

# Prospective study of liver dysfunction in pregnancy in Southwest Wales

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**Background:** Liver dysfunction in pregnancy has serious consequences. Its frequency and characteristics have not been systematically documented in Britain. We have prospectively determined incidence, causes, and outcome of liver dysfunction in pregnancy in an obstetric unit in Southwest Wales, UK.

**Methods:** A central laboratory identified all abnormal liver tests (bilirubin >25 µmol/l, aspartate transaminase >40 U/l, or γ glutamyl transpeptidase >35 U/l) from patients in antenatal clinics and wards of an obstetric unit serving a population of 250 000. Patients with abnormal liver tests were assessed and followed through after pregnancy. Medical advice was provided to obstetric teams.

**Findings:** There were 4377 deliveries during the 15 month study. A total of 142 patients had abnormal liver tests. There were 206 contributing diagnoses, the great majority being pregnancy specific. Among the most important were pre-eclampsia (68), HELLP (haemolysis, elevated liver enzymes, low platelets) syndrome (30), obstetric cholestasis (23), hyperemesis gravidarum (11), acute fatty liver of pregnancy (five), and hepatic infarct (one). Sepsis, postoperative factors, and placental pathology (51) were not uncommonly responsible but incidental or pre-existing hepatobiliary disease was infrequent (17). Sixty five patients were delivered early by induction or caesarean section because of liver dysfunction. Despite substantial liver related morbidity, there were no maternal deaths and only two intra-uterine deaths.

**Conclusions:** Liver dysfunction was seen in 3% of deliveries during a 15 month prospective study and was usually directly related to pregnancy with spontaneous recovery in the puerperium. Incidence of the most serious conditions, acute fatty liver of pregnancy and HELLP syndrome, was much greater than previously reported. Profound effects on maternal and infant health were observed but close medical and obstetric collaboration ensured low mortality.

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Pregnancy may be complicated by severe liver problems including liver failure. Some liver disorders are specific to pregnancy. The two most serious, acute fatty liver of pregnancy and HELLP syndrome (haemolysis, elevated liver enzymes, low platelets), are rare whereas obstetric cholestasis, liver dysfunction associated with pre-eclampsia, and hyperemesis gravidarum are commoner. Certain other hepatobiliary disorders are also important either because they are more likely to occur in pregnancy—for example, gall stones and hepatic vein thrombosis—or because they run a more severe course than in the non-pregnant state—for example, acute hepatitis E. While these pregnancy specific or pregnancy predisposed hepatobiliary diseases are well described, their epidemiology in the UK is poorly documented. It is likely that they are under reported and there is evidence from the lay press<sup>1</sup> and parliamentary questions<sup>2</sup> that obstetric teams and health care professionals may be unaware of their frequency and clinical impact.

In 1999 we decided on a prospective evaluation of abnormal liver function during pregnancy in an obstetric unit which provides all obstetric services for a very stable and ethnically uniform population of approximately 250 000 in Southwest Wales. Before embarking on the prospective study, we performed a retrospective analysis of abnormal liver function tests identified in obstetric patients from the same population during 1997 and 1998 and searched the database of the Trust coding office for any diagnosis of liver or biliary disease during pregnancy over the same time period. On the basis of our retrospective analysis we anticipated encountering about 50 cases of liver dysfunction among 3500 pregnancies during the course of one year. Thus we planned a prospective study of up to two years duration to allow study of at least 100 consecutive cases of liver dysfunction in pregnancy.

## METHODS

### Study population

The obstetric unit of Swansea NHS Trust is based primarily in Singleton Hospital with subsidiary units and antenatal clinics in Neath General, Morriston, Prince Philip, and Amman Valley Hospitals. There are no other obstetric services within this area and therefore the great majority of pregnant women use the services of this obstetric unit.

The population is defined by the Unitary Authority of Swansea as follows: city of Swansea (postcodes SA1-SA9) population 226 000; part of the surrounding rural area (postcodes SA14, 15, and 18) population 25 000. This population is 51.9% female, 48.1% male, and is predominantly of Caucasian ethnic origin (98.2%). ONS figures for 1999–2000 showed a 0.3% population growth with 3% migration and 3% immigration.

One biochemistry laboratory serves all of these hospitals and the general practices of the area. We endeavoured to trace all abnormal liver tests occurring in pregnant women in this geographical area using the computer database of the biochemistry laboratory. The principal biochemist flagged up all abnormal liver tests which originated from obstetric wards or antenatal clinics or were requested by obstetric staff or midwives.

