to three days is not the optimal time for scanning as bone healing is only just beginning and soft tissue hyperaemia may interfere with the image. A more reliable delay after trauma is seven to 10 days.[2] Isotope scans are indeed less expensive and more sensitive than conventional radiographs.

Our aim is to give medical staff, especially junior doctors, confidence to treat this condition by adequate soft tissue splintage when they do not have access to isotope departments.

M R A YOUNG

Ulster Hospital,
Dundonald,
Belfast BT16 0RH

1 Young MRA, Lowry JH, Laird JD, Ferguson WR. ^{99m}Tc-MDP bone scanning of injuries of the carpal scaphoid. *Injury* 1988;19:14-7.
2 Fordman EW, Ramachandran PC. Radionuclide imaging of osseous trauma. *Semin Nucl Med* 1974;4:411-28.

Drug points

Addendum to guidelines for reporting adverse drug reactions

Drs LOUISE GLASSNER COHEN and JOHN P ROVERS (Department of Pharmacy Services, Brigham and Women's Hospital, Boston, Massachusetts) write: Accurate reporting of adverse drug reactions requires that they be adequately identified and reported in complete detail. Several algorithms have been published as aids to this.[1,2] Venulet *et al* evaluated 5737 such reports and determined that only 19% included complete information.[3] Minimal guidelines for reports have been published,[4] but we would include one additional requirement. Both the outpatient and inpatient records should be checked when preparing reports of adverse drug reactions.

A patient with sepsis secondary to AIDS had had previous adverse drug reactions. After receiving treatment with a new antimicrobial agent he noticed a rash and was readmitted to hospital with a condition resembling toxic epidermal necrolysis, to which he eventually succumbed. His illness was consistent with other reports of drug induced toxic epidermal necrolysis. Literature searches and information from the manufacturer showed no reports of reactions of this type with this drug. The inpatient chart was used to prepare a report for publication. As a final check the outpatient chart was obtained, and, unlike the inpatient chart, this record indicated that he had previously undergone a skin biopsy, whose result had been suggestive of erythema multiforme. We re-evaluated the cause and effect relation of this adverse drug reaction and did not submit it for publication.

Like most adverse drug reaction reports ours concerned a patient in hospital.[5] Presumably many such reports relied solely on the inpatient record. In large teaching hospitals the patient may not be known to the team, and the history obtained from an abbreviated summary may be incomplete. Therefore reports prepared from only inpatient documents may lack relevant information.

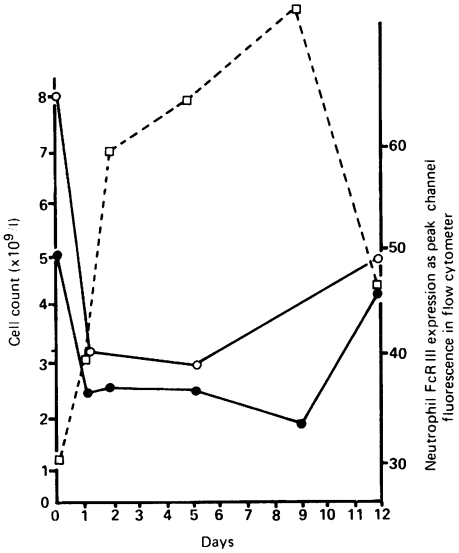
New drugs are often held responsible for otherwise unexplained clinical situations. Using only inpatient documents the published algorithms classify our case as a possible adverse drug reaction.[1,2] Consequently, even objectively identified reports which include the requisite information[4] may be incorrect. We concur with previously proposed requirements and additionally recommend that the patient's outpatient record should be consulted before the clinician concludes that an adverse drug reaction has occurred.

1 Kramer MS, Leventhal JM, Hutchinson TA, Feinstein AR. An algorithm for the operational assessment of adverse drug reactions. 1. Background, description and instructions for use. *JAMA* 1979;242:623-32.
2 Karch FE, Lasagna L. Toward the operational identification of adverse drug reactions. *Clin Pharmacol Ther* 1977;21:247-54.
3 Venulet J, Blattner R, Von Bulow J, Berneker GC. How good are articles on adverse drug reactions? *Br Med J* 1982;284:252-4.
4 Venulet J. Informativity of adverse drug reactions data in medical publications. *Drug Information Journal* 1985;19:357-65.
5 Karch FE, Lasagna L. Adverse drug reactions. A critical review. *JAMA* 1975;234:1236-41.

Neutropenia following intravenous immunoglobulin

Drs P A VEYS, M G MACEY, C M OWENS, and A C NEWLAND (Department of Haematology, The London Hospital, London E1 1BB) write: Drs R V Majer and P J Green reported the occurrence of temporary neutropenia in two patients receiving high dose intravenous immunoglobulin (30 April, p 1262) and concluded that this was a side effect that had not been reported previously. This is, however, a frequently observed although not widely reported effect.

We studied the neutrophil counts in 48 patients with idiopathic thrombocytopenic purpura who received intravenous immunoglobulin. There was a significant decrease ($p<0{\cdot}001$) from the count before treatment (mean $6{\cdot}0\times10^9$/l) to that on days three and four (mean $3{\cdot}0\times10^9$/l). There was a correlation between the decrease in neutrophil count and the increase in platelet count ($p<0{\cdot}01$). The neutropenic period was brief, and counts returned to normal by day seven.



Platelet count (□), neutrophil count (●), and FcR III expression (○) after intravenous immunoglobulin given on days 0 and 1 to a patient with longstanding idiopathic thrombocytopenic purpura.

