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Each summary contains the name of the first author, the title of the paper, the Vancouver reference and/or doi number, and a link to the abstract of the paper. In the majority of cases these are subscription journals, so to view the full text you will need to subscribe to the journal or pay to view on an individual article basis.

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Asthma

Excitement over fixed-dose ciclesonide/ formoterol?

Korn and Buhl, Efficacy of a fixed combination of ciclesonide and formoterol: the EXCITED study.
Resp Med 2012;**106**:57-67.
http://dx.doi.org/10.1016/j.rmed.2011.08.010

This Phase II multi-centre randomised parallel group non-inferiority study is the first to evaluate the efficacy and safety of Altana Pharma's fixed-dose ciclesonide/formoterol 320/9 combination dry-powder inhaler (DPI) against a fluticasone/salmeterol 250/50 DPI. 160 patients were randomised, and treatment was for 6 weeks. The primary outcome was change in FEV_1 from randomisation to the final study visit; secondary outcomes were percentage of days without asthma symptoms, and use of rescue medication during the final 4 weeks of treatment. Comparable statistically significant improvements in primary and secondary outcomes occurred in both treatment groups. Ciclesonide/formoterol fixed-dose combination was not inferior to the flixotide/salmeterol combination in terms of efficacy and tolerability. We await further studies on how ciclesonide/formoterol compares with the currently available fixed-dose combination inhalers.

"Doctor, is this pollution making my asthma worse?"

Andersen *et al*. Long-term exposure to air pollution and asthma hospitalisations in older adults: a cohort study.
Thorax 2012;**67**:6-11.
http://dx.doi.org/10.1136/thoraxjnl-2011-200711

The authors followed-up the 57,000 subjects in the Danish Diet, Cancer and Health cohort (aged 50-65 at baseline in 1993-1997) for 10 years to obtain data on first hospital admission for asthma, and correlated this with annual nitrogen dioxide (NO_2) levels used as a proxy for traffic-related air pollution around their homes since 1971. Using Cox regression models to assess the association between the two, NO_2 levels were associated with an increased risk of asthma hospitalisation and first-ever admissions, with the highest risk in people with pre-existing asthma or COPD. In his linked editorial, Kunzli highlights the two primary hypotheses relevant to research on air pollution and chronic respiratory diseases: that exposure supports the development of the underlying chronic pathology thus increasing the pool of patients prone to acute exacerbations; or that exposure triggers an acute event among those with the disease. We need more studies to ascertain which is correct…

"I can tell you're going to have an asthma exacerbation…"

Schatz *et al*. The relationship of asthma impairment determined by psychometric tools to future asthma exacerbations.
Chest 2012;**141**:66-72.
http://dx.doi.org/10.1378/chest.11-0574

These authors compared three validated questionnaires which evaluate the effect that asthma has on patients' lives ('asthma impairment') and assessed their ability to predict asthma exacerbations. 2680 patients with persistent asthma completed the Asthma Control Test (ACT), mini-Asthma Quality of Life Questionnaire (mAQLQ), and Asthma Impact Survey (AIS-6), and documented any exacerbations over the previous 12 months. Responses to the three questionnaires were analysed, and individual patient scores were calculated. Scores on each of the three questionnaires were significantly related to future asthma exacerbations, notwithstanding any previous exacerbations in that particular patient (relative risk 1.3). Three factors – symptoms, activity and 'bother' – were each significantly associated ($P < 0.0001$) with future asthma exacerbations. The authors conclude that interference with activities is the primary subjective component of asthma impairment that is related to future exacerbation risk. This sounds eminently like common sense…

Risk of asthma is lower following RSV versus non-RSV bronchiolitis in infancy

Koponen *et al*. Preschool asthma after bronchiolitis in infancy.
Eur Respir J 2012;**39**:76-80
http://dx.doi.org/10.1183/09031936.00040211

This study confirms what we thought previously: that the risk of childhood asthma is lower after respiratory syncytial virus (RSV) infection compared with non-RSV infection in infancy. Out of 205 infants aged < 6 months hospitalised for bronchiolitis, 166 (81%) were able to provide follow-up data either in a face-to-face consultation or by telephone 6 years later (mean age 6.5 years). Identical structured questionnaires were used. The viral aetiology of the bronchiolitis was proven in 97% of cases. Current asthma was present in 8.2% in the RSV bronchiolitis group versus 24% in the non-RSV patients. 45 of the 166 children (27%) had ever had asthma. In adjusted analyses, atopic dermatitis, non-RSV bronchiolitis and maternal asthma were independent early-life risk factors for asthma. So, the risk of asthma is lower after RSV bronchiolitis than after bronchiolitis caused by other viruses in children who were hospitalised at < 6 months old.

