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are accruing about postpartum thyroid disease to justify a detailed evaluation of a screening strategy.

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Treatment of persistent otitis media

SIR—van Balen and colleagues (Sept 14, p 713)¹ mention that most children in the Netherlands receive xylometazoline 0.25% nose drops, one drop thrice daily, for middle ear effusion. We are concerned about the routine use of these drops because they are known to cause rhinitis medicamentosa, a condition characterised by rebound nasal mucosal swelling, and prolonged use induces a tendency towards abuse. The imidazoles (to which xylometazoline belongs) are more likely than other drugs to cause rebound congestion and rhinitis medicamentosa because of their long duration of action.²

Xylometazoline drops used in paediatric practice come in a strength of 0.05% (British National Formulary). The use of the 0.25% strength would be clearly harmful in these children. Moreover, van Balen and colleagues do not mention the preservative used, which is benzalkonium chloride. The combination of both these factors accentuates the deleterious effects on the nasal mucosa within 10 days.³ van Balen et al also fail to clearly indicate whether these drops were used only for the time of the study or longer. It seems illogical to discuss the lack of efficacy of decongestants (used orally) in their introduction,⁴ but to use them in the study nevertheless.

26% of general practitioners prescribe topical decongestants for allergic rhinitis,⁵ which suggests that misuse of these drugs is widespread. Education should be targeted towards general practitioners. If as noted in the paper, "in the Netherlands most patients with middle-ear effusion receive decongestant nosedrops (one drop of xylometazoline 0.25%, three times a day)", then we suggest that the lower dose of xylometazoline (0.05%) is substituted and the period of use restricted to less than 10 days.

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Author's reply

SIR—Parikh and Scadding rightfully point at the harmful side-effects of xylometazoline nosedrops. In the Netherlands many general practitioners use xylometazoline nosedrops for upper respiratory tract infections, which include nasal catarrh and otitis media. The use of these nosedrops never exceeds 5-7 days. This is carefully explained in the product information package insert. It is my experience that patients are very well aware of this time restriction. In our study we used the nosedrops for 7 days in the strength of 0.25% instead of 0.05%. This was for practical and logistic reasons. Both the pharmaceutical company and the consulted pharmacists saw no difficulties in the use of this strength in children under 6 years of age. I agree that it has never been shown that decongestant nosedrops has any effect in the management of otitis media with effusion, and our guidelines do not advise the use of these nosedrops. The reason for their use in our study was that treatment in all included children had to be the same, apart from the antibiotic treatment. Because we expected that at least some of the participating general practitioners would prescribe these nosedrops, we included them in the baseline therapy.

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SIR—van Balen and colleagues¹ report a positive effect of antibiotic treatment for persistent middle-ear infection. They found that treatment with co-amoxiclav for 2 weeks led to higher rates of resolution at the end of therapy than placebo. Other studies have also shown a short-term beneficial effect in terms of resolution of the effusion, but there is still the question of how long the positive effects of antibiotic treatment of otitis media with effusion will last.^{2,3} Long-term effects have not been properly investigated. In his meta-analysis Rosenfeld² suggested that because of the modest impact of antibiotics on otitis media, other factors are important for clinical resolution. One of these factors is the natural course of the disease: at least half the otitis media with effusion episodes resolve spontaneously within 3 months.⁴ It should be noted that only a few children with this condition will benefit from treatment with antibiotics, and probably only for a short time. Furthermore, widespread antibiotic resistance has been reported in children medically treated for otitis media with effusion.²

Before treatment can be recommended, short-term and long-term risks and costs for the population should be taken into consideration and balanced against short-term and long term benefits.

Following the recommendation of Van Balen—ie, giving antibiotics to children with isolated (persistent) disease—would mean a change of current policy of many general practitioners. Before implementation of these research findings, long-term effects and sequels should be further investigated.

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Repeated cytogenetic culture failure as an indicator of immunodeficiency

SIR—Leucocyte cultures for chromosome analysis generally rely on the glycoprotein phytohaemagglutinin to stimulate T-cells into a transient blastic transformation so that metaphase chromosomes can be obtained after 3 days in culture.¹ Success rates are greater than 98% (UK NEQAS data) and a single repeat sample is usually sufficient to produce a result whenever an initial culture fails. Over the past 5 years, however, we have encountered three patients in whom cultures failed on more than two occasions and in each case a diagnosis associated with immunodeficiency was reached.

