receive 80 mg fenfluramine daily. It is associated with an increase in intrasleep restlessness, during which more frequent spontaneous shifts to stage 1 sleep occur.¹⁹ Patients may be more conscious of their dreams during the periods of intrasleep restlessness. Phenothiazines, monoamine oxidase inhibitors, tricyclic antidepressants, amphetamines, and alcohol reduce REM sleep to below normal levels.²⁰⁻²² When these drugs are withdrawn an REM sleep rebound takes place, and the patient spends a higher proportion of the night than usual in dreaming sleep. Dreams become particularly vivid and disturbing.²⁰ Total withdrawal of vitamin C from the diet did not change the dream pattern induced by fenfluramine when compared with the pattern reported by subjects receiving a daily intake of 40 mg with the fenfluramine. Dreaming has not been reported in scorbutic patients,²³ and dreaming is not described as a mental change that accompanies scurvy.²⁴ Our results show that there is a definite relation between the dose of fenfluramine administered and the degree of change in sleep pattern.

Depression and acute psychotic episodes have been reported during or immediately after fenfluramine treatment.²⁵⁻²⁷ It seems that fenfluramine played a part in precipitating psychotic decompensation in three patients, in two of whom there was a previous history of mental illness.²⁸ One patient in our study complained of nightmares while on fenfluramine and developed a severe depressive illness. Fenfluramine was discontinued and her depression rapidly resolved. Hence, as well as its dose-related weight-reducing and anorectic actions, fenfluramine also exerts dose-related central effects, which may assume undesirable toxic proportions. Patients who dream or have nightmares while on fenfluramine may develop an acute psychotic episode. This possibility should be recognised when its use is contemplated in patients with a history of mental disease or in whom the disease is inadequately controlled with other drugs.

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Influence of simultaneous low amniotomy and oxytocin infusion and other maternal factors on neonatal jaundice: a prospective study

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Summary

In a prospective study of 196 consecutive single births a significant increase in serum bilirubin concentrations was found in infants born after low amniotomy induction and oxytocin infusion compared with those born spontaneously. This relationship was not dose-dependent and may have been associated with artificial interruption of pregnancy rather than the oxytocin itself. Infants delivered after spontaneous labour accelerated by oxytocin showed no such increase. The hormonal surge at the spontaneous onset of labour may affect fetal enzyme induction, but other factors, such as methods of infant feeding and oral contraceptive use, were found not to be significant.

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Introduction

The use of oxytocin infusion to induce labour is now routine in many centres. Simultaneous surgical and medical induction has been advocated,^{1 2} and the interval between induction and delivery has been reduced to about eight hours.^{3 4} Hazards of these procedures, however, include fetal distress and low Apgar scores.⁵ Oxytocin has been implicated in an increased incidence of neonatal jaundice,⁶⁻⁸ though other workers have failed to confirm this.⁹⁻¹¹

We have carried out a prospective study of the factors implicated in neonatal jaundice and report here the results.

Patients and methods

A total of 217 consecutive single deliveries at this hospital were considered for the study. Of these, 21 babies were excluded because of incomplete bilirubin data, birth weight below 2500 g, haemolytic disease, neonatal infection, or discharge from hospital within 48 hours. A further 15 infants were delivered by caesarean section. The remaining 181 babies were divided into three groups: A (54 infants), spontaneous onset of labour, no oxytocin used; B (28 infants), spontaneous onset of labour, oxytocin used to accelerate labour; C (99 infants),

labour induced by low amniotomy and simultaneous oxytocin infusion.

The Tekmar pump was used to administer the intravenous oxytocin. In group C two infusion regimens were used, in 75 cases a low-dose regimen—initially 2 units at 5 drops/min, increasing by 5 drops/min every 30 minutes to a maximum of 4 units at 40 drops/min—and in 24 cases an accelerated high-dose regimen initially 2 units at 10 drops/min, increasing by 10 drops/min every 20 minutes to a maximum of 10 units at 60 drops/min. In all cases the infusion rate was adjusted to a maintenance level in which contractions were moderately strong, occurring every two to three minutes, and lasting for 45 seconds.

Cord blood was obtained after delivery (day 1), and the infant's blood collected by heel-prick on the third and sixth postnatal days. Total serum bilirubin was estimated with a spectrophotometer within 24 hours of birth,¹² the upper limit of normal being taken as 205.2 $\mu\text{mol/l}$ (12.0 mg/100 ml).

