2.5 (0.95-6.58)	10.6 (4.1-29.1)	2.9 (1.04-8.00)	-	3.6 (1.02-13.1)
Nasal congestion	0.89 (0.37-2.25)	0.94 (0.46-1.91)	0.92 (0.53-1.61)	1.16 (0.48-2.88)	1.14 (0.55-2.38)
Hoarse	0.95 (0.50-1.82)	2.28 (1.16-4.48)	1.17 (0.72-1.90)	6.62 (1.94-22.8)	1.03 (0.50-2.02)
Loss of voice	4.66 (1.80-12.3)	1.42 (0.58-3.97)	3.02 (1.51-6.09)	2.24 (0.94-6.02)	1.93 (0.90-4.16)
Shortness of breath	1.26 (0.70-2.20)	1.90 (0.71-5.06)	1.11 (0.68-1.83)	1.97 (0.85-4.60)	1.69 (0.89-3.08)
Loss of smell	0.76 (0.41-1.39)	6.49 (2.26-17.9)	0.71 (0.41-1.26)	0.69 (0.35-1.40)	0.71 (0.38-1.31)
Wheezing	1.44 (0.87-2.35)	2.07 (1.07-3.94)	1.36 (0.69-2.23)	1.89 (0.75-5.37)	2.07 (1.11-3.87)
Continuous Variables, odds ratio (95% confidence interval)**					
Age† (units = 5)	0.95 (0.89-1.01)	0.95 (0.88-1.02)	0.94 (0.88-0.99)	0.97 (0.90-1.04)	0.92 (0.86-0.98)
Self-rated health status	1.22 (0.62-2.40)	0.66 (0.40-1.10)	1.02 (0.69-1.50)	1.9 (1.16-3.04)	0.96 (0.76-1.20)
Rating of health at enrollment	0.99 (0.62-1.61)	0.99 (0.61-1.68)	1.02 (0.65-1.60)	0.89 (0.61-0.98)	0.93 (0.66-1.30)
Days from illness onset to enrollment (n = 5)	0.98 (0.84-1.15)	1.07 (0.90-1.27)	1.07 (0.93-1.22)	0.99 (0.81-1.22)	1.06 (0.89-1.26)
Days of exercise per month (n = 5)	0.91 (0.74-1.10)	1.00 (0.81-1.23)	0.94 (0.80-1.10)	0.68 (0.47-0.96)	1.01 (0.87-1.18)



Длительность клинических проявлений при респираторных инфекциях различной этиологии



American Family Physician[®]



Overview

- [AAP Releases Practice Guideline on Diagnosis, Management, and Prevention of Bronchiolitis \[Practice Guidelines\] \(04/15/2015\)](#)
- [AAP Releases Guideline on Diagnosis and Management of Acute Bacterial Sinusitis in Children One to 18 Years of Age \[Practice Guidelines\] \(04/15/2014\)](#)
- [IDSA Updates Guideline for Managing Group A Streptococcal Pharyngitis \[Practice Guidelines\] \(09/01/2013\)](#)
- [IDSA Releases Guidelines for Management of Acute Bacterial Rhinosinusitis \[Practice Guidelines\] \(03/15/2013\)](#)
- [Acute Rhinosinusitis in Adults \(05/01/2011\)](#)
- [Croup: An Overview \(05/01/2011\)](#)
- [Diagnosis and Treatment of Acute Bronchitis \(12/01/2010\)](#)
- [Diagnosis and Treatment of Streptococcal Pharyngitis \(03/01/2009\)](#)
- [Pharyngitis \(03/15/2004\)](#)
- [Diagnosis and Management of Group A Streptococcal Pharyngitis \[Practice Guidelines\] \(02/15/2003\)](#)
- [Guidelines for the Diagnosis and Management of Rhinosinusitis in Adults \[Practice Guidelines\] \(12/01/2007\)](#)

Screening and Diagnosis

- [Diagnosis of Streptococcal Pharyngitis \[Point-of-Care Guides\] \(06/15/2014\)](#)
- [Risk Stratification of Children with Bronchiolitis \[Point-of-Care Guides\] \(08/01/2012\)](#)
- [Usefulness of Procalcitonin Measurement in Reducing Antibiotic Use and Identifying Serious Bacterial Illness \[AFP Journal Club\] \(07/15/2011\)](#)

Prevention

- [AAP Updates Guidelines on Immunoprophylaxis for RSV Infection \[Practice Guidelines\] \(09/01/2010\)](#)

Treatment

- [Bronchodilators for Bronchiolitis \[Cochrane for Clinicians\] \(11/01/2014\)](#)
- [Intranasal Corticosteroids for Acute Bacterial Sinusitis \[Cochrane for Clinicians\] \(09/01/2014\)](#)
- [Antibiotics for Sore Throat \[Cochrane for Clinicians\] \(07/01/2014\)](#)
- [Corticosteroids for the Treatment of Sore Throat \[Cochrane for Clinicians\] \(01/01/2014\)](#)
- [Treatments for Symptoms of the Common Cold \[FPIN's Clinical Inquiries\] \(12/15/2013\)](#)
- [Oral Antihistamine/Decongestant/Analgesic Combinations for the Common Cold \[Cochrane for Clinicians\] \(11/01/2012\)](#)
- [Antibiotic Use in Acute Upper Respiratory Tract Infections \(11/01/2012\)](#)
- [Treatment of the Common Cold in Children and Adults \(07/15/2012\)](#)
- [Common Cold \[Clinical Evidence Handbook\] \(12/15/2011\)](#)
- [Antibiotics for Viral Upper Respiratory Tract Infections in Children \[FPIN's Clinical Inquiries\] \(03/15/2011\)](#)
- [Respiratory Syncytial Virus Infection in Children \(01/15/2011\)](#)
- [Saline Nasal Irrigation for Upper Respiratory Conditions \(11/15/2009\)](#)
- [Antibiotics for Acute Maxillary Sinusitis \[Cochrane for Clinicians\] \(05/01/2009\)](#)
- [Sinusitis \(Acute\) \[Clinical Evidence Handbook\] \(02/15/2009\)](#)
- [Radiologic Imaging in the Management of Sinusitis \(11/15/2002\)](#)
- [AAP Issues Recommendations for the Management of Sinusitis in Children \[Practice Guidelines\] \(03/15/2002\)](#)
- [Bronchitis \(Acute\) \[Clinical Evidence Handbook\] \(08/01/2004\)](#)
- [Antihistamines for the Common Cold \[Cochrane for Clinicians\] \(08/01/2004\)](#)
- [Upper Respiratory Tract Infection \[Clinical Evidence Handbook\] \(12/01/2002\)](#)
- [Should We Prescribe Antibiotics for Acute Bronchitis? \[Cochrane for Clinicians\] \(07/01/2001\)](#)

Editorials and Letters

- [Appropriate Antibiotic Use: Family Physicians Have the Power of the Pen \[Editorials\] \(11/01/2012\)](#)
- [Avoiding Sore Throat Morbidity and Mortality: When Is It Not "Just a Sore Throat?" \[Editorials\] \(01/01/2011\)](#)



Критерии антибиотикотерапии ОРИ (бактериальной инфекции)

- **Длительная, более 3 дней лихорадка;**
- Появление слизисто-гнойного отделяемого;
- Одышка без бронхообструкции;
- Асимметрия хрипов;
- Наличие лейкоцитоза, нейтрофилеза со сдвигом влево.

?



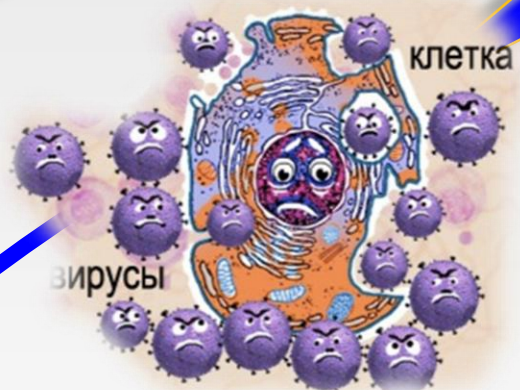
Патогенез и симптоматика ОРИ



Инфекционная нагрузка

Лихорадка

Респираторные СИМПТОМЫ



Размножение, персистенция инфекционного агента

Элиминация, гибель возбудителя

Регрессия воспаления, разрешение симптомов, реконвалесценция



Этапы течения вирусной респираторной патологии



Интоксикационный синдром

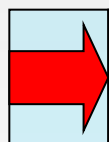
«Местные» симптомы
Симптомы осложнений

«Местные» симптомы

Астенический синдром
Симптомы ятрогении

Астенический синдром

Симптомы ятрогении



2-8 дней

5-14 дней

0-7 дней

Продром

Острый
воспалительный
период

Период регрессии
воспаления и
восстановления
слизистой

Период
формирования
иммунитета и
астении



РИНО-ВИРУСНАЯ инфекция

Пикорнавирус
100 серотипов

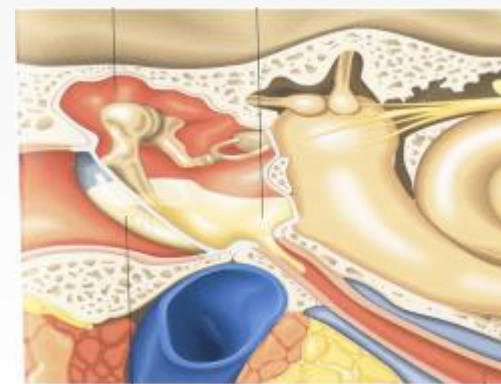
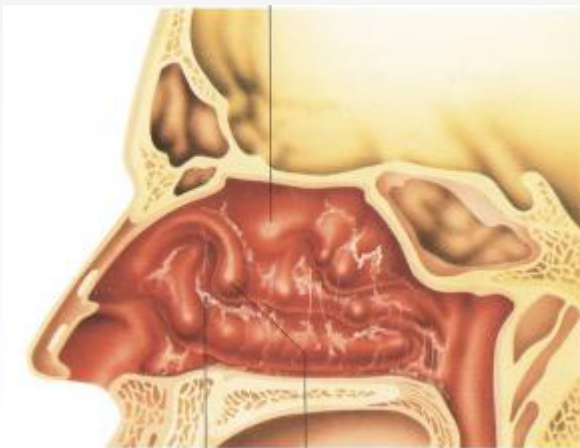


