- 10 Feenstra P. Leprosy control through general health services and/or combined programmes. *Lepr Rev* 1993;64:89-96.
- 11 Lienhardt C, Fine PEM. Type 1 reaction, neuritis and disability in leprosy. What is the current epidemiological situation? *Lepr Rev* 1994;65:9-33.
- 12 Lockwood DNJ, Vinayakumar S, Stanley JNA, McAdam KPWJ, Colston MJ. Clinical features and outcome of reversal (type 1) reactions in Hyderabad, India. *Int J Lepr* 1993;60:8-15.
- 13 Becq-Bleumink M, Berhe D. Occurrence of reactions, their diagnosis and management in leprosy patients treated with multidrug therapy: experience in the leprosy control program of the All Africa Leprosy and Rehabilitation Training Center (ALERT) in Ethiopia. *Int J Lepr* 1992;60:173-84.
- 14 Khanolkar-Young S, Young DB, Colston MJ, Stanley JNA, Lockwood DNJ. Nerve and skin damage in leprosy is associated with increased intra-lesional heat shock protein. *Clin Exp Immunol* 1994;96:208-13.
- 15 Eiglmeier K, Honore N, Woods SA, Caudron B, Cole ST. Use of an ordered cosmid library to deduce the genomic organisation of *Mycobacterium leprae*. *Mol Microbiol* 1993;7:197-206.
- 16 Telenti A, Imboden P, Marchesi F, Lowrie D, Cole ST, Colston MJ, et al. Detection of rifampicin-resistance mutations in *Mycobacterium tuberculosis*. *Lancet* 1993;341:647-50.
- 17 Honore N, Cole ST. The molecular basis of rifampicin-resistance in *Mycobacterium leprae*. *Antimicrobial Agents and Chemotherapy* 1993;37:414-8.
- 18 Britton WJ. Immunology of leprosy. *Trans Roy Soc Trop Med Hyg* 1993;87:508-14.
- 19 Yamamura M, Uyemura K, Deans RJ, Weinberg K, Rea TH, Bloom TBR, et al. Defining protective responses to pathogens: cytokine profiles in leprosy lesions. *Science* 1991;254:277-9.
- 20 Ponnighaus JM, Fine PEM, Sterne JAC, Wilson RJ, Msosa E, Gruer PJK, et al. Efficacy of BCG vaccine against leprosy and tuberculosis in northern Malawi. *Lancet* 1992;339:636-9.
- 21 Convit J, Sampson C, Zuniga M, Smith PG, Plata J, Silva J, et al. Immunoprophylactic trial with combined *Mycobacterium leprae*/BCG vaccine against leprosy: preliminary results. *Lancet* 1992;339:446-50.
- 22 Magill A, Grogil M, Gasser RA, Sun W, Oster CN. Visceral infection caused by *Leishmania tropica* in veterans of operation Desert Storm. *N Engl J Med* 1993;328:1383-7.
- 23 Lockwood DNJ. Sudan: kala-azar should be in the news. *Lancet* 1991;338:624-5.
- 24 Singla N, Singh GS, Sundar S, Vinayak VK. Evaluation of the direct agglutination test as an immunodiagnostic tool for kala-azar in India. *Trans Roy Soc Trop Med Hyg* 1993;87:276-8.
- 25 Zijlstra EE, Siddig Ali M, El-Hassan AM, El-Toum IA, Satti M, Ghalib HW, et al. Kala-azar: a comparative study of parasitological methods and the direct agglutination test in diagnosis. *Trans Roy Soc Trop Med Hyg* 1992;86:505-7.
- 26 Okong'o-Odera EA, Wamachi A, Kagai JM, Kurtzhals JAL, Githure JI, Hey AS, et al. Field application of an ELISA using redefined *Leishmania* antigens for the detection of visceral leishmaniasis. *Trans Roy Soc Trop Med Hyg* 1993;87:423-4.
