EVOLUTION IN THE THERAPEUTICS OF
RESPIRATORY VIRAL INFECTIONS

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Asst Professor of Internal Medicine & Infectious Diseases
University of Athens Medical School
Respiratory viral infections

- Respiratory syncytial virus
- Rhinovirus
- Influenza A, B, and C viruses
- Human metapneumovirus
- Parainfluenza viruses types 1, 2, 3, and 4
- Human bocavirus*
- Coronavirus types 229E, OC43, NL63, HKU1, SARS
- Adenovirus
- Enteroviruses
- Varicella-zoster virus
- Hantavirus
- Parechoviruses
- Epstein-Barr virus
- Human herpesvirus 6 and 7
- Herpes simplex virus
- Mimivirus
- Cytomegalovirus†
- Measles†
Lower RTIs - Associations

- **Bronchiolitis**  
  RSV, hMPV, PIV, adeno

- **Wheezing/Asthma**  
  RSV, hMPV, rhinovirus

- **Croup**  
  PIV

- **Pneumonia**  
  flu, PIV, adeno, RSV

- **Pneumonitis Tx**  
  RSV, PIV, flu, hMPV, adeno
VIRAL PNEUMONONIAS

Most frequent causes

- Influenza
- Respiratory syncytial virus (RSV)
- Parainfluenza
- Human metapneumovirus
- Human bocavirus
- Rhinoviruses
- Coronaviruses
- Adenoviruses
- Echo, Coxsackie

Lancet 2011; 377: 1264–75
CAP - Viruses vs. Bacteria

✓ NO clinical algorithm exists
  • to clearly distinguish viral vs. bacterial

✓ NO clear consensus
  • pts w obvious viral CAP & need for Abx

Lancet 2011; 377: 1264–75
CAP - Viruses vs. Bacteria

<table>
<thead>
<tr>
<th>Suggests viral cause</th>
<th>Suggests bacterial cause</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Younger than 5 years</td>
</tr>
<tr>
<td><strong>Epidemic situation</strong></td>
<td>Ongoing viral epidemic</td>
</tr>
<tr>
<td><strong>History of illness</strong></td>
<td>Slow onset</td>
</tr>
<tr>
<td><strong>Clinical profile</strong></td>
<td>Rhinitis, wheezing</td>
</tr>
<tr>
<td><strong>Biomarkers</strong></td>
<td></td>
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<tr>
<td>Total white-blood cell count</td>
<td>&lt;10×10⁹ cells per L</td>
</tr>
<tr>
<td>C-reactive protein concentration in serum</td>
<td>&lt;20 mg/L</td>
</tr>
<tr>
<td>Procalcitonin concentration in serum</td>
<td>&lt;0.1 µg/L</td>
</tr>
<tr>
<td><strong>Chest radiograph findings</strong></td>
<td>Sole interstitial infiltrates, bilaterally</td>
</tr>
<tr>
<td><strong>Response to antibiotic treatment</strong></td>
<td>Slow or non-responsive</td>
</tr>
</tbody>
</table>

*Lancet 2011; 377: 1264–75*
SPECIFIC PATHOGENS
Influenza is here every year !!!
Antiviral Therapies for Influenza

Neuraminidase (NA)
- NA Inhibitors
  - Oseltamivir
  - Zanamivir

Matrix protein (M2)
- M2 Inhibitors
  - Amantadine
  - Rimantadine
Neuraminidase inhibition prevents the virus from escaping and spreading to other cells.
# Influenza & Antivirals

<table>
<thead>
<tr>
<th>Outcome</th>
<th>AM/RM</th>
<th>ZNV</th>
<th>OSEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ symptoms</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Prevent complications</td>
<td>?</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>↓ Abx use</td>
<td>?</td>
<td>28%</td>
<td>24-40%</td>
</tr>
<tr>
<td>↓ Hospitalization</td>
<td>?</td>
<td>?</td>
<td>~50%</td>
</tr>
<tr>
<td>Treat complications</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>↓ transmission</td>
<td>? (30%)</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

?= No placebo-controlled study or not reported
Duration of viral shedding (Days)

Day of illness

p=0.000 by Kruskal-Wallis test

CID 2010:50 (1 April) • Ling et al
HPA guidance on use of antiviral agents for the treatment and prophylaxis of influenza