ЛИХОРАДКА – 1-3 дня, слабовыраженная

Общая длительность – 5-7 дней

Осложнения – синусит, отит

Клинические проявления - **РИНИТ**



Floyd W. Denny, Jr., 2012



АДЕНО-ВИРУСНАЯ инфекция

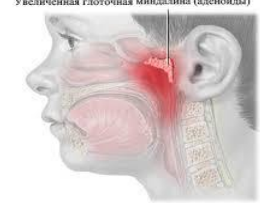
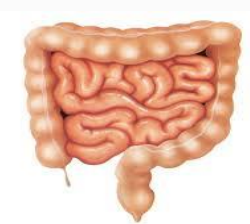
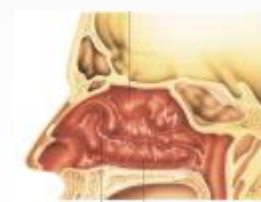
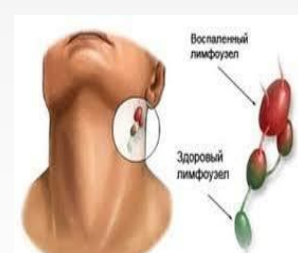
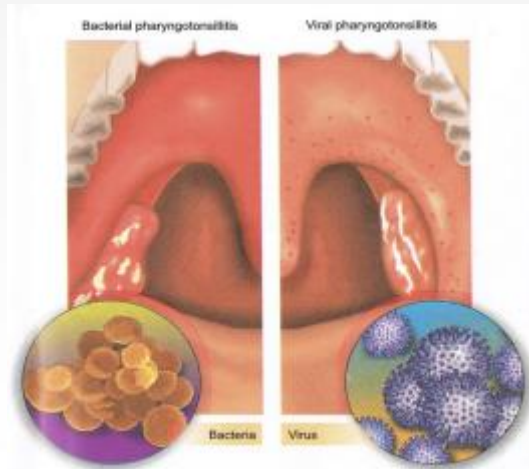
32 типа
в т.ч. РСF*



ЛИХОРАДКА – до 6-14 дней,
выраженная, часто двухволновая
Общая длительность – до 2-3 недель
Осложнения – пневмония

**Клинические проявления – тонзилофарингит,
ринит, аденопатия, конъюнктивит, энтерит**

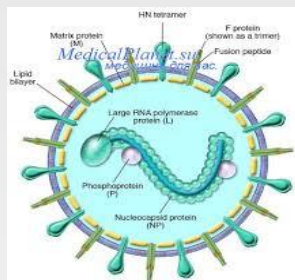
Widmer K, Zhu Y, 2012



*pharyngoconjunctival fever-PCF — англ.



РЕСПИРАТОРНО-СЕНТИЦИАЛЬНЫЙ вирус

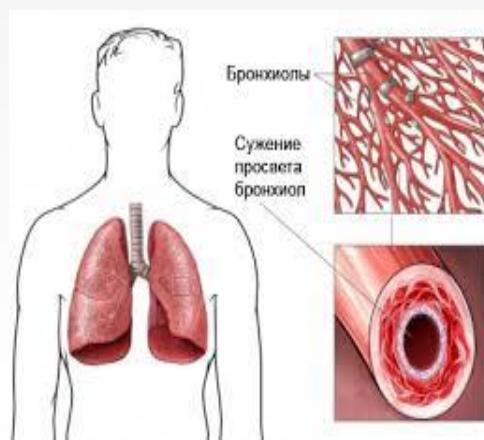
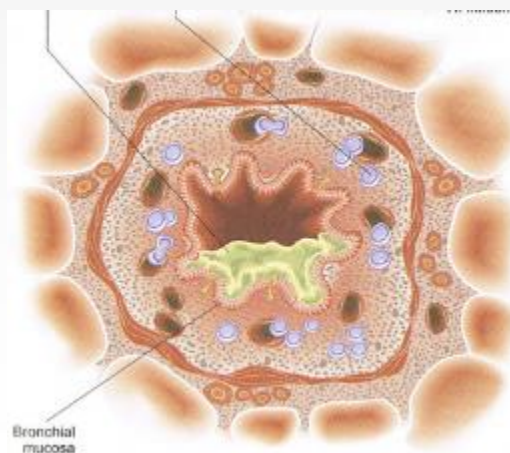


ЛИХОРАДКА – до 7 дней, выраженная

Общая длительность – до 3 недель

Осложнения – ДН

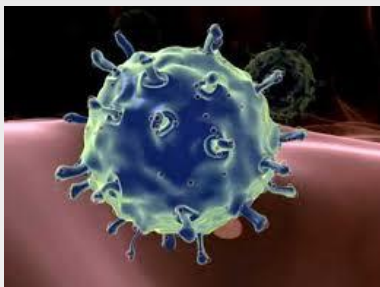
Клинические проявления – обструктивный бронхит, бронхиолит, пневмония





ПАРАГРИПП

4 типа вирусов



ЛИХОРАДКА – 4-5 дней, не выраженная

Общая длительность – **до 2-4 недель**

Осложнения – **«вирусный круп»**

Клиника – рино-фаринго-ларинго-трахеит





Критерии антибиотикотерапии ОРИ (бактериальной инфекции)

- Длительная, более 3 дней лихорадка;
- **Появление слизисто-гнойного отделяемого;**
- Одышка без бронхообструкции;
- Асимметрия хрипов;
- Наличие лейкоцитоза, нейтрофилеза со сдвигом влево.

?



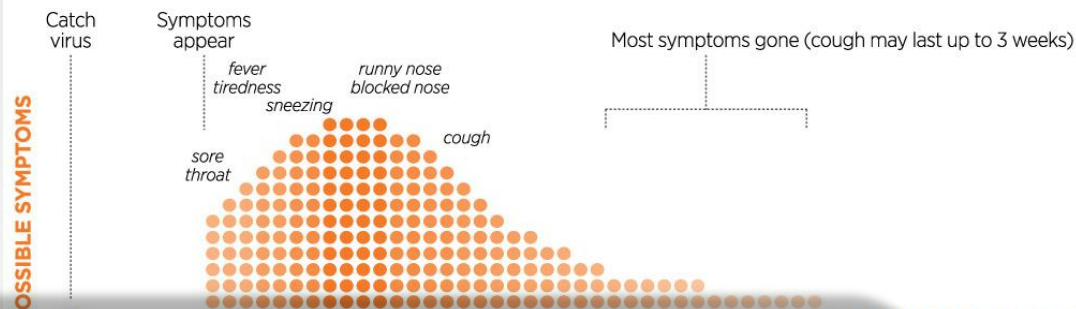
Цвет патологического носового секрета



SNEEZES AND COUGHS SPREAD COLDS

▶ A handy guide to when you're most infectious

Keep colds to yourself and stay at home when you are unwell



Medscape

News & Perspective Drugs & Diseases CME

Upper Respiratory Tract Infection

Author: Anne Meneghini, MD, Chief Editor: Zach Mosenifar, MD

Overview Presentation DDx Workup

Practice Essentials

Background

Pathophysiology

Etiology

Epidemiology

Prognosis

Patient Education

Show All

Multimedia Library

Tables

References

Evolution of nasal secretions in viral nasopharyngitis:

прозрачный жидкий – мутный светлый жидкий – мутный светлый густой – желтый (светло-зеленый) густой

Source: nps.org.au



Клеточный состав слизи дыхательных путей



54

Zuberbier, T. Pseudoallergy or nonallergic hypersensitivity / T. Zuberbier // Allergy. 1999. - Vol. 54. - P. 397-398.

	NET %	MKF %	EPC %	LIMF %	EOZ %
Норма у некурящего человека	20,1	70,8	3,6	4,6	0,9
Бронхиальная астма неконтролируемая	18,3	25,6	19,4	10,6	26,1
Острый бронхит вирусной этиологии	21,1	13,2	5,8	37,0	22,9
Острый бронхит бактериальной этиологии	43,0	15,4	10,7	11,2	19,7



Asthma and natural colds: inflammatory induced in induced sputum. A feasibility study / E. Pizzichini, M. Pizzichini, A. Efthimiadis et al. // Am. J. Respir. Crit. Care Med.- 1998.-Vol. 158.-P. 1178-1184.



- Этот тест
покажет нужны
ли еще тесты...

