

administration of a grass pollen extract is beneficial in established seasonal allergic rhinitis.²⁹

Conclusion

Using molecular biology to find new ways to inhibit allergic tissue responses is becoming a reality. Particularly promising are the use of vaccines and pharmacological agents to reduce the polarised Th2 response seen in atopic subjects by enhancing production of interferon γ . Selective inhibition of specific mediators such as interleukin 4, interleukin 5, interleukin 13, and eotaxin should lead to a new class of anti-cytokine therapeutic agents. At the cellular level, more effective inhibition of mast cell activation and strategies to remove IgE as the triggering stimulus hold promise. With the discovery of genes increasing susceptibility to allergic disease, the next decade is likely to witness substantial advances in knowledge of induction mechanisms and disease prevention.

With the current epidemic of allergic disease there is an urgent need to identify those environmental factors that are responsible so that appropriate interventions can be introduced. In genetically susceptible individuals these might include changes to the maternal and infant diet to programme the developing immune response or the early introduction of a protective vaccine to reset the T lymphocyte balance more in favour of Th1 cells. In this regard the development of synthetic bacterial DNA and antigen specific DNA vaccines looks especially promising.

In established allergic disease, the task of reversing sensitisation is daunting. Safer and more efficacious allergen vaccines, whether based on DNA or peptides, offer the most promising approach for fundamentally changing the allergic immune response. Patients would also greatly benefit from more effective, orally administered inhibitors of mast cells and small molecules that could either remove IgE or interrupt its capacity to signal through its cell surface receptors.

Competing interests: None declared.

- 1 Peat JK, Li J. Reversing the trend: reducing the prevalence of asthma. *J Allergy Clin Immunol* 1999;103:1-10.
- 2 Palmer EM, van Seventer GA. Human T helper cell differentiation is regulated by the combined action of cytokines and accessory cell-dependent co-stimulatory signals. *J Immunol* 1997;158:2654-62.
- 3 Jung T, Moessner R, Kieckhoff K, Heidrich S, Neumann C. Mechanisms of deficient interferon- γ production in atopic diseases. *Clin Exp Allergy* 1999;29:912-9.
- 4 Shirikawa T, Enomoto T, Shimazu SI, Hopkin JM. The inverse association between tuberculin response and atopic disorder. *Science* 1997;275:77-9.
- 5 Martinez FD, Holt PG. Role of microbial burden in aetiology of allergy and asthma. *Lancet* 1999;354(paediatrics suppl II):S112-5.
- 6 Wang C-C, Rook AW. Inhibition of an established allergic response to ovalbumin in BALB/c mice by killed *Mycobacterium vaccae*. *Immunology* 1998;93:307-13.
- 7 Hopkin JM, Shaldan S, Ferry B, Coull P, Antrobus P, Enomoto T, et al. Mycobacterial immunisation in grass pollen immunisation and rhinitis. *Thorax* 1998;53(suppl.4):A16.
- 8 Wagner H. Bacterial CpG DNA activates immune cells to signal infectious danger. *Adv Immunol* 1999;73:329-68.
- 9 Chu RS, Targoni OS, Krieg AM, Lehmann PV, Harding CV. CpG oligodeoxynucleotides act as adjuvants that switch on T-helper 1 (Th-1) immunity. *J Exp Med* 1997;186:1623-8.
- 10 Patalano F. Injection of anti-IgE antibodies will suppress IgE and allergic symptoms. *Allergy* 1999;54:103-10.
- 11 Casale T, Bernstein IL, Busse WW, La Force CF, Tinkelman DG, Stoltz RR, et al. Use of an anti-IgE humanised monoclonal antibody in ragweed-induced allergic rhinitis. *J Allergy Clin Immunol* 1997;100:110-21.
- 12 Stanworth DR, Jones VM, Lavin IV, Naggar S. Allergy treatment with a peptide vaccine. *Lancet* 1990;336:1279-81.
- 13 Romanski B, Bartuzi Z, Stanworth DR. Assessment of a novel anti-allergy vaccine in subjects with severe food allergy and at risk of anaphylaxis to food. *Int Rev Allergol Clin Immunol* 1998;4:164-73.
- 14 Rudolf MP, Vogel M, Kricsek F, Ruf C, Zürcher AW, Reuschel R, et al. Epitope specific antibody response to IgE by mimotope immunisation. *J Immunol* 1998;160:3315-21.

