The Thoracic Society of Australia and New Zealand (TSANZ) Annual Scientific Meeting (ASM) Conference Report

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**Topic: Don’t forget to breathe: A resource for those with COPD.**
**Presenter: Sue Ward Respiratory CNS Hastings Hospital**

This was an excellent presentation by Sue Ward from Hawkes Bay DHB, regarding an evidence-based e-book that she and other colleagues produced for individuals with a diagnosis of COPD. It provided further information and support on COPD and the aim was for this to be readily available and free of charge for consumers.

The ‘Don’t forget to breathe’ resource is now on its second edition and is freely available on the website [www.don'tforgettobreathe.org.nz](http://www.don'tforgettobreathe.org.nz). It is published under a creative commons licence, to enable people to copy and share the work as widely as possible and has been downloaded in 32 countries worldwide. Each GP practice throughout Hawkes Bay has at least one copy to use as a teaching aid, as well as hospital wards and the physiotherapy department. Sue advised that the copies had been requested from both the US and UK health professionals to print and they use the resource in their pulmonary rehabilitation programmes and Breathe Easy support groups.

Given that COPD affects 200,000 New Zealanders and up to 15% of adults over the age of 45 may have COPD, many of these people will not be aware that this is the case. While there is a lot of information available on COPD, much of it is dispersed in small or non-cohesive fragments and scattered through various resources. Also, much of the information available on the Internet is not relevant to our situation in New Zealand. This e-book brings together the information in a way that is applicable to a New Zealand audience.

**Topic: Cost implication for missed malnutrition. A common complication in COPD.**
**Presenter: Jenna Storestreet, Dietician, Adelaide Hospital**

Malnutrition is implicated in:
- Muscle loss weakness
- Delayed health recovery
- Falls
- Increased ALOS
- Increased costs

**A result of a study involving 176 people:**
Malnutrition is common but there is no recommended cut-off to decide when it is best to intervene and this means there are a number of issues regarding missed malnutrition. 50/50 were male and female. Of the group that undertook a screening, 42% were found to be malnourished. Of the malnourished group only 62% had been referred and 32% were not referred at all.
**Current practice:**
Malnutrition is usually identified by nurses, sometimes on admission, using the Malnutrition Screening Tool (MST). It includes weight loss and poor eating history. This is a screening tool only and the diagnosis of malnutrition is much more complex. The tool dieticians’ use is the Subjective Global Assessment. BMI can be used as well if the person is younger than 18, but does not measure muscle loss.

**Summary:**
Many patients miss out on appropriate referrals if malnutrition is not identified and malnutrition is highly prevalent in COPD. It is important for clinicians to understand the criteria for malnutrition, but unfortunately the guidelines are not standardised in what the actual cut-off point of malnutrition is. The BTS recommend a BMI of 21 and should alert clinicians to those patients who are highly compromised. An improved MST screening score is currently being trialled. It is hoped that the high malnutrition rates, which are likely to impact on inpatients have inpatient stay, could be improved. This is a topic to be watched for in the future.

**Presenter: Dr Marie Williams, Adelaide University**

**Topic: Dyspnoea is influenced by context but not severity of COPD**
This presentation described the landscape of breathlessness, including both the science and what patients describe (symptoms). It is important to assess intensity, the sensory qualities and the different tools used to assess these, including the neural mechanisms, the social responses and the level of distress.

There are two new scales for breathlessness. One is the “Dyspnoea 12”. This is the global score of dyspnoea and includes 12 items and 2 domains, one being physical and one being affective.

The ATS recommends that we classify the tools used to describe dyspnoea, as these are now quite varied, as the different tools assess different aspects, not just breathlessness. This includes what is troubling the patient, how it feels and what the impact is.

In GOLD there is no difference in the tools described in terms of context, daily life, but there are often differences in total response.