Does SMART apply to smokers as well as non-smokers?

Van Schayck *et al*. Do asthmatic smokers benefit as much as non-smokers on budesonide/formoterol maintenance and reliever therapy? Results of an open label study.
Resp Med 2012;**106**:189-96.
http://dx.doi.org/10.1016/j.rmed.2011.10.017

If our patients have asthma and still smoke, they're almost guaranteed to have a degree of 'steroid non-responsive' asthma – i.e. smoking dramatically reduces the effectiveness of inhaled corticosteroids (ICS) at the steroid receptor. This paper reports data on 886 smokers and matched controls

from the EuroSMART study, an open, randomised, 6-month study comparing budesonide/formoterol (200/6) as Single inhaler Maintenance And Reliever Therapy (SMART) at two different maintenance doses (1 or 2 puffs twice-daily [bd]) in patients who were symptomatic despite ICS and long-acting beta2-agonists. Severe asthma exacerbations and changes in the 5-item Asthma Control Questionnaire (ACQ-5) were calculated. Mean time to first severe exacerbation was not statistically different between the two groups. For smokers there was a statistically significant prolonged time to first severe exacerbation for those on the higher maintenance dose of ICS. But these were mild smokers less than 40 years old or with a smoking history less than 10 pack-years – so the authors are careful to qualify their advice in declaring that SMART may benefit patients with a 'limited' smoking history…

What characterises adolescent-onset asthma?

Kurukulaaratchy *et al*. Characterisation of asthma that develops during adolescence: findings from the Isle of Wight birth Cohort.
Resp Med 2012;**106**:329-37.
http://dx.doi.org/10.1016/j.rmed.2011.12.006

Here, the authors report data from a longitudinal birth cohort study (the Isle of Wight Whole Population Birth Cohort, n = 1456, recruited in 1989) and reviewed the children at age 1,2,4, 10 and 18. 'Adolescent-onset asthma' was defined as asthma at age 18 without any previous history of asthma, and 'persistent-adolescent asthma' as asthma at age 10 and 18. Adolescent-onset asthma accounted for 28.3% of the asthma prevalence at age 18, and was of similar severity to persistent-adolescent asthma. The adolescent-onset asthma patients showed elevated bronchial hyperresponsiveness (BHR) and atopy at age 10 and 18, and at age 18 their BHR, bronchodilator reversibility and sputum eosinophilia were comparable to the persistent-adolescent group. In children aged 10 who later went on to have adolescent-onset asthma, the boys already had impaired lung function whereas the girls developed reduced lung function in their mid-teens. Predisposing factors for adolescent-onset asthma were atopy (odds ratio [OR] 2.35; 95% CI = 1.08-5.09), rhinitis (OR 2.35; 1.11-5.01) and BHR (OR 3.42; 1.55-7.59) at age 10. A further reminder that good history-taking, focussing on any past history of atopic disease, is important in diagnosing asthma in teenagers…

Age, obesity and lung function in asthma

Lang *et al*. Does age impact the obese phenotype? Longitudinal asthma control, airway function, and airflow perception among mild persistent asthmatics.
Chest 2011;**140**:1524-33.
http://dx.doi.org/10.1378/chest.11-0675

We know that obesity can cause dyspnoea in the absence of any other pathology, and that it typically produces a restrictive defect on spirometry. But what impact does obesity have in the presence of pre-existing asthma? Previous studies have shown conflicting results. These authors set out to see whether age modifies the effect of obesity on asthma using a post hoc analysis of a well-phenotyped cohort of 490 patients with mild persistent asthma. In children aged 6-11, obesity caused a large reduction in lung function but the obese children reported fewer asthma symptoms than the non-obese children. In 12-17 year-olds, the obese tended to have greater airflow obstruction and asthma symptoms than the non-obese – and this was particularly so for girls. In adults, the impact of obesity was only noticeable in women aged 18-44. Therefore, obesity has the greatest impact on asthma in children and in women. An important consideration when assessing the reasons for poor asthma control in these patients…

Allergy

Vitamin D in asthma and allergy

Hollams *et al*. Vitamin D and atopy and asthma phenotypes in children: a longitudinal cohort study.
Eur Respir J 2011;**38**:1320-7.
http://dx.doi.org/10.1183/09031936.00029011

Previous studies have shown links between vitamin D and atopic and asthma phenotypes. Here, using previously ascertained phenotypic data, the authors assessed vitamin D levels as a risk modifier for respiratory and allergic outcomes in 989 6-year olds and 1,380 14-year olds (689 children were assessed longitudinally at age 6 and then 8 years later) in Perth, Western Australia. They conclude that, in this large unselected cohort, children – particularly boys – with inadequate vitamin D at 6 and 14 years of age had increased atopy and bronchial hyperresponsiveness, and that low vitamin D at age 6 is a predictor of atopy and asthma at age 14. Future potential for therapeutic intervention?…We shall see.

