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COPD exacerbation

Chronic obstructive pulmonary disease exacerbation and risk of pulmonary embolism

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Pulmonary embolism is not a common feature in patients with chronic obstructive pulmonary disease with uncomplicated exacerbations

Exacerbations of chronic obstructive pulmonary disease (COPD) are episodes of acute deterioration in respiratory symptoms¹ that are accompanied by physiological changes² and associated with increases in airway and systemic inflammation.^{3–4} These episodes are responsible for considerable morbidity and mortality, especially in patients with more severe COPD.⁵ There is consequently much interest in understanding the underlying pathophysiology of exacerbations and determining their triggers, so that appropriate interventions can be designed to prevent these events, reduce their severity and thus improve health status.

We now recognise that respiratory infections are important triggers of exacerbation. Respiratory viral infections, especially with human rhinovirus (the

cause of the common cold), influenza and respiratory syncytial virus may be isolated from up to 60% of exacerbations.^{6–7} Exacerbations where a virus is isolated have increased airway and systemic inflammatory changes.^{3–8} The role of bacteria at exacerbation has been more difficult to determine as airway bacteria are also found in stable patients with COPD, especially those with more severe COPD. However, we now know that bacterial strain change may play a part in triggering exacerbation.⁹ Airway bacteria may be present in up to 70% of COPD exacerbations, and their isolation is accompanied by increased airway inflammatory changes.¹⁰ Viruses and bacteria may also be co-isolated from the same exacerbation, and recent studies have suggested that the presence of both

pathogens may have a synergistic effect on the degree of airway inflammation, especially when exacerbations are severe.^{8–12} Thus, airway infection can be implicated as a trigger in most COPD exacerbations, even taking into account difficulties in sampling these patients that can lead to underestimating the significance of airway infection.

There is also interest in other causes of COPD exacerbation. Air pollution has been associated with an increase in hospital admissions in patients with COPD, although these effects are relatively small.¹³ As COPD exacerbations are closely linked to respiratory infections, the hypothesis has been put forward that pollutants can increase susceptibility to viral infection. One study has suggested that with higher personal nitrogen dioxide exposure, there is a greater risk of an asthmatic exacerbation after respiratory infection.¹⁴ Similar mechanisms might be operating in patients with COPD and further studies investigating the associations between pollution and infection are required.

Exacerbations therefore result from further insult to the COPD airway, but a number of conditions may mimic exacerbation by causing worsening dyspnoea in patients with underlying COPD. One such condition is pulmonary embolism, a disorder of the vasculature rather than the airway. Although pulmonary embolism is not thought to predispose to exacerbation, there have been a number of reports suggesting that the prevalence of deep venous thrombosis and pulmonary

embolism is increased in patients with COPD exacerbation (although earlier results were based on small studies in selected hospitalised patients^{15–16}). The hypothesis that COPD exacerbations may trigger pulmonary embolic events is plausible as acute infections are known to predispose to deep venous thrombosis and pulmonary embolism.¹⁷ Furthermore, patients with COPD are often elderly, may be immobile, and often have systemic inflammation and co-morbid conditions, all of which increase susceptibility to venous thromboembolism. There may also be diagnostic difficulties as both COPD exacerbations and pulmonary embolism may present solely with dyspnoea. A recent study by Tillie-Leblond *et al*¹⁸ reported a 25% prevalence of pulmonary embolism in patients with COPD hospitalised for severe exacerbations “of unknown origin”. An unusual feature of this study was that the authors excluded all patients in whom a potential infective cause for exacerbation was identified: they excluded exacerbations associated with increased sputum volume or sputum purulence, or a history of colds and sore throats, which indicates viral infection. Thus, the patients recruited into this study were highly selected and not representative of most exacerbations presenting to primary or secondary care that are usually accompanied by some manifestation of airway infection. In this study, exacerbations were defined as an acute deterioration requiring hospitalisation, and it is not clear whether patients just presented with worsening symptoms of dyspnoea or may have developed other conditions such as heart failure that could increase the risk of pulmonary embolism.

In this issue of *Thorax*, Rutschmann *et al*¹⁹ describe a further interesting study investigating the prevalence of pulmonary embolism at COPD exacerbations. (see page 121) In contrast with the study by Tillie-Leblond, Rutschmann *et al* included consecutive patients admitted to emergency departments with COPD exacerbations and investigated all the patients for pulmonary embolism, regardless of clinical suspicion. Investigation involved a standardised algorithm based on D-dimer testing, lower limb venous ultrasonography and multidetector helical computerised tomography scan. The data showed that the prevalence of pulmonary embolism was 6.2% in patients with COPD with clinical suspicion of pulmonary embolism, and only 1.3% where there was no clinical suspicion of pulmonary embolism. The authors conclude that as the prevalence of pulmonary embolism is so low, systematic investigation in patients presenting with COPD exacerbations is not required.

So is this the final conclusion: that pulmonary embolism is not an issue in patients with COPD with uncomplicated exacerbations? The results of this study are consistent with the clinical observation that most moderate to severe exacerbations in patients with COPD last between 7 and 10 days, respond well to therapy, and recover to their baseline symptoms and lung function. Some patients with COPD are prone to frequent exacerbations; they may be susceptible to respiratory viral infections²⁰ and are these patients more prone to develop PE? Perhaps, however, these patients are more prone to developing pulmonary embolism. Furthermore, we also recognise that in some patients, an index COPD exacerbation may be followed closely in time by another “recurrent” exacerbation,²¹ and this is consistent with the observation that patients admitted to hospital with exacerbations are subsequently at an increased risk of readmission.²² It is thus possible that in addition to airway infection, venous thromboembolism may play a part in exacerbation recurrence.

Airway infection is the most important trigger of COPD exacerbations, and strategies to reduce airway viruses and bacteria should be the most effective interventions to prevent or reduce these events. The paper by Rutschmann *et al* suggests that pulmonary embolism is not a common feature of the uncomplicated exacerbation at presentation. However, some exacerbations can have prolonged recovery periods, complicated by respiratory failure and co-morbidity, when the risk of pulmonary embolism may become greater. It is these exacerbations that have particular health economic implications and require our future efforts.

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