There is now a new multi-dimension dyspnoea profile (MDP) which measures the sensation of dyspnoea. This is important as we know dyspnoea is important, but the sensation may be the big driver for patient behaviour change. (As the BORG is a physiological measure, the new score may be better as it is more likely to influence behaviour).

**Reflection:**
This was an interesting presentation; however there are no simple solutions to manage breathlessness and it is likely that multiple tools be used, as well as multiple interventions, as there are so many factors involved.

**Presenter: Dr Vanessa Tee, Adelaide**

**Topic: NIV positive pressure for treatment of respiratory failure due to COPD - The Cochrane systemic review**
Traditionally patients who were not responsive to typical therapy were commenced on NIV. There was a need to evaluate efficacy and safety of NIV with regards to reducing mortality and to assess for treatment success or failure. The Cochrane review also undertook to assess if NIV was an appropriate clinical alternative to intubation. Treatment outcomes included review of ABG, ALOS, symptom score, and complications. Although there were over 100 initial or potential studies for assessment, only 30 articles were considered, including eight new studies for the metanalysis.

**Outcomes:**

**Primary outcome:**
Treatment failure is less likely with NIV use, with 56% relative risk to reduction. There was also a significant reduction in the requirement for intubation. The outcomes were similar if NIV was used in the inpatient ward or in ICU.

**Secondary outcome:**
ABG improved within one hour with NIV. Average length of stay improved with NIV. Symptom burden reduced with NIV and there were fewer complications in favour of NIV. However the comment was made that there were no low numbers in the total number of studies and so the advice was to treat this with caution.

**Discussion:**
There was good evidence for the use of NIV in COPD respiratory failure. The authors considered there was low utilisation of this, from a lack of knowledge and equipment and the usage also remains highly variable. The use of NIV significantly reduces the need for intubation, it is safe, it is well tolerated, reduces average length of stay and symptoms. It can be offered for all patients with acute hypercapnia and is effective on the ward, as well as ICU and is generally well tolerated.

**Presenter:** Dr Anuk Kriavit, Darwin

**Topic: Physician outreach clinics in the Northern Territory**

Dr Kriavit reported on an advanced trainee project that discussed the results of a two year retrospective data study, from physician outreach clinics in the NT, to assess the burden of chronic respiratory disease in the remote population in the top end of NT. The aim was to undertake a chronic respiratory disease profile, to maximise service delivery, redistribute resources and implement and measure the new programme. The results of 444 patients were included, current smokers being 45% and current ex smokers being 46%, at the average age of 54 years. The respiratory diagnoses included COPD (47%), asthma (10%) and bronchiectasis (6-10%).

**Findings:**
Included is a 70% higher incidence of COPD in the population compared to the urban population and a 40% higher incidence of bronchiectasis.

**Discussion:**
The factors influencing the results were predominantly the high incidence of smoking, being over (90%). With smoking cessation being a key factor in all health planning, COPD and bronchiectasis contribute a very high burden in this population and that rural areas have minimal access or support from health professionals in general.
Reflection:
The data illustrated the severity of poor health in this population group. The presenter acknowledged the crucial role of Aboriginal health care workers being pivotal.

Presenter: Professor Marc Miravitlles, Barcelona Spain
Topic: The treatment of COPD according to phenotypes.
Professor Miravitlles has an extensive and widely published academic background is a leading European Respiratory physician and a member of the European Guidelines group.

What is important in determining the treatment of COPD?

- Biomarkers?
- Clinical signs?
- Imaging?
(As clinicians we must always treat the patient not just the genetic of biological findings)

Different phenotypes have different responses to treatment
Generally there are many well studied frameworks that describe the various groups of COPD patients.
Broadly these are:

1. Non exacerbators
2. Exacerbators with bronchitis
3. Exacerbators with emphysema
4. Asthma/COPD overlap (ACOS)

Diagnosis is not always clear with 19% of the ACOS group we can’t actually tell if they have asthma or COPD even after a bronchodilator challenge, they have features that fulfil both criteria for diagnosis and also features that overlap. Additionally, even for the patients who have has been identified as having high levels of eosinophils in sputum when treated with ICS do not all respond the same..

