that of COPD. Evidence from a large prospective study of patients with COPD showed that systemic inflammation conferred its greatest risk on susceptibility to lung cancer. A recent population-based study showed that statin therapy reduced mortality for a number of cancers by about 20% to 30%, particularly those linked with smoking and obesity. In absolute terms, we estimate that 42% of all the lives saved with statin therapy were from a reduction in death from lung cancer specifically. That statins reduce the risk of lung cancer or deaths from lung cancer is consistent with the literature and concurs with our understanding of the adverse effects of systemic inflammation on epithelial cancers. Moreover, Arimura and colleagues recently showed that systemic inflammation was responsible for DNA damage in the airways of mice and was mediated through macrophages, further implicating systemic inflammation in lung cancer (reverse effect) (Fig 1).

We conclude that statin therapy provides a powerful immunomodulatory action that has a profound effect on the innate immune system in the lung, specifically cytokine-driven inflammation that characterizes aerropolllutant-based airways disease (ie, COPD and its comorbidities). We suggest that it is time to examine statins as adjunct therapy to inhaler-based treatment in COPD.

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**REFERENCES**


**Routine Pneumocystis Pneumonia Prophylaxis in Patients Treated With Rituximab?**

To the Editor:

I was pleased to read the article by Martin-Garrido et al in this issue of CHEST (see page 258) on *Pneumocystis* pneumonia (PcP) risk in patients treated with rituximab at the Mayo Clinic in Rochester, Minnesota, from 1998 to 2011. Thirty of 230 patients with PcP had received rituximab, compared with 23 patients with HIV-associated PcP. However, to determine the incidence of PcP in patients treated with rituximab, I would like to know how many patients were treated with rituximab during the study period.

A systematic review and meta-analysis of randomized controlled trials recommended PcP prophylaxis in patients without HIV infection when the risk for PcP is > 3.5%. In transplantation medicine, routine PcP prophylaxis is used in patient groups with a fixed, high incidence of disease > 3% to 5%. PcP incidence in patients treated with rituximab is, therefore, of clinical importance to assess the risk-benefit ratio of routine, primary PcP prophylaxis. I agree with the authors that primary PcP prophylaxis should be considered in patients treated with rituximab, but not solely for the duration of B-cell depletion.
Response

To the Editor:

I appreciate Dr Besada’s interest in our article on the potential risks of developing Pneumocystis pneumonia (PCP) in immunocompromised patients receiving rituximab. We too wish to know the overall incidence of this often lethal complication following the administration of this medication. Unfortunately, under the design of the study, this is not currently possible. During this time frame, a significant number of patients received rituximab at outside institutions either before or after care at the Mayo Clinic. Thus, there were no means to accurately obtain the total number of patients who were exposed to rituximab over this time period in the entire patient population. We simply raised concern that PCP may develop as a complication in patients receiving rituximab and that this infection has a high attendant mortality (about 30%).

Our study is unique in that three of the patients in the cohort received rituximab as the only immunosuppressive agent associated with the development of PCP. Earlier series reported this infection in transplant recipients. We simply raised concern that PCP has a high attendant mortality (about 30%).

We support the general recommendations of Green et al, advocating routine prophylaxis in patient populations where the overall incidence of PCP exceeds 3.5%. Unfortunately, at this time, the true incidence of PCP in patients receiving rituximab either alone or in combination with other immunosuppressive drugs remains unknown and must await additional monitoring of patients receiving this medication. However, in light of the potential risk of this infection and the high mortality associated with PCP, we recommend that clinicians use their judgment, carefully weighing the risk of the prophylaxis regimens against the potential risks of PCP. Such decisions are, of course, tempered by the overall clinical setting. It is for these reasons that we intentionally did not use the term “routine” in characterizing the decision to administer prophylaxis to these patients, although antibiotic prophylaxis often may well be considered and offered to many such immunosuppressed individuals.

References


Pathophysiology of Intrapulmonary Right-to-Left Shunt in Infants With Obstructive Apnea

To the Editor:

We read with great interest the article by Shaikh et al1 in CHEST (January 2013). The authors concluded that in adults with severe sleep apnea syndrome, closure of the patent foramen ovale is not followed by a reduction in nocturnal desaturation, suggesting the coexistence of an alternative mechanism of residual right-to-left shunt (RLS). Here we propose a potential source of residual RLS.

In infants with Pierre Robin syndrome, with choanal atresia, or with esophageal atresia, the pathogenic mechanism of glossoptosis apnea is similar to that of sleep apnea. The main difference is that in infancy, sleep is not an essential prerequisite for the development of glossoptosis apnea. The study of breathing patterns during respiratory distress shows that these infants present recurrent obstructed inspiratory efforts (an equivalent of Müller maneuver). The obstructed inspiration is followed by a prolonged and interrupted expiratory flow; despite a positive inspiratory intrathoracic pressure (an equivalent of Valsalva maneuver), and then by a retarded expiratory flow (grunting expiration). The association between obstructive apnea and expiratory grunt suggests that the functional upper airway obstruction...