respiratory acidosis as a result of pulmonary oedema consequent on her congestive cardiac failure, and this may simply have been a result of fluid overload from the volume of infusion she was receiving (the actual fluid volume infused is not stated). If this was in fact the case, infusion of bicarbonate may have compounded the problem by raising blood PCO_2 .

This case presentation demonstrates that measurement of blood PCO_2 , pH, and standard bicarbonate is mandatory to determine whether the patient has a metabolic or respiratory acidosis, as appropriate treatment will differ according to which type of acidosis is present.

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SIR,—We read with interest the "Lesson of the Week" by Mr M I Whitehead and others (17 May, p 1221) entitled "Acute congestive cardiac failure in a hypertensive woman receiving salbutamol for premature labour." We agree with the importance of the increased circulating blood volume in the pathogenesis of cardiac failure, but we would like to draw attention to the similar problem of ergometrine administration to the patient who has had salbutamol by intravenous infusion.¹

Ergometrine causes arterial and, probably more important, venous vasoconstriction. This decreases the vascular compartment, thus effectively increasing the circulating blood volume and the strain on the right side of the heart. The central venous pressure is known to increase by about 6 cm of water after intravenous ergometrine and the effects last over one hour.² It would be interesting to know if this patient and those reported in other papers received ergometrine. A combination of drugs is always potentially dangerous. Salbutamol with its widespread effect on the sympathetic system would seem potentially hazardous in labour, where alterations in blood volume occur anyway. The role of corticosteroids is not clear, but the addition of drugs like ergometrine and hypotensive agents which act on the vascular tree can only compound adverse effects.

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¹ Davies AE, Robertson MJS. *Br J Obstet* (in press).
² Vaughan Williams C, Johnson A, Leward R. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 1974;81:596.

SIR,—The reported case by Mr M I Whitehead and others (17 May, p 1221) of acute congestive cardiac failure in a hypertensive woman receiving salbutamol for premature labour provides a timely lesson on the dangers of obstetrical polypharmacy. One must question the necessity for such potentially dangerous drug therapy in a pregnant patient. The authors claim that Redman *et al*¹ showed that controlling hypertension during pregnancy has been associated with "a pronounced improvement in fetal survival." In fact, Redman's carefully controlled trial showed mainly a reduction in second trimester fetal losses in patients with chronic hypertension treated from early in pregnancy.² There is little evidence as yet that starting treatment at 27 weeks, as in the case reported, will alter the fetal prognosis.

In a modern neonatal unit the survival of infants of 32 weeks weighing 1500 grams is in excess of 85%. Continued intrauterine existence in the presence of severe hypertension may carry a greater risk than premature delivery. The administration of salbutamol in the case described may have been an attempt to thwart a physiological *deus ex machina*.

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¹ Redman CWG, Beilin LJ, Bonnar J. *Br J Obstet Gynaecol* 1977;84:419-26.

² Redman CWG, Beilin LJ, Bonnar J, Dunsted MK. *Lancet* 1976;ii:753-6.

*.*We sent copies of these letters to the authors, whose reply appears below.—Ed, *BMJ*.

SIR,—We welcome the correspondence resulting from our case report. These comments appear to have been prompted, firstly, by misinterpretation of the text and, secondly, by our failure to provide complete information. We did not *conclude*, as is stated by Dr P Davies, that salbutamol caused congestive cardiac failure but only *suggested* an association; and this misunderstanding may have arisen in part because the wording of this "Lesson of the Week" was an editorial comment, not our own comment. The mechanism that we discussed was again only a suggestion and we are delighted that three alternatives have been offered.

Our patient went into cardiac failure on two occasions, 10 hours apart. In reply to the question of Dr Robinson and Miss A Davies, neither was associated with the use of ergometrine. The second episode almost certainly resulted from cardiovascular changes at delivery further compromising an already ill patient who, as Dr Fogarty correctly surmised, was most probably fluid overloaded. The input in these 10 hours was 1500 ml and the output was 375 ml. The events preceding the first episode of heart failure were somewhat different and are presented in greater detail.