Some new studies that could influence clinical decision making underway include the use of TH2 use as a biomarker on COPD. Twenty percent of patients with COPD have elevated TH2 cells and are more likely to to respond to ICS +/- LABD. Those patients who have no TH2 signature have no response to ICS/bronchodilator

The concentration of blood eosinophils is likely to be a good indicator of patients likely to respond to bronchodilator especially if the level is >2%. Additionally there is a dose response relationship.

Also in this group, these is a low dose of ICS to treat (i.e. 100mcg BDP is as good or better than a high dose)

Summary of the ACOS phenotype

- 10-20%
- Have more reversibility
- TH2 signature marker
- No reliable easily sought biomarkers

Group 2 – the frequent exacerbators

Bronchitis (chronic)

- Some have bacterial isolation
Some don’t
Therefore THESE ARE DIFFERENT DISEASES

**Type 1: chronic bronchitis (this is both a symptom and a risk factor)**

**Type 2: infective bronchitis**
- This group has dark sputum even when well
- Accounts for 30% of Ch bronchitis

Mucopurelent sputum was previously referred to as colonisation, this is now considered a ‘chronic bronchial infection’

Risk factors: (also worse outcomes)
- More than one pathogen identified within a 12 month period
- If the patient required an admission
- If the patient had evidence of any bronchiectasis
- Also worse prognosis if the patient was colonised with pseudomonas and had bronchiectasis

Therefore it is a different phenotype of patients who experience coloured sputum when well.

The treatment challenge therefore it is impossible to stop the bacteria and that this group may respond to long term antibiotics, e.g. Azithromycin. There was a recent paper in The Lancet 2014 regarding this therapy for patients, even with maximum therapy, to continue to give macrolides in the long term and this study outcome was, there was a 42% response reduction in exacerbations over a 12 month period.

Other option treatments include Quinolones such as Moxifloxacin for five days, every two months for a 12 month period. This of course is likely to lead to a much higher risk of resistance.

**Non-exacerbators**

*The Instead study* which reviewed treatments of inhaled corticosteroids and long-acting beta agonists, compared with treatment with just long-acting beta agonists. The outcome in this group showed there was no difference in outcomes.

*The Illuminate study* was similar as it had no inhaled corticosteroids, but it included a combination of a long-acting beta agonist in combination with a short-acting beta agonist and in fact this showed better outcomes over 12 months.

LAMA/LABA showed improved outcomes when just LAMA was used on its own.

Treatment studies of patients with inhaled corticosteroids, which were treated in conjunction with sputum eosinophils, according to the BTS Guidelines showed this group had more exacerbations.

**Presenter: Prof Gary Yee (Perth, WA)**

**Topic: Advances in pleural infection management**

Effusion and empyema were discussed and the use of surgical intervention reviewed. By far the majority of empyemas and effusions are cured by
antibiotics and chest drainage and do not require surgical intervention. A new prognostic score was discussed - ‘RAPID’

R - Renal impairment
A - Age >70 years
P - Pus
I – Inpatient (worse prognosis if already an inpatient)
D – Diet (poor nutritional state the longer the ALOS)

Professor Yee described the group who scored highly in the RAPID score as being the ‘crumbling’ patient. The existence of pleural infection was also a marker of frailty and that these patients are more likely to die from factors associated with their co morbidities than the pleural infection.

Provided that the pleura infection settles then the residual opacity will resolve over time – i.e. there is no need to rush into surgery so “treat the patient not the x-ray”

If the infection persists then the use of fibrolytics to evacuate the pleural pus is key.

The insertion of chest drains should always be image guided due to the risk of perforating major vessels especially the ones that sit under both lips of the ribs.