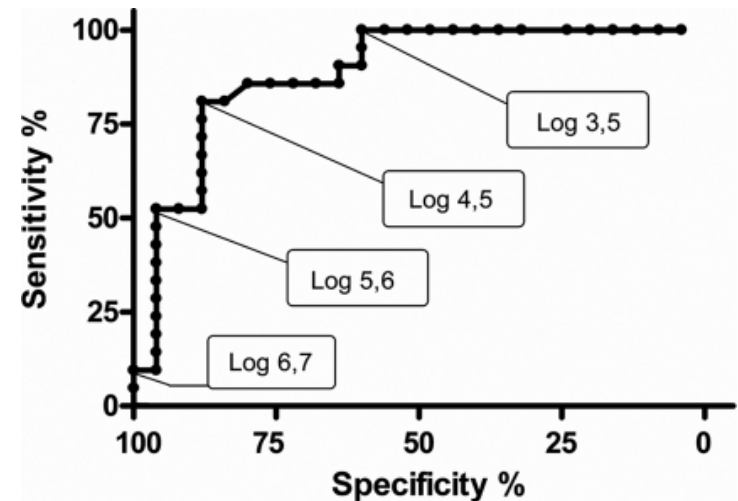
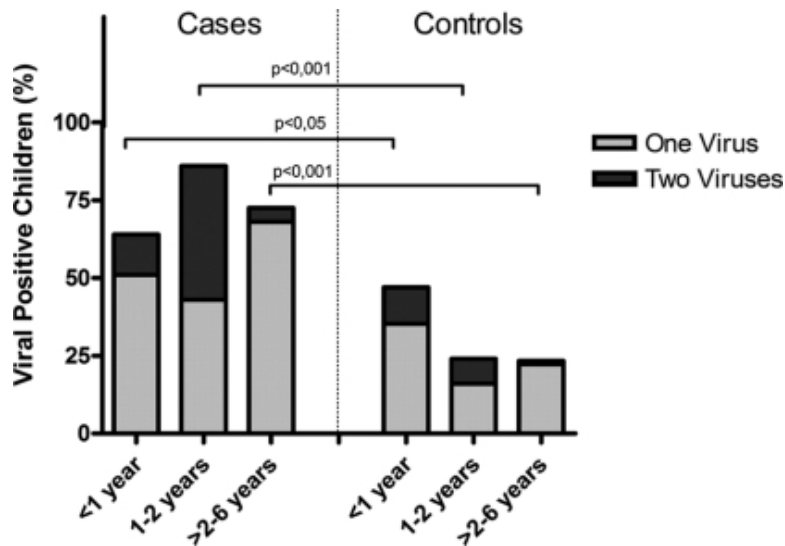


"This test is to see if we need to do more tests."



Frequent Detection of Respiratory Viruses without Symptoms: Toward Defining Clinically Relevant Cutoff Values ∇

Rogier R. Jansen, Joanne Wieringa, [...], and Janke Schinkel





A Novel Host-Proteome Signature for Distinguishing between Acute Bacterial and Viral Infections

Kfir Oved^{1*}, Asi Cohen¹, Olga Boico¹, Roy Navon¹, Tom Friedman^{1,2}, Liat Etshtein^{1,3}, Or Kriger^{1a}, Ellen Bamberger^{1,3,5}, Yura Fonar^{1a,b}, Renata Yacobov⁴, Ron Wolchinsky⁶, Galit Denkberg⁷, Yaniv Dotan^{3,8}, Amit Hochberg⁴, Yoram Reiter⁶, Moti Grupper^{3,9}, Isaac Srugo^{3,5}, Paul Feigin¹⁰, Malka Gorfine¹⁰, Irina Chistyakov^{3,5}, Ron Dagan¹¹, Adi Klein⁴, Israel Potasman^{3,9}, Eran Eden^{1*}

1 MeMed Diagnostics, Tirat Carmel, Israel, 2 Rambam Medical Center, Haifa, Israel, 3 Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel, 4 Department of Pediatrics, Hillel Yaffe Medical Center, Hadera, Israel, 5 Department of Pediatrics, Bnai-Zion Medical Center, Haifa, Israel, 6 Faculty of Biology, Technion-Israel Institute of Technology, Haifa, Israel, 7 Applied Immune Technologies, Haifa, Israel, 8 Department of Internal Medicine, Bnai-Zion Medical Center, Haifa, Israel, 9 Infectious Diseases Unit, Bnai-Zion Medical Center, Haifa, Israel, 10 Faculty of Industrial Engineering and Management, Technion-Israel Institute of Technology, Haifa, Israel, 11 Pediatric Infectious Disease Unit and Clinical Microbiology Laboratory, Soroka Medical Center, Beer-Sheva, Israel

Новая протеомная
идентификация
характеризующая острую
бактериальную и вирусную
инфекции

Published: March 18, 2015

Procalcitonin,
C-reactive protein,
Interleukin-6

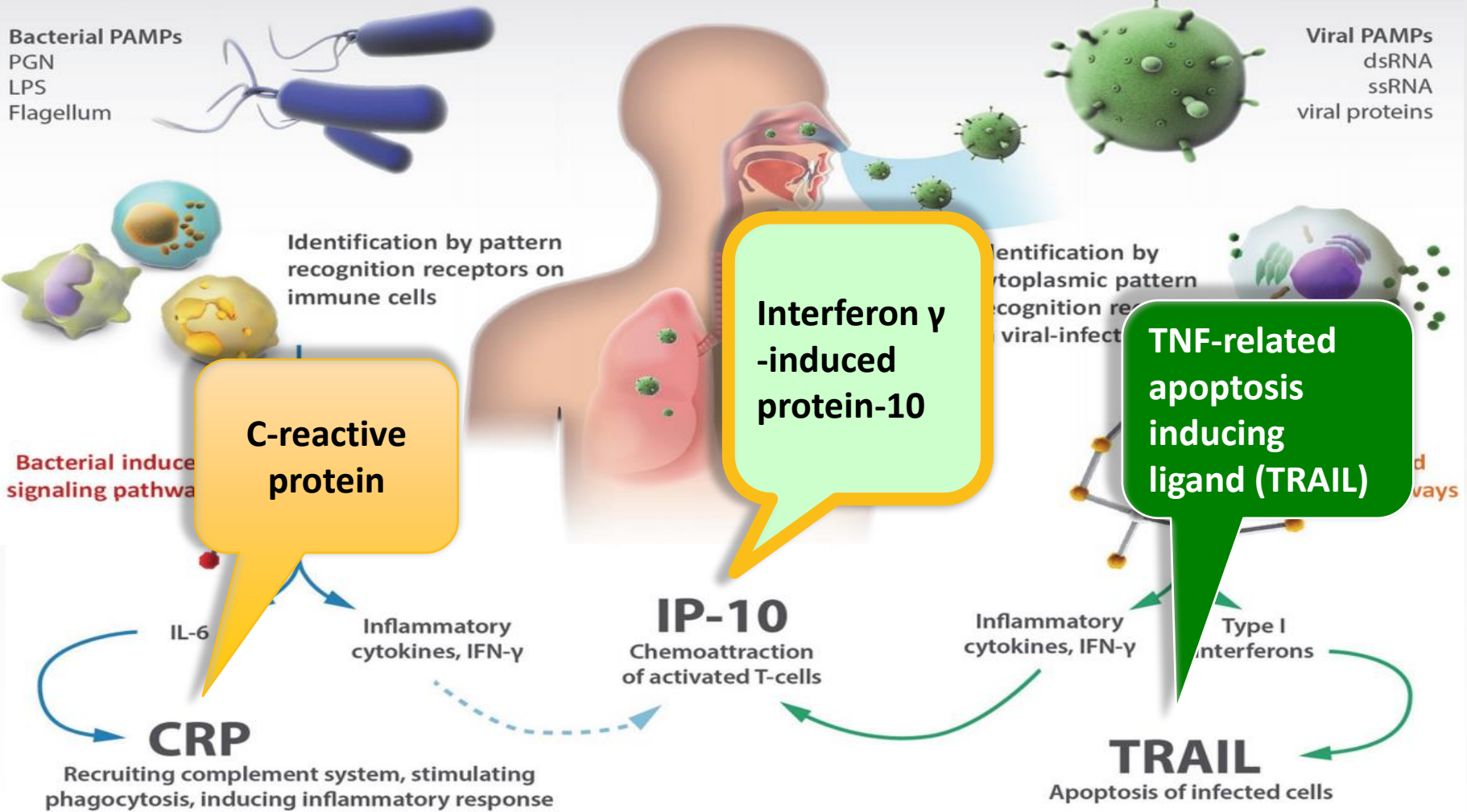


**TNF-related apoptosis
inducing ligand (TRAIL)**, γ -INF,
Interferon γ -induced protein-10



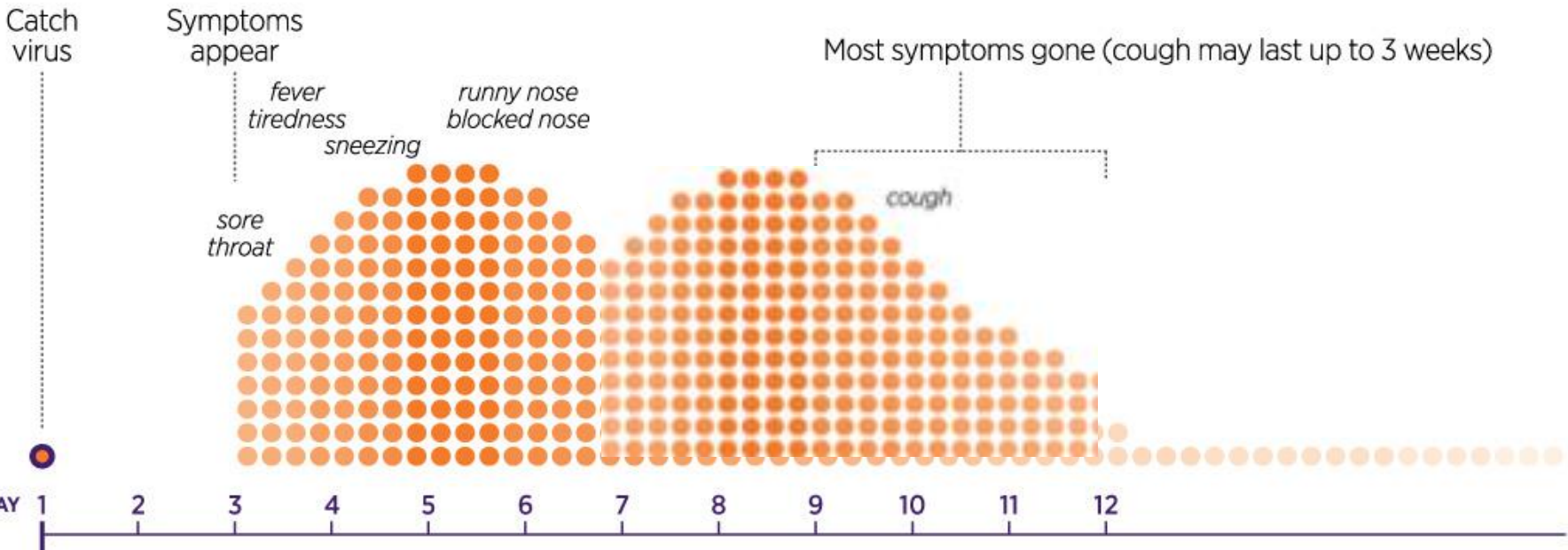
BACTERIAL INFECTION

VIRAL INFECTION



POSSIBLE SYMPTOMS

INFECTIOUS PERIOD



Virus or bacterial reinfection



Peak infectious period due to sneezing and coughing



Варианты бактериальных осложнений ОРВИ



РАННИЕ

**Вирусно-
бактериальные
ассоциации**

**Макролид или (и)
Амоксициллин**

World Health Organization. Pocket Book of Hospital Care: Guidelines for the Management of Common Illnesses With Limited Resources. WHO press, Geneva, Switzerland.



