glucose tolerance in these children (A Bavdekar et al). The fetal origins hypothesis predicts high rates of type 2 diabetes for them later in life. The prevalence of diabetes in India is likely to go on increasing and to constitute a major health burden.

Can fetal growth be improved in pregnancies at risk for fetal growth retardation? Improving the mother's growth and nutrition before pregnancy is the ideal strategy, but animal studies show that more than one generation of improved maternal nutrition may be needed to optimise fetal growth. Later marriage and childbearing would allow Indian mothers to start pregnancy better grown (W P T James and J M Wallace). Only limited evidence exists that nutritional supplements in pregnancy improve fetal growth in undernourished mothers (A M Prentice). Furthermore, the effects of supplements vary according to the stage of pregnancy: giving them early in pregnancy may even worsen fetal growth.

The thrifty phenotype is a paradigm that has stimulated animal as well as human research on fetal growth retardation; its neuroendocrine and metabolic effects; and the possible mechanism by which metabolism, body composition, and growth may be permanently affected. It was widely if not universally accepted by the congress as a model to explain the link between fetal growth retardation and later diseases. Of the existence of that link there is no doubt, and in the 21st century it may matter most in the Indian subcontinent.

Roger Robinson *associate editor, BMJ*

The *BMJ* provided financial support to the congress. RR wrote an introductory chapter to *Fetal and infant origins of adult disease.*[1]

*Papers presented at the congress are indicated here by their authors' names in parentheses. Abstracts will be published in a supplement to *Pediatric Research*, July 2001.

1 Barker DJP, ed. *Fetal and infant origins of adult disease.* London: BMJ Books, 1992.
2 Hales CN, Barker DJP. Type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. *Diabetologia* 1992;35:595-601.

The protective effect of childhood infections

The next challenge is to mimic safely this protection against allergy and asthma

Papers p 390

Although infectious diseases are by no means defeated, the past 100 years have seen a dramatic decline in some previously common childhood infections. Many serious viral and bacterial infections can now be prevented or treated by vaccination or antibiotics. In contrast, the prevalence of asthma and atopic disease has increased, particularly during the past 30 years. This increase is certainly not accounted for by a change in genetic risk factors: genetically similar populations in East and West Germany had very different rates of asthma before unification (although former east Germany is now catching up with the west[1]). In a landmark study of hayfever, hygiene, and household size in 1989 Strachan proposed that improved hygiene was the factor that explained this rise.[2]

The immunological arguments that underlie this "hygiene" hypothesis can be summarised as follows. Many common viral infections induce a strong protective host response dominated by the production of interferon γ (IFNγ). This type 1 response is more effective at eliminating viruses than the alternative type 2 response (characterised by the production of interleukin 4 and interleukin 5), which promotes IgE production, eosinophilia, atopy, and asthma. Children are born with strong type 2 responses but mature their type 1 responses in the first year or so of life under environmental influence, mainly that of common childhood infections. Children born to atopic parents are slower to do this than those born to non-atopic parents.[3]

Thus, having many older siblings; attending day care at an early age[4]; growing up on a farm and in frequent contact with cattle, poultry, and cats; and having childhood measles[5] and orofaecal infections such as hepatitis A[6] are all helpful (directly or by association) in promoting normal immunological maturation and in preventing atopic disease. By contrast, living in a small family group in hygienic conditions and taking antibiotics in early life[7] may promote the development of asthma and atopy.

In this issue of the *BMJ*, Illi et al show that episodes of uncomplicated common colds (runny nose) during infancy may also protect against episodes of wheezing in later childhood (p 390).[8] Other childhood infections such as herpetic stomatitis, exanthema subitum, and chickenpox also seemed protective. By contrast, episodes of wheezy lower respiratory tract infection were strongly associated with subsequent episodes of wheezing by the age of 7 (odds ratio >6). In other words, children with frequent simple infantile colds are less likely to develop wheezing by the age of 7, while children with wheezy lower respiratory illnesses in the first year are more likely to wheeze later on.

The authors acknowledge the difficulty of showing cause and effect in observational studies of this type. Importantly, no attempt was made to confirm the clinical diagnosis of viral colds by laboratory studies, and the authors were unable to determine whether rhinovirus, coronavirus, or respiratory syncytial virus had different effects. However, the important conclusion is that the risk of a diagnosis of asthma by the age of 7 is reduced by about 50% percent in children with two or more reported episodes of common cold (without associated wheeze) by the age of 1 year.

The challenge before us is to find ways of reproducing the protective effects of early childhood infections, while at the same time reducing the burden of serious (and less serious but still troublesome) infectious diseases. With increasing numbers of effective vaccines, antiviral treatments, and antibiotics and with increasing affluence, how can we prevent the continued rise in asthma and atopic disease? Perhaps different common cold viruses have different effects. Since there is evidence that respiratory syncytial virus bronchiolitis is a risk

BMJ 2001;322:376–7

factor for later asthma,[9] preventing it by vaccination or passive immunotherapy[10] might reduce the frequency of childhood wheezing in later life, while Illi et al's study suggests that preventing colds might have the opposite effect. Knowing exactly which "dirt" provides the best education for the immune system and how to mimic its effects in a cleaner environment seems to be the key to reversing the rise in atopic diseases.

