conjugated oestrogen treatment there was, however, a significant acceleration in platelet aggregation in both groups ($P < 0.05$). The shortening was still present six months later, at the end of the follow-up.

Thromboelastography—There was no change in reaction time (r), thrombin phase (k), or maximum amplitude (ma).

Discussion

Prothrombin time and clotting times in factor VII and X assays are accelerated in women who have had three months' hormone replacement treatment with conjugated equine oestrogens, but there is no evidence from these tests of a cumulative effect. The pattern of increase of factors VII and X was similar to that recorded with combined oestrogen-progestogen oral contraception,[2 3] but, unlike the contraceptive, conjugated oestrogens produced no further acceleration in these assays when they were given for longer than three months.

At 12 months the thrombin phase of platelet aggregation, measured by the Chandler's tube technique, also became significantly accelerated. This test is a sensitive index of changes in intrinsic clotting that affect the thrombin phase of platelet aggregation and is not specific for platelet function. The importance of this finding is not clear, but the result does suggest that there is a widened spectrum of adverse effects and that other changes may be taking place in the coagulation mechanism in addition to those monitored.

The absence of any changes in the PTT test and thromboelastography in this study might suggest that conjugated equine oestrogens have less overall effect on intrinsic blood coagulation than combined synthetic oestrogen-progestogen contraceptives. After six months' treatment with the latter there was a significant reduction of PTT and of r values in the thromboelastogram.[3] The oral contraceptive study was, however, performed on larger groups, though only when these were combined was a significant result achieved. Groups of 31 and 34 women on different individual formulations of combined oestrogen-progestogen preparations did not show a significant shortening of the PTT. The present group of 20 menopausal women studied for 18 months of continual oestrogen administration is much smaller than the groups in our oral contraceptive studies. Too much reliance, therefore, cannot be placed on the negative findings.

Different dose regimens or dose equivalents of oestrogen may produce varying effects in haemostatic tests. Alternatively, Davies *et al*[4] found smaller changes in blood clotting with oestriol succinate treatment than with the synthetic oestrogen ethinyloestradiol in a group of menopausal women who were treated sequentially. This might be taken to support the view that different types of oestrogen cause varying rates of acceleration of the haemostatic mechanism. These problems still need to be resolved.

Further efforts are therefore still required to find formulations and doses of oestrogens which, while relieving menopausal symptoms, do not accelerate blood clotting and platelet aggregation.

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References

1 Coope, J, Thomson, J M, and Poller, L, *British Medical Journal*, 1975, **2**, 139.
2 Poller, L, Tabiowo, A, and Thomson, J M, *British Medical Journal*, 1968, **3**, 218.
3 Poller, L, Priest, C M, and Thomson, J M, *British Medical Journal*, 1969, **4**, 273.
4 Davies, T, Fieldhouse, G, and McNicol, G P, *Thrombosis and Haemostasis*, 1976, **35**, 403.

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Evaluation of fetal wellbeing by antepartum fetal heart monitoring

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Summary

The value of antenatal fetal heart rate monitoring was assessed in 301 patients. Tracings from each patient were classified as "reactive" or "non-reactive." Perinatal mortality, fetal distress in labour, caesarean section for fetal distress, and the incidence of low Apgar scores were all significantly increased in the non-reactive group.

Introduction

Since the results of intrapartum fetal monitoring correlate closely with the immediate neonatal outcome,[1-4] close attention to fetal heart rate patterns during the antenatal period might be of value in assessing fetal wellbeing. Antepartum fetal heart rate patterns may be studied by means of the oxytocin challenge test or a "non-stress" test. Though the oxytocin challenge test is useful in evaluating the condition of the fetus before birth,[5-8] it is time-consuming, may cause hyperstimulation, and is not easily repeatable. We therefore report the results of a non-stress[9-12] approach to antepartum fetal heart monitoring.