**Острый
воспалительный
период**

**Период регрессии
воспаления и
восстановления
слизистой**



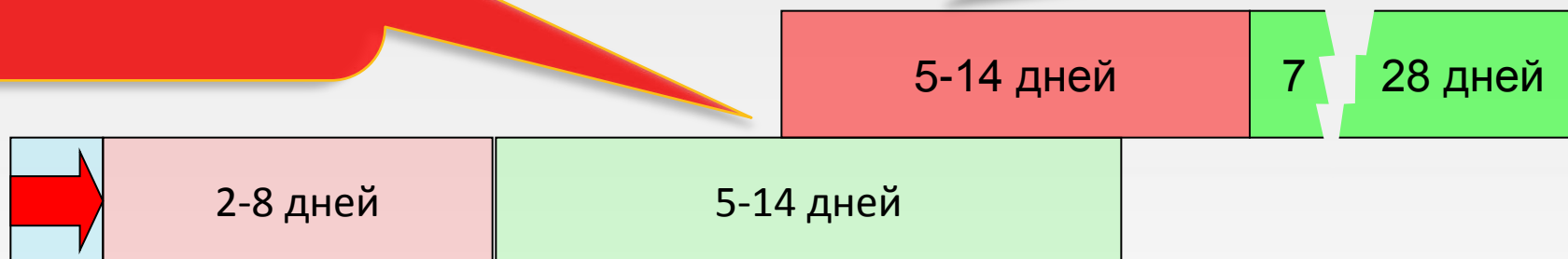
Варианты бактериальных осложнений ОРВИ



ПОЗДНИЕ

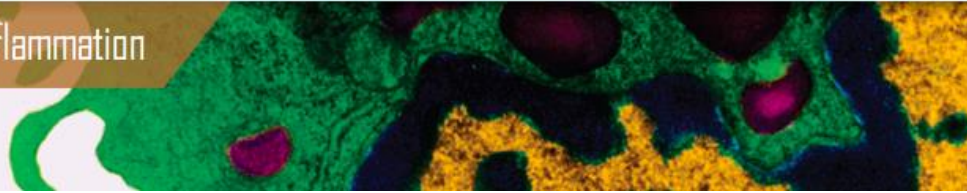
Вторичная инфекция

- Цефалоспорины, карбапенемы и макролид.
- АБТ госпитальных возбудителей и макролид.



**Острый
воспалительный
период**

**Период регрессии
воспаления и
восстановления
слизистой**



Review Article

Macrolide Therapy in Respiratory Viral Infections

Jin-Young Min and Yong Ju Jang

Department of Otolaryngology, Asan Medical Center, University of Ulsan College of Medicine, 388-1 Pungnap-2dong, Songpa-gu, Seoul 138-736, Republic of Korea

Correspondence should be addressed to Yong Ju Jang, jangyj@amc.seoul.kr

Received 20 February 2012; Revised 8 April 2012; Accepted 10 April 2012

Academic Editor: Kazuhito Asano

Respiratory Research

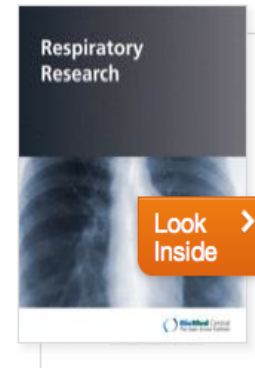
May 2013, 14:52,

[Open Access](#)

Date: 10 May 2013

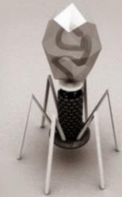
Anti-inflammatory effects of clarithromycin in ventilator-induced lung injury

Laura Amado-Rodríguez, Adrián González-López, Inés López-Alonso, Alina Aguirre, Aurora Astudillo, Estefanía Batalla-Solís, Jorge Blazquez-Prieto, Emilio García-Prieto, Guillermo M Albaiceta



BACTERIOPHAGES 2015

AGENDA



27th Jan - 29 Jan
London, UK

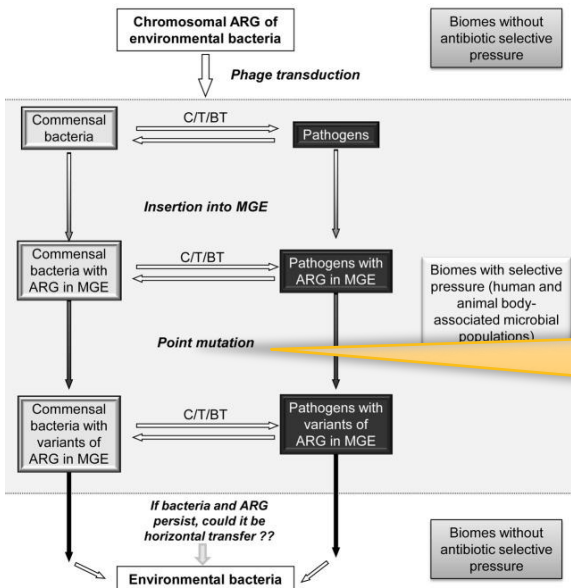
EuroSciCon 



Could bacteriophages transfer antibiotic resistance genes from environmental bacteria to human-body associated bacterial populations?

Maite Muniesa, Marta Colomer-Lluch and Juan Jofre*
Department of Microbiology; University of Barcelona; Barcelona, Spain

Могут ли **бактериофаги** передавать гены устойчивости к антибиотикам из окружающей среды бактериям человеческого тела.



Транс-горизонтальный перенос антибиотико-резистентных генов при **бактериофаговой** трансдукции



Bottlenecks in the transferability of antibiotic resistance from natural ecosystems to human bacterial pathogens

José L. Martínez*

Departamento de Biotecnología Microbiana, Centro Nacional de Biotecnología-Consejo Superior de In-

Edited by:

Stefania Stefani, University of Catania, Italy

Reviewed by:

Julian Davies, University of British Columbia, Canada

Teresa M. Coque, Hospital Universitario Ramón y Cajal, Spain

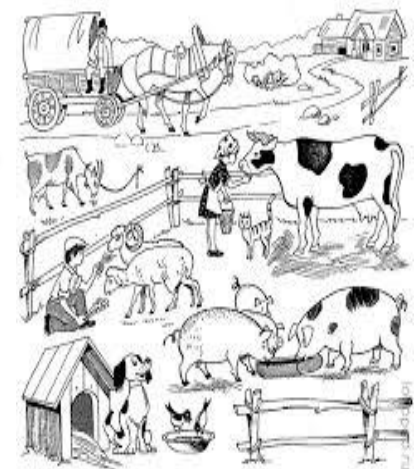
***Correspondence:**

*José L. Martínez, Departamento de Biotecnología Microbiana, Centro Nacional de Biotecnología-Consejo Superior de Investigaciones Científicas, Darwin 3, Cantoblanco, 28049 Madrid, Spain.
e-mail: jlmartnez@cnb.csic.es*

It is generally accepted that resistance genes are transferred by horizontal gene transfer originated in environmental sequences, there is increasing concern on the role that bottlenecks may play in the evolution of resistance. Recent studies have identified determinants that can provide antibiotic resistance to a host is much larger than what is actually found in the environment. Bottlenecks modulating the transfer of resistance genes. In this review, the role that different factors such as connectivity, fitness costs, or second-order selection may play in the evolution of resistance in a population.

Keywords: horizontal gene transfer, antibiotic resistance, bottlenecks, second-order selection

Узкие места переноса антибиотикорезистентности от природных экосистем в бактериальных патогенов человека.