We studied six patients in detail. Five developed a significant but brief reduction in absolute neutrophil count during the infusion of immunoglobulin. Using flow cytometric studies of patient and donor leucocytes we confirmed specific binding of intravenous immunoglobulin to the neutrophil surface in vivo and in vitro.[1] Ultracentrifugation of the immunoglobulin to remove IgG aggregates before testing reduced the amount of IgG binding in vitro. The expression of neutrophil FcR III, a receptor which has a low affinity for monomeric IgG,[2] varied in a reciprocal fashion to the amount of bound IgG, suggesting that the small amount of IgG aggregates remaining in the intravenous immunoglobulin is responsible for the specific binding of IgG to the FcR III.

Clarkson *et al* reported a temporary platelet increment accompanied by a profound neutropenia in a patient with refractory idiopathic thrombocytopenic purpura after a monoclonal antibody to the FcR III was given.[3] This also suggests that the neutropenia might be mediated through this receptor.

In one patient with longstanding idiopathic thrombocytopenic purpura who had a temporary platelet response to intravenous immunoglobulin there was a reduction in the absolute neutrophil count from $5{\cdot}1$ to $2{\cdot}2\times10^9$/l after the first two infusions. The count remained low for about 10 days (figure). The neutrophil FcR III expression was reduced in the same manner, returning to normal only with the cessation of the platelet response.

We suggest that the reduction in neutrophil count after intravenous immunoglobulin is not just a side effect. Indeed, a reduction in neutrophil phagocytic capability and mononuclear phagocyte blockade by neutrophils coated with IgG might contribute to the platelet increment in some patients with idiopathic thrombocytopenic purpura. None of our 54 patients suffered any infective complications during the neutropenic episodes, and we think that, while fairly common, the neutropenia after intravenous immunoglobulin is of little clinical concern.

1 Minchinton RM, McGrath K. Binding and antibody blocking effects of intravenous IgG preparation on peripheral blood cells. *Clin Lab Haematol* 1987;9:49-58.
2 Anderson CL, Looney RJ. Human leucocyte IgG Fc receptors. *Immunology Today* 1986;7:264-6.
3 Clarkson SB, Bussel JB, Kimberly RP, *et al*. Treatment of refractory immune thrombocytopenic purpura with an anti-Fc gamma-receptor antibody. *N Engl J Med* 1986;314:1236-9.

Henoch-Schönlein purpura after influenza vaccination

Drs UDAY PATEL, JOHN R BRADLEY, and DAVID V HAMILTON (Department of Renal Medicine, West Norwich Hospital, Norwich NR2 3TU) write: Vaccination against influenza is recommended for patients at increased risk of lower respiratory tract infections. The safety of the vaccine is well established, the usual side effects being a mild serum sickness with fever, malaise, and myalgia.[1]

A 77 year old man developed malaise, diarrhoea, and arthralgia 10 days after receiving 0·5 ml of inactivated influenza vaccine surface antigen (Influvac). On admission his blood pressure was 95/60 mm Hg, and ankle and sacral oedema were present. His abdomen was distended, and bowel sounds were reduced. A purpuric rash was present over his buttocks and legs, and the knee and ankle joints were tender.

The haemoglobin concentration was 147 g/l, the white cell count $13{\cdot}6\times10^9$/l (92% neutrophils), the platelet count 407×10^9/l, and the erythrocyte sedimentation rate 30 mm in the first hour. Plasma urea and creatinine concentrations were raised at 21·1 mmol/l and 204 μmol/l respectively, and the albumin concentration was reduced at 30 g/l. A midstream urine specimen contained 50×10^9 red cells/l and showed pronounced proteinuria.

After admission the patient developed haematemesis and melaena. Renal function deteriorated further, and percutaneous renal biopsy was performed. All of the glomeruli were abnormal with an increase in mesangial cells and matrix and patchy deposition of IgA, IgM, and C2 in relation to glomerular capillaries. The tubules and interstitial tissue were unremarkable. Oral prednisolone 60 mg daily was started. Renal function improved and the rash, arthralgia, and gastrointestinal disturbance resolved. Four week later the plasma creatinine concentration was 137 μmol/l, and there was no blood or protein on analysis of urine.

Immunological investigations were performed on serum collected 10 days after admission. No antibodies to influenza A or B, cytomegalovirus, *Mycoplasma pneumoniae*, chlamydia, or Q fever were detectable by complement fixation tests, but antibodies to Influvac (IgG 1/12800, IgA 1/400) were detected by enzyme linked immunosorbent assay (ELISA). No antibodies to ovalbumin were detected.

Henoch-Schönlein purpura is commonly preceded by symptoms of an upper respiratory tract infection, and relapses may be related to further infections. Pre-existing Henoch-Schönlein purpura may be exacerbated by influenza vaccination[2] but we are unaware of any report of Henoch-Schönlein purpura caused by the vaccination. Hypersensitivity reactions to influenza vaccine are thought to relate to allergy to vaccine components such as egg protein. It is possible, however, that immune complexes may form as a result of interaction between influenza vaccine antigens and native antibodies, initiating a vasculitic syndrome.[3]

1 Centers for Disease Control. Influenza vaccine 1980-1981. Recommendations of the public health service immunization practices advisory committee. *Ann Intern Med* 1980;93:466-8.
2 Damjanov J, Amato JA. Progression of renal disease in Henoch-Schönlein purpura after influenza vaccination. *JAMA* 1979;242:2555-6.
3 Blumberg S, Bienfang D, Kantrowitz FG. A possible association between influenza vaccination and small-vessel vasculitis. *Arch Intern Med* 1980;140:847-8.