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An evaluation of electronic fetal monitoring with clinical validation of ST waveform analysis during labour

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An evaluation of electronic fetal monitoring with clinical validation of ST waveform analysis during labour.

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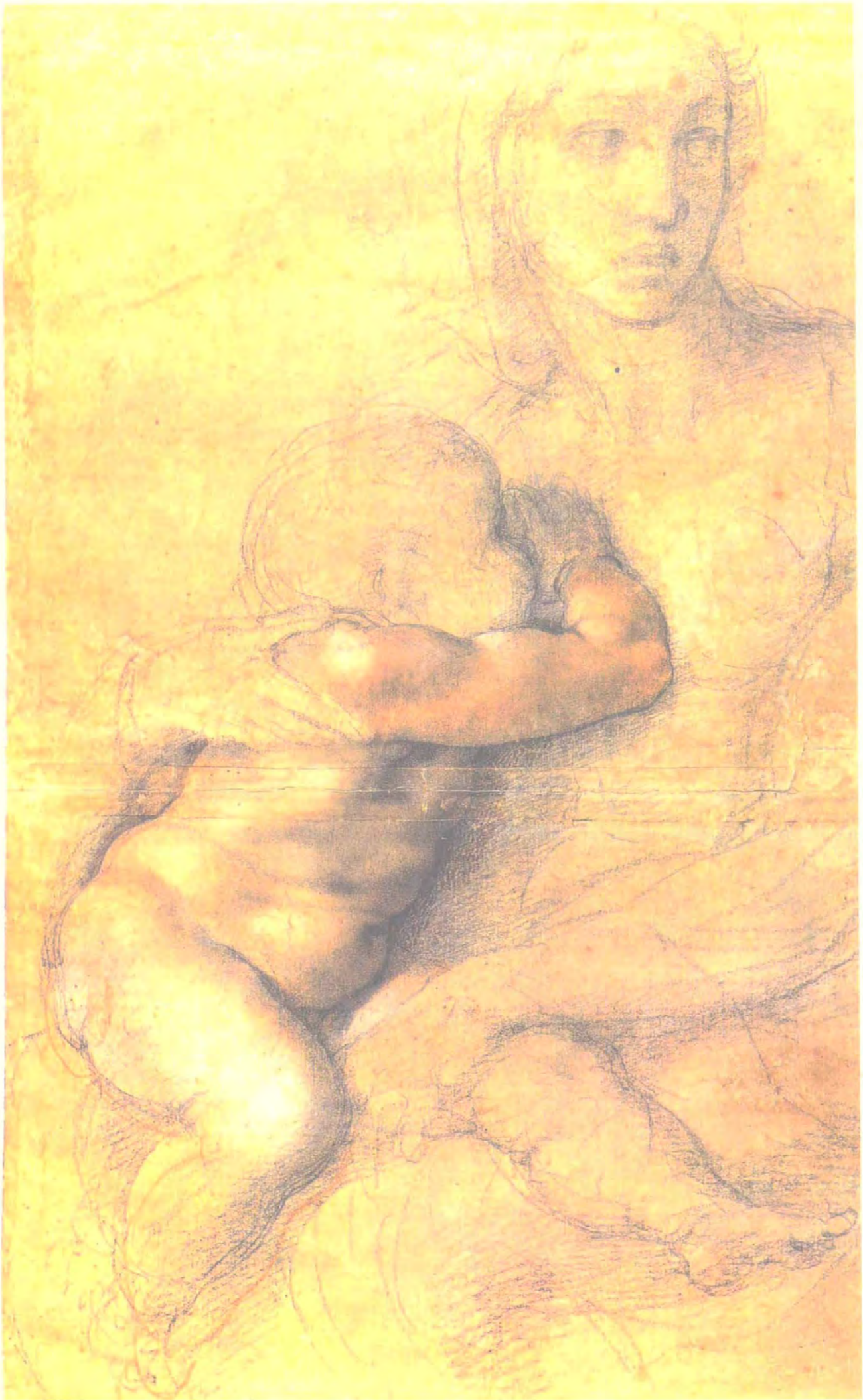
Figure; Madonna and Child by Michelangelo
Edizioni Monumenti, Musei e Gallerie Pontifice

For Thou didst form me in my inward parts;
Thou didst weave me in my mother's womb.
I will give thanks to Thee for I am fearfully
and wonderfully made;
Wonderful are Thy works,
And my soul knows it very well.

Psalm 139: 13-14



Abstract. Westgate J. **An evaluation of electronic fetal monitoring with clinical validation of ST waveform analysis during labour.**

Dissatisfaction with the electronic recording of fetal heart rate and uterine contractions (the cardiotocogram or CTG) has resulted in a search for new techniques of monitoring the fetus during labour. It is important that each method has a sound physiological and pathophysiological basis, that a model for the interpretation of changes is elucidated and that each method is thoroughly evaluated before introduction into clinical practice. Analysis of the ST waveform of the fetal electrocardiogram (FECG) is the most advanced of the new techniques under investigation. Experimental studies have shown that elevation of the ST waveform occurs with a switch to myocardial anaerobic metabolism and a negative waveform occurs during direct myocardial ischaemia. Human observational studies have suggested that a combination of ST waveform and CTG analysis may improve the specificity of intrapartum monitoring and reduce unnecessary intervention.

A high quality FECG signal is necessary for waveform analysis. The FECG can be recorded from a scalp electrode (FSE) during labour. The suitability of 5 commonly available FSEs for ECG waveform analysis was compared. Single spiral FSEs had the most favourable physical and electrical properties and produced the best quality signals in a randomised clinical trial of 50 fetuses in labour.

Intervention rates and neonatal outcome in labours monitored with CTG alone were compared with those monitored with the combination of ST waveform analysis plus CTG (ST+CTG) in a randomised clinical trial of 2434 high risk labours in a large district general hospital over an 18 month period. There was a 46% reduction in operative intervention for fetal distress in the ST+CTG group ($p<0.001$, OR 1.96 [1.42-2.71]). There was a trend to less neonatal metabolic acidemia ($p = 0.09$, OR 2.63 [0.93-7.39]) and fewer low five minute Apgar scores ($p = 0.12$, OR 1.62 [0.92-2.85]) in the ST+CTG arm.

All recordings were reviewed retrospectively, blind to outcome and the CTG classified as normal, intermediate or abnormal according to the trial protocol. There was no significant difference in the proportion of recordings in each category between the trial arms. Operative intervention in the ST+CTG arm was significantly reduced in recordings classified as normal and intermediate by the review (12/1043 ST+CTG arm versus 48/1066 CTG arm, $p <0.001$). Three patterns of ST+CTG change were identified. **1. Normal CTG, persistent stable ST waveform elevation.** These fetuses had good outcome and a significantly higher mean pH (7.29) and lower base deficit (1.1 mmol/l) at delivery. The raised ST waveform may reflect sympathoadrenal stimulation from the general arousal of labour or a response to mild but compensated hypoxaemia and is in keeping with experimental data. **2. CTG abnormal, progressive elevation in ST waveform.** All cases occurred towards the end of second stage. These fetuses had a significantly lower mean pH (7.05) and higher base deficit (7.6 mmol/l) than all other groups. This combination identified fetuses who were developing a metabolic acidosis as a result of significant hypoxia. **3. Abnormal CTG and a negative ST waveform.** All cases with persistently negative waveforms were depressed at birth, required resuscitation and had low arterial pHs (where available). This high risk group probably had depleted myocardial glycogen reserves and suffered direct myocardial hypoxia, as seen in animal studies. These findings indicate that ST waveform analysis can discriminate CTG change during labour, the combination can result in a reduction in unnecessary intervention and has the potential to more accurately identify fetuses at risk of neonatal morbidity.

The term 'monitoring' implies a degree of automatic surveillance but this is not the case as CTG and ST+CTG records are subjectively interpreted, frequently by junior, inexperienced staff. The retrospective review of cases in the trial revealed significant errors in the use of fetal blood sampling and the interpretation of both CTG and ST+CTG recordings during the study. The feasibility of representing expert clinical knowledge in a decision support tool to provide consistent, accurate interpretation of the CTG was demonstrated in two clinical studies. The full potential of ST+CTG analysis may only be achieved with some degree of automatic data processing and interpretation.

The randomised trial also demonstrated the lack of appropriate measures of neonatal outcome with which to judge the effectiveness of fetal monitoring. Analysis of cord artery and vein blood gas status at delivery can provide useful information about fetal oxygenation prior to delivery but currently the information is poorly used, if at all. Use of erroneous data, inappropriate measures of 'acidemia', failure to distinguish between respiratory and metabolic components and unphysiological expectations about relationships to other measures of neonatal outcome were some of the problems highlighted. The use of generic terminology such as 'birth asphyxia' or 'acidosis' which have varying definitions has caused much confusion and should be avoided. There is unlikely to be one 'gold standard' measure of neonatal condition at delivery.

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Publications arising from the work;

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Plymouth randomised controlled trial of 2400 cases - ST waveform plus CTG versus CTG alone for intrapartum monitoring. 26th British Congress of Obstetrics and Gynaecology, Manchester 7-10 July 1992.

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INFANT - an intelligent support tool for the management of labour. Poster. VIIIth International Congress The fetus as a Patient, Oulu, Finland, 15-18 September, 1992.

An assessment of the reliability and analysis of cord blood gas data. Society for the Study of Fetal Physiology, 20th Annual Meeting, Plymouth, 16 - 19th May, 1993.

Expert systems in medicine. Poster. Society for the Study of Fetal Physiology, 20th Annual Meeting, Plymouth, 16 - 19th May, 1993.

Presentations; invited.
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Analysis of the fetal ECG during labour. VIIIth International Congress The fetus as a Patient, Oulu, Finland, 15-18 September, 1992.

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Fetal ST waveform analysis during labour. Workshop on fetal O_2 monitoring sub partu. Munich, Germany, June 4, 1993.

Signed .....

Date 19/4/93.....

Chapter One

Introduction

Health technology assessment.

Praise without end the go ahead zeal,
Of who ever it was who invented the wheel.
But never a thought for the poor souls' sake,
Who thought ahead and invented the brake.

Howard Nemerov, New York Times, 1989.

The technological achievements of the last 30 years have been immense; space travel, satellite communications and the microprocessor to name but a few. Advances in health care technology have been impressive too, for example, doppler ultrasound, computer aided tomography, and nuclear magnetic resonance imaging are now virtually routine diagnostic techniques. It seems that scarcely a medical journal is published without reference to a new technology which, it is frequently claimed, will revolutionise some aspect of medical practice. However, there is growing recognition that new techniques need to be thoroughly evaluated before introduction into clinical practice if patients and the health service are not to be endangered by unsafe, unhelpful and costly treatments (Jennett, 1992). For years now pharmaceutical companies have followed a standard procedure for the introduction of new drugs into clinical practice. This is based on a progression from animal studies to observational studies in man and finally to randomised clinical trials. The United States requires a similar formal assessment of new health care technology through the Federal Drug Administration Bureau. As yet, no such provisions exist in Europe, but they are not far away. Recently, an Advisory Group convened by the Department of Health, concluded that "rigorous assessment of both new and existing technologies is essential to evaluate their effectiveness and safety, their cost effectiveness and their social, ethical and organisational impacts." (Health Care Advisory Group, 1992).

It is against this background of an increase in technology and calls for proper assessment of that technology that intrapartum fetal monitoring needs to be re-evaluated. Despite the major technological advances alluded to above, intrapartum monitoring has changed very little in the last 25 years. Intermittent auscultation of the fetal heart rate was performed regularly in the 1950s, fetal scalp blood sampling was introduced in the early 1960s (Saling & Schneider, 1967) and continuous electronic recording of the fetal heart rate and uterine contractions (the cardiotocogram or CTG) began in the late 1960s (Beard et al, 1971). Use of the CTG has never quite fulfilled its promise to reduce long-term neurological handicap and is regarded by many as a "disappointing" (Editorial, N Eng J Med, 1990) or an "unsatisfactory" technique (Neilson, 1993). Many alternatives to the CTG have been considered in the past and currently many new techniques are under investigation. Before these technologies can be evaluated, requirements for methods of intrapartum surveillance need to be considered. These are listed in the following Table.

Table 1.1 Requirements for methods of intrapartum surveillance.

1. A sound physiological and pathophysiological basis for measurement of the variable.
2. Technology which is robust enough to allow reliable measurement of the variable in clinical practice.
3. A model of interpretation which identifies both the normal and the abnormal.
4. Evidence from clinical studies and randomised trials to show that the new technique is as good as, or better than, existing techniques.
5. Cost-effectiveness.

The requirement for a sound physiological and pathophysiological basis for measurement of any variable used to assess fetal condition is most important. Knowledge of fetal responses to labour should form the basis of the search for new indices of fetal condition and for the assessment of indices already in use or under investigation. These responses will be reviewed in the following section.

Physiology of fetal responses to labour.

The fetus lives and grows down-stream from maternal oxygen supply in partial pressures of oxygen which are so low that the term 'Mount Everest in utero' was coined to describe its supposedly perilous existence (Barcroft, 1946). Yet the fetus has a number of special adaptive mechanisms which enable it to cope so well with this situation that it normally has a surplus of oxygen for its requirements. In the event of a further reduction in oxygen supply, important defence mechanisms are activated, mediated by beta-adrenergic receptors, to maintain the function of high priority organs; blood flow is redirected to the priority organs and organ function can be maintained by anaerobic metabolism. These mechanisms will be reviewed in more detail.

Oxygen supply.

The placenta is the organ of gas exchange for the fetus. Oxygenated maternal blood enters the intervillous spaces from spiral arterioles and flows around the fetal chorionic villi. Deoxygenated fetal blood reaches the villi via the two umbilical arteries. Oxygen diffuses from maternal blood into fetal blood across the placental membrane whilst carbon dioxide passes readily in the opposite direction. Oxygenated fetal blood returns to the fetus in the

single umbilical vein. A number of mechanisms active both **before** and **during** labour may alter this process and result in a reduction in fetal oxygen supply (Figure 1.1).

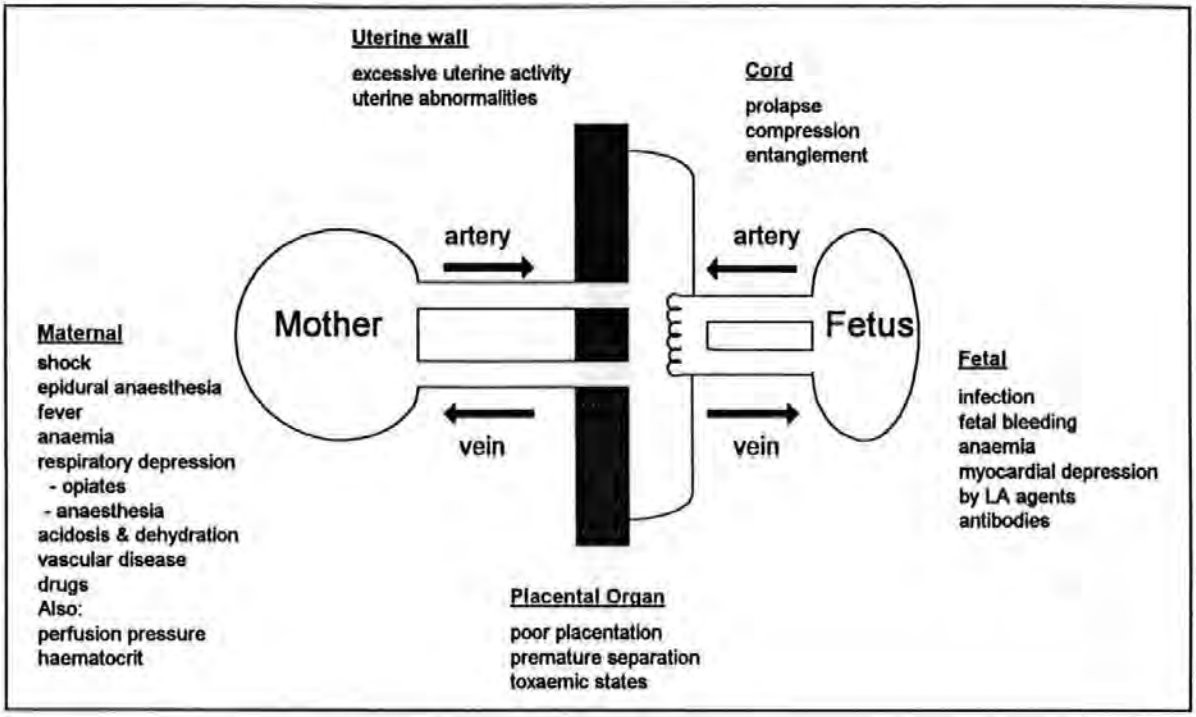


Figure 1.1 Mechanisms by which fetal oxygen supply may be impaired.

Labour is a critical time for the fetus. During labour maternal blood supply to the placenta is normally interrupted during uterine contractions so that oxygen levels in fetal blood fall during contractions and recover once placental blood flow resumes (Figure 1.2). Thus a relative oxygen deficiency is a part of normal labour.

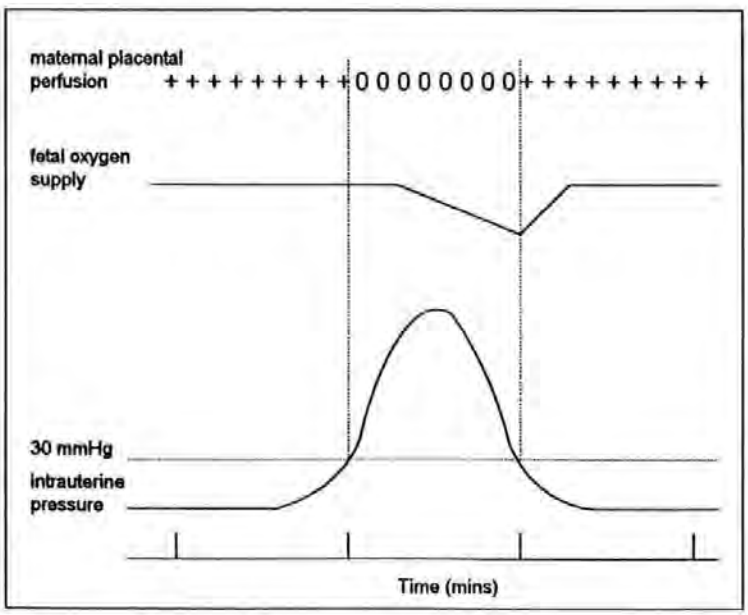


Figure 1.2 The effect of uterine contractions on placental perfusion and fetal oxygen supply (modified from Steer, 1977b).

Frequently, reduced oxygen supply is described by the terms hypoxaemia (reduced oxygen in the blood), hypoxia (oxygen supply does not meet tissue demands) and asphyxia (hypoxia plus acidosis causing impairment of organ function). A more helpful physiological approach is illustrated in Figure 1.3 and 1.4. Figure 1.3 summarises how the fetus aims to balance oxygen supply and requirements so as to maintain aerobic metabolism.

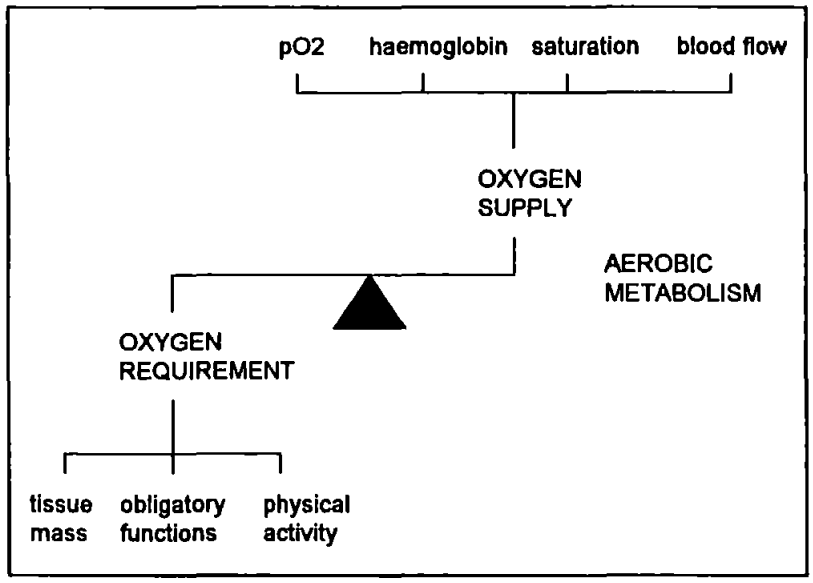


Figure 1.3 The factors which determine oxygen supply and requirement. Aerobic metabolism occurs when these are in balance.

The oxygen available to the fetus is not just dependent upon the partial pressure of oxygen in the blood (pO_2) but also on the haemoglobin concentration, the type of haemoglobin and the oxygen saturation. The increased oxygen-carrying capacity of fetal blood is partly due to its higher haemoglobin concentration and the greater affinity of fetal haemoglobin for oxygen. This enables it to become saturated with oxygen at low partial pressures of oxygen. The amount of blood flow to an organ will also determine its oxygen supply. Fetal cardiac output is approximately four times higher than that of the adult per kilo of body weight (Cohn et al, 1974, Peeters et al 1979). As a result fetal organs are normally supplied with more oxygen than they require.

Oxygen requirement is determined by fetal size, fetal activity and essential fetal metabolic processes. If supply and requirement are in balance the fetus has adequate oxygen to metabolise glucose aerobically to produce the energy required for organ function. If oxygen supply is inadequate the fetus can produce energy by anaerobic metabolism (Figure 1.4).

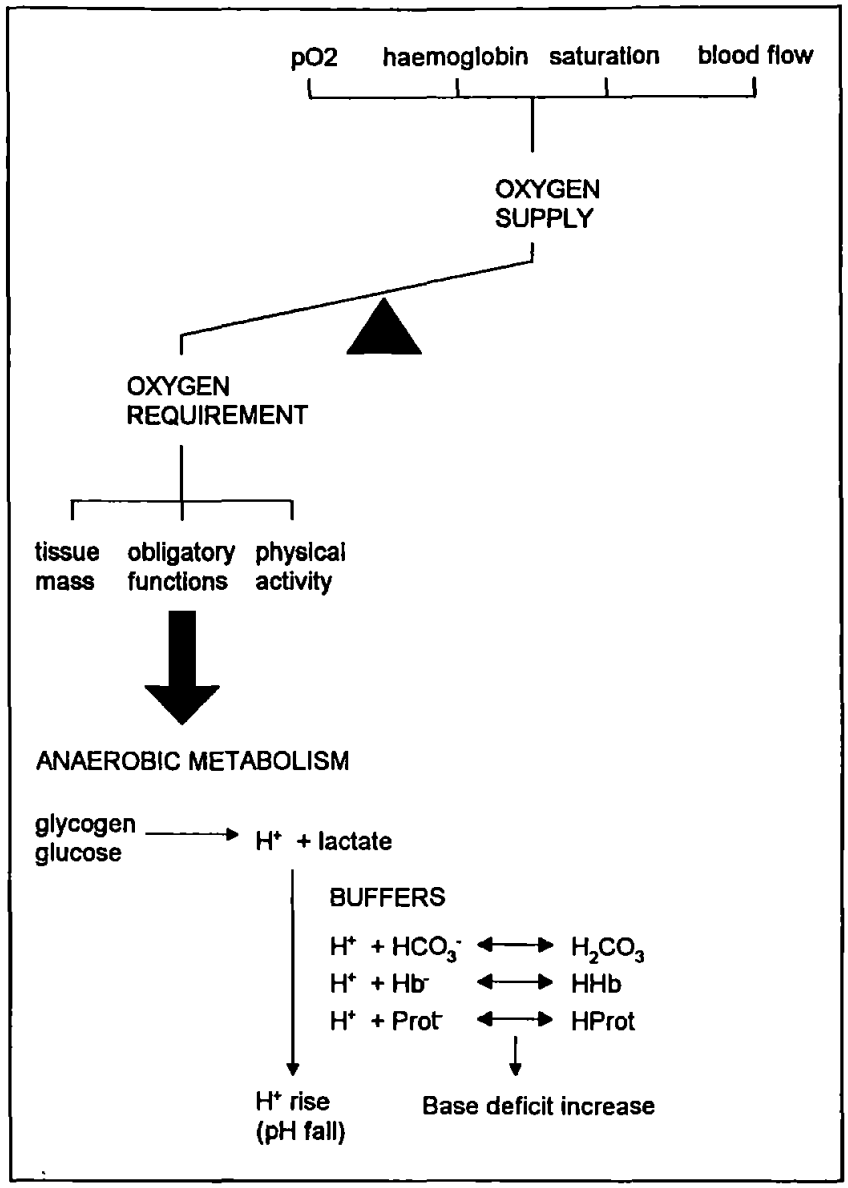


Figure 1.4 Anaerobic metabolism. When oxygen supply is insufficient to meet requirements energy is produced by the anaerobic metabolism of glycogen and glucose.

Fetal defence mechanisms.

The fetus is able to adjust to periods of reduced oxygen supply in order to maintain the balance illustrated in Figure 1.3 by means of a number of hormonal, cardiovascular, metabolic, and behavioural mechanisms. However, it is important to recognise that the time of onset, duration and severity of oxygen deficiency may vary greatly from fetus to fetus and will affect the success of fetal compensatory mechanisms. The effect of an acute oxygen lack during labour in a healthy fetus may be different from the same insult in a fetus who has already experienced a chronic oxygen deficiency throughout pregnancy.

Hormonal adjustments. The important cardiovascular and metabolic adjustments which will be described in the following sections are mediated by neural and humoral mechanisms.

Hypoxia results in an increase in sympathetic and parasympathetic (vagal) nervous system activity initiated by an increase in autonomic activity (Dawes, 1968, Parer, 1983, 1984) and an increase in the secretion of catecholamines, vasopressin, adenine, adenosine, and prostaglandins (Comline et al, 1965, Jones & Ritchie, 1978a, 1978b, Rurak, 1978, LaGamma et al, 1982, Lagercrantz & Slotkin, 1986). Large amounts of catecholamines are released from the adrenal medulla in response to both direct hypoxia and increased sympathetic activity (Comline et al, 1965, Jones & Robinson, 1975). They stimulate specific adrenergic receptors which induce both cardiovascular and metabolic responses (Phillippe, 1984). After an uneventful vaginal delivery catecholamine levels in umbilical cord arterial blood are far higher than levels found in adults performing heavy exercise. Levels in asphyxiated infants are higher than those found in patients with phaeochromocytoma (Lagercrantz & Bistoletti, 1977). The surge of catecholamines during labour and delivery probably have an important role in facilitating postnatal adaptation to extrauterine life (Lagercrantz & Slotkin, 1986). In experimental studies beta-adrenergic receptor blockade significantly impaired fetal ability to survive during periods of hypoxia (Dagbjartsson et al, 1985).

Cardiovascular adjustments. As fetal organs are relatively over perfused in relation to their oxygen requirements, they have a certain oxygen reserve. Fetal haemoglobin has a high affinity for oxygen and chronic hypoxaemia results in increased erythropoiesis to further increase the oxygen carrying capacity of fetal blood (Soothill et al, 1987). Fetal tissues can also increase the amount of oxygen they extract from the blood. In fetal sheep this compensatory increase in fractional oxygen extraction can maintain tissue oxygenation until oxygen delivery is reduced by 50% (Richardson, 1989). Blood flow is preferentially distributed to vital organs (brain, heart, adrenals) to maintain their oxygen supply at the expense of peripheral organs (gut, skin, liver, muscles, kidneys) while placental blood flow is maintained (Cohn et al, 1974, Rudolph, 1984). Chronic redistribution of blood flow away from peripheral organs can result in peripheral organ dysfunction in the neonate. Renal failure, necrotising enterocolitis, hepatic damage, coagulopathy and respiratory distress are all recognised sequelae of chronic hypoxaemia and can be used in an overall assessment of its severity (Portman et al, 1990, Shankaran et al, 1991).

Unlike the brain, the heart cannot reduce its oxygen requirements during hypoxia and, indeed, is forced to work harder as a result of the catecholamine surge. Indeed, unlike the adult, the fetal heart is often the last organ to fail during hypoxia. The result of severe myocardial hypoxia is bradycardia, hypotension and, ultimately, cardiac standstill. Neonatal cardiac dysfunction is a recognised complication of severe hypoxia and may manifest itself as cardiogenic shock, left ventricular failure as a result of global myocardial ischaemia or, particularly, right-sided failure as a result of tricuspid papillary muscle necrosis (Setzer et al, 1980, Walther et al, 1985). Ischaemic myocardial damage is relatively common in infants

who have suffered a severe oxygen deficiency and die in the first seven days of life (Donnelly et al, 1980).

Metabolic adjustments. If these cardiovascular adjustments fail to maintain adequate oxygen delivery, glucose and glycogen are metabolised anaerobically to provide the energy required to maintain cell and organ function (Figure 1.4). The lactic acid formed during anaerobic glycolysis releases hydrogen ions which are buffered primarily by bicarbonate ions but also by haemoglobin and proteins. As hydrogen ion concentration increases these buffers are consumed and a progressive metabolic acidosis develops with a fall in pH and a rise in the base deficit of the extracellular fluid. Glycogen stores are consumed rapidly during this process; 1 mole of glucose provides only 4 moles of ATP compared to the 38 moles available from aerobic metabolism (Ganong, 1983). The importance of anaerobic metabolism to the maintenance of myocardial function (and survival of the fetus) is long established and depends on the prehypoxic glycogen content of the myocardium (Dawes et al, 1959).

Anaerobic glycogenolysis results in the rapid depletion of glycogen stores which places the neonate at risk of hypoglycaemia and may accentuate hypoxic ischaemic brain damage (Vannucci & Yager, 1992). Damage to liver enzymes or hyperinsulinism may prevent adequate neonatal gluconeogenesis resulting in persistent hypoglycaemia (Collins & Leonard, 1984, Sann, 1990). These metabolic events may also contribute to difficulty with thermoregulation as a result of a depletion of brown fat (Hull, 1966).

Behavioural adjustments. Other adjustments can be made to reduce oxygen requirements such as reduced physical activity, behavioural state alterations and reduced growth rate. Knowledge of these adjustments is the rational for the biophysical assessment of fetal well-being (Manning et al, 1980), however there is recent evidence that a significant reduction in fetal activity may be a relatively late sign of fetal hypoxia. It has been found that electrocortical activity, electroocular activity and breathing movements in fetal sheep during 4 days of prolonged, graded hypoxaemia did not change significantly until fetal arterial oxygen saturation was less than 30% and fetal acidemia had occurred (Richardson et al, 1992).

The central nervous system. The brain's first response to severe hypoxia is cerebral vasodilatation and a redistribution of blood flow to the brainstem, midbrain and cerebellum (Kjellmer, 1988). Control of FHR variability originates from higher centres in the cerebral cortex, so loss of variability may be one of the first signs of cerebral hypoxia (Court & Parer, 1982, Parer, 1984). The brain can also reduce its oxygen consumption during hypoxia (Kjellmer, 1988, Richardson et al, 1989). Damage can occur as a result of both neural necrosis and ischaemic lesions and appears to involve 3 mechanisms; the release of excitatory amino acids, activation of the arachidonic cascade and the production of oxygen

free radicals (Kjellmer, 1991, Espinoza & Parer, 1991). In addition, damage occurs in two phases; firstly during hypoxia and secondly, and perhaps more significantly, during resuscitation and reoxygenation (Kjellmer, 1988). The neonate who has suffered from intrapartum oxygen deficiency severe enough to cause cerebral damage would be expected to show evidence of depression at birth which required active resuscitation (American Academy of Pediatrics, 1986, Gilstrap et al, 1989, Freeman & Freeman 1992). The occurrence of subsequent neonatal neurological disturbance and, ultimately, long term damage would depend on the degree of both primary and secondary neuronal damage.

Many fetuses who have experienced chronic hypoxaemia seem to have significant short and long term alterations in the way they develop and interact with their environment. Growth retarded fetuses have altered cerebral evoked potentials at birth (Kjellmer et al, 1992), an increased risk of perinatal complications and long term neurological abnormalities (Harvey et al, 1982, Chiswick, 1985). In addition they are at increased risk of developing arterial hypertension later in life (Gennser et al, 1988) and of dying from ischaemic heart disease (Barker et al, 1989). Recently it has been shown that under basal conditions, compared to normally grown rats, the brain tissue of growth retarded rats had lower concentrations of serotonin and aspartate, two factors which sustain trophic function in brain development (Thordstein, 1991). Growth retarded fetuses display an inappropriate increase in serotonin synthesis and an increase in lipid peroxidation in response to hypoxia (Thordstein, 1991). These findings suggest that brain development in growth retarded fetuses may be delayed and that their central nervous system is more vulnerable to the effects of hypoxia.

Conclusions.

The response of any individual fetus to the stress of labour will be determined by the duration and severity of hypoxaemia encountered before and during labour, balanced by the effectiveness of its cardiovascular responses and its energy reserves. **Given the complexity of this situation it is unlikely that any single variable will totally reflect fetal condition during labour.** Ideally, measurement of variables which reflect the function of the heart and brain and which indicate the level of hypoxaemia at which compensatory mechanisms come into play and then begin to fail is required.

The present state of CTG monitoring during labour.

The term 'electronic fetal monitoring' (EFM) has been used to describe both CTG monitoring alone (Haverkamp et al, 1979, Leveno et al, 1986) and CTG monitoring plus fetal blood sampling (Banta & Thacker, 1979, MacDonald et al, 1985). This term now also encompasses most of the alternative technologies under investigation. In order to avoid confusion, use of the term EFM will be avoided; the CTG will be used to describe continuous electronic recording of fetal heart rate and additional use of fetal blood sampling (FBS) will be specified separately.

The present state of CTG monitoring during labour can be summarised according to the points listed in Table 1.1.

Physiology and pathophysiology.

Although the heart is a vital central organ, fetal heart rate (FHR) changes during labour occur as the result of a complex interaction of many factors which act on the heart. Present understanding of the physiological and pathophysiological basis of these changes is limited (Court & Parer, 1984, Ball & Parer, 1992). As a result it can be difficult to separate FHR changes which indicate appropriate fetal compensatory responses from those which indicate decompensation.

Technology.

