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 nodine does affect the response of the thyroid to antithyroid drugs, directly by altering Iodine does affect the hormones, of indirecty by increasing response out tion.3 tion on.

Therefore, we consider the recent report by Jude et al.3 that 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 a test dose under antithyroid medical supervision; a negative perchlorate test indicating an inadequate blockade of iodide organisation and thus a possible carbimazole resistance, a positive test indicating the possibility of some degree of iodide organisation 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 prohormones, therefore delaying the response to treatment.4 Such mechanisms are involved in the resistance to antithyroid drugs of amiodarone- or iodine-induced thyrotoxicosis which may persist for months. On the basis of our previous observations, iodine-contaminated, drug 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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3 Li H, O'Mahony, AKATZU 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.

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 motility imbalance leading to small bowel bacterial overgrowth with malabsorption is an attractive hypothesis. Davies et al.7 recently used the lactulose hydrogen breath test to study whether increased orocecal 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 not present. We object to this conclusion for several reasons. First, the lactulose hydrogen breath test is a questionable tool to diagnose small bowel bacterial overgrowth.8 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.9 Therefore, the fact that none of the patients studied by Davies et al.7 had an early rise of hydrogen excretion does not exclude small bowel bacterial overgrowth. Furthermore, the authors cite the study by Metz et al.10 as evidence that the lactulose hydrogen breath test is a reliable measure for intestinal bacterial overgrowth. However, this study in fact showed that the lactulose hydrogen breath test has a rather poor sensitivity (approximately 67%).11 Preferentially, the authors should have followed the recommendation of Metz et al.10 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 microbiological 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.3

Second, one would have expected to find small bowel bacterial overgrowth since orocecal transit time was increased in 10 of the 15 patients with Parkinson’s disease. Disturbed small bowel bacterial overgrowth 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.7 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.7 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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2 Nieuwenhuis VB, Akkermans LM. The intractable infection. Eight years with bowel G6PD-deficient patient confirmed by rechallenge.

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 lumbar 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 prior bowel 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, haemoglobin 20.4%, reticulocyte count 4.5%, whole blood count 12.4 × 10^11/l, platelet count 224 × 10^11/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 margin and the spleen was not palpable. Serum bilirubin was 2.9 mg/dl (normal <1.0 mg/dl) with preponderant unconjugated bilirubin fraction (2.8 mg/
The journal club

Sir,

Valentino and Daniels' article1 was illuminating—both for those who might be interested in organising new journal clubs and those wishing to resurrect defunct ones. However, one important function of the journal club was not covered in the article, which may be of interest to those just starting out in the publications game. Sackett suggested that a journal club can be a useful forum in which to develop and enhance critical appraisal skills.2

The acquisition of critical appraisal skills should not be an end in itself, but a means to an end. Journal clubs can serve as the springboard for the production of corresponences to editors of journals following critical appraisal of articles. Critical appraisal skills may also lead to production of views that may influence policies. Correspondence to editors, for example, in the form of critical comments on specific articles, form important and integral parts of most journals. Those that get published are usually original, contain assertions supported by data or by citation, and are written in a clear prose style.3 That generation of correspondence to editors is an important but relatively untapped function of journal clubs is highlighted by the experience of Sandifer et al.4 In their evaluation of their journal club's activities in the first six months of its existence, the impact on commissioning policy and the publication of letters to the editor of the journal from which the articles were selected were used as outcome measures. Six out of 10 letters generated after collective appraisal were published. They identified their club as one of the regular attenders and the relevance of the articles to everyday practice as critical factors which influence the success of a journal club. One of the cardinal rules for successful critical appraisal of articles is to avoid prejudging the articles on the basis of source, authors or preconceptions. This can be most successfully performed in the ambience of a journal club meeting because of the variation in the composition of its membership in terms of seniority and experience.

3 BMJ. Advice to authors. BMJ 1997; 314: 370.

Anticoagulants for venous thrombosis

Sir,

Dr Tobh1 hopes that a major benefit of outpatient treatment of deep venous thrombosis using low-molecular-weight heparin will be to reduce bed shortenages. Our initial experience of home treatment of deep vein thrombosis may challenge that view.

Over the first three months of our service we anticoagulated 15 patients for deep venous thrombosis as out-patients using low-molecular-weight heparin as initial therapy. However, we identified 30 patients from the hospital inpatient computerised administration system that were treated for deep venous thrombosis as in-patients during this time. In fact, the mean number treated per week as in-patients in the three months after introduction of outpatient treatment (1.2, SD 1.0), was not significantly less than the number treated per week in the previous nine months (1.1, SD 0.9). As a result the weekly total treated (in- and out-patients) was greater in the three-month period (2.3, SD 1.4).

If our initial observation is confirmed, it suggests that a service offering ready access to radiological investigation and avoidance of a stay in hospital increases the demand for deep vein thrombosis treatment. Some patients previously would have gone undiagnosed and untreated and been at risk of pulmonary embolism and post-phlebitic leg. Whilst outpatient treatment is popular with many patients, it may not save beds and could increase radiology and haematology workloads.

Oxidative haemolysis after spiramycin.

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