Title: Early origins of COPD
Citation: Seminars in Fetal and Neonatal Medicine, April 2012, vol./is. 17/2(112-118)
Author(s): Narang I., Bush A.

Abstract: Chronic obstructive pulmonary disease is a major cause of morbidity and mortality worldwide and a significant challenge for adult physicians. However, there is a misconception that COPD is a disease of only adult smokers. There is a growing body of evidence to support the hypothesis that chronic respiratory diseases such as COPD have their origins in early life. In particular, adverse maternal factors will interact with the environment in a susceptible host promoting altered lung growth and development antenatally and in early childhood. Subsequent lung injury and further gene-environment interactions may result in permanent lung injury manifest by airway obstruction predisposing to COPD.

Title: Thorax in focus: Chronic obstructive pulmonary disease
Citation: Thorax, February 2012, vol./is. 67/2(164-169)
Author(s): Hodgson D.B., Saini G., Bolton C.E.

Abstract: Keeping up to date with scientific developments in any field of medicine is challenging, and chronic obstructive pulmonary disease (COPD) is no exception. Thorax has played an important part in the communication of key developments to its readership. In this article we review original research published in the journal over the last 2-3 years. We consider scientific and clinical developments in the epidemiology, mechanisms and treatment of COPD, placing these articles in the context of other relevant literature in COPD.
Title: Machine learning algorithms and forced oscillation measurements applied to the automatic identification of chronic obstructive pulmonary disease

Citation: Computer Methods and Programs in Biomedicine, March 2012, vol./is. 105/3(183-193), Author(s): Amaral J.L.M., Lopes A.J., Jansen J.M.

Abstract: The purpose of this study is to develop a clinical decision support system based on machine learning (ML) algorithms to help the diagnostic of chronic obstructive pulmonary disease (COPD) using forced oscillation (FO) measurements. To this end, the performances of classification algorithms based on Linear Bayes Normal Classifier, K nearest neighbor (KNN), decision trees, artificial neural networks (ANN) and support vector machines (SVM) were compared in order to the search for the best classifier. Four feature selection methods were also used in order to identify a reduced set of the most relevant parameters. The available dataset consists of 7 possible input features (FO parameters) of 150 measurements made in 50 volunteers (COPD, n=25; healthy, n=25). The performance of the classifiers and reduced data sets were evaluated by the determination of sensitivity (Se), specificity (Sp) and area under the ROC curve (AUC). Among the studied classifiers, KNN, SVM and ANN classifiers were the most adequate, reaching values that allow a very accurate clinical diagnosis (Se > 87%, Sp > 94%, and AUC > 0.95). The use of the analysis of correlation as a ranking index of the FOT parameters, allowed us to simplify the analysis of the FOT parameters, while still maintaining a high degree of accuracy. In conclusion, the results of this study indicate that the proposed classifiers may contribute to easy the diagnostic of COPD by using forced oscillation measurements.

Title: Should androgenic anabolic steroids be considered in the treatment regime of selected chronic obstructive pulmonary disease patients?

Citation: Current Opinion in Pulmonary Medicine, March 2012, vol./is. 18/2(118-124), Author(s): Velema M.S., Kwa B.H.B., De Ronde