- 27 Howard MK, Ogunkolade W, Bryceson ADM, Davidson RN, Moody AH, Miles MA. A DNA probe for human visceral leishmaniasis. *Trans Roy Soc Trop Med Hyg* 1992;86:35-6.
- 28 Davidson RN, Di Martino L, Gradoni L, Giacchino R, Russo R, Gaeta GB, et al. Liposomal amphotericin B (Ambisome) in Mediterranean visceral leishmaniasis: a multicentre trial. *Q J Med* 1994;87:75-81.
- 29 Alvar J. Leishmaniasis and AIDS co-infection: the Spanish example. *Parasitology Today* 1994;10:160-3.
- 30 Mabey DM. Ivermectin and onchocercal optic nerve lesions. *Lancet* 1993;341:153-4.
- 31 Abiose A, Jones BR, Cousens SN, Murdoch I, Cassels-Brown A, Babalola OE, et al. Reduction in incidence of optic nerve disease with annual ivermectin to control onchocerciasis. *Lancet* 1993;341:130-4.
- 32 Ramachandran CP. Improved immunodiagnostic tests to monitor onchocerciasis control programmes—a multicenter effort. *Parasitology Today* 1993;9:76-9.
- 33 Bradley JE, Trenholme KR, Gillespie AJ, Guderian R, Titanji V, Hong Y, et al. A sensitive serodiagnostic test for onchocerciasis using a cocktail of recombinant antigens. *Am J Trop Med Hyg* 1993;48:198-204.
- 34 Bradley JE, Gillespie AJ, Trenholme KR, Karam M. The effects of vector control on the antibody response to antigens of *Onchocerca volvulus*. *Parasitology* 1993;106:363-70.
- 35 Zimmerman PA, Guderian RH, Araujo E. Polymerase chain reaction-based diagnosis of *Onchocerca volvulus* infection: improved detection of patients with onchocerciasis. *J Infect Dis* 1994;169:686-9.
- 36 Dafa'Alla YH, Ghalib HW, Abdelmaged A, Williams JF. The profile of IgG and IgG subclasses of onchocerciasis patients. *Clin Exp Immunol* 1992;88:258-63.
- 37 Elson LH, Guderian RH, Araujo E, Bradley JE, Days A, Nutman TB. Immunity to onchocerciasis: identification of a putatively immune population in a hyperendemic area of Ecuador. *J Infect Dis* 1994;169:588-94.
- 38 Gilks CF. The clinical challenge of the HIV epidemic in the developing world. *Lancet* 1993;342:1037-9.
- 39 Gilks CF, Otieno LS, Brindle RJ, Newnham RS, Lule GN, Were JBO, et al. The presentation and outcome of HIV-related disease in Nairobi. *Q J Med* 1992;82:25-32.
- 40 Nunn P, Brindle RJ, Carpenter L, Odhiambo J, Wasunna K, Newnham RS, et al. Cohort study of human immunodeficiency virus infection in patients with tuberculosis in Nairobi, Kenya. *Am Rev Respir Dis* 1992;146:849-54.
- 41 De Cock KM, Coulibaly IM, Lucas SB. Tuberculosis and HIV infection in sub-Saharan Africa. *JAMA* 1992;268:1581-7.
- 42 Lucas SB, Hounnou A, Pecock C, Beaumel A, Djomand G, N'Gbhich JM, et al. The mortality and pathology of HIV infection in a West African city. *AIDS* 1993;7:1569-79.
- 43 Hawken M, Nunn P, Gathua S, Brindle R, Godfrey-Fausett P, Githui W, et al. Increased recurrence of tuberculosis in HIV-1-infected patients in Kenya. *Lancet* 1993;342:332-7.
- 44 De Cock K. Impact of interaction with HIV. In: Porter JDH, McAdam KPWJ, eds. *Tuberculosis: back to the future*. Chichester: Wiley, 1994;35-49.

