cases (1, 3, and 4) were the highest values of 1,25-$(OH)_2D$ (during the summer months) over 200 pmol/l (80 pg/ml). The fluctuations in the other subjects were within the above-mentioned normal range of 50-180 pmol/l. The range of 1,25-$(OH)_2D$ levels in normal subjects as indicated by Chesney *et al*,[5] in a paper to which Dr Tjellesen and others refer, is even larger—that is, 26-266 pmol/l. Therefore we do not agree that our serum levels of 1,25-$(OH)_2D$ would on average be double those found by others.

On the question of the reliability of the determination of metabolites of vitamin D in human serum we would like to refer also to an interlaboratory study which was undertaken in the Netherlands, in which we participated and the results of which were presented at the 16th European Symposium on Calcified Tissue.[6] With regard to the explanation put forward by Dr Tjellesen and others to account for the discrepancy between our data and theirs, we previously excluded a possible interference of high concentrations of 25-OHD and 24,25-$(OH)_2D$ with the assay of 1,25-$(OH)_2D$, as indicated in table II of our article. As to 25,26-$(OH)_2D$ we did not add this substance to a standard serum for evaluation of possible interference with the 1,25-$(OH)_2D$ assay, but we found (like others[7]) that with high-pressure liquid chromatography using a Radial Pack B Column eluted with hexane/isopropranolol (90/10, v/v) at a flowrate of 1·8 ml/min and UV detection at 254 nm an excellent separation of all the vitamin D metabolites that have been mentioned is obtained, including 25,26-$(OH)_2D$, which comes off the column in the 8-10-minute fractions while 1,25-$(OH)_2D$ appears after 13-15 minutes. So in our hands no interference of 25,26-$(OH)_2D$ with the radioimmunoassay of 1,25-$(OH)_2D$ is to be expected.

A satisfying explanation for the obvious discrepancy between the results of the longitudinal study of Dr Tjellesen and colleagues and ours is at this stage hard to give. The influence, however, of varying intakes of calcium and vitamin D, of sex, and of age have to be further explored.

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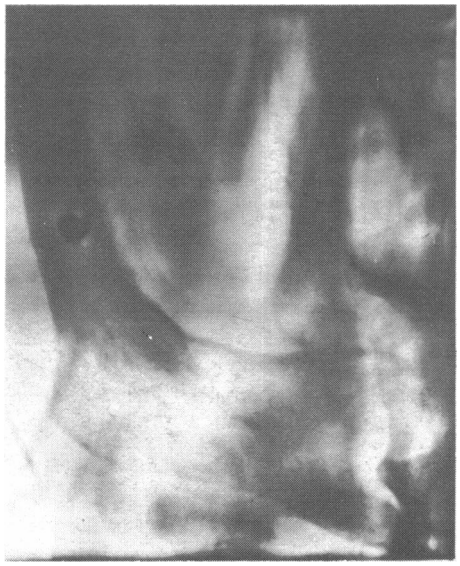
Shrapnel presenting with symptoms 62 years after wounding



Radiographie montrant le shrapnel dans la mandibule.

MONSIEUR,—En lisant la *Gazette Médicale* du 6 novembre, j'ai été très intéressé par une sélection du *British Medical Journal* et en particulier par l'article intitulé "Présence d'un éclat de shrapnel révélé par des symptomes 62 ans après blessure" de Dr John Knox et Mr Alan Wilkinson (18 juillet, p 193); car le 26 octobre j'ai opéré un patient né le 30 mai 1895 qui présentait un éclat de shrapnel dans la mandibule depuis au moins 1917. Ce morceau était long de 8 mm sur 5 environ; jamais il n'avait fait l'object d'une gène quelconque et la première manifestation remonte au 15 octobre où notre vieux "poilu" s'est retrouvé avec une grosse fluxion.

Le patient a consulté un otorhinolaryngologiste, et celui-ci ouvrit la collection et vida l'abcès; l'homme me fut envoyé pour rechercher l'origine de cette cellulite suppurée. La radiographie (figure) montrait un corps étranger; après un interrogatoire nous apprenions que cet homme avait été blessé trois fois pendant la guerre de 1914-8 et que cette blessure était passée inaperçue. La dernière fois qu'il fut blessé, et par shrapnel, remontait en 1917. Donc nous pouvons par cette observation affirmer que nous détenons le plus long intervalle de temps décrit pour un corps étranger entre la blessure initiale et la survenue de symptomes—c'est à dire, 64 ans.

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Lithium treatment and preoperative fluid deprivation

SIR,—Professor M Schou (7 November, p 1253) recommends that patients on lithium treatment who are admitted to hospital for surgery should receive intravenous fluids the night before operation. This is in order to avert lithium intoxication, which may develop if there is fluid deprivation. We would like to draw your readers' attention to the additional possibility of interaction between lithium and anaesthetic agents.