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Materials and methods

From 1 July 1975 to 30 June 1976, 800 tracings were obtained from 301 patients with singleton pregnancies. The indications for monitoring are listed in table III. Heart rate and fetal activity patterns were recorded with three conventional fetal heart rate monitors: the Roche CTG5 (phonocardiography; 225 tracings), the Roche 540 (ultrasonography; 554 tracings), and the Hewlett-Packard 8030ACTG (electrocardiography; 21 tracings).

Fetal movements may be detected (*a*) by auscultation via the fetal heart rate sensor, (*b*) by observing or palpating the maternal abdominal wall, (*c*) subjectively by the patient, or (*d*) from a transient rise on the uterine contraction channel. Fetal movements were sometimes not noticed by the patient or shown on the uterine contraction record or

both when the observer had detected one by auscultation, observation, or palpation. In 100 consecutive patients, in all of whom fetal movements were detected by the observer, 64 were felt by the patient and 78 were recorded on the uterine contraction channel.

Patients were examined on a couch at 60° to the horizontal. For the last 10 minutes of each recording the patient was turned on her side. Maternal blood pressure and pulse were checked at the beginning and end of each recording. Three patients showed a rise in blood pressure on change to the left lateral position: there was no change in the fetal heart rate pattern.

Tracings were defined as either "reactive" (fig 1) or "non-reactive" (fig 2). Reactive tracings showed (*a*) accelerations in fetal heart rate of 15 beats/min in response to fetal movements (four such responses in 20 minutes; (*b*) a "baseline variability" of 5-20 beats/min; and (*c*) a basal fetal heart rate of 120-160 beats/min. Non-reactive tracings were those that did not show these features. Recordings were continued for at least 20 minutes when the heart rate pattern was reactive, and for at least 40 minutes when the pattern was non-reactive. These times were used following the suggestion that fetuses have rest-activity cycles of 20-40 minutes' duration.[13]

When the tracing was reactive the procedure was repeated one week later unless there was an earlier deterioration in the clinical condition —for example, a rising blood pressure, increased proteinuria, or diminished fetal movements. Non-reactive tracings were repeated within 24-48 hours; if the patient had been taking drugs such as diazepam or nitrazepam, which we found could depress fetal activity, these were discontinued when possible before the repeat tracing. Sixty-two patients had been prescribed a sedative, and of these, 25 showed a non-reactive tracing. When tested again 24-48 hours after stopping the drug 20 showed reactive tracings (table I).

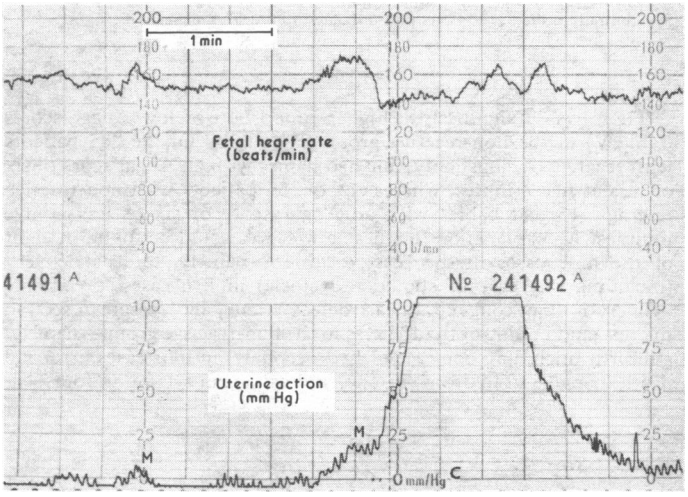

FIG 1—Reactive tracing. Acceleration of fetal heart rate occurs with fetal movements (M). No deceleration occurs with uterine contraction (C).