Presenter: Professor Gary Anderson Sydney University
Topic: What do we really know about anticholinergic bronchodilator

Professor Anderson discussed the principle that the treatment for bronchospasm usually focuses on the airway smooth muscle, but a reminder that this smooth muscle goes all the way to ducts of the alveoli. The primary focus of COPD usually involves defects in the small airways, but these do not show up when measuring FEV1. The small airways are a critical disease focus. Density of cholinergic nerve is greatest in the small airways, but of course occurs throughout the whole lung.

M2 receptors are important in the feedback mechanism, if they are simulated, then there is a greater release of acetylcholine. Therefore we must target the specific M3 receptors.

Inflamed tissue can also produce acetylcholine (that is not released from nerves). Professor Anderson asked then if acetylcholine is stimulated inflammation. The muscarinic pathways affect disease progression. There is nothing known in human studies, but there is some mouse data to suggest that there is an increase in mucus production.

M2 receptors are present in the heart and mediate the sympathetic tone. If they are blocked they can also increase the heart rate and therefore oxygen demand. Therefore medication that subsequently blocks the M2 receptors should be avoided. M2 receptors however may have some benefit, as they impair beta2 cells from working properly. They are also found mostly in the heart, whereas M3 receptors are found throughout the smooth airway, therefore of course it is preferable to have an M3 blocker to use in airway disease.
M2 and M3 receptors were closely evolved together and are linked. They are very close in molecular binding sites, so it is very difficult to target just with an M3 blocker. As yet no drug can have relative M3 acidic selectivity. There is a secondary part of receptor so it is possible to make drugs that bind tightly to M3 and are released at the M2 site. There is some affinity to M2 and M3, but do disassociate from the M2, therefore selectively target the M3 (this is described as kinetic selectivity). Both Aclidinium and Tiotropium are selective and they have a much faster disassociation for the M2 receptors and are therefore M3 enriched. Both drugs provide persistent bronchodilation without any cardiac irritability (hence their use). Aclidinium is hydrophilic, i.e. this makes the drug break down very quickly in plasma and it is therefore rapidly metabolised and excreted.

**Summary:**
M2 and M3 targeted medications
As the M2 and M3 receptors have co-evolution factors, it makes absolute selectivity very difficult. Maximum anti-muscarinic effect is limited by the structural basis for airflow limitation.

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**Presenter:** Professor Alvar Aquisti, Madrid, Spain

**Topic:** Treatable aspects of COPD

Professor Aquisti looked at what were the treatable aspects and how we can manage them.

He described a previous treatment being based on sequential thinking, focusing on FEV1 and other factors including exercise, breathlessness, exacerbations and quality of life.

Phenotypes labelled A, B, C and D were determined in 2010, however these focus on FEV1 (FEV1 was not the only way to express or understand the burden of COPD).

Over time clinicians have realised that FEV1 was not the best way to know or understand the burden and other factors associated with COPD and this involved more complex parallel thinking. COPD is complex and heterogeneous. Complex meaning there are several elements, (FEV1, MMI, exacerbations, biomarkers, imaging, symptoms, perception, co-morbidities). Heterogeneous meaning not all of these elements are present always and in all patients (i.e. it is dynamic).

COPD Phenotypes are more useful for research rather than clinical practice and his point was that it was important to apply treatable characteristics to practice. He discussed what we were missing:

1. **Information:** Is it pulmonary, is it systemic?
2. **Disease activity:** This includes FEV1 and other parameters
3. **Information:** pulmonary and systemic
4. **Disease activity – FEV1 – biomarkers**
5. **Lung cancer – DLCO**
6. **Micro biome**
7. **Imaging – is this emphysema, bronchiectasis and molecular imaging.**

All these have the potential for specific treatment characteristics.
A new way of assessing the treatable aspects of COPD: A Customised Control Panel

With regards to FEV1 and COPD. Professor Agusti reminded us that in COPD, this usually defines disease and is essential for diagnosis. It is also important and useful for follow up to monitor lung function decline. It is required today also for some drug administration, but there is a poor relationship with the things that matter to patients, such as symptoms and exacerbations. Therefore the question must be asked, is FEV1 actually needed to prescribe treatment.

