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Risks of Pneumonia in Patients with Asthma Taking Inhaled Corticosteroids

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Endothelial Cells Are Central Orchestrators of Cytokine Amplification during Influenza Virus Infection

Authors: Teijaro J R, Walsh K B, Cahalan S et al.
Reference: Cell, 2011, 146, 980–991
URL: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3176439/
Comments: Pandemic virus infection is one of the public disasters in past few years. The high mortality due to exaggerated lung inflammation and injury warrants further mechanism study. In this article, the author provided solid evidence indicating endothelium is the key and center for virus induced inflammation amplification through sphingosine-1-phosphate (S1P) signaling pathway in a murine model. S1P receptor agonist inhibits early pro-inflammatory cytokine production and recruitment of innate immune cells without affecting viral proliferation. The significant improvement of survival after S1P agonist treatment implicates potential new therapies of virus induced lung injury.

Exudate Macrophages Attenuate Lung Injury by the Release of IL-1 Receptor Antagonist in Gram-negative Pneumonia

Authors: Herold S, Tabar TS, Janßen H et al.
URL: http://ajrccm.atsjournals.org/content/183/10/1380.long
Comments: Alveolar Exudate macrophages play an important role in bacterial killing and initiating inflammation. However, potential role of exudates macrophages in anti-inflammation and barrier-protection has not been demonstrated in detail in a LPS induced lung injury model. In this study, the authors used in vitro alveolar epithelial cell culture and CCR2-deficient mice model showing lung recruited exudate macrophages reduce alveolar inflammation and epithelial damage through releasing IL-1 receptor antagonist without compromising host-defense function.

Nebulized Ceftazidime and Amikacin in Ventilator-associated Pneumonia Caused by Pseudomonas aeruginosa

Authors: Lu Q, Yang J, Liu Z et al.
URL: http://ajrccm.atsjournals.org/content/184/1/106.long
Comments: P. aeruginosa is one of the leading gram negative bacteria frequently isolated from ICU patients. Treating P. aeruginosa lung infection need balance between efficacy and induction of antibiotic resistance. In this study, intravenous injection and nebulization of ceftazidime were directly compared for treatment efficacy and induction of antibiotics resistance. The results showed similar treatment response between intravenous injection and nebulization of ceftazidime while less possibility to acquire antibiotic resistance through nebulization.
Dexamethasone and length of hospital stay in patients with community-acquired pneumonia: a randomised, double-blind, placebo-controlled trial

Authors: Meijvis SCA, Hardeman H, Remmelts HHF et al.
URL: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)60607-7/fulltext
Comments: The effects of steroid on community-acquired pneumonia are still not clear. In this study, 304 non-severe CAP patients were enrolled and half were treated with regular antibiotics while the other half had 5-mg dexamethasone for 4 days added to the antibiotics treatment. The results showed 1 day reduction of hospital stay in steroid treated group plus better quality of life compared to control, suggesting that dexamethasone could facilitate patient recovery from CAP. However, potential adverse effects using dexamethasone such as gastrointestinal disturbance and hyperglycemia need careful evaluation in individual CAP patient.

Implementation of guidelines for management of possible multidrug-resistant pneumonia in intensive care: an observational, multicentre cohort study

Authors: Kett DH, Cano E, Quartin AA et al.
URL: http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(10)70314-5/fulltext
Comments: Considering unavailability of bacteria isolation in many ICU patients, the ATS/IDSA recommended empirical antibiotics treatment in suspected HAP and VAP patients. However, it is not clear whether it is useful or not to adhere closely with the guideline for treatment efficiency. In this study, 303 patients at risk for multi-drug resistant pneumonia were assigned separately into guideline compliant and non-compliant groups, followed with 28-day survival rate or mortality record. The results showed survival rate in compliant group was 65% while in non-compliant group, the survival rate was 79% (P=0.0042). Because adherence with empirical treatment was associated with increased mortality, a randomized trial need to be done before further implementation of these guidelines.

