Hot topics from the Assemblies

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Prevalence of pulmonary embolism in patients with syncope: findings from the Pulmonary Embolism in Syncope Italian Trial (PESIT)

Authors: Prandoni P, Lensing AW, Prins MH, *et al.* *N Engl J Med* 2016; 375: 1524–1531

Summary: Syncope is a transient loss of consciousness typically due to cerebral hypoperfusion with many causes, including pulmonary embolism. The prevalence of pulmonary embolism in patients with syncope is unknown; hence, in a prospective study, Prandoni *et al.* and the PESIT investigators report in the *New England Journal of Medicine* the prevalence of pulmonary embolism in 560 patients admitted for a first episode of syncope at 11 medical centres in Italy.

All patients had a comprehensive evaluation including a detailed history and physical examination, a chest radiograph, an ECG, arterial blood gas analysis and a D-dimer assay. This was followed by risk stratification using a pre-test probability assessment using the simplified Well's score. Pulmonary embolism was excluded in 330 (59%) patients on the bases of a low pre-test probability and a negative D-dimer test.

In the remaining 230 patients, 135 (58.7%) had a positive D-dimer test, three (1.3 %) had a high pre-test probability while 92 (40%) had both positive D-dimer and high probability. A computed tomography pulmonary angiogram or ventilation/perfusion scan was performed as appropriate in all three groups and a pulmonary embolism was diagnosed in 97 (42.2%) patients on imaging or at autopsy. The authors estimated that one in six patients hospitalised for a first episode of syncope had a pulmonary embolus as an underlying cause.

This important study that demonstrates that pulmonary embolism is a common cause of syncope and therefore a systematic evaluation should be conducted in patients with syncope with a view to exclude this diagnosis.

Reviewed by: Sunkaru Touray (USA, Assembly 6)

Spatiotemporal microbial evolution on antibiotic landscapes

Authors: Baym M, Lieberman TD, Kelsic ED, *et al.* *Science* 2016; 353: 1147–1151

Summary: In the last few years, there has been growing interest in studies of phenotypic and genotypic evolution of antibiotic resistance. Baym *et al.* reported details of a novel experimental device, the MEGA (microbial evolution and growth arena) plate, a giant square acrylic dish (120×60 cm). Different concentrations of antibiotics (trimethoprim or ciprofloxacin) with an exponential increase of minimum inhibitory concentration from periphery to centre were overlaid by soft agar allowing bacterial motility. The drug-free outermost rims of the dish were inoculated with *Escherichia coli* and bacteria spread by chemotaxis to subsequent sections with a 10-fold increase in dose. Time-lapse photography allowed observation of bacterial evolution, competition, mutation and survival. The successful mutants that reached a further level were unable to grow, then secondary mutations arose and the process repeated. To study the intermediate steps in evolution, the authors inoculated bacteria from the region with no drug to that with a high level directly and through one middle region. Bacteria could not adapt directly from zero to the highest concentration, but intermediate mutants, trapped beyond the propagating front, were able to grow in a region where the front could not and had also increased resistance. Nowadays, high-level multiantibiotic resistance is emerging and spreading globally, and the proposed method allows evolutionary and diversity researche of mutational pathways to resistance.

Reviewed by: Rustem Shamuraytov (Russia, Assembly 10)

Prevalence and predictors of obstructive sleep apnoea in young children with Down syndrome

Authors: Hill CM, Evans HJ, Elphick H, *et al.* *Sleep Med* 2016; 27-28: 99–106

Summary: Children with Down syndrome are vulnerable to obstructive sleep apnoea (OSA) because of their unique craniofacial anatomy and hypotonia. Timely recognition and treatment of OSA in these children is an important goal for their optimal cognitive function and quality of life. Although guidelines recommend routine OSA screening in young children with Down syndrome, there is a lack of reliable data in this group.

The aim of the study by Hill *et al.* was to recruit a large cohort of young children with Down syndrome to determine the prevalence and predictors of moderate-to-severe OSA. In total, 188 participants aged from 6 months to 6 years were studied. 169 studies were completed

at home and 19 in a sleep laboratory. OSA was found in 44% and 14% had moderate-to-severe OSA. This was not predicted by age, tonsillar size or standardised body mass index centile.