Abstract: Chronic obstructive pulmonary disease is a widespread disease with high morbidity rates. Advanced stages can be complicated by unintentional weight loss and muscle wasting, which may contribute to increased morbidity and mortality. Reversal of weight loss increases muscle strength and exercise capacity and improves survival. This can partly be achieved by nutritional support, preferably combined with increase in exercise. Androgenic anabolic steroids (AASs), of which testosterone is the parent hormone, increase muscle size and strength. Due to these anabolic effects, AASs may emerge as a treatment option in COPD patients suffering from muscle wasting. RECENT FINDINGS: Seven trials investigated the effects of AASs in patients with COPD. Some studies also included nutritional therapy and/or a pulmonary rehabilitation program. Compared with placebo, AASs increase lean body mass (LBM) and muscle size. However, no consistent effects on muscle strength, exercise capacity, or pulmonary function are seen. SUMMARY: AASs increase LBM in patients with advanced stages of COPD. No consistent beneficial effect on other endpoints was demonstrated in the reviewed trials. However, probably higher doses of AASs are needed to exert a clinically meaningful effect on muscle strength or exercise capacity. Currently, no evidence is available to recommend AASs to all patients with COPD. In individual cases, treatment with AASs can be considered, particularly in men with advanced COPD, moderate-to-severe functional impairment, muscle wasting and on chronic corticosteroid therapy. Treatment with AASs should preferably be combined with a rehabilitation program and nutritional support. AASs should not be used in women or in men with symptomatic heart disease. When treatment with AASs is considered, intramuscular nandrolone-decanoate is preferred in a dose of 50-200mg per week for a period of 12 weeks. However, the efficacy of AAS treatment in COPD patients needs further clarification in clinical studies.

Title: The prognostic variables predictive of mortality in patients with an exacerbation of COPD admitted to the ICU: An integrative review

Citation: QJM, February 2012, vol./is. 105/2(115-126), Author(s): Messer B., Griffiths J., Baudouin S.V.

Abstract: Chronic Obstructive Pulmonary Disease frequently presents with an acute exacerbation. Debate exists as to whether these patients should be admitted to intensive care units (ICUs). An integrative review was performed to determine whether clinical variables available at the time of ICU admission are predictive of the intermediate-term mortality of patients with an AECOPD. Results: The integrative review search strategy identified 28 studies assessing prognostic variables in this setting. Prognostic variables associated with intermediate-term mortality were low Glasgow Coma Scale (GCS) on admission to ICU, cardiorespiratory arrest prior to ICU admission, cardiac dysrhythmia prior to ICU admission, length of hospital stay prior to ICU admission and higher values of acute physiology scoring systems. Premorbid variables such as age, functional capacity, pulmonary function tests, prior hospital or ICU admissions, body mass index and long-term oxygen therapy were not found to be associated with intermediate-term mortality nor was the diagnosis attributed to the cause of the AECOPD. A scoring system is proposed to assess studies of prognosis in AECOPD.
Title: Chronic obstructive pulmonary disease  
Citation: Current Opinion in Anaesthesiology, February 2012, vol./is. 25/1(24-29)  
Author(s): Spieth P.M., Guldner A., De Abreu M.G.

Abstract: Chronic obstructive pulmonary disease (COPD) is a common cause of primary hospital admission and also a common coexisting disease among surgical patients. This review focused on recent studies related to the perioperative care of COPD patients. In addition to the crucial role of smoking cessation, the use of corticosteroids, antibiotics, regional anesthesia techniques and noninvasive ventilation has become a focus in the perioperative management of the COPD patient. SUMMARY: Perioperative management as well as modern intensive care concepts are based on avoidance of tracheal intubation if possible, use of regional anesthesia techniques and the early liberation from invasive mechanical ventilation. Noninvasive ventilation has become more and more utilized in recent years to stabilize patients with acute exacerbations of COPD and to treat postoperative pulmonary complications in order to avoid reintubation.

Title: The role of nebulized therapy in the management of COPD: Evidence and recommendations  
Citation: COPD: Journal of Chronic Obstructive Pulmonary Disease, February 2012, vol./is. 9/1(58-72)  
Author(s): Dhand R., Dolovich M., Chipps B.

