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Letters to the Editor

Carbimazole – resistant thyrotoxicosis

Sir,

We read with interest the report of two cases of thyrotoxicosis apparently resistant to high doses of carbimazole.[1] In searching for the cause of a poor therapeutic response to antithyroid drugs, several possibilities must be considered. As pointed out by Cooper,[2] noncompliance is the most probable cause of treatment failure. In his study, among nine patients referred for nonresponse to high doses of propylthiouracil, only one was finally considered as possibly resistant. However, even if it is unusual, Li *et al* recently reported a case of true resistance to methimazole confirmed by the determination of serum and intrathyroidal methimazole concentration.[3] In the two cases reported by Jude, drug levels were not measured. However, the hypothesis of resistance to carbimazole could have been tested alternatively by performing a perchlorate discharge test four hours after taking carbimazole under medical supervision; a negative perchlorate test indicating an inadequate blockade of iodide organification and thus a possible carbimazole resistance, a positive test indicating the possibility of some degree of iodide organification block, and, therefore a possible lack of compliance.[2]

Regardless of the problem of compliance, iodine contamination should have been ruled out by measuring urinary iodine excretion. Iodine does affect the response of the thyroid to antithyroid drugs, directly by altering the intrathyroidal metabolism of the drug and indirectly by increasing the thyroidal stores of preformed hormones, therefore delaying the response to treatment.[4] Such mechanisms are involved in the resistance to antithyroidal drugs of amiodarone- or iodine-induced throtoxicosis which may persist for months. On the other hand, iodine-contaminated patients partially or totally resistant to antithyroid drugs may show a dramatic response to glucocorticoids,[5,6] as the two cases reported here show. Therefore, we think that an unsuspected iodine contamination may have played a role in the unresponsiveness of these two patients to high doses of carbimazole and should have been discussed.

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1 Jude EB, Dale J, Kumar S, Dodson PM. Treatment of thyrotoxicosis resistant to carbimazole with corticosteroids. *Postgrad Med J* 1996; **72:** 489–91.
2 Cooper DS. Propylthiouracil levels in hyperthyroid patients unresponsive to large doses. *Ann Intern Med* 1985; **102:** 328–1.
3 Li H, Okuda J, Akamizu T, Mori T. A hyperthyroid patient with Graves' disease who was strongly resistant to methimazole: investigation on possible mechanisms of resistance. *Endocrine J* 1995; **42:** 697–704.
4 Hall R, Lazarus JH. Changing iodine intake and the effect on thyroid disease. *BMJ* 1987; **294:** 721–2.
5 Leger AF, Massin JP, Laurent MF, *et al.* Iodine-induced thyrotoxicosis: analysis of eighty-five consecutive cases. *Eur J Clin Invest* 1984; **14:** 449–55.
6 Broussole C, Ducottet X, Martin C, *et al.* Rapid effectiveness of prednisone and thionamides combined therapy in severe amiodarone iodine-induced thyrotoxicosis. Comparison of two groups with apparently normal thyroid glands. *J Endocrinol Invest* 1989; **12:** 37–42

Gastrointestinal disorders in Parkinson's disease

Sir,

Gastrointestinal disorders are common in Parkinson's disease. Although the underlying pathophysiology remains largely unknown, enteric nervous dysfunction and subsequent gastrointestinal dysmotility leading to small bowel bacterial overgrowth with malabsorption is an attractive hypothesis. Davies *et al*[1] recently used the lactulose hydrogen breath test to study whether increased orocaecal transit time and small bowel bacterial overgrowth could explain weight loss in Parkinson's disease. None of their 15 patients showed an early rise in breath hydrogen, which led the authors to conclude that bacterial overgrowth was absent. We object to this conclusion for several reasons. First, the lactulose hydrogen breath test is a questionable tool to diagnose small bowel bacterial overgrowth.[2] The *conditio-sine-qua-non* for this test is the presence of a hydrogen-producing flora, but in 15–20% of tested subjects the gut flora will not meet this condition.[3] Therefore, the fact that none of the patients studied by Davies *et al*[1] had an early rise of breath hydrogen excretion does not exclude small bowel bacterial overgrowth. Furthermore, the authors cite the study by Metz *et al*[4] as evidence that the lactualose hydrogen breath test is a reliable measure of small bowel bacterial overgrowth. However, this study in fact showed that the lactualose hydrogen breath test has a rather poor sensitivity (approximately 67%).[4] Preferentially, the authors should have followed the recommendation of Metz *et al*[4] to use a combination of breath tests to screen for small bowel bacterial overgrowth. Alternatively, the authors could have used the more invasive method of quantitative microbial culturing of duodenal or jejunal aspirates, which remains the most accurate diagnostic tool to demonstrate small bowel bacterial overgrowth, especially when gastrointestinal motility disorders are suspected.[5]

