4678
Potential economic savings of administration of home intravenous antibiotic therapy to patients with acute respiratory infections in Ireland.
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Introduction: Acute respiratory infections (ARI) account for a significant proportion of prolonged hospital stays. Intermediate care initiatives supporting home intravenous antibiotics (HIVA) aim to facilitate early discharge and avoid unnecessary admissions. Numerous studies have demonstrated the efficacy of HIVA for acute infections. International studies have shown increased patient satisfaction, improved quality of life, fewer investigations, decreased social disruptions and increased cost-effectiveness.

Objective: The purpose of this study was to analyse the potential cost-effectiveness of HIVA in patients with ARI in Ireland.

Methods: Using the Health Service Executive (HSE) Casemix and assuming a 60% uptake of ARI patients satisfying HIVA criteria with a length of stay (LOS) of 1-3 days, cost-estimates relating to cost/bed and LOS were used to calculate cost/bed-day savings if HIVA is introduced.

Results: The approximate annual admission rate for ARI conditions such as pneumonia, COPD, asthma, CF and bronchiectasis is 26,700 patients/yr with an average cost per admission of €70,600. Based on an average LOS of 9.2 days at a cost/bed/day of €1,920, the cost/ARI admission is €17,664. This equates to €473/1. An LOS of 1-3 days would result in cost-estimates of €51,415-154.2/m, a gross difference of €318.8/m. Accounting for expenses such as capacity, staff, training, equipment, travel and others, we estimate bed-day savings of €200-220/m/yr.

Conclusion: HIVA administration is a safe, cost-effective alternative in suitable patients with ARI, potentially providing significant savings to the health service in Ireland.

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A prospective re-audit of admissions and discharge delays occurring in patients admitted to a district general hospital’s respiratory ward in the United Kingdom
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Introduction: The National Confidential Enquiry into Patient Outcome and Death recommends that following initial assessment and treatment, patients should be transferred to a ward which is appropriate for their clinical condition.

Objective: To assess delays prior to discharge for patients (respiratory vs non-respiratory) whom are medically fit for discharge, following a reduction in respiratory beds from 62 to 46 as recommended by Sarker et al 2010.

Methods: A prospective 2-week audit was conducted on respiratory wards and in-
evaluated. The fluid samples were examined for Gram stain, acid-fast bacilli smear together with specific bacterial, fungal and mycobacterial cultures. 

Conclusions: A reduction in respiratory beds lead to a reduction in patients with delayed discharge regardless of the underlying medical diagnosis. All delays were statistically significant. Efficient transfer to appropriate wards on admission will further reduce the number of delayed discharges.

4680  
The attitude of physicians for asthma treatment and results in the inhaler market between 2004-2009 in Turkey  

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We evaluated the effects Turkey Conversion Programme in Health in 2004 on drug market in the treatment of asthma. We analyzed the data from IMS the programme following the drug market and the data from the Social Security Institution (SSI) for comparative studies. In 2004 SSI paid nearly 4.0 billion Euro for drugs which increased to 8.5 billion (180%) Inhaled dust asthma drugs was 88.9 million and increased to 280.6 million (3.16 fold). Drug prescribed was 6.037.142 and increased to 20.848.058 boxes (3.45 fold).In the market of subgroup for inhaler dust asthma drugs distribution was: the rescue drugs 31.5%, combined drugs 17.7%, nebulizer 10.5%. The rates in 2009 were 20.2%, 29.6% and 18% respectively. Economically distribution was; 48.4% for combined drugs, 6.3% for nebulizer and 6.3% for rescue drugs.Rates for 2004 was 58.4%, 9.2% and 4.1%. The number of rescue drugs increased, from 1.901.938 boxes to 4.220.664 (2.2 fold). The financial increase was 4.62 fold from 5.570.177 to 27.539.326. The number for nebulizer was 631.184 and increased to 3.762.806 (5.96 fold) the cost for them was 5.570.177 increased to 27.539.326 (4.62 fold). The combined drug subgroup the number of prescriptions were 1.066.486 increased to 6.178.315 (5.79 fold).The cost was 43.006.559 and increased to 163.814.343. There has been an increase in the costs for inhaler drugs used for asthma treat- ment. Our analyses showed that this increase mostly caused by increase in the number of prescribed combined drugs. This increase we believe decreased the need for rescue drugs but had no effect on the nebulizer that has been used.