**Abbreviations:** HELLP, haemolysis, elevated liver enzymes, low platelets; LFT, liver function tests; AST, aspartate aminotransferase; γGT, gamma glutamyl transpeptidase; USS, ultrasound scan; ERCP, endoscopic retrograde cholangiopancreatogram; LDH, lactate dehydrogenase; OC, obstetric cholestasis; AFLP, acute fatty liver of pregnancy.

Abnormal liver function tests (LFT) were defined as:

- bilirubin >25 µmol/l;
- aspartate aminotransferase (AST) > 40 iu/l;
- gamma glutamyl transpeptidase (γGT) >35 iu/l.

### Retrospective analysis

For this analysis the total number of pregnant patients between January 1997 and December 1998 who had any abnormality of liver function, as defined above, was extracted from the Central Laboratory Computer Database. All ICD codes O26.6, O90.4, O99.6, K70 to K83, K87, I81, and I82 in the presence of pregnancy taken from hospital discharge summaries between January 1997 and December 1998 were also recorded.

### Prospective analysis

Between March 1999 and May 2000 all abnormal LFT observed in serum samples from pregnant patients from any clinical setting were identified by the central biochemistry laboratory. It should be stressed that liver function was not assessed as routine in all pregnancies. LFT were only requested by the obstetric staff, midwife, or general practitioner on clinical grounds. The main indications were abdominal pain, nausea/vomiting, itching, pre-eclampsia, and clinical evidence of infection. LFT were also performed in patients with non-specific symptoms because of concern for maternal/fetal well being. The demographic details of those patients with abnormal LFT were relayed to the department of gastroenterology on the day of analysis to enable either of two physicians to review the patient and/or case record. The medical aspects of the pregnancy were then followed prospectively and investigated as clinically appropriate. These investigations included serum bile acids, iron and copper studies, hepatitis A, B, and C serology, autoantibodies, hepatobiliary ultrasonography, endoscopic retrograde cholangiopancreatogram (ERCP), and liver biopsy. Diagnostic criteria for the specific liver disorders of pregnancy were based on clinical findings and investigations as follows.

### Acute fatty liver of pregnancy (AFLP)<sup>3-5</sup>

Six or more of the following features in the absence of another explanation:

- Vomiting
- Abdominal pain
- Polydipsia/polyuria
- Encephalopathy
- Elevated bilirubin
- Hypoglycaemia
- Elevated urate
- Leucocytosis
- Ascites or bright liver on ultrasound scan (USS)
- Elevated transaminases
- Elevated ammonia
- Renal impairment
- Coagulopathy
- Microvesicular steatosis on liver biopsy

### HELLP syndrome<sup>6-8</sup>

For complete HELLP syndrome:

- Elevated AST >70 iu/l
- Low platelet count <100×10<sup>9</sup>/l
- Haemolysis (lactate dehydrogenase (LDH) >600 U/l).

For partial HELLP syndrome:

- Elevated AST >40 iu/l

- Low platelet count <150×10<sup>9</sup>/l
- Absence or presence of haemolysis.

### Obstetric cholestasis (OC)<sup>9</sup>

Pruritus with elevated serum transaminases and/or bile acids in the second or third trimester.

### Pre-eclamptic liver dysfunction<sup>10</sup>

Elevated liver enzymes or bilirubin in the presence of hypertension, proteinuria, and oedema after 20 weeks of gestation.

### Hyperemesis gravidarum with liver dysfunction<sup>10</sup>

Elevated liver enzymes or bilirubin in the presence of persistent vomiting for more than one week during the first or second trimester.

## RESULTS

### Retrospective survey

A retrospective search of the laboratory database over the two year period 1997–1998 identified 88 pregnant patients with abnormal LFT. However, over the same period only 13 cases of hepatobiliary disorders during pregnancy were recorded by the coding office. Thus 75 of 88 (85%) pregnant patients with deranged liver function did not have a hepatobiliary diagnosis recorded on the hospital discharge summary. This may reflect lack of a specific diagnosis within the coding nomenclature or a defect in the coding process but more likely the abnormal liver tests were not noticed or not correctly interpreted by the obstetric teams.

### Prospective survey

LFT abnormalities were investigated in 4377 deliveries during the 15 month study period. A total of 142 patients were found to have abnormal LFT (3% of all pregnancies).

- AST elevated in 119 of 142 (84%) (median 70 U/l (range 41–9299)).
- γGT elevated in 56 of 142 (39%) (median 51 U/l (range 36–278)).
- Bilirubin elevated in 24 of 142 (17%) (median 32 µmol/l (range 26–155)).
- Bile acids elevated in 20 (median 50 µmol/l (range 17–179); normal range <14 µmol/l).

