In September, 2006, a 66-year-old man was admitted to our hospital with a 6-week history of nausea, dysphagia to solids, and abdominal discomfort after eating. His appetite was much reduced, and he reported that he felt sated after eating little food; he had lost 10 kg in weight, and was constantly tired. His past medical history included hypertension, dyslipidaemia, and coronary artery disease; his regular medications were enalapril, atenolol, simvastatin, and aspirin.

Other than epigastric tenderness, nothing of note was found on physical examination. The blood tests showed no abnormality. Nor did ultrasonography of the abdomen; upper gastrointestinal endoscopy; a barium swallow test; endoscopic ultrasonography of the upper gastrointestinal tract; colonoscopy; CT of the chest, abdomen, and head; and a whole-body gallium-67 scan was done. This too showed no abnormality (figure). Meanwhile, the patient developed joint pains, and continued to lose weight. Repeated blood tests, including thyroid function tests and an extensive autoantibody screen. Eventually, a whole-body gallium-67 scan was done. This too showed no abnormality (figure). Meanwhile, the patient developed joint pains, and continued to lose weight. Repeated blood tests showed a low serum albumin concentration (29 g/L), as well as normocytic anaemia (haemoglobin 113 g/L), and eosinophilia (0·6×10⁹/L). The combination of unexplained weight loss or abdominal symptoms. 2 In up to a quarter of patients, no definitive aetiology can be established. 1 The possibility of cortisol deficiency should be considered in all patients with unexplained weight loss or abdominal symptoms. 2,3 Eosinophilia and anaemia can also be caused by cortisol deficiency, as can arthralgia. Unusually, our patient’s cortisol deficiency was secondary to dysfunction of the pituitary or hypothalamus. Chronic understimulation of the adrenal cortex by corticotropin causes an impaired response on the short corticotropin-stimulation test, which does not necessarily indicate Addison’s disease. 2 Since there was no evidence of generalised hypopituitarism, and no evidence of hypothalamic damage on MRI, we made a diagnosis of isolated corticotropin deficiency—a rare disorder, sometimes caused by lymphocytic hypophysitis, which may be of autoimmune aetiology. 1 Our patient’s recovery strikingly illustrated the diagnostic usefulness of Occam’s razor. 1

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were followed up longitudinally, with the data being presented as geometric means for each community. Any sampling variability would be random and be accounted for in the statistical analyses. Comparisons were made with pretreatment microfilaria counts and analyses were done on individuals over time. Furthermore, in a subsequent unpublished study on these communities, adult worms, embryos, and larval stages in the vector have been examined and the conclusions from these additional results are consistent with those reported.

Our results cannot be explained by the alternative hypotheses suggested, which strengthens the concern that ivermectin resistance, manifested as an increase in the rate of microfilaria repopulation by adult worms, is developing. As suggested by many of the correspondents, this suggestion warrants increased monitoring for ivermectin resistance and an acceleration of efforts to develop better tools for such monitoring and for new means of onchocerciasis control.

We declare that we have no conflict of interest.

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The report by Mike Osei-Atweneboana and colleagues1 concerning possible ivermectin resistance in onchocerciasis is of concern. Although the microfilaricidal effects of ivermectin seemed undiminished, the study suggests that the poorly understood inhibition of embryogenesis in female macrofilariae was reduced in four of ten villages.

Any suggestion of compromised effectiveness is of great concern for the Mectizan Donation Program, one of the most effective public-health mass treatment programmes of all time. The rates of repopulation of microfilariae were relatively small and occurred in an area where treatment coverage has not been particularly high. This is also an area where active transmission of Onchocerca volvulus continues. Nonetheless, this report is a warning against complacency and a call to redouble efforts in the search for a macrofilaricidal drug and for drugs that can affect embryogenesis through an alternative mechanism. Further it is an urgent message for increased scrutiny of populations after treatment.

Some believe that elimination of onchocerciasis is possible in many foci through interruption of transmission through more aggressive treatment programmes with higher levels of population coverage.2,4 The findings from Ghana might encourage such efforts.