Second, one would have expected to find small bowel bacterial overgrowth since orocaecal transit time was increased in 10 of the 15 patients with Parkinson's disease. Disturbed small bowel motility is an important risk factor for small bowel bacterial overgrowth.[6] Histological observations suggest that impaired gastrointestinal motility might be related to impairment of the gastrointestinal myenteric plexus, which appears to be affected in Parkinson's disease.[7]

Third, Davies *et al*[1] found high lactulose/mannitol ratios in their patients, suggesting a reduction in the absorptive surface area of the small intestine. This might indicate the existence of small bowel bacterial overgrowth, since it is a well known cause of intestinal mucosal injury, loss of brush border enzyme activity and resultant malabsorption.[8] In conclusion, the study of Davies *et al*[1] does not exclude the possibility that small bowel bacterial overgrowth, due to disturbed small bowel motility, may at least partially explain weight loss, malabsorption and other gastrointestinal disorders in Parkinson's disease.

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1 Davies KN, King D, Billington D, Barrett JA. Intestinal permeabilitity and orocaecal transit time in elderly patients with Parkinson's disease. *Postgrad Med J* 1996; **72:** 164–7.
2 Nieuwenhuijs VB, Akkermans LMA. The intestinal microflora and small bowel bacterial overgrowth. In: Quigley EMM, Marsh M, eds. *The small intestine.* Cambridge, MA, USA: Blackwell Science, Inc. (in press)
3 King CE, Toskes PP. Breath test in the diagnosis of small intestine bacterial overgrowth. *Crit Rev Clin Lab Sci* 1984; **21:** 269–81.
4 Metz G, Drasar BS, Gassull MA, Jenkins DJA, Blendis LM. Breath-hydrogen test for small-intestinal bacterial overgrowth. *Lancet* 1976, **1:** 668–9.
5 Valdovinos MA, Camilleri M, Thomforde GM, Frie C. Reduced accuracy of ^{14}C-d-xylose breath test for detecting bacterial overgrowth in gastrointestinal motility disorders. *Scand J Gastroenterol* 1993; **28:** 963–8.
6 Stotzer P-O, Björnsson ES, Abrahamsson H. Interdigestive and postprandial motility in small-intestinal bacterial overgrowth. *Scand J Gastroenterol* 1996; **31:** 875–80.
7 Wakabayashi K, Takahashi H, Ohama E, Ikuta F. Parkinson's disease: an immunohistochemical study of Lewy body-containing neurons in the enteric nervous system. *Acta Neuropathol* 1990; **79:** 581–3.
8 Toskes PP, Giannella RA, Jervis HR, Rout WR, Takeuchi A. Small intestinal mucosal injury in the experimental blind loop syndrome. *Gastroenterology* 1975; **68:** 1193–203..

Oxidative haemolysis after spiramycin

Sir,

I report a case of spiramycin-induced acute haemolysis in a glucose-6-phosphate dehydrogenase (G6PD)-deficient patient confirmed by rechallenge.

A 48-year-old-woman was hospitalised with complaints of malaise, weakness, abdominal and lumber pain 24 h after initiation of treatment with oral spiramycin (1 g bid) for fever and symptoms of an upper respiratory tract infection. Eight years previously G6PD A-deficiency was diagnosed, when she suffered from several sulfonamide- and acetanilide-induced haemolytic episodes requiring blood transfusions. The laboratory data were: haemoglobin 7.7 g/dl, haematocrit 22.4%, reticulocyte count 4.5%, whole blood count 12.4×10^9/l, platelet count 224×10^9/l. The lactate dehydrogenase concentration was markedly elevated (1823 U/l; normal < 300). Three days after the spiramycin therapy, she was afebrile but nauseated, icteric, and passing dark urine. The liver was 3 cm below the right costal margain and the spleen was not palpable. Serum total bilirubin was 2.9 mg/dl (normal < 1.0 mg/dl) with preponderant unconjugated bilirubin fraction (2.8 mg/