4681  
Stepping up the controller medication in asthma patients: Impact of various treatment options on costs  
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Introduction: To compare asthma-related costs among adults who step-up their controller medication. 

Methods: A population-based study was conducted using the administrative health data, the rescue drugs and asthma drugs, Canada (1997 to 2007). Hospitalization, physician visits, and prescription records were used to identify asthma patients (age 14-65) and calculate direct costs. Four cohorts were constructed as those who: increased the dose of inhaled corticosteroids (ICS) group, switched to ICS/long-acting beta-agonist (LABA) in a single formulation (ICS/LABA group), added LABA in separate formulations (ICS+LABA group), or added leukotriene receptor antagonist (ICS+LTRA group). The outcome was the direct cost of asthma (2008 CAD) in the year after the step-up, adjusted for multiple demographic, resource use, and comorbidity variables from the previous year.

Results: 52.640 patients (average age 43.3; 60.3% female) were included (7,115 ICS+, 19,457 ICS/LABA, 4,086 ICS+LABA, and 1,982 ICS/LRA). The average costs of asthma for the year after the index date for the ICS+ group was 550$. Compared to ICS+, all other groups had significantly positive incremental costs: +358.0 for ICS/LABA, +550.4 for ICS+LABA, and +554.1 for ICS/LRA (all P<0.01). Higher age, higher resource use, and higher cumulative dose of rescue medication in the year prior to the step-up date were predictors of higher costs after the step-up date (all P<0.01).

Conclusions: Based on relatively large sample and adjusted for several potential confounders, increasing ICS dose as a step-up approach was associated with the lower costs compared to addition of a second class of controller medication.

4682  
The cost and diagnostic efficacy of microbiological evaluation of exudative pleural effusion  
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Purpose: To evaluate the cost and diagnostic efficacy of microbiological studies of pleural fluids. 

Method: Hospitalized patients with exudative pleural effusion were prospectively evaluated. The fluid samples were examined for Gram stain, acid-fast bacilli smear together with specific bacterial, fungal and mycobacterial cultures. 

Results: Bacteriologic and EZN stains of the pleural fluids were negative in 89 cases included whereas fluid cultures were positive in 9 (10.1%) cases [3 (12.5%) of the 24 with tuberculous pleurisy and 6 (28.5%) of the 21 with empyema or other parapneumonic pleural effusion]. The cultures of the malignant, nonspec- ific and paramalignant fluids were negative. In cases with empyema or other parapneumonic pleural effusion and tuberculous pleurisy, no significant difference was determined between culture-positive and culture-negative cases regarding age, gender, fever or fluid LDH and glucose levels; positive cultures were more frequent in the presence of fluid purulence (55.6% versus 8.3%, p=0.046). In 5 (83.3%) of the 6 culture-positive and in 6 (40%) of the 15 culture-negative cases with empyema or other parapneumonic effusion, change in antibiotic treatment was necessary. The costs of the microbiological studies was 39.4 Euro for each case and 1735 Euro and 1419 Euro for cases with noninfectious and infectious fluids, respectively.

Conclusion: Diagnostic yield of the routine microbiological studies of pleural flui- ds was determined low. It was concluded that requesting microbiological studies of pleural fluids in cases strongly considered to have infection on clinical basis in cases with purulent fluid would be more beneficial regarding diagnostic yield and cost.

484. Translational models of airway disease

4683  
Bitter taste receptor agonists as a novel class of bronchodilators in guinea-pig airways  
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Rationale: Desh mendie et al. (Nat Med 2010) reported that several bitter taste receptor (TAS2R) agonists evoked relaxation of mice and human airways. We examined the effects of three prototype agonists in segments of guinea pig trachea (GPT).

Methods: GPT was pre-contracted with 0.1 µM carbachol in both absence and presence of 3 µM indomethacin or prostaglandin antagonists. The segments were either exposed to denatonium, chloroquine or saccharin, or kept untreated. Ex- pression of TAS2Rs in guinea pig tracheal epithelium and smooth muscle was measured with real-time PCR.