In the six hours prior to this first episode salbutamol and hydralazine were infused in 5% dextrose for three hours; the blood pressure ranged from 100/60 to 120/80 mm Hg and the pulse from 100 to 120 beats/min, and the fluid input equalled output at 300 ml. Hydralazine was then discontinued and salbutamol infused alone for a further three hours. During this time the blood pressure and pulse remained within the same ranges; the input was 390 ml and the patient became anuric. The plasma urea was 5.0 mmol/l (30 mg/100 ml) and the venous pH was 7.39 and 7.41.

Hydralazine increases cardiac output and work¹ and, as pointed out by Dr Fogarty, could have contributed to the cardiac failure. However, in our patient hydralazine therapy was not associated with a precipitous fall in blood pressure or with prolonged severe hypotension, and no rebound rise in blood pressure was observed when hydralazine was discontinued. The blood urea remained within the normal range. The total volume of fluid infused was relatively small and we would be surprised if this volume contributed to circulatory overload. We would agree with Dr P Davies that differentiation between respiratory and metabolic acidosis requires measurements of PCO_2 , pH, and standard bicarbonate. However, salbutamol is known to induce a

metabolic acidosis^{2,3} and in our opinion the observed pH and standard bicarbonate levels are more in favour of a compensated metabolic acidosis than respiratory acidosis. Thus although the suggestions of Dr Fogarty and Dr P Davies are valid we do not believe that their hypotheses are any more likely to be correct than ours.

Dr Poole-Wilson's proposal that the underlying mechanism was tachycardia is also perfectly valid, especially as the patient's pulse seldom fell below 95 beats/min in the 10 hours between the first and second episodes of cardiac failure. This proposal raises important issues related to clinical management as in our experience tachycardia of from 110 to 120 beats/min can be induced in most pregnant patients when salbutamol is given in low dosages of 5-10 $\mu\text{g}/\text{min}$. If this degree of tachycardia did indeed initiate the cardiac failure then should pregnancy-associated hypertension, which is not uncommonly associated with preterm labour, be regarded as a contraindication to salbutamol therapy?

Although, as Miss Crowley states, the fetal survival in modern neonatal units is now 85% at 32 weeks' gestation it is 95% at 35 weeks' gestation. Abrupt rises in maternal blood pressure can be transient and following effective therapy the pregnancy may progress until the fetal wastage is only 5% and not 15%. For these reasons obstetric polypharmacy is likely to continue, but we are in total agreement with Dr Robinson, Miss A Davies, and Miss Crowley concerning its potential dangers. The mechanism responsible for heart failure in this patient was almost certainly multifactorial and our view of this "Lesson of the Week" is best stated by re-emphasising our original conclusions concerning the need for careful monitoring in these situations.

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¹ Chattejee K, Parmley WW, Massie B, Wermer J, Klausner S, Norman A. *Circulation* 1976;54:879-83.

² Thomas DJB, Dove AF, Alberti KGM. *Br J Obstet Gynaecol* 1977;84:497-9.

³ Leopold D, McEvoy A. *Br Med J* 1977;ii:1152-3.

Progesterone, fluid, and electrolytes in premenstrual syndrome

SIR,—Mr P M S O'Brien and others (10 May, p 1161) have attempted to assess the relative roles of progesterone, fluid, and electrolyte changes in premenstrual syndrome. I would agree with their statement that the aetiology of premenstrual syndrome remains undetermined.

We have previously attempted to assess the importance of hormonal and electrolyte changes in premenstrual syndrome. Five women with premenstrual symptoms were studied in a metabolic unit during both an untreated and a progesterone-treated menstrual cycle. Mood was assessed by daily menstrual distress questionnaires,¹ and early morning temperature and weight were recorded daily. Blood samples were assayed for progesterone and 17-oestradiol. Twenty-four-hour urine samples were collected and androsterone, etiocholanolone, dehydroepiandrosterone, 11-oxoandrosterone, 11-oxoetiocholanolone, pregnanolone, 11-hydroxyandrosterone, 11-hydroxyetiocholanolone, allo-pregnenediol, and pregnane-

diol were measured.² We found no consistent pattern of hormonal or electrolyte change in the five subjects, and no consistent pattern of weight change in relation to menstruation. Interestingly, no obvious natriuretic effects were observed in any of the patients during progesterone administration, even (in one subject) with daily intramuscular injections of 100 mg progesterone.