OPEN ACCESS Freely available online

PLOS ONE

Use of a Bacteriophage Lysin to Identify a Novel Target for Antimicrobial Development

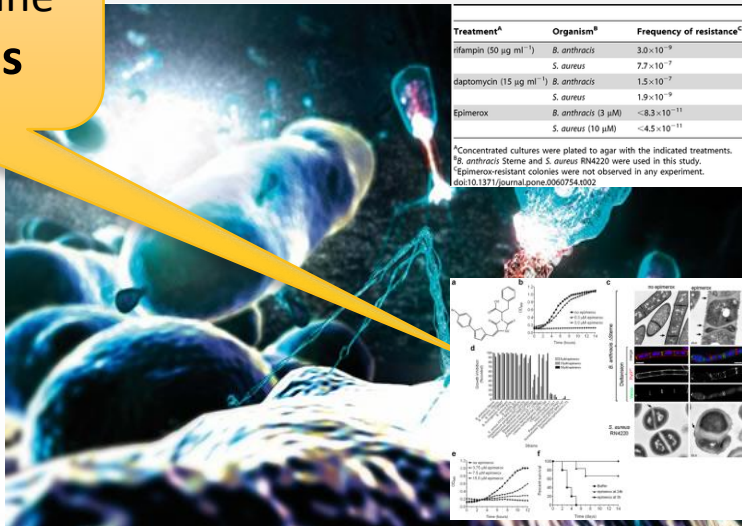
Raymond Schuch^{1*}, Adam J. Pelzek¹, Benjamin Y. Winer¹, Andrew Farnsworth³, Adrienne Clifford⁵, David J. Bearss⁵, Haripriya Vincent A. Fischetti¹

¹ Laboratory of Bacterial Pathogenesis and Immunology, The Rockefeller University, New York, New York, United States of America, ² Information Systems and Biotechnology, The Rockefeller University, New York, New York, United States of America, ³ Department of Structural Microbiology, The Rockefeller University, New York, New York, United States of America, ⁴ Department of Microbiology, The University of California, San Francisco, San Francisco, California, United States of America, ⁵ Department of Microbiology, The University of California, San Francisco, San Francisco, California, United States of America

Использование лизинов бактериофагов в определении новых мишеней антимикробной эволюции

UDP- N - acetylglucosamine 2-epimerases

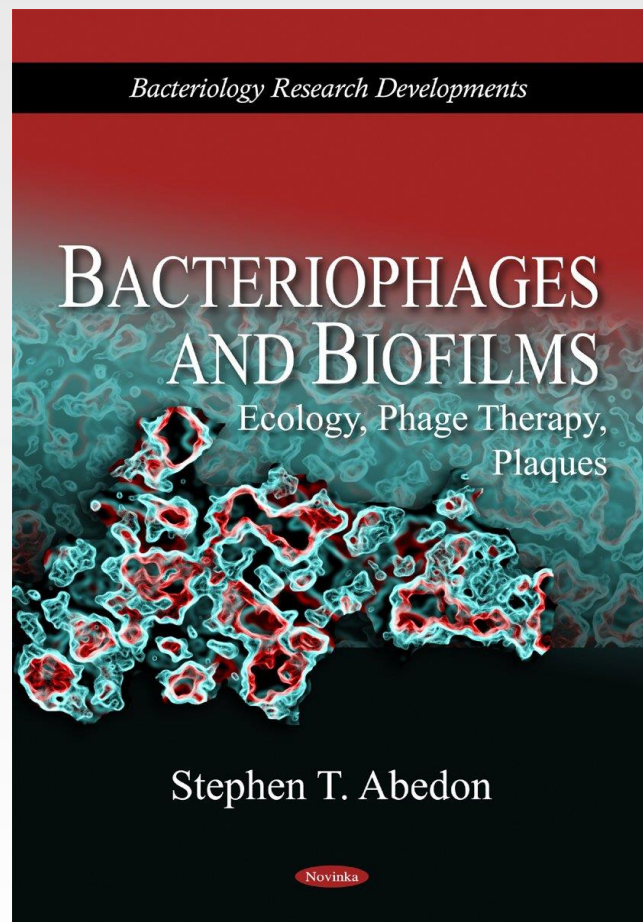
Schuch R et al. 2013. Use of a Bacteriophage Lysin to Identify a Novel Target for Antimicrobial Development. PLoS ONE 8(4): e60754. doi:10.1371/journal.pone.0060754



Аллостерический ингибитор бактериальной 2-эпимеразы



Бактериофаги и биопленки

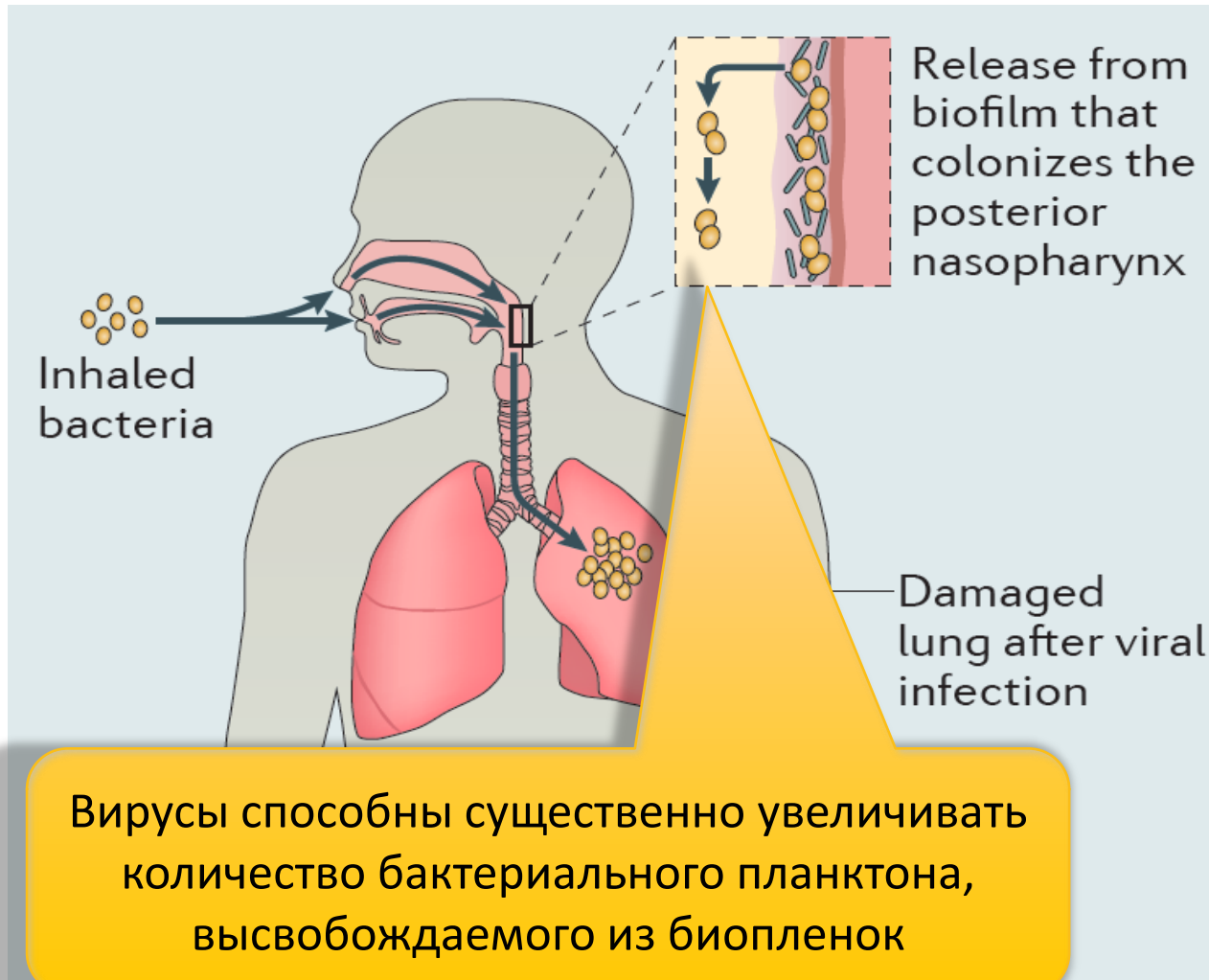




Вирусы «вспахивают» биопленки !?



The co-pathogenesis of influenza viruses with bacteria in the lung, NATURE | APRIL 2014 | VOLUME 12



Jonathan A. McCullers, 2014



Туберкулез (ТБ)

[Туберкулез](#)

[Стратегия "Остановить ТБ"](#)

[Стратегия ДOTS](#)

[ТБ/ВИЧ и ТБ с лекарственной устойчивостью](#)

[Поставщики медицинских услуг](#)

[Больные туберкулезом](#)

[Публикации о ТБ](#)

[О департаменте](#)

Воздушно-капельная инфекция

Взгляд на проблемы, связанные с прекращением распространения МЛУ-ТБ и ШЛУ-ТБ, и пути их решения



"Воздушно-капельная инфекция" – это книга о борьбе с распространением туберкулеза с множественной и широкой лекарственной устойчивостью (МЛУ-ТБ и ШЛУ-ТБ) во всем мире. Книга, написанная Джоном Доннели, представляет собой сборник интервью, репортажей и фотографий из разных уголков мира.

Я МОГУ остановить ТБ

Всемирный день борьбы с туберкулезом 2014 г.

В центре внимания



Доклад ВОЗ о борьбе с ТБ, 2014 г.



Стратегия борьбы с ТБ Основные положения

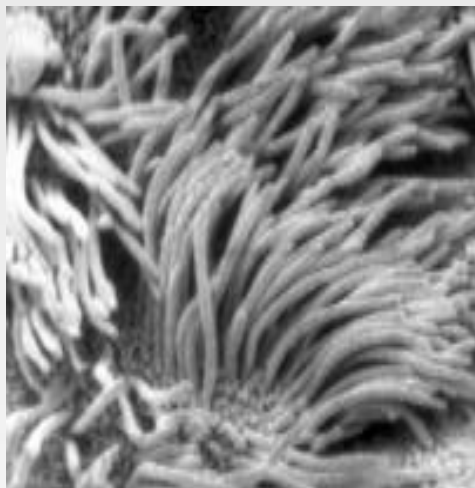


Аэрогенная или воздушно-капельная...?

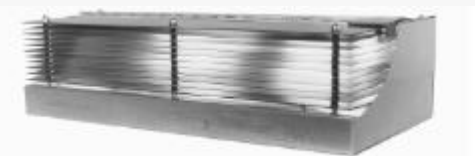




Аэрогенная или воздушно-капельная...?



- Туберкулез
- Пандемический грипп
- Вирусные и бактериальные патогены при ИД



- **Экранированные УФБО.**
- **Маски** на кашляющих пациентах.
- **Респираторы** на посетителях, персонале, ряде пациентов.