The CTG was introduced in the late 1960s and the instruments soon became widely available. FHR can be measured directly from a fetal scalp electrode (FSE) applied to the fetal presenting part or indirectly from a doppler ultrasound transducer applied to the maternal abdomen. Both methods are susceptible to signal noise (particularly doppler techniques) which primarily affects estimations of FHR variability. Improvements in signal processing and the introduction of wide range ultrasound transducers and autocorrelation have improved the accuracy of FHR detection although artefacts may still occur (Carter, 1986, Dawes et al, 1990). However, generally, the technology is robust and user-friendly but requires subjective interpretation.

Model of interpretation.

The model of interpretation of CTG changes was largely based on empirical observations of thousands of hours of recordings during human labour (Hon & Quilligan, 1967, Beard et al, 1971) and is still reproduced in modern textbooks (Llewellyn-Jones, 1986, Miller & Callander, 1989). The detailed knowledge these early workers gained from their

observations has not been represented in the simplistic classifications used and even their original terminology has become corrupted with time (Donker, 1991).

Clinical evaluation.

In the late 1960s and early 1970s there were a large number of observational studies which favourably compared the CTG with intermittent auscultation using historical or non-randomised concurrent controls (e.g. Paul & Hon, 1974, Tipton & Lewis, 1975, Lee & Baggish, 1976, Neutra et al, 1978). It is impossible to be sure that other factors did not contribute to the improvements noted (e.g. a fall in high parity pregnancies, earlier diagnosis of congenital abnormalities, improvements in neonatal resuscitation). The results of the first randomised controlled trial which compared the CTG with intermittent auscultation of FHR did not appear until 1976 (Renou et al, 1976) and supported the use of the CTG in high risk labours. Since then 7 other randomised trials have been published. Their findings can be summarised as follows;

Operative intervention rates are increased with the use of CTG alone (Kelso et al, 1978, Haverkamp, et al, 1979, Leveno et al, 1986, Neldam et al, 1986, Luthy et al, 1987).

The addition of fetal blood sampling to assess fetal acid-base status during labour can reduce operative intervention (Haverkamp et al, 1979, Young et al, 1980, MacDonald et al, 1985) but is an intermittent procedure which is used in less than 45% of UK hospitals (Whebble et al, 1989). Furthermore, there is very little information on how frequently and how effectively it is used in clinical practice (Murphy et al, 1990).

Neonatal outcome. Only two of the randomised controlled trials have shown an improvement in neonatal condition with use of the CTG (Renou et al, 1976, MacDonald et al, 1985). The main effect appears to be a reduction in neonatal seizures (Grant, 1991), but follow-up of a proportion of cases from the Dublin study (MacDonald et al, 1985) has shown no difference in outcome at 4 years of age (Grant et al, 1989).

There is no accepted definition for 'birth asphyxia' and many different measures of neonatal outcome have been used in various studies. However, hypoxia is not the only cause of neonatal seizures (Nelson & Leviton, 1992), a low Apgar score or neonatal ventilatory requirements (American Academy of Pediatrics, 1986). Routine measurement of cord artery and vein blood gas parameters are recommended as objective measures of neonatal condition (Thorp et al, 1989, Johnson et al, 1990) but there is much confusion about their value (Ruth & Raivio, 1988, Dennis et al, 1989). There is no longer any consensus of opinion as to which measures of outcome are appropriate, or more appropriate than others.

Two other important points can be noted from the large number of additional clinical studies which have investigated various aspects of CTG monitoring.

Large intra- and inter-observer differences in the interpretation of CTG recordings have been reported (Trimbos & Keirse, 1982, Lotgering et al, 1982, Lidegaard, et al, 1992) and apparently even 'experts' cannot agree (Donker, 1991). There is growing evidence that the interpretation of CTG changes is a major problem for practising obstetricians and that improper interpretation and management is implicated in a large proportion of 'birth asphyxia' cases (Murphy et al, 1990) and is the cause of a substantial proportion of litigation for birth related events (Ennis & Vincent, 1990, Chamberlain & Orr, 1990).

Cerebral palsy rates have not decreased. When the CTG was introduced in the 1960s, there was much optimism that it would prevent fetal death in labour and reduce long term neurological handicap. Despite the dramatic decline in intrapartum stillbirth rates in developed countries (Parer, 1979, Shepherd et al, 1983, Errkola et al, 1984, Georgsdottir et al, 1989), cerebral palsy rates in both preterm and term fetuses have increased (Nelson & Ellenburg, 1986, Stanley & Watson, 1988, Dowding & Barry, 1988, Hagberg & Hagberg, 1989, Pharoah et al, 1990). Given the fall in intrapartum stillbirth rates, it is possible that use of the CTG has caused a shift from death to handicap. This implies that intrapartum events may only exacerbate existing damage and is consistent with both the physiology and pathophysiology just reviewed and with recent evidence that less than 10% of cerebral palsy is related to intrapartum events (Nelson, 1988, Blair & Stanley, 1988).

Cost effectiveness.

The cost-effectiveness of the CTG to the health service has rarely been addressed. In their review of electronic fetal monitoring published in 1979, Banta & Thacker estimated that EFM cost the country $411 million in 1977-78. Their calculations were challenged by Hobbins et al (1979) who claimed the cost of EFM was closer to $80 million. In 1991 it was estimated that the cost for an emergency caesarean section was £1172, 3 times that of a normal vaginal delivery and double that of an operative vaginal delivery (Clark et al, 1991). It is obvious that use of this technology results in a significant increase in cost to the health service. The increased incidence of repeat caesarean section in subsequent pregnancies also needs to be included in any financial equation. Other important factors are more difficult to put a figure on, for example, the impact of an operative delivery on the psyche of the mother and its effect on maternal-infant bonding. In comparison, the cost-effectiveness of CTG monitoring for commercial companies was obvious at an early stage. By 1976 one commercial company had sold over 800 CTG monitors at a cost of over 2 million pounds, provoking the comment that the technique had moved from the realms of research into big business (Steer, 1977a).

Consideration of cost-effectiveness is now complicated by the issue of litigation. If the FHR is not recorded during labour and there is a poor infant outcome, it is becoming increasingly difficult to mount a defence against accusations of mismanagement. The growing numbers and escalating costs of these cases threatens the financial stability of the entire health service. The number of claims against obstetricians and gynaecologists has trebled in the last 5 years and in many cases successful settlements exceed £1 million (Symonds, 1991). As the costs for these cases are now being absorbed by district health authorities, it is inevitable that local health services will be affected by a diversion of funds to cover settlement of these cases.

Summary.

The CTG was introduced into clinical practice without a clear understanding of the physiological and pathophysiological basis of interpretation and without a thorough assessment of its value in clinical practice. As a result the whole area of intrapartum fetal monitoring is in confusion. On the one hand clinicians know that use of the CTG will result in unnecessary operative deliveries, whilst on the other, failure to monitor may leave them open to litigation, as may its inappropriate use.

Alternatives to CTG monitoring.

There seem to be three possible responses to the confusion about the value of CTG monitoring during labour.

Do nothing.

Should we abandon all forms of intrapartum monitoring? Perinatal mortality rates in third world countries where intrapartum care is not widely available do not encourage much confidence in this approach. As the general standard of nutrition, health and hygiene in these countries is far below that enjoyed in most western countries, the comparison may not be entirely valid. However, comparable data is available from a religious sect in Indiana in the United States who do not believe in medical care. Their women receive no antenatal care and deliver at home without trained attendants. From 1975 to 1982, a conservative estimate of the perinatal mortality in this group was three times higher than that of the whole state. These findings were unexplained by demographic data as sect members were predominantly white, aged 24 to 35, married, and had at least a high school education (Kaunitz et al, 1984). It is salutary to note that the maternal mortality rate in this group was 100 times higher than the whole state population.

Use intermittent auscultation only.

Another simple, but less extreme alternative, is to abandon the CTG in favour of intermittent auscultation of FHR. Whilst results of the randomised trials indicate that this approach may be suitable for low risk labours, the only study of high risk labours demonstrated a significant advantage for the CTG (Renou et al, 1976). A number of other points also need to be considered.

Firstly, there is evidence that the performance of a randomised trial may have influenced the use of intermittent auscultation during the Dublin randomised trial of intermittent auscultation versus CTG (MacDonald et al, 1985). Figure 1.5 shows the intrapartum stillbirth and perinatal mortality rates in the National Maternity Hospital, Dublin before, during and after their trial. Before the trial intermittent auscultation was used exclusively. The CTG was only introduced into the hospital a few months before the randomised trial began (an interesting point which raises questions about staff inexperience with the technology).

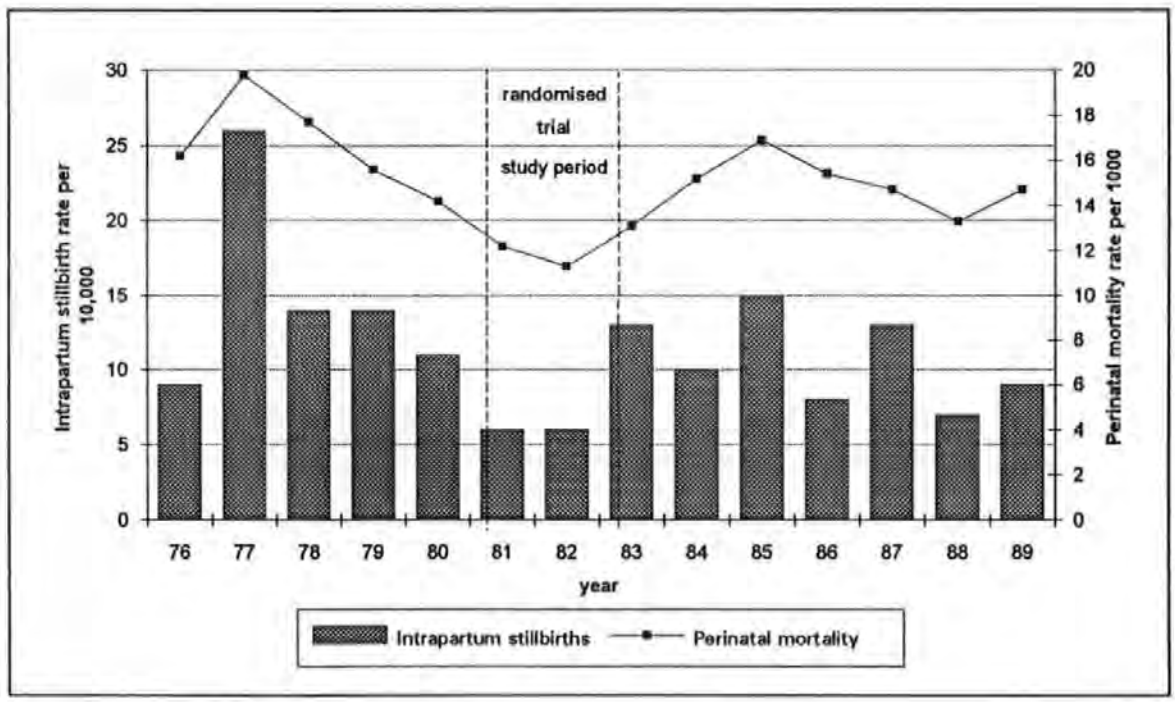


Figure 1.5 Intrapartum stillbirth and perinatal mortality rates at the National Maternity Hospital in Dublin from 1976 to 1989. (Figures obtained from Dr P Boylan, personal communication).

There was a clear decrease in total hospital mortality rates during the trial period (a Hawthorne effect). This not only reduced the chance of detecting a difference between the two monitoring techniques but also suggests that the quality of intermittent auscultation was improved by the performance of the trial.

Secondly, it is has been repeatedly demonstrated that errors in counting FHR by auscultation can be significant. Observers were more likely to bias baseline estimations towards normal when the FHR is fast or slow (Day et al, 1968, Schifrin et al, 1992) and a significant proportion of decelerations were missed (Miller et al, 1984, Schifrin et al, 1992, Strong & Jarles, 1993).

Thirdly, a very important practical problem is that most labour wards cannot provide the one to one staffing level required to perform auscultation as frequently as required. One group only managed to successfully monitor 7.5% of 423 labours by intermittent auscultation (Morrison et al, 1991). Staff unavailability was the main reason for failure. The immediate response to this problem is to suggest that health care funding would be better spent on personnel and not machines. But despite a one to one midwife:patient ratio in a highly motivated group of mothers (and midwives), there was a two to sevenfold increase in asphyxia related perinatal deaths in home delivery cases in South Australia where intrapartum monitoring is only by intermittent auscultation (Henderson-Smart, 1991).

Continue the search for new measures of fetal condition during labour.

Over the last 30 years there have many attempts to investigate new variables; transcutaneous measurements of pO_2 (Huch et al, 1980), continuous tissue pH (Weber & Hahn-Pedersen, 1979, Nickelsen & Weber, 1991), pCO_2 (Schmidt et al, 1982, Schmidt & Saling, 1987), systolic time intervals (Robinson et al, 1978), fetal oxygen saturation by pulse oximetry (Johnson, 1991), changes in the ST waveform (Rosén et al, 1991) and time constants (Murray, 1986) of the fetal electrocardiogram (Greene, 1987), and cerebral blood flow by near infrared spectroscopy (NIR) (Peebles et al, 1992a &b) .

The majority of these approaches must overcome considerable technical problems to reliably obtain the required signal. The techniques currently under investigation are summarised in Appendix 1 according to the present state of pathophysiological knowledge, the available technology and potential clinical usefulness.

One of the most advanced of these new methods of intrapartum fetal surveillance is analysis of changes in the ST waveform of the fetal electrocardiogram (ECG). It reflects the function of a central organ, the heart, and, over the last 18 years the physiological basis for changes in the waveform have been determined in a series of animal experiments A number of preliminary human observational studies have been performed with promising results. This information will now be reviewed in detail.

The ST waveform of the fetal electrocardiogram.

The fetal electrocardiogram (FECG), like that of the adult, consists of P, QRS and T waves separated by PR and ST intervals (Figure 1.6). These represent the summation of the electrical events within the heart as seen from the body surface. The P wave represents atrial contraction, the QRS complex ventricular contraction, and the ST waveform (ST segment and T wave) ventricular repolarisation.

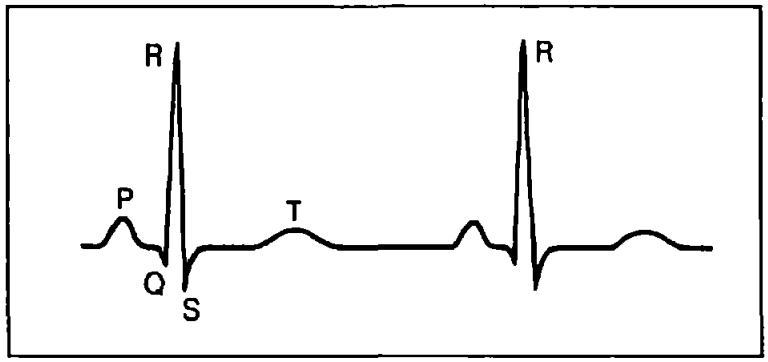


Figure 1.6 The ECG waveform.

Changes seen on the surface ECG occur as a result of changes in the relationships of the action potentials in different parts of the ventricular muscle at different points in time. The ST segment is usually isoelectric because the ventricular cells come simultaneously to nearly the same depolarised potential and no current flows between them. As some areas repolarise before others, current flows between cells to produced the T wave. Normally the base of the heart and the endocardium depolarise before the apex and epicardium but, as their action potentials last longer, repolarisation proceeds in the reverse direction which results in the positive ST waveform shown in Figure 1.7A.

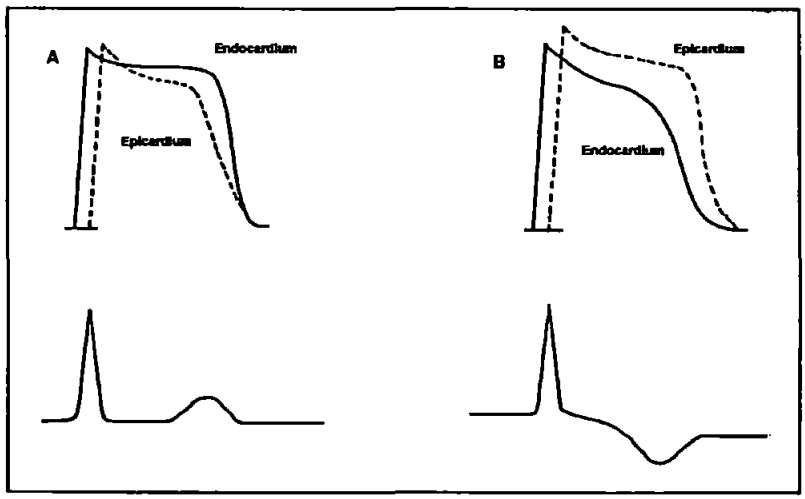


Figure 1.7 The relationship between action potentials in the endocardium and epicardium which give (A) a positive and (B) a negative T wave. The ST segment reflects the plateau phase of the action potential and the T wave the time difference between repolarisation of different parts of the myocardium (after Wohlfart, 1987).

If the endocardium depolarises before the epicardium, or the base before the apex, as for example during an extrasystole, the T wave will be negative (Figure 1.7B). The shape of the action potentials, and therefore the ST waveform, are affected by pressure gradients across the ventricular wall (Kirk & Honig, 1964) and by metabolic and ionic events around the myocardial cell which influence the sodium/potassium pump and probably calcium and chloride currents (Noble, 1979). The ST waveform can be assessed qualitatively by its shape, and quantitatively by measurement of the T wave height relative to that of the QRS complex (T/QRS ratio, Figure 1.8).

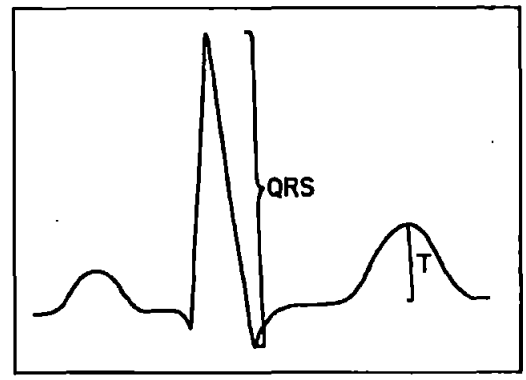


Figure 1.8 The T/QRS ratio.

In adults the ST waveform is affected by a number of normal and pathological conditions. Clinical analysis of the waveform is used to determine the size and progress of myocardial infarcts (Braunwald & Maroko, 1976) and to diagnosis coronary insufficiency during an exercise ECG (Sokolow & McIlroy, 1981). Over the last 18 years a series of experimental animal and clinical observational studies have provided a basis for understanding ST waveform change in the fetus (reviews by Greene, 1987, Greene & Westgate, 1993).

Pathophysiology.

There have been many incidental observations of ST segment and T wave change in the fetus in the past; with acute asphyxia by cord occlusion in goats (Towell, 1971), by maternal aortic occlusion or abnormal uterine activity in monkeys (Myers, 1972, Morishima et al, 1975) and in human fetuses before death (Hon & Lee, 1963) and in association with an abnormal CTG (Pardi et al, 1971). Initially, these changes were thought to be too variable to be useful but then a number of acute experiments performed specifically to examine the ST waveform showed that this may not be the case.

Acute preparations. In 1975, Rosén noted that hypoxia with acidemia caused a progressive increase in the amplitude of the ST waveform in the exteriorised fetal lamb (Rosén & Kjellmer, 1975). These changes preceded heart rate changes and a steadily increasing T wave height (T/QRS ratio >1.0) always preceded signs of failing cardiovascular function (Rosén et al, 1976a) and occurred contemporaneously with serial

changes in the somatosensory evoked electroencephalogram (EEG) (Rosén et al, 1976b). A strong correlation was also demonstrated between the T/QRS ratio and the depletion of myocardial glycogen and creatine-phosphate (Rosén & Isaksson, 1976) and between T/QRS ratio and lactate rise (Rosén et al, 1976a). Later Hökegård et al (1981) demonstrated a strong correlation between the increase in T wave amplitude during hypoxia with the rate of myocardial glycogenolysis as measured by a decrease in myocardial glycogen, creatinine phosphate and ATP measured on serial biopsies from the hearts of fetal lambs.

Chronic preparations. The evidence from acute experiments strongly linked ST elevation with myocardial glycogenolysis which was already known to be of great importance for the maintenance of myocardial function and fetal survival during hypoxia (Dawes et al, 1959). The study of ST waveform in chronically instrumented fetal lambs added further information.

ST waveform elevation. Fetal lambs with a normal baseline ST waveform had different responses to hypoxaemia (Greene et al, 1982, Greene, 1983). Despite similar falls in the partial pressure of oxygen (pO_2) (to 1.8 kPa or 13.5 mmHg) some lambs displayed little change in ST waveform or lactate while others had marked ST elevation which was related to the rate of lactate accumulation. These findings were confirmed by Rosén et al (1986a) who also demonstrated that an elevation of catecholamine levels during hypoxia only occurred in fetuses with lactate and ST waveform changes (Figure 1.9). The different responses to hypoxia seen in these fetuses were clearly important. It was postulated that fetuses that did not display ST waveform, lactate or catecholamine changes were able to compensate for decreased pO_2 with increased myocardial blood flow and hence were able maintain myocardial oxygen supply (Greene, 1983). Oxygen supply is the product of blood flow and oxygen content. Myocardial blood flow can increase by 350-500% to maintain oxygen supply despite a 70-80% reduction in arterial oxygen content (Peeters et al, 1979).

In comparison, it seems that the group of lamb fetuses that were unable to fully compensate for hypoxia with increased blood flow switched to anaerobic metabolism to maintain myocardial function. As a result their ST waveform, as measured by the T/QRS ratio, and lactate levels rose, in keeping with the acute experimental data. The degree of ST waveform elevation may also provide information about the effectiveness of fetal compensatory mechanisms. Dagbjartsson (1989) found a linear correlation between T/QRS ratio increase and myocardial workload in exteriorised lambs and recently a correlation between the degree of ST elevation and the development of fetal acidosis during repetitive cord compressions in chronic fetal sheep preparations has been reported (Watanabe et al, 1992). A T/QRS ratio >0.5 during cord compression was associated with fetal hypotension, lowered catecholamine levels and fetal acidosis.

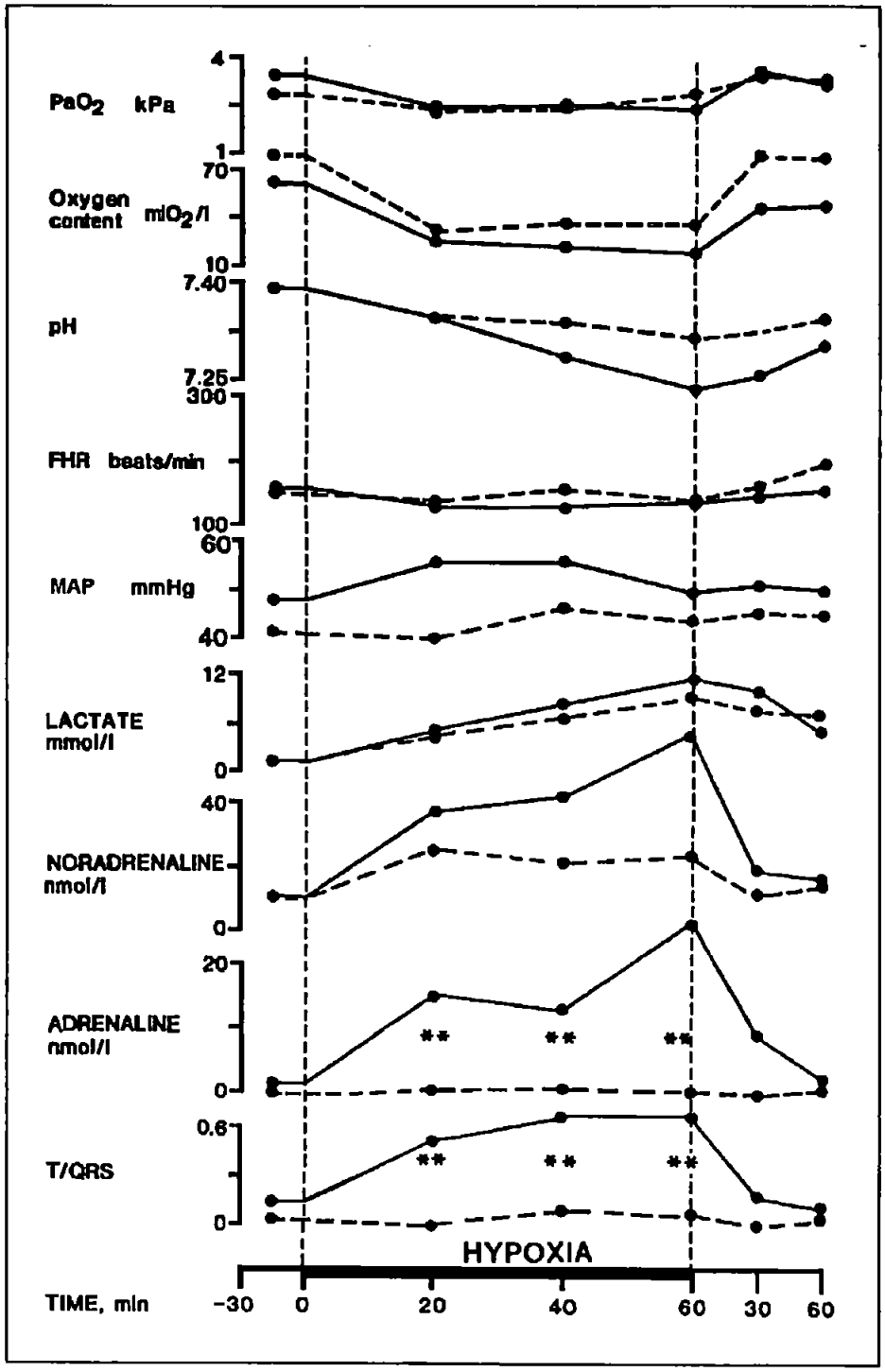


Figure 1.9 Alterations in the mean values of PaO_2, arterial oxygen content, fetal heart rate (FHR), mean arterial blood pressure (MAP), lactate, noradrenaline, adrenaline and T/QRS before, during and after a 1 hour period of hypoxia. Dashed lines indicate a group of fetuses with no changes in ST waveform during hypoxia; solid lines indicate the group with an increase in T wave amplitude. The level of significance between the 2 groups is indicated (**$p<0.01$). Reproduced from Rosén et al, 1984, with permission.

As a result of these investigations, a mechanism for ST waveform elevation was proposed (Figure 1.10). Anaerobic metabolism results in an alteration in ionic currents about the myocardial cell which affects the cell membrane potential and thus ST waveform shape.

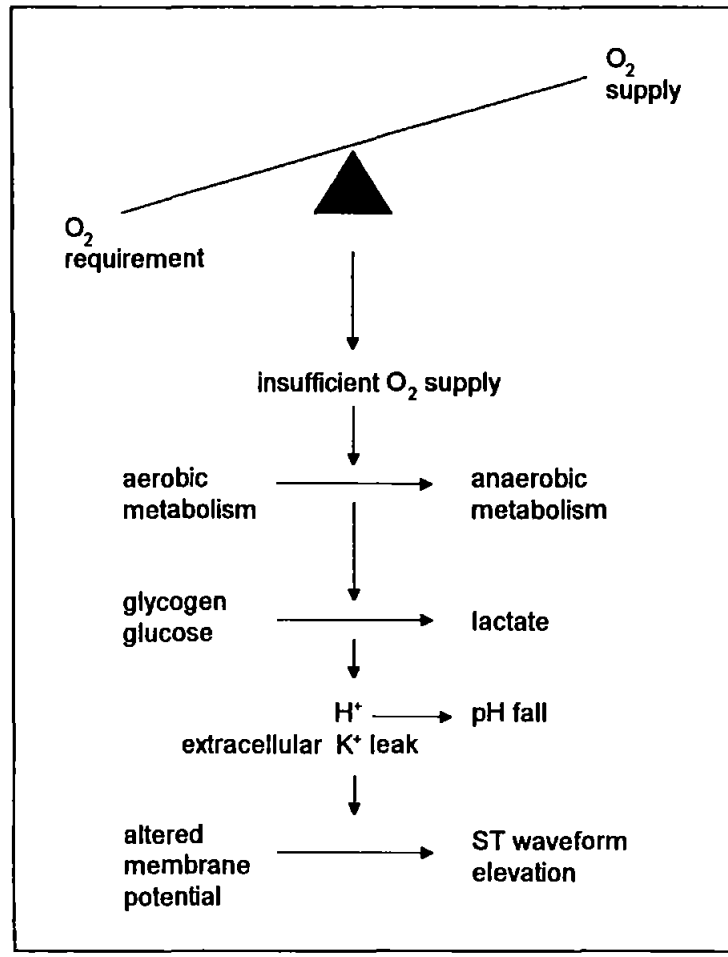


Figure 1.10 A schematic representation of the mechanisms underlying ST waveform elevation (modified from Greene, 1987).

Circulating catecholamines and the autonomic nervous system play a vital part in the fetal responses to hypoxaemia. ST waveform elevation was produced by infusion of the beta-agonist isoprenaline in the exteriorised lamb (Hökegård et al, 1979). Increasing doses (0.04 to 9.0 μg/kg/min) produced a progressive increase in T/QRS ratio but the value never exceeded 0.60. Propranolol blocked these changes and those produced during mild hypoxia, but not during severe hypoxia. Hypoxia and isoprenaline infusion had an additive effect on ST waveform change and produced higher T/QRS ratios than those seen with isoprenaline alone. In the chronic fetal lamb adrenaline infusion did not cause ST elevation (Greene, 1983) but this may have been related to the lower dose of beta-mimetic (0.3-0.7μg/kg/min) and/or the use of a less cardioselective agent (adrenaline). Dagbjartsson (et al, 1989) showed that exteriorised lamb fetuses subjected to maternal infusion of varying doses of terbutaline had a much more marked response in heart rate, myocardial contractility, blood pressure, and ST waveform change with hypoxia than did control fetuses. This suggests that

hypoxia may increase myocardial beta-receptor sensitivity. The observation that ST waveform change promptly returned to normal following hypoxia even though circulating catecholamines were still raised (Greene, 1983) supports this hypothesis. Mild hypoxia may induce ST change by beta-receptor activation whilst severe hypoxia may have a more direct effect on myocardial cells.

In some chronically instrumented fetal lambs a persistently elevated waveform (T/QRS ratio 0.48) was associated with chronic hypotension and/or anaemia despite normal blood gases (Greene, 1983). No fetus with these changes survived labour (Greene & Rosén, 1989). In one fetus the chronically elevated ST waveform became markedly negative with a sinusoidal heart rate and blood pressure pattern at the onset of a hypoxic insult for one hour during labour and the fetus died shortly afterwards.

Negative ST waveform. The unilateral uterine artery ligation model (Lafaber et al, 1984) was used in the guinea pig to examine the ST waveform of growth retarded fetuses compared with their normally grown littermates (Widmark et al, 1991). The majority of runted guinea pigs showed ST depression with and without negative T waves whilst their normally grown litter mates showed ST elevation (Figure 1.11).

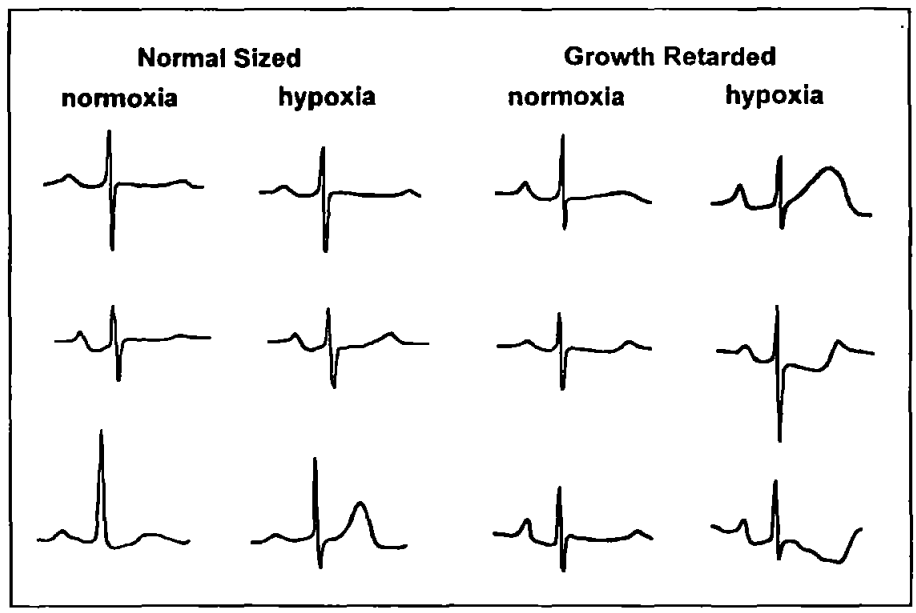


Figure 1.11 ST waveform change during hypoxia in normal sized and growth retarded guinea pig fetuses (modified from Widmark et al, 1991).

Normal sized controls showed a 4 to 7 fold increase in plasma catecholamines compared to the 2 to 3 fold increase seen in runted fetuses. These runted fetuses probably had depleted myocardial glycogen reserves, a blunted sympathoadrenal response to hypoxia and consequently ineffective myocardial anaerobic metabolism. This data fits well with much earlier observations by Gelli & Gyulai (1969). They examined the effects of pre-delivery glucose loading in rabbits subject to anoxia by complete placental separation. In untreated

controls the ECG initially showed high peaked T waves after the onset of anoxia which subsequently became depressed with negative T waves after 49 minutes. Half of the glucose loaded fetuses continued to show large positive T waves for 87 minutes before demise and although the remainder developed negative T waves, this occurred 13 minutes later than controls. So it would seem the development of a negative ST waveform is related to a lack of substrate and failing myocardial function. In the sheep fetus, negative T waves were associated with reduced myocardial contractility and a reduction in stroke volume (Rosén, personal communication).

The finding of negative ST waveforms can be explained by the effect of hypoxia on myocardial cell action potentials (Wohlfart, 1987). If energy balance cannot be maintained either by myocardial vasodilatation and aerobic metabolism supplemented by anaerobic metabolism, ischaemic hypoxia occurs first in the deeper layers of the myocardium (endocardium) compared with the epicardium. This alters the sequence of repolarisation to produce a negative ST waveform (Figure 1.7B). ST depression with T wave elevation (a biphasic ST waveform) is also seen when myocardial ischaemia occurs in adults and may represent an earlier stage in the development of myocardial ischaemic hypoxia when the action potential change is not uniform throughout the myocardium.