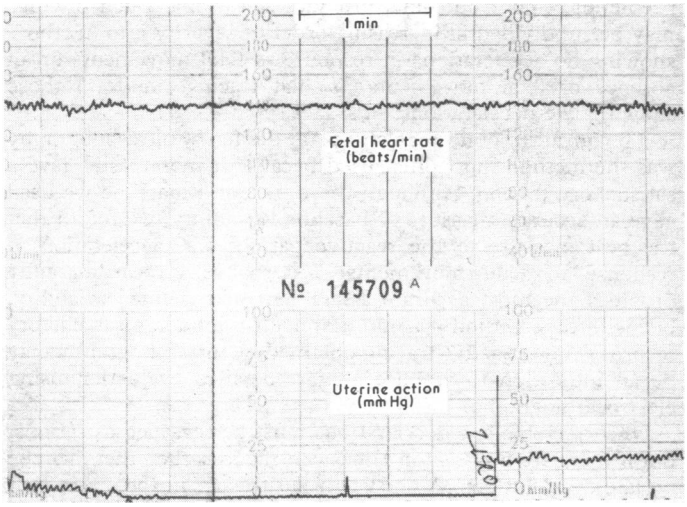

FIG 2—Non-reactive tracing. No fetal movements or fetal heart accelerations are present.

TABLE I—*Effect on non-reactive tracings of discontinuing sedatives*

Sedative	Total No of patients using drug	Patients with non-reactive tracings initially		
		Total	Repeat tracing 24-48 hours after stopping drug	
			Reactive	Non-reactive
Diazepam	32	14	12	2
Nitrazepam	26	9	7	2
Phenobarbitone	1	1	1	
Phenytoin	2			
Amitriptyline	1	1		1
Total	62	25	20	5

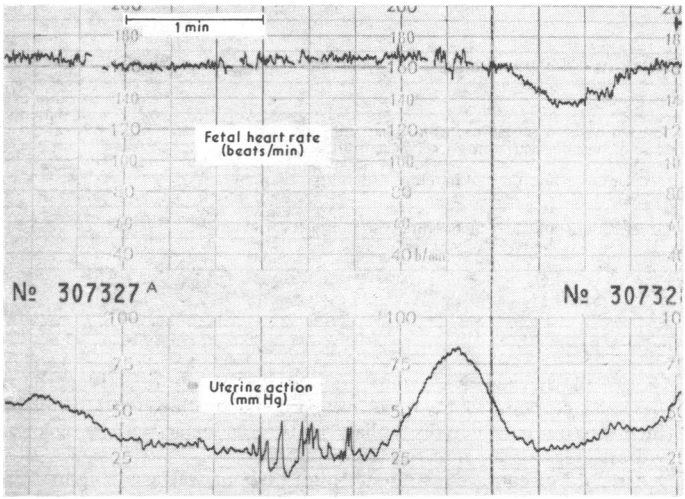

FIG 3—Late deceleration. Fetal heart slows towards end of uterine contraction and remains below basal level for one minute.

When decelerations (fig 3) occurred the patient, if not already an inpatient, was admitted to hospital. Urgent consultation was sought with the clinician in charge, and if delivery was not quickly effected the tracing was performed at least twice daily with continued consultation and appraisal of the whole clinical picture.

Our ultrasound machine has a "depth-ranging" capability and displays a running three-beat average of the heart rate.[14] We compared the external fetal heart rate record in labour obtained with this machine with the direct electrocardiogram in the same patient and found a close correlation.

Results

Altogether 245 patients had reactive and 56 non-reactive tracings. Five patients in the non-reactive group showed late decelerations. Satisfactory tracings were obtained in all cases examined by ultrasonography, but we failed to obtain a satisfactory tracing on 50 occasions when using phonocardiography and on 13 occasions when using electrocardiography. The gestational ages and complications of pregnancy in the reactive and non-reactive groups are shown in tables II and III. Table IV lists the abnormalities of fetal heart rate in the non-reactive group.