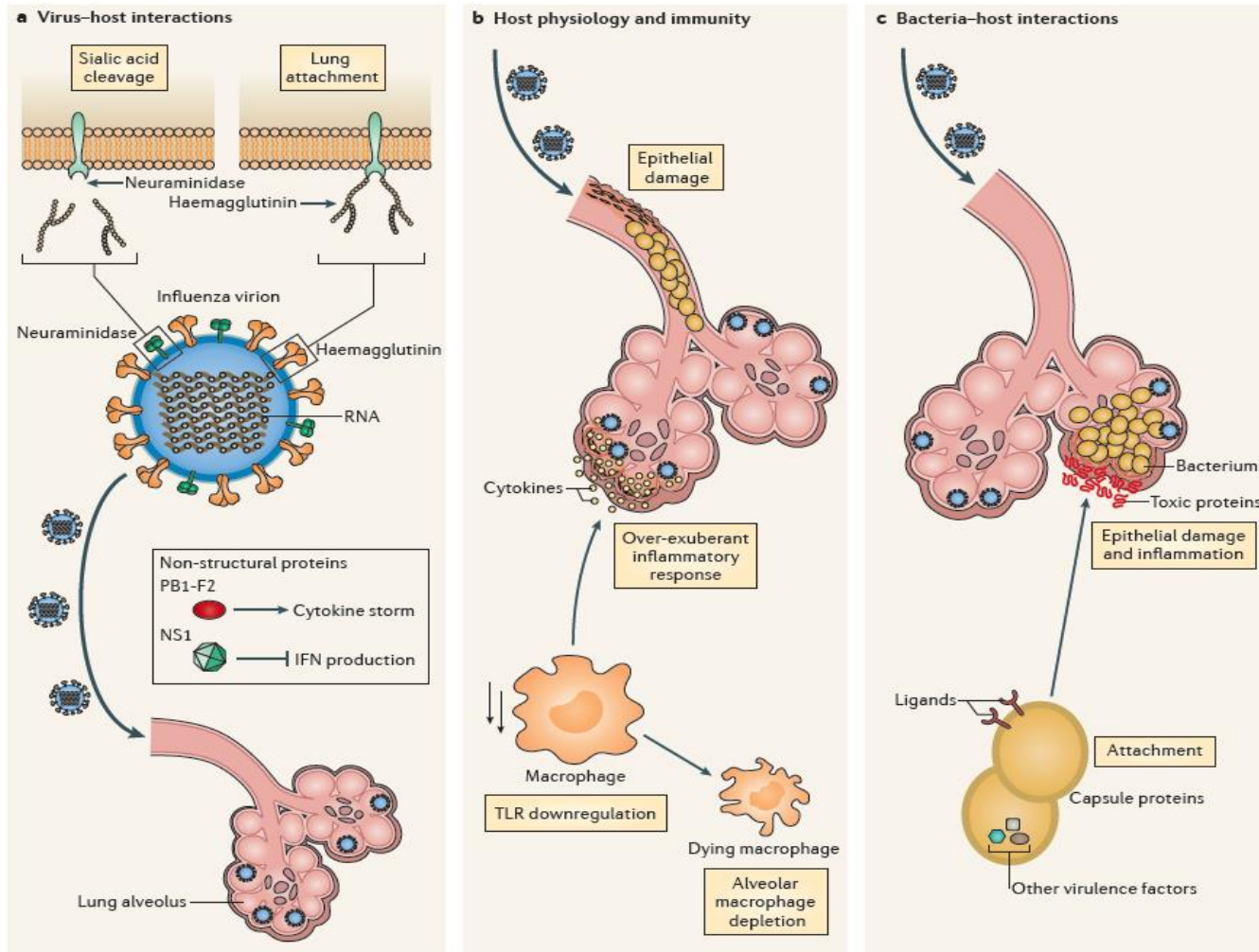




Аэрогенное инфицирование вирусом как триггер бактериальной пневмонии



The co-pathogenesis of influenza viruses with bacteria in the lung, NATURE | APRIL 2014 | VOLUME 12



Jonathan A. McCullers, 2014



Google

natural folk treatment of respiratory infection



Поиск

Новости

Картинки

Видео

Ещё ▾

Инструменты поиска

Результатов: примерно 187 000 (0,58 сек.)

www.rd.com/slideshows/natural-cough-remedies/ ▾ [Перевести эту страницу](#)

Thyme is an officially approved German **treatment** for coughs, upper **respiratory infections**, **bronchitis**, and whooping cough, with good reason: Those tiny leaves ...

Folk Medicine

www.rice.edu/projects/.../Courses/.../mod7.html ▾ [Перевести эту страницу](#)

Folk Medicine in Hispanics in the Southwestern United States ... The term "disease" generally signifies any **organic illness**. Upper **respiratory infection**.

Bronchitis Remedies on Pinterest | Sinus Infection Cure ...

<https://www.pinterest.com/explore/bronchitis-remedies/> ▾

Lungs Formula, Home Remedies, **Bronchitis**, Cough, **Nature Remedies**, Jill, Asthma, Complete **Cure**, Folk Remedies, Treats **Bronchitis**, Laryngitis Remedies.

Vanquishing Viruses - 10 Natural Antiviral Remedies ...

www.ion.ac.uk/information/.../vanquishingviru... ▾ [Перевести эту страницу](#)

But what about **natural treatments** that can actually kill viruses and shorten the ... patients with **respiratory tract infections** and 120 out of 172 patients with viral skin ... been used in **folk medicine** to treat a wide range of illnesses, including colds, ...



1 首先, 上呼吸道感染又称为普通感冒, 广义上包括: 普通感冒、病毒性咽炎等等, 狭义的上呼吸道感染又称普通感冒, 是最常见的急性呼吸道感染性疾病, 患者大多数由病毒引起, 少数由细菌引起。



2 其次, 一般情况下有明显的急性鼻炎和上呼吸道炎症表现, 通常不会发热, 无中毒症状, 往往症状都较轻, 包括有: 咳嗽、打喷嚏、流鼻涕、咽喉痛, 还可能有痰或是头痛的症状, 我们不能忽视它建议及时治疗。

3 最后, 患者要注意对因治疗和对症治疗, 对症治疗包括: 休息、解热镇痛、镇咳剂, 如果频繁打喷嚏、流鼻涕, 可选用马来酸氯苯那敏等抗组胺药; 病因治疗包括有: 抗菌药物治疗、抗病毒药物治疗。



999感冒灵颗粒

功能主治: 解热镇痛。本品用于感冒引起的头痛, 发...[\[查看说明书\]](#)

参考价格: ¥9.9 103条患者评价



白加黑

功能主治: 本品适用于治疗和减轻感冒引起的发热、...[\[查看说明书\]](#)

参考价格: ¥6.5 1条患者评价



阿斯美(复方甲氧那明胶囊)

本品用于支气管哮喘和喘息性支气管炎, 以及其他呼吸系统疾病引起的咳嗽、咳痰、喘息等症状。...[\[查看说明书\]](#)

参考价格: ¥48 5条患者评价



e-docteur
Analysez vos symptômes



ANALYSEZ >

Santé, froid, hve...

Amygdales, végétations

Angine

Dépression hivernale, luminothérapie

Fatigue hivernale

Mal de gorge

Otite

Peau en hiver

Rhino bébé

Rhume, nez bouché

Tweeter

+1 1

J'aime 130

Favoris

AAA

★★★★☆ 76 avis

Témoignages (0)

Dossier Soigner un rhume au naturel

RHUME, GRIPPE, COMMENT TRAITER SIMPLEMENT UNE INFECTION VIRALE ?



Nez qui coule, gorge qui gratte, voire **fièvre** et **courbatures**, que faire contre ces symptômes indiquant une **infection virale** telle un **rhume** ou une **grippe** ?

Il existe des traitements très simples pour rapidement améliorer votre état.

- Rhume ou grippe : vous avez de la fièvre ?
- Rhume ou grippe : vous avez des courbatures ?

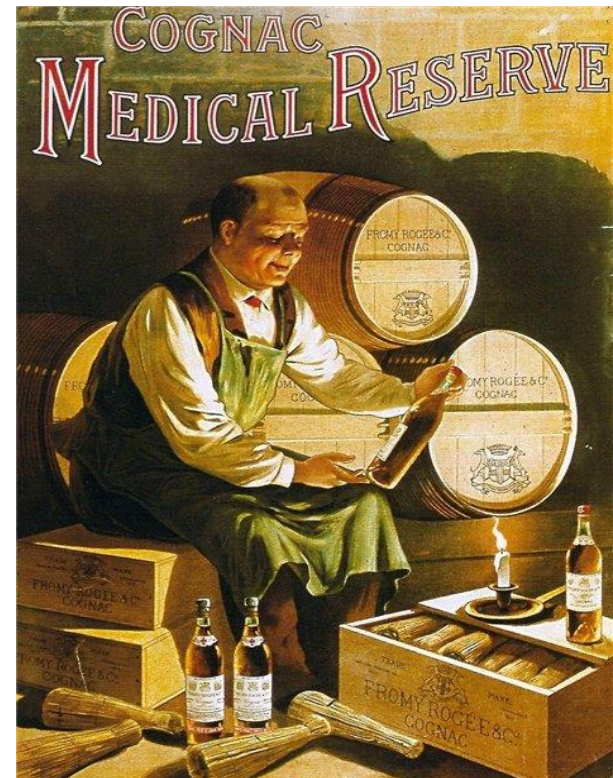
courbatures ?

- Rhume ou grippe : vous avez le nez bouché ?
- Rhume ou grippe : vous avez mal à la gorge ?
- Rhume ou grippe : vous tousssez ?



VIDÉOS

TOUTES LES VIDÉOS >





Common Cold Overview

Written by the Healthline Editorial Team | Published on 30 Июль 2014 г.
 Medically Reviewed by [Kenneth R. Hirsch, MD](#) on 30 Июль 2014 г.



Overview

How It's Contracted

Cold Duration

Read This Next

Part 1 of 3: Overview

Overview

A cold is a common viral infection of the upper respiratory tract—namely, your nose and throat. According to the [National Institutes of Health \(NIH\)](#), Americans “catch” an estimated one billion colds every year. Typical cold symptoms include a runny nose, nasal congestion, sneezing, coughing, and a sore throat. Colds can occur at any time during the year but are most common in the winter months.