Summary ST waveform elevation indicates compensated hypoxic myocardial stress and a switch to anaerobic myocardial metabolism. A progressive rise in T/QRS ratio represents continuing anaerobic metabolism with a risk of eventual decompensation due to depletion of myocardial glycogen stores and a progressive metabolic acidosis. Biphasic and negative waveform changes probably indicate myocardial decompensation as a result of direct myocardial ischaemic hypoxia.

Technology.

The FECG in the Greene and Rosén animal experiments was recorded from subcutaneous silver/silver-chloride precordial chest leads. In contrast the human FECG is recorded from an electrode attached to the fetal scalp. This results in a number of problems.

Signal noise is increased significantly as attachment of a FSE to the scalp is not as secure as implanted precordial leads. This adds movement artefact to the signal. Several different types and designs of FSE are available in clinical practice. The ideal FSE for ECG waveform analysis has not been previously determined. Signal noise affects the shape of the ECG waveform (Figure 1.12) and must be removed before ST waveform analysis can reliably be performed (Greene, 1989).

Filtering is the easiest way to remove unwanted signal noise. Conventional CTG recorders heavily filter FECG signals to obtain a stable baseline from which QRS complexes are easily

counted to obtain the heart rate. However, the frequency content of the FECG is 0.05 to 100 Hz and high pass filtering to remove baseline noise will also remove the low frequency components of the slow moving parts of the waveform (the P wave, ST segment and T wave) and distort waveform shape. Early investigators used considerable filtering (e.g. Hon & Lee, 1963, bandpass 8-50 Hz) which would have obscured all but gross waveform changes. Others failed to quote the filter characteristics of their recording systems (e.g. Hioki, 1975). This may explain the inconsistencies in early reports of ST waveform change in the human fetus.

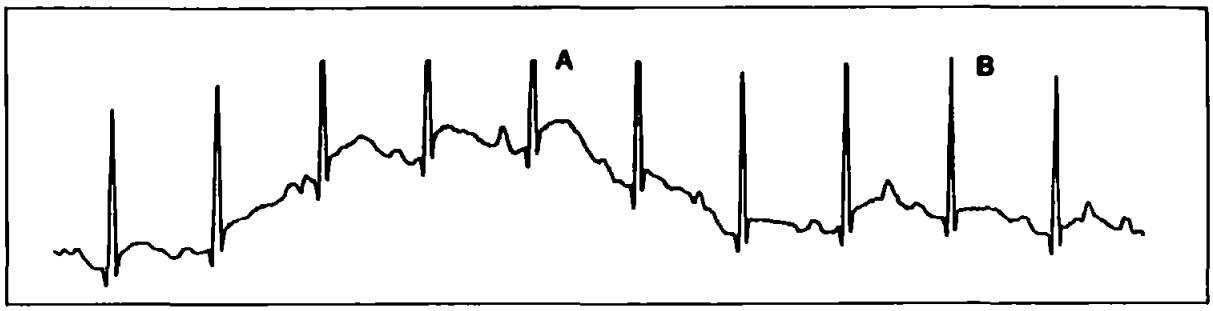


Figure 1.12 A strip of raw FECG recorded from a fetal scalp electrode. The baseline noise results in apparent alterations in ST waveform shape (compare complexes A and B). Reproduced from Greene, 1987, with permission.

Signal processing. Improvements in signal processing and the development of smaller, faster computers allowed signal noise to be removed with minimal filtering with the use of signal averaging (Marvell et al, 1980, Wickham, 1982, Lindecrantz, 1983). This technique recovers a wanted repetitive signal from background noise by averaging several signals. The repetitive signal is enhanced by n, the number of signals averaged, but random background noise is only enhanced by $\sqrt{n}$. A transient rejection algorithm was added to prevent obviously aberrant complexes from affecting the average (Greene, 1983). Signal averaging relies on a software algorithm to detect the QRS wave in every complex. If the signal contains too much noise the detection point will vary (jitter) and misalignment of the complexes will result in a distortion of the average. This will tend to reduce the height of the QRS complex and increase the calculated T/QRS ratio. This was overcome by producing parallel signals and filtering one to obtain a clean trigger from which to average the raw signal (Greene, 1983, Rosén & Lindecrantz, 1989). Inconsistencies between the QRS trigger and the rest of the signal such as may occur with physiological variation in heart rate may cause a smoothing of the T wave but this is unlikely to be a significant problem if the averaging period is kept short (Greene, 1983).

Systems for fetal ST waveform collection and analysis. A dedicated on-line microprocessor-based system for ST waveform analysis has been developed in Sweden as a result of the investigations detailed above (Rosén & Lindecrantz, 1989). It filters the signal for waveform analysis between 0.05 and 100 Hz at a sampling frequency of 500 Hz with 8

bit resolution. The electrode lead configuration used is different from that used by a conventional CTG recorder. A maternal skin electrode is used as the reference electrode in order to standardise the T wave vector so that it is unaffected by fetal rotation (Lindecrantz et al, 1988). This ST Analyser (STAN, Cinventa, AB, Sweden) has been used successfully in a number of observational studies (Arulkumaran et al, 1990, Rosén et al, 1992).

Another system for on-line FECG analysis has been designed in Nottingham (Marvell et al, 1980) and used in several studies (Jenkins et al, 1986, Murray et al, 1986). The FECG is recorded with a conventional lead system by a CTG recorder. The signal is initially filtered from 3 to 250 Hz with subsequent enhancement of low frequencies down to 0.16 Hz. It analyses many other features of the FECG in addition to ST waveform amplitude. On-line analysis was initially performed by a computer in a separate room but a PC-based bedside version has recently been developed. The technology is patented and there are no published reports of its performance or clinical value.

An off-line ST waveform analysis system has been developed in Southampton (Newbold et al, 1989). It uses a conventional lead system and collects the FECG from a CTG recorder (bandwidth 0.3 to 50 Hz). The FECG and uterine contraction data are recorded onto an FM tape recorder for subsequent analysis. The low frequency components of the FECG are electronically enhanced down to 0.16 Hz. The sampling frequency is 1000 Hz with 12 bit resolution. It has been used in two studies (Newbold et al, 1989, 1991).

Clinical studies.

Human intrapartum studies with appropriate filter characteristics (Pardi et al, 1974, Marvell et al, 1980, Lilja et al, 1985, Jenkins et al, 1986) showed the fetal scalp ECG has a T wave which is usually isoelectric or has a positive T wave no larger than the P wave. These, and other studies confirmed that the FECG could be recorded from a FSE for on-line analysis and helped to develop the technology to the stage where larger observational studies could be performed (Lilja et al, 1988, Lilja et al, 1989). Normally the ST waveform and T/QRS ratio remain relatively stable throughout labour for a given fetus (Newbold et al, 1989) and reported mean values are similar; 0.15 (SD 0.05) Lilja et al, 1988, and 0.10 (SD 0.05) Newbold et al, 1989.

Initial studies suggested that a combination of ST waveform and CTG change identified fetuses at risk of poor outcome. All 3 cases of asphyxia reported by Arulkumaran et al (1990) had acute ST elevation and CTG change. All had a metabolic acidosis at delivery (arterial pH <7.05, BDecf >12 mmol/l) and all had low Apgar scores at delivery. The development of negative ST changes in association with CTG changes has been reported in two cases (Rosén et al, 1989, Rosén et al, 1992). Both were growth retarded and asphyxiated and one died.

It has been speculated that the addition of ST waveform analysis to the CTG may help prevent unnecessary operative intervention. One of the first clinical studies (Lilja et al, 1985) showed only 26% of 48 high risk cases had a continuously normal CTG, whereas 67% had a continuously normal ST waveform. The operative delivery rate for fetal distress was 20% but fetal outcome was good in all cases. In another study, 12 of 44 cases with an abnormal CTG were delivered for fetal distress, but none were significantly acidotic and none had ST waveform change (Newbold et al, 1991). The CTG was abnormal in 55% of 201 cases studied by Arulkumaran et al, (1990) but the T/QRS was abnormal in only 27%. Twenty-seven had an operative delivery for fetal distress but only 11 had T/QRS changes and all fetuses with a cord artery pH<7.15 or a standard bicarbonate <15 mmol/l were identified by ST waveform change.

The technology of the ST ANalyser appeared sufficiently advanced to allow clinical research. Arulkumaran et al (1990) reported 77% of their cases had continuous T/QRS ratios available and the other 23% had intermittent values recorded.

Model of interpretation.

The evidence from these clinical observational studies supported the animal experimental findings and enabled us to develop a model of interpretation based on the combination of CTG and ST waveform change (Figure 1.13). The next step was to examine the value of ST waveform analysis in randomised clinical trials using this model of interpretation.

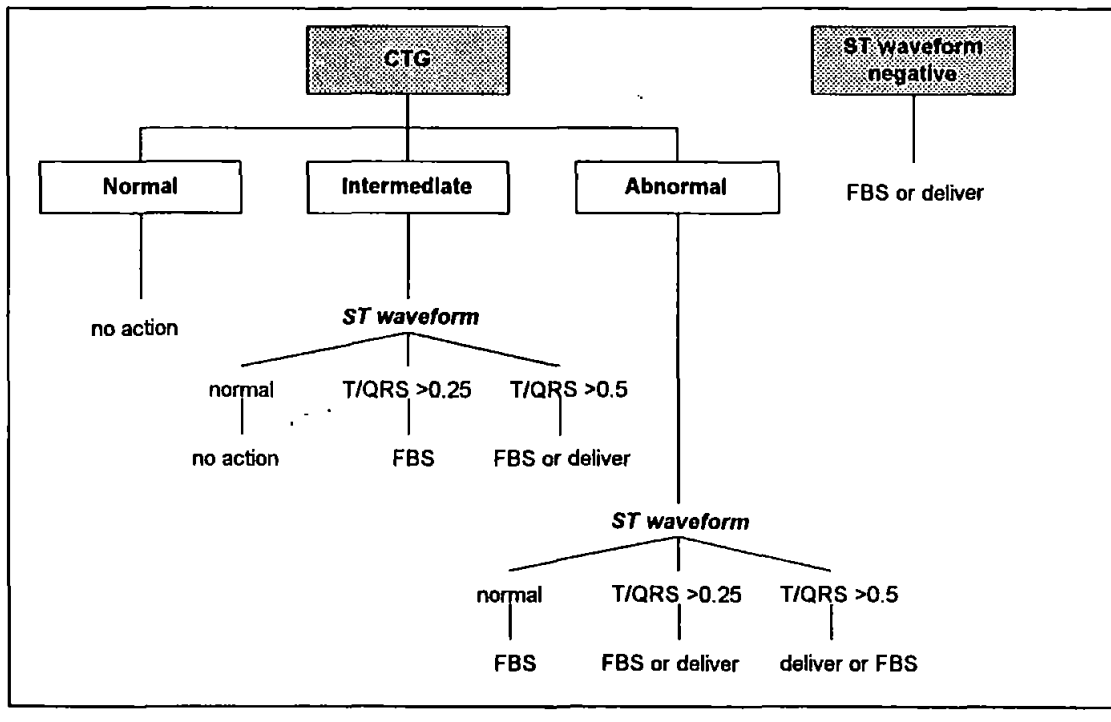


Figure 1.13 Model of interpretation for CTG plus ST waveform changes. Action on the basis of ST change alone is only recommended for persistently negative waveforms.

Objectives and structure of thesis.

It had always been proposed that ST waveform analysis of the fetal ECG should be appropriately validated before introduction into clinical practice (Greene, 1983, Rosén et al, 1986, Greene, 1987). Since 1975 a steady, progressive line of experimental and clinical investigations have determined the pathophysiological basis for ST waveform change, developed the required technology and gathered enough clinical information for a model of interpretation to be developed. This thesis examines and reports the final stages of that validation process from validation of a collection system from the fetal scalp electrode through to the final monitor output and, then a randomised trial to test the clinical value of the addition of ST waveform analysis to the CTG using this equipment.

The randomised trial also provided an opportunity to examine how CTG monitoring was used in clinical practice and to assess the value of umbilical cord blood gas analysis as an objective measure of neonatal outcome.

The work will be presented in the following chapters;

Chapter 2. Part I. An investigation of fetal scalp electrodes.
Part II. Validation of the data collection system.

Chapter 3. Randomised clinical trial of CTG alone or with ST waveform analysis for intrapartum monitoring.

Chapter 4. Assessment of current monitoring practice.

Chapter 5. Assessment of umbilical cord blood gas analysis.

Chapter 6. Future developments in intrapartum fetal monitoring.

Chapter Two

Optimising the acquisition of the fetal ECG in clinical practice.

Part I Fetal scalp electrodes

Part II Validation of the FECG data collection system

Analysis of the ST waveform of the fetal ECG is a more technically demanding method for intrapartum fetal assessment than CTG analysis. Considerable signal processing is necessary to extract the signal from unwanted background noise without distorting its biological components. Any system for signal analysis is only as good as the quality of data it receives; or to put it more plainly, rubbish in, rubbish out. It was therefore important to validate the FECG collection system to be used before further clinical studies were attempted.

The work will be presented in two parts; Part I deals with fetal scalp electrodes (FSEs) and Part II with examination of the remaining aspects of data collection and analysis with particular reference to the ST ANalyser (STAN, Cinventa AB, Mölndal, Sweden).

Part I. An examination of currently available fetal scalp electrodes.

Introduction.

Electrode function In body tissue.

The patient-electrode interface is the first stage of any biological signal recording system and is frequently the factor which most limits the performance of these systems (Gatzke, 1974). Physiological signals are carried by ionic currents in the body, whilst electrical currents are carried by electrons in cables. An electrode must act as a transducer to change ionic currents into electrical currents. Some materials are better suited for this purpose than others. Two important factors which determine the function of an electrode in body tissue are, firstly, the electrode's offset potential and, secondly, its susceptibility to movement artefact.

Electrode offset potential. When an electrode is placed in a conducting solution metal ions transfer from the metal into the solution and from the solution onto the metallic surface to form a bipolar layer. One polarity of charge becomes dominant on the surface of the metal and the opposite polarity is distributed in excess in the electrolyte immediately adjacent to the electrode (Figure 2.1). This cloud or double layer of charged ions at the electrode surface allows electron transfer between metal and tissues but results in a difference in electrical potential between the electrode/electrolyte interface and the rest of the electrolyte solution (Geddes, 1972). This is referred to as the electrode offset potential. Ideally, the offset potential of an electrode should be as low as possible as changes in the potential add noise to the signal being measured (Cooper et al, 1974). Different metals

have different offset potentials and thus some are more suited to use as electrodes than others. Metals such as stainless steel which do not ionise readily form a large double layer of ions and have a high offset potential. In comparison, silver-chloride coated silver electrodes (silver/silver-chloride) have a low offset potential as the silver-chloride dissociates to silver and chloride ions which move freely between electrode and electrolyte, allowing electron transfer without the formation of a double layer of charge.

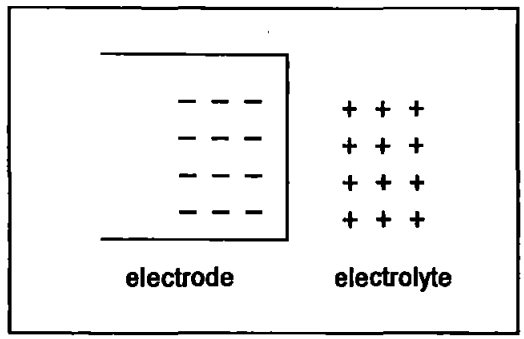


Figure 2.1 The electrode offset potential.
A double layer of charged ions forms at the electrode /electrolyte interface and results in a difference in electrical potential between the interface and the rest of the electrolyte solution. This is the electrode offset potential.

Movement artefact. Movement at the electrode/electrolyte interface results in a disturbance of ions in the double layer which alters the electrode potential, affects electron transfer and adds artefacts to the recorded signal. Electrodes with a high offset potential have more disturbance of their large ionic cloud during movement and thus produce more movement artefact than low offset potential electrodes. Susceptibility to movement artefact is also determined by the security of electrode attachment to the body surface. The less secure the attachment, the more movement at the electrode/electrolyte interface and the more artefact is likely to be added to the signal.

Ideally, the electrodes used for FECG recording should have a low offset potential and a secure method of attachment to the fetus.

Fetal scalp electrodes.

FSE Development. FSEs were first designed to record the fetal ECG. The first FSE was made from a nickel-silver surgical skin clip which had to be attached to the fetal scalp through an amniscope with a long-handled forcep (Hon, 1963). The metal used for the electrode was later changed to silver/silver-chloride with a marked improvement in signal quality (Hon, 1967). The design was also changed to a single wire spiral which was attached to the fetus by a disposable plastic applicator. However, problems with the silver-chloride coating process frequently resulted in flakes of the material being deposited in fetal scalp tissues. This was obviously unsatisfactory but, at that time, choice of an alternative material was influenced by Hon's observations on heart rate and ECG changes in the dying fetus (Hon et al, 1959). Hon only detected FECG waveform changes immediately prior to death and concluded that FHR changes would be more useful for fetal monitoring purposes. As a result the material used for the FSEs was changed to stainless

steel. Hon acknowledged this produced a far noisier ECG signal but showed it was still suitable for ***heart rate*** detection when used with a bandpass filter of 1.5 to 100 Hz (Paul & Hon, 1973).

FSE Design. All FSEs have the same basic design; an active electrode which attaches to the fetal presenting part (scalp or bottom) and a reference electrode which makes contact with the vaginal vault via cervical secretions and amniotic fluid. Each electrode is attached to a wire which runs to a connecting device attached to the mother's leg. On the back of this device is a metal plate which rests on the mother's leg and acts as the signal reference point.

There are two major types of FSE in use today; the spiral types, which are attached to the fetus with either a single or double spiral and the Copeland types which are attached with a semicircular clip (Figure 2.2). Both types are made from stainless steel.

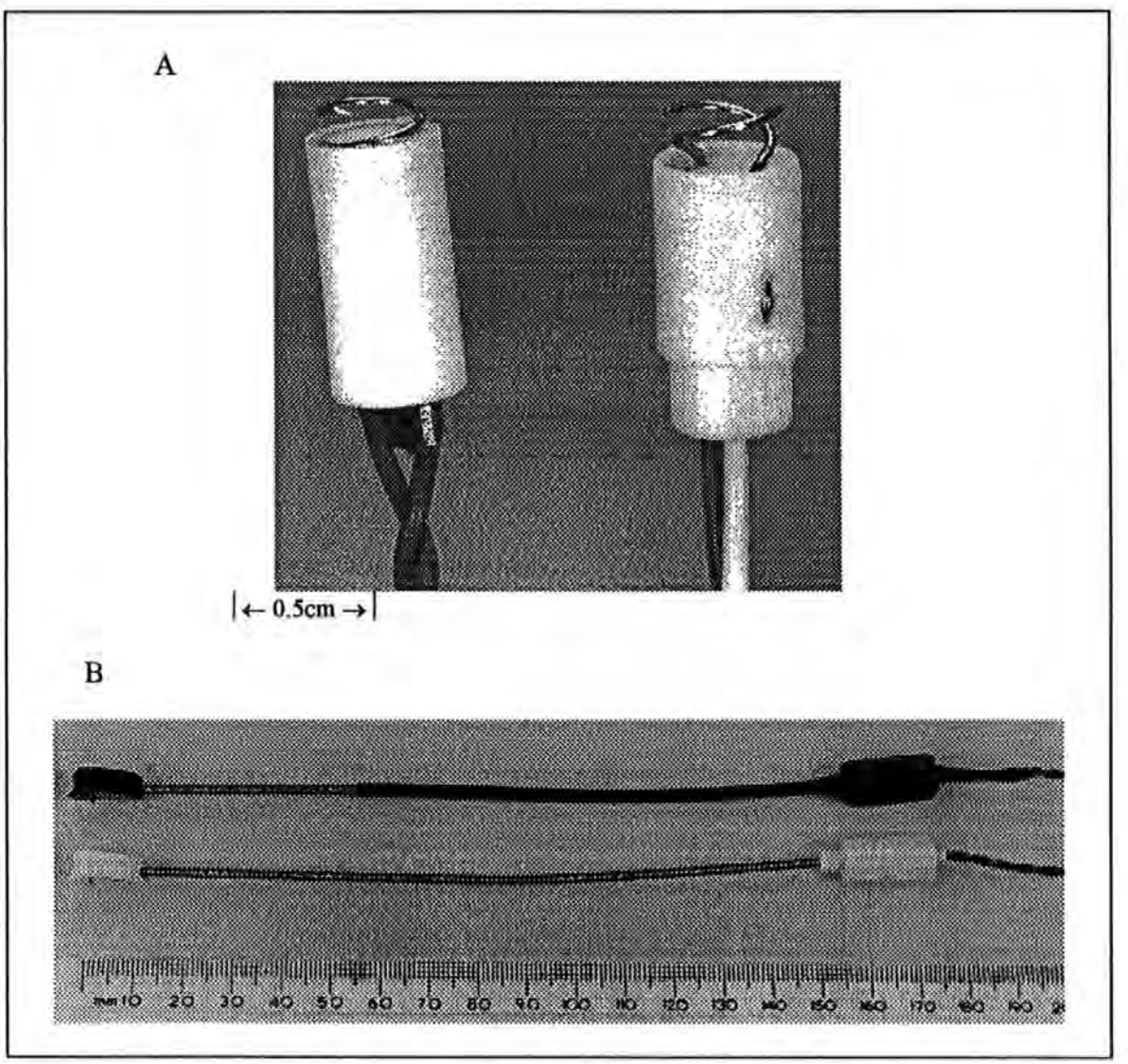


Figure 2.2 A. Corometrics single (left) and Hewlett-Packard double (right) spiral FSEs.
B. Copeland Reusable (top) and Disposable (bottom) FSEs.

As all the FSEs now used to collect FECG signals are made from stainless steel, they are particularly susceptible to movement artefact. Their different designs, different means of attachment to the fetus and different effects on the primary ECG signal have not previously been considered. Given the renewed interest in FECG waveform changes and their significance during labour, it was important that these differences be investigated. In view of this, a study was designed to compare and contrast five commonly available FSEs by examining their physical and electrical characteristics and then assessing the quality of the fetal ECG signal obtained from each in a randomised clinical trial.

The five types of FSE investigated were the single spiralled Corometrics (Corometrics Medical Systems Inc. USA) and Cetro (Cetro AB, Sweden), the double spiralled Hewlett-Packard (Hewlett-Packard Medical, UK) and both the Copeland Reusable and Disposable (Surgicraft Ltd, UK).

Methods.

Physical characteristics.

The construction of each FSE was examined under a hand lens and the clinical method of application to the fetus critically reviewed.

Electrical characteristics.

An in-vitro experiment was designed to record and compare the FSE frequency responses and then the frequency responses were modelled using digital filters to assess the effect of the FSEs on the ECG waveform shape. The work for this section was performed in conjunction with R. Keith and is also presented in his PhD thesis (Keith, 1993).

In-vitro experiment. The frequency responses of the FSEs were obtained in an in-vitro experiment in order to assess the ability of the electrodes to faithfully reproduce the ECG waveform (Figure 2.3). Optimal attachment was ensured for each electrode. The Solatron 1170 Frequency Response Analyser was used to produce input signals between 0.01 and 200 Hz which were passed through each FSE. The output signal from each was fed back to the Solatron and compared with the input signal. Any change in amplitude (gain) or timing (phase) was measured.

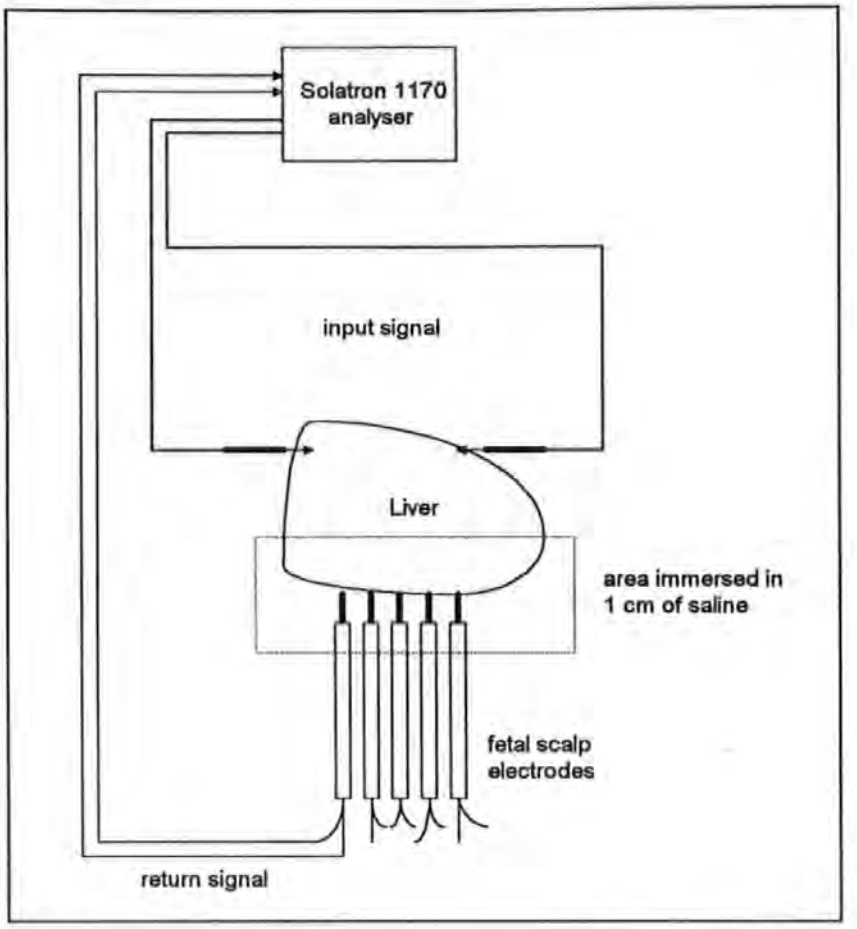


Figure 2.3 Experimental set-up for in-vitro measurement of FSE frequency responses.

Digital filter model. A digital filter with a frequency response equivalent to that of each FSE was obtained using the frequency sampling method (Lockhart and Cheetham, 1989). The digital filter was used to process ECG data obtained from 4 neonates within 1 hour of birth. The neonate data was collected using precordial silver/silver-chloride skin electrodes to avoid the influence of the FSEs under investigation. The data acquisition system used for this purpose had a bandwidth of 0.05 - 200 Hz, with a 12-bit resolution and a sampling frequency of 1000 Hz. The lower frequency of 0.05 Hz was chosen to conform to the recommendations of the American Heart Associations Committee on Electrocardiography (1975).

Randomised clinical trial of FSEs.

The five types of FSE were randomly allocated to a group of 50 women in labour. Women were entered into the trial after the decision to use a FSE was made by Labour Ward staff and informed consent obtained. The electrode to be used was determined by opening a sealed opaque envelope. Only new electrodes of each type were used. All spiral electrodes and most Copelands were applied by one investigator (the author). The others were applied by experienced midwives.

The ST ANalyser was used as the FECG recorder for this study. The FECG signal was recorded differentially between the electrode on the scalp and a standard skin electrode placed on the maternal thigh with the vaginal electrode as the common mode point for the amplifier. The data collection system and processor was assessed prior to the FSE clinical trial and the findings will be presented in Part II of this chapter.

An example of a STAN recording is shown in Figure 2.4. The FHR and uterine activity are displayed as on a standard CTG recording and the T/QRS ratio is plotted continuously just above the contraction channel. Averaged ECG complexes and their T/QRS ratio are printed every 2 to 2.5 minutes to allow waveform shape and signal quality to be assessed.

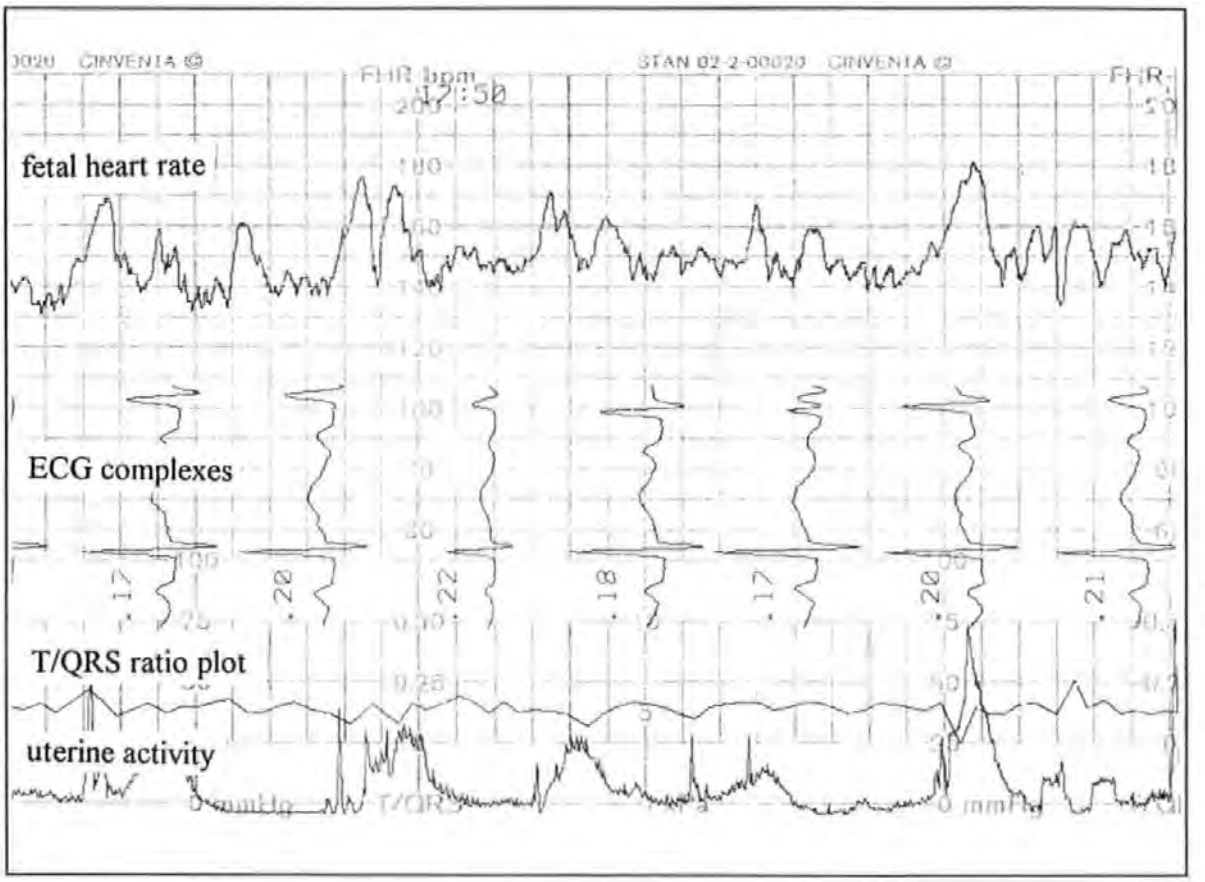


Figure 2.4 An example of a STAN recording.

A subjective assessment of signal quality was made at the bedside at intervals through-out data collection. If the FHR or ECG recordings showed excessive signal loss or interference the electrode was reapplied. At a later stage the complete STAN CTG and ECG waveform trace was divided into 30 minute epochs and analysed. The first and second stages of labour were considered separately.

Each FHR record was graded 1 (excellent), 2 (fair - adequate for monitoring purposes), or 3 (poor - inadequate for clinical use, Figure 2.5). These gradings were based on the

amount of signal loss and interference seen on the trace.

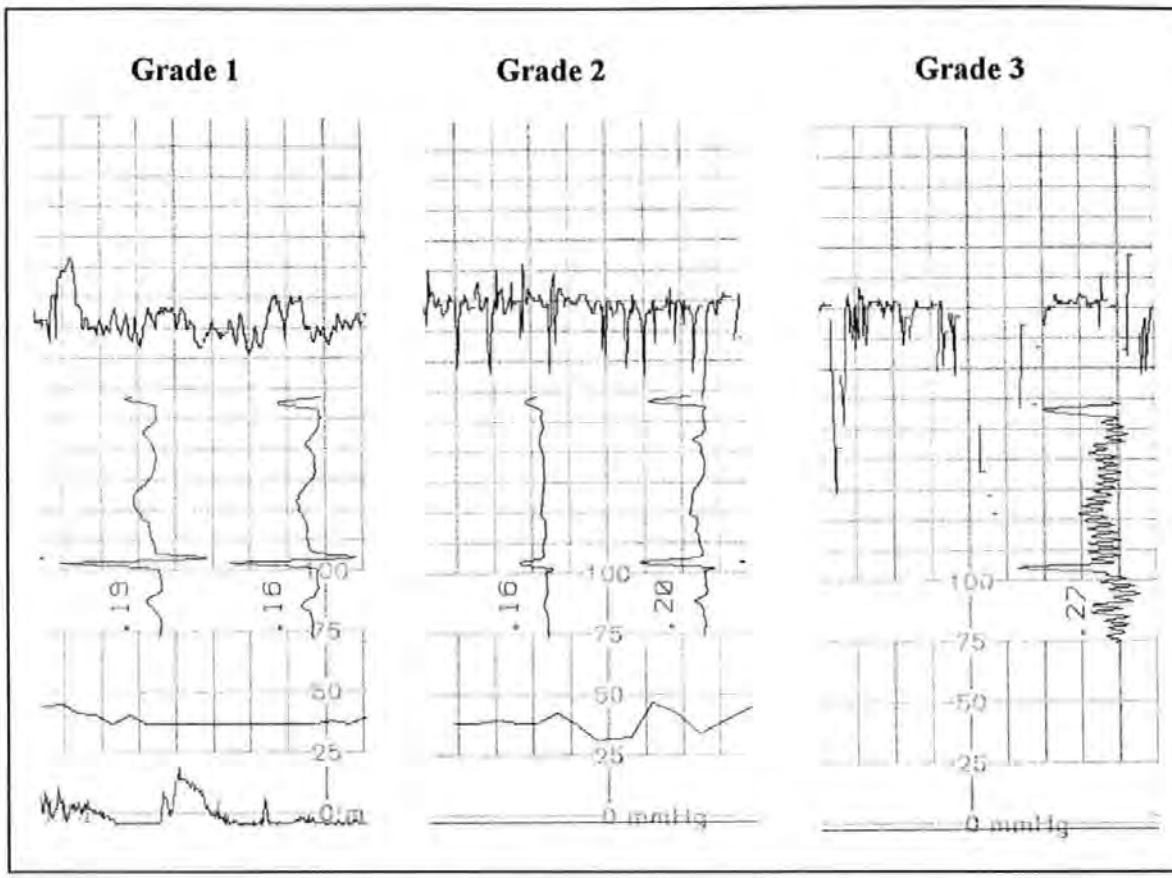


Figure 2.5 Fetal heart rate quality grades 1 (excellent), 2 (fair - adequate for clinical use) and 3 (poor - inadequate for clinical use).

