

colleagues, is reassuring about the usefulness of meta-analyses for assessing the effects of health care. Systematic reviews—with the use of meta-analysis when appropriate—clearly represent an advance over commonly used haphazard approaches.<sup>3</sup> Nevertheless, this young science of research synthesis needs additional empirical research to guide its development.

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## Reversible hypopituitarism after interferon- $\alpha$ therapy

SIR—Autoimmune endocrinopathies such as hyperthyroidism, hypothyroidism, and insulin-dependent diabetes mellitus have been reported as side-effects of interferon therapy.<sup>1–3</sup> However, hypopituitarism related to this agent has not been reported.

A 44-year-old woman diagnosed as having chronic hepatitis C in December, 1992, had been treated with recombinant interferon- $\alpha$  2b  $\times 10^6$  units three times a week for 3 months at another hospital. She complained of general fatigue, oedema, and amenorrhoea 2 weeks after starting therapy but treatment was continued until March, 1993.

She was referred to our hospital in April, 1993. She had facial and pretibial oedema but no goitre. Her serum free thyroxine was 1.1 ng/dL (normal 0.85–2.15), free triiodothyronine 2.4 pg/dL (2.8–6.0), and thyrotropin (TSH) 0.1  $\mu$ U/mL (0.3–3.5). Basal serum cortisol and corticotropin were 4.0  $\mu$ g/mL (4.4–17.4) and 1.2 pg/mL (6.1–55.0), respectively. Basal levels of other hormones (growth hormone, luteinising hormone, follicle stimulating hormone, prolactin) were normal. Serum cortisol and corticotropin did not respond to insulin-induced hypoglycaemia and lysine-vasopressin. However, serum cortisol rose to 26.6  $\mu$ g/dL after corticotropin stimulation, suggesting recent onset of corticotropin deficiency. TSH responses to TSH-releasing hormone and growth hormone responses to arginine were blunted.

Autoantibodies against thyroid microsomal antigen and thyroglobulin (haemagglutination kits, Sanko Pure Chemical, Tokyo) were not detected, but pituitary antibody for GH<sub>3</sub> cells was positive. Ovarian autoantibodies were not tested. Magnetic resonance imaging showed no abnormality in the pituitary gland.

The diagnosis was hypopituitarism and the patient was put on replacement with 10 mg hydrocortisone and 100  $\mu$ g thyroxine daily for 11 months. Her fatigue and oedema disappeared and menstruation resumed. We discontinued replacement therapy and basal levels of cortisol and corticotropin and responses to insulin-induced hypoglycaemia and lysine-vasopressin returned to normal. Growth hormone responses to arginine became normal too, as did serum free thyroxine (1.5 ng/dL) and free triiodothyronine (3.9 pg/mL).

Interferon treatment has been reported to induce organ or non-organ specific autoantibodies,<sup>1,2</sup> sometimes leading to autoimmune endocrinopathy.<sup>1–3</sup> Long-term treatment with interferon- $\alpha$  is not thought to influence pituitary hormones,<sup>4</sup> although Crockett et al<sup>5</sup> reported growth retardation (without measurement of growth hormone levels) in children on long-term interferon. In our patient

hypopituitarism developed during interferon therapy, and she recovered 11 months after that treatment stopped. An autoimmune process induced by interferon may have resulted in a reversible hypopituitarism. Our case suggests that patients on interferon therapy should be monitored for pituitary function.

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## When to use fluconazole

SIR—Denning (March 4, p 584) points out an error in our commentary (Jan 7, p 6). We agree that fluconazole is not beneficial in diseases caused by *Aspergillus* spp, and we did not imply that it did. The reference to his work<sup>1</sup> on the use of itraconazole for invasive aspergillosis was correctly cited; the statement about the lack of usefulness of in-vitro susceptibility testing to guide therapy with antifungal drugs was incorrectly attributed to his publication,<sup>1</sup> and Como and Dismukes<sup>2</sup> report should have been cited instead. We apologise for this error.

As we say, laboratory and epidemiology data confirm the emergence of both in-vitro and clinical resistance to fluconazole among *Candida* spp. Data cited by Rex and colleagues<sup>3</sup> suggest a correlation between in-vitro susceptibility testing and in-vivo efficacy when the proper test conditions are selected. Both the references Denning cites to further substantiate this correlation were published late in 1994, and were not available when we submitted our commentary for publication.

Considerable progress has been made in the field of antifungal susceptibility testing; however, reliable antifungal susceptibility testing is available from only a few specialised reference laboratories. Even if a firm correlation between in-vitro testing and clinical outcome is established, routine measurements of minimum inhibitory concentrations for antifungal agents cannot be widely endorsed until a standardised dependable procedure can be made available to all hospital microbiology laboratories. The clinician could obtain timely results and patient management would benefit. Antifungal susceptibility testing should be reserved for patients in whom there is treatment failure or as dictated by forthcoming investigational protocols.

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