Results: Denatonium and chloroquine induced concentration-dependent relax- ations whereas saccharin had no effect. In consistency with these findings, there was expression of TAS2R4 and TAS2R10 in mouse and human airways. We examined the effects of three prototype agonists in segments of guinea pig trachea (GPT).

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4684  
Prostacyclin modifies VEGF synthesis in fibroblasts from healthy and COPD patients  
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Background: Involvement of vascular remodelling in the lung is a characteristic feature of chronic obstructive lung disease (COPD). The vascular mediator prostacy- clin may regulate fibroblast activity. The objective was to study the effects of prostacyclin on synthesis of vascular endothelial growth factor (VEGF) and its interac- tions with transforming growth factor β1(TGF β1) in distal lung fibroblasts from patients with COPD and control subjects.

Methods: Primary human lung fibroblast cultures were established from periph- eral airway biopsy samples from healthy individuals (controls, n=5) and after lung resection from patients with COPD (GOLD IV) (n=7). The lung fibroblasts were cultured in 0.4% medium and stimulated with the cyclooxygenase inhibitor indomethacin 3 µM in combination with the prostacyclin analogue iloprost 1 µM and TGF-B 10ng/ml for 24h. VEGF production was measured in the cell culture supernatant by ELISA.
Iloprost enhanced VEGF synthesis in fibroblasts from control subjects (p < 0.05) but not in COPD patients.

**Conclusions:** Iloprost enhanced VEGF synthesis in fibroblasts from both healthy and patients with COPD. Though, ioprost had no effect on VEGF after TGF-β stimulation, whereas indomethacin reduced VEGF production in fibroblasts from patients with COPD (p < 0.01). However, ioprost showed no effect on VEGF synthesis after TGF-B stimulation, whereas indomethacin reduced VEGF production in fibroblasts from patients with COPD (p < 0.05) and 6-1-fold from patients with COPD to 0.01). However, ioprost showed no effect on VEGF synthesis after TGF-B stimulation, whereas indomethacin reduced VEGF production in fibroblasts from patients with COPD (p < 0.05) and 6-1-fold from patients with COPD.

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Potential involvement of the CCR10/CCL28 axis was recently reported in a murine model of allergic asthma [1]. Blockade of the CCR10 receptor might therefore represent a novel alternative to the current treatment of asthma. We have investigated the effect of the PEM CCR10 antagonist, POL7085, in an allergic model of asthma in mice. Nine week-old male Balb/c mice were sensitized to ovalbumin (OVA) administered intraperitoneally in the presence of alum (D0 and D7), and challenged to OVA administered intranasally (D18 to D21). POL7085 was administered once daily 1 hour before each OVA challenge at 9 and 18mg/kg intra-nasally (I.N.) x 5 days. De novo gene synthesis of IL-13 was studied by RT-qPCR.

In conclusion, the PEM CCR10 antagonist, POL7085, significantly and dose-dependently decreased asthma symptoms after once daily local administration in particular AHR and eosinophilia. Blocking the CCR10 chemokine receptor therefore appears as a promising novel approach for treating asthma.

**References**


**4687**

**Protective effect of a protein epitope mimic (PEM) CCR10 antagonist, POL7085, in an allergic model of asthma**

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Potential involvement of the CCR10/CCL28 axis was recently reported in a murine model of allergic asthma [1]. Blockade of the CCR10 receptor might therefore represent a novel alternative to the current treatment of asthma. We have investigated the effect of the CCR10 antagonist, POL7085, in an allergic model of asthma in mice. Nine week-old male Balb/c mice were sensitized to ovalbumin (OVA) administered intraperitoneally in the presence of alum (D0 and D7), and challenged to OVA administered intranasally (D18 to D21). POL7085 was administered once daily 1 hour before each OVA challenge at 9 and 18mg/kg intra-nasally (I.N.) x 5 days. De novo gene synthesis of IL-13 was studied by RT-qPCR.

