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 iodine does affect the response of the thyroid to antithyroid drugs, directly by altering iodine contamination should have been considered. As such, the hypothesis of resistance to carbimazole could have been tested alternatively by performing a perchlorate discharge test four hours after taking carbimazole under antithyroid drug suppression; 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.3

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 thyroid stores of propranolol, delaying the negative feedback response to treatment.4 Such mechanisms are involved in the resistance to antithyroidal drugs of amiodarone- or iodine-induced thyrotoxicosis which may persist for months. One possible explanation for the high levels of carbimazole reported by Li et al was a possible overgrowth, another possible reason of the high doses of carbimazole and should have been discussed.

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3 Li H, Obiela, Akentezi T, Mor I. A hyperthyroid patient with Graves' disease who was strongly resistant to carbimazole: investigations on possible mechanisms of resistance. Endocrinology 1995; 42: 677–704.

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 dysfunction leading to small bowel bacterial overgrowth with malabsorption is an attractive hypothesis. Davies et al recently used the lactulose hydrogen breath test to study whether increased oroacaeal 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 is an important cause. 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 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 al2 had an early rise of breath hydrogen excretion does not exclude small bowel bacterial overgrowth. Furthermore, the authors cite the study by Metz et al4 as evidence that the lactulose hydrogen breath test is a reliable measure for small bowel bacterial overgrowth. However, this study in fact showed that the lactulose hydrogen breath test has a rather poor sensitivity (approximately 67%).5 Preferentially, the authors should have followed the recommendation of Metz et al6 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 cultures 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 oroacaeal 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 al2 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 mucousal injury, loss of brush border enzyme activity and resultant malabsorption.8 In conclusion, the study of Davies et al2 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 some gastrointestinal disorders in Parkinson's disease.

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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. 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 x 10^6/l, platelet count 224 x 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 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/
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crisis.
similar
induced by
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Within
2
was obtained and
haemoglobinuria. Coomb's
test
after discharge.

bodies,
polychromatophilia, poikilocytosis,

coagulative disorders.

Six weeks after recovery, informed consent
was obtained and spiramycin re-instituted.
Within 2 h of rechallenge, acute haemolysis
had recurred. The clinical and laboratory
abnormalities settled rapidly within four
days after ceasing spiramycin. The patient is well
14 days after discharge.

A variety of drugs, toxins, and infections
cause haemolysis in G6PD-deficient indivi-
duals by posing oxidant threat to erythro-
cytes.1,2 The macrolide spiramycin has been
used in a similar way to erythromycin in
susceptible infections.3 The adverse effects
of spiramycin are also similar to those of ery-
thromycin; the most frequent being gastro-
intestinal disturbances, and skin hyper-
sensitivity.4 In our case, the acute haemolysis
induced by spiramycin after complete recovery
from the febrile illness suggests the drug to be
the triggering oxidative agent of the haemoly-
tic crisis. I am unable to find any reports of
similar adverse reaction to spiramycin.

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The journal club

Sir,
Valentini and Danis’ 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 mean
to an end. Journal clubs can serve as the
springboard for the production of correspon-
dences 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 Sander 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
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
the need for more team of 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.

Anticoagulants for venous thrombosis

Sir,
Dr Toh1 hopes that a major benefit of out-
patient treatment of deep vein thrombosis
using low-molecular-weight heparin will be to
reduce bed shortages. Our initial experience
of home treatment for deep vein thrombosis
may challenge that view.

Over the first three months of our service
we anticoagulated 15 patients for deep vein
thrombosis as out-patients using low-molecu-
lar-weight heparin as initial therapy. However,
we identified 30 patients from the hospital in-
patient computerised administration system
that were treated for deep vein 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 out-
patient 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 out-
patient treatment is popular with many
patients, it may not save beds and could
increase radiology and haematology work-
loads.

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1 Toh CH. Anticoagulants for venous thrombosis.
Oxidative haemolysis after spiramycin.

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