Reviewed October 2012
Influenza in the Community

- Mild forms
  - Fever, coryza
  - General sx
    - headache, malaise, myalgia/arthralgia & GI Sxs
    - NO evidence of complications
Influenza in the Community

**UNCOMPPLICATED**

- Previously healthy
  - **No treatment** OR **oseltamivir PO**
    - if physician feels patient is at serious risk of developing complications
- **Atrisk group**
  - **Severely immunosuppressed?**
    - **YES:** zanamivir INH (Diskhaler) OR if unable to take inhaled preparation, **oseltamivir PO** and clinical follow up
    - **NO:** PO oseltamivir within 48 hours of onset, or later at clinical discretion

**e.g.** >65yrs, chronic dz, pregnancy, BMI>40

**e.g.** ChemoRx, BMT, SOT, HIV w CD4< 200
Influenza in the Community

- **Severe forms - Complications**
  - Requiring hospital admission
  - Sxs & signs of LRTI
    - hypoxemia, dyspnea, lung infiltrate on CxR
  - CNS involvement
  - Exacerbation of underlying medical condition
Influenza in the Community

Severe immunosuppression

COMPPLICATED

NO: first line: oseltamivir PO/NG

2nd line: zanamivir INH, NEB OR IV

YES: zanamivir INH, NEB or IV

E.g. ChemoRx, BMT, SOT, HIV w CD4 < 200
MAIN POINTS FOR INFLUENZA Rx

Mild uncomplicated influenza
Rx only population at ↑ risk for complications

Complicated influenza or worsening
Rx all
# Post exposure prophylaxis

<table>
<thead>
<tr>
<th>Previously healthy (excluding pregnant women)</th>
<th>Exposed to circulating influenza H1N1 (2009), H3N2, or B</th>
<th>Exposed to suspected or confirmed oseltamivir resistant influenza</th>
</tr>
</thead>
<tbody>
<tr>
<td>No prophylaxis</td>
<td>No prophylaxis</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>At risk of complicated influenza (including pregnant women but excluding severely immunosuppressed patients and children under 5 years)</th>
<th>Oseltamivir PO 10 days once daily if therapy can be started within 48 hrs of last contact; or after 48 hrs on specialist advice only.</th>
<th>Zanamivir INH 10 days once daily if therapy can be started within 36 hrs of last contact; or after 36 hrs on specialist advice only.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previously healthy (excluding pregnant women)</td>
<td>If unable to administer zanamivir INH, <strong>oseltamivir PO 10 days</strong> (if therapy can be started within 48 hrs of last contact; or after 48 hours on specialist advice only).</td>
<td>If unable to administer zanamivir INH, discuss with specialist and consider nebulised aqueous zanamivir (unlicensed) after individual risk assessment.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severely immunosuppressed patients (excluding children under 5 years)</th>
<th>Zanamivir INH 10 days if therapy can be started within 36 hrs of last contact; or after 36 hrs on specialist advice only.</th>
<th>Zanamivir INH 10 days only if therapy can be started within 36 hrs of last contact; or after 36 hrs on specialist advice only.</th>
</tr>
</thead>
</table>
Adverse effects

- **Oseltamivir**
  - GI tract
    - nausea
    - vomit
      - Take w food

- ? Encephalitis

- Allergic rash

- ? Neuro-psych effects
Body temperature

38°C
37°C

AMS

Intensive Care Unit

Plasma OC
Creatinine

800
600
400
200
0

5 6 7 8 9 10 11 12
Days after onset of fever

Serum Creatinine (mg/dL)

Oseltamivir 150 mg bid
Near Peak
Oseltamivir 75 mg bid

CID 2010:50 (1 April) • BRIEF REPORT
Relenza® (zanamivir for inhalation)
Rotadisk® and Diskhaler®
Fatal Respiratory Events
Caused by Zanamivir
Nebulization

Clinical Infectious Diseases 2010;50:620
Oseltamivir
Drug - Drug interactions

❖ Clopidogrel

→ Oseltamivir hydrolysis to active metabolite

J Pharmac Exp Ther 2006
Infections With Oseltamivir-Resistant Influenza A(H1N1) Virus in the United States

Nila J. Dharan; Larisa V. Gubareva; John J. Meyer; et al.


http://jama.ama-assn.org/cgi/content/full/301/10/1034
### Australian influenza report 2011