The range and median values for AST, γGT, and bilirubin for the specific pregnancy related liver disorders are shown in table 1.

Elevations in AST, γGT, and bilirubin were seen across the entire range of pregnancy specific liver disorders and non-specific hepatobiliary conditions. Serum total bile acids were measured very selectively and elevated levels were seen only in OC and AFLP. Clinical jaundice was a feature of three patients with AFLP, one with HELLP syndrome, one with sepsis, and one with paracetamol overdose.

Other laboratory findings among 142 patients with abnormal LFT were:

- Thrombocytopenia in 35 (25%) (median 126×10<sup>9</sup>/l (range 5–149)).
- Hyperuricaemia in 100 (70%) (median 0.38 mmol/l (range 0.28–0.70); normal range for the third trimester <0.28 mmol/l).

Thrombocytopenia was seen in complete and partial HELLP syndrome by definition but was also seen in three of five patients with AFLP. Hyperuricaemia was a prominent feature of all pregnancy specific liver disorders except hyperemesis gravidarum.

Abnormalities of imaging investigations among 142 patients with abnormal LFT were:

**Table 1** Aspartate aminotransferase (AST), gamma glutamyl transpeptidase ( $\gamma$ GT), and bilirubin values for specific pregnancy related liver disorders

	AST (U/l)	$\gamma$ GT (U/l)	Bilirubin ( $\mu$ mol/l)
Pre-eclamptic liver dysfunction	53(14–4123)	18 (4–106)	8(2–155)
HELLP syndrome	66(41–4123)	24 (6–209)	13(4–155)
Obstetric cholestasis	210(30–519)	29 (8–278)	14(6–34)
Hyperemesis gravidarum	51(9–280)	23 (2–64)	25(4–33)
AFLP	278(86–542)	50 (22–209)	50(19–61)

Values are median (range).

HELLP, haemolysis, elevated liver enzymes, low platelets; AFLP, acute fatty liver of pregnancy.

- Common bile duct stones in three patients (USS and ERCP).
- Gall bladder stones in three patients (USS).
- Hepatic infarct and subcapsular haematoma complicating one case of HELLP syndrome (USS and computerised axial tomography).
- Ascites and intra-abdominal bleeding complicating one case of HELLP syndrome (USS).
- Ascites and bright liver texture in one case of AFLP (USS).

#### Diagnoses accounting for abnormal liver tests

A total of 206 contributory diagnoses were made among 128 patients while in 14 patients abnormal liver tests remained unexplained (table 2).

#### Pregnancy specific conditions

Pre-eclampsia was the commonest underlying abnormality—68 patients (48%). Complete HELLP syndrome as defined by Sibai and colleagues<sup>6</sup> occurred in five patients (4%) while incomplete HELLP syndrome<sup>7,8</sup> was diagnosed in 25 (18%). Twenty nine of 30 HELLP syndrome patients had pre-eclampsia. In most of those patients with incomplete HELLP syndrome, platelet count decreased abruptly by more than 50% in parallel with abnormal liver tests. OC was diagnosed in 23 patients (16%). Eleven patients (8%) had deranged LFT associated with hyperemesis gravidarum; all responded well to conservative management or oral steroids. AFLP was diagnosed in five patients (4%), three of whom needed prolonged postnatal hospitalisation because of multi-organ involvement. Clinical details of these patients have been presented and published recently.<sup>11,12</sup>

#### Other contributory conditions

Seventeen patients had abnormal liver tests in association with sepsis, most commonly caused by urinary tract infection (nine patients). In 22 patients LFT became abnormal or abruptly deteriorated immediately after caesarean section. The main indications for caesarean section were pre-eclampsia, placental abruption, and failure to progress. Of these 22 patients, 14 had pre-eclampsia with normal liver tests prior to caesarean section but seven of these 14 had platelet counts of  $100\text{--}150 \times 10^9/\text{l}$ , possibly representing incomplete HELLP syndrome. Of the 22 patients, four had urinary tract infections and two had postpartum haemorrhage. In four patients abnormal liver tests were drug related: three were due to anticonvulsants and one to an overdose of paracetamol. Three patients had common bile duct stones diagnosed by ultrasound and subsequently treated endoscopically in the postnatal period. Viral hepatitis was rare with only two identified cases of chronic hepatitis C, one of which was known before pregnancy and the other was discovered in association with OC. Poorly controlled diabetes was noted in eight patients, five of whom had gestational diabetes; the abnormal liver tests in these patients may reflect hepatic steatosis. Various placental pathologies were noted in 12 patients: five postpartum haemorrhage, three antepartum haemorrhage, one placental infection with sepsis, one abruption, one placental infarction, and one with both placental infarction and abruption. Abnormal liver tests were noted at the onset of placental pathology or during resuscitation; 12 patients required blood transfusions. Alcohol was not considered to be a contributing factor in any patient although in two with unexplained liver dysfunction alcohol consumption was not accurately ascertained.