Abstract: Current guidelines recommend inhalation therapy as the preferred route of drug administration for treating chronic obstructive pulmonary disease. Previous systematic reviews in COPD patients found similar clinical outcomes for drugs delivered by handheld inhalers - pressurized metered-dose inhalers (pMDIs), dry powder inhalers (DPIs) - and nebulizers, provided the devices were used correctly. However, in routine clinical practice critical errors in using handheld inhalers are highly prevalent and frequently result in inadequate symptom relief. In comparison with pMDIs and DPIs, effective drug delivery with conventional pneumatic nebulizers requires less intensive patient training. Moreover, by design, newer nebulizers are more portable and more efficient than traditional jet nebulizers. The current evidence regarding nebulizer use for maintenance therapy in patients with moderate-to-severe COPD, including use during exacerbations, suggests that the efficacy of long-term nebulizer therapy is similar, and in some respects superior, to that with pMDI/DPIs. Therefore, despite several known drawbacks associated with nebulized therapy, we recommend that maintenance therapy with nebulizers should be employed in elderly patients, those with severe disease and frequent exacerbations, and those with physical and/or cognitive limitations. For some patients, using both nebulizers and pMDI/DPI may provide the best combination of efficacy and convenience. The impact of maintenance nebulizer treatment on other relevant clinical outcomes in patients with COPD, especially the progressive decline in lung function and frequency of exacerbations, needs further investigation.

Title: Indacaterol: A review of its use as maintenance therapy in patients with COPD  
Citation: Drugs, 2012, vol./is. 72/4(543-563)  
Author(s): McKeage K.

Abstract: Indacaterol inhalation powder (Onbrez Breezhaler) is a long-acting, selective beta2-adrenoceptor agonist that is indicated for the maintenance bronchodilator treatment of airflow obstruction in adults with chronic obstructive pulmonary disease. This article reviews the clinical efficacy and tolerability of indacaterol 150 and 300μg once daily in adults with moderate to severe COPD, as well as reviewing indacaterol's pharmacological properties and results of a cost-utility analysis. Indacaterol has a fast onset of action after the first dose and is effective over 24 hours, allowing for once-daily administration. In short-term trials (<=21 days) in patients with COPD, once-daily indacaterol 150 or 300μg significantly improved lung function, exercise endurance and lung hyperinflation relative to placebo. In large, longer-term clinical studies (12 weeks to 1 year) in patients with moderate to severe COPD, once-daily indacaterol 150 or 300μg improved lung function (primary endpoint) significantly more than placebo, and improvements were significantly greater than twice-daily formoterol 12μg or salmeterol 50μg, and noninferior to once-daily tiotropium bromide 18μg (all agents were administered via inhalation). Overall, indacaterol improved dyspnoea, use of rescue medication and general health status significantly more than placebo, salmeterol or tiotropium bromide, and the degree of improvement in these endpoints was similar to or greater than that achieved with formoterol. Improvements were sustained over the long term (1 year), with no evidence of tolerance. Combination therapy with indacaterol plus tiotropium bromide improved lung function, dyspnoea, rescue medication use and general health status significantly more than tiotropium bromide alone in patients with moderate to severe COPD.
severe COPD. Indacaterol is generally well tolerated when used alone or in combination with tiotropium bromide in patients with COPD and has not been associated with any safety issues. The most common adverse event in clinical trials was COPD worsening, which occurred more commonly with placebo than indacaterol. Indacaterol was not associated with an increased risk of cardiovascular adverse events. In a cost-utility analysis from a German healthcare payer perspective, once-daily indacaterol 150 μg was dominant (i.e. more effective with lower total costs) to once-daily tiotropium bromide 18 μg and twice-daily salmeterol 50 μg in the treatment of patients with COPD. In conclusion, indacaterol provides a valuable option for the maintenance treatment of adults with COPD.

