large placenta would be expected to have a high placental flow to compensate for anaemic anoxia of the fetus. The uptake was 19·5 m.c.p.—above 2 S.D. of normal. The patient with the large fibroid uterus would have a distorted and abnormally high uterine flow superimposed on the placental flow, and her uptake was 21·6 m.c.p.

With this supporting clinical evidence we felt justified in relating the uptake to the outcome of the pregnancy. Analysis of the results showed that the isotope uptake by anterior placentae was significantly reduced in pregnancies resulting in growth-retarded babies. This association also seemed to apply to lateral placentae but not to posterior placentae. As we did not adjust the probe to try to eliminate erratic absorption from posterior placentae by the fetus, liquor, and uterine muscle these factors may explain the inconsistency.

We appreciate antepartum haemorrhage may be expected to interfere with and impair placental function but it was essential to include these cases in a retrospective study of this type. Their inclusion was supported by the fact that there was no significant difference in uptakes between patients delivering normal babies who had bled and those who had not.

The isotope uptake by the placenta was statistically unrelated to the gestation of the pregnancy. This is of considerable potential clinical value because all available serial placental function tests depend on an accurate estimation of the maturity of the pregnancy, which it is often impossible to make. If our results are substantiated by a prospective study then random single sample tests of placental function and fetal wellbeing could be performed regardless of estimated maturity.

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SHORT REPORTS

Uterine Rupture in Labour

Rupture of the uterus may result from obstetric mismanagement; dehiscence of a previous caesarean scar; hyperstimulation of the intact uterus; direct trauma during delivery; or a combination of these factors. The policy of allowing women who have had a previous caesarean section for non-repetitive causes to have a trial of spontaneous labour has meant that more women are at risk of uterine rupture: thus of 143 cases, 43 followed a previous caesarean section.[1] Only two of the 18 maternal deaths from uterine rupture reported in the most recent maternal mortality report[2] were scar ruptures and only three of the 18 had received intravenous oxytocin but this report covers 1967-9, before the current tendency to use high doses, with resultant risk of hyperstimulation of the uterus.

The danger of rupture may be increased when epidural analgesia is used because hyperstimulation is less easily detected. Difficult vaginal delivery and intrauterine manipulation may tear the lower uterine segment, particularly if it has been weakened by a previous caesarean section, or is very thin because of high parity or hyperstimulation. A combination of any two of these factors is especially dangerous. We have therefore reviewed five cases of uterine rupture in labour occurring in the King's College Hospital Group during an 18-month period in 1973-4.

Patients

The total number of deliveries during this period was 5835, an incidence of rupture of 1 in 1166. All patients were multigravida; oxytocin stimulation was used in three of the five cases and intravenous prostaglandin E.2. in another. Three patients (cases 1, 3, and 5) had epidural analgesia. The clinical features and treatment are analysed in the table.

Discussion

Delfe and Eastman reported an incidence of uterine rupture of 1 in 1000 at Johns Hopkins Hospital.[3] Three decades later the incidence of rupture at King's College Hospital is 1 in 1166. The traditional view that the combination of oxytocin and high parity is dangerous should still be respected—as the experience of two grandmultipara bears out, especially when oxytocin is given in high dosage.[4] When oxytocin is used in grandmultipara or in patients with a previous caesarean scar very careful supervision is called for.

The commonly held view that epidural analgesia is unsuitable for a patient with a previous caesarean section scar has been challenged.[5] Nevertheless, the removal of pain as a warning symptom may lead to delay in diagnosis, even though the local analgesia induced permits palpation of the lower segment during the course of vaginal examination.

The difficulty in diagnosis is the crux of the problem and is well illustrated by cases 4 and 5. In case 4 the diagnosis of uterine rupture was unsuspected until an emergency caesarean section was performed because of a prolapsed cord. In case 5 the possibility that the previous scar might rupture was kept constantly in mind and the lower segment palpated at regular intervals during labour. Nevertheless, the rupture was missed on palpation even when the fetus developed an unexplained tachycardia suggesting that rupture had occurred.

Continuous monitoring of the uterine contractions and fetal heart rate offer the best chance of avoiding hyperstimulation and of diagnosing fetal distress indicating that rupture may be occurring.

Analysis of Five Cases of Uterine Rupture

Case no.	Age	Parity	Previous Caesareans	Induction	Stimulation	Duration of labour	Hyperstimulation	Monitoring in labour	Mode of delivery	Diagnosis	Treatment
1	32	4	Nil	Yes	PG.E.2 2mgm/ 500 ml	6 hours 30 min	Yes	Yes	Forceps	III stage PPH E.U.A.	Hysterectomy
2	33	4	Nil	No	Oxytocin 4 units/ 500 ml	8 hours 15 min	Yes	No	Abdominal	I stage Fetal death	Repair of rent. Sterilization
3	32	4	One	Yes	Oxytocin 4 units/ 500 ml	22 hours	No	Yes	Vaccum ext.	III stage P.P.H. E.U.A.	Hysterectomy
4	25	2	One	No	None	1 hour 30 min	No	No	Abdominal	I stage Cord prolapse	Repair of rent. Sterilization
5	31	1	One	Yes	Oxytocin 8 units/ 500 ml	7 hours 10 min	No	Yes	Abdominal	I stage Fetal tachycardia	Repair of rent. Sterilization

P.P.H. = Postpartum haemorrhage. E.U.A = Examination under anaesthesia.