I am Chair of the Mectizan Expert Committee, which is a voluntary position without pay.

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Coeliac disease and lymphocytic hypophysitis

Ami Schattner and Taiba Zornitzki describe a man with anaemia, arthralgia, and gastrointestinal involvement (June 30, p 2214).1 Many ancillary tests were done, resulting in an eventual diagnosis of corticotropin deficiency possibly caused by lymphocytic hypophysitis. One test that was not done was for coeliac disease. This disease is very common and has protein manifestations2,3 matching most findings in Schattner and Zornitzki’s patient. Steroids are also used in its treatment,2 and the patient’s recovery might therefore be due to their effect on coeliac disease, which can occur with lymphocytic hypophysitis.4,5 Finally, as well as heeding Occam’s razor,1 “When you hear hoofbeats, don’t think zebras” should also be kept in mind.

I declare that I have no conflict of interest.

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1 Schattner A, Zornitzki T. When the whole-body scan shows no abnormality. Lancet 2007; 369: 2214.


3 Ciclitira PJ, King AL, Fraser JS. AGA technical review on celiac sprue. Gastroenterology 2001; 120: 3526–40.


Authors’ reply

We applaud the brilliant suggestion by Weekitt Kittisupamongkol that our patient’s isolated corticotropin deficiency could have been due to associated unrecognised coeliac disease. As many as 3.8% of blood donors in Israel have positive serology for coeliac disease, and when they undergo
intestinal biopsies a prevalence of at least one in 157 is found.1 With such a high prevalence in Israel and other countries, one should be wary of associations that might be no more than coincidental. However, as an autoimmune disease, coeliac disease is often associated with other endocrine and non-endocrine autoimmune disorders. Only the associations with type 1 diabetes and with thyroid disease are well established by large controlled studies (about 6% and 5% of patients with coeliac disease, respectively), whereas concomitant occurrence of Addison’s disease or autoimmune hypophysitis in coeliac disease is limited to case reports.2

Impaired growth hormone was identified in five of seven children with coeliac disease whose growth did not catch up after more than a year of gluten-free diet; in four of them, high titres of antipituitary antibodies were discovered and the MRI was normal.3

We declare that we have no conflict of interest.

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Dual inhibition of the renin system by aliskiren and valsartan

We would like to clarify some aspects of our study (July 21, p 221)1 in light of the selective reporting of our findings in the Comment by Willem Birkenhager and Jan Staessen.2 Although drugs that inhibit the renin system are known to lead to modest increases in potassium concentrations,3 the Comment gives an exaggerated picture of the risks associated with combined aliskiren/valsartan. As we report, most potassium increases to above 5.5 mmol/L were transient, with concentrations returning to normal at study end without any interruptions to treatment. Potassium concentrations of 6.0 mmol/L or more, the danger level referenced in the Comment, were more common with placebo (six patients; 1%) than combination treatment (two patients; 0.5%). In a previous study,4 only two of 118 patients who received the aliskiren/valsartan combination had potassium concentrations above 5.5 mmol/L; none had concentrations above 6.0 mmol/L.

We also disagree with Birkenhager and Staessen that our findings have limited generalisability. Although diastolic blood pressure was used for patients’ selection, the mean systolic blood pressure in all treatment groups at baseline ranged from 152.8 to 154.1 mm Hg, with 86-6% of patients having systolic blood pressure of 140 mm Hg or greater. 8-h ambulatory blood pressure monitoring was used to exclude those with white-coat hypertension. Other baseline characteristics, including age, ethnic origin, duration of hypertension, and the proportion of patients with obesity and metabolic syndrome, indicate that our study population was representative of hypertensive patients seen in clinical practice. Both diastolic and systolic blood pressure were assessed as efficacy endpoints in the study.

Finally, the claim that this combination “is unlikely to make it to general practice or even to primary prevention in specialist care” vastly overstates the issue of hyperkalaemia. The requirement for biochemical monitoring with the aliskiren/valsartan combination is no greater than that needed for patients receiving moderate diuretic doses in combination with other classes of antihypertensive drugs.

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