Emerging Infectious Diseases, Vol. 17, 2011;653-660

<table>
<thead>
<tr>
<th>WHO Region</th>
<th>AFRO</th>
<th>EMRO</th>
<th>EURO</th>
<th>PAHO</th>
<th>SEARO</th>
<th>WPRO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of oseltamivir resistant isolates</td>
<td>1</td>
<td>1</td>
<td>191</td>
<td>95</td>
<td>0</td>
<td>159</td>
</tr>
</tbody>
</table>

**Pie Chart:**
- Immunosuppressed patients (1): 24%
- Associated with drug use, including treatment and prophylaxis (2): 27%
- No known association with drug use, including known or suspected cases of person to person transmission (3): 37%
- Preliminary notification (4): 12%
• 594 isolates
  – 238 Interntl  84 pH1N1, 76 A(H3N2), 78 B
  – 356 USA 30 pH1N1, 158 A(H3N2), 168 B

• All A (H3N2) susceptible to NAIs

• 1 pH1N1 US oselt R, zana S (H275Y)
• < 1% of 3000 tested viruses were R to NAIs
• All R to adamantanes
1374 viruses tested

- 11 A(H1N1)pdm09 H275Y mutation oselt R
- 1 A(H1N1)pdm09 Y155H mutation oselt/zan R
- 1 A(H3N2)pdm09 D151N mutation oselt/zan R
- 1 B virus I221T mutation oselt R /zan S
- All A (H3N2), A(H1N1)pdm09 tested adamantane R
Neuraminidase Inhibitor resistance

<table>
<thead>
<tr>
<th>Substitution</th>
<th>N2 No.</th>
<th>Reduced Inhibitor Sensitivity</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Oseffamivir</td>
<td>Zanamivir</td>
</tr>
<tr>
<td>H275Y</td>
<td>274</td>
<td>221-2597</td>
<td>1-3</td>
</tr>
</tbody>
</table>

Substitutions in NA that are known to occur clinically and cause clinical resistance.

<table>
<thead>
<tr>
<th>Substitution</th>
<th>Reduced Inhibitor Sensitivity</th>
<th>References</th>
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<tbody>
<tr>
<td></td>
<td>Oseffamivir</td>
<td>Zanamivir</td>
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<tr>
<td>N1 NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H275Y</td>
<td>221-2597</td>
<td>1-3</td>
</tr>
</tbody>
</table>

Substitutions in NA that are known to occur clinically and cause reduced sensitivity in vitro but the clinical impact is currently unknown.

<table>
<thead>
<tr>
<th>Substitution</th>
<th>Reduced Inhibitor Sensitivity</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oseffamivir</td>
<td>Zanamivir</td>
</tr>
<tr>
<td>N1 NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D199N</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>I223R</td>
<td>28-45</td>
<td>10-12</td>
</tr>
<tr>
<td>N295S</td>
<td>12-208</td>
<td>3-5</td>
</tr>
</tbody>
</table>

N2 NA

<table>
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<tr>
<th>Substitution</th>
<th>Reduced Inhibitor Sensitivity</th>
<th>References</th>
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<tbody>
<tr>
<td></td>
<td>Oseffamivir</td>
<td>Zanamivir</td>
</tr>
<tr>
<td>E119V</td>
<td>18-2057</td>
<td>1-3</td>
</tr>
<tr>
<td>R292K</td>
<td>&gt;10000</td>
<td>3-20</td>
</tr>
<tr>
<td>N294S</td>
<td>300-1379</td>
<td>8</td>
</tr>
</tbody>
</table>

Influenza B

<table>
<thead>
<tr>
<th>Substitution</th>
<th>Reduced Inhibitor Sensitivity</th>
<th>References</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Oseffamivir</td>
<td>Zanamivir</td>
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<tr>
<td>R150K</td>
<td>38-252</td>
<td>5-1000</td>
</tr>
<tr>
<td>D197E</td>
<td>12-26</td>
<td>6-7</td>
</tr>
<tr>
<td>D197N</td>
<td>4-10</td>
<td>3-10</td>
</tr>
<tr>
<td>I221T</td>
<td>6-7</td>
<td>2-5</td>
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<tr>
<td>N294S</td>
<td>17-23</td>
<td>1</td>
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<tr>
<td>G407S</td>
<td>4</td>
<td>7</td>
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</table>