**Title:** Tiotropium bromide inhalation powder: A review of its use in the management of COPD

**Citation:** Drugs, 2012, vol./is. 72/2(273-300)

**Author(s):** Keating G.M.

**Abstract:** The anticholinergic agent tiotropium bromide (Spiriva) is a long-acting bronchodilator that is indicated for the treatment of chronic obstructive pulmonary disease (COPD). This article reviews the clinical efficacy and tolerability of tiotropium bromide inhalation powder, administered using the HandiHaler device, in patients with COPD, as well as reviewing its pharmacological properties and the results of pharmacoeconomic analyses. Shorter-term placebo-controlled trials in patients with COPD demonstrated significantly higher trough forced expiratory volume in 1 second (FEV1) responses with tiotropium bromide than with placebo, confirming it has a duration of action of >=24 hours and is suitable for once-daily administration. Lung function improved to a greater extent with tiotropium bromide than with ipratropium bromide or, in most instances, salmeterol. Indacaterol was shown to be noninferior to tiotropium bromide in terms of the trough FEV1/sub>1/sub> response. The large, 4-year UPLIFT trial did not show a significant reduction in the annual rate of decline in FEV1 with tiotropium bromide versus placebo in patients with COPD, although subgroup analyses demonstrated a significantly lower rate of decline with tiotropium bromide than with placebo in some patient groups (e.g. patients with moderate COPD, patients aged >=50 years, patients not receiving maintenance therapy at baseline). Tiotropium bromide prevented exacerbations in patients with COPD, with a significantly lower exacerbation rate and a significantly longer time to first exacerbation seen with tiotropium bromide than with placebo or salmeterol. Exacerbation rates did not significantly differ between patients receiving tiotropium bromide and those receiving salmeterolfluticasone propionate. Tiotropium bromide also had beneficial effects on health-related quality of life (HR-QOL) and other endpoints, such as dyspnoea and rescue medication use. Combination therapy with tiotropium bromide plus formoterol with or without budesonide improved lung function to a significantly greater extent than tiotropium bromide alone in patients with COPD. In addition, exacerbation rates were lower and HR-QOL was improved with tiotropium bromide plus budesonideformoterol versus tiotropium bromide alone. Although the addition of salmeterolfluticasone propionate to tiotropium bromide did not reduce the COPD exacerbation rate, it did improve lung function and HR-QOL. Tiotropium bromide inhalation powder is generally well tolerated in patients with COPD, with anticholinergic adverse events (e.g. dry mouth, constipation, gastrointestinal obstruction, dysuria) among the most commonly reported adverse events. The UPLIFT trial showed no significant difference between tiotropium bromide and placebo recipients in the risk of stroke, and the risk of serious cardiac adverse events (including congestive heart failure and myocardial infarction) was significantly lower with tiotropium bromide than with placebo. The absence of a detrimental effect on cardiovascular outcomes was supported by the results of a meta-analysis and pooled analyses. In addition, on-treatment mortality was lower with tiotropium bromide than with placebo in the UPLIFT trial. Pooled analyses showed significantly lower cardiovascular mortality with tiotropium bromide than with placebo, with a meta-analysis demonstrating no significant difference between patients receiving tiotropium bromide and controls in cardiovascular mortality. Results of modelled pharmacoeconomic analyses conducted from a healthcare payer perspective in several developed countries suggest that tiotropium bromide is a cost-effective option in patients with COPD. In conclusion, tiotropium bromide inhalation powder is a useful option for the maintenance treatment of patients with COPD.

**Title:** Advance care planning in COPD

**Citation:** Respirology, Jan 2012, vol./is. 17/1(72-78)

**Author(s):** Patel K., Janssen D.J.A., Curtis J.R.

**Abstract:** The review aims to discuss current concepts in advance care planning (ACP) for patients with COPD, and to provide a narrative review of recent trends in ACP and end-of-life care for patients with COPD. ACP, which involves patient-clinician communication about end-of-life care, can improve outcomes for patients and their families, and may be especially relevant for patients with COPD. Effective patient-clinician communication is needed to inform and prepare patients about their diagnosis, treatment, prognosis and what dying might be like. It is important for clinicians to understand patients' values and preferences for life-sustaining treatments as well for their site of terminal care. Unfortunately, discussions about ACP and end-of-life care in current practice are scarce, and their quality is often poor. ACP can improve outcomes for patients and their relatives. The challenge remains in the practical implementation of ACP in the clinical setting, especially for patients with COPD. ACP should be implemented alongside curative-restorative care for patients with advanced COPD. The disease course of COPD is such that there will rarely be a clear transition point predicting the timing of the need for initiation of end-of-life care. Future studies should focus on interventions that facilitate concurrent ACP and prepare patients for making in-the-moment decisions, with the goal of improving the quality of end-of-life care.
Title: Efficacy of indacaterol in the treatment of patients with COPD
Citation: Primary Care Respiratory Journal, December 2011, vol./is. 20/4(380-388)
Author(s): Jones P.W., Barnes N., Vogelmeier C.

