treatment. Antiarrhythmic treatment was changed to procainamide. The electrocardiogram was unchanged, creatine kinase activity remained normal, and serum potassium concentration was 4·1 mmol/l. Besides premature ventricular beats, decreasing in frequency, the patient's further course was uneventful and he was discharged five days later. Serum mianserin concentrations measured by high performance liquid chromatography had a peak of 8·3 μmol/l (2·2 mg/l). The terminal half life (43·5 hours) was comparable with published values.[6] The peak concentration of the main metabolite, desmethylmianserin, was 0·19 μmol/l (0·76 mg/l). Only traces of other antidepressants, known to have been prescribed to the patient in the past, and of their metabolites were found (for example, desipramine 0·10 mg/l and mesoridazine 0·13 mg/l).

Although arrhythmogenic properties of mianserin have been reported in animal models[7] and changes of systolic time intervals during treatment with mianserin have been shown in humans,[8] cardiac arrhythmia is unusual, even in the case of intoxication.[1] To our knowledge the mianserin concentrations in the case reported here are the highest published values, exceeding therapeutic levels by about 20 to 50 times.[9] In view of the excessive drug concentration and the absence of other reasons we believe that mianserin induced life threatening rhythm disorders in this patient. His pre-existing coronary heart disease may have increased his susceptibility to arrhythmogenic events. The low concentrations of tricyclic compounds detected were, however, unlikely to provoke rhythm disturbances. After excessive doses mianserin, too, may induce potentially fatal ventricular arrhythmia, and close monitoring for at least 48 hours is advisable.

1 Chand S, Crome P, Dawling S. One hundred cases of acute intoxication with mianserin hydrochloride. *Pharmakopsychiatrie* 1981;**14**:15-7.
2 Crome P, Newman B. Poisoning with maprotiline and mianserin. *BMJ* 1977;ii:260.
3 Green SDR, Kendall-Taylor P. Heart block in mianserin hydrochloride overdose. *BMJ* 1977;ii:1190.
4 Huet C, Roul J, Guerot C, Valere PE. Inversion massive de l'onde T au cours d'un traitement par la miansérine (Athymil®). *Therapie* 1987;**42**:253-4.
5 Westermann GMA, Koerselman GF. How safe is "safe"? A case of fatal autointoxication with mianserin and flurazepam. *Ned Tijdschr Geneeskd* 1987;**131**:1182-4.
6 Shami M, Elliott HL, Kelman AW, Whiting B. The pharmacokinetics of mianserin. *Br J Clin Pharmacol* 1983;**15**:313S-22S.
7 Wouters W, Deiman W. Acute cardiac effects of fluvoxamine and other antidepressants in conscious rabbits. *Arch Int Pharmacodyn Ther* 1983;**263**:197-207.
8 Møller M, Thayssen P, Kragh-Sørensen P, *et al.* Mianserin: cardiovascular effects in elderly patients. *Psychopharmacology* 1983;**80**:174-7.
9 Yokoyama T, Kuroda K, Uemoto M, Masui M, Ide H, Mita T. Mianserin plasma levels and clinical response in primary depression. *Kobe J Med Sci* 1986;**32**:171-7.

Convulsions and transient cortical blindness after cisplatin

Drs P A PHILIP, J CARMICHAEL, and A L HARRIS (Imperial Cancer Research Fund Oncology Unit, Churchill Hospital, Oxford OX3 7LJ) write:

Cisplatin is a cytotoxic drug increasingly used to treat patients with a wide range of cancers such as germ cell tumours, ovarian carcinoma, bladder cancer, and small cell lung cancer. Although renal toxicity and gastrointestinal toxicity are commonly dose limiting, several neurological complications have been described, particularly after high doses. The main neurological side effects are peripheral sensory neuropathy predominantly and ototoxicity, which may be irreversible. Focal encephalopathy or seizures are rare and are often reversible.