* The corresponding position in N2 neuraminidase is indicated

* Fold changes in IC50 compared to wild-type (NAI sensitive) viruses is shown: unk = currently unknown

* References relating to the substitutions indicated are given after the Table

* These substitutions (and I223V; refs 4, 25) are known to synergise with H275Y

* Occurrence with I222V can yield greater fold changes in IC50 compared to wild-type (NAI sensitive) viruses

* Substitutions table developed by the WHO GISRS antiviral susceptibility expert working group (AVWG). WER No. 39, 2012. 87, p 372
<table>
<thead>
<tr>
<th>Water</th>
<th>WC</th>
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**Carriage number 8**

- **Case C**
- **Case D**
- **Case E**
- **Case F**
- **Contact 1**
- **Contact 2**
- **Contact 3**
- **Contact 4**

The NEW ENGLAND JOURNAL of MEDICINE

Volume 362:86-87    January 7, 2010    Number 1
Oseltamivir-Resistant Pandemic (H1N1) 2009 Treated with Nebulized Zanamivir
Other antivirals for influenza

- Research level or compassionate use
  - iv zanamivir, aqueous solution zanamivir
  - iv oseltamivir
  - iv peramivir
  - inh Laninamivir
  - iv ribavirin
  - Monoclonal Ab
    - DAS181, favipiravir, nitazoxanide and AVI-7100
Peramivir is the Most Potent in vitro against H1N1 among those studied

Data courtesy of Dr. Larisa V Gubareva, MD, PhD
Team Leader, Molecular Epidemiology
Virus Surveillance and Diagnosis Branch
Influenza Division, NCIRD, CCID,
Centers for Disease Control & Prevention
Phase III Randomized, Double-Blind Study Comparing Single-Dose Intravenous Peramivir with Oral Oseltamivir in Patients with Seasonal Influenza Virus Infection¹

Shigeru Kohno,¹* Muh-Yong Yen,² Hee-Jin Cheong,³ Nobuo Hirotsu,⁴ Tadashi Ishida,⁵ Jun-ichi Kadota,⁶ Masashi Mizuguchi,⁷ Hiroshi Kida,⁸ and Jingoro Shimada⁹ for the S-021812 Clinical Study Group

![Graph showing comparison of influenza virus titer between Peramivir and Oseltamivir.](image)
Correspondence

Parenteral Peramivir Treatment for Oseltamivir-Resistant 2009 Pandemic Influenza A H1N1 Viruses

Parenteral peramivir for H275Y neuraminidase mutants [10]. The prophylactic activity of intramuscular peramivir was evaluated in mice infected with wild-type and infection with H275Y mutant influenza viruses is being evaluated in further experiments. Although the outcome of the single case treated with intravenous

JID 2011:204 (15 November) • 1641
H7N9 INFLUENZA – China 2013

Geographical location

Confirmed human cases of avian influenza A(H7N9) reported to WHO

Data as of 30 May 2013, 16:46 GMT-1
Source: WHO/GIP
Clinical Findings in 111 Cases of Influenza A (H7N9) Virus Infection

- 108/111 pts Rx
  - received NAIs
  - oseltamivir or peramivir
- Median t 7 days !!!
  - 9.9% within 48 hrs
- Abxs 71.2%
Human monoclonal antibody CR8020 with broad neutralizing activity against most group 2 viruses, including H3N2 and H7N7

Science, 2011: 843-850
Figure 8. The pockets on the predicted structures explored by AutoDock based on a subunit:

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0037790
Rhinovirus Therapeutics

- Antivirals – Pleconaril
- 3C protease inhibitors (e.g. nasal spray of ruprintrivir)
- Interferon alpha-2b for prophylaxis
- Soluble ICAM-1 (Tremacamra)
  - JAMA 1999; 281:1797
- VLDL and LDL receptor fragments
Rhinoviruses

Thibaut HJ et al. Biochemical pharmacology. 2012;83(2):185-92
Rhinoviruses

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

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Home > Find Studies > Study Record Detail

A Phase 2 Study of BTA798 in Asthmatic Adults With Symptomatic Human Rhinovirus Infection (RHINO)

This study has been completed.
Sponsor:
Biota Scientific Management Pty Ltd
Information provided by (Responsible Party):
Biota Scientific Management Pty Ltd