Results

On days 1, 3, and 6 the mean serum bilirubin concentrations in group C were significantly higher than those in group A ($P < 0.05$) (table I). There were no significant differences, however, between groups A and B ($P > 0.05$). Fifteen of the 99 infants in group C had serum bilirubin concentrations above 205.2 $\mu\text{mol/l}$ compared with only one of the 54 infants in group A. There were no significant differences in mean gestational age or birth weight between the three groups (table II).

Table III shows the mean serum bilirubin concentrations for all 196 infants—that is, including the 15 delivered by caesarean section—related to factors known to affect those concentrations. Similar values were found whether the infants were delivered spontaneously, with assistance or by caesarean section. There were no significant differences in concentrations between breast-fed infants and those fed artificially, nor between infants born to mothers who had or had not used oral contraceptives in the previous year.

TABLE I—Mean ($\pm$ SD) total serum bilirubin concentrations ($\mu\text{mol/l}$) in the three infant groups

	Group A (n=54)	Group B (n=28)	Group C (n=99)
Day 1	39.2 $\pm$ 10.1	39.0 $\pm$ 10.8	44.0 $\pm$ 16.6
Day 3	104.3 $\pm$ 46.7	106.2 $\pm$ 51.0	127.9 $\pm$ 55.9
Day 6	78.0 $\pm$ 48.7	80.9 $\pm$ 45.5	111.8 $\pm$ 58.5

Conversion: SI to traditional units—Serum bilirubin: 1 $\mu\text{mol/l} \approx 0.06$ mg/100 ml.

TABLE II—Mean birth weight and gestational age in the three infant groups

	Group A (n=54)	Group B (n=28)	Group C (n=99)
Birth weight (g)	3350	3320	3300
Gestational age (weeks)	39.2	39.5	39.1

TABLE III—Mean ($\pm$ SD) neonatal serum bilirubin concentrations ($\mu\text{mol/l}$) relation to certain maternal and fetal factors

Factors	No of infants	Serum bilirubin concentration
Spontaneous vaginal delivery	158	108.4 $\pm$ 55.9
Assisted vaginal delivery	23	113.2 $\pm$ 62.2
Caesarean section	15	111.2 $\pm$ 49.2
Previous oral contraceptive use	61	114.7 $\pm$ 55.2
No previous use of oral contraception	92	119.4 $\pm$ 56.4
Breast-feeding	65	109.8 $\pm$ 52.1
Artificial feeding	113	113.5 $\pm$ 53.7

Discussion

Our finding of significantly increased serum bilirubin concentrations in babies delivered by surgical induction and

oxytocin infusion agrees with that of Davies *et al*⁷ and of Ghosh and Hudson⁶ but differs from the findings of Gould *et al*¹⁰ and Davidson *et al*.⁹ Davidson *et al* found that the mean total bilirubin concentration in cord blood was lower in babies delivered after oxytocin-induced labour. Their sample included only 14 cases, however, and the difference was not statistically significant.

Serum bilirubin concentrations above 205.2 $\mu\text{mol/l}$ in full-term infants should always be regarded as abnormal.¹³ In our series 15 of the 99 infants delivered by oxytocin induction had serum bilirubin concentrations greater than 205.2 $\mu\text{mol/l}$ compared with one of the 54 delivered without oxytocin.

Beazley and Alderman¹⁴ found a dose-dependent, progressive increase in serum bilirubin in infants delivered by high-dose or prolonged oxytocin infusion techniques. Our results did not support this finding, nor did the serum bilirubin concentrations differ significantly between the high- and low-dose regimens of group C ($P > 0.05$). We cannot therefore agree with Ghosh and Hudson,¹⁵ who contended that a reduced oxytocin dosage would "virtually eliminate neonatal hyperbilirubinaemia of unknown origin." Calder *et al*¹⁶ suggested that interruption of pregnancy rather than the direct effect of oxytocin causes hyperbilirubinaemia. Induced labour may lack the normal hormonal surge of spontaneous labour^{17,18} that may be responsible for fetal hepatic enzyme induction. Thus in induced labour there would be no enzyme induction.¹⁹

The direct association between oxytocin and a raised bilirubin concentration may be spurious. Indeed, Calder *et al*¹⁶ found higher neonatal bilirubin concentrations after labour induced by either oxytocin or dinoprostone than in those of spontaneous onset. Our findings agree with those of Gould *et al*¹⁰ but differ from those of Wong and Wood²⁰ and Arthur *et al*,²¹ as we could find no significant difference between breast-fed and artificially fed babies. We also could not confirm that previous oral contraceptive use had any icterogenic effect on the newborn.²²

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