A total of 189 patients (160 in the reactive group and 29 in the non-reactive group) had a normal delivery, 56 (48 in the reactive group and 8 in the non-reactive group) an operative vaginal delivery, and

TABLE II—*Distribution of gestational ages among patients in reactive and non-reactive groups. Figures are numbers of patients*

	Gestation in weeks			Total
	28–36	37–40	>40	
Reactive group	34	117	94	245
Non-reactive group	16	18	22	56

TABLE III—*Complications of pregnancy necessitating monitoring in reactive and non-reactive groups of patients*

	Reactive	Non-reactive	Total
Normal	16		16
Suspected late for dates	94	22	116
Suspected intrauterine growth retardation and bad obstetric history	81	18	99
Oedema, hypertension, and proteinuria in pregnancy	35	4	39
Antepartum haemorrhage	6	3	9
Rhesus isoimmunisation	4	5	9
Diabetes	3	1	4
Other (external cephalic version, threatened premature labour, etc)	6	3	9
Total	245	56	301

TABLE IV—*Abnormalities of fetal heart rate tracing in non-reactive group*

		No of patients
Normal baseline variability (5–20 beats/min)		21
Loss of baseline variability (<5 beats/min)		20
Decelerations and normal baseline variability	Early	4
	Variable	4
	Late	1
Decelerations and loss of baseline variability	Early	1
	Variable	1
	Late	4
	Total	56

56 (37 in the reactive group and 19 in the non-reactive group) caesarean section. There were five perinatal deaths—four stillbirths (including one case of hydrocephaly) and one neonatal death (congenital hydrops)—all in the non-reactive group.

A record of continuous monitoring in labour was available for 228 patients (191 in the reactive group and 37 in the non-reactive group) (table V). Fetal distress during labour, as evidenced by a pathological fetal heart rate pattern, occurred in two patients in the reactive group and 17 in the non-reactive group, this difference being significant ($P < 0.001$). Details of the pathological fetal heart rate pattern in labour and the antepartum fetal heart rate pattern of patients with the labour abnormality are shown in table VI. Of the two patients in the reactive

TABLE V—*Analysis of features present in reactive and non-reactive groups*

	Reactive (n = 245)	Non-reactive (n = 56)	Significance of difference (χ^2 test)
Perinatal deaths		5	P<0·001
Continuous monitoring in labour	191	37	
Pathological fetal heart rate pattern in labour	2	17	P<0·001
Caesarean section for fetal distress:			
Before labour		1	P<0·001
During labour	1	7	
Apgar score ≤6 at one minute	24	29	P<0·001
Apgar score ≤6 at five minutes	9	13	P<0·001

group with fetal distress in labour, one was found to have an unsuspected placenta praevia and was delivered by caesarean section, and the other was delivered vaginally; both infants did well. Of the 17 patients in the non-reactive group with fetal distress in labour, seven were delivered by caesarean section (one neonatal death from congenital hydrops) and 10 were delivered vaginally (one hydrocephalic stillbirth). All 15 surviving infants had low Apgar scores but subsequently did well.

Five patients showed late decelerations on antepartum monitoring. Fetal death before labour occurred in two, 12 and 72 hours after these decelerations were first detected. In the first case caesarean section was delayed because of heparin treatment, while in the second case the fetus was thought to be too premature to affect delivery (28 weeks' gestation). One patient underwent caesarean section at 33 weeks of gestation. The 1100-g infant showed evidence of growth retardation but subsequently did well. The placenta was grossly infarcted. Induction of labour was effected in a non-diabetic patient, who delivered a 3960-g infant at 41 weeks of gestation. The neonatal course resembled that of an infant of a diabetic mother: the infant subsequently did well. In one case late decelerations occurred immediately after external cephalic version. These gradually improved, and two weeks later the patient had a spontaneous vertex delivery by the vaginal route of a healthy infant.

A patient with a "flat" tracing—that is, no baseline variability (by phonocardiography)—in the antepartum period defaulted from follow-up and returned two weeks later, when intrauterine death was diagnosed.