Sebastian L Johnston *professor of respiratory medicine*
Peter J M Openshaw *professor of experimental medicine*

Department of Respiratory Medicine, National Heart and Lung Institute, Imperial College School of Medicine at St Mary's, Norfolk Place, London W2 IPG

1 von Mutius E, Weiland SK, Fritzsch C, Duhme H, Keil U. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. *Lancet* 1998;351:862-6.
2 Strachan DP. Hay fever, hygiene and household size. *BMJ* 1989;299: 1259-60.
3 Prescott SL, Macaubas C, Smallacombe T, Holt BJ, Sly PD, Holt PG. Development of allergen-specific T-cell memory in atopic and normal children. *Lancet* 1999;353:196-200.
4 Ball TM, Castro-Rodriguez JA, Griffith KA, Holberg CJ, Martinez FD, Wright AL. Siblings, day-care attendance, and the risk of asthma and wheezing during childhood. *N Engl J Med* 2000;343:538-43.
5 Shaheen SO, Aaby P, Hall AJ, Barker DJ, Hayes CB, Shiell AW, et al. Measles and atopy in Guinea-Bissau. *Lancet* 1996;347:1792-6.
6 Matricardi PM, Rosmini F, Riondino S, Fortini M, Ferrigno L, Raicetta M, et al. Exposure to foodbourne and orofecal microbes versus airbourne viruses in relation to atopy and allergic asthma: epidemiological study. *BMJ* 2000;320:412-7.
7 Hopkin JM. Early life receipt of antibiotics and atopic disorder. *Clin Exp Allergy* 1999;29:733-4.
8 Illi S, von Mutius E, Lau S, Bergmann R, Niggeman B, Sommerfeld C, et al. Early childhood infectious diseases and the development of asthma up to school age: a birth cohort study. *BMJ* 2001;322:390-5.
9 Sigurs N, Bjarnason R, Sigurbergsson F, Kjellman B. Respiratory syncytial virus bronchiolitis in infancy is an important risk factor for asthma and allergy at age 7. *Am J Respir Crit Care Med* 2000;161:1501-7.
10 Wenzel SE, Gibbs R, Lehr M, Park N, Simoes EAF. Asthma related clinical and physiologic outcomes in high risk children 5-9 years after prophylaxis with RSV Ig IV. *Am J Respir Crit Care Med* 2000;161:A898.

Type 2 diabetes in children

Exemplifies the growing problem of chronic diseases

Type 2 diabetes mellitus in children is an emotionally charged issue and an emerging public health problem.[1 2] Until recently most children with diabetes mellitus had type 1, one of the most common[3] and increasingly prevalent[4] chronic diseases in children. Increasingly, however, type 2 diabetes is being reported in children from the United States, Canada, Japan, Hong Kong, Australia, New Zealand, Libya, and Bangladesh.[5]

The prevalence of type 2 diabetes in children ranges from 4.1 per 1000 12-19 year olds in the US to 50.9 per 1000 15-19 year old Pima Indians of Arizona.[1 2] Between 8% and 45% of recently diagnosed cases of diabetes among children and adolescents in the United States is type 2, and the magnitude of this disease may be underestimated.[1 2] The prevalence of the disease is on the rise in North America, and its incidence almost doubled in Japan between 1976-80 and 1991-5—from 7.3 to 13.9 per 100 000 junior high school children.[5] These trends coincide with the rising prevalence of overweight and physical inactivity world wide.[5 6–8]

Among US children the mean age at diagnosis of type 2 diabetes is between 12 and 14 years, corresponding with puberty; the disease affects girls more than boys, predominantly people of non-European origin, and is associated with obesity, physical inactivity, a family history of type 2 diabetes, exposure to diabetes in utero, and signs of insulin resistance.[1 2] At diagnosis the affected child may present with weight loss, ketosis, and acidosis.[1 2] Insulin and C peptide levels are often raised and antibodies absent, which may help differentiate type 1 from type 2 diabetes, but insulin secretion may well be blunted at diagnosis.[1] Haemoglobin A_{1c} levels may range from 10% to 13%, and a sizeable proportion of patients have hypertension, hypertriglyceridemia, albuminuria, sleep apnoea, and depression,[2] and these factors may worsen over time.[9] However, treatment protocols vary considerably, and several of the drugs used for glycaemic, blood pressure, and lipid control are not approved for use in children.[1 2]

To respond to this emerging problem, the American Diabetes Association and the American Academy of Pediatrics issued a joint consensus statement, and the Committee for Native American Child Health is developing treatment guidelines based on expert opinion. The National Institutes of Health and the Centers for Disease Control and Prevention have each embarked on new research programmes to improve gaps in our knowledge. So, what do we need to know and do?

Firstly, we need to develop case definition(s) that will differentiate between types of diabetes in children, and will be suitable for estimating the magnitude of the disease in populations[2] and for clinical diagnosis.[1] Case definitions for public health surveillance and clinical purposes should involve simple low cost tests, an issue of importance to poor countries and communities.

Secondly, epidemiological data on the magnitude of the problem, its secular trends, and follow up of incident cases are needed for several at risk populations.[1 2] Limited data are available in selected populations such as the American Indians, but few data exist for several parts of the world where the disease is prevalent.

Thirdly, adult studies have shown efficacious interventions for type 2 diabetes, but their safety and efficacy in children is not known. Also needed are well coordinated, multicentre trials testing the feasibility of multiple risk factor reduction in children and its benefits for practical health outcomes, such as the early stages of vascular disease.

Fourthly, despite efficacious treatments, the quality of care for adults with type 2 diabetes remains suboptimal.[10] This situation is likely to be worse for children and adolescents[1 2] because this is a new problem for clinicians; adolescents may be particularly reluctant to make behavioural changes, manage their disease, and accept follow up; and access to health care may be inadequate. Carefully conducted studies of quality of care and of potential interventions among children are needed.

BMJ 2001;322:377–8