In one such reported case,[1] a patient anaesthetised with sodium methohexitone and suxamethonium bromide for electric convulsion therapy could not be roused for two hours, although spontaneous respiration had returned within the expected time. The serum lithium concentration was found to be high (3·4 mmol/l (4·9 mg/100 ml)). A week later, when her serum lithium concentration was 0·5 mmol/l (0·7 mg/100 ml) this patient recovered normally from anaesthesia, suggesting that the abnormally raised serum lithium concentration was responsible for the earlier complication. In another case,[2] a surgical patient receiving lithium carbonate therapy was reported to have prolonged neuromuscular blockade, which was attributed to pancuronium bromide, although this patient had also received sodium thiamylal, succinylcholine, nitrous oxide, and fentanyl. The serum lithium concentration was only 0·9 mmol/l (1·3 mg/100 ml). A further report[3] of interaction between lithium and a neuromuscular blocking agent concerned a patient taking lithium carbonate who underwent caesarean section, for which anaesthesia was induced with pancuronium bromide, thiopental, and succinylcholine. Postoperatively the patient remained apnoeic for four hours. The possibility of lithium potentiation of succinylcholine was further evaluated and confirmed in experiments in dogs.

We therefore consider it preferable to discontinue lithium 24-48 hours before an operation and to recommence it only when the patient is safely over the immediate postoperative period and back to normal fluid balance. For patients receiving lithium and electric convulsion therapy concurrently, it may not be practicable to interrupt lithium therapy repeatedly. In such cases, in addition to maintaining fluid balance as emphasised by Professor Schou, the serum lithium concentration should be checked beforehand and the anaesthetist should be alert to the possibility of delayed recovery. If lithium is withheld during surgical or other procedures this should not be for longer than necessary, as relapse may occur within 7-10 days of discontinuation of lithium therapy even in patients whose psychiatric disorder has been well controlled for a number of years.

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Intravenous amiodarone in atrial fibrillation complicating myocardial infarction

SIR,—Atrial fibrillation as an early complication of myocardial infarction may be life threatening and thus requires immediate control.

Intravenous amiodarone is effective soon after administration, as pointed out by Dr Roger Blandford (2 January, p 16). One point worth bearing in mind, however, is that the half life of this drug is 28 days, and therefore if long-term treatment of an unstable tachyarrhythmia is contemplated the regimen should commence with 10 days of intravenous administration, started at the same time as oral therapy. This allows plasma levels to attain and remain within a therapeutic range. I stress this point because in Dr Blandford's case 2 intravenous therapy was given for only 24 hours, tablets being administered thereafter; this may explain, in part, the subsequent runs of atrial fibrillation experienced by the patient.

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Hyperkalaemic cardiac arrhythmia caused by potassium citrate mixture

SIR,—With reference to the short case report "Hyperkalaemic cardiac arrhythmia caused by potassium citrate mixture" by Drs J J Browning and K S Channer (21 November, p 1366), we would like to report a similar case to

emphasise the potential danger of this medication, especially in the elderly.

A 77-year-old man presented with alteration of bowel habit, rectal bleeding, and tenesmus. He was found to have a rectal carcinoma invading the prostate and underwent an abdominoperineal resection of the tumour. He developed urinary retention postoperatively and required intermittent catheterisation. After withdrawal of the catheter he was given 10 ml potassium citrate *BP* three times a day and co-trimoxazole for a urinary tract infection. On admission his serum creatinine was 161 μmol/l (1·8 mg/100 ml), blood urea nitrogen 9·7 mmol/l (13·6 mg/100 ml), and serum potassium 3·7 mmol(mEq)/l. One week later he became unwell with excessive shaking of his limbs and with a coarse hand tremor. His serum potassium level was found to be 7·0 mmol/l; an electrocardiogram showed elevated T-waves but was otherwise normal. He was on no other medications. His potassium citrate was discontinued and his symptoms stopped. The serum potassium level fell to 4·9 mmol/l over the ensuing three days.

This case illustrates that potassium citrate mixture is not a harmless preparation even when given in acceptable dosage to patients with normal renal function in a hospital setting. It should be emphasised that the medication contains 9·25 mmol of potassium ion per gram and that specific warnings are not given about the dangers of hyperkalaemia in either *Martindale's Extra Pharmacopoeia*[1] or in the *United States Dispensary*.[2] We feel that care should be exercised when this mixture is prescribed, especially in the elderly and in those patients with impaired renal function.

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Interaction of indomethacin and warfarin

SIR,—Dr Alex Paton, in his answer to the question concerning the use of antirheumatic drugs in patients receiving long-term anticoagulant therapy (21 November, p 1379), states that indomethacin potentiates the effect of warfarin.