Abstract: Effective bronchodilation is an important part of the management of patients with chronic obstructive pulmonary disease and can improve breathlessness and ability to undertake physical activities. Indacaterol is a new once-daily, long-acting inhaled bronchodilator for COPD. We review the efficacy of indacaterol as a bronchodilator, including its impact upon symptoms and health status. Its effect on symptoms and health status was similar or significantly greater than the other bronchodilators. The safety profile was similar to placebo. Once-daily indacaterol is an effective and beneficial maintenance bronchodilator treatment for patients with moderate-to-severe COPD.

Title: Reconsidering sex-based stereotypes of COPD
Citation: Primary Care Respiratory Journal, December 2011, vol./is. 20/4(370-378)
Author(s): Ohar J., Fromer L., Donohue J.F.

Abstract: Chronic obstructive pulmonary disease (COPD) has historically been considered a disease of older, white, male smokers, as illustrated in Frank Netter's classic images of the 'pink puffer' and 'blue bloater'. However, women may be more susceptible to COPD than men, and the disease course may be reflective of that increased susceptibility. From a review of epidemiological data of COPD, we found differences in the way men and women present with COPD symptoms, a bias in the way COPD symptoms are treated in men and women, and differences in susceptibility to airway obstruction based on age, sex, and smoking history. These data show that classic stereotypes of COPD - including male predominance - should be abandoned, and that there are not two but multiple COPD phenotypes, which are characterised by differences between women and men in susceptibility, symptoms, and disease progression. These differences impact on physician perception. Although further research into this concept is needed, the differences we found should prompt, in the short term, changes in the way (and in whom) COPD is evaluated, diagnosed, and treated; in the long term, these differences should prompt research into the prognosis of COPD based on sex differences.

Title: New horizons in early stage COPD - Improving knowledge, detection and treatment
Citation: Respiratory Medicine, November 2011, vol./is. 105/6(1125-1141)
Author(s): Decramer M., Miravitlles M., Price D.

Abstract: Early stage COPD carries a significant healthcare burden that is currently underrecognised, underdiagnosed and undertreated. Furthermore, patients at this stage can rapidly decline to advanced disease, especially if they continue to smoke. The natural history of the disease in early stages remains largely unknown, and emerging evidence indicates that we are able to reduce lung function decline and exacerbations, and improve quality of life, in early stage COPD, mainly through smoking cessation. But new evidence from randomised clinical trials also suggests an impact of pharmacotherapy on clinical outcomes in early disease. Guidelines need to be updated to reflect this greater understanding of early stage disease, and trials need to be conducted to definitively show the benefits of intensive treatment so that we can meet the large, unmet clinical needs of this important patient group.

Title: Cardioselective beta-blockers for chronic obstructive pulmonary disease: A meta-analysis
Citation: Respirology, Nov 2011, vol./is. 16(99-100)
Author(s): Ni Y.

Abstract: Results: Five studies of non-selective beta-blockers and four studies of cardio-selective beta-blockers were included. Sample size for the cardio-selective beta-blockers was 85 cases, non-selective beta-blockers 46. The results showed that FEV<sub>1</sub> decline 0.14L with the use of non-selective beta-blockers (z = 6.78, p < 0.0001), and with the use of cardio-selective beta-blockers decline 0.03L (z = 2.08, p = 0.04). Non-selective beta-blockers decrease the response to beta2-agonist of FEV<sub>1</sub> significantly by 13.42% (z = 10.68, p < 0.0001). Cardio-selective beta-blockers produced no significant change in response to beta2-agonist of FEV<sub>1</sub> (z = 0.46, p = 0.65). Conclusion: Our study showed an adverse effect of beta-blockers on lung function in patients with COPD. But the cardioselective beta-blockers has a little effect on the lung function and produce no change in the reactivity of airway to bronchodilators. Given their demonstrated benefit in conditions such as heart failure, coronary artery disease and hypertension, cardioselective beta-blockers should be considered for patients with COPD with prudence.

