

be achieved, and they identify a need for more rapid seizure treatment to lessen the increased morbidity and mortality of prolonged status epilepticus. Longer seizure duration might also lessen the effectiveness of benzodiazepine doses in seizure cessation.⁶ Treatment should be started before arrival at hospital, but requires trained health-care personnel or families, availability of an affordable benzodiazepine that can be easily stored and administered via a transmucosal route, and proximity to a medical resource for further assessment and treatment. This opportunity is not yet available for many children. Furthermore, because several benzodiazepines show efficacy via various delivery routes in the acute setting, perhaps the search for one drug delivered via one route should no longer be the main concern. Instead we may need to keep many options available in our intervention for prolonged seizures and

tailor the treatment for each individual patient, with the reminder that access to care is the first step.

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Worms, asthma, and the hygiene hypothesis

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IgE was discovered in the 1960s,¹ and it was quickly linked to allergic asthma² and helminthic infections.³ Pathogenetic links between these two conditions were claimed, and it was proposed that helminths contributed to allergy and asthma through potentiation of allergen-specific IgE responses or, by contrast, to protect from allergy and asthma either through the saturation of Fc_ε receptors on mast cells and basophils (by polyclonal IgE) or by induction of IgG blocking antibodies.⁴ Helminthic infections were associated with asthma in a few studies, but not in others.⁴ This area re-emerged when the immunosuppressive properties of helminths were re-evaluated by combining two new concepts: the “anti-inflammatory network” (interleukin 10, transforming growth factor β, T-regulatory cells) and the “hygiene hypothesis”.⁵ Now helminths were considered to prevent allergy and asthma by stimulating the anti-inflammatory network and the allergy epidemic was attributed to the sharp decline of helminthic infections.⁵ Indeed chronic intestinal helminth infection can protect children from atopic reactivity in a various settings in developing countries.^{6–10} Similarly, worm infestation early in life (mainly *Ascaris*, *Oxyuris* spp) was negatively associated with subsequent eczema in a large population of East German children.¹¹ By contrast, transient, delayed, or milder helminthic infections

in children were positively associated with atopic disorders.^{6,12} To explain these new inconsistencies, it was speculated that early, heavy, and chronic helminthic infections protect children of endemic countries against allergies (eg, by stimulating T-regulatory cells), whereas sporadic, delayed, or transient infection potentiates allergy in sensitised children through bystander T-helper-2 stimulation.^{5,13}

Cross-sectional studies are clearly insufficient to answer whether helminths promote or suppress allergy and asthma. Theoretically, such a link could be experimentally investigated by monitoring either allergic children during a new helminthic infection or children chronically infected by helminths during deworming treatment. With the latter approach, Venezuelan children chronically infected mostly with *Ascaris lumbricoides* and *Trichuris trichuria* developed or increased their atopic reactivity to mites after treatment with anthelmintic drugs.¹⁴ Similarly, Gabonese children chronically infected with *A lumbricoides* and *T trichuria* transiently increased their reactivity to locally relevant airborne allergens during a 3-year follow-up after anthelmintic treatment.¹⁵ By contrast, Philip Cooper and colleagues¹⁶ report in today's *Lancet* that an anthelmintic programme in Ecuadorian schoolchildren reduced helminthiasis without promoting atopic sensitisation,

allergic symptoms, and exercise-induced bronchospasm during a 1-year follow-up.