There have, in fact, been a number of studies of concomitant administration of indomethacin and anticoagulants of the coumarin group showing no such interaction.[1-3] Vessell *et al*[3] carried out two double-blind, placebo-controlled studies in normal volunteers. In the first of these the prothrombin time was stabilised at one-and-a-half to two-and-a-half times normal on a constant dose of warfarin, and then regular indomethacin or placebo was introduced with no subsequent change in prothrombin time. In the second study they demonstrated no difference in prothrombin time or warfarin plasma half-life between an indomethacin group and a control group when a loading dose of warfarin was given. In their data sheet for indomethacin Thomas Morson Pharmaceuticals states that "controlled clinical studies have shown that Indocid did not influence the hypoprothrombinaemia produced by anticoagulants in patients and normal subjects." They do, however, recommend that the prothrombin time is observed closely when indomethacin is given to a patient receiving oral anticoagulants. Apart from individual interaction with warfarin there is, of course, always a danger that patients on non-steroidal anti-inflammatory drugs may develop gastrointestinal bleeding, and this is a further point to bear in mind before undertaking anticoagulation.

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Perforated duodenal ulcer after perioperative steroid treatment

SIR,—I refer to the recent article "Perforated duodenal ulcer after perioperative steroid treatment" by Mr J L Beynon and others (12 December, p 1591). The use of steroids in large doses has been routine in transplant surgery for many years, though there has been a recent tendency to lower doses. Patients waiting for transplant are screened preoperatively for evidence of peptic ulceration or hyperacidity, and appropriate therapy is started. All patients prophylactically have cimetidine administered to them. Since we started the use of cimetidine about two years ago, the incidence of overt peptic ulcer symptoms, and their complications, has been negligible. Initially we used cimetidine in a dosage of 200 mg three times a day and 400 mg at night, but we now tend to use 200 mg three times a day in the presence of good renal function. The patients who cannot take oral medication immediately following operation have parenteral cimetidine.

There is little doubt that patients undergoing any form of surgery are under acute stress and this, coupled with the ingestion of steroids, must make peptic ulceration almost inevitable. The use of enteric-coated tablets has failed to reduce the incidence of this problem, and we are convinced that cimetidine needs to be started preoperatively and continued until the steroid dosage is reduced.

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Assessment of iron stores in inflammation by assay of serum ferritin concentrations

SIR,—The paper by Dr D R Blake and others (31 October, p 1147) seeks to deal with the interpretation of serum ferritin concentrations in patients with inflammatory diseases. The reason for measuring serum ferritin is to single out those patients who would benefit from iron therapy by assessing the level of their iron stores. Excessive ferritin release from damaged tissues, particularly the liver, can make interpretation difficult but this is not usually a problem in inflammatory disease.[1]

The abstract of the paper by Dr Blake and his colleagues suggests that serum ferritin concentration may rise with storage iron levels but may also be directly influenced by the inflammatory process. This is at variance with the data and conclusions expressed in the main body of the paper. The changes in haemoglobin concentration which took place in the patients are given in only one case—a 22-year-old woman with classical rheumatoid arthritis. Her disease remitted spontaneously over the course of six months and during that time her haemoglobin concentration rose from 8 to 13 g/dl. This change alone would be expected to account for a decrease of the order of 100 μg/l serum ferritin,[2] and indeed the serum ferritin concentration fell from 55 μg/l to an unstated figure less than 15 μg/l. When she was anaemic she had normal levels of storage iron but when the disease remitted and the marrow again resumed its normal activity the demand for iron exhausted the stores. There is no evidence that the serum ferritin concentration did not simply reflect the level of iron stores at each given instant. Whether or not the level of storage iron indicated by the serum ferritin concentration is adequate for future demands is a separate issue.

In addition, this brief paper makes a number of remarkable statements. We are told that the haemoglobin concentration and "red cell variables" are a reliable index of iron stores in normal subjects. Iron stores in normal subjects range from 0 to over 2 g and are not known to be correlated with either haemoglobin concentration, mean cell volume, or any other red cell variable. The authors also state that the word ferritin, as in "serum ferritin," is a misnomer. This is not so. The term apoferritin is used specifically to describe the protein in its iron-free state. Serum ferritin may contain relatively little iron but it does contain detectable quantities[1] and is properly called ferritin. The fact that all serum ferritin assays are based on the detection of the ferritin protein rather than its iron does not affect its proper nomenclature.

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**We sent this letter to Dr Blake, who replies below.—ED, *BMJ*.

SIR,—The three points raised by Dr D P Bentley and others in their letter are valid, clinically important, and discussed in our paper.

The clinical questions we sought to answer were simple. What is an appropriate lower limit of normality for a serum ferritin estimation in a rheumatoid population and at what level of serum ferritin should we consider investigating the cause of the patient's iron deficiency? In a healthy population serum ferritin under 15 μg/l indicates low iron stores. Dr Worwood (their ref 1), referring to patients with infection, inflammation, and chronic disease, has stated that "a ferritin concentration in excess of 50 μg/l should rule out iron deficiency in such patients but further studies are needed to confirm the statement." Our study would confirm the statement as the figure derived from our data is 55 μg/l.