There was a discussion which included the patients with a history of a high FENO and evidence of eosinophilia with reversibility proven, suggests that this is a different patient group and deserves different approaches.

Presenter: Jane Walsh, Physiotherapist, Western Australia
Topic: The focus of exercise, not quality of life, on subsequent health care utilisation following exacerbation of COPD.

The presenter discussed the evidence of variable response to pulmonary rehab, which can reduce hospital admissions and length of stay in a 12 month period. It is however unknown if a favourable response is in actual exercise capacity. The best responders are the ones who are weaker overall when they start, especially in the leg muscles, as they receive better outcomes in pulmonary rehab. Plus co-morbidities are likely to have a significant effect. Co morbidities including cerebrovascular and cardiovascular disease did occur frequently in exacerbations of COPD and it is unsure of how these affect the long term outcome. Nonetheless, COPD remains the 5th biggest killer in Australia in 2012 and co-morbidities are common:
- 40% have hypertension
- 29% have cerebrovascular disease
- Hypercholesterolemia in diabetes are also very high

**New Australian Guidelines, The use of Omalizumab (Xolair) in severe allergic asthma**

Dr Vanessa McDonald is a clinical nurse consultant in respiratory medicine and a post-doctoral researcher in the University of Newcastle Priority Research Centre for Asthma and Respiratory Disease. She was part of an extensive panel of contributors who wrote a practical management guideline for the use of Omalizumab (a monoclonal anti-immunoglobulin E Antibody). This medication, which is administered subcutaneously on a two or four weekly programme, is directed for patients with severe allergic asthma, who have exaggerated IgE responses to common environmental allergens.

Classifying the severity of asthma involves assessing both the severity of the underlying disease, as well as responsiveness to treatment. (These factors may also change over time). Severe asthma is defined by the ATS and ERS as asthma that required high intensity treatments to maintain good control or where, despite such treatment, good control is not achieved. The WHO defines severe as “uncontrolled asthma which can result in risk of frequent and severe exacerbations or death and/or adverse reactions to medications and/or chronic morbidity”.

Goals of asthma treatment remain to prevent death, to prevent asthma exacerbations, to achieve and maintain control of symptoms, to minimise adverse affects from medication, to improve quality of life by maintaining normal activity levels and normal lung function.

Disease management issues that people with asthma face include the burden of long term use of inhaled or oral corticosteroids, adherence issues, affordability and acceptability.

**Recognising and assessing uncontrolled allergic asthma.**

Patients with uncontrolled allergic asthma remain symptomatic despite receiving optimised conventional therapies, including inhaled corticosteroids, LABA and oral corticosteroids. This puts them at high risk of severe exacerbations and loss of lung function. Factors such as incorrect diagnosis, poor adherence to therapy and inadequate inhaler technique, need to be excluded before a diagnosis of uncontrolled asthma can be made.

Co-morbidities are often associated with uncontrolled asthma, including GORD, obesity (with or without OSA), chronic rhinosinusitis, vocal cord dysfunction, anxiety and depression. Individuals with asthma may also have therapy-induced co-morbidities of systemic corticosteroid use and co-morbidities can also exacerbate symptoms and affect asthma control.

There are a number of tests to confirm asthma and exclude alternative diagnoses and to meet the criteria for the use of Omalizumab, patients must have a total serum IgE level assessed and an allergic sensitisation documented. Disease confirmation occurs by either spirometry, before and after bronchodilator, or peak flow variability, or bronchial provocation challenge. Allergic sensitisation is documented by skin prick testing or in-vitro specific IgE measurements. The testing should include a panel of a common inhalant allergen such as house dust mite, grass, pollens, cat and fungi.
Additionally, investigation may be required in some patients to exclude alternative diagnoses or co-morbidities. These include: blood eosinophil, Aspergillus precipitins test, static lung volumes and diffusing capacity, CT, CT of sinus, flow volume loops and laryngoscopy, oesophageal pH monitoring or a trial with medications with a proton pump inhibitor for three months, sweat chloride test, measurement of serum immunoglobulin levels, sleep study.