A 59 year old woman presented with metastatic adenocarcinoma of unknown origin with left supraclavicular lymphadenopathy, pleural effusion and ascites, and no cerebral metastases. She received a combination of hydroxyurea (36 g) and cisplatin (75 mg/m^2) given every three weeks. Restaging investigations showed partial remission in the assessable disease sites in the retroperitoneal region. She developed confusion and then status epilepticus four days after the third course of treatment. Total cumulative dose of cisplatin was 225 mg/m^2, which was commenced eight weeks before this episode.

Investigations showed normal results of haematological and biochemical tests, including platelet count; clotting screen; and serum glucose, sodium, and calcium concentrations. A lumbar puncture was not performed. Computed tomography of the brain showed a few small ill defined abnormalities, which at the time were not diagnostic. She was treated with phenytoin, diazepam, and high dose dexamethasone and remained unconscious for 36 hours. She recovered consciousness fully on the fifth day but had reduced visual acuity of 6/60 bilaterally (Snellen's test) and complained of frontal headaches. There were no focal neurological signs, and her fundi were normal. Visual acuity slowly improved and was normal (6/6) on the 10th day. Repeat computed tomography on the 14th day showed no abnormality, and dexamethasone was gradually discontinued and anticonvulsants stopped. Neurological examination one month later showed no abnormality.

The incidence of convulsions induced by cisplatin has been estimated at 10%, and they may occur from six hours to three months after treatment.[1] Focal encephalopathy and cortical blindness have been reported in a few patients.[2-6] Our patient did not have any of the possible precipitating factors for encephalopathy after cisplatin treatment.[2] Her creatinine clearance was 82 ml/minute before the last course of treatment. To our knowledge hydroxyurea has no neurological side effects, although appreciable concentrations in the cerebrospinal fluid may occur with high doses. As convulsions may not occur until up to three months after receiving cisplatin it is important to include cisplatin induced fits and cortical blindness in the differential diagnosis of focal cerebral signs in patients who are undergoing treatment with cisplatin. Such patients may be wrongly assumed to have either progressive disease in the central nervous system or other complications of treatment, such as sepsis, with serious consequences. Moreover, active or supportive treatment may be withheld on the assumption of disease progression or recurrence in the brain.

1 Mead GM, Arnold AM, Green JA, Macbeth FR, Williams CJ, Whitehouse J. Epileptic seizures associated with cisplatin administration. *Cancer Treat Rep* 1982;**66**:1719-22.
2 Gorman DJ, Kefford R, Stuart-Harris R. Focal encephalopathy after cisplatin therapy. *Med J Aust* 1989;**150**:399-401.
3 Berman IJ, Mann MP. Seizures and transient cortical blindness associated with cis-platinum (II) diamminedichloride (PDD) therapy in a thirty-year-old man. *Cancer* 1980;**45**:764-6.
4 Lindeman G, Kefford R, Stuart-Harris R. Cisplatin neurotoxicity. *N Engl J Med* 1990;**323**:64-5.
5 Cattaneo MT, Filipazzi V, Piazza E, Damiani E, Mancarella G. Transient blindness and seizures associated with cisplatin therapy. *J Cancer Res Clin Oncol* 1988;**114**:528-30.
6 Diamond SB, Rudolph SH, Lubicz SS, Deppe G, Cohen CJ. Cerebral blindness in association with cis-platinum chemotherapy for advanced carcinoma of the fallopian tube. *Obstet Gynecol* 1982;**59**(suppl 6):84-6S.