**Table 2** Diagnoses accounting for abnormal liver tests

	n	No with $\uparrow$ AST	No with $\uparrow$ $\gamma$ GT	No with $\uparrow$ bilirubin	No with $\uparrow$ urate	No with $\downarrow$ platelets
Group 1—Pregnancy specific						
Pre-eclampsia	68	62	23	7	61	26
HELLP syndrome						
Complete	5	5	2	3	5	5
Partial	25	25	10	7	24	25
Obstetric cholestasis	23	22	10	2	17	0
Hyperemesis gravidarum	11	7	4	5	3	1
Acute fatty liver of pregnancy	5	5	3	4	5	3
Hepatic infarct/haematoma	1	1	1	1	1	1
Group 2—Other conditions						
Postoperative (caesarean section)	22	21	10	3	21	7
Sepsis	17	17	6	2	12	2
Placental pathologies	12	11	4	3	9	3
Diabetes	8	6	5	1	5	4
Drug related	4	1	4	1	N/A	2
Bile duct stones	3	3	2	2	1	0
Hepatitis C	2	2	1	0	0	0
Group 3—Diagnosis obscure	14	8	4	1	6	0

N/A, not available.

**Table 3** Timing of liver dysfunction. Onset of specific pregnancy related liver disorders (in weeks' gestation)

Pre-eclamptic liver dysfunction	37 (25–40)
HELLP syndrome	36 (25–38)
Obstetric cholestasis	35 (21–39)
Hyperemesis gravidarum with liver dysfunction	9 (6–14)
AFLP	38 (32–38)

Values are median (range).  
HELLP, haemolysis, elevated liver enzymes, low platelets; AFLP, acute fatty liver of pregnancy.

### Timing of liver dysfunction

Abnormal liver tests were first noted between six weeks' gestation and six days postpartum. The range and median values for the onset of specific pregnancy related liver disorders are presented in table 3.

### Pregnancy outcome

No maternal deaths occurred in association with liver dysfunction during the 15 month study period. There was a termination of an unwanted pregnancy at eight weeks' gestation associated with hyperemesis. There were two intrauterine deaths: one at 30 weeks' gestation in association with pre-eclamptic liver dysfunction and one in the first trimester following paracetamol overdose with severe hepatic necrosis. Forty two of 153 live babies (27%) required admission to the special care baby unit for further management. The Apgar score for babies born to mothers with abnormal liver tests during pregnancy was 8.1 (95% confidence interval (CI) 7.8–8.3) at one minute and 9.3 (95% CI 9.1–9.5) at five minutes, in contrast with 8.4 (95% CI 8.3–8.6) and 9.6 (95% CI 9.5–9.7), respectively, for a control group of 267 babies born consecutively during the month of March 2001 ( $p < 0.007$  and  $p < 0.002$ , respectively). There was no significant difference between Apgar scores according to specific maternal diagnosis. Median stay in the special care baby unit was 14 days (range 1–121 days).

Sixty five patients (46%) were delivered early (induction of labour, elective or emergency Caesarean section) because of deteriorating liver function or the implications of the underlying liver dysfunction. Median gestation of the 141 affected pregnancies (excluding the therapeutic termination) was 38 weeks (range 12–42 weeks). There were 11 twin, 1 triplet, and 130 singleton pregnancies.

### DISCUSSION

The epidemiology of most pregnancy related liver disorders is either unknown or only patchily recorded and there are no published prospective data from the UK. OC is especially common in Chile and 20 years ago was reported in over 10% of all pregnancies but it has become progressively less common in that country in recent years (currently approximately 1.5%).<sup>13</sup> Its incidence in the UK has received little attention but it is certainly commoner than the official estimates of less than 1 case per 1000 given in answer to a parliamentary question in 1995.<sup>2</sup> A recent retrospective analysis from Birmingham<sup>14</sup> gave an incidence of OC of 1:160 in a white population—a value similar to ours. AFLP and HELLP syndrome are generally considered to be rare.<sup>5–18</sup> Standard texts and recent reviews give incidence values for AFLP of 1:7000–16 000 pregnancies<sup>4 15 17</sup> and for HELLP syndrome of 1:900–2000 pregnancies.<sup>6 18 19</sup> Our prospective study contrasts strongly with these estimates and has shown that liver dysfunction in pregnancy is surprisingly common.

