[Indian J Chest Dis Allied Sci 2017;59:201-203]

Abstracts' Service

Pulmonary Exacerbation in Adults with Bronchiectasis: A Consensus Definition for Clinical Research

Adam T. Hill, Charles S. Haworth, Stefano Aliberti, Alan Barker, Francesco Blasi, Wim Boersma, James D. Chalmers, Anthony De Soyza, Katerina Dimakou, J. Stuart Elborn, Charles Feldman, Patrick Flume, Pieter C. Goeminne, Michael R. Loebinger, Rosario Menendez, Lucy Morgan, Marlene Murris, Eva Polverino, Alexandra Quittner, Felix C. Ringshausen, Gregory Tino, Antoni Torres, Montserrat Vendrell, Tobias Welte, Rob Wilson, Conroy Wong, Anne O'Donnell and Timothy Aksamit

European Respiratory Journal 2017;49: 1700051

There is a need for a clear definition of exacerbations used in clinical trials in patients with bronchiectasis. An expert conference was convened to develop a consensus definition of an exacerbation for use in clinical research.

A systematic review of exacerbation definitions used in clinical trials from January 2000 until December 2015 and involving adults with bronchiectasis was conducted. A Delphi process followed by a round-table meeting involving bronchiectasis experts was organised to reach a consensus definition. These experts came from Europe (representing the European Multicentre Bronchiectasis Research Collaboration), North America (representing the US Bronchiectasis Research Registry/ COPD Foundation), Australasia and South Africa.

The definition was unanimously approved by the working group as: a person with bronchiectasis with a deterioration in three or more of the following key symptoms for at least 48 h: cough; sputum volume and/or consistency; sputum purulence; breathlessness and/or exercise tolerance; fatigue and/or malaise; haemoptysis AND a clinician determines that a change in bronchiectasis treatment is required.

The working group proposes the use of this consensus-based definition for bronchiectasis exacerbation in future clinical research involving adults with bronchiectasis.

Burden of Disease and Change in Practice in Critically Ill Infants with Bronchiolitis

Luregn J. Schlapbach, Lahn Straney, Ben Gelbart, Janet Alexander, Donna Franklin, John Beca, Jennifer A. Whitty, Subodh Ganu, Barry Wilkins, Anthony Slater, Elizabeth Croston, Simon Erickson and Andreas Schibler on behalf of the Australian & New Zealand Intensive Care Society (ANZICS) Centre for Outcomes & Resource Evaluation (CORE) and the Australian & New Zealand Intensive Care Society (ANZICS) Paediatric Study Group

European Respiratory Journal 2017;49: 1601648

Bronchiolitis represents the most common cause of non-elective admission to paediatric intensive care units (ICUs).

We assessed changes in admission rate, respiratory support, and outcomes of infants <24 months with bronchiolitis admitted to ICU between 2002 and 2014 in Australia and New Zealand.

During the study period, bronchiolitis was responsible for 9628 (27.6%) of 34 829 non-elective ICU admissions. The estimated population-based ICU admission rate due to bronchiolitis increased by 11.76 per 100 000 each year (95% CI 8.11-15.41). The proportion of bronchiolitis patients requiring intubation decreased from 36.8% in 2002, to 10.8% in 2014 (adjusted OR 0.35, 95% CI 0.27-0.46), whilst a dramatic increase in high-flow nasal cannula therapy use to 72.6% was observed ($p<0.001$). We observed considerable variability in practice between units, with six-fold differences in risk-adjusted intubation rates that were not explained by ICU type, size, or major patient factors. Annual direct hospitalisation costs due to severe bronchiolitis increased to over USD30 million in 2014.

We observed an increasing healthcare burden due to severe bronchiolitis, with a major change in practice in the management from invasive to non-invasive support that suggests thresholds to admittance of bronchiolitis patients to ICU have changed. Future studies should assess strategies for management of bronchiolitis outside ICUs.