I believe that both our failure to find any consistent changes and the inconsistent progesterone findings of Mr O'Brien and other workers^{3,4} are a reflection of at least two factors. Firstly, it is difficult to elucidate the aetiology of any condition until one has an accurate definition of the condition. There are many problems in defining the type, timing, and intensity of premenstrual symptoms. Sampson and Jenner¹ report on a control study in which 71% of subjects reported premenstrual symptoms, 82% recorded significant changes in fluid retention premenstrually, and 53% had significant changes in mood premenstrually. The suggestion is therefore that some mood and fluid retention changes are normal and not pathological. Where then is the borderline between "normal" and "having premenstrual syndrome?" Clinical studies^{5,6} find that the majority of women actively seeking treatment for premenstrual symptoms are parous and in their later reproductive years (30-50 years). However, many of the studies on the aetiology of premenstrual syndrome were undertaken on women who were not actively seeking help, their age range is younger, and they are childless. Most studies use different definitions of "premenstrual syndrome" and because of this results from differing studies are not comparable.

Secondly, the failure to find one consistent aetiological factor for premenstrual syndrome is that, as in other psychosomatic disorders, many aetiological factors are implicated. It appears logical that in a disorder which fluctuates regularly in relation to menstruation there will be hormonal changes which both precede and follow the symptoms of the disorder. Our understanding of the normal physiological and psychological changes of menstruation is growing and, hopefully, we will with time be able to quantify which physiological and psychological changes are normal and which become abnormal in that group of women we classify as having premenstrual syndrome.

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¹ Sampson GA, Jenner FA. *Br J Psychiat* 1977;130:265-71.

² Fenoughty M. M Med Sc thesis, University of Sheffield, 1975.

³ Backstrom T, Mattson B. *Neuropsychiatry* 1975;1:80-6.

⁴ Munday M. *Curr Med Res Opin* 1977;4, suppl 4:16-22.

⁵ Dalton K. *The premenstrual syndrome and progesterone therapy*. London: William Heinemann, 1977.

⁶ Sampson GA. *Br J Psychiat* 1979;135:209-15.

Circumcision and undescended testis

SIR,—In my opinion there is a definite place for the treatment of retraction of foreskin and applying hydrocortisone cream to prevent fibrosis and bring the skin forward in certain cases of non-retractile prepuces (28 June, p 1591). This can be done by the mother—either the mother is successful in retracting

this skin and the condition is cured or the mother fails and no further attempt for retraction is carried out after a month; therefore the question of adhesions does not arise. One can also break the adhesions and the prepuce under general anaesthesia rather than carrying out the full procedure of circumcision.

There are two more indications for circumcision before the age of 4 years: (1) Posthitis—a surprising number of doctors are not familiar with the treatment for inflammation of the prepuce only. (2) Pinhole opening in the prepuce, produced by fibrosis. In Moslem boys circumcision is recommended in the first seven days of life, though if this is not feasible it may be performed much later, as mentioned in the article.

In practical terms, to say that the mother would have noted whether the testes are both in the scrotum after a hot bath is not really very helpful, as a number of cases are still missed despite family doctors and school health clinics. Examining the child after putting him in a squatting position is helpful in bringing the retractile testes into the scrotum, and both sides can be examined at the same time.

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Unanswered questions on ectopic pregnancy

SIR,—Your recent leading article on ectopic pregnancy (3 May, p 1127) attempted to assess the demography of ectopic pregnancy. You adduced some statistics reflecting its current incidence, but a rise in incidence, you noted, might only signify better diagnosis of the condition so that it occupies a more prominent place on the diagnostic index. I believe that a truly meaningful demographic analysis of ectopic pregnancy must await clarification of its aetiology, which still remains obscure.