**Role of IgE**

IgE is a key mediator of allergic reactions in asthma, including chronic airway inflammation and asthma-related symptoms. The role of Omalizumab is to bind to circulating IgE, regardless of allergen specificity. This prevents IgE from binding to its receptor on the mast cells and basophils. The treatment with Omalizumab reduces both the early and late phase responses to inhaled allergen challenge. A number of trials were described to demonstrate the efficacy of Omalizumab as an add-on therapy (INNOVATE study).

**Particulars of benefit of Omalizumab**

- Baseline characteristics do not appear to be a reliable predictor
- Age, gender and baseline serum IgE are also not a reliable predictor
- Greater absolute benefit was observed in patients with more severe asthma, (defined as lower FEV1 at baseline).

Vanessa discussed the development of the new Guidelines and the use of Omalizumab in her severe asthma clinic. She reinforced that both serum levels of total IgE and evidence of sensitivity to a specific allergen is required, before this is indicated. The clinical trials show that this medication used as an add-on therapy, has a significant improvement in the rate of asthma exacerbations, reduces the use of corticosteroids and bronchodilator, improves symptoms in lung function and quality of life. (A number of well validated tools such as the Asthma Control Questionnaire and Asthma Quality of Life Questionnaire were used).

There are safety considerations. Anaphylaxis reactions are rare but have been reported and usually occur. The time of onset varies widely, approximately a third occur in the first 30 minutes, a second third occur between 30 minutes and six hours and another third occurred more than six hours after administration, with 5% of those exceeding 24 hours. Therefore this must be administered in an environment where appropriate precautions for potential anaphylaxis are available, including availability of Adrenalin for immediate administration, oxygen and IV therapy, if the patient becomes hypotensive. Allergic reactions were also noted and if these were local, then they did not indicate to the patient they should not have further doses.

Vanessa also discussed setting up a Severe Asthma Service. This included the requirement for appropriately qualified personnel including respiratory physicians, respiratory CNS, access to immunologist or allergist, pulmonary function scientist, speech pathology physiotherapy. Additionally access to preferably a sputum processing laboratory if available (it isn’t in NZ), or availability of FENO measurements is recommended. I have requested a copy of this paper from the library and will share with the team.
Presenter: Dr Tanja Effing, Epidemiologist, Adelaide
Topic: Association between the baseline characteristics of COPD patients with associated co-morbidities (Preliminary results)

Co-morbidities frequently co-exist, this leads to frequent complications when exacerbations are experienced and the incorrect treatment is put in place. There is limited information in the literature regarding this and one large RCT was actually stopped due to a high proportion of deaths.

Discussion: need to tailor interventions; treatment is complicated by a higher number of co-morbidities and the cognitive challenges for patients who have complicated actions plans.

The ‘COPE111’ (COPD and co-morbidities) trial is underway in SA, n=174

Inclusion criteria:

- Diagnosis of COPD (As per GOLD criteria)
- CHF
- IHD
- Diabetes
- Anxiety
- Depression
- More than 3 exacerbations

Exclusion – cognitive impairment

Extensive assessment undertaken including respiratory assessment, Quality of life, MMSE, knowledge and behaviours, pain, anxious feelings, BMI, CAT score, CRQ, smoking, health literacy (confidence in filling out medical related forms).

Worse scores were experienced in the co-morbid group and all scores increased the higher number of co-morbidities which is not surprising however three variables were identified as being significant

1. Anxious feelings have high impact
2. low cognition
3. BODE score (breathlessness)

Discussion:

If clinicians are aware of what variables associated with higher co-morbid loads then interventions can be tailored. Anxiety, although this is high in people with COPD it is likely to be much higher the more co-morbidities that are experienced. That studies and interventions regarding self management must take into account the complexity of co-morbidities.