The Diaphragm Acts as a Brake during Expiration to Prevent Lung Collapse

Mariangela Pellegrini, Goran Hedenstierna, Agneta Roneus, Monica Segelsjo, Anders Larsson and Gaetano Perchiazzi

American Journal of Respiratory and Critical Care Medicine 2017;195:1608–16

Rationale. The diaphragm is the major inspiratory muscle and is assumed to relax during expiration. However, electrical postinspiratory activity has been observed. Whether there is an expiratory diaphragmatic contraction that preserves lung patency has yet to be explored.

Objectives. We hypothesized the occurrence of an expiratory diaphragmatic contraction directed at stabilizing peripheral airways and preventing or reducing cyclic expiratory lung collapse.

Methods. Mild acute respiratory distress syndrome was induced in 10 anesthetized, spontaneously breathing pigs. Lung volume was decreased by lowering end-expiratory airway pressure in a stepwise manner. We recorded the diaphragmatic electric activity during expiration, dynamic computed tomographic scans, and respiratory mechanics. In five pigs, the same protocol was repeated during mechanical ventilation after muscle paralysis.

Measurements and Main Results. Diaphragmatic electric activity during expiration increased by decreasing end-expiratory lung volume during spontaneous breathing. This enhanced the diaphragm muscle force, to a greater extent with lower lung volume, indicating a diaphragmatic electromechanical coupling during spontaneous expiration. In turn, the resulting diaphragmatic contraction delayed and reduced the expiratory collapse and increased lung aeration compared with mechanical ventilation with muscle paralysis and absence of diaphragmatic activity.

Conclusions. The diaphragm is an important regulator of expiration. Its expiratory activity seems to preserve lung volume and to protect against lung collapse. The loss of diaphragmatic expiratory contraction during mechanical ventilation and muscle paralysis may be a contributing factor to unsuccessful respiratory support.

Extreme Trait Whole-Genome Sequencing Identifies *PTPRO* as a Novel Candidate Gene in Emphysema with Severe Airflow Obstruction

Josiah E. Radder, Yingze Zhang, Alyssa D. Gregory, Shibing Yu, Neil J. Kelly, Joseph K. Leader, Naftali Kaminski, Frank C. Sciurba and Steven D. Shapiro

American Journal of Respiratory and Critical Care Medicine 2017;196:159–71

Rationale. Genetic association studies in chronic obstructive pulmonary disease have primarily tested for association with common variants, the results of which explain only a portion of disease heritability. Because rare variation is also likely to contribute to susceptibility, we used whole-genome sequencing of subjects with clinically extreme phenotypes to identify genomic regions enriched for rare variation contributing to chronic obstructive pulmonary disease susceptibility.

Objectives. To identify regions of rare genetic variation contributing to emphysema with severe airflow obstruction.

Methods. We identified heavy smokers that were resistant (n = 65) or susceptible (n = 64) to emphysema with severe airflow obstruction in the Pittsburgh Specialized Center of Clinically Oriented Research cohort. We filtered whole-genome sequencing results to include only rare variants and conducted single variant tests, region-based tests across the genome, gene-based tests, and exome-wide tests.

Measurements and Main Results. We identified several suggestive associations with emphysema with severe airflow obstruction, including a suggestive association of all rare variation in a region within the gene *ZNF816* (19q13.41; $P = 4.5 \times 10^{-6}$), and a suggestive association of nonsynonymous coding rare variation in the gene *PTPRO* ($P = 4.0 \times 10^{-5}$). Association of rs61754411, a rare nonsynonymous variant in PTPRO, with emphysema and obstruction was demonstrated in all non-Hispanic white individuals in the Pittsburgh Specialized Center of Clinically Oriented Research cohort. We found that cells containing this variant have decreased signaling in cellular pathways necessary for survival and proliferation.