The risk to the patient and the fetus if the uterus ruptures is serious and even when mother and baby survive the mother's future childbearing capacity is usually lost. Clearly, uterine hyperstimulation must always be avoided and oxytocin and prostaglandin should not generally be used in the grandmultipara or the patient who has previously had a caesarean section. If it is felt necessary to use these agents then continuous monitoring of labour is essential, especially if epidural analgesia is to be employed.

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Busulphan Toxicity Syndrome caused by Chlorambucil

The well-recognized syndrome of busulphan toxicity comprises diffuse interstitial fibrosis, cutaneous pigmentation, and symptoms resembling adrenal cortical insufficiency.[1] These complications tend to occur after relatively long-term treatment and this paper records two patients who developed toxicity during treatment with chlorambucil for chronic lymphocytic leukaemia for three years.

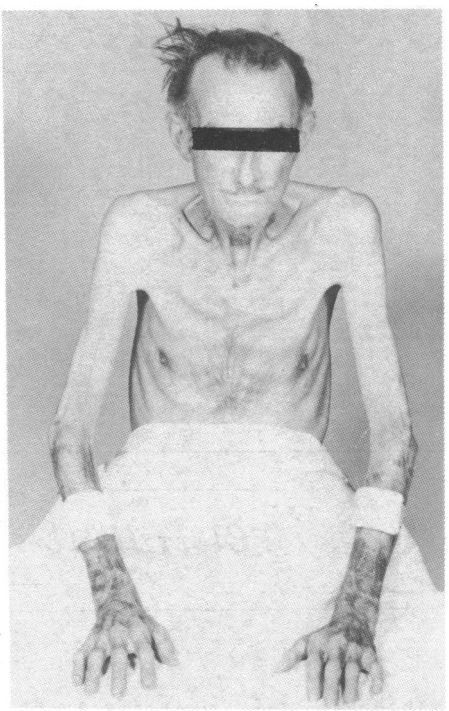
Case Histories

A.B., aged 60, had responded well to corticosteroid treatment and was on a low dose of prednisolone for three years. But chlorambucil was prescribed when signs of deterioration developed. After a year his weight began to fall and he again showed clinical deterioration. Chlorambucil and prednisolone were increased. Despite regression of the leukaemia the patient got worse (see figure). Endeavours to identify a coexistent malignancy were unsuccessful. At this clinical nadir the platelet count was 7×10^9/l, the bone marrow was densely lymphocytic, but normal haemapoietic cells were represented. A dose of two mg vincristine was given and within a week the platelet count rose to 50×10^9/l. This could either be attributed to vincristine or to recovery from chlorambucil myelosuppression. But the count fell again and complications attributed to vincristine toxicity developed—urinary obstruction and the syndrome of inappropriate A.D.H. secretion.

C.D. was 67 when she was prescribed chlorambucil for chronic lymphocytic leukaemia. There was a rapid haematological response, so chlorambucil was stopped for one year and restarted for submandibular lymph node enlargement. After taking two mg chlorambucil daily for three months she became weak and breathless. Chlorambucil was again withheld and the respiratory symptoms and radiological signs dispersed during the following months. Twenty months later chlorambucil was prescribed again, and she had repeated episodes of breathlessness, attributed to lower respiratory tract infections. Gross pulmonary changes due to chlorambucil may have produced a particular susceptibility to acute respiratory infections.

Discussion

The pulmonary changes originally described in association with busulphan treatment[1] have since been seen to complicate the course of patients receiving other cytotoxic drugs.[2] Fatal interstitial pulmonary changes have been described in four patients receiving chlorambucil for chronic lymphocytic leukaemia.[3] The more remarkable syndrome of multiple toxic side effects associated with busulphan administration has not been described during chlorambucil treatment, or indeed with other cytotoxic drugs.



Gross emaciation of patient while in leukaemic regression.

Though the term "interstitial pulmonary fibrosis" has been used to describe the lung changes seen, the histological features indicate alveolar cell proliferation with morphological abnormalities. The fact that the pulmonary changes are reversible suggests that clinical dysfunction precedes the development of fibrosis. Thus the reaction may not be predominantly fibrosis and the alternative descriptive term "pulmonary alveolar cell proliferation" may be preferable. Pulmonary function studies performed in patients during early stages of cytotoxic treatment displayed severe abnormalities in the absence of clinical symptoms or radiographic changes in the lungs.[4]

Patient A.B. has died. Necropsy showed nothing to contradict the conclusion that he was suffering untoward consequences of chlorambucil treatment. Had the drug administered been busulphan there would have been no hesitation in accepting this view.

These cases show that busulphan-associated complications may occur during chlorambucil administration and should be borne in mind as a possible consequence of treatment with cytotoxic drugs in general. As Dameshek and Gunz said: "It is of extreme importance to recognise the beginning of the syndrome since the drug(s) can be discontinued and the patient may recover; if this is not done, an irreversible situation with extreme wasting culminating in death will develop."[5]

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