We based the normal ranges for AST,  $\gamma$ GT, and bilirubin in pregnancy on those of the non-pregnant state and have not taken into account possible physiological fluctuations related to the stage of gestation. Girling and colleagues<sup>20</sup> from St

Mary's Hospital have reported lower normal values of AST and bilirubin during pregnancy but their observations have not been validated independently and contradict previous work.<sup>21</sup> Thus we decided to use our own laboratory's normal range. If we had applied Girling's normal values of AST for the third trimester, a further 112 patients would have been identified with slightly raised values of between 31 and 40 U/l. Hence we have possibly understated the incidence of biochemical liver dysfunction in pregnancy.

We encountered more liver abnormalities in our prospective study than predicted by our retrospective analysis. This suggests that the study itself uncovered more disease by raising awareness of the possibility of liver problems, encouraging more testing by obstetric staff, and promoting a culture of diagnostic accuracy. Our methodology only enabled liver dysfunction to be detected when there was a clinical reason for a liver function test to be requested. Thus both the retrospective and prospective studies probably underestimated the true prevalence of liver dysfunction in this population. The high incidence of the most serious specific liver diseases of pregnancy (AFLP, HELLP syndrome, and OC) is partly explained by detection of cases which might have escaped diagnosis had the study not been in progress. We know from our retrospective survey that cases, which on review of clinical data could be confidently ascribed to HELLP syndrome, AFLP, or OC, were not at the time given a diagnosis. Important obstetric liver problems may pass unnoticed by clinicians without experience in these diseases when jaundice is absent. With attentive obstetric and medical supervision, many cases can be recognised early and managed effectively so preventing progression to life threatening disease. Recognition of less florid cases of AFLP has been recently reported from Los Angeles<sup>17</sup> and contrasts with descriptions of the disease from the same institution 20 years earlier.<sup>4</sup> OC is underdiagnosed because itching in pregnancy is often accepted as normal by patients and medical attendants. The correct diagnosis will not be made unless serum transaminases and/or bile acids are checked. OC is an important diagnosis because of its association with sudden intrauterine death in late pregnancy,<sup>9 22</sup> a risk which can be largely avoided by delivery before 37 weeks.<sup>1 2 9 13</sup>

Our previous studies<sup>23</sup> have shown viral hepatitis to be uncommon among women of childbearing age in Southwest Wales. Only two patients with hepatitis C were identified in our present study cohort but in one of these the cause of abnormal LFT was OC and her liver tests returned to normal after delivery. No patients with hepatitis A or B were identified.

It is sometimes difficult to be certain of the cause of liver dysfunction in pregnancy, either because full diagnostic criteria are not met or because of overlapping features of pregnancy specific disorders. Thus some of our pre-eclamptic patients had elevated transaminases and a falling platelet count yet did not qualify for a diagnosis of complete HELLP syndrome because the degree of laboratory abnormality did not reach those levels chosen in Memphis, Tennessee for disease definition.<sup>6</sup> There is now general agreement that HELLP syndrome can be partial or incomplete<sup>7 8</sup> but it is essential that investigators define their diagnostic criteria to allow for comparisons of incidence and outcome. There is good evidence to show that enzyme peaks and platelet nadirs have prognostic significance.<sup>24</sup> We believe that HELLP syndrome covers a wide spectrum of liver dysfunction in pre-eclamptic patients and can exist in mild forms. At the other extreme are patients with severe multisystem disease who may show features of both HELLP syndrome and AFLP although in our experience one or other of the conditions will be dominant.