The STAN prints the average of 30 ECG complexes every 2½ minutes. The number of complexes printed reflects the time taken to accept 30 ECG complexes into the average and shape of these complexes gives a measure of signal quality. The total number of complexes in each epoch was counted (maximum = 14) and each complex graded as follows:

1 optimal, no baseline shift, no high frequency components;
2 fair, some interference from high frequency components but waveform components still well-defined;
3 bad, baseline shift or excessive high frequency components or very low amplitude signals (Figure 2.6).

The ratio of the T wave height to the QRS complex height is plotted continuously as the T/QRS ratio. The number of minutes that this ratio was plotted in each 30 minute epoch was measured from the trace. On 13 patients the raw ECG data from the STAN was recorded and stored onto a PC-based Optical Disc (Reflections Systems Ltd, Essex) for later analysis

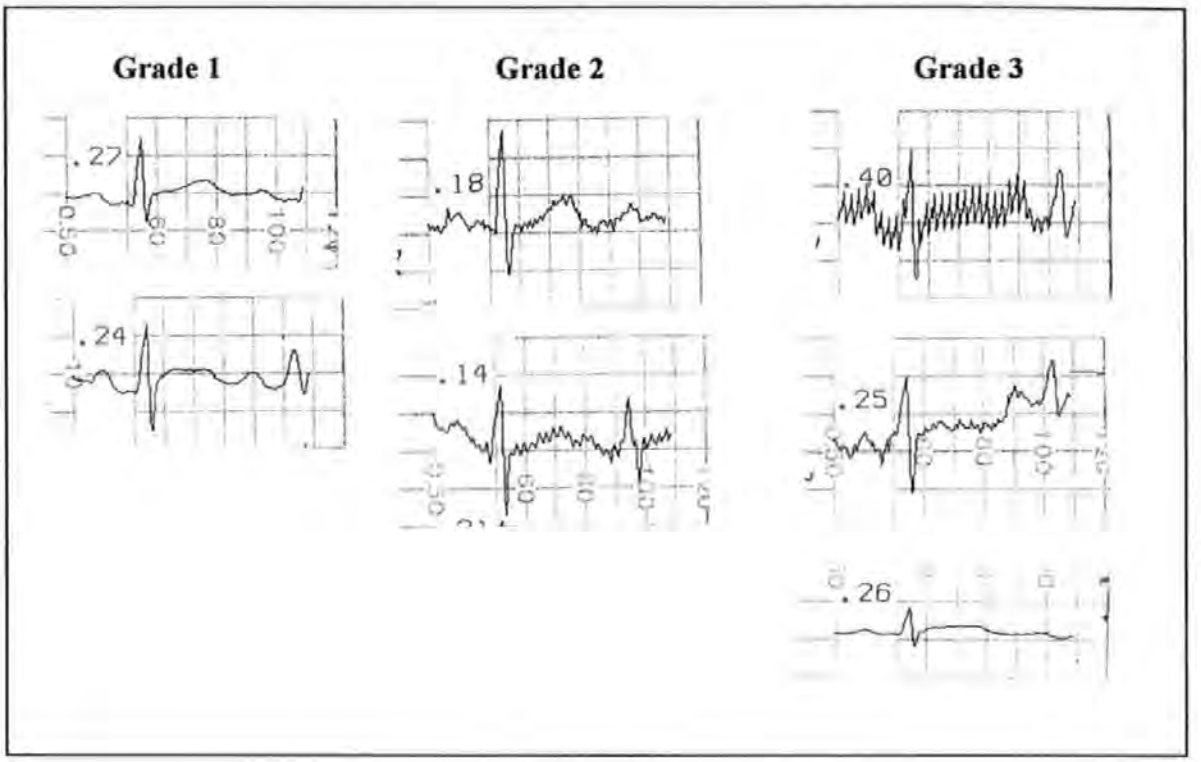


Figure 2.6 ECG quality grades 1 (optimal), 2 (fair - some high frequency noise but waveform components still well-defined) and 3 (poor - excessive high frequency noise, wandering baseline or very low amplitude ECG).

Statistical analysis was by One Way Analysis of Variance using the "Minitab" Version 7 statistical software package run on a prime mainframe computer.

Results.

Physical characteristics.

Spiral FSEs. The spiral electrodes are attached to the fetus with the aid of two PVC plastic tubes - a driving tube and a guide tube. These slip respectively onto and over the electrode facilitating safe introduction into the vagina and rotation of the spiral into the fetal scalp. These tubes are withdrawn once the electrode is applied leaving only the electrode wires emerging from the vagina. All of these FSEs are designed for a single use and then are discarded.

The applicator tubes for the Hewlett-Packard double spirals are larger and more rigid than the single spiral applicators. This made ideal positioning and application to the fetal head difficult, especially early in labour with a posterior cervix. Despite providing a large surface area for signal collection, the double spiral only allowed a 180 degree clockwise rotation for attachment compared to the 360 degree rotation of the single spiral. As a result double

spirals were more likely to become detached during labour than single spirals. Interestingly, it was found that the wires from both the Corometrics and Hewlett-Packard electrodes were wound in the opposite direction to the needle rotation which tended to encourage un-winding with maternal movement. This was especially noticeable with the Hewlett-Packard.

Copeland FSEs. The Copeland FSEs are either reusable or disposable and have a spring action - twisting the base of the electrode anticlockwise rotates the needle semi-circle at the electrode head into a recess. Once the head of the electrode is pressed firmly against the fetus, the base is twisted clockwise causing the round-bodied needle to emerge from the recess and rotate into the fetal scalp (Figure 2.7). The length of electrode which protrudes from the vagina increases as descent of the fetal head occurs through the maternal pelvis. The Reusable Copelands are cleaned, tested for electrical continuity and re-sterilised before reuse.

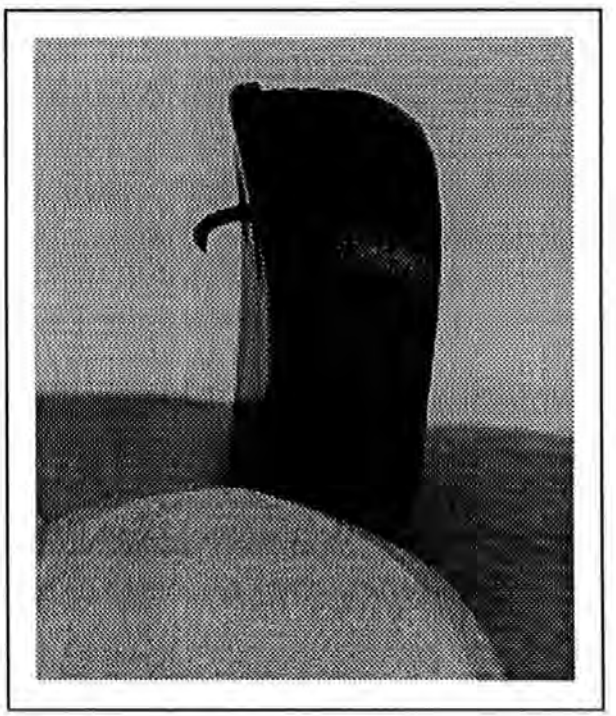


Figure 2.7 Copeland FSE showing the round- bodied needle half rotated out of the recess in the FSE head.

The long, semi-rigid design of the Copelands made them susceptible to movement artefact as the entire length of the electrode was suspended from its point of insertion into the fetal scalp (Figure 2.8). Furthermore, it was found that the round-bodied needle of the Copeland FSE approached the tough fetal scalp at an oblique angle and often failed to penetrate completely or merely pinched the skin without penetrating it. This not only increased susceptibility to movement artefact but also resulted in only a small area of electrode coming into contact with fetal subcutaneous tissues.

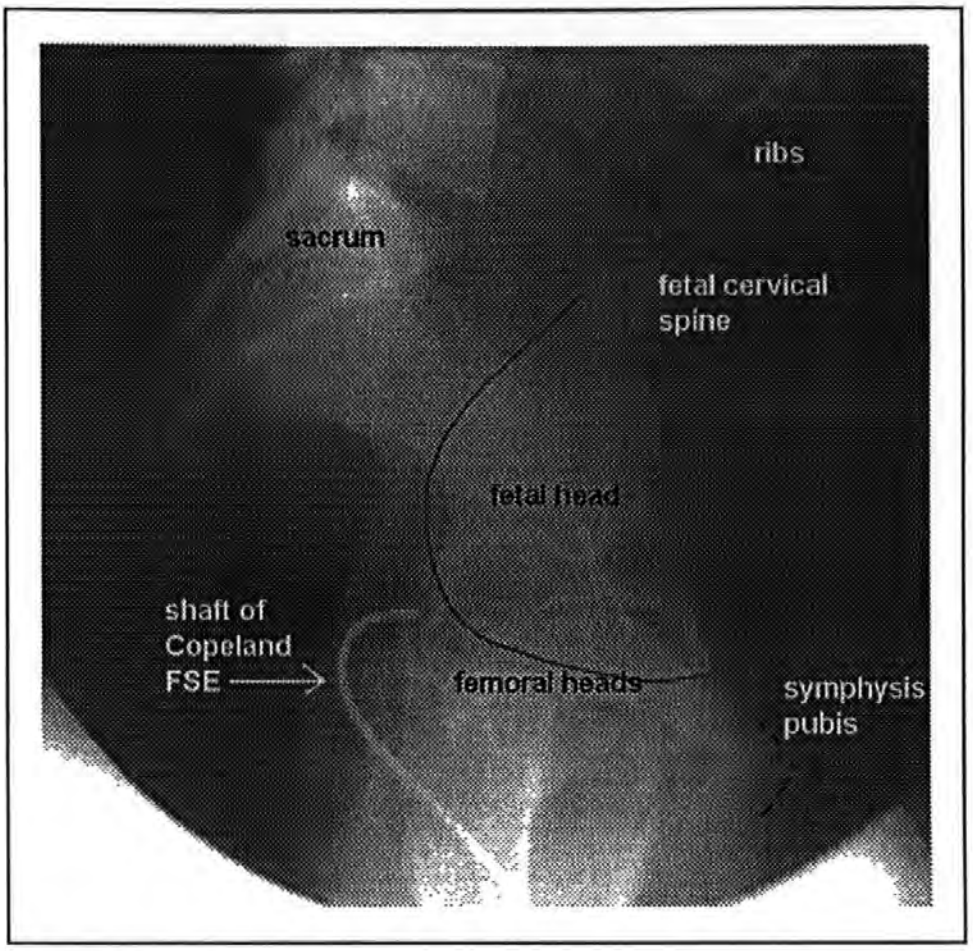


Figure 2.8 A serendipitous X-ray taken in early labour (because of a mistaken diagnosis of a breech presentation). A Copeland FSE has been applied to the fetal head. There is a gap between the fetal head and the shaft of the FSE because the plastic head of the FSE is not visible on the X-ray. Note the curve on the shaft of the FSE as it follows the axis of the vagina which is likely to cause tension at the electrode/scalp interface.

Electrical characteristics.

The magnitude frequency response for each electrode is shown in Figure 2.9. The phase response of the FSEs was considered negligible as the maximum phase change measured was only 14 degrees (Copeland Reusable).

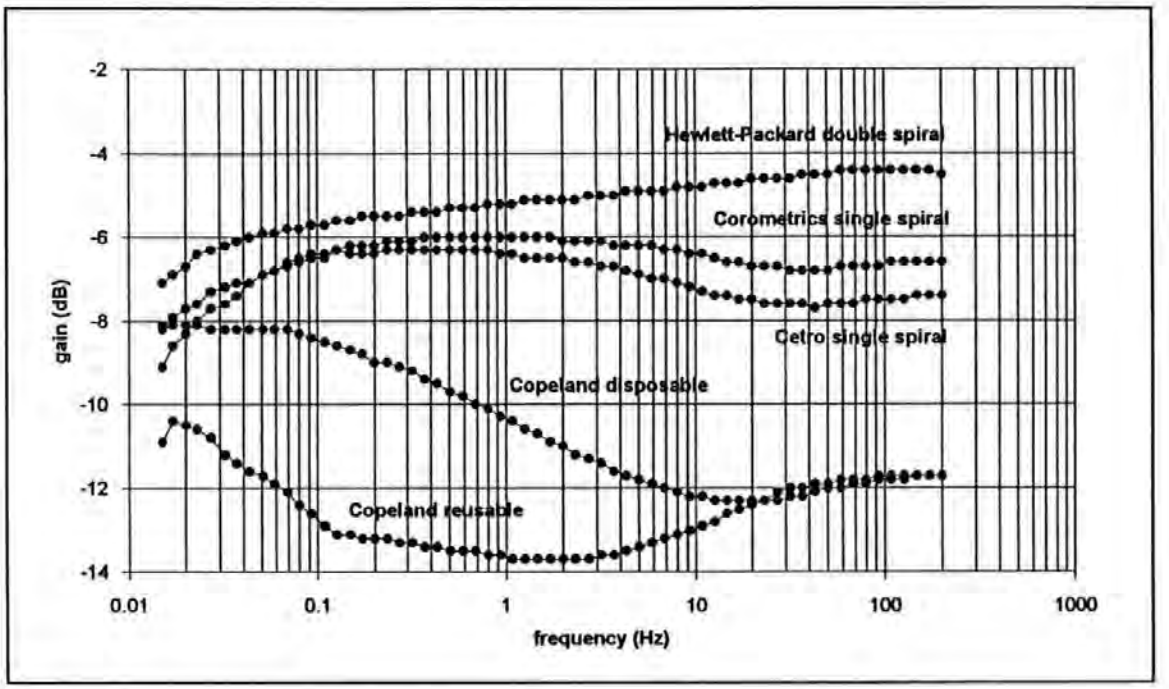


Figure 2.9 FSE frequency responses.

The electrodes could be divided into two groups on the basis of their frequency responses. It was found that the magnitude response for the spiral FSEs approached the ideal electrode response, being nearly flat within the frequency band of interest (0.05-100 Hz). The Copeland FSEs attenuated the higher frequency FECG components by 4 to 8 dB more than the spirals but only attenuated the very low frequency components (which are responsible for baseline shifts) by an extra 2 to 4 dB.

Typical filtered and unfiltered sections from a Corometrics single spiral and a Copeland reusable FSE simulation are shown in Figure 2.10. As expected, visual examination showed that both FSEs attenuated the signal, but the peak to peak amplitude of the Copeland signal was only 54% of that of the Corometrics. Whilst there did not appear to be any major changes in the waveform shape, there were small modifications in the P and T wave regions with the Copeland FSE.

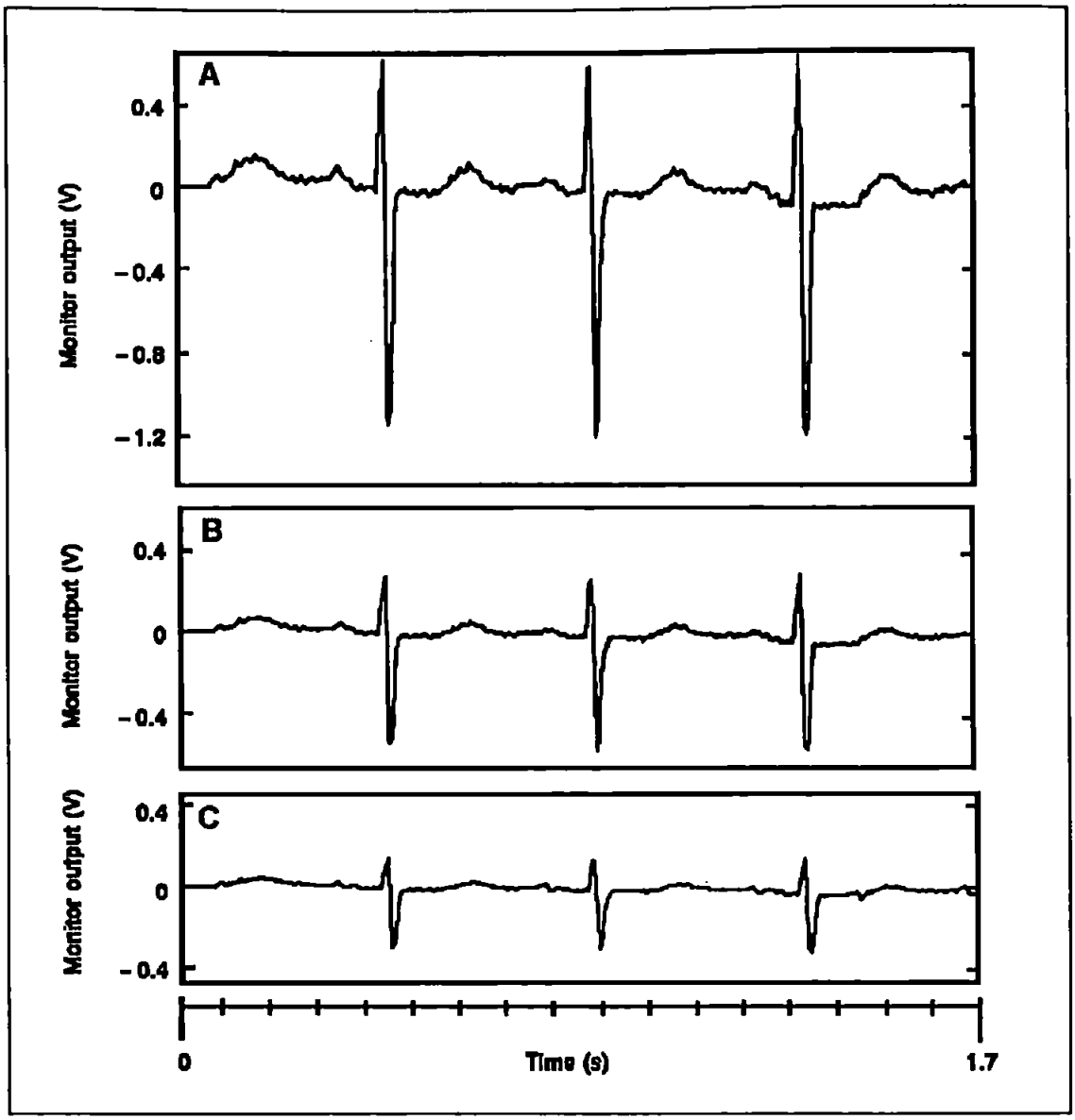


Figure 2.10 Effects of simulated FSE frequency responses on a segment of neonatal ECG recorded with precordial silver/silver-chloride electrodes; A. raw neonatal ECG, B. after the Corometrics single spiral filter, C. after the Copeland Reusable filter.

Clinical trial.

First stage. The first stage results are summarised in Table 2.1. The Copeland Disposable electrode had a significantly lower proportion of Grade 1 FHR epochs compared to the spiral FSEs ($p<0.05$) and a significantly higher proportion of Grade 2 epochs compared to the Corometrics single spiral and Hewlett-Packard double spiral ($p<0.05$). There were no significant differences in first stage total ECG complex numbers but differences are apparent in the quality of the complexes. The Copeland Disposable FSE had a significantly lower proportion of Grade 1 complexes than all spirals ($p<0.005$) and a significantly higher proportion of Grade 3 complexes than the single spirals ($p<0.005$) and double spirals ($p<0.01$). Copeland Reusables had significantly less Grade 1 and more Grade 3 complexes

than the single spirals ($p<0.05$). Copeland Disposable FSEs had a significantly lower average duration of T/QRS ratio plots than all the spirals ($p<0.005$) and the Copeland Reusable FSEs ($p<0.05$).

Second stage. The results from the second stage of labour followed the same trend with single spiral FSEs producing the best quality heart rate and ECG signals (Table 2.2). Overall second stage quality was not as good as first stage quality for each FSE type.

Reapplication rates. Only one reapplication of a Corometrics single spiral FSE was required in one patient during the study because the FSE became dislodged during a vaginal examination. The Cetro single spiral required two reapplications in two patients in attempts to improve poor signal quality. The Hewlett-Packard double spiral required four reapplications in four patients - two because the FSE fell off, two to improve poor signal quality. In comparison reapplication rates on account of poor signal quality were much higher with the Copeland types; 11 in four patients for the Reusable and 17 in six patients in the Disposable groups respectively.

Cost comparisons. The Corometrics single spirals were the least expensive disposable FSE at £3.20 each; the Hewlett-Packard double spirals cost £4.50 each and the Copeland Disposables £6.50 each (the Cetro FSE was not available in the UK). The Copeland Reusables cost £18 each but had an average life of 10 patients. They cost 30 pence to clean, package and resterilise making the total cost £2.10 per patient. However, because of their design it was difficult to ensure that all fetal material was removed from the recess in the head of the device. The Central Sterilisation Unit manager could not guarantee that all material was removed and recommended a change to a disposable FSE (J Barker, personal communication).

Table 2.1. First stage FHR and ECG signal quality for each fetal scalp electrode type.
10 recordings for each type, each record assessed over 30 minute epochs and averaged.
Averaged results for each FSE type shown.

Fetal scalp Electrode	Total no. 30 min. epochs	FHR Quality			ECG complexes				T/QRS ratio Duration of plot per 30 min. ± SD
		% of epochs			No. complexes per 30 min.	% of complexes			
		Grade 1	Grade 2	Grade 3		Grade 1	Grade 2	Grade 3	
Corometrics	81	84.0	6.1	9.9	12.5	87.8	8.9	3.3	23.8 ± 6.0
Cetro	69	85.5	14.5	0.0	13.2	80.3	17.3	2.4	25.5 ± 3.8
Hewlett-Packard	65	83.1	10.8	6.1	13.2	76.5	11.6	11.9	24.9 ± 2.9
Copeland Reusable	73	57.5	23.3	19.2	12.2	61.6[1]	18.9	19.5[1]	21.5 ± 6.1
Copeland Disposable	64	39.1[2]	39.1[3]	21.8	10.7	39.1[4]	22.2	38.1[5]	15.0 ± 6.5[6]

1 $p<0.05$ compared to Corometrics and Cetro single spirals

2 $p<0.05$ compared to Corometrics, Cetro and Hewlett-Packard spirals

3 $p<0.05$ compared to Corometrics and Hewlett-Packard spirals

4 $p<0.005$ compared to Corometrics, Cetro and Hewlett-Packard spirals

5 $p<0.005$ compared to Corometrics and Cetro, $p<0.01$ compared to Hewlett-Packard spirals

6 $p<0.005$ compared to Corometrics, Cetro and Hewlett-Packard spirals, $p<0.05$ compared to Copeland Reusables

All by One Way Analysis of Variance.

Table 2.2. Second stage FHR and ECG signal quality for each fetal scalp electrode type.
Available recordings for each type, each record assessed over 30 minute epochs and averaged.
Averaged results for each FSE type shown.

Fetal scalp Electrode (number)[1]	Total no. 30 min. epochs	FHR Quality			ECG complexes				T/QRS ratio Duration of plot per 30 min. ± SD
		% of epochs			No. complexes per 30 min.	% of complexes			
		Grade 1	Grade 2	Grade 3		Grade 1	Grade 2	Grade 3	
Corometrics (8)	12	61.5[2]	23.1	15.4	8.3	64.6[2]	19.2	16.2	16.7 ± 7.5
Cetro (7)	9	66.7[2]	22.2	11.1	10.2	71.7[2]	17.4	10.9	15.7 ± 11.2
Hewlett-Packard (8)	10	50.0	0.0	50.0	6.8	44.1	20.6	35.3	12.9 ± 9.3
Copeland Reusable (7)	13	53.8[3]	23.1	23.1	9.3	28.9	37.2	33.9	14.9 ± 6.6
Copeland Disposable (7)	9	11.1	55.6	33.3	7.6	45.0	27.5	27.5	9.0 ± 7.3

1 Details of missing numbers; Corometrics & Cetro - operative delivery before second stage (2 and 3 cases respectively), Hewlett-Packard - FSE fell off in second stage (2 cases), Copeland Reusable - abandoned poor quality (2 cases) & LSCS in first stage (1 case), Copeland Disposable - abandoned poor quality (1 case) & LSCS first stage (2 cases).

2 $p<0.05$ compared to Hewlett-Packard, and both Copelands.

3 $p<0.05$ compared to Copeland Disposable

All by One Way Analysis of Variance.

Discussion.

These investigations showed that single spiral FSEs were the most suitable for ECG waveform collection. They were the easiest to apply optimally, appeared to produce the most stable attachment and were least prone to movement artefact problems. They had a near ideal signal transfer function and, although they produced more signal attenuation than the double spirals, their greater security of attachment produced a more favourable signal to baseline noise ratio. They were also the cheapest of the disposable types.

Double spiral FSEs showed the least signal attenuation in the in-vitro experiment. However, despite their near ideal frequency response, problems in applying and maintaining attachment in-vivo made them less suitable for data collection. Some of these problems could be overcome by the simple expedient of twisting the lead wires in the same direction as the spiral needles so the FSE is not so easily dislodged by traction on the wires during maternal movement.

The Copeland FSEs showed most signal attenuation in-vitro. Their frequency response indicated that they attenuated the low frequency noise less than the principle ECG signal. This resulted in the poorest signal to noise ratio of all the FSEs; the smallest ECG signal with the largest baseline swings. Their long, semi-rigid design and the difficulty in obtaining optimal attachment resulted in increased signal noise. Fixation problems could immediately be improved by making the point of the needle taper-cut rather than round-bodied and by meticulously ensuring optimal attachment, though movement artefact is likely to remain a problem.

The subjective results of the clinical trial have been confirmed by an automatic analysis of signal quality performed on the 13 traces which were recorded onto optical disc (Keith, 1993). The most important determinants of signal quality were found to be the amount of baseline noise and signal size. Baseline noise is related to security of attachment, as already discussed, and signal size is related to the surface area of the active electrode in contact with the fetal tissues. Double spiral FSEs had the largest surface area but their poor attachment negated this advantage. Copeland FSEs had the smallest surface area which compounded their problems of signal attenuation and high baseline noise.

Spiral FSEs are used extensively throughout Europe, Australasia and America while Copelands are most popular in the UK. Disposables are now used more than Reusables due to concerns about cleaning and re-sterilisation. The geographical difference in use may relate to a DHSS Safety Bulletin (1985) produced in response to a number of case reports concerning improper application or removal of spiral electrodes (e.g. Sharp and Couriel, 1985) or inappropriate application sites (e.g. Thomas and Blackwell, 1975). It discussed

certain design features and the necessity for correct application techniques, and although not intended to discourage the use of spiral electrodes, it effectively did so in the UK.

The one randomised clinical trial of FSEs reported prior to the present study compared the quality of *fetal heart rate* recordings and found no difference between Copeland Disposable and Corometrics FSEs in complication rates. There was less heart rate signal loss in the second stage of labour with the Copeland but no difference in the first stage of labour (Nickelsen et al, 1989). A second trial, published since the work of this thesis, compared *fetal heart rate* quality with 2 double spirals (Rocket-Rolon and Hewlett-Packard) and the Copeland disposable (Needs et al, 1992). The Copeland was least likely to become detached, the Rolon-Rocket most likely. There was no difference in scalp trauma. The heart rate records in the Hewlett-Packard group were more likely to be of good quality and these FSEs were least likely to be replaced because of poor signal quality. These findings are entirely consistent with those reported here for FECG signal quality and also with our experience with Rocket-Rolon double spirals during preparation for the study. They appeared to be quite poorly made compared to the Hewlett-Packard double spirals and as every one applied fell off at some stage, they were not considered worthy of study.

In theory, a significant improvement in ECG signal quality could be obtained if silver/silver-chloride FSEs could be used. New membrane coating techniques developed by Surgicraft Ltd may make this possible (Penman et al, 1990). This technique silver plates, partly chloridises and then coats a conventional stainless steel Copeland FSE with a biocompatible electrically conducting polymer which should prevent silver-chloride deposition in tissues without affecting the electrical properties (Figure 2.11).

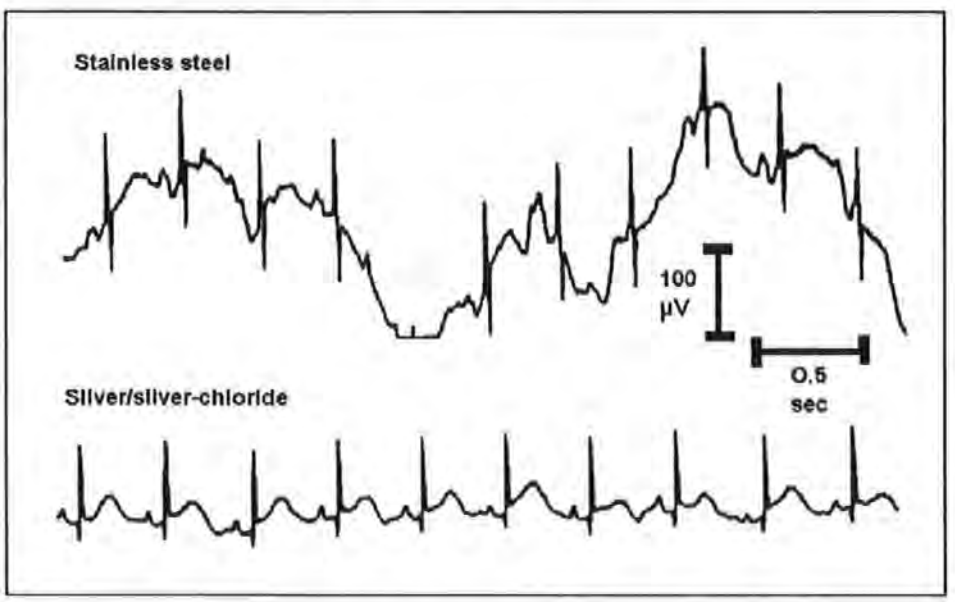


Figure 2.11 Comparison of a recording from a stainless steel FSE and from a silver/silver-chloride coated FSE (from Penman et al, 1992, reproduced with permission).

As can be seen from the figure, the ECG recording from a conventional Copeland showed large baseline swings whilst that from the new low resistance Copeland had a very stable baseline. Although a promising idea, this data is somewhat misleading as the recordings were not made simultaneously from the same patient (the RR intervals are different).

Several prototypes of the low resistance Copeland have been tested by our group using the model described in the in-vitro experiment. Overall signal attenuation was increased by 2 to 4 dBs compared to conventional Copelands but 2 of the 4 prototypes displayed much flatter frequency responses. The thickness of the membrane coating may have contributed to the increase in attenuation. A small number of these FSEs were used in the clinical situation on a trial basis without much success even though the needle was taper cut rather than round-bodied. This is probably related to the basic Copeland design with its long semi-rigid arm which predisposes to movement artefact. This technology, however, has promise but may be more applicable to single spiral FSE designs.

There has been renewed interest in non-penetrative FSEs recently because of the increasing incidence of AIDS. Suction FSEs have been developed in the past (Walker et al, 1969, Goodlin & Fabricant, 1970) but never achieved widespread use probably due to difficulty in maintaining attachment to the presenting part. More recently, one group has designed a 40 cm long multichannel sensor which uses surface electrodes for FECG detection (Allman et al, 1991). The quality of FECG signal obtained has not been reported. Another design where suction is applied through holes drilled in a metal plate has been reported (Hofmeyer et al, 1992). This is apparently suitable for fetal heart rate detection but no assessment of ECG quality has yet been made. The use of a silver/silver-chloride disc might make this design particularly useful for FECG recording.

In summary, a single spiral FSE was the best of the available fetal scalp electrodes for ST waveform analysis of the FECG and was used in all further studies in our hospital.

Part II. Examination of a Fetal ECG Data Acquisition System

Introduction.

A data collection system for ST waveform analysis has been designed based on the work of Greene and Wickham and Rosén and Lindecrantz reported in Chapter One. Before this system was used in a randomised trial to test the clinical value of ST waveform analysis, it was important to validate the collection system itself. A block diagram of the STAN system is shown in Figure 2.12.

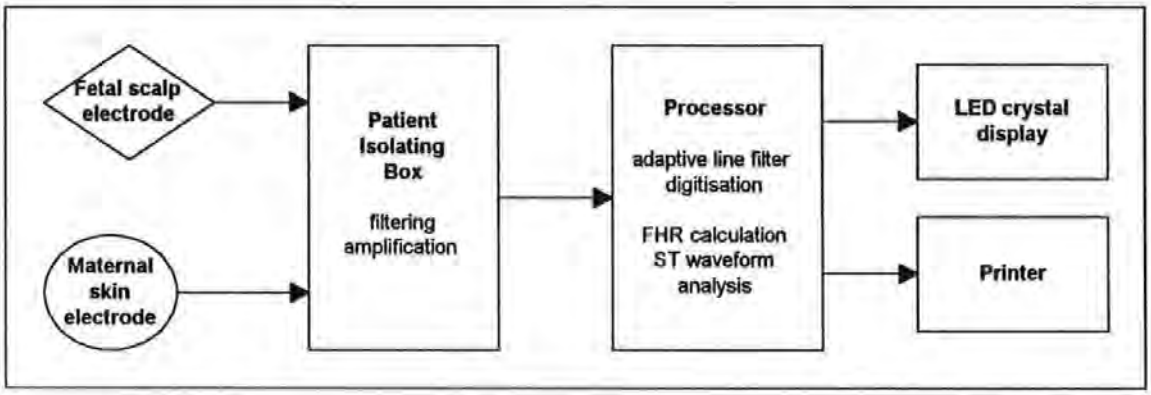


Figure 2.12 Block diagram of STAN system .

The signal recorded differentially from a FSE and a maternal skin electrode is collected by the Patient Isolating Box (PIB) where it is high pass filtered at 0.05 Hz (1st order high-pass filter), amplified, isolated from the patient and transmitted down a cable to the STAN processor where an adaptive line filter (operating at 50 Hz in the UK) removes mains frequency noise (Rosén & Lindecrantz, 1989). The signal for ECG waveform analysis is low pass filtered at 100 Hz (4th order Butterworth low-pass filter), and bandpass filtered for heart rate analysis between 4 and 26 Hz. The signal is digitised at 8 bits at a sampling frequency of 500 Hz.