Title: Chronic obstructive pulmonary disease: A concise review
Citation: Medical Clinics of North America, November 2011, vol./is. 95/6(1125-1141)
Author(s): Balkissoon R., Lommatzsch S., Carolan B.

Abstract: Globally, chronic obstructive pulmonary disease (COPD) is a major cause of significant morbidity and mortality, and is now the third leading cause of death in the United States. Over the past 15 years there has been a surge of bench and translational research regarding the genetics and pathogenesis of COPD, and several large-scale clinical trials have introduced new treatment paradigms for COPD. Current research also demonstrates that COPD is not just a lung disease and that there are several potential extrapulmonary manifestations and comorbidities that should be evaluated and treated when one identifies an individual as having COPD.
Title: Exercise assessment and training in pulmonary rehabilitation for patients with COPD
Citation: European Journal of Physical and Rehabilitation Medicine, September 2011, vol./is. 47/3(483-497)
Author(s): Singh S., Harrison S., Houchen L., Wagg K.

Abstract: Patients with COPD frequently complain of dyspnoea and leg fatigue on exertion. Pulmonary rehabilitation (PR) is an established intervention for the management of patients with COPD. The purpose of this article is to describe the assessment process, exercise intervention and its anticipated benefits, in the context of a rehabilitation programme for individuals with COPD. This has been sub-divided into aerobic, skeletal muscle resistance and inspiratory muscle rationale, assessment and training. The evidence supporting the incorporation of aerobic and skeletal muscle resistance training in PR is well established. The benefit of including inspiratory muscle training (IMT) as an adjunct to PR is less clear.

Title: Effects of medical and psychological treatment of depression in patients with COPD - A review
Citation: Respiratory Medicine, October 2011, vol./is. 105/10(1422-1433)
Author(s): Fritzsche A., Clamor A., Von Leupoldt A.

Abstract: Chronic Obstructive Pulmonary Disease is a chronic inflammatory lung disease characterized by progressive and only partially reversible symptoms and by considerable negative consequences such as reductions in functional status and quality of life. Comorbid depression is highly prevalent in patients with COPD and related to a worse course of the disease. Despite its negative impact, depression often remains unrecognized and untreated in COPD patients. This review summarizes the current state of findings from studies examining the effects of antidepressant treatments in patients with COPD. Reviewed treatment options are antidepressant medical therapy and cognitive-behavioral therapy (CBT). Antidepressant medical trials include treatments with selective serotonin reuptake inhibitors (SSRI) or tricyclic antidepressants (TCA); CBT was applied using various components. Across both treatment types, the majority of studies included patients with a wide range of psychiatric conditions and especially comorbid symptoms of anxiety were often not controlled. Furthermore, greatly varying instruments and methods for assessing depressive symptoms, small sample sizes and rather heterogeneous results were observed. This makes the comparison of treatment options rather difficult and prevents definite conclusions. However, some important implications valuable for further research were obtained. Some limited data suggested that SSRI might show fewer side effects than TCA. A few antidepressants as well as beneficial effects in other outcomes were observed after antidepressant medical treatment. More clearly, CBT showed some potential in terms of improvements in depressive symptoms, and also in other outcome measures. Patient compliance seems more promising for CBT than for antidepressant medical treatment. Overall, the reviewed studies suggest some promising effects for both treatment types and effect sizes in studies with significant antidepressant effects were reasonable. However, future randomized controlled trials comparing antidepressant medical and cognitive-behavioral therapy will be essential to assess distinct and most favorable treatment effects.

