We read with interest the article ‘Henoch–Scho¨nlein purpura and Graves’ disease’ by Lee et al. [1]. They reported the first case of a patient with Graves’ disease who developed Henoch–Scho¨nlein purpura (HSP) after a propylthiouracil overdose. We wondered whether HSP would have occurred if she had maintained the prescribed dosage. Although a causal relationship between HSP and Graves’ disease or propylthiouracil use is unclear, we recently reported the case of a patient who developed Graves’ disease during ciclosporin treatment for severe HSP nephritis [2], and speculated that these two diseases might be related. In the past 10 years, we have experienced two additional cases of HSP associated with Graves’ disease.

**Patient 1**

A 28-year-old previously healthy woman presented with a skin eruption starting at 12 weeks gestation. Physical examination revealed palpable purpura of the lower extremities extending to the knees, but otherwise was unremarkable. Her past medical history revealed that she had been diagnosed with Graves’ disease 4 years previously and had been treated with propylthiouracil for 3 years. One year ago, she came to maintain euthyroid state without propylthiouracil treatment. Family history revealed that her mother and younger sister had hypothyroidism. Her blood pressure was normal, and laboratory tests, including complete blood count, BUN, creatinine, aminotransferases, alkaline phosphatase, urinalysis, hepatitis B and C and human immunodeficiency virus serologies, were negative or normal. Erythrocyte sedimentation rate (ESR) was 59 mm/h and serum IgA level 429 mg/dl (normal reference values <300). About 1 month later, she experienced a cutaneous flare, which persisted several weeks, without evidence of renal disease or hypertension.

**Patient 2**

A 12-year-old girl was admitted to the hospital with a history of fatigue, abdominal pain, vomiting and dark urine. On admission, she had arthralgia, oedema and a palpable purpuric rash on the lower extremities. Past medical history revealed that a tonsillectomy had been performed at the age of 9 years, and Graves’ disease was diagnosed at the age of 10 years. She was commenced on propylthiouracil and subsequently remained euthyroid state on a stable dose of propylthiouracil. She was hypertensive, and laboratory investigations were: ESR 59 mm/h, BUN 74 mg/dl, serum creatinine 4.8, serum albumin 3.2 g/dl, cholesterol 177 mg/dl, serum IgA 291 mg/dl, creatinine clearance 13 ml/min/1.73 m², antinuclear antibody negative and anti-ds DNA antibody negative. Urinalysis showed many RBCs/HPF and proteinuria 30 mg/dl. She was diagnosed as having acute nephritic type of HSP nephritis, and treated with methylprednisolone pulse therapy followed by prednisolone, calcium-channel blocker (Madipine) and propylthiouracil. She achieved complete remission of HSP nephritis including resolution of haematuria and proteinuria at 1.4 years of follow-up. About 3 years after the development of HSP, the patient is still in complete remission without recurrence of vasculitis.

Our cases suggest that HSP may develop in a patient with Graves’ disease receiving the usual dose of propylthiouracil or no treatment. Therefore, it is likely that not only propylthiouracil use but also Graves’ disease itself may be a triggering factor for the development of HSP in susceptible individuals. However, a large prospective study may further elucidate the clear relationship between HSP and Graves’ disease or propylthiouracil use.

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**Cloudy dialysate due to lercanidipine**

Sir,

Cloudy dialysate in a patient on continuous ambulatory peritoneal dialysis (CAPD) results from a diverse group of aetiologies. Most commonly, it reflects an increased number of leucocytes secondary to bacterial peritonitis. However, an occasional patient presents with leucocyte-negative, cloudy dialysate. Dihydropyridine type calcium channel blockers would cause turbid peritoneal dialysate [1]. In our study, we investigated whether patients on CAPD having lercanidipine (dihydropyridine type calcium channel blocker) treatment had turbidity of peritoneal dialysate. We evaluated 23 patients with end stage renal disease on CAPD, 14 female and nine male, with the mean age of 45.3 ± 17.6 years. The mean time on CAPD was 15.9 ± 11.6 months. The patients who enrolled in this study were given lercanidipine 5 mg/day. Peritoneal dialysate was evaluated in terms of turbidity of dialysate on the first day. Our diagnostic criteria for drug-induced turbidity of dialysate as its development within the first day after the treatment, absence of clinical symptoms of peritoneal inflammation and the peritoneal dialysate containing normal...
leucocyte counts. In our patients, three out of 23 (13.04%) CAPD patients given lercanidipine developed non-infective turbid peritoneal dialysis.