A prostaglandin analogue as a probable cause of myocardial infarction in a young woman

Drs ERIC FLIERS, DONALD R DÜREN, and PIETER A VAN ZWIETEN (Academic Medical Centre, 1105 AZ Amsterdam, The Netherlands) write:

A 32 year old woman presented with dyspnoea in May 1990. In September 1989 her first pregnancy had ended in an intrauterine fetal death at 24 weeks' gestation, and during induction of labour by intravenous administration of sulprostone (Nalador) (maximum dose 500 μg/h) she developed an anteroseptal myocardial infarction (creatine kinase maximal 2300 U/l, aspartate aminotransferase maximal 354 U/l). Her electrocardiogram had been normal before induction of labour. After complete recovery a diagnostic cardiac catheterisation was performed in November 1989. During coronary angiography an anterolateral myocardial infarction developed. Although the procedure had to be terminated prematurely, the coronary arteries had been visualised and did not show striking abnormalities. Extensive laboratory investigation for abnormal haemostasis was negative. Subsequently, exertional dyspnoea and fatigue developed followed by upper abdominal discomfort and facial oedema. In spite of diuretic treatment these complaints progressed until she was admitted to our department.

On examination her blood pressure was 105/75 mm Hg and the pulse rate was 100/min. The jugular veins were distended with a positive abdominojugular reflux. The apex beat was displaced laterally. Systolic pulsations were palpable along the left sternal border. The first heart sound was normal and was followed by a pansystolic murmur, grade 3/6, which radiated into the axilla. There were crepitant rales over the posterior lung bases. The liver was enlarged and there was some pretibial oedema. A chest *x* ray film showed an enlarged left and right ventricle (cardiothoracic ratio 16·5:26), enlarged pulmonary vessels, and Kerley B lines. The electrocardiogram showed sinus tachycardia with left atrial involvement, normal PR interval and QRS width, low voltages, and QS waves in V1 and V2. Left ventricular ejection fraction was 13%. Cardiac catheterisation showed a pulmonary artery pressure of 70/25 mm Hg, a mean pulmonary artery wedge pressure of 25 mm Hg, and a left ventricular pressure of 120/24 mm Hg. The cardiac index was 2·9 l/min.m^2. Cineangiography showed apical and diaphragmal akinesia with hypokinesia of the other segments. There was a grade III/IV mitral regurgitation. Coronary arteriography showed a normal left and a normal dominant right coronary artery.

The patient was treated with digoxin, frusemide, captopril, and nicoumalone. She is currently being evaluated for heart transplantation.

This young woman had two myocardial infarctions within one year, leading to severe cardiac failure. Apart from mild, reversible hypertension associated with oral contraception, she had always been healthy. The first myocardial infarction occurred during administration of a prostaglandin E_2 analogue. This time course is highly suggestive of a causal relation between the drug and coronary spasm leading to ischaemia.

Several prostaglandins are synthesised and released by the heart and coronary vessels.[1] The role of prostaglandins in cardiac disease remains controversial, although there is experimental evidence that strongly suggests a role for cardiac prostaglandins in modulating coronary tone and vascular resistance in isolated coronary artery strips and perfused hearts.[2] Recent studies even suggest a physiological role for coronary prostaglandins in modulating coronary vascular response to sympathetic stimulation in non-ischaemic patients.[3] That sulprostone, a prostaglandin analogue, led to coronary spasm in this patient is further substantiated by two observations: the coronary angiogram did not show any abnormalities, and the first catheterisation was complicated by an unexplained myocardial infarction during coronary angiography, possibly indicating a high susceptibility to coronary spasm in this patient.

1 Beamish RE, Das PK, Karmazyn M, Dhalla NS. Prostaglandins and heart disease. *Can J Cardiol* 1985;**1**:66-74.
2 Evers AS, Murphree S, Saffitz JE, Jakschick BA, Needleman P. Effects of endogenously produced leukotrienes, thromboxane and prostaglandins on coronary vascular resistance in rabbit myocardial infarction. *J Clin Invest* 1985;**75**:992-9.
3 Neri Serneri GG, Gensini GF, Abbate R, *et al.* Physiologic role of coronary PG12 and PGE2 in modulating vascular response to sympathetic stimulation. *Am Heart J* 1990;**119**:848-54.