ClinicalTrials.gov Identifier:
NCT01175226
First received: August 3, 2010
Last updated: February 14, 2013
Last verified: February 2013
History of Changes

Biota Announces Positive Phase IIb Data for Asthmatic Patients With Human Rhinovirus Infection (HRV)

Oral Treatment for HRV Infection Shows Statistically Significant Reduction of Cold-Like Symptoms

MELBOURNE, AUSTRALIA--(Marketwire - Mar 28, 2012) - Biota Holdings Limited (ASX: BTA) today announced that the Phase II clinical study of its oral antiviral BTA798 (vapendavir) for the treatment of naturally acquired human rhinovirus (HRV) infection in asthmatics resulted in a statistically significant reduction in cold symptoms compared to a placebo.
Rhinoviruses

Effects of Pleconaril Nasal Spray on Common Cold Symptoms and Asthma Exacerbations Following Rhinovirus Exposure (Study P04295AM2)(COMPLETED)

This study has been completed.

First Received on October 31, 2006. Last Updated on June 22, 2007  History of Changes

<table>
<thead>
<tr>
<th>Sponsors</th>
<th>Schering-Plough</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information provided by:</td>
<td>Schering-Plough</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier:</td>
<td>NCT00394914</td>
</tr>
</tbody>
</table>

RESULTS HAVE NOT BEEN REPORTED TO DATE !!! ???
Enterovirus

- Wide range of clinical manifestations
- Several serotypes → respiratory dz
- Pharyngitis common
• Several targets for inhibition of viral replication
  – viral 3C protease
  – the putative 2C helicase
  – the 3D RNA-dependent RNA polymerase

• Inhibitors against host cell factors, IVIG
Enteroviruses

A. Pleconaril

B. Compound 1

C. Ribavirin

D. Geldanamycin

Molecules targeting enterovirus capsid
Molecules targeting enterovirus 3C protease
Molecules targeting enterovirus RNA replication
Molecules targeting host factors

Thibaut HJ et al. Biochemical pharmacology. 2012;83(2):185-92
Parainfluenza virus

- Croup (types 1, 2), laryngitis
- Pneumonia (type 3) in children 6 m – 3 yrs
- Pneumonia in immunocompromised
  - BMT units (type 3)
- Rx: ribavirin, ? NAIs, recombinant sialidase fusion protein (DAS 181)

RSV Alveolar obstruction

- Syncytia formation
- Inflammatory cell infiltrate
- Sloughing of respiratory epithelium
Prevention

- Palivizumab = Synagis
  - RSV-F protein-specif. humanized monoclonal Ab
    - Impairs fusion & resp epithelium entry, **NO role in Rx**
  - Children < 2 yrs & ↑ risk
    - Prematurity, bronchopulmonary dysplasia, neuromuscular dz, congenital heart disease, CLD, immunodeficiency
  - Children w recurrent wheezing that had RSV infxn
    - ↑↑↑↑ cost
Motavizumab

RSV Hospitalization
- CHD
- Premature/CLD

Combined Analysis

RSV Outpatient MALRI
- CHD
- Premature/CLD

Combined Analysis

Relative Risk

Noninferiority Margin = 1.265

Favors Motavizumab

RSV Rx

- Supportive, Abx if mixed bacterial infection
- RSV IG
- Ribavirin
  - NOT as routine Rx
  - LRTI, severe dz
RSV Rx – novel agents

- Monoclonal Ab against G protein
  - Experimental data, mice

- Small molecules
  - BMS-433771, TMC353121, JNJ-2408068, VP14637
  - NMSO3, YM-53404, RSV604

- si RNAs

A randomized, double-blind, placebo-controlled study of an RNAi-based therapy directed against respiratory syncytial virus

John DeVincenzo, Robert Lambkin-Williams, Tom Wilkinson, Jeffrey Gehelsky, Sara Nochur, Edward Walsh, Rachel Meyers, Jared Gollob, and Akshay Vaishnaw

*Departments of Pediatrics and Molecular Sciences, University of Tennessee School of Medicine and The Children's Foundation Research Center, Memphis, TN 38103; †Retroscreen Virology Ltd., Centre for Infectious Diseases, Queen Mary University of London, London E1 4NS, United Kingdom; ‡Southampton University School of Medicine, Division of Infection, Inflammation, and Immunity, Southampton General Hospital, Southampton SO16 6YD, United Kingdom; 
§Alnylam Pharmaceuticals, Inc., Cambridge, MA 02142; and ¶University of Rochester School of Medicine and Dentistry, Infectious Diseases Unit, Rochester