Conclusions. *PTPRO* is a novel candidate gene in emphysema with severe airflow obstruction, and rs61754411 is a previously unreported rare variant contributing to emphysema susceptibility. Other suggestive candidate genes, such as *ZNF816*, are of interest for future studies.

Prevalence & Factors Associated with Depression Among Schoolgoing Adolescents in Chandigarh, North India

Man Mohan Singh, Madhu Gupta and Sandeep Grover

Indian Journal of Medical Research 2017;146;205–15

Background & objectives. Depression among adolescents is a rising problem globally. There is a need to understand the factors associated with depression among adolescents. This study was conducted to ascertain the prevalence of depressive disorders and associated factors among schoolgoing adolescents in government and private schools in Chandigarh, India.

Methods. A cross-sectional study was conducted among 542 randomly selected schoolgoing adolescents (13-18 yr), from eight schools by multistage sampling technique. Depression was assessed using Patient Health Questionnaire-9 (PHQ-9) and associated factors by pretested semistructured interview schedule. Multivariate analysis was done to identify significant associated factors.

Results. Two-fifth (40%) of adolescents had depressive disorders, 7.6 per cent major depressive disorders and 32.5 per cent other depressive disorders. In terms of severity, 29.7 per cent had mild depression, 15.5 per cent had moderate depression, 3.7 per cent had moderately severe depression and 1.1 per cent had severe depression. Significant associated factors included being in a government school, studying in class X^{th} and XII^{th}, rural locality, physical abuse by family members, alcohol use and smoking by father, lack of supportive environment in school, spending less time in studies, lower level of participation in cultural activities and having a boy/girlfriend. Significant predictors on binary logistic regression analysis were being in class X^{th} [odds ratio (OR)=5.3] and lack of self-satisfaction with own academic performance (OR=5.1).

Interpretation & conclusions. Our study showed that a significant proportion of schoolgoing adolescents suffered from depression. The presence of depression was associated with a large number of modifiable risk factors. There is a need to modify the home as well as school environment to reduce the risk of depression.

A Simplified Multiplex PCR-based Typing Method for Common *Salmonella Enterica* Serovars Supported by Online Server-based Detection System

Probodh Borah, Steffen Porwollik, Prerak Desai, Prakash Nayak, Partha Pratim Borah, Pui Cheng and Michael McClelland

Indian Journal of Medical Research 2017;146;272–80

Background & objectives. A rapid and simple alternative method is needed to replace the laborious, time-consuming *Salmonella* serotyping. The objective of the present study was to improve and simplify a previously reported multiplex polymerase chain reaction (PCR)-based method and to create an online server to enable rapid determination of serovars.

Methods. A method of multiplex PCR-based genome typing (MPGT) was standardized using 59 *Salmonella* isolates of 31 serovars. Several previously reported primers were modified to obtain a more accurate performance. The screen was separated into four different multiplex reactions distinguishable on standard electrophoresis. A blind study was subsequently performed with 81 isolates of 10 serovars most prevalent in India. Whole genome information from 440 *Salmonella* isolates was used to confirm the usefulness of this method and concurrence of *in silico* predictions and PCR results were investigated. A public server *(http://www.mpgt-salmonella.res.in)* was established for data storage and determination of closest previously observed *Salmonella* isolates based on obtained MPGT patterns.

Results. The 16 target genes amplified showed variability in their presence in strains from different serotypes. Hence, identical amplification patterns suggested genetic relatedness of strains and usually identical serological behaviour. The observed absence/presence patterns of genes were converted to an MPGT code. Altogether, 83 different codes were predicted *in silico* based on the whole genome information of 440 strains. Results confirmed that major serovars usually displayed unique MPGT codes.

Interpretation & conclusions. The multiplex PCR assay resulted in specific binary codes for isolates from each of the 31 *Salmonella* serovars tested. The online server allowed the user to compare obtained PCR results with stored previous patterns. Simplicity, speed and cost-effectiveness make this tool useful for quick outbreak management.