The FSE, the first step in the collection system, was investigated in Part I. In this second part other aspects of the collection system which may influence signal quality and ultimately affect the clinical usefulness of the system were considered. The following observations were made during preparation for the randomised trial of fetal scalp electrodes reported in Part I of this chapter.

Observations and Investigations.

Location of the maternal skin electrode.

The original instructions suggested that this electrode be placed on the lower abdomen, just above the inguinal ligament. However, this resulted in the recording of such large maternal ECG signals that the smaller FECG signals were swamped. This was probably due to the close proximity of the electrode to the femoral vessels. Placing the skin electrode on the lateral thigh resolved the problem but increased signal artefact due to muscle movement. During the clinical FSE trial it was observed that signal quality was better in patients with epidural analgesia than without (although this was not significant because of small numbers) and deteriorated in the second stage. These observations would be consistent with the effect of muscle movement artefact.

FECG lead configuration.

It is possible to minimise noise recorded with a biological signal by the technique of common mode amplification where only the difference between the voltage recorded at two points on a preparation is amplified. A conventional CTG lead system records one signal from the active element on the fetal scalp, the other from the vaginal element of the FSE and uses the metal leg plate as the common mode reference point. In this way noise from the leg plate connection will be present on both signals but its effect will be minimised as only the difference between the two signals is amplified. In the STAN system the vaginal element is used as the common mode reference point so that any muscle artefact from the maternal skin electrode will not be removed by common mode rejection. This means that the ECG signal recorded with the STAN lead configuration may be more susceptible to maternal movement artefact and would fit with the deterioration in signal quality seen in the second stage recordings during the randomised FSE study reported earlier.

This alteration in lead configuration arose because of uncertainty as to where the vaginal element of an FSE makes its contact. Any instability of contact would be a source of signal noise. Lilja et al (1985) obtained a signal with a more stable baseline than the conventional lead system by recording differentially from two scalp electrodes attached to the presenting part with the common mode reference point either on an intrauterine catheter or on the maternal thigh. However, Lindecrantz & Widmark (1989) claimed that both this and the conventional CTG lead arrangement was only sensitive to changes in the ECG vector in the horizontal plane - parallel to a line through the two electrodes - and that rotation of the fetal head could cause changes in the shape of the FECG recorded by the electrodes (Figure 2.13A). They reported one case where the FECG became completely inverted as labour progressed as a result of rotation of the fetal head. They suggested recording the FECG differentially from the active element of the FSE and from a skin electrode placed

on the maternal thigh with the vaginal element of the FSE as the common mode reference point. This configuration could be sensitive to FECG changes in the longitudinal axis of the fetus and therefore may be more appropriate for detecting T wave changes (Figure 2.13B). This configuration could also minimise noise from the vaginal element.

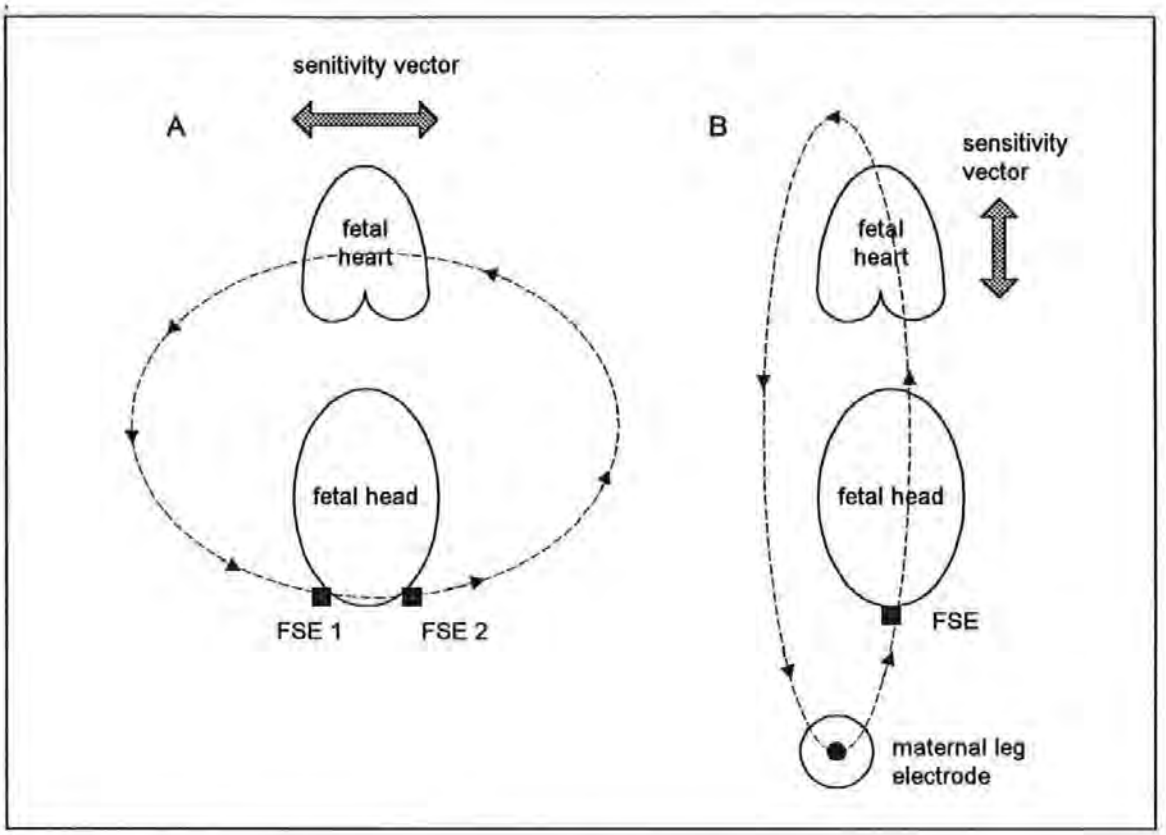


Figure 2.13.. Possible ECG sensitivity vectors obtained by recording FECG differentially;
A. from two FSEs attached to the fetal head. The vector may be in the horizontal plane (similar to leads I and II of an ECG recorded from limb leads);
B. from one FSE and from a maternal leg electrode. The vector may be in the longitudinal plane (similar to leads III and AVF from an ECG recorded from limb leads).
After Lindecrantz & Widmark, 1989.

The theoretical considerations which led to the choice of this lead configuration have never been examined further, nor has signal quality with different configurations been compared. Given the importance of FECG signal quality, it was clear that this area required further investigation.

An investigation of FECG electrode configuration connections.

In an attempt to clarify the questions raised by the STAN configuration, a study was designed to investigate different lead configurations and their effect on signal quality and FECG waveform shape and to attempt to detect changes in the ECG shape with rotation of the fetal head during delivery. This work was performed in conjunction with John Curnow,

Biomedical Engineer, Department of Medical Physics, Plymouth General Hospital.

Method. Informed consent to apply two single spiral FSEs to the fetal scalp was obtained from six women in early labour. Ethical Committee approval was obtained for the study. The data collection system is shown in Figure 2.14.

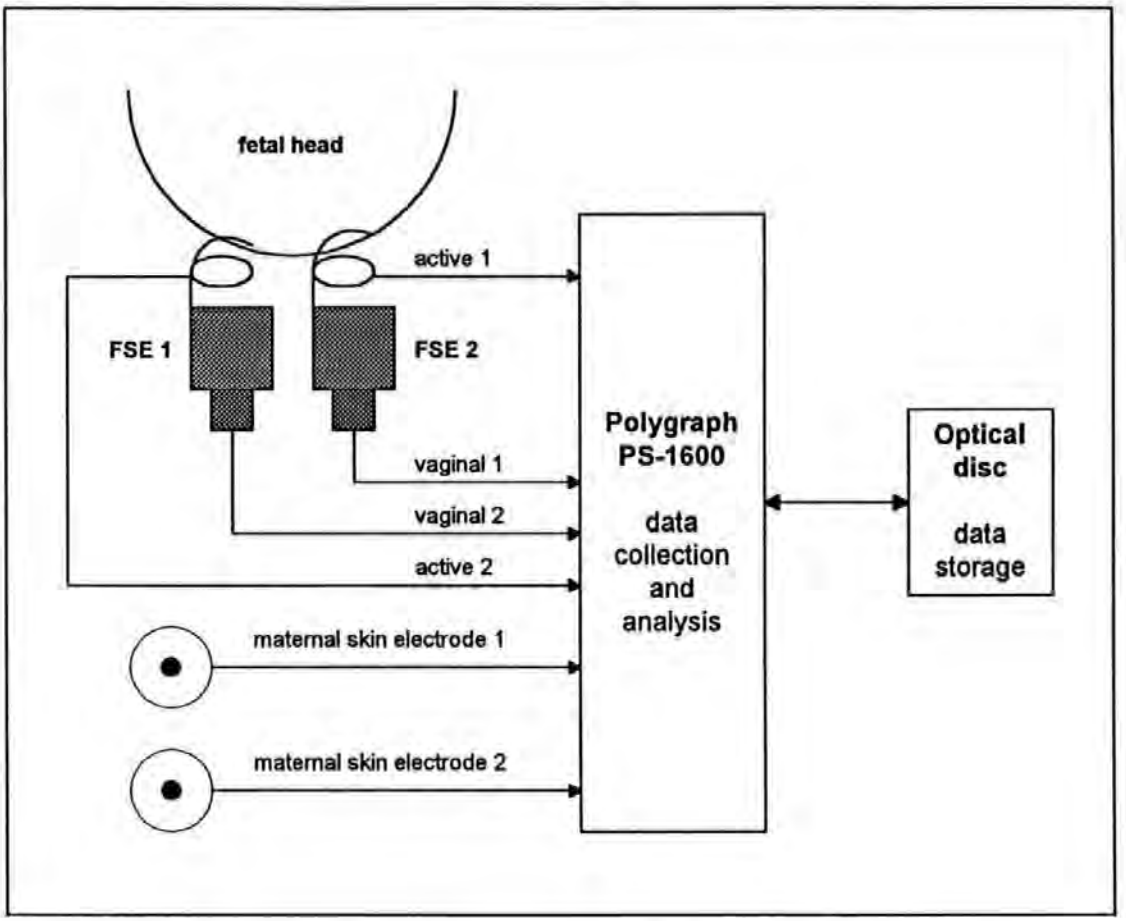


Figure 2.14 The data collection system used for the lead configuration study.

Signals were collected independently from each element of each FSE (the active and vaginal elements) and from two maternal thigh skin electrodes and then passed to a multichannel data collection, analysis and storage system which combined the individual signals to produce the desired lead configurations (Polygraph PS-1600, Twenty Technology Transfer, Holland). Data was collected at a sampling rate of 500 Hz with a 12 bit Analogue to Digital Converter (ADC) and band pass filtered between 0.05 and 120 Hz then archived on an optical disc for later analysis. The study aimed to compare three lead configurations; first the conventional (FECG recorded differentially from the active and vaginal elements of one FSE with the leg electrode as the common mode point, Figure 2.13A), second the STAN configuration (FECG recorded differentially from active element of FSE and leg electrode with the vaginal element as the common mode point, Figure 2.13B) and third, a configuration suggested by Lindecrantz & Widmark (FECG recorded differentially from the active element of one FSEs and a leg electrode with the active

element of a second FSE as the common mode point). A 13 lead neonatal ECG was performed within 24 hours of birth to compare with the lead configurations recorded during labour.

In order to compare the low, medium and high frequency content of the signal from each lead configuration, the first hour of data from the conventional and the STAN configurations in every patient was filtered with simple first order filters to obtain the frequency content <1 Hz, from 1 - 50 Hz and > 50 Hz.

Results.

ECG shape during labour. The ECG complexes produced by each lead configuration were compared at five minute intervals throughout each labour. Rotation of the fetal head from a transverse position to an occipito-anterior position occurred in 4 of the 6 cases, one delivered vaginally in an occipito-posterior position and the other had a LSCS for failure to progress. There was no difference in waveform shape between the three lead configurations, nor were there longitudinal changes in either configuration during labour.

Neonatal ECG comparison. The ECG shape recorded by all three lead configurations during labour was very similar to the neonatal waveform shape recorded in leads aVF, and III, i.e. in the longitudinal plane of the fetus. If the conventional lead configuration had recorded the fetal ECG in the transverse plane, the waveform shape should have been similar to that seen in leads I and II of the neonate, but this was not the case.

Frequency content. The results of the signal filtering for the conventional and STAN configurations are shown in Table 2.3. As the STAN and Lindecrantz & Widmark configurations produced identical recordings a separate analysis has not been performed for the latter configuration. One of the patients generated two files so seven files were analysed. The mean power for each frequency range was calculated with and without File 6 as visual inspection of the data indicated that a problem with electrode or lead attachment may have occurred during the recording in that case.

The STAN lead configuration signals contained proportionally more low frequency content and less high frequency content compared to the conventional configuration. This confirms that the STAN configuration has an increased susceptibility to baseline noise. The increase in high frequency noise with the conventional configuration may be related to the vaginal element of the FSE which, on visual inspection of the recordings from that electrode element alone, did seem to contain more high frequency content.

Table 2.3 Percentage low, medium and high frequency content for each lead configuration in each patient for the first hour of recording.

File number	Conventional configuration frequency content (%)			STAN configuration frequency content (%)		
	low < 1 Hz	medium 1-50 Hz	high > 50 Hz	low < 1 Hz	medium 1-50 Hz	high > 50 Hz
1	68.3	3.2	28.5	97.2	2.1	0.7
2	80.2	9.9	9.9	83.3	10.8	5.9
3	3.7	1.5	94.8	77.3	20.2	2.5
4	4.8	2.0	93.2	74.3	23.2	2.5
5	36.7	8.8	54.5	26.2	9.9	63.9
6	85.4	14.6	0.03	42.7	44.1	13.2
7	1.4	3.6	95.0	10.7	9.1	80.2
Mean -of all	40.1	6.2	53.7	58.5	17.1	24.1
-excluding File 6	32.5	4.8	62.7	61.5	12.5	26.0

Discussion. This preliminary investigation has not revealed any differences in ECG waveform shape between the lead configurations. Unfortunately, none of the babies studied rotated 180 degrees from occipito-posterior to occipito-anterior during labour and delivery so the study is not conclusive. In the original work, Lindecrantz et al (1989) used two FSEs attached almost to opposite sides of the fetal head, whereas this study mimicked the clinical situation where the two elements of one FSE are less than 1 cm apart. This may also explain the lack of rotational changes seen here.

Although the STAN lead configuration is not obviously wrong, it does predispose to problems with low frequency baseline noise which is the most problematic for ECG waveform analysis. The high proportion of high frequency noise seen with the conventional lead configuration is not a major problem for signal analysis as high frequency noise is far easier to remove than low frequency noise.

This is an area which requires further work in a larger number of labours over a spectrum of positive and negative ST waveform changes. A method of recording both lead configurations from a single FSE and two maternal leg electrodes has been devised which will improve patient recruitment rates. However, before this is done a method for

automatic analysis of ECG waveform shape is being developed to obviate visual assessment of the data (N. Outram, PhD project, University of Plymouth). A more refined method for signal noise analysis is also under investigation. Until this is complete, no change in the STAN lead configuration can be recommended.

Cable and leads.

Cables and leads can add noise to a signal from mains interference or cable motion artefact. Electrode lead wires can act as antennae to pick up airborne electrical noise, particularly mains frequency noise (50 Hz). This can be minimised by keeping leads and cables as short as possible, using shielded cables or optical fibres as cables and by using differential input amplifier systems (Gatzke, 1974). The only problem found with the STAN system was with the lead to the maternal skin electrode. This was initially 20 cm long and unscreened and acted as a very effective aerial for airborne noise, especially 50 Hz noise. This was reduced by shortening the lead to 8 cm.

Data acquisition electronics

The STAN uses a standard differential common mode amplifier and there was no evidence that the choice of amplifier itself contributed significantly to signal noise.

Amplification and gain settings. The signal is amplified by a factor of 600 in the PIB before it is passed to the processor. The default gain setting of the processor was normally just over 2000 but could be halved or increased by a factor of 2 or 4 as judged by visual inspection of the FECG display. Frequent adjustment of the gain settings was necessary in some cases. This would be impractical in the routine clinical situation. An automatic gain setting was recommended and subsequently introduced. However, this automatic gain adjustment only took effect after amplification in the PIB. It was felt that the amplification factor was too large as saturation and signal dropout still frequently occurred as a result of large baseline changes. The PIB amplification was eventually reduced in June 1992 with immediate improvements in signal quality on subjective assessments of recordings.

Signal processing.

The signal from the PIB is transmitted down a cable to the STAN for processing. An adaptive line filter (operating at 50 Hz in the UK) is used to eliminate mains frequency noise. The ECG is then split into two channels; one for QRS detection, the other for waveform analysis. Finally the signals are digitised by an analogue to digital converter (ADC) before heart rate calculation and waveform analysis. Each step of this process was examined as part of a report prepared for Cinventa (Plymouth Perinatal Research Group, 1989). The filter characteristics quoted in the STAN maintenance manual were confirmed

and were suitable for waveform analysis.

The major problem identified by this work related to the resolution of the STAN system. It is clear that baseline noise will remain the major problem of FECG waveform analysis as long as stainless steel FSEs and the STAN lead configuration are used. The speed of the relatively old STAN processor limits the system to only 8 bit resolution. This means that the whole signal - ECG and baseline noise - must be represented in 2^8 bits or 256 values. If very large baseline swings occur the size of the signal will have to be reduced to fit into 256 values, so most values will be taken up representing baseline changes. This may leave only 50 values or so to represent the ECG waveform, and the T wave itself may only be represented by 2 or 4 values. This clearly causes problems for ST waveform analysis. The situation could be improved by a factor of 16 by increasing the resolution of the system to 2^{12} bits.

Display and printout.

Heart rate and T/QRS ratio were displayed on the liquid crystal display (LCD) but were too small to be read more than a half a metre away from the screen. This was clearly impractical and a larger numerical display was recommended and introduced.

The first versions of STAN tested had a recorder which had different coloured pens in a rotating pen holder device. The fine parts involved were not robust enough for continual use and the rotating pen holders frequently became stuck with the pens lifted off the paper. All eventually broke. This mechanism was replaced by a single colour non-rotating pen which was satisfactory. The printer mechanism itself was very noisy and was replaced by a thermal printer in 1992.

Summary

This investigation identified several important areas where relatively simple improvements to STAN design were possible; the maternal electrode lead wire, signal amplification, gain control, signal display and printout. This demonstrated the value of informed clinical input into the design of new technology. Engineers are not always aware of the requirements and restrictions of clinical monitoring equipment, especially in a high stress area such as the labour ward. Ideally, clinicians with some understanding of signal analysis technology should be involved at an early stage in the design of new technology and in early clinical studies.

The questions about the STAN lead configuration were unable to be resolved and must await a larger, more detailed study. The lead configuration used is not wrong, but does rather disadvantage ST waveform analysis by increasing baseline noise which is a particular problem in the second stage of labour. It may be that an update of the now rather old STAN processor to provide more signal processing capabilities would allow this noise to be removed more effectively without distorting the signal. However, processing can never add information to a signal and it would be better to maximise initial signal quality than rely on increased processing to cope with a poor quality signal. Although faster processors are now available, the expense and time required to incorporate these into a new model of STAN could not be justified until data from a randomised trial demonstrated some actual clinical benefit for the new technology.

Chapter Three

Randomised trial of CTG alone or with ST Waveform analysis for intrapartum monitoring.

Introduction

As discussed in Chapter One, a series of experimental studies over the last 17 years have identified a physiological basis for changes in the ST waveform shape of the fetal ECG. Human observational studies have indicated that a combination of fetal heart rate and ST waveform changes might be of clinical value by allowing a reduction in operative intervention without adversely affecting neonatal outcome (Lilja et al, 1985, Greene, 1987, Arulkumaran et al, 1990). The main purpose of this randomised clinical trial was to investigate the significance of any reduction in operative intervention by comparing intervention rates and neonatal outcome in labours monitored with CTG alone or in combination with ST waveform analysis. The results are presented and discussed in this chapter.

The trial also provided an opportunity to examine current monitoring practice and to assess the value of cord blood gas analysis. These findings are presented and discussed in Chapters Four and Five respectively.

Methods

Plymouth General Hospital is one of the largest obstetric units in the UK with more than 5,200 deliveries per annum. In 1989, prior to this trial, the total caesarean section rate was 9.5%, the forceps rate 8.5% and the perinatal mortality rate was 6.1 per 1000 live births. The overall operative delivery rate for 'fetal distress' was 4.5% while the rate for those monitored continuously with a fetal scalp electrode was 11%.

Calculation of sample size.

It was calculated that a sample size of 450 in each arm would give a 90% chance (power) of detecting a 50% difference from an 11% 'fetal distress' delivery rate at the 5% level using a two sided test to compare proportions (Casagrande & Pike, 1978). The trial size required to assess an affect on neonatal morbidity was more difficult to calculate due to the lack of recognised endpoints. Objective assessment of immediate outcome was possible with umbilical cord acid-base assessment. If a 2% incidence of metabolic acidosis was assumed (Low, 1988) then a sample size of 1300 in each arm would give a 50% chance of detecting a 50% difference at the 5% level in a two-sided test. Based on the above calculations, the estimated recruitment rate and the available resources a total sample size of 2400 was chosen with an interim analysis at 1200. Although the power for neonatal outcome was relatively low, the sample size provided sufficient data to examine low incidence outcomes for exploratory purposes.

The recorders used were a HP 8040A CTG recorder (Hewlett-Packard Ltd, Böblingen, Germany) for the CTG arm and a STAN 8801 recorder (Cinventa AB, Mölndal, Sweden) for the ST waveform plus CTG (ST+CTG) arm.

Study entry and randomisation.

All pregnancies of more than 34 weeks gestation with no gross fetal abnormality were eligible for trial entry. Entry to either arm was decided by draw of a sealed opaque envelope once the decision to apply a scalp electrode was made. The hospital policy for continuous internal monitoring was selective for all high risk pregnancies (pre-eclampsia, antepartum haemorrhage, growth retardation, diabetes, previous caesarean section), an abnormal antenatal or early labour external CTG, inductions or augmented labour, the presence of meconium liquor, epidural analgesia or breech presentation. The study was approved by the local Ethical Committee and all patients approached gave informed consent before entry into the trial.

Preparation for the trial.

Extensive education and training of labour ward staff on the use of the STAN recorder and the concepts of CTG and ST waveform analysis was provided before and continued throughout the trial on a weekly basis. A pilot phase of 100 cases using the trial protocol was run as a 'dress rehearsal' immediately before the trial commenced but none of the pilot data has been included in the analysis.

Protocols for management in labour.

All cases in the trial were managed by medical and midwifery staff and not by research staff. The following protocols for management were derived before trial commenced.

CTG arm. The interpretation of CTG traces and management followed accepted clinical guidelines including an FBS option. These are summarised in Table 3.1.

ST+CTG arm. The interpretation of first stage traces followed the same CTG classification as shown in Table 3.1 but included certain modifications based on the T/QRS ratio according to the model of interpretation shown in Figure 1.13 (Table 3.2). In the second stage acutely emerging changes in the ST waveform over a five minute period were regarded as significant.

FBS guidelines. A FBS pH of >7.25 was considered normal but if the pattern which prompted the FBS persisted, a repeat FBS was indicated in 60 minutes and if the pattern deteriorated the repeat FBS was to be obtained earlier. A pH of 7.20 to 7.25 was suspicious and the FBS was to be repeated in 45 minutes or earlier if the trace deteriorated, while a pH of <7.20 was abnormal and required immediate delivery.

Measurement of outcome

Intervention. The frequency of fetal blood sampling (both total numbers of FBS performed and numbers of cases with an FBS) was recorded as were the indications for FBS given in

the hospital notes. Operative deliveries were recorded according to the primary indication given by the operator. Deliveries for 'fetal distress' included both deliveries performed on account of an abnormal scalp pH and those performed because of concern about an abnormal trace. Deliveries for 'failure to progress' included deliveries for inadequate progress in either the first or second stage of labour and elective forceps deliveries performed on account of maternal condition (e.g. hypertension).

Table 3.1 Protocol for CTG interpretation and recommended action.

Classification	Baseline	Variability	Decelerations	Action
Normal	110-160 bpm	10-25 bpm	none	Continue recording
Intermediate	100-110 bpm 160-180 bpm	>25 bpm <5 bpm	early mild variable[1]	Any two >30 mins; FBS. Repeat 1 hour[2].
Abnormal	<100 bpm with accelerations >180 bpm	<5 bpm, no accelerations in the absence of sedation.	severe variable[3] late	Any one > 30 mins; FBS. Any two >15 mins; FBS. Repeat 1 hour[2].
Preterminal	Persistent bradycardia, no accelerations exceeding 100 bpm and believe this will be persistent.			Deliver; if not FBS.

1. < 60 dropped beats, < 60 seconds duration.
2. FBS earlier if CTG deteriorates.
3. >60 dropped beats, > 60 seconds.

Table 3.2 Protocol for ST waveform plus CTG (ST+CTG) interpretation and recommended action.

Classification	Normal ST (T/QRS 0.05-0.24)	Intermediate ST (T/QRS >0.24 >30 mins)	Abnormal ST (T/QRS >0.5 >15 mins)	Negative ST [1]
CTG normal	continue recording	monitor closely	FBS	FBS or deliver
CTG intermediate	continue recording	FBS	FBS or deliver	FBS or deliver
CTG abnormal	> 30 mins FBS	FBS or deliver	deliver	deliver
CTG preterminal	deliver	deliver	deliver	deliver

1. Negative T wave or ST segment depression with positive T waves.

Neonatal outcome. This was assessed by;

1. Umbilical cord artery and vein blood gas analysis. A Corning 178 Blood Gas Analyser (CIBA Corning Ltd, UK) was used throughout. In the first 400 cases cord blood gas analysis was restricted to those cases having an operative delivery or FBS. When a second and dedicated blood gas analyser became available analysis was performed on all deliveries. The cord was double clamped immediately after delivery and 1 to 5 ml of blood withdrawn from an artery and the vein into separate preheparinised syringes. If samples could not be analysed within 10 minutes of delivery they were placed on ice and were analysed within 40 minutes of delivery. The base deficit (BD) calculated from the blood compartment was corrected to that in the extracellular fluid compartment (BDecf) by using the Siggaard-Andersen Acid Base Chart (Siggaard-Andersen, 1971) as this is more appropriate in the perinatal period (Rosén & Murphy, 1991). The methodology of cord blood sampling is discussed further in Chapter Five.
2. Apgar scores at 1 and 5 minutes.
3. Details of any resuscitation.
4. Postnatal course - babies were followed up daily to discharge. Any abnormalities in the postnatal period were noted together with details of admissions to neonatal intensive care (Special Care Baby Unit or SCBU), treatment given and diagnosis at discharge.

For the purposes of this study, a diagnosis of **birth asphyxia** was derived from the following references; Low et al, 1984, American Academy of Pediatrics, 1986, Gilstrap et al, 1989 and Murphy et al, 1990. It required all of the following;

i. cord artery pH <7.05 and extracellular fluid Base Deficit (BDecf) > 12 mmol/l;
ii. Apgar score at 5 minutes of ≤ 7;
iii. active resuscitation for ≥ 4 minutes;
iv. one of the following problems in the postnatal period;
   - hypoglycaemia (BM stix < 1.6 mmol/l) within the first 12 hours (mild asphyxia),
   - neurological abnormalities or a requirement for assisted ventilation in the first 48 hours (moderate asphyxia)
   - death (severe asphyxia).

A copy of the Case Record Form used for the study is given in Appendix 2.

Retrospective quality assessment.

All traces were reviewed by a single observer and given separate quality scores for heart rate and uterine contraction recordings according to how useful the recordings were for monitoring purposes (1= excellent, 2= satisfactory, 3 = unsatisfactory). The ST+CTG traces were also given an additional score for the quality of the ECG complexes.

Retrospective, blinded review of traces.

It is inevitable that clinical staff do not adhere to protocols on occasions. All traces were therefore reviewed retrospectively, blind to outcome, by the author. This enabled clinical CTG and ST+CTG interpretation and management to be compared with that recommended by the trial protocol as interpreted by an experienced clinician. It also allowed patterns of ST+CTG change to be recorded. The review started at the beginning of each trace and worked to the end in 30 minute segments without preview. Classification was strictly according to the trial protocol and blind to neonatal outcome. The CTG for each trace was classified as normal, intermediate or abnormal based on the classification shown in Table 3.1. In addition the ST+CTG traces were also classified as normal T/QRS ratio (<0.25), raised (>0.24) or negative. Finally it was noted whether any intervention had been performed on the basis of CTG or ST+CTG changes - either fetal blood sampling or an operative delivery for 'fetal distress'.

Statistical methods.

Tests of significance for continuous variables was by Student's 't' test and for discrete variables by Chi Squared analysis. Significance levels were taken at 'p' levels of < 0.05. The odds ratios and 95% confidence intervals were also calculated (Gardener et al, 1989). Multivariate analysis was performed using ANOVA with the Minitab, Version 7.1 statistical software package running on a prime mainframe computer. Kruskal-Wallis and Mann-Whitney U tests were performed on nonparametric data.

Results.

Trial entries.

During the trial period (21.6.90 to 13.12.91) there were 6798 deliveries from pregnancies of at least 34 weeks gestation. Of these, 2434 (36%) fulfilled the entry criteria and were recruited to the trial (1215 CTG arm, 1219 ST+CTG arm). No patient approached refused entry. Thirty-four patients did not receive the allocated recorder and are discussed below. In total 1212 cases in the CTG arm and 1188 in the ST+CTG arm received the intended recorder. Results are given according to intention to treat by original randomisation. A secondary analysis by treatment received has been performed and does not alter the statistical significance of the results (See Appendix 3).

Randomisation details are shown in Table 3.3. The CTG arm had significantly fewer inductions and trends to fewer post-dates pregnancies, total antenatal complications and epidural analgesia. These features are likely to be related.

Table 3.3 Randomisation details.

	CTG n=1215	ST+CTG n=1219	p value	Odds ratio (95% CI)
Maternal age (years) mean SD	26.5 5.4	26.2 5.3	>.05	(-0.13-0.73)[1]
Gestational age (weeks) mean SD	39.6 1.6	39.6 1.6	>.05	(-0.13-0.13)[1]
Primigravidae	822	825	.98	0.99 (0.84-1.18)
Antenatal complications Total	230	262	.13	0.85 (0.70-1.04)
- preclampsia	33	40	.82	0.82 (0.52-1.31)
- previous LSCS	17	19	.87	0.90 (0.46-1.73)
- growth retardation	27	25	.88	1.09 (0.63-1.88)
- antepartum haemorrhage	19	12	.27	1.60 (0.77-3.31)
- post dates (≥42 weeks)	76	99	.09	0.75 (0.55-1.04)
- others[2]	58	67	.47	0.86 (0.60-1.24)
Breech	25	30	.59	0.83 (0.49-1.42)
Inductions	394	443	.05	0.84 (0.71-0.99)
Epidural analgesia	673	712	.14	0.88 (0.75-1.04)
Meconium liquor	202	201	.97	1.01 (0.82-1.25)
Birth weight (grams) mean SD	3363 503	3381 518	>.05	(-58.6-22.6)[1]
Birth weight < 10th centile	43	39	.73	1.11 (0.71-1.73)

1. For these continuous variables the 95% CI for differences between means has been calculated.
2. hypertension, diabetes, reduced fetal movements, urinary tract infection, asthma, polyhydramnios, anaemia.

Non-compliance with allocated recorder.

There were three cases in the CTG arm. In two a recording was unobtainable on the CTG recorder (although in one it was possible on a ST+CTG recorder.) In the third no CTG recorder was available. Two had normal deliveries and one had a caesarean section for 'failure to progress'. All had normal neonatal outcome with no asphyxia.

There were 31 cases in the ST+CTG arm. Ten of these were protocol failures and four were technical failures - two printer mechanisms and two broken cables. In 17 cases no satisfactory heart rate or ECG trace could be obtained despite reapplication of the scalp electrode and checking the recorder. In 13 of these a satisfactory CTG trace was obtained

on a CTG recorder whilst in the other four cases this also failed to produce a satisfactory heart rate.

Of these 31, 20 had uneventful labours and normal deliveries, eight had operative deliveries for 'failure to progress', two had FBS followed by a normal delivery, and one had a forceps delivery for 'fetal distress'. All had normal neonatal outcome with no asphyxia.

Intervention.

Fetal blood sampling. The frequncy of fetal blood sampling is shown in Table 3.4. Although the FBS rate in the two arms is not significantly different (9.4% CTG, 7.6% ST+CTG), there were significantly more samples taken in the CTG arm (168 versus 129 in the ST+CTG arm).

Table 3.4 Fetal blood sampling by numbers of cases and number of samples.

	CTG n=1215	ST+CTG n=1219	p value	odds ratio	95% CI
Number of cases	114	93	.14	1.25	(0.94-1.67)
Number of samples	168	129	.02	1.36	(1.06-1.73)

Operative delivery. Table 3.5 shows the indications for the operative deliveries. There was a highly significant reduction in total operative deliveries for 'fetal distress' in the ST+CTG arm. The method of delivery for these cases is shown in Table 3.6. Both LSCS and non-rotational forceps deliveries have been significantly reduced. Importantly, there are no differences in the number of operative deliveries for 'failure to progress'. This group acts as an internal control and indicates that there has not merely been a change in the indications for operative delivery in the ST+CTG group.

Table 3.5 Indications for operative delivery.

	CTG n=1215	ST+CTG n=1219	p value	odds ratio	95% CI
Abnormal FBS pH	19	15	.60	1.28	(0.65-5.52)
Abnormal trace	92	46	<.001	2.09	(1.45-3.00)
Total deliveries for 'fetal distress'	**111**	**61**	**<.001**	**1.96**	**(1.42-2.71)**
Deliveries for 'failure to progress'	272	283	.69	0.96	(0.96-1.16)

Table 3.6 Mode of delivery for 'fetal distress'.

	CTG n=1215	ST+CTG n=1219	p value	odds ratio	95% CI
LSCS	30	15	.03	2.03	(1.09-3.80)
Rotational forceps	13	9	.52	1.45	(0.62-3.41)
Vacuum	10	5	.30	2.01	(0.68-5.91)
Non rotational forceps	58	32	.007	1.86	(1.20-2.88)
Total	**111**	**61**	**<.001**	**1.96**	**(1.42-2.71)**

Neonatal outcome.