Title: Chronic obstructive pulmonary disease: Pathophysiology, current methods of treatment and the potential for simvastatin in disease management
Citation: Expert Opinion on Drug Delivery, September 2011, vol./is. 8/9(1205-1220)
Author(s): Marin L., Colombo P., Bebawy M

Abstract: This review focuses on the patho-physiology of COPD, explores current approaches to alleviate and treat the disease, and discusses the potential use of statins for treatment. Specifically, the mechanism of action and metabolism of simvastatin, the most known and studied molecule among the statin family, are critically reviewed. Various cellular pathways have been implicated in COPD, with alveolar macrophages emerging as pivotal inflammatory mediators in the COPD patho-physiology. Recently, emerging anti-cytokine therapies, such as PDE4 inhibitors and ACE inhibitors, have shown good anti-inflammatory properties that can be useful in COPD treatment. Recently, statins as a drug class have gained much interest with respect to COPD management, following studies which show simvastatin to exert effective anti-inflammatory effects, via inhibition of the mevalonic acid cascade in alveolar macrophages.

Title: Maintenance pharmacotherapy of mild and moderate COPD: What is the evidence?
Citation: Respiratory Medicine, September 2011, vol./is. 105/9(1268-1274)
Author(s): Ferguson G.T.

Abstract: Chronic obstructive pulmonary disease affects more than 24 million individuals in the United States, although at least half of the cases are not diagnosed. Proactive diagnosis and limitation of risk exposure from smoking or pollutants are important to improve prognosis. Pharmacologic treatments are prescribed according to COPD stage and symptoms. Mild COPD is symptomatically treated 'as needed' with short-acting bronchodilators; major guidelines recommend starting maintenance treatment at the moderate COPD stage with long-acting bronchodilators; inhaled corticosteroids may be added for patients with more severe disease and frequent exacerbations. Maintenance therapy preserves 24-h airway patency, reduces exacerbations, and improves activity tolerance and health-related quality of life. Recent post-hoc analyses of large clinical trials that contain subgroups of patients with less severe COPD suggest that, similar to those with advanced disease, patients with moderate disease benefit from long-term maintenance therapies. Studies suggest symptomatic mild patients may also benefit. Proactive identification and pharmacologic intervention has the potential to alter clinical outcomes throughout the disease course.

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survival. Numerous endpoints have been proposed for response to therapy, decline in lung function, and airway inflammation. Airway inflammation is involved in increased bronchial tone, mucus hypersecretion and loss of parenchymal elastic structures. Oxidative stress impairs tissue integrity, accelerates lung ageing and reduces the efficacy of corticosteroids by decreasing levels of histone deacetylase-2. Protease-antiprotease imbalance impairs tissues and is involved in inflammatory processes. Inflammation is also present in the pulmonary artery wall and at the systemic level COPD patients, and may be involved in COPD-associated comorbidities. Proximal airways inflammation contributes to symptoms of chronic bronchitis while distal and parenchymal inflammation relates to airflow obstruction, emphysema and hyperinflation. Basal levels of airways and systemic inflammation are increased in frequent exacerbators. Inhaled corticosteroids are much less effective in COPD than in asthma, which relates to the intrinsically poor reversibility of COPD-related airflow obstruction and to molecular mechanisms of resistance relating to oxidative stress. Ongoing research aims at developing new drugs targeting more intimately COPD-specific mechanisms of inflammation, hypersecretion and tissue destruction and repair. Among new anti-inflammatory agents, phosphodiesterase-4 inhibitors have been the first to emerge.

Abstract: Despite an increasing evidence base, some important controversies in COPD management still exist. The classic way to define COPD has been based on spirometric criteria, but more relevant diagnostic methods are needed that can be used to describe COPD severity and comorbidity. Initiation of interventions earlier in the natural history of the disease to slow disease progression is debatable, there are many controversies about the role of inhaled corticosteroids in the management of COPD, and long-term antibiotics for prevention of exacerbation have had a resurgence in interest. Novel therapeutic drugs are urgently needed for optimum management of the acute COPD exacerbation. COPD is a complex disease and consists of several clinically relevant phenotypes that in future will guide its management.

