generalized cutaneous rash and oedema. Supine blood pressure was 110/70 mmHg and abdominal palpation revealed that the size of the uterus corresponded to gestational week. Laboratory studies reported haemoglobin 8.9 g/dl, haematocrit 26%, creatinine 3.7 mg/dl, urea 117 mg/dl, white cell count 10 000 µl, with eosinophils 200 µl and platelet count 190 000 µl. Serum glucose 90 mg/dl, creatinine 3.7 mg/dl, urea 117 mg/dl, total proteins 5.6 g/l, bilirubin 3.2 mg/dl, AST 24 IU/l, ALT 9 IU/l, LDH 414 IU/l, CPK 11 IU/l and platelet count 190 000 µl. Serum glucose 90 mg/dl, creatinine 3.7 mg/dl, urea 117 mg/dl, total proteins 5.6 g/l, bilirubin 3.2 mg/dl, AST 24 IU/l, ALT 9 IU/l, LDH 414 IU/l, CPK 11 IU/l and total alkaline phosphatase 311 IU/l. Antinuclear antibodies, c-ANCA, p-ANCA and anti-MBG were negative. Tests for serum antibodies to hepatitis C virus, hepatitis B surface antigen and anti-HIV were also negative. Serum levels of complement C3 and C4, serum immunoglobulins and TSH were normal. A renal ultrasound revealed normal sized and symmetric kidneys. Blood smear did not reveal schizocytes or eosinophilia. Urinary protein excretion was 0.8 g/24 h and the sediment revealed three red blood cells and leucocyturia. Obstetric ultrasound scan showed oligohydramnios with an amniotic fluid index of 2 (normal value 5–24.0 cm [1]). With parenteral fluids, a renal ultrasound revealed a normal sized and symmetrical kidney. Blood smear did not reveal schizocytes or eosinophilia. Urinary protein excretion was 0.8 g/24 h and the sediment revealed three red blood cells and leucocyturia. Obstetric ultrasound scan showed oligohydramnios with an amniotic fluid index of 2 (normal value 5–24.0 cm [1]). With parenteral fluids, a renal ultrasound revealed a normal sized and symmetrical kidney. Blood smear did not reveal schizocytes or eosinophilia. Urinary protein excretion was 0.8 g/24 h and the sediment revealed three red blood cells and leucocyturia.

We describe a case of acute renal failure and oligohydramnios induced by magnesium dypirone (metamizol, Nolotil®). Magnesium dypirone is a prostaglandin synthetase inhibitor widely used as analgesic or anti-pyretic drug. It is advised to be used with caution in pregnancy. Although other prostaglandin synthetase inhibitors have been associated with oligohydramnios [2–5], only in one case report has magnesium dypirone been involved where its use did not induce acute renal failure [6]. The mechanism of oligohydramnios with these drugs is unknown. It could be related to fetal oliguria due to the increase of arginine vasopressin in the fetal collecting duct induced by prostaglandin inhibition, as has been shown in animal models [7]. In our patient, the dose of self-administered magnesium dypirone was high, and probably part of the drug entered the fetal circulation transplacentally.

Magnesium dypirone can induce two different forms of acute renal failure: (i) reversible renal ischaemia secondary to inhibition of prostaglandin synthesis, appearing 3–7 days after initiation of therapy when drug levels inhibit prostaglandin synthesis [8]; and (ii) acute tubulointerstitial nephritis [9]. In our patient, the diagnosis of acute tubulointerstitial nephritis was made according to clinical and biochemical data as well as after a detailed history record, but both forms of renal disease associated with magnesium dypirone were probably present. Moreover, withdrawal of dypirone was associated with a dramatic improvement of renal function and the oligohydramnios, as has been described previously [6].

We conclude that magnesium dypirone may induce reversible acute renal failure and oligohydramnios in pregnancy. It should be used with caution, with monitoring of renal function and amniotic fluid volume.

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Striking increase in circulating hepatocyte growth factor during enoxaparin-anticoagulated haemodialysis

Sir,

Hepatocyte growth factor (HGF) is a multipotent cytokine of growing importance in tissue development, apoptosis, regeneration and repair of injuries. In chronic haemodialysis (HD) patients, serum HGF levels are increased, directly related to the extent of arteriosclerosis and chronic inflammation, and the prevalence of cardiovascular disease and viral hepatitis, and may stimulate erythropoiesis [1,2]. They also independently predict mortality in dialysis patients [2]. Increased HGF may thus be viewed as a marker of co-morbidity and poor survival, and at the same time as an indicator of the activated body repair in this population.