Lesson of the Week

Upper abdominal pain in pregnancy may indicate pre-eclampsia

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Clinical and laboratory tests for pre-eclampsia must be undertaken in all women with upper abdominal pain in pregnancy

Pre-eclampsia is one of the prime causes of maternal and perinatal morbidity and mortality. The syndrome is highly variable, and the clinical presentation is often atypical. We describe the case histories of three women who presented with epigastric pain as the first outward manifestation of the disorder and in whom the diagnosis was initially overlooked.

Case reports

CASE 1

A 28 year old primigravida attended her general practitioner's surgery at 34 weeks' gestation with pain in the right upper quadrant, nausea, and vomiting. An antacid was prescribed for presumed reflux oesophagitis. Her blood pressure was not measured and her urine was not tested for protein. The symptoms persisted, and five days later she presented to the hospital antenatal clinic. On examination her blood pressure was 140/80 mm Hg and urine analysis showed proteinuria (2+). She had appreciable tenderness of the right hypochondrium. Further investigation disclosed a moderate thrombocytopenia ($56 \times 10^9/l$) and raised serum concentrations of aspartate aminotransferase (225 U/l) and uric acid (0.37 mmol/l). Concentrations of haemoglobin, urea, alkaline phosphatase, and albumin all lay within the normal ranges for pregnancy. There was no evidence of haemolysis, and

the standard clotting times were not prolonged. A midstream urine sample was clear of white and red cells at microscopy. Pre-eclampsia with raised liver enzyme concentrations and a low platelet count was diagnosed. As the cervix was unfavourable caesarean section was performed to deliver the baby, a girl weighing 2100 g; she required minimal resuscitation. With intensive monitoring and supportive care, the woman made a complete recovery over 72 hours, her blood pressure, aspartate aminotransferase concentration, and platelet count all returning to within normal limits.

CASE 2

A 26 year old woman complained of epigastric pain at 36 weeks in her first pregnancy. Her general practitioner diagnosed dyspepsia and prescribed an antacid mixture. Her blood pressure and urine were not checked. The pain continued, and at a routine antenatal visit two days later she was found to be hypertensive (135/105 mm Hg) and to have proteinuria (2+). On investigation in hospital that day she had moderate thrombocytopenia ($78 \times 10^9/l$) and raised serum concentrations of aspartate aminotransferase (142 U/l) and uric acid (0.41 mmol/l). Standard clotting times were normal and there was no evidence of haemolysis. The fetus was normally grown and had a reactive heart rate pattern. An attempt was made to induce labour with dinoprostone gel (2 mg, two doses,

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six hours apart; Prostin E2 gel, Upjohn). Twelve hours later labour had not progressed and her platelet count had fallen further to $39 \times 10^9/l$. A caesarean section was performed under general anaesthetic, with a platelet transfusion being given during surgery. A girl weighing 2300 g was delivered in excellent condition. The woman's platelet count rose steadily to $120 \times 10^9/l$ and her liver enzyme abnormality reversed within 48 hours of delivery. Her hypertension settled by the fifth day.

CASE 3

A 27 year old woman complained of epigastric pain at 22 weeks' gestation in her second pregnancy; her first pregnancy had ended as a spontaneous abortion at 18 weeks. Analysis of urine showed proteinuria (1+), but her blood pressure was not measured. Her general practitioner diagnosed a urinary tract infection and prescribed an antibiotic. Four days later she had a moderate antepartum haemorrhage (<500 ml) and was transferred to hospital. By the time of admission the bleeding had stopped. The uterus was soft and not tender, but she was tender in the right hypochondrium. Her blood pressure was 160/110 mm Hg, and a urine sample tested positive for protein (3+). Detailed investigation showed a mildly raised serum concentration of aspartate transaminase (84 U/l) and thrombocytopenia ($91 \times 10^9/l$). Her serum albumin concentration was low (28 g/l), but there was no evidence of haemolysis or disseminated intravascular coagulation. A urine sample was clear at microscopy. The fetal heart pattern was reactive, but an ultrasound scan showed the fetus to have symmetrical growth retardation with oligohydramnios. Doppler umbilical artery blood flow analysis showed reversed flow in diastole. An attempt was made to control the hypertension with methyldopa (500 mg thrice daily) and nifedipine (10 mg thrice daily; Bayer), but without success. Repeat blood sampling confirmed the initial results. Delivery was considered necessary to prevent severe maternal complications, and, in view of the fetus's extreme prematurity, labour was induced using a prostaglandin E₂ pessary (2.5 mg; inhouse preparation). The fetus died shortly after uterine contractions started. A normally formed male fetus weighing 450 g was delivered spontaneously 12 hours later. Thereafter, the woman recovered rapidly, and she was discharged home three days later.