Pre-eclampsia was very common among our patients with pregnancy related liver disorders: it was present in 29 of 30 with HELLP syndrome, two of those with OC, and a large proportion (37) of those with abnormal LFT without a more specific hepatic diagnosis. The association of pre-eclampsia with

other pregnancy specific liver disorders is well documented<sup>25-27</sup> and suggests some common ground in the aetiology of the conditions. Some patients with undoubted HELLP syndrome showed microvesicular fat within hepatocytes on biopsy,<sup>28</sup> a feature previously considered diagnostic of AFLP, while other patients with typical AFLP developed thrombocytopenia<sup>3</sup> and had elevated transaminases and LDH. Mitochondrial fatty acid beta-oxidation defects, particularly LCHAD (long chain 3-hydroxyacyl CoA dehydrogenase) deficiency, have been described in babies born to mothers suffering from either HELLP syndrome or AFLP, or both.<sup>29-31</sup> In clinical presentation there are many similarities too; vomiting and abdominal pain are the cardinal early symptoms of both disorders while polyuria, polydipsia, and even frank diabetes insipidus, although most commonly described in AFLP, are sometimes seen in HELLP syndrome also.<sup>32</sup>

In our study the incidence of AFLP was found to be 1 in 1000 and that of OC 1 in 190 deliveries. Following the formal study period, we continued to monitor new cases of AFLP and OC presenting to the obstetric unit for a further 12 month period. Four more cases of AFLP and 20 of OC were diagnosed and therefore the incidence of the two conditions remained unchanged at 1 in 1000 and 1 in 190, respectively. These high incidence values may reflect increased awareness and interest within our obstetric and gastroenterology departments but we cannot exclude a particular susceptibility of the indigenous Celtic population.

We acknowledge that there are no properly conducted trials to judge the merits of any particular line of treatment. There is no uniformity of management protocols for any of the specific liver disorders of pregnancy and expert opinion is divided, particularly in HELLP syndrome<sup>17-18</sup> where there is no consensus as to whether conservative treatment, aggressive medical treatment, or premature delivery gives superior results. There is more agreement about the importance of rapid early delivery in the management of AFLP<sup>3-5, 17-33</sup> but again this is based on clinical observation and comparison with historical reports rather than controlled trials.

During this study, we observed a high incidence of pregnancy specific liver disorders yet encountered no maternal deaths and very low fetal mortality. We attribute this to close cooperation between gastroenterologists and obstetricians, and a proactive policy of early delivery.

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### Bleeding peptic ulcer

We read with interest the paper on prediction of therapeutic failure after adrenaline injection plus heater probe treatment in patients with bleeding peptic ulcer by Wong and colleagues (*Gut* 2002;50:322-5). Even though the authors qualified their generalisation, the statement that "elderly patients often succumb to their concomitant illnesses rather than the bleeding itself" needs to be challenged as being unnecessarily defeatist, given the fact that timeliness of surgical intervention<sup>1</sup> and, as shown below, postoperative management at the intensive care level, may be more crucial to survival than comorbidity as such.

### Case report

A 70 year old woman with congestive cardiac failure (including radiographically validated left ventricular failure) and chronic obstructive airways disease experienced an episode of haematemesis and melaena with an associated blood pressure of 78/48 mm Hg on the 1 March 2002, which was the eighth day of her hospital stay. Endoscopy revealed a large actively bleeding duodenal ulcer, which was managed with endoscopic haemostasis, rapidly followed by definitive laparotomy and under running of the bleeding vessel. She was then transferred to a neighbouring hospital for postoperative intensive care management, and this included a 24 hour period of artificial ventilation. On the 11th postoperative day, having been repatriated to our hospital, she was clinically much improved even though

her arterial blood tensions while breathing room air were as follows: partial oxygen tension (paO<sub>2</sub>) 4.9 kPa (normal range 10-14), partial carbon dioxide tension (paCO<sub>2</sub>) 6.9 kPa (normal range 4.5-6.1), and oxygen saturation 70%, with concurrent transcutaneous oxygen saturation 72% (normal range 95-98%). Her clinical status continued to improve on diuretics, angiotensin converting enzyme inhibitors, bronchodilators, and supplemental oxygen. On her 25th postoperative day, lung function tests revealed a one second forced expiratory volume (FEV<sub>1</sub>) of 0.86 litres (40% predicted), forced vital capacity (FVC) of 1.59 litres (61% predicted), and an FEV<sub>1</sub>/FVC ratio of 54% (typically less than 70% in airflow obstruction). She could now perform a modified version of the "shuttle" walk<sup>2</sup> for a distance of 30 m briskly, without stopping for breath, and also without supplemental oxygen. Repeat arterial blood gas tensions on 30 March 2002 showed paO<sub>2</sub> 7.7 kPa and paCO<sub>2</sub> 5.8 kPa while breathing room air.

### Comment

On the basis of age, comorbidity, shock at presentation, and endoscopic stigmata of recent haemorrhage, this patient had a high risk of death with or without surgical intervention.<sup>3</sup> Only timely intervention and impeccable postoperative care could tip the scales in her favour, hence the successful outcome documented here.