Colds affect young children more often than adults. Most adults suffer from about two to four colds per year. According to Boston Children’s Hospital, children—those ages 6 and under in particular—may experience up to six to 10 colds annually. According to the [Centers for Disease Control and Prevention \(CDC\)](#),



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Document heading doi: 10.1016/S2221-1691(13)60146-X © 2013 by the Asian Pacific Journal of Tropical Biomedicine. All rights reserved.

Combined antibacterial activity of stingless bee (*Apis mellipodae*) honey and garlic (*Allium sativum*) extracts against standard and clinical pathogenic bacteria

Berhanu Andualem*

Department of Biotechnology, Natural and Computational Sciences Faculty, University of Gondar, Gondar, Ethiopia

PEER REVIEW

Peer reviewer

Amare Gessesse, PhD in Applied Microbiology, Associate Professor, Addis Ababa University, Institute of Biotechnology, Addis Ababa, Ethiopia. Tel: +251914708989 E-mail: amare.gessesse@gmail.com

Comments

This is a very good finding in which the author investigated the synergistic antimicrobial activity of mixture of garlic extract and *Apis mellipodae*

ABSTRACT

Objective: To investigate the synergic antibacterial activity of garlic and tazma honey against standard and clinical pathogenic bacteria.

Methods: Antimicrobial activity of tazma honey, garlic and mixture of them against pathogenic bacteria were determined. Chloramphenicol and water were used as positive and negative controls, respectively. Minimum inhibitory concentration (MIC) and minimum bactericidal concentration of antimicrobial samples were determined using standard methods.

Results: Inhibition zone of mixture of garlic and tazma honey against all tested pathogens was significantly ($P \leq 0.05$) greater than garlic and tazma honey alone. The diameter zone of inhibition ranged from (18 ± 1) to (35 ± 1) mm for mixture of garlic and tazma honey, (12 ± 1) to (20 ± 1) mm for tazma honey and (14 ± 1) to (22 ± 1) mm for garlic as compared with (10 ± 1) to (30 ± 1) mm for chloramphenicol. The combination of garlic and tazma honey (30–35 mm) was more significantly ($P \leq 0.05$) effective against *Salmonella* (NCTC 8385), *Staphylococcus aureus* (ATCC 25923), *Lysiria moncytogenes* (ATCC 19116) and *Streptococcus pneumonia* (ATCC 63). Results also showed considerable antimicrobial activity of garlic and tazma honey. MIC of mixture of garlic and tazma

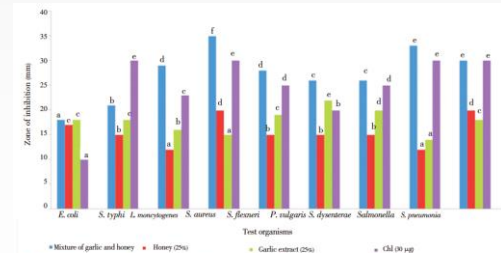


Figure 1. Antibacterial activity of different concentrations of garlic, honey and mixture of garlic and honey with agar well diffusion method. Chl: Chloramphenicol. Values are means of triplicate determinations. Values of the same color bars followed by different letters are significantly different (P<0.05).



Two Major Medicinal Honeys Have Different Mechanisms of Bactericidal Activity

Paulus H. S. Kwakman¹, Anje A. te Velde², Leonie de Boer¹, Christina M. J. E. Vandenbroucke-Grauls^{1,3}, Sebastian A. J. Zaat^{1*}

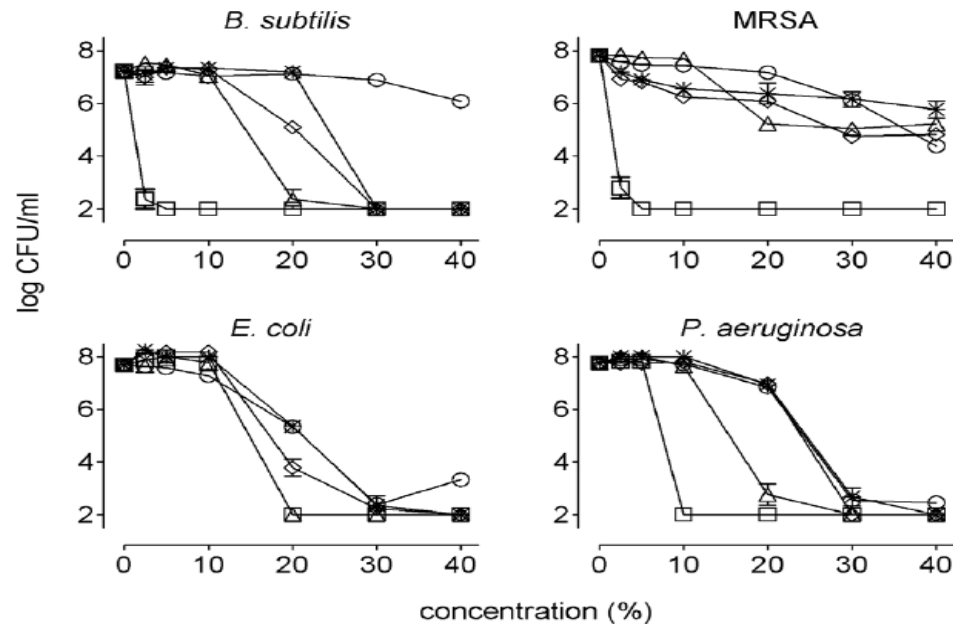


Figure 3. Contribution of MGO to the bactericidal activity of manuka honey. The indicated bacteria were incubated in various concentrations (v/v) of manuka honey in incubation buffer (squares), in manuka with addition of glyoxalase I (triangles) or glyoxalase I and SPS without (diamonds) or with adjustment of the pH to 7.0 (asterisks), or in a honey-equivalent sugar solution (circles). After 24 hours, numbers of surviving bacteria were determined. doi:10.1371/journal.pone.0017709.g003



Visiting a sauna: does inhaling hot dry air reduce common cold symptoms? A randomised controlled trial



Daniel Pach, Bettina Knöchel, Rainer Lüdtkke, Katja Wittmann, Stefan N Willich and Claudia M Witt



Med J Aust 2010; 193 (11): 730-734

The common cold, mainly caused by rhinoviruses or coronaviruses,^{1,2} is a frequent problem all over the world. Although the symptoms are generally benign, viral colds result in significant costs to the economy due to lost workdays and school attendance.³ Convincing treatment options without side effects are not known.⁴ Traditionally, the local application of heat is used to treat the symptoms of the common cold — for example, ingesting hot fluids such as tea or chicken soup,⁵ or inhaling hot vapour.⁶ Moreover, few clinical trials have been conducted to evaluate such treatment options.⁶⁻⁸ It has been suggested that local hyperthermia of the nasal mucosa can affect rhinovirus replication.⁷⁻⁹ A Cochrane review of six trials — one from Israel, two from the United Kingdom, and three from the United States — found that only the studies from Israel and UK showed that steam was beneficial for relief of common cold symptoms.⁶ Results on symptom indices were equivocal; therefore, it was concluded that steam inhalation cannot be recommended for the routine treatment of common cold symptoms and further blind randomised controlled trials needed to be conducted.

In the German city of Essen, a sauna with dry air heated to 90°C exists (www.unperfekthaus.de/projekte/angezogen-sauna) where people can visit dressed in street clothes for the relief of common cold symptoms. This type of sauna is widely available and offers enough dry air to heat the throat, and wetness of the skin is only caused by sweating, not by high humidity. With the aim of heating the throat, people stay in this sauna for only a short period to avoid

ABSTRACT

Objective:

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symptom

Design:

treatment
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Results: No significant difference between groups was observed for AUC representing symptom severity over time (intervention group mean, 31.2 [SEM, 1.8]; control group mean, 35.1 [SEM, 2.3]; group difference, -3.9 [95% CI, -9.7 to 1.9]; $P=0.19$). However, significant differences between groups were found for medication use on Day 1 ($P=0.01$), symptom severity score on Day 2 ($P=0.04$), and participants' ratings of the effectiveness of the therapy on Day 7 ($P=0.03$).

Conclusion: Inhaling hot air while in a sauna has no significant impact on overall symptom severity of the common cold.

Trial registration: ClinicalTrials.gov identifier NCT00552981.

MJA 2010; 193: 730-734

acquired common cold, using a symptom severity score.

METHODS

Design

A randomised single-blind controlled trial was conducted, in which participants were randomly assigned to an intervention group (inhaling hot air within a hot sauna) or a

ceuticals for Human Use Guideline for Good Clinical Practice (ICH GCP), and was approved by the local ethics committee (Charité University Medical Center).

Participants

Employees of the Charité University Medical Center, medical students and people working near the Charité campus were recruited between November 2007 and March 2008

Посещая сауну: вдыхать ли горячий воздух для уменьшения симптомов простуды? Рандомизированное контролируемое исследование

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по Г.А.Войтовичу/ ... 6.Уриновое голодание. /По Г.П. **Малахову**/ ... Голодание при острых вирусных инфекциях /ОРЗ, **грипп**/. Голодать ... голодание. **Лечение**

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ГАЗЕТА МАЛАХОВ PRO

ФОРУМ

МАГАЗИН

- **Пить по утрам среднюю порцию свежей урины - 50-100 г (залпом или нечетное количество глотков). Если человек брезглив и не может пить урину, можно делать компрессы из свежей или старой урины на горло, это эффективно при ангине.**
 - Для профилактики простудных заболеваний промывать носоглотку 1-2 раза в день и чаще свежей уриной. Если урина очень концентрирована солями и раздражает носоглотку - разбавить ее теплой водой. Для усиления эффекта можно использовать упаренные виды урины: 1/2 1/3 1/4, как разведенную со свежей, так и без нее.
 - Для излечения от инфекции, попавшей в легкие, и очищения их от слизи рекомендуется в течение 5-15 мин дышать парами старой урины.