This is the largest study reported to date describing the prevalence and predictors of OSA in a European population of children with Down syndrome. The authors concluded that young children with Down syndrome should be routinely screened for OSA using objective measures and that domiciliary cardiorespiratory polygraphy is an acceptable screening approach. Further studies in larger independent populations of children with Down syndrome are required to establish the OSA severity thresholds associated with the increased risk of neurocognitive and cardiovascular morbidity.

Reviewed by: Monique Slaats (Belgium, Assembly 7)

Effectiveness of fluticasone furoate–vilanterol for COPD in clinical practice

Authors: Vestbo J, Leather D, Diar Bakerly N, *et al. N Engl J Med* 2016; 375: 1253–1260

Summary: One of the greatest limitations in interpreting the results of randomised controlled trials of drug efficacy in patients with chronic obstructive pulmonary disease (COPD) is applicability to real-world patients. This is due to strict inclusion and exclusion criteria and close monitoring during studies by healthcare professionals. The Salford Lung Study investigators took a unique approach in understanding the real-life effectiveness of the once-daily inhaled combination of fluticasone furoate and vilanterol (FF-VI) (100/25 µg), compared with maintenance therapy. This was made possible by performing an effectiveness trial across 75 general practices in Manchester, UK, served by one hospital, which were linked by one integrated electronic health record system. This study was a prospective, 12-month, open-label, parallel-group, randomised trial in 2799 patients with COPD. The key finding was that in those randomised to receive once-daily FF-VI, there was 8.4% reduction (95% CI 1.1–15.2%) in the rate of moderate or severe exacerbations, defined as an increase in symptoms requiring antibiotics, steroids or both, or a scheduled or unscheduled admission to hospital. This study shows that a broad heterogeneous population of patients with COPD do benefit from once-daily FF-VI.

Reviewed by: Imran Satia (UK, Assembly 5)

Dexamethasone and supportive care with or without whole brain radiotherapy in treating patients with non-small cell lung cancer with brain metastases unsuitable for resection or stereotactic radiotherapy (QUARTZ): results from a phase 3, non-inferiority, randomised trial

Authors: Mulvenna P, Nankivell M, Barton R, *et al. Lancet* 2016; 388: 2004–2014

Summary: Whole-brain radiotherapy (WBRT) is a frequently used therapy for non-small cell lung cancer (NSCLC) patients with brain metastases who are unsuitable for resection or stereotactic radiotherapy. The evidence base for use of this therapy is limited.

To further address this, Mulvenna *et al.* performed a phase III trial, QUARTZ (The Quality of Life After Treatment for Brain Metastases), investigating the use of dexamethasone and optimal supportive care (OSC) with or without whole-brain irradiation (20 Gy in five daily fractions) in patients with NSCLC and brain metastases. The primary end-point of this noninferiority trial was quality-adjusted life-years (QALYs). The study randomised 538 patients across UK and Australia.

QALYs in the supportive care plus WBRT group were 46.4 days compared to 41.7 days in the group receiving supportive care alone, a difference of –4.7 QALY days in favour of WBRT (90% CI –12.7–3.3 days). Overall survival in both groups was similar (hazard ratio 1.06, 95% CI 0.90–1.26; p=0.81) with a median survival for patients with WBRT of 9.2 weeks and 8.5 weeks for those treated with OSC plus WBRT and OSC alone, and only a small difference in side-effects between the groups. Quality of life was similar between groups. Subgroup analyses showed significant effect in favour of WBRT in the subgroup aged <60 years (p=0.0062) while no significant effect of WBRT was observed in other subgroups (stratified according to sex, Karnofsky Performance Status, disease control and presence of extracranial metastases).

This is the first adequately powered randomised study in patients with NSCLC and cerebral metastases, demonstrating the noninferiority of OSC alone *versus* OSC plus WBRT. The results suggest that use of WBRT in patients under 60 years of age is most likely to offer survival benefit. However, given the rapidly evolving systemic and local treatment paradigms in lung cancer patients with brain metastases, uncertainties remain regarding the optimum group of patients who will benefit from whole brain radiotherapy.

Reviewed by: Markus Glatzer (Switzerland, Assembly 11)

Hot topics are short (approx. 200 words) summaries of recent important articles in respiratory medicine written by Junior ERS members. To become a hot topic author, please contact Aran Singanayagam: e-mail: aransinga@gmail.com