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### References

- 1 Wheatley KE, Snyman JH, Brearley S, *et al*. Mortality in patients with bleeding ulcer when those aged 60 or over are operated on early. *Br Med J* 1990;301:272.
- 2 Singh SJ, Morgan MDL, Scott S, *et al*. Development of a shuttle walking test of disability in patients with chronic airways obstruction. *Thorax* 1992;47:1019-24.
- 3 Rockall TA. Management and outcome of patients undergoing surgery after acute upper gastrointestinal haemorrhage. *J R Soc Med* 1998;91:518-23.

## CORRECTIONS

The authors of Marchbank *et al* (*Gut* 2002;51:787-92) in the December issue of the journal, have noted a typographical error in their paper. In the results section, it should

state that the pH of the two subjects who were taking proton pump inhibitors who did not show a change to the larger form of TGF $\alpha$  had a pH of less than, and not greater than 4 as published. The authors apologise for the error.

The following errors occurred in the paper "Prospective study of liver dysfunction in pregnancy in Southwest Wales" in the December issue by Ch'ng *et al* (*Gut* 2002;51:876-80) as final author corrections were not included. The published version does not clearly distinguish those patients in whom pre-eclampsia was the sole identifiable cause of liver dysfunction from those in whom pre-eclampsia co-existed with another cause such as HELLP syndrome, obstetric cholestasis, or sepsis. The corrections are to the abstract, tables 1, 2, and 3, and part of the text of the results section on page 878 under the sub-heading "Diagnoses accounting for abnormal liver tests", and to two of the references. The journal apologises for the errors.

In the abstract, under methods, the second sentence should read "Patients with abnormal liver tests were assessed and followed throughout and after pregnancy. Medical advice was provided to obstetric teams."

### Pregnancy specific conditions

Pre-eclampsia was a common underlying abnormality seen in 68 patients (48%) but was the sole identifiable cause of liver dysfunction in only 15. Complete<sup>6</sup> and incomplete<sup>7</sup> HELLP syndrome occurred in 30 patients of whom 29 were pre-eclamptic making this the commonest diagnosis accounting for abnormal liver tests. In most of those patients with incomplete or partial HELLP syndrome, the platelet count dropped abruptly by more than 50% in parallel with abnormal liver tests. OC was diagnosed in 23 patients (16%); two of whom had pre-eclampsia. Eleven patients (8%) had deranged LFT associated with hyperemesis gravidarum and all responded well to conservative management or oral steroids; none of these developed pre-eclamptic liver dysfunction later in pregnancy. AFLP was diagnosed in five patients (4%), three of whom needed prolonged post-natal hospitalisation because of multi-organ involvement; none of these five patients had pre-eclampsia. Clinical details of these patients have been presented and published recently.<sup>11 12</sup>

In "Other contributory conditions" the first sentence should read "Seventeen patients had abnormal liver tests in association with sepsis,

**Table 1** Aspartate aminotransferase (AST), gamma glutamyl transpeptidase ( $\gamma$ GT), and bilirubin values for specific pregnancy related liver disorders

	AST (U/l)	$\gamma$ GT (U/l)	Bilirubin ( $\mu$ mol/l)
HELLP syndrome	66 (41-1123)	24 (6-209)	13 (4-155)
Obstetric cholestasis	210 (30-519)	29 (8-278)	14 (6-34)
Pre-eclamptic liver dysfunction alone	68 (36-210)	18 (7-51)	7 (3-12)
Hyperemesis gravidarum	51 (9-280)	23 (2-64)	25 (4-33)
AFLP	278 (86-542)	50 (22-209)	50 (19-61)

Values are median (range).

HELLP, haemolysis, elevated liver enzymes, low platelets; AFLP, acute fatty liver of pregnancy.

**Table 2** Diagnoses accounting for abnormal liver tests

	n	No with ↑ AST	No with ↑ γGT	No with ↑ bilirubin	No with ↑ urate	No with low platelets
Group 1—Pregnancy specific						
HELLP syndrome (5 complete, 25 partial)	30	30	12	10	29	30
Obstetric cholestasis	23	22	10	2	17	0
Pre-eclampsia alone	15	14	4	0	13	0
Hyperemesis gravidarum	11	7	4	5	3	1
Acute fatty liver of pregnancy	5	5	3	4	5	3
Hepatic infarct/haematoma	1	1	1	1	1	1
Group 2—Other conditions						
Postoperative (caesarean section)	22	21	10	3	21	7
Sepsis	17	17	6	2	12	2
Placental pathologies	12	11	4	3	9	3
Diabetes	8	6	5	1	5	4
Drug related	4	1	4	1	N/A	2
Bile duct stones	3	3	2	2	1	0
Hepatitis C	2	2	1	0	0	0
Group 3—Diagnosis obscure	14	8	4	1	6	0

N/A, not available.