Patient 1 was referred at 13 months of age for global developmental delay, gross motor delay, and macrocephaly. A few poor-quality metaphases with apparently normal chromosomes were obtained and two further samples at 19 and 21 months yielded no metaphases. Subsequently, however, biochemical analysis² revealed purine nucleotide phosphorylase (PNP) deficiency which is an established cause of severe T-cell dysfunction. PNP is an autosomal recessive condition in which mutations of the PNP gene have been described, heterozygote carriers identified, and prenatal diagnosis made available. This patient has been progressing well since bone marrow transplantation.

Patient 2 was referred at birth for respiratory difficulties, small genitalia, simple low-set ears, and small eyes. No metaphases were obtained from three samples taken at 1, 7, and 16 days despite the use of T-cell mitogens and B-cell mitogens on the third sample. A ventricular septal defect, low calcium, and absent thymus suggested DiGeorge syndrome, but a skin sample had normal chromosomes with no evidence of the characteristic deletion with the use of in situ hybridisation.³ The child died at 5 months of age. Immunostaining of spleen showed some T-lymphocytes suggestive of ectopic thymic tissue. A diagnosis of primary immunodeficiency of unspecified type was made.

Patient 3 was first referred at the age of 1 year for short stature. No metaphases were obtained from three samples despite the use of additional mitogens on the third. She had chronic cough, recurrent infections, and offensive diarrhoea. T-cell and B-cell depletion (especially CD4) was confirmed and a diagnosis of combined immunodeficiency rather than severe combined immunodeficiency made in view of evidence of low-level T-cell immunity. Adenosine deaminase deficiency (ADA) was excluded, treatment with intravenous immunoglobulin was ineffective, and the patient died at 2 years of age.

These patients underline the importance of considering a diagnosis of immunodeficiency as soon as two consecutive lymphocyte cultures fail without any obvious cause. Further attempts at culture should make use of a cocktail of T-cell and B-cell mitogens including phytohaemagglutinin, pokeweed, and TPA (tetradecanoyl phorbol acetate). If successful, cytogeneticists should bear in mind the instability of chromosomes 1, 9, and 16 associated with the immunodeficiency, centromeric instability, and facial anomalies (ICF) syndrome.⁴ The immunodeficiencies are a heterogeneous group of conditions but the success of bone marrow transplantation and feasibility of gene therapy are

already transforming the prognosis for conditions such as PNP and ADA.⁵ It is vital that correct classification of these disorders is made as early as possible so that appropriate prognosis, therapy, and recurrence risks can be provided.

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Photocopier toner dust and lung disease

SIR—Ambruster and colleagues (Sept 7, p 690)¹ conclude that photocopier toner dust caused chronic lung disease in a 39-year-old man. Their diagnosis of granulomatous pneumonitis and mediastinal lymphadenopathy attributable to toner dust inhalation is based on comparison of X-ray spectrograms of the toner and intracellular particles in lung and mediastinal lymph-nodes.

Apart from copper the toner also contains iron, as follows from the spectrogram. However, it seems that no iron was detected in the spectrogram of the lung and lymph-node biopsy specimens. If that was the case, then the conclusion that toner dust caused the illness would be inappropriate. Furthermore, information is lacking about the patient's exposure to toner dust in terms of airborne concentration, and duration, and the very relevant question as to whether others in the same working environment contracted similar lung disease. What about possible exposure to other dusts in the patient's personal environment? Finally, if, as they state, "lymphadenopathy is usually linked to chronic beryllium disease", then this possible cause must be excluded. The more so because beryllium has not been mentioned to be a component of the toner.

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- 1 Ambruster C, Dekan G, Hovorka A. Granulomatous pneumonitis and mediastinal lymphadenopathy due to photocopier toner dust. *Lancet* 1996; 348: 690.

Authors' reply

SIR—Wieriks correctly points out that toner dust also contains iron. Most of the particles in the lung tissue of our patient contained silicon, copper, and iron. Some contained silicon and copper only, and a few aluminium also. All these elements were also detectable in the toner. We did not