31. **Murphey LJ,** Williams MK, Sanchez SC, *et al*. Quantification of the major urinary metabolite of PGE_2 by a liquid chromatographic/mass spectrometric assay: determination of cyclooxygenase-specific PGE_2 synthesis in healthy humans and those with lung cancer. *Anal Biochem* 2004;**334**:266–75.
32. **Szczeklik A.** Prostaglandin E_2 and aspirin-induced asthma. *Lancet* 1995;**345**:1056.
33. **Pavord ID,** Tattersfield AE. Bronchoprotective role for endogenous prostaglandin E_2. *Lancet* 1994;**344**:436–8.
34. **Kowalski ML,** Pawliczak R, Woźniak J, *et al*. Differential metabolism of arachidonic acid in nasal polyp epithelial cells cultured from aspirin-sensitive and aspirin-tolerant patients. *Am J Respir Crit Care Med* 2000;**161**:391–8.
35. **Kowalski ML,** Ptasińska A, Bienkiewicz B, *et al*. Differential effects of aspirin and misoprostol on 15-hydroxyeicosatetraenoic acid generation by leukocytes from aspirin-sensitive asthmatic patients. *J Allergy Clin Immunol* 2003;**112**:505–12.
36. **Pierzchalska M,** Szabo Z, Sanak M, *et al*. Deficient prostaglandin E_2 production by bronchial fibroblasts of asthmatic patients with special reference to aspirin-induced asthma. *J Allergy Clin Immunol* 2003;**111**:1041–8.
37. **Picado C,** Fernandez-Morata JC, Juan M, *et al*. Cyclooxygenase-2 mRNA is downexpressed in nasal polyps from aspirin-sensitive asthmatics. *Am J Respir Crit Care Med* 1999;**160**:291–6.
38. **Perez-Novo CA,** Watelet JB, Claeys C, *et al*. Prostaglandin, leukotriene, and lipoxin balance in chronic rhinosinusitis with and without nasal polyposis. *J Allergy Clin Immunol* 2005;**115**:1189–96.
39. **Ying S,** Meng Q, Scadding G, *et al*. H. Aspirin sensitive rhinosinusitis is associated with reduce E-prostanoid 2 (EP2) receptor expression on nasal mucosal inflammatory cells. *J Allergy Clin Immunol* 2006;**117**:312–8.
40. **Jinnai N,** Sakagami T, Sekigawa T, *et al*. Polymorphisms in the prostaglandin E_2 receptor subtype 2 gene confer susceptibility to aspirin-intolerant asthma: a candidate gene approach. *Hum Mol Genet* 2004;**13**:3203–17.
41. **Lee SH,** Rhim T, Choi YS, Min JW, *et al*. Complement C3a and C4a increased in plasma of patients with aspirin-induced asthma. *Am J Respir Crit Care Med* 2006;**173**:370–8.
42. **Bochenek G,** Nagraba K, Nizankowska E,*et al*. A controlled study of 9alpha, 11beta-PGF2 (a prostaglandin D2 metabolite) in plasma and urine of patients with bronchial asthma and healthy controls after aspirin challenge. *J Allergy Clin Immunol* 2003;**111**:743–9.
43. **O'Sullivan S,** Dahlen B, Dahlen SE, *et al*. Increased urinary excretion of the prostaglandin D_2 metabolite 9 alpha, 11 beta-prostaglandin F_2 after aspirin challenge supports mast cell activation in aspirin-induced airway obstruction. *J Allergy Clin Immunol* 1996;**98**:421–32.
44. **Szczeklik A,** Nizankowska E, Bochenek G, *et al*. Safety of a specific COX-2 inhibitor in aspirin-induced asthma. *Clin Exp Allergy* 2001;**31**:219–25.
45. **Ferreri NR,** Howland WC, Stevenson DD, *et al*. Release of leukotrienes, prostaglandins and histamine into nasal secretions of aspirin sensitive asthmatics during reactions to aspirin. *Am Rev Respir Dis* 1988;**137**:847–54.
46. **Fischer AR,** Rosenberg MA, Lilly CM, *et al*. Direct evidence for a role of the mast cell in the nasal response to aspirin in aspirin-sensitive asthma. *J Allergy Clin Immunol* 1994;**94**:1046–56.
47. **Kowalski ML,** Sliwinska-Kowalska M, Igarashi Y, *et al*. Nasal secretions in response to acetylsalicylic acid. *J Allergy Clin Immunol* 1993;**91**:580–98.
48. **Szczeklik A,** Sladek K, Dworski R, *et al*. Bronchial aspirin challenge causes specific eicosanoid response in aspirin-sensitive asthmatics. *Am J Respir Crit Care Med* 1996;**154**:1608–14.
49. **Sladek K,** Szczeklik A. Cysteinyl leukotrienes overproduction and mast cell activation in aspirin-provoked bronchospasm in asthma. *Eur Respir J* 1993;**6**:391–9.
50. **Trudeau J,** Hu H, Chibana K, *et al*. Selective downregulation of prostaglandin E2-related pathways by the Th2 cytokine IL-13. *J Allergy Clin Immunol* 2006;**117**:1446–54.
51. **Szczeklik A,** Sanak M. The broken balance in aspirin hypersensitivity. *Eur J Pharmacol* 2006;**533**:145–55.
52. **Gyllfors P,** Bochenek G, Overholt J, *et al*. Biochemical and clinical evidence that aspirin-intolerant asthmatic subjects tolerate the cyclooxygenase 2-selective analgetic drug celecoxib. *J Allergy Clin Immunol* 2003;**111**:1116–21.

Lung alert

Inhibition of NKCC1 may be beneficial in sepsis

Mortality related to bacteraemic pneumonia remains high, and previous studies have shown that the Na^+–K^+–Cl cotransporter (NKCC1) may have an important role in causing acute lung injury secondary to compromise of the alveolar-capillary barrier. Under normal physiological conditions, NKCC1 plays a central role in salt transport and volume regulation in epithelial and non-epithelial cells. This study investigated the host response to *Klebsiella pneumoniae* infection in an experimental model of bacteraemia in congenic mice lacking NKCC1 expression (NKCC1−/−) and control mice (NKCC1+/+).

Mice were infected with *K pneumoniae* and bronchalveolar lavage fluid (BALF) was analysed 48 h later. NKCC1−/− mice had significantly higher numbers of cells in BALF, in particular increased numbers of neutrophils and interleukin (IL)-10. There was also a 10-fold decrease in bacterial colony forming units (CFUs) in NKCC1−/− mice compared with controls. Hypothermia was also significantly less in NKCC1−/− mice 48 h after infection. Similar changes were noted in a model of acute inflammation after lipopolysaccharide stimulation, with significantly higher neutrophils, macrophages and IL-6 in NKCC1−/− mice. However, these effects were observed primarily in the pneumonic model and not in the peritonitic model.

This study shows that NKCC1 contributes to changes in pulmonary vascular permeability during inflammation, and loss of NKCC1 expression shows a protective effect against hypothermic sepsis and bacteraemia. Inhibitors specific for NKCC1 might provide a novel means of limiting sepsis in individuals with bacterial pneumonia.

► Nguyen M, Pace AJ, Koller BH. Mice lacking NKCC1 are protected from development of bacteremia and hypothermic sepsis secondary to bacterial pneumonia. *J Exp Med* 2007;**204**:1383–93

B Jayaraman

Correspondence to: B Jayaraman, Respiratory SpR, Royal Bournemouth Hospital, Bournemouth, UK; Bhagi.jayaraman@gmail.com