Заблуждения о кашле



- Что-то мне докторша назначила..., а **мокроты то нет...**



- А ты в аптеке купи термопсиса и солодки – **рекой потечет...**

Кокрановский обзор, 2010



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Independent high-quality evidence for health care decisions
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Intervention Review

Over-the-counter (OTC) medications for acute cough in children and adults in ambulatory settings

Susan M Smith^{1,*}, Knut Schroeder², Tom Fahey³ Database Title

Editorial Group: [Cochrane Acute Respiratory Infections Group](#)

Published Online: 7 OCT 2009

Assessed as up-to-date: 7 APR 2010

DOI: [10.1002/14651858.CD001831.pub3](https://doi.org/10.1002/14651858.CD001831.pub3)

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«Не существует убедительных доказательств в пользу использования экспекторантов в лечении острой инфекционной патологии...»

Metanalysis Twenty-six trials (18 in adults, eight in children) involving 40371 people were included.

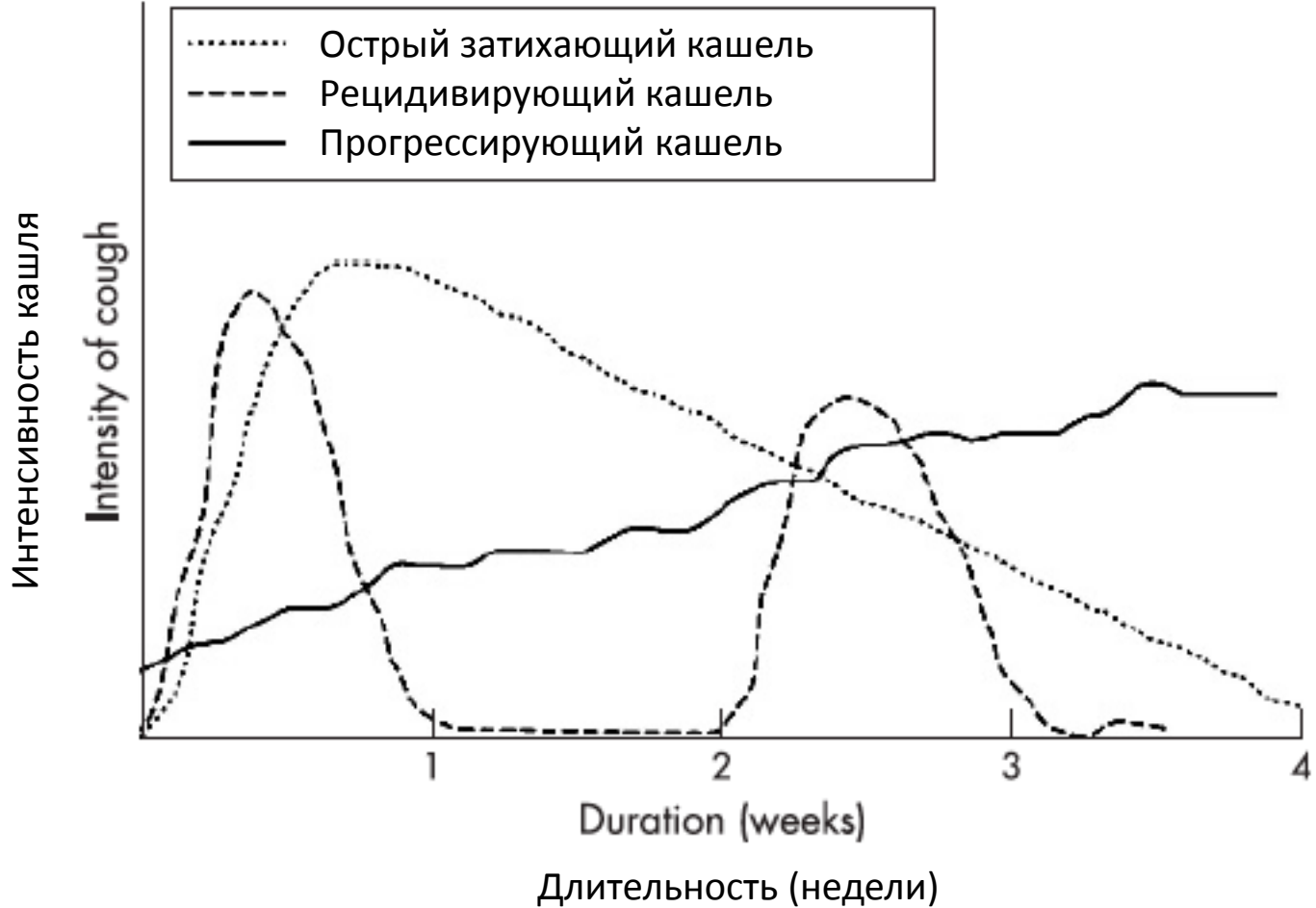
- Женщины врачи существенно чаще назначают АБ при ОРИ.
- В 54% АБП назначались без показаний, «на всякий случай».
- **Вирусы VS. Бактерии не является ключевым вопросом.**
- В 36% пациентов (родителей) влияли на назначение АБП.
- **Длительный кашель потенцирует использование АБ**
- Обучение врачей снизило частоту выписки АБП при ОРИ в 2,1 раза

Applying psychological theories to evidence-based clinical practice: Identifying factors predictive of managing upper respiratory tract infections without antibiotics

[Martin P Eccles](#),¹ [Jeremy M Grimshaw](#),² [Marie Perle](#),³ [Nick Steen](#),¹ [Nigel B Pitts](#),⁴ [Ruth Thomas](#),⁵ [Elizabeth Glidewell](#),⁵ [Graeme MacLennan](#),⁵ [Debbie Bonetti](#),⁴ [A](#)⁵

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Использование психологических теорий в реальной клинической практике: прогностические факторы ведения инфекции верхних дыхательных путей без антибиотиков





D M Fleming, A M Ross, K W Cross and H Kendall

The reducing incidence of respiratory tract infection and its relation to antibiotic prescribing

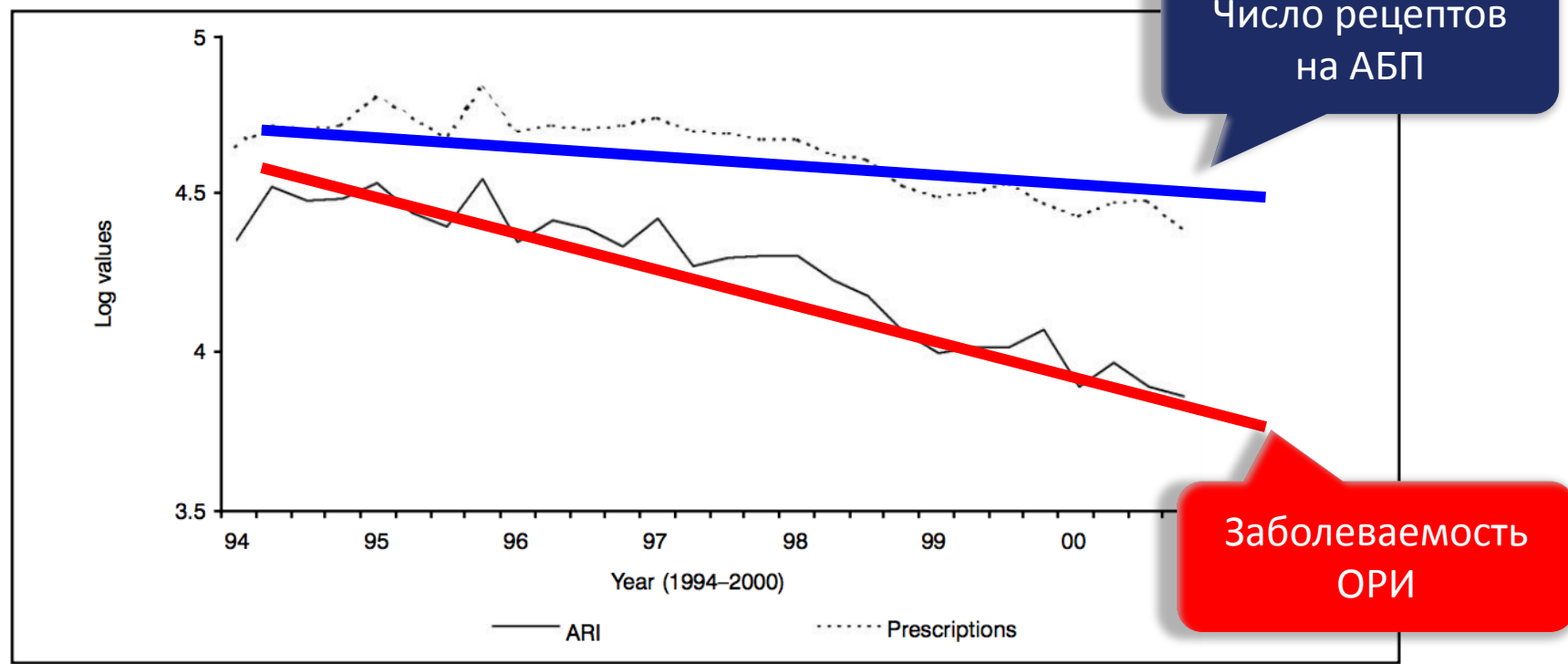


Figure 5. Seasonally adjusted trends in incidence of acute respiratory tract infections (ARI [per 1000]) and antibiotic prescriptions (per 100 000): quarterly data logged.

Доктор, не лечите меня каждый раз антибиотиком...





Coniuncte !!!





Рузанов Дмитрий Юрьевич

druzanoff@mail.ru



СПАСИБО ЗА ВНИМАНИЕ