PAI-1 is an essential component of the pulmonary host response during Pseudomonas aeruginosa pneumonia in mice

Authors: Goolaerts A, Lafargue M, Song Y et al.
URL: http://www.ncbi.nlm.nih.gov PMC/articles/PMC3282176/
Comments: High coagulation activity and down-regulated fibrinolysis in alveolar space are associated with increased mortality in ARDS and pneumonia patients. Deletion of PAI-1 showed protection in acute lung injury induced by hypoxia and bleomycin, but controversial results in gram negative and positive bacterial induced pneumonia model. In this study, the authors found that deletion of PAI-1 was protective in early stages of P. aeruginosa induced pneumonia but had high mortality and worsened lung injury in later stages. One of the mechanism is that PAI-1 deletion decreased neutrophils recruitment in the lungs so lung injury would be reduced before bacteria proliferates to certain number of colonies. Cell culture studies further clarified that PAI-1 inhibition could reduced endothelial permeability though inhibition of RhoA signaling pathway. These results highlights the complexity of coagulation factors in pneumonia.
**Procalcitonin and C-Reactive Protein in Hospitalized Adult Patients With Community-Acquired Pneumonia or Exacerbation of Asthma or COPD**

**Authors:** Bafadhel M, Clark TW, Reid C et al.


**URL:** [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3109646/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3109646/)

**Comments:** Pneumonia is sometimes difficult to differentiate from acute exacerbation of asthma or chronic obstructive pulmonary disease. While rapid assessment and empirical antibiotic treatment is indicated for Pneumonia; viral infection is often the cause of acute exacerbation of asthma and COPD and therefore does not require systematic antibiotic treatment. A method to differentiate rapidly and easily these conditions would be helpful to guide antibiotic use in order to optimize treatment and reduce antibiotics resistance. Procalcitonin (PCT) and C-reactive protein (CRP) were quantified in three groups of patients, pneumonia, asthma and COPD. The results showed both PCT and CRP could distinguish pneumonia from asthma and COPD exacerbation while CPR could be used to guide antibiotic use in hospitalized patients with acute respiratory illness.

**Recombinant Tissue Factor Pathway Inhibitor in Severe Community-acquired Pneumonia-- A Randomized Trial**

**Authors:** Wunderink RG, Laterre PF, Francois B et al.

**Reference:** Am J Respir Crit Care Med, 2011, 183:1561-1568

**URL:** [http://ajrccm.atsjournals.org/content/183/11/1561.long](http://ajrccm.atsjournals.org/content/183/11/1561.long)

**Comments:** Severe pneumonia is the leading cause of death in ICU worldwide. Tissue factor over expression is the initial reaction of coagulopathy during pneumonia and provokes extrinsic thrombosis in vascular compartment. Previous studies showed Tissue factor inhibition beneficial in CAP patients with sepsis. However, in this multicenter, randomized double blinded and placebo controlled clinical trial, Tifacogin, the Tissue Factor Pathway Inhibitor, did not have any effects on mortality and adverse effects in severe CAP patients. Possible reason include tissue factor expression is an event in pneumonia and it may be irreversibly activated before administration of Tifacogin. Future studies are in need for coagulation/fibrinolysis activity modulations in pneumonia and sepsis.

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Risks of Pneumonia in Patients with Asthma Taking Inhaled Corticosteroids

Authors: O’Byrne PM, Pedersen S, Carlsson LG et al.
URL: http://ajrccm.atsjournals.org/content/183/5/589.long

Comments: Corticosteroid inhalation is the mainstay for treatment of asthma according to GINA. There are some reports showing association of steroid inhalation and increased risk of pneumonia in chronic obstructive pulmonary disease, but it is not clear whether steroid inhalation has any impact on pneumonia incidents in asthma patients. In this retrospective study based on 26 trials on budesonide and comparator, 60 trials on budesonide and fluticasone, the authors did not find any difference on pneumonia incidence or severe adverse effects between those two groups of population. These results do not support any increased risk of pneumonia in patients with asthma using inhaled corticosteroid.

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