You cite as possible causes of ectopic pregnancy pelvic sepsis and usage of intra-uterine contraceptive devices (IUCDs). What of pelvic sepsis in this connection? There is certainly clinical confirmation of this relationship, perhaps more in women with primary infertility, though pelvic inflammatory states by no means always underlie involuntary childlessness or ectopic pregnancy. I reviewed the records of 325 consecutive patients diagnosed as having an ectopic pregnancy at operation in four large London hospitals during 1967-79, and found that pelvic inflammatory disease was uncommon (11%). The remaining 89% in this series had no demonstrable organic condition to explain their ectopic pregnancies, but 12% of patients had IUCDs and a further 2% were accounted for by progesterone-only contraceptive-pill failures.

How then do IUCDs relate to ectopic pregnancy? On circumstantial evidence, in part statistical^{1,2} as well as anatomical,³ and in the knowledge that ovulation and sperm penetration of the female genital tract are unaffected by IUCDs *in situ*,^{4,5} the following hypothesis for the mode of action of IUCDs was formulated.³ Effective intrauterine contraception induces an antifertility state by *inhibiting* tubal ovum migration, though with occurrence of the occasional ovarian pregnancy. Failed intrauterine contraception results in pregnancy but with an incidence of ectopic,

mainly tubal, implantation by reason of *disturbed* ovum migration along the oviduct.

Quite how failure of progesterone-only oral contraceptives fits into this hypothesis is difficult to rationalise. The consequences of this failure do seem similar to those of failed intrauterine contraception and this is documented in the literature (see Rantakylä⁶ for references). Perhaps a wider view of the imperfections besetting human reproduction should be taken. Maybe that involuntary and unexplained infertility preceding eventual pregnancy and effective antifertility states achieved by IUCDs and progesterone-only oral contraceptives are both manifestations of transiently aberrant tubal function, whereas ectopic, especially tubal, pregnancy and even early spontaneous abortion reflect disturbed tubal function causing errors in zygote nidation.

I suggest that the physiology of the human oviduct has been taken for granted for too long. Much is known about the workings of the hypothalamic-pituitary-ovarian axis and yet many common aberrations of human reproduction, iatrogenic and spontaneous, remain ill understood.

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¹ Vessey MP, Johnson B, Doll R, *et al. Lancet* 1974;ii:495-8.

² Lehfeldt H, Tietze C, Gorstein F. *Am J Obstet Gynec* 1970;108:1005-9.

³ Jonas EG. *Br Med J* 1975;iii:467.

⁴ Faucher GL, Ellegood JO, Mahesh VB, *et al. Am J Obstet Gynec* 1969;104:502-7.

⁵ Malkani PK, Suján S. *Am J Obstet Gynec* 1964;88:963-4.

⁶ Rantakylä P, Ylöstalo P, Järvinen PA, *et al. Acta Obstet Gynec Scand* 1977;56:61-2.

Quality of prescribing for children

SIR,—We read with interest the recent paper by Dr J C Catford (14 June, p 1435). Nine local general practitioners have participated in a prescribing study, from which it has been possible to identify all drugs prescribed for children under 12 years, dosage, quantity, and associated morbidity over a three-month period ending December 1979. We used Dr Catford's criteria of quality and our findings were similar to his own, 24 prescriptions out of a total of 1784 (1%) being for hazardous or undesirable drugs.

However, the fact that only a few drugs considered by Dr Catford to be hazardous or undesirable were prescribed for children says little about the quality of prescribing. This cannot be adequately assessed by simply recording the drugs used by doctors. Prescribing requires the doctor to consider and decide on appropriate and rational responses to a number of questions relating to a specific patient and problem: Is a drug required? If so, which one (or possibly more)? Which route and which preparation? What dose? How often? For how long? Will the drug be taken, and can I influence this by means other than those considered in previous questions? Relevant and important information such as the proportion of children who presented to the general practitioners and were not given drugs was unknown to Dr Catford, but he has restricted himself unnecessarily to a very small area of prescribing by describing only the drugs prescribed for children without knowledge of their indications, when presumably data on dose, dose-frequency, formulation, and the planned duration of therapy were available to him.