B

Quantitative Culture

Cumulative % of Subjects Infected

Day

p = 0.0029

RSV

Placebo

A

Symptoms (Infected Only)

Daily Mean Symptom Score

Study Day

0 1 2 3 4 5 6 7 8 9 10 11

Placebo (N=37)  ALN-RSV01 (N=29)

p = NS

RSV

ALN-RSV01 or Placebo

A

qRT-PCR

Cumulative % of Subjects Infected

Day

p = 0.0321

RSV

Placebo

ALN-RSV01
Review

Progress in understanding and controlling respiratory syncytial virus: Still crazy after all these years

Peter L. Collins\textsuperscript{a,}\textsuperscript{c,*}, José A. Melero\textsuperscript{b}

\textsuperscript{a}Department of Microbiology and Immunology, \textsuperscript{b}Department of Medicine, \textsuperscript{c}Departments of Microbiology and Pediatrics, \textsuperscript{*}Corresponding author. Tel.: +1 212 606 1986; fax: +1 212 587 4768.

Virus Research 162 (2011) 80–99

Contents lists available at SciVerse ScienceDirect

Virus Research

journal homepage: www.elsevier.com/locate/virusres
Human Metapneumovirus and Lower Respiratory Tract Disease in Otherwise Healthy Infants and Children

John V. Williams, M.D., Paul A. Harris, Ph.D., Sharon J. Tollefson, B.A., Lisa L. Halburnt-Rush, M.Ed., Joyce M. Pingsterhaus, B.A., Kathryn M. Edwards, M.D., Peter F. Wright, M.D., and James E. Crowe, Jr., M.D.
Human Metapneumovirus

- Epi & clinical picture similar to RSV
- Max incidence between 4-6 months of age
- Frequent coinfection w RSV
- Frequently mild or asymptomatic infection

J. Williams et al. NEJM 2004;350:5
HMPV in immunosuppression

Human Metapneumovirus Rx

- Ribavirin iv vs. oral vs. nebulized (SPAG)
- Ribavirin + IVIG
- Monoclonal Abs
- siRNA ?

Virology Journal 2012, 9:105
ADENOVIRUS

- 51 serotypes
  - Pharyngo-conjunctivitis / association w pools
  - Immunocompromised, BMT (60 % mortality)
  - Military recruits - CAP 10-20%

**Rx:** Ribavirin ± IVIG, Cidofovir, Vidarabine

*Transplantation* 2007; 13(1): 74-81
Bone Marrow Transplant. 2013 Mar 18
SARS

- Ribavirin
- NA
- Protease inhibitors
  - Lopinavir/ritonavir
  - Nelfinavir
- Human interferons
- Statins
- Convalescent serum
- Monoclonal Abs
Other Coronaviruses

CHLOROQUINE ANTIVIRAL ACTIVITY AGAINST HCoV-OC43

(A)

% Survival

0 20 40 60 80 100

0 1 2 3 4 5 6 7 8 9 10 28

Time (days post infection)

15 mg/kg CQ (n=70, N=9)
5 mg/kg CQ (n=42, N=5)
1 mg/kg CQ (n=21, N=4)
0 mg/kg CQ (n=132, N=19)

Els Keyaerts et al. AAC 2009;53:3416-3421
New coronavirus - MERS-CoV

Severe respiratory disease associated with Middle East respiratory syndrome coronavirus (MERS-CoV)

17 June 2013
New coronavirus - MERS-CoV

• ? interferons (types I and III)
  – MERS-CoV ->50 to 100 times more sensitive to interferon-alpha (IFN-α) Rx than SARS-CoV

• ? Cyclosporin A
  – inhibitor of MERS-CoV replication in cell culture
New coronavirus - MERS-CoV

INTERIM GUIDANCE DOCUMENT

Clinical management of severe acute respiratory infections when novel coronavirus is suspected: What to do and what not to do

World Health Organization
OTHER VIRAL PNEUMONIAS

- Herpesviruses
  - VZV, HSV
    - Immunocompromised, pregnancy, HIV
  - CMV

- Systemic dz
  - Measles, Hantavirus

- Others...
  - Bocavirus, Parechovirus, Mimivirus