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**References**


**4688**

**Characterisation of TNF-α alpha lectin-like domain derived peptides associated with improved alveolar fluid clearance in pulmonary oedema**

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The beneficial effect of the lectin-like domain of TNF-alpha, including the TIP peptide which mimics this domain, on activation of oedema resorption, improved alveolar clearance and protection of lung function after transplantation, is well documented from several independent studies in vitro and in vivo studies using animal models. The effect is mediated by activation of sodium current through ENaC in A549 cells with the patch clamp technique. For all ENaC-activating TIP peptides a maximum effect was observed at 120 nM. Compared to TNF-alpha (EC50 8.2 nM) and the original human TIP peptide (24.3±3 vs 44.3±3 for DEX).

In conclusion, the PEM CCR10 antagonist, POL7085, significantly and dose-dependently decreased asthma symptoms after once daily local administration in particular AHR and eosinophilia. Blocking the CCR10 chemokine receptor therefore appears as a promising novel approach for treating asthma.

**References**


**4689**

**Consequences of chronic pulmonary TLR9 activation in the lung and beyond**

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Potential involvement of the CCR10/CCL28 axis was recently reported in a murine model of allergic asthma [1]. Blockade of the CCR10 receptor might therefore represent a novel alternative to the current treatment of asthma. We have investigated the effect of the CCR10 antagonist, POL7085, in an allergic model of asthma in mice. Nine week-old male Balb/c mice were sensitized to ovalbumin (OVA) administered intraperitoneally in the presence of alum (D0 and D7), and challenged to OVA administered intranasally (D18 to D21). POL7085 was administered once daily 1 hour before each OVA challenge at 9 and 18mg/kg intra-nasally (I.N.) x 5 days. De novo gene synthesis of IL-13 was studied by RT-qPCR.

In conclusion, the PEM CCR10 antagonist, POL7085, significantly and dose-dependently decreased asthma symptoms after once daily local administration in particular AHR and eosinophilia. Blocking the CCR10 chemokine receptor therefore appears as a promising novel approach for treating asthma.

**References**

Results: Total BAL cells were increased in all CpG-ODN mice (p < 0.05). PMNs were increased in blood (30%) and BAL (39%) which persistent upon prolonged exposure duration. Blood lymphocytes were subchronically 19% decreased which was reflected in an abundant pulmonary (sub-) chronic lymphocyte influx. Chronic exposure leads to 21% decreased peak expiratory flow (ml/sec) and 71% increased airway resistance (cm H2O/ml/sec). Right ventricle heart hypertrophy was observed upon chronic exposure; ratio right ventricle weight/total heart weight CpG-ODN=0.23±0.007; control=0.19±0.008. Wet lung weight was 15.2% increased subchronically and 70.8% chronically.

Conclusion: An interplay between neutrophils and lymphocytes could possibly play a role in TLR9 induced adverse pulmonary and cardiovascular effects. Caution is needed when CpG-ODNs are chronically administered for therapeutic purposes.

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Efficacy of the TRPV1 antagonist SB-705498 in an MRI guinea pig model of rhinitis

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Rationale: Antagonism of nasal TRPV1 receptors is a potential target for inhibition of symptoms associated with rhinitis. Here, we explore the pharmacology of SB-705498 on the contralateral nasal secretory response to ipsilateral nasal capsaicin challenge in the guinea pig.

Methods: Experiments were conducted on intranasally sensitised guinea pigs. Absolute nasal fluid volumes were measured using MRI techniques that provide images of the total nasal cavity of the guinea pig. Animals were pre-treated with SB-705498 or vehicle (-1, -6 and -24h) and MRI scanned to produce first a baseline measurement and then a further measurement at 10 minutes post capsaicin challenge (0.3mM; 50ul).

Results: 1 hour pre-treatment with SB-705498 resulted in approximately 50% inhibition of the secretory response at 10mg/kg (oral; p < 0.05), 1mg/kg (intranasal suspension; p < 0.005) and 0.1mg/kg (intranasal particle reduced suspension; p < 0.0005). At 12 hour pre-treatment, approximately 60% inhibition (p < 0.0001) was observed with SB-705498 at 1mg/kg (intranasal particle reduced suspension); at 24h this had reduced to ∼50% inhibition (p < 0.01).

Conclusion: These studies demonstrate that SB-705498 inhibits capsaicin-induced intranasal parasympathetic responses in guinea pig. Topical application of SB-705498 was associated with a further improvement in intranasal potency.