Cooper and colleagues' study is good public-health news: intensive anthelmintic treatment in highly endemic areas does not promote allergic diseases in the short term. However, we believe that this study does not totally rule out helminths as protecting against atopic responses to airborne allergens and the development of allergic diseases. Indeed a possibility is that the intensity and chronicity of helminthic infections in Ecuadorian children was less than that in the Gabonese children studied by Van den Biggelaar and colleagues.¹⁵ The prevalence of individuals infected by *T trichuria* approached 80% in Gabonese children over the 3-year study period, but was only 53% at baseline in Ecuadorian children, suggesting a lower circulation of this geohelminth infection in the latter group. Nor are helminths the only infections in Ecuadorian children, in whom tuberculosis, salmonellosis, food poisoning, and other foodborne and faecal-oral infections abound¹⁷ and whose burden could not be modified by anthelmintic treatment programmes. *T trichuria* and *A lumbricoides* are a hallmark of faecal contamination. Foodborne and faecal-oral infections are a source of immunostimulating agents which protect against atopic sensitisation and allergic asthma.^{18,19} Cooper and colleagues noted that children with helminthic infection at baseline (before any intervention) had significantly less atopic sensitisation than those not infected (OR 0.78, 95% CI 0.65–0.95, $p=0.013$).¹⁶ Thus the elimination of just one category of protective agent through deworming is likely to be insufficient to produce a rise in allergy within the 1-year follow-up. Actually the overall effect of deworming on atopy in Gabonese children was transient and seen mostly after the first year of follow-up;¹⁵ thus it is conceivable that small and transient variations could not be recorded in the shorter study done by Cooper and colleagues in Ecuadorian children.¹⁶ Accordingly, studies in migrants from developing to developed countries have clearly shown that even more profound changes of lifestyle require many years, not simply some months, to induce changes in the immune response against allergens.²⁰

The exposure to infectious agents is so complex that studies on the hygiene hypothesis require new strategies of investigations. This complex system can

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Whipworm (*Trichuris trichiura*)

be better examined through systemic analysis (eg, neural networks) to discriminate and map a relative protective role against atopy and reciprocal interaction of any single category of infections circulating in a given human community. More specifically, an opposite strategy might theoretically be proposed to investigate the role of worms in allergy. Instead of testing whether allergies appear in endemic areas after deworming, the test might be whether allergies disappear by administering helminths or their products to the allergic patient. Indeed, the regular administration of larvae of *T suis* has been reported to be safe and effective in the treatment of other immune disorders, such as inflammatory bowel disease, in which its action is attributed to an anti-inflammatory response.²¹ A similar experimental approach has been successfully tested in animal models of allergy and asthma.²² Trials with *Necator americanus* have been planned in volunteers with asthma or other allergies.²³

The extremely complex field of the hygiene hypothesis cannot be approached any more through "simple" studies and will require systemic thinking and intervention studies adopting original and safe approaches.

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Surgery for ovarian cancer: how to improve survival

Worldwide there are 204 449 new cases of ovarian cancer diagnosed annually, accounting for about 4% of female cancers, with an estimated 124 860 disease-related deaths.¹ In the USA and the UK, ovarian cancer is the leading cause of gynaecological cancer-related death.¹ In 1994, the National Institutes of Health convened a 14-member panel of experts in the management of ovarian cancer to generate a consensus statement of recommendations.² The panel concluded that: “Adequate and complete surgical intervention is mandatory primary therapy for ovarian cancer, permitting precise staging, accurate diagnosis, and optimal cytoreduction. The procedure is best conducted by a qualified gynecologic oncologist when there is a high probability of ovarian cancer...all women with suspected ovarian cancer should be offered a preoperative consultation with a gynecologic oncologist.”²

During the past decade, compelling published work has accumulated to lend support to these consensus recommendations. These reports show that initial surgery for ovarian cancer is most appropriately done by gynaecological oncologists, preferably in centres with

expertise in the multidisciplinary management of this disease. Mirjam Engelen and colleagues recently described a population-based observational study of patterns of care for 680 women with ovarian cancer in the northern Netherlands.³ The patients were treated between 1994 and 1997. The main objective was to study the effect of surgery by a gynaecological oncologist on the quality of surgery and survival outcome compared with surgery by gynaecologists without subspecialty training. In all disease stages, patients more often received surgical treatment according to prevailing surgical guidelines when a gynaecological oncologist operated. The risk of death for patients who did not have surgery according to accepted guidelines was almost twice that for patients who had surgery according to the guidelines.

In Engelen and colleagues’ study for patients with stage I/II disease, gynaecological oncologists were substantially more likely to do the necessary staging than were general gynaecological surgeons, resulting in a more accurate assignment of disease stage and administration of adjuvant treatment. For patients with stage III disease, 5-year survival was 32% when the