COPD

Measuring self-efficacy after pulmonary rehabilitation

Vincent *et al*. Measuring a change in self-efficacy following pulmonary rehabilitation. An evaluation of the PRAISE tool.
Chest 2011;**140**:1534-9.
http://dx.doi.org/10.1378/chest.10-2649

The role of pulmonary rehabilitation (PR) in the management of COPD is well established. What is less well known is how to predict which patients will do well. Self-efficacy explores emotional functioning and coping skills, and is purported to be a strong predictor of health behaviours. The authors investigated the reproducibility and sensitivity of the PRAISE tool (adapted from another self-efficacy scale) in 29 stable COPD patients who completed the tool during PR assessment and seven days later, and in 225 patients who completed it before and after a 7-week course of PR. Other assessments included the incremental shuttle walk test, MRC dyspnoea scale, and CRQ-SR and HADS questionnaires. PRAISE was shown to have test-retest reliability, but could not predict a successful outcome of PR.

Rapid decliners, slow decliners, and sustainers: different COPD phenotypes based on rate of FEV_1 decline

Nishimura *et al*. Annual change in pulmonary finction and clinical phenotype in chronic obstructive pulmonary disease.
Am J Resp Crit Care Med 2012;**185**:44-52.
http://dx.doi.org/10.1164/rccm.201106-0992OC

According to the Fletcher-Peto curve, our FEV_1 peaks at age 25 and then declines – and this rate of FEV_1 decline is worse in susceptible smokers. This is the whole rationale for encouraging smoking cessation in all COPD patients who continue to smoke. But aside from the smoker/non-smoker divide, what else determines the rate of FEV_1 decline? This was a 5-year observational cohort study of 261 patients with COPD (26% stage I, 45% stage II, 24% stage III, 5% stage IV) who had detailed pulmonary function assessment at baseline with spirometry at 6-monthly intervals thereafter, and disease severity assessed by CT scanning and annual measurements of carbon monoxide (CO) transfer coefficient. Average annual decline in FEV_1 was -32 +/- 24 [SD] mL/year but there was considerable variability: the lowest quartile were termed 'Rapid decliners', the middle two quartiles 'Slow decliners', and the highest quartile 'Sustainers'. The 'Rapid decliners' had more severe emphysema as assessed by CT and CO transfer coefficient (rather than FEV_1 % predicted). The authors conclude that these 'Rapid decliners' require much more attention in clinical practice…

COPD and its co-morbidities…again

Macchia *et al*. Unrecognised ventricular dysfunction in COPD.
Eur Respir J 2012;**39**:51-8.
http://dx.doi.org/10.1183/09031936.00044411

These authors used a prospective 2-year cohort study design to assess the prevalence and prognostic implications of previously undiagnosed coexistent congestive heart failure (CHF) in patients with COPD, and the presence of (undiagnosed) airway obstruction in patients with CHF. All patients were aged 60 or over. 201 patients with echocardiographically-confirmed CHF underwent routine spirometry, and 218 patients with clinically and spirometry-confirmed COPD had routine echocardiography and B-type natriuretic peptide (BNP) measurement. 37.3% of the CHF patients had airway obstruction, and 17% of the COPD patients had CHF. The presence of CHF in patients with COPD tended to increase mortality over the 2-year

follow-up period (hazard ratio 2.34, 95% CI 0.99-5.54; P = 0.053), but the presence of airway obstruction in patients with CHF did not alter survival rates. This is yet more evidence that we need to think holistically and consider other co-morbidities when managing our COPD patients…

Infections

Worldwide respiratory infections in children secondary to influenza

Nair *et al*. Global burden of respiratory infections due to seasonal influenza in young children: a systematic review and meta-analysis.
Lancet 2011;**378**(9807):1917-30.
http://dx.doi.org/10.1016/S0140-6736(11)61051-9

The incidence of (and mortality from) acute lower respiratory infections (ALRI) secondary to influenza in children is unknown. Funded by WHO and the Bill and Melinda Gates Foundation, this large group of international authors systematically reviewed 43 studies with data on 8 million children. Age-stratified incidence estimates for influenza episodes and influenza-associated ALRI were then applied to global population estimates for 2008. Estimated mortality rates were obtained by combining these incidence data with case fatality ratios from hospital- and population-based data. The authors estimate that there were up to 111,000 deaths worldwide in children aged under 5 attributable to influenza-associated ALRI in 2008, 99% of which occurred in developing countries. A challenge for us all…