Recently, we reported in this journal that the use of unfractionated heparin (UFH) vs low molecular weight (LMW) enoxaparin during intermittent HD could be directly predictive of increased serum HGF levels [1]. We also found a direct association between pre-dialysis levels of the cytokine and a dose of UFH. Therefore, we hypothesized that heparin could be a specific stimulus for the HGF release in maintenance HD patients [1]. In the present study, we followed serum HGF levels during dialysis [by enzyme-linked immunosorbent assay (ELISA) from R&D Systems, Inc., Minneapolis MN] in 14 patients anticoagulated with enoxaparin (Clexane, Bellon Rhône-Poulenc Rorer,
The heparin was injected into the arterial line as a bolus of 40 (20–60) mg (0.70 ± 0.22 mg/kg) at the onset of HD, following the initial rinse of the circuit with 1000 ml of isotonic saline containing 2.0 IU/ml of UFH. The anticoagulation regimen had been employed effectively for at least 2 months prior to the study.

Serum HGF levels were 1.82 (1.20–5.70) ng/ml predialysis, 31.0 (15.4–83.7) ng/ml after 10 min, and 8.97 ± 3.56 ng/ml after 180 min from the start of HD and after enoxaparin injection (Friedman’s ANOVA /C31 2 for the change = 28.0, P < 0.0001). As shown in Figure 1A, HGF strikingly increased by a mean of 1596 ± 650% after 10 min of HD compared with baseline (Wilcoxon’s P = 0.001). After 180 min, it was higher by 349 ± 190% vs predialysis, and lower vs the 10 min level (both P = 0.001). The 10 min percentage increase in HGF (Spearman’s ρ = 0.594, P = 0.025, Figure 1B) but not that at 180 min (ρ = 0.268, P = 0.353) significantly correlated with the dose of enoxaparin.

This study shows an abrupt and sustained increase in serum HGF during enoxaparin-anticoagulated HD. To our knowledge, the magnitude of the early rise in circulating HGF cannot be compared with any other moiety studied in this clinical setting so far. Similar behaviour of HGF was evidenced previously in non-dialysis subjects receiving i.v. heparin [3,4]. After 5 min following the injection of 3000 IU of UFH, serum HGF increased by as much as 2500% [3]. In another study, the peak increment in circulating HGF in response to administration of the LMW dalteparin at a mean dose of 0.36 mg/kg amounted to ~800% and was noted after 10 min [4]. The HGF increase lasted up to 4 h post-injection [4]. The reason for a rapid increase in circulating HGF due to heparin may be the displacement of the cytokine from heparan sulfate proteoglycans [3–5]. The prolonged increment in the growth factor may be explained by a lower clearance of HGF–heparin complexes and an enhanced production of the cytokine by heparin [3–5].

This study shows the first time that the early increase in serum HGF directly depends on the dose of enoxaparin used for blood anticoagulation during intermittent HD procedures. It implies that heparin may be a modulator of the biological effects of HGF in chronic HD patients, especially as the cytokine also acts as a classic hormone exerting its distant effects in a concentration-dependent manner. The consequences of such marked and prolonged elevations in serum HGF due to repeated heparin administration may be important in HD patients. They deserve further detailed evaluation because HGF augments organ repair but may also propagate cancer metastases due to its angiogenic effects.

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2. Malatino LS, Mallamaci M, Benedetto FA et al. Hepatocyte growth factor predicts survival and relates to inflammation and


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### Tenckhoff catheters: the pull technique

**Sir,**

We are writing as a follow up to our previously published article [1] describing the ‘pull’ technique for removing Tenckhoff peritoneal dialysis catheters as a day case procedure, not requiring a general anaesthetic. We have been routinely using this technique in the Oxford Transplant Centre successfully for the last 3 years and now perform it exclusively on the ward. We would like to provide a warning regarding a catheter that snapped whilst being pulled out, by not following the described technique. However, it did remain attached to the inner cuff anchored to the abdominal wall and was removed safely under a local anaesthetic, as had been predicted theoretically in the original paper.

A 67-year-old male, with end-stage renal failure on ambulatory peritoneal dialysis with chronic obstructive pulmonary disease and a history of myocardial infarction in the last 3 months, had the catheter ‘pulled’ on the ward. The outer cuff was surrounded by granulation tissue and as described in the original paper, was dissected out under a local anaesthetic to be removed with the catheter. The catheter was grasped by a Spencer Wells forceps and during the pull it snapped at the point of clamping. The patient subsequently underwent a wound exploration under local anaesthesia and as predicted the catheter was fixed to the anterior abdominal wall anchored by the inner cuff. The cuff along with the catheter was removed successfully and the patient discharged home the same day.

This case illustrates the importance of a steady pull technique applied by hand only. Grasping the catheter by an instrument has the definite risk of fracturing the catheter. Pulling by hand spreads the load more evenly and provides feed back as to the degree of traction being applied. Continued use of the pull technique in our and other units, which have taken up the technique since the original publication, is supported by its low complication rate, economic advantages and patient acceptability.

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