Title: Advances in drug delivery: Is triple therapy the future for the treatment of chronic obstructive pulmonary disease?
Citation: Expert Opinion on Pharmacotherapy, August 2011, vol./is. 12/12(1913-1932)
Author(s): Salama R.O., Young P.M., Rogueda P.

Abstract: Current therapies for chronic obstructive pulmonary disease focus on the improvement of clinical symptoms via the use of bronchodilators: beta<sub>2</sub>-adrenoreceptor agonists and muscarinic (M3) acetylcholine receptor antagonists. The combination of inhaled corticosteroids (ICSs) and long-acting beta<sub>2</sub>-agonists (LABAs), or LABAs and anticholinergics has become an efficient alternative to single therapies. These combinations consist of a LABA and an ICS together with an anticholinergic, such as ipratropium or tiotropium. This review summarizes the latest thinking and findings on the usefulness of triple therapy in the treatment and management of COPD. It aims to provide an overview to understand the efficacy and need for COPD triple therapy. The reader will gain an in-depth view of the triple therapy approach in managing COPD, existing molecules in the market or in development as well as new chemical entities. Clinical evidence in support of triple therapy, formulations and products are also discussed. Expert opinion: There is limited documented clinical evidence for the use of triple therapy in COPD, reflected in the lack of commercial activity in the field. The future for the management of COPD may lie with triple therapy, but may equally rest on a better understanding of the disease and subsequent development of new chemical entities, such as dimer molecules, longer-acting beta-agonists and antimuscarinics.
Title: Assessment and management of chronic obstructive pulmonary disease in the emergency department and beyond
Citation: Expert Review of Respiratory Medicine, August 2011, vol./is. 5/4(549-559)
Author(s): Rowe B.H., Bhutani M., Stickland M.K.

Abstract: Acute exacerbations of chronic obstructive pulmonary disease are common, can result in emergency department presentation and often result in hospitalization. After confirming the diagnosis and treating comorbidities, management of severe AECOPD includes bronchodilators, systemic corticosteroids, antibiotics, noninvasive ventilation and, occasionally, endotracheal intubation. Once discharged, delayed follow-up and suboptimal management often occurs. Antibiotics, systemic corticosteroids and optimization of nonpharmacological interventions (e.g., smoking cessation, immunization and pulmonary rehabilitation) are important discharge considerations. Improving linkages to primary providers who adhere to management involving a pharmacological and nonpharmacological treatment plan is critical to preventing future AECOPDs, reducing healthcare utilization and maintaining the quality of life of patients following an AECOPD.

Title: The role of pharmacotherapy in mild to moderate chronic obstructive pulmonary disease
Citation: Therapeutic Advances in Respiratory Disease, August 2011, vol./is. 5/4(245-254)
Author(s): Raghavan N., Guenette J.A.

Abstract: COPD is a major health problem worldwide and most of those afflicted have mild to moderate disease as measured by spirometry. There is mounting evidence that even mild airway obstruction is associated with activity-related dyspnea, exercise limitation, impaired quality of life, increased hospitalization and mortality. There is increasing interest in the potential impact of therapeutic interventions beyond smoking cessation. Unfortunately, few clinical trials have included patients with mild to moderate disease and the evidence base for pharmacological treatment in this subpopulation is currently lacking. Recent short-term mechanistic studies confirm that reversal of airway smooth muscle cholinergic tone consistently improves respiratory mechanics during rest and exercise in mild COPD but long-term clinical benefits remain to be evaluated. Secondary analysis of large, prospective studies designed to evaluate the efficacy of long-acting bronchodilators, inhaled corticosteroids and combination therapy indicate that patients with moderate COPD achieve comparable benefits to those with advanced disease. Treatment choices are driven mainly by clinical presentation: for those with persistent and troublesome activity-related dyspnea a trial of inhaled bronchodilator therapy is justified; for those with a propensity for recurrent infective exacerbations, consideration of additional anti-inflammatory treatment seems reasonable. In this paper, we review the current knowledge base and emerging paradigm for the pharmacological treatment of mild to moderate COPD.