5. **Biron CA.** Role of early cytokines, including alpha and beta inteferons (IFN-α/β) in innate adaptive immune responses to viral infections. *Immunology* 1998;**10**:383—90.
6. **Ank N,** West H, Paludan SR. IFN-lambda: novel antiviral cytokines. *J Interferon Cytokine Res* 2006;**26**:373—9.
7. **Schatz M,** Dombroski MP, Wise R, *et al*. Asthma morbidity during pregnancy can be predicted by severity classification. *J Allergy Clin Immunol* 2003;**112**:283—8.
8. **Nicholson KG,** Kent J, Ireland DC. Respiratory viruses and exacerbations of asthma in adults. *BMJ* 1993;**307**:982—6.
9. **Johnston SL,** Pattermore PK, Sanderson G, *et al*. Community study of the role of viral infections in exacerbations of asthma in 9-11 year old children. *BMJ* 1995;**310**:1225—9.
10. **Minerbi-Codish I,** Fraser D, Avnun L, *et al*. Influence of asthma in pregnancy on labour and the newborn. *Respiration* 1998;**65**:103—35.
11. **Cox S,** Posner SF, McPheeters M, *et al*. Hospitalizations with respiratory illness among pregnant women during influenza season. *J Obstet Gynaecol* 2006;**107**:1315—22.
12. **Hartert TV,** Neuzil KM, Shintani AK, *et al*. Maternal morbidity and perinatal outcomes among pregnant women with respiratory hospitilizations during influenza season. *J Obstet Gynaecol* 2003;**189**:1705—12.
13. **Contoli M,** Message SD, Laza-Stanca V, *et al*. Role of deficient type III interferon-λ production in asthma exacerbations. *Nat Med* 2006;**12**:1023—6.
14. **Gehlhar K,** Bilitewski C, Reintz-Rademecher K, *et al*. Impaired virus-induced interferon-alpha2 release in adult asthmatic patients. *Clin Exp Allergy* 2006;**36**:331—7.
15. **Wark PA,** Johnston SL, Bucchieri F, *et al*. Asthmatic bronchial epithelial cells have a deficient innate immune response to infection with rhinovirus. *J Exp Med* 2005;**201**:937—47.
16. **McLaughlin K,** Murphy V, McCaffery K, *et al*. The relationship between patient perceived risk of inhaled corticosteroids in pregnancy and medication adherence. *Respirology* 2009;**14**:A42.
17. **Powell H,** Smart J, Wood L, *et al*. Validity of the common cold questionnaire (CCQ) in asthma exacerbations. *PLoS ONE* 2008;**3**:e1802.
18. **Juniper EF,** Bousquet J, Abetz L, *et al*. Identifying 'well-controlled' and 'not well-controlled' asthma using the Asthma Control Questionnaire *Respir Med* 2006;**100**:616—21.
19. **Papi A,** Johnston SL. Rhinovirus infection induces expression of its own receptor intercellular adhesion molecule 1 (ICAM-1) via increased NF-κB-mediated transcription. *J Biol Chem* 1999;**274**:9707—20.
20. **Dupont WD,** Plummer WD. PS power and sample size program for free on the Internet. *Control Clin Trials* 1997;**18**:274.
21. **Dodds L,** McNeil SA, Fell DB, *et al*. Impact of influenza exposure on rates of hospital admissions and physician visits because of respiratory illness among pregnant women. *CMAJ* 2007;**176**:463—8.
22. **Neuzil KM,** Reed GW, Mitchel EF, *et al*. Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women. *Am J Epidemiol* 1998;**148**:1094—102.
23. **Groer MW,** Davis MW, Smith K, *et al*. Immunity, inflammation and infection in post-partum breast and formula feeders. *Am J Reprod Immunol* 2005;**54**:222—31.
24. **Yang K,** Puel A, Zhang S, *et al*. Human TLR-7-, -8-, and -9- mediated induction of IFN-α/β and -λ is IRAK-4 dependent and redundant for protective immunity to viruses. *Immunity* 2005;**23**:465—78.
25. **Birmachu W,** Gleason R, Bulbulian B, *et al*. Transcriptional networks in plasmacytoid dendritic cells stimulated with synthetic TLR 7 agonists. *BMC Immunol* 2007;**8**:26.
26. **Coccia E,** Severa M, Giacomini E, *et al*. Viral infection and toll-like receptor agonists induce a differential expression of type I and λ interferons in human plasmacytoid and monocyte-derived dendritic cells. *Eur J Immunol* 2004;**34**:796—805.
27. **Gibson SJ,** Lindh JM, Riter TR, *et al*. Plasmacytoid dendritic cells produce cytokines and mature in response to the TLR7 agonists, imiquimod and resiquimod. *Cell Immunol* 2002;**218**:74—86.
28. **Ito T,** Wang Y-H, Liu Y-J. Plasmacytoid dendritic cell precursors/type I interferon-producing cells sense viral infection by Toll-like receptor (TLR) 7 and TLR9 *Springer Semin Immunopathol* 2005;**26**:221—9.
29. **Lund JM,** Alexopoulou L, Sato A, *et al*. Recognition of single-stranded RNA viruses by Toll-like receptor 7. *Proc Natl Acad Sci U S A* 2004;**101**:5598—603.
30. **Li X,** Xu Y, Ma L, *et al*. 17beta-estradiol enhances the response of plasmacytoid dendritic cell to CpG. *PLoS ONE*. 2009;**4**:e8412.
31. Asthma in Australia: findings from the 2004-05 National Health Survey2007. http://www.aihw.gov.au/publications/index.cfm/title/10416 (accessed Jul 2009).
32. **Murphy VE,** Gibson P, Talbot PI, *et al*. Severe asthma exacerbations during pregnancy. *J Obstet Gynaecol* 2005;**106**:1046—54.
33. **Kelly JT,** Busse WW. Host immune responses to rhinovirus: mechanisms in asthma. *J Allergy Clin Immunol* 2008;**122**:671—82.

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A possible mechanism of drug tolerance in mycobacteria

In this study, the authors investigated possible mechanisms of drug tolerance in mycobacteria and identified a key mediator to target with drug therapy, with the aim of shortening current treatment and moving towards eradication.

Using an in vivo model, they found that drug tolerant mycobacteria existed in macrophages prior to granuloma formation, indicating that the granuloma is not essential for developing tolerance, but is important for dissemination. By monitoring the movement of individual macrophages from a particular granuloma they observed that these macrophages could leave the granuloma and recruit other macrophages to create new granulomas, often at sites distant from the original. This explained a well-established phenomenon in human tuberculosis infection.

The group confirmed the importance of macrophages in the induction of drug tolerance and showed that efflux pumps are essential for both bacterial growth and development of drug tolerance. They found that bacteria retained intracellularly induced tolerance when they became extracellular. This explained how tolerant extracellular bacteria could arise in the granuloma's necrotic core in human tuberculosis infection.

By challenging current dogma, the researchers have established the important role of macrophages and granulomas in inducing and disseminating tolerance. They have found efflux pumps to be a useful specific target of drug therapy due to their role in tolerance and bacterial growth.

► **Adams KN**, Takaki K, Connolly LE, *et al*. Drug tolerance in replicating mycobacteria mediated by a macrophage-induced efflux mechanism. *Cell* 2011;**145**:39—53.

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