There were more cases of cord artery metabolic acidosis (13 versus 5) and more low 5 minute Apgar scores (32 versus 20) in the CTG arm. Although these differences did not achieve statistical significance (p=.09 and .12 respectively) the odds ratios and 95% confidence intervals (2.63 [0.93-7.39] and 1.62 [0.92-2.85] respectively) show a trend to improved short term neonatal outcome in the ST+CTG arm. There were no other significant differences in outcome (Table 3.7).

Table 3.7 Neonatal outcome.

	CTG n=1215	ST+CTG n=1219	p value	odds ratio	95% CI
Cord artery pH<7.15	101	110	.58	0.91	(0.69-1.21)
Cord artery pH<7.05	25	23	.86	1.09	(0.62-1.94)
Metabolic acidosis; cord artery pH <7.05 & BDecf>12mmol/l	13	5	.09	2.63	(0.93-7.39)
Apgar at 5 min. <7	32	20	.12	1.62	(0.92-2.85)
SCBU admissions	31	24	.41	1.30	(0.76-2.23)
Birth asphyxia	4	3			

Birth asphyxia. The cases of birth asphyxia which occurred in trial entries are summarised in Table 3.8. (IPPV = intermittent positive pressure ventilation).

Table 3.8. Summary of birth asphyxia cases which occurred in trial entries.

Case No., parity & gestation	Intrapartum trace	Mode of delivery	Weight (grams)	artery & vein pH & BDecf (mmol/l)	Apgars at 1 5' & 10'	Resuscitation	Neonatal course
CTG arm							
251 Multip, 40 W	1st stage; reduced variability 2hr 2nd stage: 5 min. only, bradycardia.	SVD	3200	6.87, 16 7.08, 17	5, 7, 8	4 min. IPPV	Hypoglycaemia
1129 Primip, 40 W	1st stage: tachycardia, decreased variability & late decelerations on admission at 3cm dilation.	LSCS	2380	7.03, 13 7.10, 13	5, 6, 8	5 min. IPPV	Ventilated 48h. Spastic hemiplegia at 1 year
1591 Primip, 37 W	1st stage: variable decelerations 90 min., tachycardia & reduced variability 30 min. Cord prolapse	LSCS	3850	6.81, 16 7.20, NA	3, 7, 9	4 min. IPPV	Fitted at 10 hours
2009 Primip, 37 W	1st stage: late decelerations 90 min., tachycardia & reduced variability 30 min. FBS at 8cm pH 7.07. Rapid progress.	SVD	2610	7.04, 13 7.08, 13	3, 6, 9	8 min. IPPV	Hypoglycaemia
ST+CTG arm							
106 Multip, 38 W ? IUGR	1st stage: normal 2 hours. 2nd stage: tachycardia, reduced variability, late decelerations. Negative T wave, T/QRS ratio negative 40 minutes.	SVD	2800	NA NA	4, 6, 7	15 min. IPPV	Hypoglycaemia Jittery 48 hr
1372 Primip, 40 W Absent fetal movement 24 h abnormal CTG	ARM, syntocinon: heart rate 160, absent variability, late decelerations then bradycardia. Wide QRS, ST segment depressed, T wave & T/QRS ratio positive.	LSCS	2880	NA NA	Stillborn		
1699 Primip, 40 W	1st stage: syntocinon, variable decelerations 50 min., T/QRS ratio 0.9. FBS at 9cm, pH 7.34. Then severe variable decelerations 120 min., tachycardia & reduced variability 30 min., rise in T/QRS ratio to 0.32, terminal bradycardia.	Forceps Cord tightly around neck	3600	6.88, 16 7.38, 4	Stillborn	Attempted resuscitation 30 min	

Retrospective review.

Four entries in the CTG arm could not be assessed due to poor quality heart rate signals. All had normal outcome. Twelve entries in the ST+CTG arm had ECG signals of such poor quality that the ST waveform could not be assessed but the CTG was satisfactory. All but one of these had normal CTGs and all had normal outcome. One developed a bradycardia late in the second stage and had a forceps delivery. The cord artery pH was 7.24, BDecf 4 mmol/l and the Apgars were 8 at 1 and 9 at 5 minutes. The 34 cases who did not receive the allocated method of monitoring (detailed above) were also excluded from the review. Thus, retrospective review of recordings according to the trial protocol was carried out on 1208 entries in the CTG arm and 1176 in the ST+CTG arm (Figure 3.1).

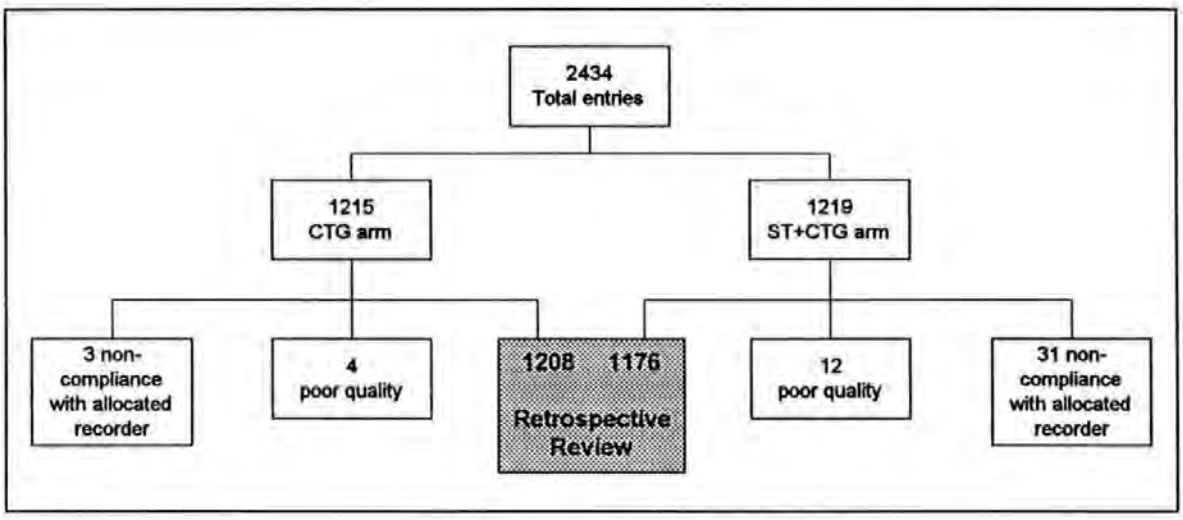


Figure 3.1 Flow chart to demonstrate how the cases assessed in the retrospective review were obtained.

Intervention for 'fetal distress'.

The CTG and ST+CTG arms of the trial had similar numbers of recordings with normal, intermediate and abnormal CTGs (Table 3.9). Operative intervention for 'fetal distress' in the normal recordings was significantly reduced in the ST+CTG arm. The proportion of operative deliveries for 'fetal distress' in the intermediate and abnormal recordings was also reduced in the ST+CTG arm, but the difference was not statistically significant.

Table 3.9 Proportion of operative intervention for 'fetal distress' by retrospective review.

Retrospective classification	CTG n=1208	ST+CTG n=1176	p value	odds ratio	95% CI
Normal					
number (% of total)	953 (78.8)	950 (80.8)	.27	0.89	(0.73-1.09)
'fetal distress' deliveries (%)	26 (2.7)	3 (0.3)	<.001	8.94	(2.57-25.3)
Intermediate					
number (% of total)	113 (9.4)	93 (7.9)	.26	1.20	(0.89-1.59)
'fetal distress' deliveries (%)	22 (19.5)	9 (9.6)	.07	2.26	(0.92-5.64)
Abnormal					
number (% of total)	142 (11.8)	133 (11.3)	.78	1.04	(0.81-1.35)
'fetal distress' deliveries (%)	63 (44.4)	47 (35.3)	.16	1.46	(0.87-2.44)

Negative ST waveform.

There were a total of 13 cases identified with negative ST waveforms. Seven had good outcome with no acidosis; three had normal CTGs (one breech with abnormal shaped ECG complexes, one with an error in the fiducial point calculation and one fetus at 34 weeks), and four had abnormal CTGs (one error in the fiducial point calculation and three with only intermittently negative waveforms in the second stage).

The remaining six cases all had persistent waveform changes and included two of the three cases of birth asphyxia in the ST+CTG arm. All asphyxiated cases except one (case 1372) had acute second stage changes in association with an abnormal CTG pattern. Three had negative T waves and a negative T/QRS ratio while three had biphasic ST waveform changes (negative ST segment, positive T wave) with a positive T/QRS ratio. All were depressed at birth and required resuscitation (one minute Apgar scores three to six). Cord artery data was available in three cases (pH 6.97, BDecf 16 mmol/l; pH 7.03, BDecf 10 mmol/l; pH 7.08, BDecf 11 mmol/l).

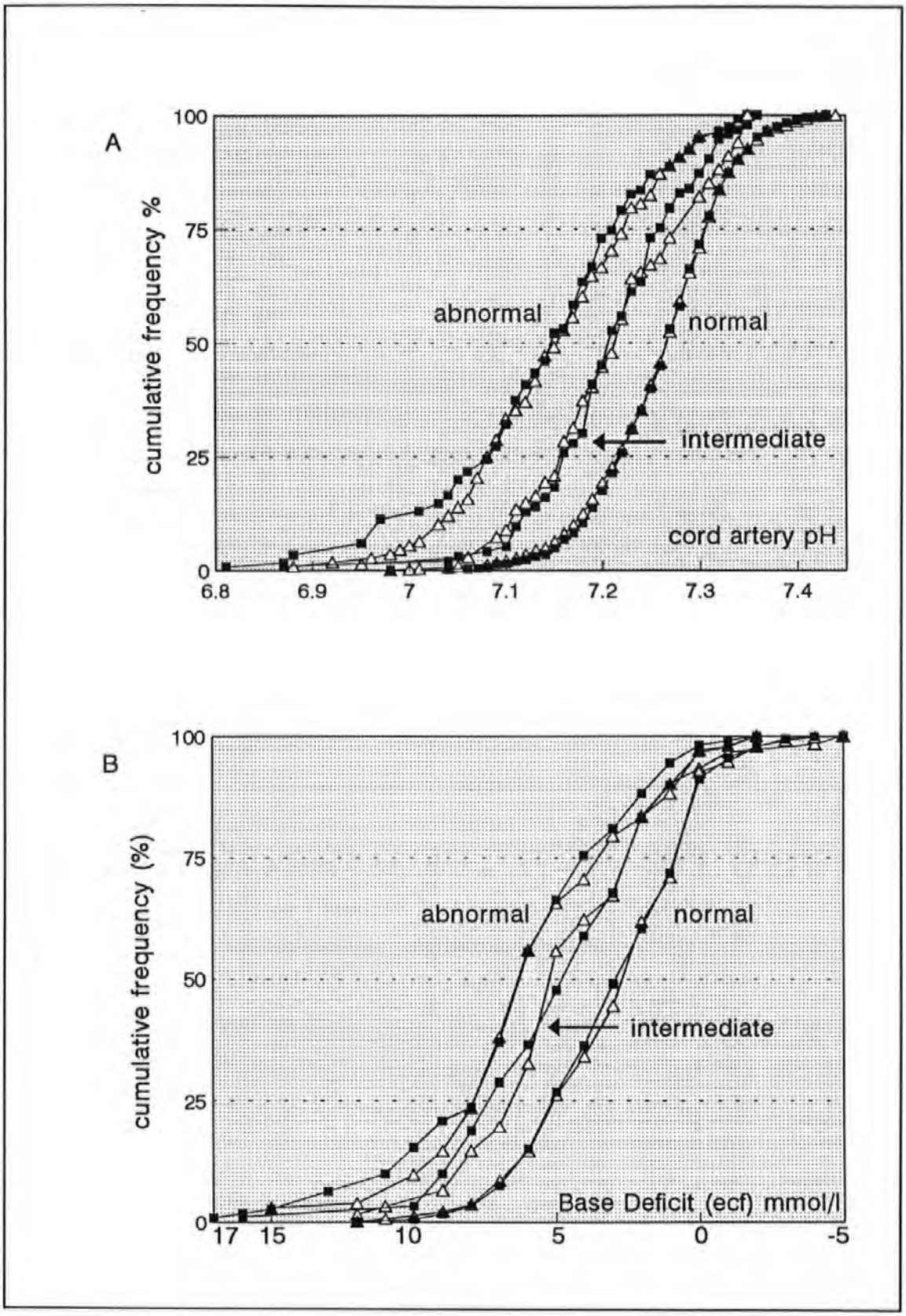


Figure 3.2 Cumulative frequency distributions for

A. cord artery pH and B. cord artery BDecf by retrospective classification.

■ CTG arm, Δ ST+CTG arm

Cord artery pH and extracellular base deficit at delivery.

The cumulative frequency distribution for cord artery pH and BDecf according to the retrospective CTG classification are shown in Figure 3.2. Both arms had similar frequency distributions for each classification (normal, intermediate and abnormal). The mean pH and BDecf are shown in Table 3.10.

The ST+CTG arm was divided into 2 subgroups for each classification; those where the ST waveform remained normal (T/QRS <0.25) and those where it was elevated (T/QRS ≥ 0.25). The small number of cases with negative waveforms were excluded from this analysis. Figures 3.3 and 3.4 show the cumulative frequencies of cord artery pH (Fig. 3.3) and BDecf (Fig. 3.4) for the CTG arm and for each subgroup in the ST+CTG arm for normal (A), intermediate (B) and abnormal (C) retrospective CTG classifications. The mean pH and BDecf and their 95% confidence intervals are also tabulated in Table 3.10. Significance testing was by ANOVA and these results are given and discussed on page 82.

Table 3.10 Mean arterial pH and extracellular base deficit (BDecf) and 95% confidence intervals by retrospective trace classification.

Retrospective CTG classification	CTG arm	ST+CTG arm		
		Total	ST normal	ST raised
Normal pH	7.26 (7.26-7.27) n=723	7.26 (7.26-7.27) n=728	7.26 (7.26-7.27) n=681	7.29 (7.27-7.30) n=47
BDecf (mmol/l)	2.0 (1.8-2.2) n=693	2.1 (1.9-2.3) n=686	2.1 (1.9-2.4) n=643	1.1 (0.3-1.9) n=43
Intermediate pH	7.21 (7.20-7.23) n = 93	7.21 (7.19-7.23) n = 68	7.21 (7.19-7.24) n = 59	7.21 (7.14-7.28) n = 9
BDecf (mmol/l)	3.9 (3.2-4.6) n= 90	3.6 (2.9-4.3) n=61	3.5 (2.7-4.2) n=53	4.6 (2.0-7.1) n=8
Abnormal pH	7.14 (7.12-7.16) n=115	7.16 (7.14-7.18) n=108	7.19 (7.17-7.20) n=88	7.05 (7.02-7.08) n=20
BDecf (mmol/l)	5.2 (4.5-5.9) n=110	4.8 (3.8-5.2) n=102	3.8 (3.1-4.5) n=84	7.6 (6.1-9.1) n=18

See page 82 for significance tests.

The frequency distribution for pH and BD in the CTG normal, ST raised group was shifted to the right of the CTG normal, ST normal group (Figure 3.3A & 3.4A). This ST raised group had the highest mean pH and lowest mean BDecf compared to all other groups in either arm. In all the T/QRS ratio was persistently elevated (0.25-0.35) for the duration of labour, all had very reactive heart rate patterns with excellent neonatal outcome.

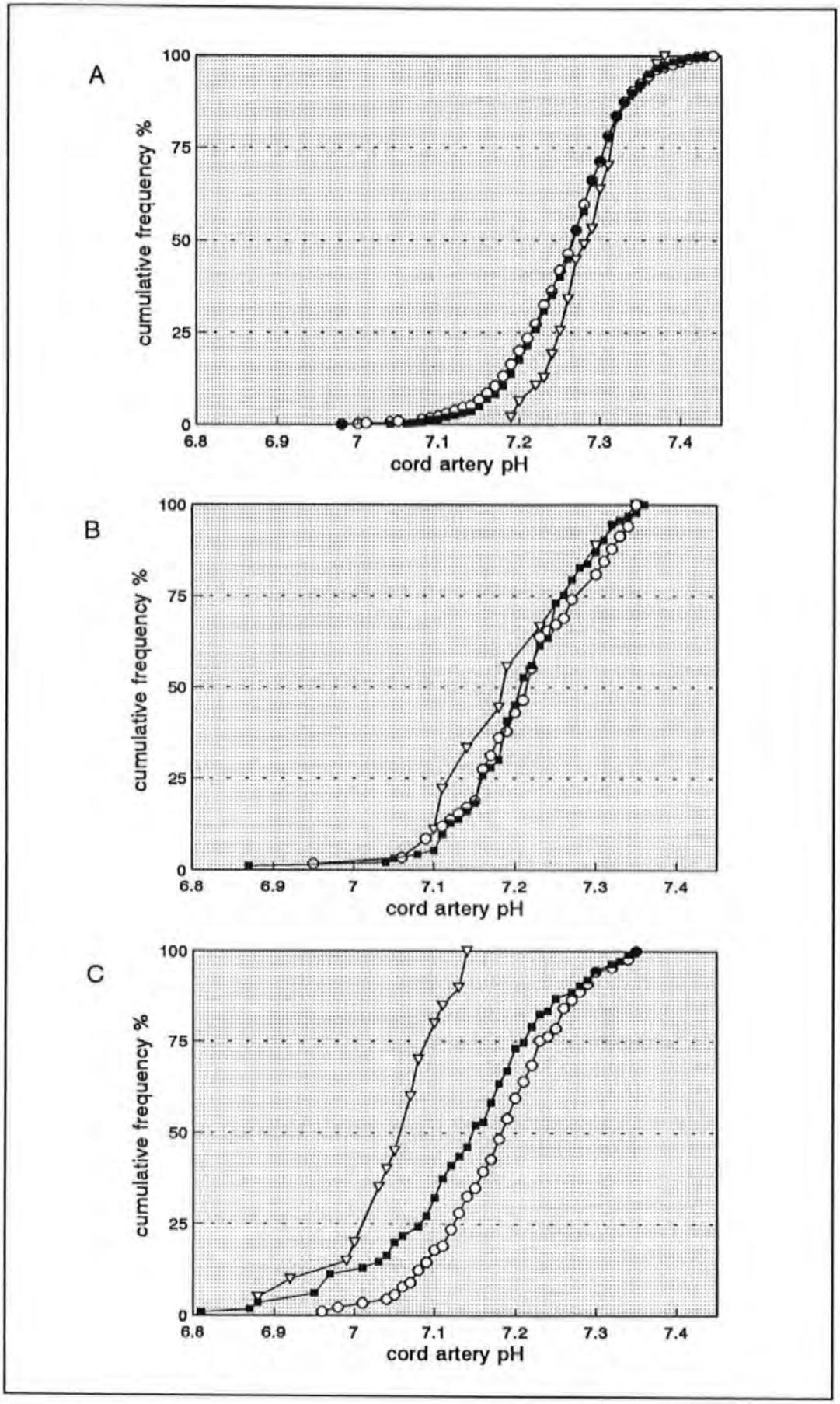


Figure 3.3 Cumulative frequencies for cord artery pH for
A. normal, B. intermediate and C. abnormal retrospective CTG classifications.
■ CTG arm, ST+CTG arm; O ST normal, ∇ ST raised.

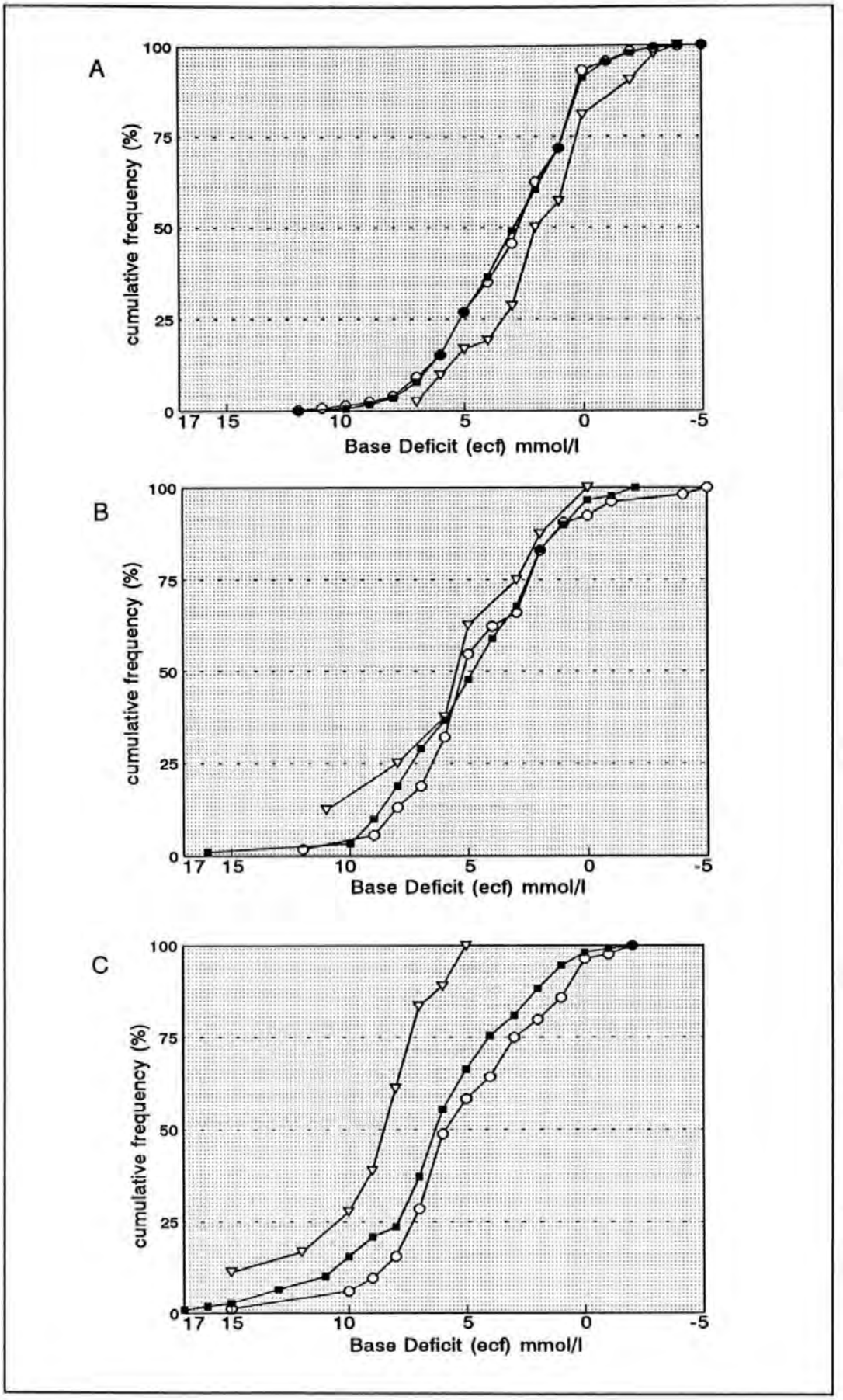


Figure 3.4 Cumulative frequencies for cord artery BDecf for
A. normal, B. intermediate and C. abnormal retrospective CTG classifications.
■ CTG arm, ST+CTG arm; O ST normal, ∇ ST raised.

The frequency distributions in the CTG intermediate groups overlapped (Figures 3.3B & 3.4B) and no effect of ST waveform change could be seen. This was probably because there were only 8 cases in the CTG intermediate, ST raised group and the 95% CIs for the means were very wide.

The frequency distributions for each ST waveform subgroup in the CTG abnormal group were clearly different (Figures 3.3C & 3.4C); the ST normal subgroup has been shifted to the right of the CTG arm frequency distribution (to higher pH and lower BDecf values) whilst the ST raised subgroup has been shifted to the right (to lower pH and higher BDecf levels). The CTG abnormal, ST raised group had the lowest mean pH and highest mean BDecf compared to all other groups. In these cases the ST elevation occurred during the second stage in parallel with progressive CTG abnormalities.

Statistical analysis. The significance of the interaction between CTG and ST waveform change on pH and BDecf was tested by ANOVA. The results are shown in the following Tables.

Table 3.11 Results of ANOVA to test the effect of CTG classification on pH and BDecf in both arms of the trial.

Factor	Degrees of Freedom	pH p value	BDecf p value
CTG classification (normal, intermediate or abnormal)	2	<0.0001	<0.0001
Arm of trial (CTG or ST+CTG)	1	0.235	0.184
CTG/Arm interaction	2	0.190	0.532

In this analysis the the effects of two variables (CTG classification and which form of monitoring was used) on pH and BDecf were tested. Any interaction between the two variables was also assessed. These results show a significant effect of CTG classification on both pH and BDecf in both arms but no effect of trial arm for each CTG classification and no interaction between trial arm and CTG. This can be illustrated in the following Figures.

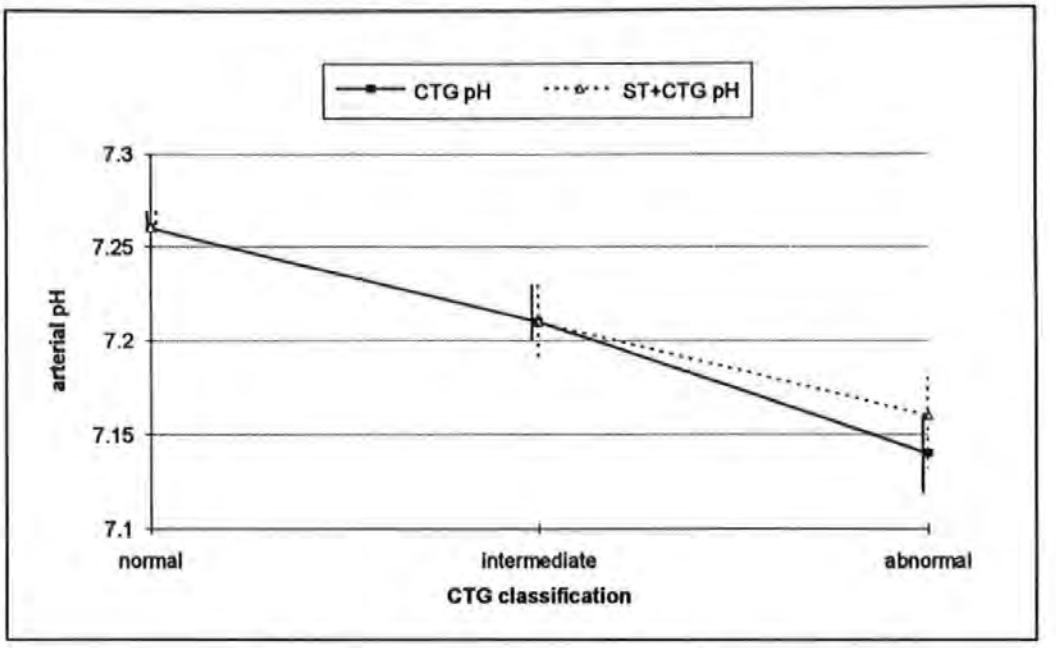


Figure 3.5 Mean pH at each CTG classification in both arms of the trial. Vertical bars show 95% confidence intervals.

As the CTG became more abnormal, the mean pH in each trial arm fell. The pH values for each arm of the trial virtually overlap and there was no significant difference between the values for each CTG classification in each arm.

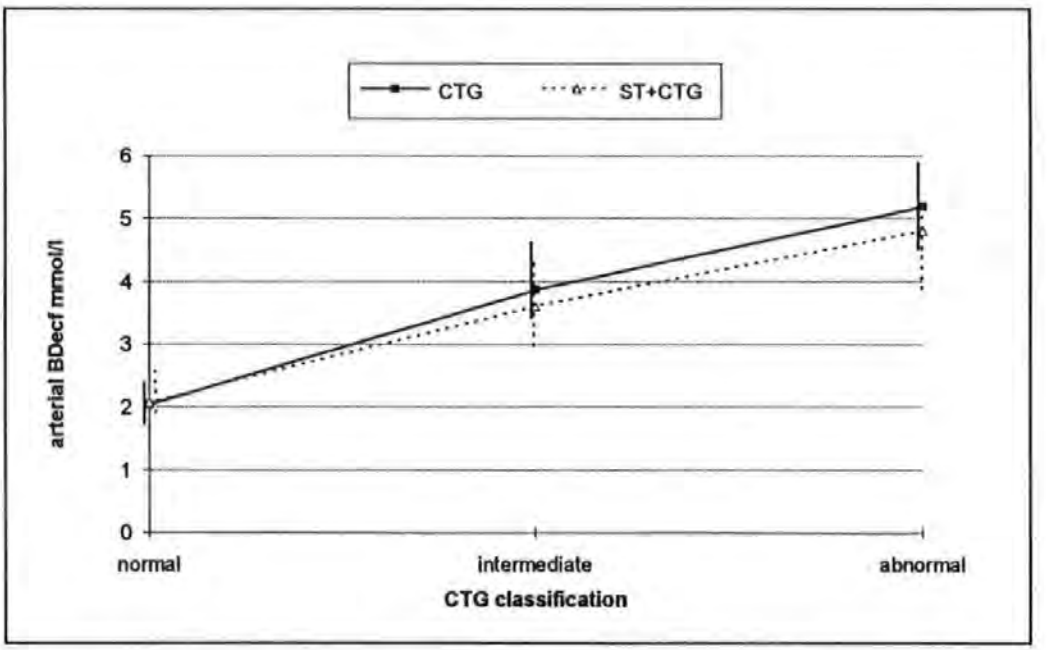


Figure 3.6 Mean BDecf at each CTG classification in both arms of the trial. Vertical bars show 95% confidence intervals.

As the CTG became more abnormal in each trial arm, the mean BDecf rose. The BD values in each arm at each CTG classification were not significantly different.

The next analysis was performed on the ST+CTG arm data only. It tested the effects of two variables (CTG classification and ST waveform pattern) on pH and BDecf. Any interaction between the two variables was also assessed.

Table 3.12 Results of ANOVA to test the effect of CTG and ST waveform classification on pH and BD in the ST+CTG arm.

Factor	Degrees of Freedom	pH p value	BDecf p value
CTG classification (normal, intermediate or abnormal)	2	<0.0001	<0.0001
ST waveform (normal or raised)	1	0.001	0.005
CTG/ST waveform interaction	2	<0.0001	<0.0001

Both CTG classification and ST waveform had a significant effect on pH and BD and there was a significant interaction between the two. This can be illustrated in the following figures.

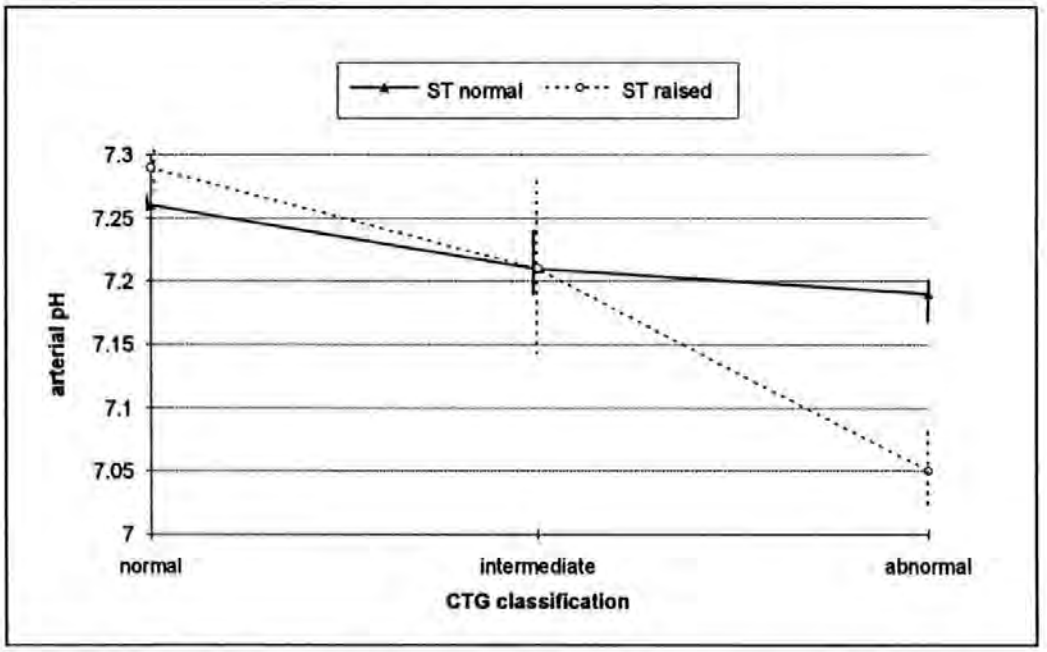


Figure 3.7 Mean pH at each CTG classification for ST normal and ST raised subgroups of the ST+CTG arm. Vertical bars show 95% confidence intervals.

As the CTG classification became more abnormal, the pH fell in both subgroups of the ST+CTG arm. However, the values are dissimilar (except for CTG intermediate) and the slopes of the two lines are different. This illustrates the significant interaction between

CTG classification and ST waveform change for pH.

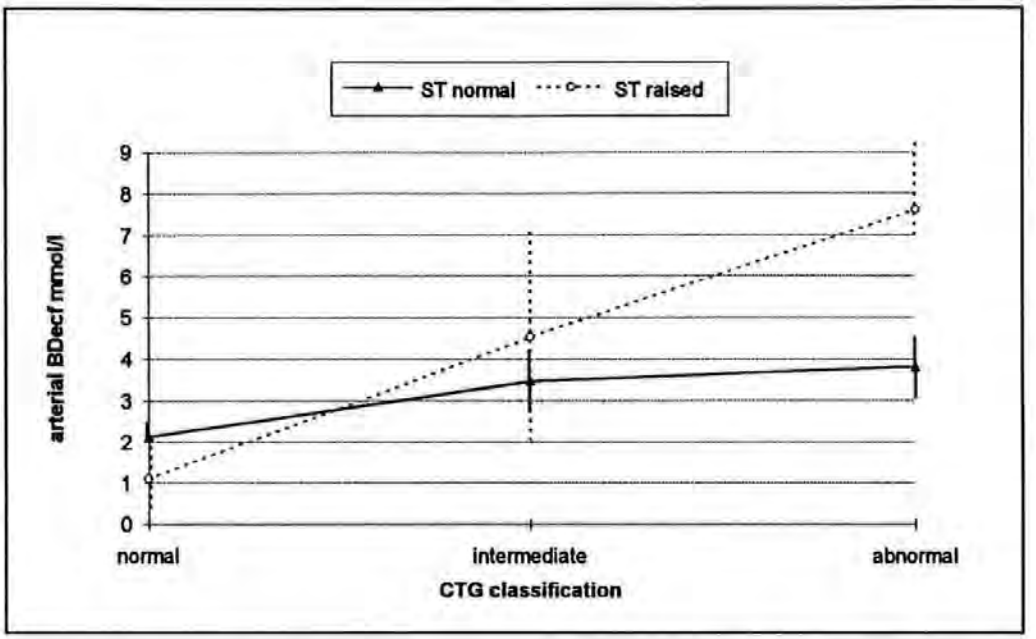


Figure 3.8 Mean BDecf at each CTG classification for ST normal and ST raised subgroups of the ST+CTG arm. Vertical bars show 95% confidence intervals.