TABLE VI—*Details of pathological fetal heart rate pattern in labour, and antepartum fetal heart rate pattern of patients with labour abnormality*

Labour	No of patients	Antepartum monitoring	No of patients
		Non-reactive:	
Late decelerations, loss of baseline variability, and severe bradycardia	3	Loss of baseline variability	3
Late decelerations and loss of baseline variability	1	Late decelerations and loss of baseline variability	1
Late decelerations alone	7	Loss of baseline variability	4
		Normal baseline variability	3
Early decelerations with loss of baseline variability	4	Loss of baseline variability	2
		Normal baseline variability	2
Variable decelerations with loss of baseline variability	1	Loss of baseline variability	1
Loss of baseline variability	1	Loss of baseline variability	1
		Reactive:	
Late decelerations alone	2	Normal	2

NB: Fetal heart abnormalities included were those that could not be corrected—for example, by correction of uterine hyperstimulation—or attributed to drugs—for example, depressants.
Normal baseline variability 5-20 beats/min.
Loss of baseline variability <5 beats/min.
Severe bradycardia <100 beats/min unrelated to uterine contractions.

There was a significantly higher proportion of low Apgar scores (table V) in the non-reactive group ($P < 0.001$). Of the 245 patients with reactive tracings, only nine had babies with an Apgar score of six or less at five minutes, whereas of the 56 patients with non-reactive tracings, 13 had babies with an Apgar score of six or less at five minutes. An explanation for these low scores could be found in eight of the nine cases in the reactive group—namely, forceps delivery (including one case of shoulder dystocia) in five cases, precipitate delivery in one, congenital heart defect in one, and caesarean section in one—and in nine of the 13 cases in the non-reactive group—namely, stillbirth (including one case of hydrocephaly) in four cases, neonatal death (congenital hydrops) in one, and caesarean section in four.

Discussion

The non-stress test is simple to use, innocuous, and provides reliable information on fetal wellbeing in pregnancy, during labour, and at delivery. A reactive tracing predicts that the fetus will tolerate labour and delivery well, and all infants in this category survived. A non-reactive tracing, although not always predicting a poor outcome, provides a warning. Such tracings may be subdivided in increasing order of severity into (*a*) those showing no accelerations in response to fetal movements or an absence of fetal movements, (*b*) flat tracings, and (*c*) those showing late decelerations.

Though ultrasound may stimulate the fetus, ultrasonography was the method most often used because it more easily gave a satisfactory tracing. Although the ultrasound machine we used gave an accurate measure of baseline variability, we found that the best measure of the reactive pattern was acceleration in response to fetal movements. External electrocardiography provides the most accurate assessment of baseline variability, but with this method it is more difficult to obtain a satisfactory record. A non-reactive tracing obtained by ultrasonography may be an indication to attempt a more-detailed evaluation using electrocardiography.

Uncorrectable late decelerations must be regarded as serious, but if there are no Braxton Hicks contractions then there will be no late decelerations. A persistent flat tracing in the absence of fetal movements when there is no correctable cause—for example, depressant drugs—should be regarded as unfavourable.

We thank our nursing, technical, and medical colleagues for co-operation, and Mr K Matthews for the statistical analysis.

References

[1] Beard, R W, *et al*, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1971, **78**, 865.
[2] Caldeyro-Barcia, R, *The Heart and Circulation in the Newborn and Infant*, p 7. New York, Cassell, 1966.
[3] Kubli, F W, *et al*, *American Journal of Obstetrics and Gynecology*, 1969, **104**, 1190.
[4] Wood, C, *et al*, *American Journal of Obstetrics and Gynecology*, 1969, **105**, 942.
[5] Cooper, J M, Soffronoff, E C, and Bolognese, R J, *Obstetrics and Gynecology*, 1975, **45**, 27.
[6] Gaziano, E M, Hill, D L, and Freeman, D W, *American Journal of Obstetrics and Gynecology*, 1975, **121**, 947.
[7] Schifrin, B, *et al*, *Obstetrics and Gynecology*, 1975, **45**, 433.
[8] Weingold, A B, de-Jesus, T P S, and O'Keiffe, J, *American Journal of Obstetrics and Gynecology*, 1975, **123**, 466.
[9] Kubli, F W, Kaeser, I, and Hinslemann, M, *The Feto-Placental Unit*, p 323. Amsterdam, Exerpta Medica, 1969.
[10] Hammacher, K, *Perinatal Medicine*, p 80. New York, Academic Press, 1970.
[11] Rochard, F, *et al*, *American Journal of Obstetrics and Gynecology*, 1976, **126**, 699.
[12] Emmen, L, *et al*, *British Journal of Obstetrics and Gynecology*, 1975, **82**, 353.
[13] Dreyfus-Brisac, C, and Blanc, C, *Encéphale*, 1956, **45**, 205.
[14] Laversen, N H, Hochberg, H M, and George, M E D, *American Journal of Obstetrics and Gynecology*, 1976, **125**, 1125.