Sleep disorders

Obstructive Sleep Apnoea, CPAP, and the metabolic syndrome

Sharma *et al*. CPAP for the metabolic syndrome in patients with obstructive sleep apnea.
NEJM 2011;**365**:2277-86.
http://www.nejm.org/doi/full/10.1056/NEJMoa1103944

In this double-blind placebo-controlled crossover trial, 86 patients with obstructive sleep apnoea (OSA) – 75 of whom had the metabolic syndrome – received three months of therapeutic continuous positive airway pressure (CPAP) followed by sham CPAP, or vice versa, with a one-month washout period in between. The measurements taken included blood pressure (BP), fasting glucose, insulin resistance, fasting lipid profile, and glycosylated haemoglobin (HbA1c) levels. CPAP treatment was associated with significant mean decreases in systolic and diastolic BP, total cholesterol, LDL, tryglcerides, and HbA1c. OSA is associated with an increased prevalence of the metabolic syndrome, and this is the first study to show that these metabolic abnormalities can at least partially be reversed by CPAP treatment.

Fibrotic lung disease

Using FVC to measure clinical status in idiopathic pulmonary fibrosis

Du Bols *et al*. Forced vital capacity in patients with idiopathic pulmonary fibrosis. Test properties and minimal clinically important difference.
Am J Resp Crit Care Med 2011;**184**:1382-9.
http://dx.doi.org/10.1164/rccm.201105-0840OC

Forced vital capacity (FVC) measurement has an established role in assessing pulmonary function in patients with idiopathic pulmonary fibrosis (IPF), but the authors of this study set out to clarify that role in terms of its reliability, validity, responsiveness, and to estimate the minimal clinically important difference (MCID) – i.e. the clinical significance of changes in the FVC over time. FVC and other measures of functional status were measured at baseline and at 24-week intervals thereafter in 1,156 randomised patients from two other clinical trials. FVC was a reliable, valid and responsive measure of clinical status in patients with IPF, and a decline of 2-6% - although seemingly a small degree of change – represented a clinically important difference.

Miscellaneous

Intravenous β2-agonists make acute respiratory distress syndrome (ARDS) worse

GaoSmith *et al*. Effect of intravenous β_2-agonist treatment on clinical outcomes in acute respiratory distress syndrome (BALT-2): a multicentre, randomised controlled trial.
Lancet 2012;**379**:229-235.
http://dx.doi.org/10.1016/S0140-6736(11)61623-1

This is an important negative study. A previous phase 2 randomised controlled trial (RCT) of intravenous (i.v.) salbutamol for up to 7 days in patients with ARDS had shown that salbutamol reduced lung fluid and airway pressure – slightly encouraging you might think… In order to assess the effects of i.v. salbutamol on overall mortality, these authors performed a multicentre placebo-controlled parallel-group RCT on intubated and mechanically ventilated adult patients who were randomised within 72 hours of ARDS onset to receive either i.v. salbutamol (15mcg/kg/hour) or placebo for up to seven days. 161 patients received salbutamol and 163 received placebo. Intravenous salbutamol increased 28-day mortality – 55/161 (34%) patients died in the salbutamol group, whereas 38/163 (23%) patients died in the placebo group [risk ratio 1.47, 95% CI 1.03-2.08]. In fact, the study was stopped early after the second interim data analysis because of safety concerns.

Marijuana and the lungs

Pletcher *et al*. Association between marijuana exposure and pulmonary function over 20 years.
JAMA 2012;**307**(2):173-81.
http://dx.doi.org/10.1001/jama.2011.1961

In this paper, the authors used data from the Coronary Artery Risk Development in Young Adults (CARDIA) study – a longitudinal study of 5115 subjects in four cities in the USA who had pulmonary function and smoking habits assessed at intervals over 20 years – and matched this with lifetime exposure to marijuana joints expressed in joint-years (1 joint-year of exposure = 365 joints or filled pipe bowls). The main outcome measures were FEV_1 and FVC. Marijuana exposure was nearly as common as tobacco exposure but was light (median 2-3 joints/month). There was a direct linear relationship between tobacco exposure and reduction in both FEV_1 and FVC, but the relationship between pulmonary function and marijuana use was non-linear: low cumulative marijuana use was not associated with any adverse effects on lung function, whereas very heavy marijuana use was significantly associated with increased changes in FVC.