As the CTG classification became more abnormal, the BDecf rose in both subgroups of the ST+CTG arm. However, the values are dissimilar and the slopes of the two lines are different. This illustrates the significant interaction between CTG classification and ST waveform change for BDecf.

Use of ANOVA assumed that the data was normally distributed with a homogeneity of variances, although this was not entirely true. Use of this test can be justified as it is well documented that ANOVA is robust for departures from normality (Glass et al, 1972). With the overwhelmingly significant effects found here, the conclusions are unlikely to be compromised by the moderate departure from normality present. As a cautionary check the effect of CTG classification in each column in Table 3.10 was analysed using the Kruskal - Wallis test, a nonparametric alternative to One Way ANOVA. This showed a highly significant ($p<0.001$) effect of CTG classification on pH and a significant effect ($p<0.01$) on BDecf with the exception of the CTG intermediate, ST normal and CTG abnormal, ST normal subgroups which were not significantly different. It was impossible to test the interaction between CTG and ST waveform with nonparametric tests as there was no nonparametric version of ANOVA which could cope with groups of unequal size. Similar results to the ANOVA were found with repeated Mann-Whitney-U tests comparing each subgroup of the data with every other group. It is recognised that such multiple comparisons would have increased the chance of finding a falsely significant result (a type I error) but the analysis was only performed as an additional check on the ANOVA results.

Quality assessment.

There were no differences in the quality scores for heart rate in the first stage between the trial arms (Table 3.13). Compared to the ST+CTG recorder, the CTG recorder produced significantly better heart rate recordings in the 2nd stage and better contraction recordings in both the first and 2nd stage. The ST+CTG recorder produced significantly worse heart rate and ECG recordings in the 2nd stage compared to first stage recordings.

Table 3.13 Subjective assessment of quality of recordings on a scale of 1 (excellent) to 3 (poor). Figures are given as percentages.

	CTG			ST+CTG		
	Grade 1	**Grade 2**	**Grade 3**	**Grade 1**	**Grade 2**	**Grade 3**
Fetal heart rate						
First stage	88	12	0	87	12	1
Second stage	84[1]	15	1	71[2]	26	3
Contractions						
First stage	88[3]	11	1	75	20	5
Second stage	83[4]	12	5	73	19	8
ECG complexes						
First stage				73	25	2
Second stage				56[5]	39	3

Fetal heart rate; 1 $p<0.001$, OR 2.13 (1.73-2.62) compared to ST+CTG second stage.
2 $p<0.001$, OR 2.83 (2.27-3.51) compared to ST+CTG first stage

Contractions; 3 $p<0.001$, OR 2.46 (1.99-3.06) compared to ST+CTG first stage.
4 $p<0.001$, OR 1.81 (1.47-2.22) compared to ST+CTG second stage

ECG complexes; 5 $p<0.001$, OR 2.14 (1.79-2.55) compared to ST+CTG first stage

All by χ^2 analysis.

Discussion.

Evaluation of the ST waveform of the fetal ECG has closely followed standard pharmaceutical procedures for the introduction of a new drug; with animal studies to investigate the basic physiology, observational studies in man to determine a clinical protocol, followed by a randomised clinical trial to establish its clinical value and practicability. This is the first time a new concept for fetal assessment which involves new technology has been tested in a randomised trial ***before*** widespread introduction into obstetric practice.

Intervention and outcome.

The main aim of the trial was to investigate the effects of ST waveform plus CTG analysis on operative intervention rates and neonatal outcome. The results show a significant reduction both in the total number of FBS samples taken and in the number of operative deliveries for 'fetal distress' with no adverse effects on neonatal outcome.

Fetal blood sampling. There was no difference in FBS in the interim analysis at 1200 entries (80 samples taken from 58 patients in the CTG arm versus 70 samples taken from 52 patients in the ST+CTG arm, p=0.56, OR 1.18[0.84-1.67]). By the completion of the trial at 2434 entries, the total number of patients who had FBS in each arm was not significantly different (114 CTG versus 93 ST+CTG, p=0.14, OR 1.26 [0.94-1.67]) but there was a significant reduction in total number of samples taken (168 CTG versus 129 ST+CTG, p=0.02, OR 1.36 [1.06-1.73]). These findings reflect the deliberately conservative trial protocol as it was important to maintain the safety of an FBS option during the introduction of a new monitoring concept. Recently, Johansen et al, (1992) measured the T/QRS ratio immediately before a FBS was performed for CTG changes in 88 cases. A T/QRS ratio <0.25 would have correctly reassured clinicians in 38 cases and all 3 cases with a metabolic acidosis would have been identified by a T/QRS ratio > 0.24. On the basis of their findings and those from this trial, it would be possible to safely reduce the FBS frequency in the CTG abnormal group.

Operative deliveries. A significant reduction in operative intervention was apparent by the interim analysis at 1200 cases (total deliveries for 'fetal distress' were 58 in the CTG arm versus 27 in the ST+CTG arm, p<0.001, OR 2.30 [1.44-3.69]) and was maintained at 2400 cases (111 CTG arm versus 61 ST+CTG arm, p<0.001, OR 1.96 [1.42-2.71]).

Based on the estimates of Clark et al, (1991) of £1172 per emergencey LSCS and £644 per operative vaginal delivery, the cost of the 'fetal distress' deliveries in the CTG arm was £87,324 and in the ST+CTG arm £47,204. Assuming the same rates of 'fetal distress'

deliveries, if all trial entries had been monitored with CTG alone, the cost of 'fetal distress' deliveries would have been in the order of £174,650 as compared to £94,410 if all entries had been monitored with ST+CTG analysis. Thus a potential saving of £80,240, or £33 per monitored patient, could have been possible with ST+CTG analysis.

The reduction in operative deliveries included both simple liftout forceps and caesarean sections and occurred in a hospital with intervention rates which were already low. The trial did not merely bias the indications given for operative delivery in the ST+CTG arm as there was no difference in the number of deliveries for failure to progress in each arm. In a stressful labour ward situation a clinician who is really concerned about a trace is more likely to deliver, and alter the indications given for delivery, than not deliver at all.

The selection of cases for operative delivery was more accurate in the ST+CTG arm. Fewer deliveries occurred in traces classified as normal or intermediate by the reviewer. ST waveform changes did not occur as frequently as CTG changes, therefore the addition of ST waveform probably acted as a reassuring variable which prevented interference in the majority of cases.

It is possible that a similar reduction in intervention could have been achieved by the addition of any other variable, whatever the source, as long as it reassured the clinician that action was not required whenever CTG changes occurred.

A possible example of such a variable is shown in Figure 3.9. This variable may prevent intervention in cases with minor CTG changes but, once changes become severe, the clinician's anxiety and desire to intervene would overcome advice to the contrary. This approach is unlikely to win the support of many Ethical Committees or pregnant women. In comparison, the use of ST waveform analysis in labour has a sound physiological basis and the neonatal outcome and cord blood gas results in this study demonstrate that the concept offers more than non-discriminatory advice to reduce intervention.

Figure 3.9 An example of an additional variable which could reduce operative intervention?

Further, clinical use of the ST waveform in other centres has been associated with decreased intervention. For example, Haugesund Hospital in Norway has 1450 deliveries per annum and uses CTG analysis without fetal blood sampling. The introduction of one

ST ANalyser in 1990 used in high risk labours was associated with a fall in operative delivery rates without an increase in perinatal mortality (Eriksen et al, 1992).

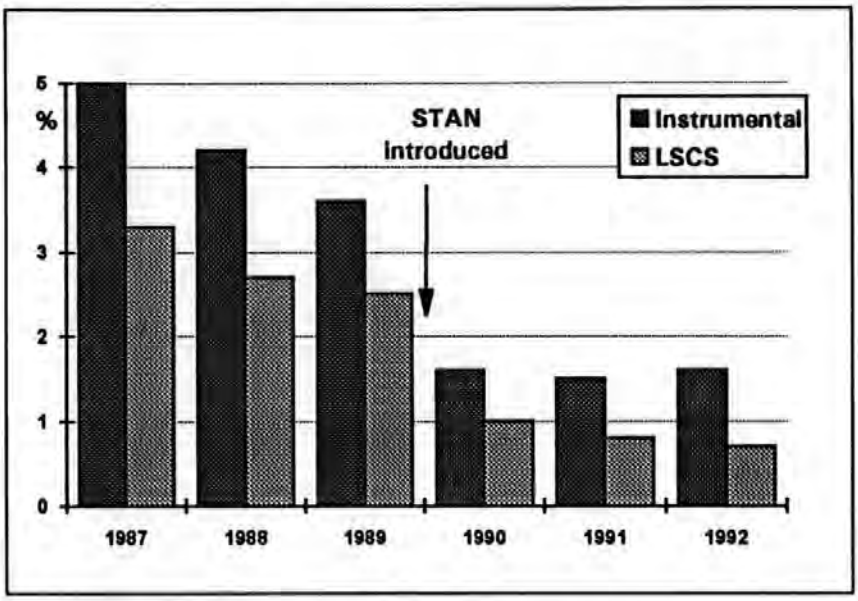


Figure 3.10 Operative delivery rates (%) at Haugesund Hospital, Norway before and after STAN introduction. Modified from Eriksen et al, 1992.

Neonatal outcome. Although the differences in operative intervention in this trial were statistically significant by the interim analysis of 1200 cases, the trial was continued to 2400 cases to investigate the effect on neonatal outcome. There were trends to less metabolic acidosis (13 CTG versus 5 ST+CTG, p=0.09 OR 2.63 [0.93-7.39]) and fewer low five minute Apgar scores (32 CTG versus 24 ST+CTG, p=0.12 OR 1.62 [0.92-2.85]). These are likely to be related and support the contention that the use of ST waveform to delay intervention had no adverse effect on immediate neonatal outcome and, further, suggest an improved outcome is possible. Given the numbers in this trial it was unlikely that significant differences in outcome would be found, but it is highly unlikely that these trends would be completely reversed with increased numbers. Further data from meta-analysis of other trials is required.

Patterns of ST waveform and CTG change.

Several interesting patterns of ST waveform and CTG change were observed in the study.

1. Persistent, stable ST elevation with a reactive CTG. (Figure 3.11)

This was seen in 4% of cases and was associated with a significantly higher mean arterial pH at delivery. This probably reflects sympathoadrenal stimulation from the general arousal of labour (Lagercrantz & Slotkin, 1986) or response to mild but compensated hypoxaemia and is in keeping with the animal data (Hökegård et al, 1979) and the increased heart rate variability seen in these fetuses.

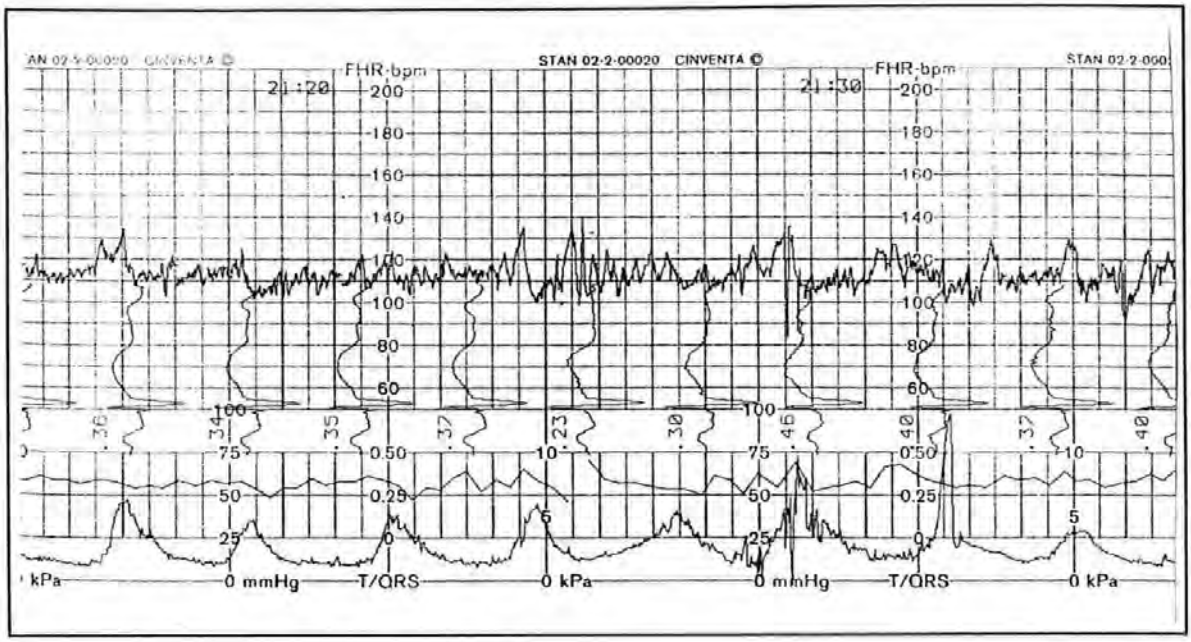


Figure 3.11 An example of a case with a persistent, stable ST waveform elevation and a reactive CTG pattern.

2. Rapid rise in ST waveform and a progressively abnormal CTG. (Figure 3.12)
Most of these cases occurred at the end of the second stage with an acute rise in T/QRS ratio over 10 to 20 minutes. The mean artery pH and BD for this group were lower than all other groups so this combination of ST and CTG change identified a group of fetuses who were developing a metabolic acidosis. These findings are consistent with the experimental data which showed that ST elevation was directly related to myocardial glycogenolysis.

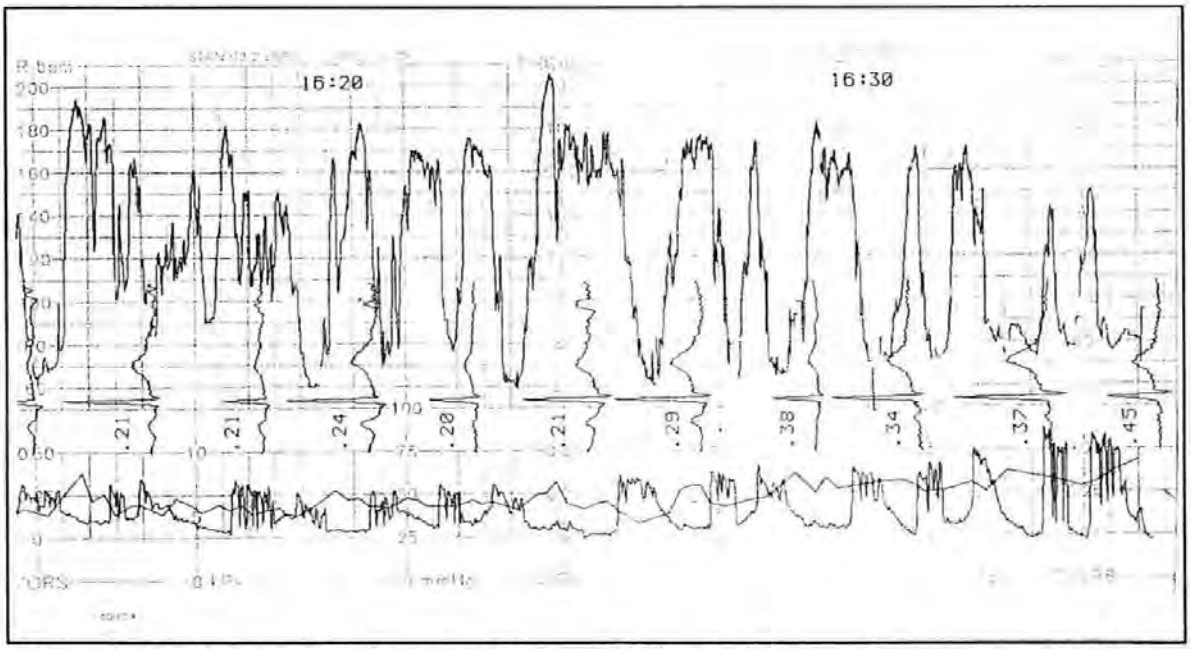


Figure 3.12 An example of a case with a rapid rise in ST waveform accompanied by a progressive deterioration in CTG.

Anaerobic metabolism is an important part of the fetal response to reduced oxygen supply. A cord artery metabolic acidosis identifies fetuses who have experienced significant hypoxia and who are, therefore, at risk of neonatal sequelae (Low, 1988). This group most clearly demonstrated the potential for ST waveform change to discriminate CTG changes.

3. Negative ST waveform and an abnormal CTG. (Figure 3.13)

These fetuses probably had an ineffective response to hypoxia. Two of the three birth asphyxia cases in this study had negative ST waveforms and all 3 cases of negative waveforms reported in other studies to date (Rosén & Lindecrantz, 1989, Rosén et al, 1992 and Murphy et al, 1992) were also asphyxiated with one death. Two were growth retarded and one was postmature. This is in keeping with the animal studies in which ST depression with and without negative T waves was observed in runted guinea pig fetuses during hypoxia (Widmark et al, 1991, Figure 1.11 in the introductory chapter). As a result of their reduced myocardial glycogen stores and a blunted sympathoadrenal response, these fetuses were unable to compensate adequately during periods of hypoxia and suffered the effects of direct hypoxia in the deeper myocardial layers. The accompanying change in cell membrane potentials produced a negative ST waveform pattern as illustrated in Figure 1.12 of the introductory chapter.

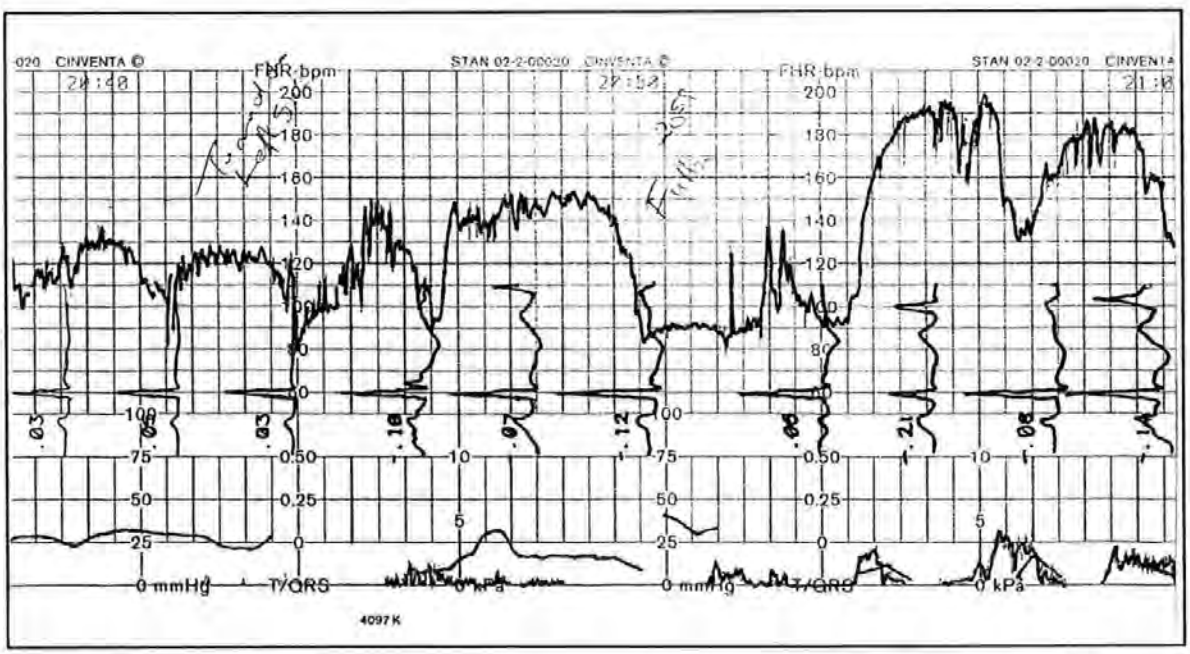


Figure 3.13 An example of a case with negative ST waveform change accompanying an abnormal CTG (Case 106 in Table 3.8, page 75).

Why do some fetuses display a biphasic waveform (ST segment depression with a positive T wave) and others both a negative ST segment and T wave? In order to investigate this further, the ST waveform changes observed in adults during an exercise ECG were reviewed. There are differences in myocardial metabolism between the fetus in labour and an adult (Su and Friedman, 1973) and global myocardial hypoxia is more likely in the fetus

whilst in adults hypoxia is usually localised to an ischaemia area. The acute hypoxic stress in the fetus is intermittent (related to contractions) not persistent. Despite these differences very similar patterns of ST waveform change were observed in the adult and the fetus. The significance of tall peaked T waves (indicative of coronary insufficiency) and ST segment depression (evidence of direct myocardial ischaemia) (Schamroth, 1984) was consistent with the model of interpretation of fetal ST waveform elevation and depression. In the adult the development of a negative ST waveform during the exercise ECG was preceded by progressive ST segment depression and T wave flattening until eventually T wave inversion occurred. The reverse was seen during the recovery period (Figure 3.14). In cases with a normal ECG prior to exercise, negative T waves are not seen without preceding biphasic changes (D. Morris, Senior Cardiology Technician, Plymouth General Hospital, personal communication). A similar progression from a positive to a biphasic and then a negative waveform was observed in a fetus during the trial (Figure 3.15).

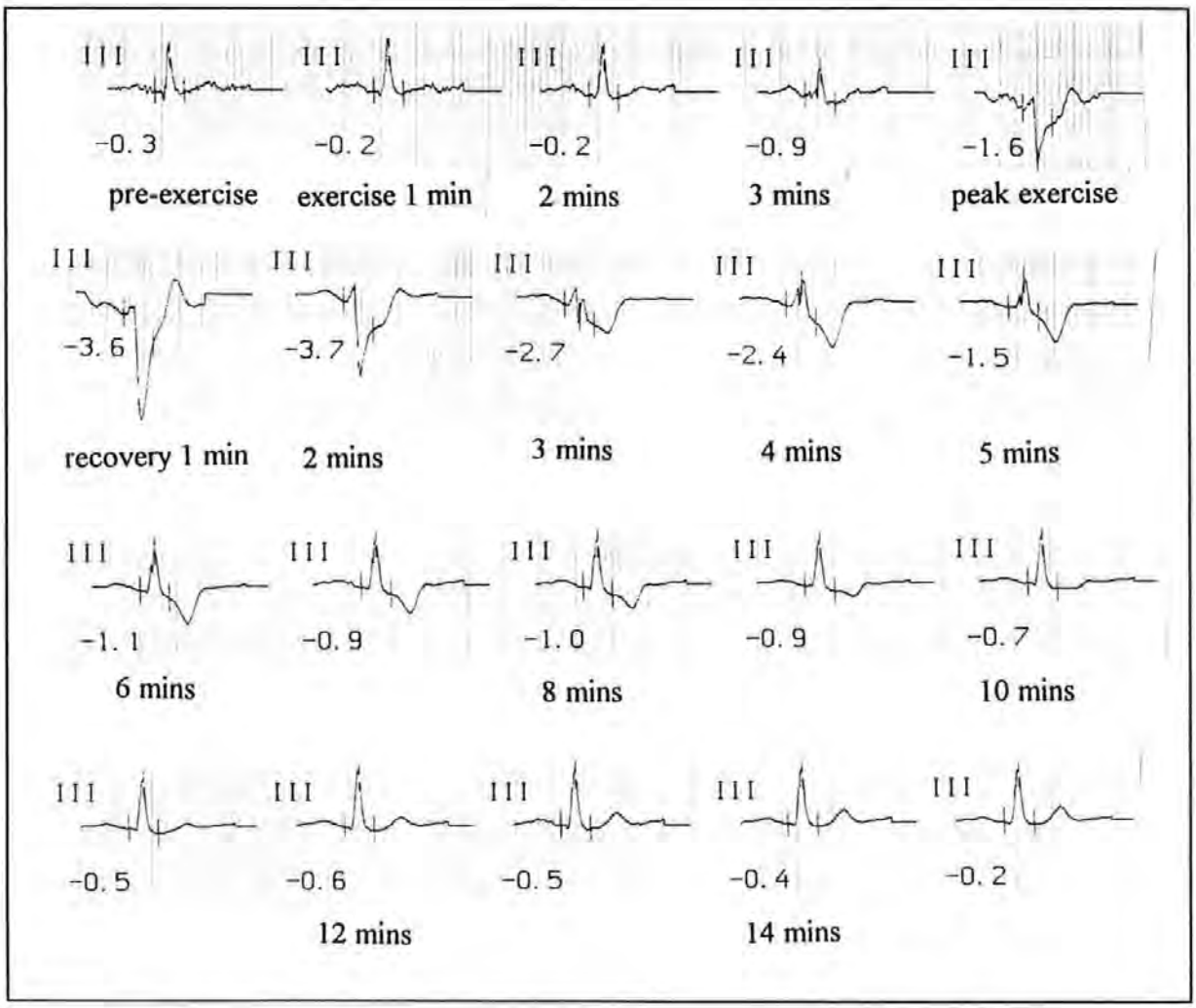


Figure 3.14 Exercise ECG changes in an adult male in lead III. Note how changes progress from a positive ST waveform to a biphasic pattern and finally a negative T wave at 6 minutes and then gradually reverse. The numbers printed by each complex are a measure of ST segment depression.

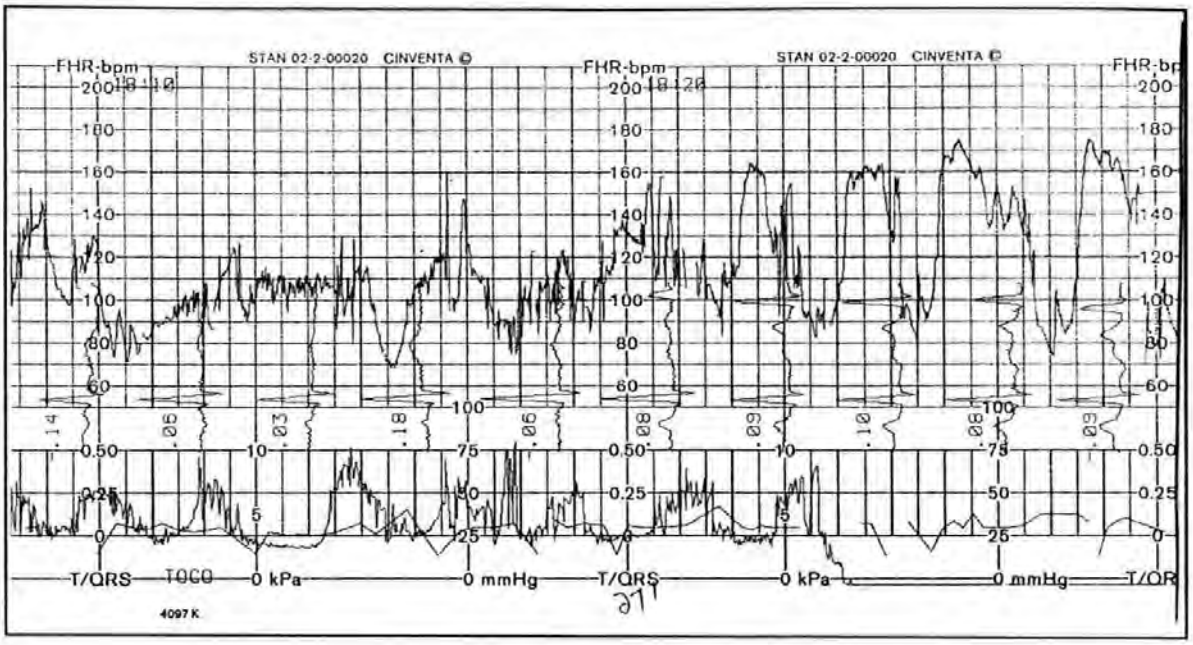


Figure 3.15 An example of a progression from a positive ST to a biphasic and then a negative waveform.

Intermittent negative changes which were related to contractions were more likely to be biphasic than negative and frequently just involved a flattening of the ST segment (Figure 3.16). A recent follow-up study found that adult men with an isoelectric, flat ST segment had higher mortality rates than those with the optimal upward sloping ST segment (Schouten et al, 1992).

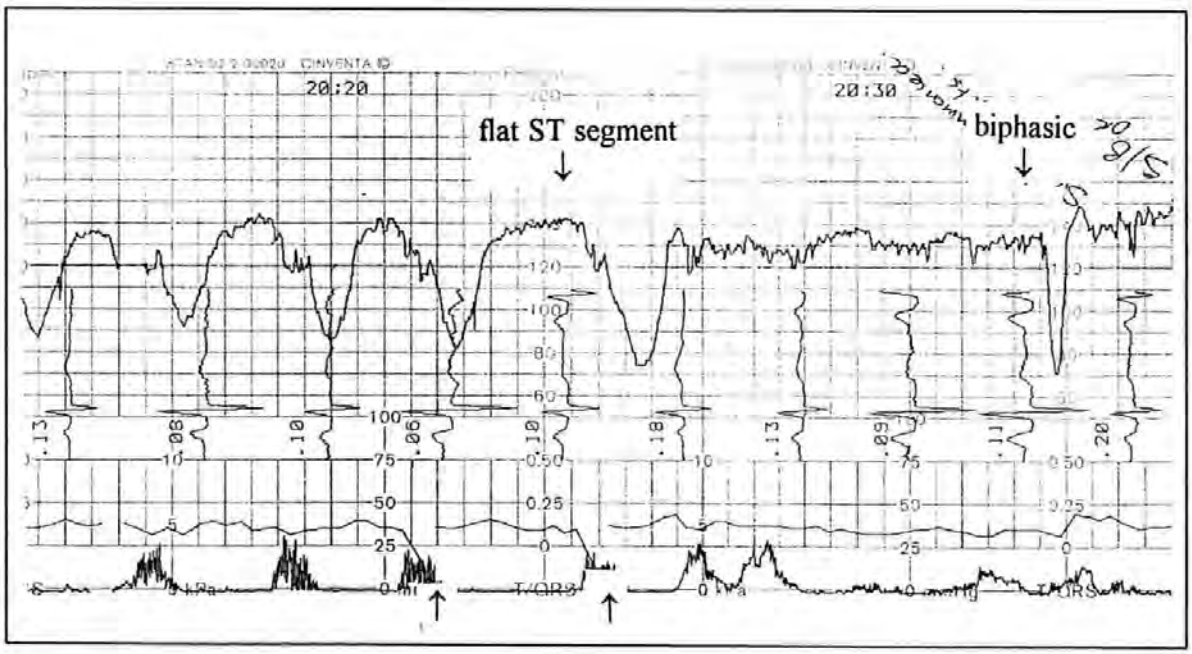


Figure 3.16 An example of intermittent biphasic ST waveform changes with ST segment flattening. Note how the T/QRS ratio plot becomes negative with the 3rd and 4th contractions.

In four cases the ST waveform became negative without any obvious transition through a biphasic waveform (Figure 3.13). All of these had flat T waves at the onset of recording. This may be a significant observation but more numbers are needed to ensure this was not a chance finding. It is possible that a rapid progression of changes from biphasic to negative may have occurred but may not have been documented due to the 2½ minute interval between printed ECG complexes.

On the basis of these observations, it would seem that ST depression with negative T waves is indicative of a more severe degree of oxygen deficiency than biphasic changes. The difference in ST waveform appearance may reflect the fact that the ECG is an average of potentials across the whole myocardium. A biphasic waveform may indicate that some areas are still able to produce energy by anaerobic metabolism whilst a negative T wave may indicate that the majority of the myocardium is hypoxic.

The occurrence of biphasic ST waveform changes highlights the need to examine the whole waveform and not just the T/QRS ratio. Important ST segment depression may be missed unless this is done. Clearly the T/QRS ratio is only one aspect of ST waveform assessment, although it has the merit of being more easily quantifiable. ST waveform area combined with the number of times the waveform crosses the isoelectric line may provide additional information (Greene, 1983). This highlights the necessity for an automated analysis of ECG waveform shape (N. Outram, PhD project, University of Plymouth).

Previous observational studies.

A number of small observational studies had been performed prior to this trial. They served two purposes; firstly to develop and refine the technology required for ST waveform analysis (Greene, 1983, Lilja et al, 1985, Lilja et al, 1988, 1989) and secondly, to test and further develop the model of interpretation for ST waveform change in the human fetus (Arulkumaran et al, 1990, Rosén et al, 1992). None of these studies included many cases with poor outcome. Arulkumaran et al (1990) had 3 cases of clinical birth asphyxia (Apgar <4 at 1 minute and <7 at 5 minutes) in 201 entries. Newbold et al (1991), using the Southampton system, found no relationship between T/QRS ratio and CTG pattern or cord artery pH in 105 fetuses. But their study did not include any cases with significant acidosis and no case with metabolic acidosis. The mean cord artery pH of their CTG abnormal group was the same as that of their overall population (7.24). The fact that no ST waveform changes were noted in this study is a positive finding (Westgate & Greene, 1991) and not a negative one as the authors have suggested. Many studies have attempted to correlate T/QRS ratio and cord artery pH over the normal range for both which is clearly inappropriate and does not test the model of interpretation. Several workers have not reported any cases with negative or biphasic waveforms, possibly because they did not have any or, possibly, because they confined analysis to the T/QRS ratio only and therefore

did not notice any biphasic changes (Newbold et al, 1991, MacLachlan et al, 1992). The randomised trial was the first study in which a group of fetuses with persistent elevation of the ST waveform have been described. The fact that this change is associated with an excellent outcome may explain the lack of correlation between T/QRS ratio and outcome measures found in other studies (Murphy et al, 1992, MacLachlan et al, 1992).

Randomised trial methodology.