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Sex-related differences among 100 patients with alcoholic liver disease

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Summary

During 1975 we studied 100 patients—77 men and 23 women—who had a history of alcohol abuse and disturbed liver function test results. On presentation the women were less likely to be suspected of alcohol abuse (9; 38%) than the men (59; 77%). Although the quantity of alcohol consumed and length of history of alcohol abuse were similar for men and women, the incidence of chronic advanced liver disease was higher among women (86%) than among men (65%). Women, however, were less likely to have developed primary liver cell cancer. Overall the women had a higher incidence of other alcohol-related disorders and were less likely to stop abusing alcohol (2; 9%) than were their male counterparts (22; 29%). Women seem to be more susceptible to alcohol-related disease.

Introduction

In 1945 Spain[1] reported that women with alcoholic cirrhosis died younger than men, and that death among women was usually secondary to hepatocellular failure, whereas in men it was related to portal hypertension. Since then few studies of alcohol-related liver disease have taken into account sex differences.[2-6] We therefore studied the drinking patterns, presentation, clinical picture, and prognosis in men and women seen at The Royal Free Hospital, London, (RFH) during 1975 who had a history of alcohol abuse and disturbed liver function test results.

Patients and methods

The medical unit at RFH has a special interest in hepatology, and the hospital, by virtue of its geographical situation, draws a fairly high percentage of its patients from the upper social classes. Both these factors affected the characteristics of the population in this study.

During 1975 516 patients with liver disease were admitted to the medical unit. All were interviewed and 100 were identified as alcohol abusers, drinking regularly above 100 g of ethanol per kg body weight per day. This level of consumption, if sustained, carries the risk of physical complications.[2] Socioeconomic circumstances and drinking habits were recorded, social class being defined by occupation[7] and highest class achieved. Married women were classed according to their husband's occupations. A family history of alcoholism was sought. The age of onset of regular drinking and of regular heavy drinking was recorded, and so far as possible the type and amount of beverage consumed per day were assessed. Patients were judged to be physically dependent on alcohol if they gave a history of tremor after a period of abstinence, which was relieved by alcohol, and of episodes of amnesia. The occurrence of episodes of delirium tremens—characterised by disorientation, delusions, visual hallucinations, and fear and accompanied by restlessness, hyperactivity, and possibly epileptiform fits—were noted. Percutaneous liver biopsy was performed in all patients except three.

While in hospital patients were forcefully and repeatedly warned of the dangers of alcohol abuse. After discharge these warnings were repeated at regular outpatient attendances. Blood ethanol concentrations were a valuable guide to continuing alcohol abuse.[8] All patients were referred to their general practitioners and when necessary to social services. Alcoholics Anonymous was discussed. Only 9% of the patients were thought to require consultant psychiatric help at the start of the study. Patients alive at the end of the year were reviewed. Data were analysed using the $2 \times 2 \chi^2$ test, Fisher's exact probability test, or the Mann-Whitney U test.[10]

Results

The 100 patients (77 men and 23 woman) who were identified as alcohol abusers accounted for 19·4% of the total admissions for liver disease. In 69% alcohol abuse had been suspected at first presentation whether at RFH or elsewhere. Women were less likely to be suspected of alcohol abuse (9; 38%) than men (59; 77%) ($P < 0.001$). Two case histories of women patients illustrate this point.

CASE 1

In April 1974 after a flu-like illness a 34-year-old married African State Registered Nurse became jaundiced, with dark urine and light stools. This was accompanied by pain in the right upper abdomen and pruritus. Her 30-year-old brother had recently died of alcoholic cirrhosis. She denied

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