- 15 Daëron M. ITIM-bearing negative coreceptors. *Immunologist* 1997;5:79-85.
- 16 Paesen GC, Adams PL, Harlos K, Nuttall PA, Stuart DI. Tick histamine-binding proteins: isolation, cloning and three-dimensional structure. *Mol Cell* 1999;3:861-71.
- 17 Renz H, Bradley K, Enssel K, Loader JE, Larsen GL, Gelfand EW. Prevention of the development of immediate hypersensitivity and airway hyper-responsiveness in vivo with soluble IL-4 receptors. *Int Arch Allergy Immunol* 1996;106:167.
- 18 Borish LC, Nelson HS, Lanz M, Claussen LR, Martin DW, Garrison L. Phase I/II study of interleukin-4 receptor (IL04r) in moderate asthma. *J Allergy Clin Immunol* 1998;101:S8-9.
- 19 Grunig G, Warnock M, Wakil AE, Venkayya R, Brombacher F, Rennick DM, et al. Requirement for IL-13 independently of IL-4 in experimental asthma. *Science* 1998;282:2261-3.
- 20 Zhu Z, Homer RJ, Wang Z, Chen Q, Geba GP, Wang J, et al. Pulmonary expression of interleukin-13 causes inflammation, mucus hypersecretion, subepithelial fibrosis, physiologic abnormalities, and eotaxin production. *J Clin Invest* 1999;103:779-88.
- 21 Tony H-P, Shen B-J, Reusch P, Sebald W. Design of human interleukin-4 antagonists to inhibiting interleukin-4-dependent and interleukin-13-dependent responses in T cells and B cells with high efficiency. *Eur J Biochem* 1994;225:659-65.
- 22 Grunewald SM, Werthemann A, Schnarr B, Klein CE, Bröcker EB, Mohrs M, et al. An antagonistic IL-4 mutant prevents type I allergy in the mouse: inhibition of the IL-4/IL-13 receptor system completely abrogates humoral immune response to allergen and development of allergic symptoms in vivo. *J Immunol* 1998;160:4004-9.
- 23 Danzig M, Cuss F. Inhibition of interleukin-5 with a monoclonal antibody attenuates allergic inflammation. *Allergy* 1997;52:787-94.
- 24 Leckie MJ, ten Brinke A, Lordan J. SB 240563, a humanised anti-IL-5 monoclonal antibody: initial single, dose safety and activity in patients with asthma. *Am J Respir Crit Care Med* 1999;159(3):A624.
- 25 Teran C. Chemokines and IL-5: major players of eosinophil recruitment in asthma. *Clin Exp Allergy* 1999;29:287-90.
- 26 Heath H, Qin S, Rao P, Wu L, La Rosa G, Kassam N, et al. The importance of CCR-3 demonstrated using an antagonistic monoclonal antibody. *J Clin Invest* 1997;99:178-84.
- 27 Durham S, Till SJ. Immunologic changes associated with allergen immunotherapy. *J Allergy Clin Immunol* 1998;102:157-64.
- 28 Roy K, Mao HQ, Haeng SK, Leong KW. Oral gene delivery with chitosan-DNA nanoparticles generate immunologic protection in a murine model of peanut allergy. *Nature Med* 1999;5:387-91.
- 29 Clavel R, Bousquet J, André C. Clinical efficacy of sublingual-swallowed immunotherapy. A double blind placebo-controlled trial of a standardised five grass pollen extract in rhinitis. *Allergy* 1998;53:493-8.

Corrections and clarifications

Revalidation of doctors in Canada

In the reference list of this article by W Dale Dauphinee (30 October, pp 1188-90), reference number 8 should have been listed as number 7, and number 7 should have been listed as number 8.

The Icelandic database: do modern times need modern sagas?

In this article by Ruth Chadwick (14 August, pp 441-4) the author wrongly attributed to the Council of Europe Steering Committee on Bioethics a view on the difficulty of identifying individuals within the Icelandic database. It should have been attributed to the Ministry of Health and Social Security of Iceland. The ministry submitted a paper to the committee on bioethics, but its authorship was not apparent on the copy sent to Dr Chadwick.

Implementing screening for colorectal cancer

The penultimate sentence of the fourth paragraph of this editorial by Wendy Atkin (6 November, pp 1212-3) quotes endoscopists as citing a sensitivity as low as 44% for adenomas of less than 1 cm; this should have read "for adenomas greater than 1 cm."

Dietary management of hepatic encephalopathy

In this editorial by Carol A Seymour and Kevin Whelan (22 May, pp 1364-5) reference 3 was wrongly attributed to Andres T; it should have been attributed to Blei AT. Moreover, Seymour and Whelan's reference to this article implied that Blei was recommending the dietary restriction mentioned; in fact they meant only to emphasise that a positive nitrogen balance benefits subjects, which is a point that Blei made in the reference cited.