Discussion

Pre-eclampsia is a progressive disorder of endothelial function that is unique to pregnancy and probably results from various microvascular diseases.¹ It arises in the placenta but may affect all major organ systems, including the brain, kidney, liver, and lung. Although most cases of pre-eclampsia are first detected at routine screening of symptom free women attending routine antenatal clinics, the mode of presentation is highly variable and a small proportion of women present with the symptoms of systemic complications such as headache, visual disturbance, and eclampsia. Pre-eclampsia complicated by raised liver enzyme concentrations and a low platelet count with or without haemolysis is at least as common as eclampsia and often more difficult to manage,¹ but it is less well recognised.³ Several authors have reported high rates of serious maternal and perinatal problems such as hepatic rupture, renal failure, pulmonary oedema, placental abruption, and

perinatal asphyxia.^{2,4-6} Early diagnosis and prompt action are essential, therefore, to help avert life threatening complications. Although the clinical progression of pre-eclampsia is usually slow, occurring over days and sometimes weeks, rapid deterioration may occur and occasionally result in multisystem failure within the course of a few hours.⁷ Detailed monitoring and supportive care may reduce the risk of complications, but ultimately the only means of controlling the condition is delivery of the fetus (and placenta). Early recognition of fulminant cases allows maximum time for assessment and stabilisation before delivery, including enhancement of fetal lung maturity with exogenous corticosteroids,⁸ and transfer to a unit adequately equipped for maternal and neonatal intensive care.

Our three case reports confirm that epigastric pain is often a grave symptom in pregnant women. They also emphasise that blood pressure must be measured and urine tested for protein in all women troubled by upper abdominal pain after 20 weeks of pregnancy. Women with pre-eclampsia complicated by raised liver enzyme concentrations and thrombocytopenia with or without haemolysis may be normotensive and aprotinuric at initial presentation.^{9,10} Therefore blood pressure measurement and urine analysis cannot be relied on to exclude the diagnosis of pre-eclampsia. Given that clinical deterioration may be rapid, women with upper abdominal pain and tenderness must be admitted to hospital immediately to test for hepatic dysfunction, haemolysis, and thrombocytopenia.

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- 1 Roberts JM, Redman CWG. Pre-eclampsia: more than pregnancy-induced hypertension. *Lancet* 1993;342:1447-51.
- 2 Weinstein L. Syndrome of hemolysis, elevated liver enzymes, and low platelet count: a severe consequence of hypertension in pregnancy. *Am J Obstet Gynecol* 1982;142:159-67.
- 3 Lim BH, Barry CL, Brown GH. HELLP syndrome: an often unrecognized complication of pre-eclampsia. *Aust NZ J Obstet Gynaecol* 1991;31:27-8.
- 4 Mackenna J, Dover NL, Brame RG. Pre-eclampsia associated with hemolysis, elevated liver enzymes, and low platelets—an obstetric emergency? *Obstet Gynecol* 1983;62:751-4.
- 5 Sibai BM, Taslimi MM, El-Nazer A, Amon E, Mabie BC, Ryan GM. Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe pre-eclampsia-eclampsia. *Am J Obstet Gynecol* 1986;155:501-9.
- 6 van Dam PA, Renier M, Backelandt M, Buytaert P, Uytendaele F. Disseminated intravascular coagulation and the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe pre-eclampsia. *Obstet Gynecol* 1989;73:97-102.
- 7 Martin JN Jr, Blake PE, Perry KG Jr. The natural history of HELLP syndrome: patterns of disease progression and regression. *Am J Obstet Gynecol* 1991;164:1500-13.
- 8 Lamont RF, Dunlop PDM, Levene MI, Elder MG. Use of glucocorticoids in pregnancies complicated by severe hypertension and proteinuria. *Br J Obstet Gynaecol* 1983;90:199-202.
- 9 Sibai BM. The HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): Much ado about nothing? *Am J Obstet Gynecol* 1990;162:311-6.
- 10 Aarnoudse JG, Houthoff HJ, Weits J, Vellenga HJ. A syndrome of liver damage and intravascular coagulation in the last trimester of normotensive pregnancy. A clinical and histopathological study. *Br J Obstet Gynaecol* 1986;93:145-55.

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Correction

Guidelines for paediatric life support

An editorial error occurred in this article by the Paediatric Life Support Working Party of the European Resuscitation Council (21 May pp 1349-55). In figure 7 (p 1354) the arrow should point from adrenaline 100 µg/kg to cardiopulmonary resuscitation for 1 minute and not the other way round.