Differential diagnosis of non-infectious cloudy peritoneal dialysis includes cellular causes (i.e. leucocyte, eosinophils, red cells and malign cells) and non-cellular causes (i.e. triglyceride and drugs) [2]. Yoshimoto et al. [1,3] reported that benidipine, manidipine, nisoldipine and nilidipine caused cloudy dialysate on CAPD patients. In their study, it was revealed that the fluid contained an elevated triglyceride concentration. As far as we know this is the first report in the literature that lercanidipine causes cloudy dialysate in the CAPD patients.

Conflict of interest statement. None declared.

Effect of creatinine assay standardization on the performance of Cockcroft–Gault and MDRD formula in predicting GFR

Sir,

The recent article of van Biesen et al. [1] illustrates the importance of standardization of serum creatinine assays when using formulas to estimate glomerular filtration rate (GFR). We provide further proof of the importance of standardization of creatinine. We previously compared the performance of the modification of diet in renal disease (MDRD) formula and the Cockcroft–Gault (CG) formula in healthy persons and normo-albuminuric diabetic patients [2]. As reported in this Journal, we concluded that the MDRD equation was less accurate than CG formula in predicting GFR (measured by inulin clearance). Our data were based upon a creatinine assay, based on the Jaffé kinetic reaction performed on a Hitachi 747 auto-analyser.

Meanwhile it has been shown that correct use of the MDRD equation necessitates calibration of the creatinine assay against the assay used by the Cleveland Clinic Laboratory [3].

The Cleveland Clinic Laboratory originally used a Beckman modified kinetic rate Jaffé reaction. Recently, samples of the MDRD study were re-analysed and compared with a creatinine assay using isotope dilution mass spectrometry (IDMS) as the gold standard [4]. IDMS results were highly correlated to enzymatic creatinine, measured by Roche technology. Therefore, this enzymatic assay should preferably be used in the MDRD equations.

We recently introduced the Roche enzymatic method in our Hospital. Comparison of the enzymatic method with our former Jaffé method according to an approved evaluation protocol [National Committee for Clinical Laboratory Standards, Evaluation Protocol number 9 (EP-9)] revealed: $y$ (enzymatic creatinine) $= 1.266 \times (\text{Jaffé creatinine}) - 29$. Based on this formula, we recalculated our creatinine data and applied the new formula [4]:

$$170 \times \left( \frac{\text{[enzymatic creatinine (mg/dl)]}}{0.95} \right)^{-0.999} \times (\text{age})^{0.176} \times \left( \frac{\text{Serum\_albumin\_nitrogen (mg/dl)}}{\text{[serum protein (g/dl)]}} \right)^{0.170} \times (\text{[alcohol (g/dl)]})^{10.318}$$

($\times 0.762$ if female; $\times 1.180$ if black).

Results are given in Table 1. It is apparent that the use of standardized creatinine assay has a major influence on the reported differences between the formula-derived GFR and the true GFR. In fact, in contrast to our earlier finding, our recalculated data indicate that the MDRD formula is probably more accurate than the CG formula, also in persons with normal GFR. Reporting of MDRD-GFR using creatinine assays that are not calibrated using a gold standard should be discouraged.

Conflict of interest statement. None declared.

Table 1. Measured and predicted GFR in healthy subjects and diabetes patients without [2] and with standardization of creatinine assay

<table>
<thead>
<tr>
<th></th>
<th>GFR (inulin clearance)</th>
<th>Former Jaffé method</th>
<th>MDRD</th>
<th>ΔMDRD - GFR</th>
<th>New enzymatic method</th>
<th>MDRD</th>
<th>ΔMDRD - GFR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CG</td>
<td>ΔCG - GFR</td>
<td></td>
<td></td>
<td>CG</td>
<td>ΔCG - GFR</td>
<td></td>
</tr>
<tr>
<td>Healthy subjects</td>
<td>107 ± 11</td>
<td>112 ± 17</td>
<td>5.0 ± 18.6</td>
<td>103 ± 13</td>
<td>−3.3 ± 16</td>
<td>128 ± 23</td>
<td>21.2 ± 23.5</td>
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<td>(n = 46)</td>
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<tr>
<td>Diabetic patients</td>
<td>122 ± 18</td>
<td>119 ± 16</td>
<td>−2.8 ± 19.7</td>
<td>108 ± 18</td>
<td>−13.9 ± 23.7</td>
<td>141 ± 24</td>
<td>18.7 ± 23.2</td>
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<td>(n = 46)</td>
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Values are expressed as means ± SD; GFR, glomerular filtration rate (ml/min/1.73 m²); CG, prediction of GFR with Cockcroft–Gault formula (ml/min/1.73 m²); MDRD, prediction of GFR with the MDRD formula (ml/min/1.73 m²).