**Table 3** Timing of liver dysfunction. Onset of specific pregnancy related liver disorders (in weeks' gestation)

HELLP syndrome	36 (25–38)
Obstetric cholestasis	35 (21–39)
Pre-eclamptic liver dysfunction	37 (25–40)
Hyperemesis gravidarum with liver dysfunction	9 (6–14)
AFLP	38 (32–38)

Values are median (range).

HELLP, haemolysis, elevated liver enzymes, low platelets; AFLP, acute fatty liver of pregnancy.

most commonly caused by urinary tract infection (9 patients); 5 of these 17 were also pre-eclamptic."

References 11 and 12 should be as follows:

- 11 **Ch'ng CL**, Morgan M, Kingham JG. Acute fatty liver of pregnancy in South Wales, UK. *J Hepatol* 2002;**36**(Suppl 1):186.
- 12 **Ch'ng CL**, Morgan M, Kingham JGC. Acute fatty liver of pregnancy in South Wales, UK. *Gastroenterology* 2002;**123**(Suppl 1):53.

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## NOTICES

### The national register of hepatitis C infections with a known date of acquisition.

The register steering group invite clinical and epidemiological researchers to submit proposals to access data held in the register. It is envisaged that a variety of studies might benefit from linkage with or access to the register, and proposals from all specialities and institutions are welcomed. Any researchers interested in applying for access to information held within the national register should contact the register co-ordinator (see below) for a list of available data and an application form. Study proposals should then be submitted to the register co-ordinator by **16 December 2002**.

Further information: Dr Helen Harris (Register Co-ordinator) or Ms Lisa Beck (Research Assistant), Immunisation Division, Communicable Diseases Surveillance Centre, Public Health Laboratory Service, 61 Colindale Avenue, London NW9 6EQ. Tel: +44 (0)20 8200 6868 ext 4496; fax: +44 (0)20 8200 7868; email: hharris@phls.nhs.uk or lbeck@phls.nhs.uk

### 17th International Workshop on Therapeutic Endoscopy

This will be held on 3–5 December 2002 in Hong Kong. Further information: Professor SC Sydney Chung, Endoscopy Centre, Prince of Wales Hospital, Shatin, NT, Hong Kong. Tel: +852 2632 2233; fax: +852 2635 0075; email: info@hksde.org

### Advances in the Inflammatory Bowel Diseases

This conference will take place on 6–7 December 2002 in New York, USA. Further information: Heather Drew, Imedex, 70 Technology Drive, Alpharetta, GA 30005-3969, USA. Tel: +1 770 751 7332; fax: +1 770 751 7334; email: h.drew@imedex.com; website: www.imedex.com

### 15th European Intensive Course (SMIER) Digestive Endoscopy

This course will take place on 16–17 December 2002 in Strasbourg, France. Further information: Michele Centonze Conseil, 6 bis Rue des Cendriers, 75020 Paris, France. Tel: +33 1 44 62 68 80; fax: +33 1 43 49 68 58.

### The Future of Gastro-entero-hepato-pancreatology is bright

This Academic Farewell Symposium of Guido NJ Tytgat will be held on 12 December 2002 in Amsterdam, the Netherlands. Deadline for registration is 1 November 2002 (no registration fee) and registration should be done via email to: j.goedkop@amc.uva.nl.

### Cancer of Oesophagus and Gastric Cardia: from Gene to Cure

This conference will be held on 13–15 December 2002 in Amsterdam, The Netherlands. Further information: European Cancer Centre, PO Box 9236, NL 1006 AE Amsterdam, The Netherlands. Tel: +31 (0)20 346 2547; fax: +31 (0)20 346 2525; email: ecc@ikca.nl

### Imaging of the Abdomen: an Update

This will be held on 23–24 January 2003 in Amsterdam, the Netherlands. Further information: visit the website www.epgs.nl or email epgs@amc.uva.nl. Tel: +31 20566 3926/4386.

### Surgery of the Foregut

This meeting will be held on 17–18 February 2003 in Florida, USA. Further information: Cleveland Clinic Florida, Office of CME, 2950 Cleveland Clinic Boulevard, Weston, FL 3331, USA. Tel: +1 954 659 5490; (toll free: +1 866 293 7866); fax: +1 954 659 5491; email: cme@ccf.org