Randomised trials have become widely accepted as the best method with which to compare alternative forms of care (Chalmers, 1991). Random allocation of patients between different treatments is used in order to balance both known prognostic factors and unrecognised and unmeasurable factors which may affect trial results (Health Care Advisory Group, 1992). Important methodological aspects of this trial will be discussed.

The randomisation process produced comparable groups for analysis. There were significantly more inductions in the ST+CTG arm at the 5% level and the number of postdates pregnancies and patients with epidural analgesia also approached significance. These variables are likely to be related. One could expect a few significant results purely by chance as a result of the large number of variables compared but this does not invalidate the comparability of the groups (Chalmers, 1991). These differences are more likely to have disadvantaged the ST+CTG arm as they are factors associated with increased intervention and poorer outcome. The use of sealed envelopes is not the ideal method for randomisation as it allows opened envelopes to be switched between patients entered into the trial at the same time. A more sophisticated randomisation process using computers or the telephone might have been preferable but would have been more costly and would have involved more work for clinical staff which would undoubtedly have prejudiced recruitment.

Observer bias. In a trial of this nature it was impossible to blind staff, patients, or the observers to the method of monitoring used so it is impossible to exclude any effect related to enthusiasm for the new technology. However it is also possible that an opposite effect may have occurred; if some staff found the new technology 'threatening', it is less likely that they would have followed the trial protocol. The observers were neither providers nor recipients of care and the outcome measures were objective 'hard data' - e.g. fetal blood sampling, operative deliveries, cord gas data, Apgar scores. This reduced the likelihood of observer bias.

The analysis of trial results has been by intention to treat, irrespective of whether the treatment was received or not. This is recommended as the only way that selection bias can be excluded (Chalmers, 1991). However, this policy may minimise or obscure differences between trial arms if the study is small or the number of cases not receiving the allocated

care is large. In the present study less than 3% of cases fell into this category and a secondary analysis which excluded those who did not receive the allocated treatment confirmed the primary results. In the Dublin randomised study of CTG and intermittent auscultation, 20% of those allocated to the CTG arm did not receive the allocated treatment yet a secondary analysis was not reported (MacDonald et al, 1985).

The number and nature of the analyses performed in this trial were pre-specified, as was the decision to analyse and publish the first 1200 entries. An interim analysis was chosen firstly because an effect on operative intervention for fetal distress should have been apparent by 1200 entries and, secondly, to ensure there was no obvious adverse effect on neonatal outcome. It could be argued that the interim analysis should have been made by an independent group, but as the analysis was performed by dedicated research personnel who were not involved in day to day labour ward management this was probably unnecessary. The results were not made available to clinical staff before the end of the study and publication post-dated completion of the study.

Protocol criticisms. There were two aspects of the trial protocol itself which could be criticised. The first is related to the inclusion of immature fetuses (34 to 36 weeks gestation). As little is known about ST waveform changes in these fetuses, trial entry should probably have been restricted to 36 weeks gestation or more. There is a progressive increase in sympathetic innervation of the tissues during development (Phillipe, 1984, Slotkin & Seidler, 1988). The cardiovascular and biophysical responses of the preterm fetal lamb to induced hypoxaemia are much less pronounced than in the more mature fetus (Matsuda et al, 1992). Thus, a different and perhaps less marked ST waveform change may occur in the immature fetus during labour. This has been noted experimentally; an equivalent degree of hypoxia was accompanied by less of a rise in plasma catecholamines and T/QRS ratio in the immature fetal lamb compared to the mature fetus (Widmark et al, 1989).

There were 26 cases less than 36 weeks gestation in the ST+CTG arm; two showed ST changes. One at 34 weeks gestation had persistently negative T waves (T/QRS –0.06 to –0.08) with a reactive CTG throughout labour. The neonate was delivered normally and was in good condition (cord artery pH 7.38, BDecf 2 mmol/l, Apgars 8 at one minute and 9 at five minutes). The other case was also at 34 weeks gestation and had intermittent negative T waves and an abnormal CTG which resulted in a forceps delivery (cord artery pH 7.15, BDecf 6 mmol/l, Apgars 9 at one, 9 at five minutes). One other immature fetus in the ST+CTG arm had a FBS at full dilatation five minutes after a prolonged deceleration to 90 bpm for 15 minutes. The ST waveform had remained normal (T/QRS ratio 0.10) The FBS pH was 7.18, BDecf 8 mmol/l and a liftout forceps delivery was done 30 minutes later (cord artery pH 7.23, BDecf 5 mmol/l , Apgars 9 at one, and 9 at five minutes). All other preterm fetuses in the ST+CTG arm and the 26 preterm fetuses in the CTG arm had

normal outcomes. As this randomised trial did not include any acidotic preterm fetuses, no comment can be made on the pattern of ST waveform change nor on the suitability of ST waveform analysis in this group.

The second criticism of the trial protocol relates to the classification of a recording with reduced variability and no accelerations in the absence of sedation for 30 minutes as abnormal. This did not allow for physiological sleep states in which variability can be less than five beats per minute and may last for more than 45 minutes in up to 5% of recordings (Spencer & Johnson, 1986). The recommended action was the same for both arms of the trial and therefore did not bias the retrospective review. However, for the purpose of future studies the duration of reduced variability required to classify an abnormal recording should be extended to 45 minutes.

Education and training. If new technology is to be compared with existing technology it is important that staff are familiar with the use of new equipment and the interpretation of results before the comparison occurs. Preparation for this trial took place over a nine month period and included written material, lectures and discussion sessions. Staff were introduced to the ST+CTG recorder during the study of fetal scalp electrodes. Finally, a pilot study was run for a month before the trial proper commenced to familiarise staff with the study procedures and to identify any aspects of the protocol which needed clarification. No randomised trial of electronic fetal heart rate monitoring performed to date has published details of any staff training and preparation for the trial. Given the increase in education and training provided during this trial, interpretation of the CTG alone should have improved. This makes the differences in intervention rates more surprising. It seems that the addition of ST waveform analysis to the CTG improved clinical interpretation of CTG traces, probably by reassuring staff that traces were normal, as has already been discussed.

The Hawthorne effect. The performance of a randomised trial may modify staff behaviour and the quality of care given (the Hawthorne effect). This effect has already been demonstrated in the review of the perinatal and intrapartum stillbirth rates from the Dublin randomised trial (Chapter 1, Figure 1.1). The effects of the Plymouth trial on overall unit figures were not obvious as only one third of total deliveries were recruited to the study and ST+CTG analysis was used in only half of these. Plymouth operative intervention rates from 1987 to 1992 are shown in Figure 3.17. It is remarkable that the reduction in LSCS for 'fetal distress' in the ST+CTG arm occurred despite the background of a steadily rising emergency LSCS rate. The increase in LSCS has been accompanied by an decrease in the operative vaginal delivery rate; obstetricians seem less likely to attempt vaginal operative deliveries in favour of LSCS. This is probably related to the increasing pressure of litigation.

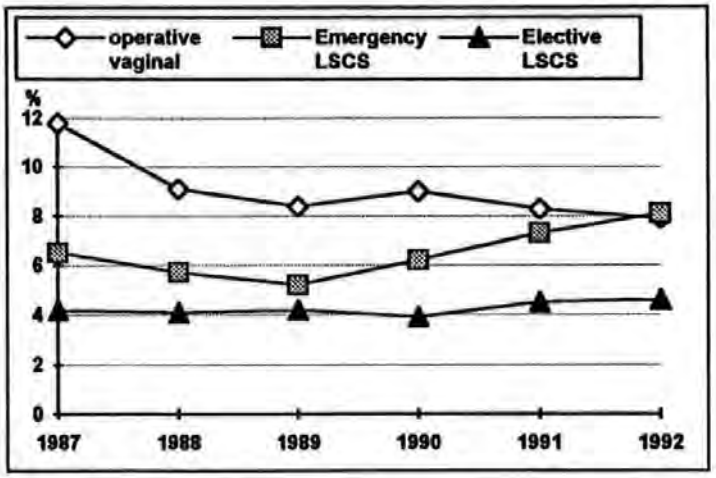


Figure 3.17 Operative delivery rates at Plymouth General Hospital. The randomised trial ran from mid 1990 to the end of 1991.

Revised guidelines for clinical action.

As a result of the observations of ST and CTG change made during this trial, recommendations for clinical action have been revised (Table 3.14). These guidelines apply to the mature fetus (≥ 36 weeks gestation).

Table 3.14 ST + CTG clinical guidelines.

CTG	ST waveform		
	Normal	**High & stable**	**Negative or rising**
Normal	No Action	No action	FBS or deliver[1]
Intermediate	No action	Wait 1 hour FBS or deliver[4]	Deliver[2]
Abnormal	Wait 1 hour FBS or deliver[4]	Deliver	Deliver[3]

1 Negative - less than -0.05 for more than 20 minutes.
Rising - rises more than 0.40 over 15 minutes
2 Negative - less than -0.05 for more than 20 minutes.
Rising - rises more than 0.15 from the baseline over 15 minutes.
3 Any negative or positive change over 5-10 minutes.
4 Repeat FBS every hour or earlier if CTG deteriorates. If CTG remains unchanged but ST shows acute change, delivery should be expedited. In second stage delivery should occur after 90 minutes as rapid deterioration can occur after this time.

In these revised guidelines the shape of the waveform, rather than just the T/QRS ratio, is emphasised. For any given healthy fetus the ST waveform (and hence the T/QRS ratio) tends to remain stable throughout labour. The impression gained during the retrospective review of recordings was that a progressive rise above the normal level for each fetus was important, irrespective of whether that rise took the T/QRS ratio above 0.25. The T/QRS ratio does have the merit of being quantifiable but assesses mainly T wave height and not ST segment changes. These will only be identified if the whole waveform is examined. Similarly, signal quality can only be assessed by checking waveform shape.

Contraction related waveform changes are important but cannot easily be incorporated into a simplified scheme such as the one shown here. In addition, the ECG complexes are only printed out every 2½ minutes so it is impossible to examine waveform shape after every contraction. However, the changes seen in this study and those found experimentally by Greene (1987) and Watanabe et al (1992) suggest that contraction related changes may identify a fetus at risk of decompensation before changes in the baseline ST waveform occur. Ideally, some way of presenting this information to the clinician should be found.

Future development of the STAN recorder.

Although the STAN monitor is satisfactory for clinical use, it is clear that improvements can be made. There were significantly more exclusions from the retrospective review because of poor signal quality in the ST+CTG arm than in the CTG arm (29 [2.3%] versus 6 [0.5%], $p<0.001$, OR 4.9 [2.03-11.87]). Considering the problems associated with FECG analysis, a 2.3% failure rate is, in fact, quite encouraging. It is likely that there will always be occasions in many labours when FECG quality is inadequate for waveform analysis. However, it is of some concern that the quality of STAN FHR recordings in the second stage and contraction recordings in both stages were not as good as the Hewlett-Packard CTG recorder. These signals do not depend on ECG waveform analysis and improvements should be possible.

The technological development of the STAN monitor now lags behind sound clinical evidence of its usefulness. There is a responsibility to correct this but, as yet, no commercial company has been willing to further the concept of ST waveform analysis and make the necessary improvements to the recorder. This is despite the fact that the concept has been developed in a logical sequence and best fulfils the requirements for a method of intrapartum fetal surveillance. This randomised trial has demonstrated the ability of ST waveform plus CTG analysis to reduce operative intervention rates. It must surely be in the best interests of both obstetrician/midwife and patient that the technology is developed further so it eventually may become available in clinical practice. The problem is, of course, both political and financial. There is little incentive for companies who already have a large share of the fetal monitoring market to spend further large sums of money developing a

similar product, though it may be a better one, which will give them no further financial gain. Given the potential reduction in operative delivery costs associated with the use of STAN in this study, the Department of Health could consider developing the technology further itself. Although thorough evaluation of new health care technology is necessary, it is ironic that the expense and politics involved may prevent or significantly delay the introduction of technology which is proven to be of better health gain than that currently used.

Summary.

The results of this randomised trial have confirmed the ability of ST waveform change to discriminate CTG change during labour. The model of interpretation used is safe and depends on the use of both variables (CTG and ST waveform), and also upon adequate education and training of staff. Further randomised trials in other units are required to confirm these findings and to provide further data to assess the possible effect on improved neonatal outcome.

Chapter Four

An assessment of current monitoring practice.

Introduction.

Effective use of the CTG for intrapartum monitoring depends upon appropriate selection of cases and the ability of midwives and obstetricians to interpret FHR patterns and take appropriate action once changes occur. A selective policy of CTG monitoring in high risk cases is usually advised (FIGO, 1987), but nearly half of UK obstetricians aim to monitor all patients continuously (Whebble et al, 1989) despite evidence that it is not beneficial in low risk patients (Grant, 1991). There is increasing evidence that staff find interpretation of CTG recordings a difficult task; misinterpretation is implicated in a large proportion of birth asphyxia cases (Murphy et al, 1990) and is the cause of a substantial proportion of litigation for birth related events (Ennis & Vincent, 1990, Chamberlain & Orr, 1990).

The use of FBS to discriminate CTG changes has been widely advocated in order to prevent unnecessary operative intervention (Saling & Schneider 1967, Beard et al, 1967, Zalar & Quilligan, 1979, Haverkamp et al, 1979, Sykes et al, 1983, MacDonald et al, 1985). Despite these recommendations less than half of UK units have facilities for its use (Whebble et al, 1989) and where it is used, FBS rates vary from 1% to 22% (Clark & Paul, 1985, van den Berg et al, 1987). There is surprisingly little information in the literature on when, and how effectively, FBS is used in clinical practice.

The randomised trial of CTG versus ST+CTG reported in the previous chapter provided an opportunity to investigate when and how well CTG plus FBS monitoring was used in clinical practice in Plymouth when regular education sessions were available. Three specific areas were addressed and will be reported here; firstly, the use of FBS in trial entries, secondly, selection of cases for operative delivery for 'fetal distress' and thirdly, the distribution of monitoring methods and their relation to outcome.

Methods.

The trial methodology was reported in the previous chapter. Additional information on the distribution of monitoring methods and neonatal outcome in babies not entered into the trial was obtained from review of the Birth Register and SCBU Admissions Book.

Results.

Fetal blood sampling.

Several aspects of FBS were studied in the retrospective review of CTG and ST+CTG recordings.

Selection of cases for FBS. Cases where FBS was indicated in the first stage of labour according to the retrospective review were compared with those who actually had FBS during the trial. The results are shown in Table 4.1. If multiple FBS procedures had been performed on the same patient, FBS was considered as appropriate as long as one of the samples taken was recommended on the retrospective review.

Table 4.1 Retrospective review of fetal blood sampling in the first stage of labour.

	CTG n=1208	ST+CTG n=1176
No. of cases where FBS done	114 (9.4%)	90 (7.7%)
Based on the retrospective review FBS was;		
- indicated & done	70	55
- not indicated but done	44	35
- indicated but not done	35	21
Total cases where FBS was indicated	105 (8.7%)	76 (6.5%)

39% of the FBS cases in each arm were performed unnecessarily, whilst 33% (CTG arm) and 23% (ST+CTG arm) of those who should have had an FBS did not have this done. This latter group included 3 of the 7 cases of birth asphyxia (1 CTG, 2 ST+CTG) and 6 of the total 48 cases with a cord artery pH <7.05 (CTG 4, ST+CTG 2).

pH at FBS and FBS response times. In order to check the accuracy of the retrospective review, scalp pH at the first FBS and the indication for FBS as assessed in the retrospective review were examined (Figure 4.1). The response times from onset of CTG change to FBS are shown in Figure 4.2.

The two arms of the trial have been combined as there were only 3 cases when ST waveform change contributed to the indication for FBS (1 intermediate CTG with a negative waveform; pH 7.28, 2 abnormal CTGs with a raised T/QRS ratio pH 7.29 and 7.33). One case with a clearly erroneous pH of 7.82 ('severely abnormal' group) was excluded from Figure 4.1 and the calculations for mean pH as the value obtained was not in the physiological range. No repeat sample was taken. The 'not indicated' group included many with minor changes (e.g. early decelerations) which did not require FBS. The

'severely abnormal' group had a combination of abnormalities (e.g. tachycardia, reduced variability and late decelerations). In the 'abnormal <30 mins' group the abnormal CTG persisted for <30 minutes and hence did not fulfil the criteria for FBS.

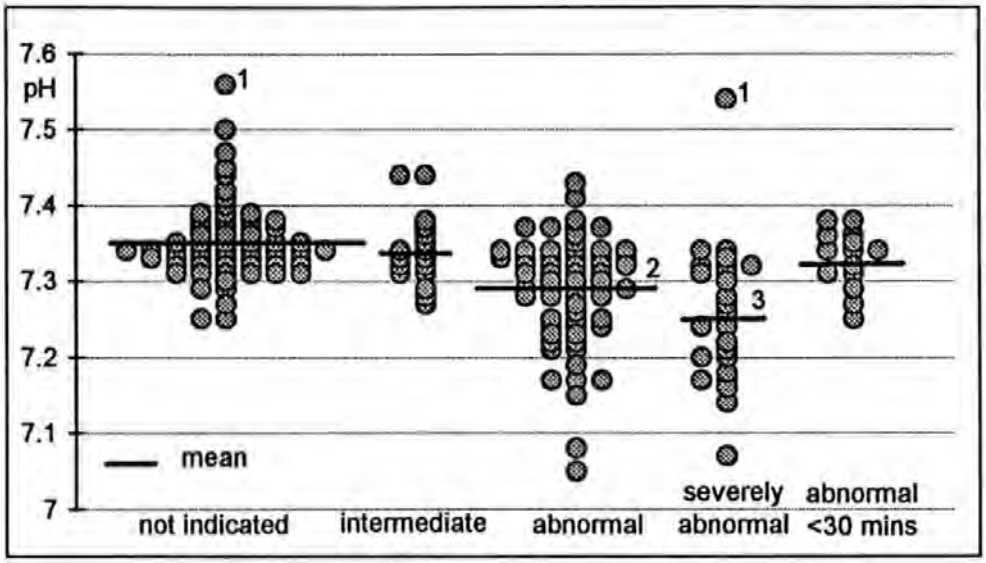


Figure 4.1 pH at the first FBS according to the indication determined by the retrospective review.

1 These two values were not used for calculation of mean pH as they were not in the physiological range.

2 Mean pH is less than 'not indicated', 'intermediate' and 'abnormal <30 mins' groups ($p<0.001$).

3 Mean pH is less than all other groups ($p<0.001$).

Significance testing by One Way Analysis of Variance.

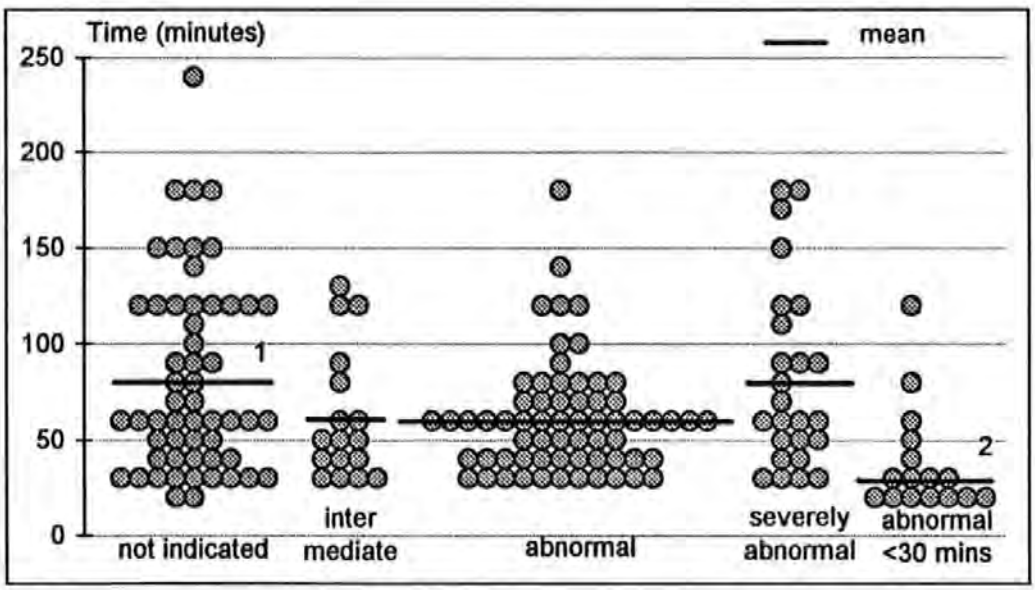


Figure 4.2 Response time from onset of CTG change to first FBS.

1 Mean time is significantly longer than the 'abnormal' group ($p<0.05$).

2 Mean time is significantly shorter than all other groups ($p<0.001$).

Significance testing by One Way Analysis of Variance.

It is encouraging for the reviewer to note that none of the cases where the FBS was 'not indicated' had a pH <7.25. This indicates the review was accurate. Although the mean pH fell as CTG changes progressed from normal to abnormal and then to severely abnormal, the majority of cases still had a pH in the normal range. The mean pH of cases with a CTG abnormality which had been present for <30 minutes was significantly higher than those in which an abnormality had been present for a longer period of time. This is consistent with the finding that a fetus may maintain a normal pH for some time in the presence of late decelerations (Beard et al, 1971, Fleischer et al, 1982) as a consequence of the fetal compensatory mechanisms discussed in the introductory chapter.

The range of response times is very similar for all categories, and it is of particular interest that a severely abnormal CTG did not prompt earlier intervention than occurred in the other groups. Similar findings have been reported in a review of the management of birth asphyxia cases (Murphy et al, 1990).

Interpretation of results and subsequent management. An understanding of acid-base balance and the normal range of results for blood gas values is necessary to interpret FBS results accurately. Three cases in which non-physiological values for pH were accepted as valid readings have already been presented. Full acid-base status needs to be assessed if a transient respiratory acidosis is to be distinguished from a more significant metabolic acidosis (Saling & Schneider, 1967, Ingemarsson & Arulkumaran, 1986), yet 22% of the FBS samples taken in this study had an unreliable pCO_2 result. Half of these cases were due to an inadequate size blood sample and in the rest the pCO_2 readings were suspiciously low for the pH value obtained. There are two possible reasons for this; a combination of operator and machine error (this will be discussed in the following chapter), or CO_2 may have diffused out of scalp blood exposed to air during sample collection. In one case an erroneous pCO_2 reading (16 mm Hg) resulted in a similarly erroneous BDecf calculation (17 mmol/l) despite a pH of 7.27. This high BDecf result was given as one of two indications for LSCS (the other was slow progress - at 4cm dilatation). In 3 cases a mild respiratory acidemia (caused by a transient bradycardia related to a known precipitating event) led to a rotational forceps delivery for 'fetal distress' - the umbilical cord gases were normal in each case.

Sixteen cases (8% of the total, 6 CTG, 10 ST+CTG) had a low cord pH at delivery (artery <7.10 or vein <7.15) despite having a FBS performed at some stage during labour. Two of these were asphyxiated at birth. Contributing factors in these 16 cases were; delay in performing the initial FBS (n=2), delay between abnormal FBS and delivery (n=4), failure to repeat FBS despite deterioration in trace (n=3), failure to record FHR adequately in second stage despite previous abnormal trace (n=2), prolonged bradycardia during rotational forceps delivery (n=1), and rapid deterioration in pH between FBS and delivery (n=4).

Operative delivery for 'fetal distress'.

The proportion of 'fetal distress' deliveries in the CTG normal, intermediate and abnormal classifications has been given in tabular form (Chapter Three, Table 3.9) and is shown graphically below.

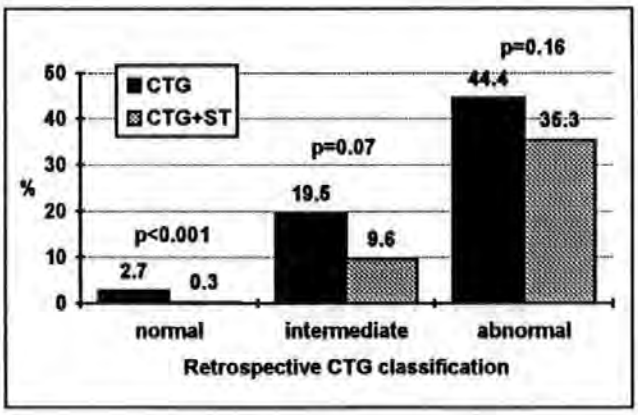


Figure 4.3 Percentage of CTG normal, intermediate and abnormal recordings in which an operative delivery for 'fetal distress' was performed.

43% of 'fetal distress' operative deliveries in the CTG arm were considered unnecessary compared to 5% in the ST+CTG arm. Further analysis revealed that 14 (18%) of abnormal traces in the CTG arm and eight (9.5%) of those in the ST+CTG arm should have had operative intervention or FBS for 'fetal distress' but did not (p=.19, OR 2.0 [0.74-5.74]). Although this group only totalled 1% and 0.6% of the total cases reviewed in each arm respectively, amongst their number were two cases of birth asphyxia from the CTG arm and one from the ST+CTG arm.

Only 43% (CTG) and 53% (ST+CTG) of the LSCS for 'fetal distress' were preceded by an FBS. Their details are shown below (Table 4.2).

Table 4.2 Details of cases who had an LSCS for 'fetal distress' without an FBS.

Relevant clinical details.	CTG n=17	ST+CTG n=7
Abnormal trace in early labour, FBS impossible	3	0
Intrapartum abruption	2	1
Cord prolapse	1	0
Prolonged bradycardia, no recovery	4	1
Temporary bradycardia, overhasty intervention	4	1
Abnormal trace with one normal FBS- later repeat FBS attempted but failed	1	2
No obvious reason why FBS not done	2	1

Many of these cases were explained by the clinical circumstances but some were clearly not. This occurred despite the trial protocol recommendations and the fact that FBS was a well established technique in the hospital long before the trial began.

Selection of cases for CTG monitoring.

The hospital has a policy of selective continuous CTG monitoring with an FSE in high risk cases. During the time of the randomised trial 6798 women of at least 34 weeks gestation went into labour and were monitored as shown in Figure 4.4.

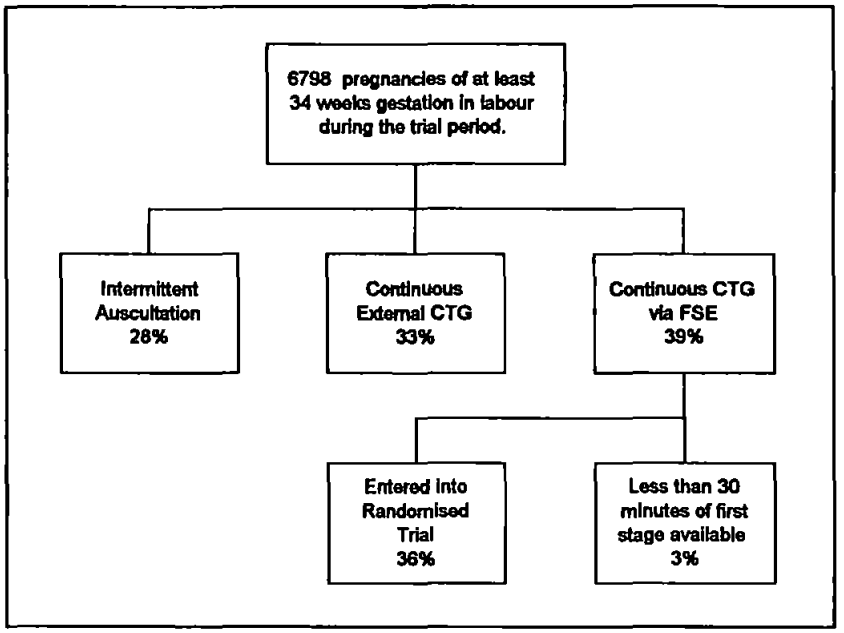


Figure 4.4 Proportion of labours monitored by different techniques during the randomised trial.

Birth asphyxia review.

The seven cases of birth asphyxia which occurred in randomised trial entries were detailed in Table 3.8 in the previous chapter. Asphyxia occurred in a further nine labours of at least 34 weeks gestation who were not entered into the trial. Details of these cases is given in Appendix Four. The distribution of birth asphyxia according to the method of intrapartum monitoring is shown in Table 4.3.

Obvious FHR changes (on intermittent auscultation or CTG) occurred in all but three cases; in two the FHR was not monitored at all for a period in the second stage and in the other (classified as intermediate on retrospective review) there was reduced variability in the first stage. It should be stressed, however, that in the remaining 13 cases the FHR changes were so astoundingly obvious that it is of some concern that they apparently went unnoticed or did not prompt earlier action. It was adjudged that appropriately timed action occurred in only one of these 13 cases, appropriate but significantly delayed action in six cases and no action at all in the remaining six.

Table 4.3 Distribution of birth asphyxia cases according to the method of intrapartum monitoring.

Birth asphyxia % of population	Intermittent auscultation 28%	Continuous external CTG 33%	Continuous CTG with FSE 39%
Severity; mild moderate severe (died)	 2 2 0	 1 0 4	 3 2 2
Total	4	5	7

The timing of the major FHR abnormalities detected on the retrospective review are shown in Table 4.4.

Table 4.4 Timing of FHR abnormalities in asphyxia cases.

Time of FHR abnormality and relevant events	Number of cases (total =16)	Outcome
Antenatal (includes 1 antenatal abruption)	4	-3 died, 1 spastic hemiplegia
First stage; cord prolapse abruption no obvious precipitating event	 1 1 2	 -fitted, normal follow-up -spastic quadriplegia -hypoglycaemia, then normal
Second stage possible vasa praevia nuchal cord no obvious relevant finding	 1 5 2	 -died -1 died, 2 spastic quadriplegia, 1 fitted then normal, 2 hypoglycaemia then normal. -hypoglycaemia then normal

The likely asphyxial insult occurred in the second stage in 50% of cases. Most of these babies had birth weights in excess of 3200g, compared to the low birth weights of those damaged in the antenatal period (birth weights 1993g and 3100g [36 weeks] and 2300g and 2880g [40 weeks]) and 3 of the 4 first stage cases (all around 2600g at term). The cord prolapse baby weighed 3850g.

The definition of 'birth asphyxia' used in the randomised trial did not require evidence of significant intrapartum hypoxia but clearly should have done as asphyxial damage occurred prior to the onset of labour in 25% of cases. It can be difficult to separate antepartum from intrapartum events, but where the distinction can be made readily (as in the 4 cases here), it should be.

Discussion.

The previous published randomised trials of CTG and intermittent auscultation (referenced in Chapter One) only assessed the effects of CTG monitoring as it was used in clinical practice in each unit. Only one group attempted to document the accuracy of interpretation and management (MacDonald et al, 1985), but this was only done in a random survey of 10% of trial entries. In the trial reported in this thesis the quality of data interpretation and management was reviewed in every case. Even so the review may not reflect everyday clinical practice as it is likely that the performance of the trial altered the way midwives and clinicians reacted to CTG changes. In addition, management protocols and twice weekly CTG teaching sessions were available where there had been none before, which should also have improved the use of the CTG.

It is also acknowledged that a retrospective review of this nature could not mimic the clinical situation; it was largely performed during daylight hours in a relatively stress free environment. Many factors which influence clinical decision making were unknown. For example, details specific to each patient, e.g. fetal growth retardation, maternal blood pressure, the effectiveness of maternal analgesia, how busy the unit as a whole was and what emergencies and other cases staff had to deal with at the time. As a result the review has not been a definitive audit of care but, nevertheless, has highlighted some important points about clinical practice in a large district general hospital which are likely to be representative of clinical practice in the UK.

Fetal blood sampling.

This review has revealed significant problems with the selection of patients for FBS, the timing of the initial FBS and subsequent repeat samples and the interpretation of results. Many of the problems highlighted here were described by Saling in 1967 in his review of intermittent auscultation plus FBS (Saling & Schneider, 1967). Three main factors contribute to these difficulties;

1. FBS is an **intermittent** variable which requires an extra **invasive** procedure. There are many practical problems associated with the technique, not least of which is the discomfort both clinician and mother can experience during the process. These problems undoubtedly contribute to its infrequent use in practice and highlight the need for simple additional variables which reflect fetal condition during labour.

2. **The decision to obtain an FBS is dependant upon interpretation of the CTG.** FBS and the CTG are not independent variables. If the level of CTG interpretation is sub-optimal, the value of FBS will be limited (as it was here). One possible solution to this

problem is to have very high FBS rates in the hope of ensuring that all acidotic fetuses are identified (van den Berg et al, 1987, Murphy et al, 1990). There is some evidence that higher rates of sampling are associated with higher mean cord arterial pH at delivery (Steer, 1987) but there is no evidence that an increased sampling rate will result in a reduction in birth asphyxia.

3. **Correct use of the information obtained at FBS requires an understanding of the events of labour and of the physiology of acid-base balance during labour.** There is plenty of scope for misinterpretation of FBS data (as illustrated here). Of particular concern was the tendency for clinicians to be reassured by one normal FBS result and, despite continued CTG abnormalities, fail to repeat the FBS at a later stage. This was a contributing factor in one asphyxia case during the study (Case 1699) and has subsequently occurred in at least one other asphyxia case since completion of the study. Much has been made of the high false positive rate of CTG changes and the fact that FBS can reduce unnecessary intervention (Steer, 1987). However, this should not be misinterpreted to mean that the CTG does not contain useful information, for clearly it does. The retrospective review of randomised trial recordings showed that there was a significant decrease in cord arterial pH and a rise in BDecf as the CTG became more abnormal (Table 3.10, Chapter Three). FBS should not replace the CTG, but should be used as an additional variable. A normal FBS does not mean abnormal CTG findings can be totally ignored. Labour is a dynamic process in which both the severity and the **duration** of hypoxic stress will affect how well and for how long any given fetus will be able to compensate for hypoxia. In the cases mentioned above this important point was not recognised and, instead, undue weight was placed on a single pH value, taken at a single point in time, with disastrous consequences. An increase in FBS rates without an improvement in knowledge of how the information should be used may not be as successful as proponents of this approach hope.

These findings have important implications for new technology; the use of extra, intermittent, time consuming, inconvenient and difficult techniques is unlikely to have a major impact, simply because they will not be used frequently enough in routine practice. ST waveform analysis has many advantages over FBS. It does not require extra invasive procedures and it provides continuous information. It is therefore more likely to influence decision making, as suggested by this study. However, the need for correct understanding and use of the available information is just as important for ST waveform analysis as it is for FBS.

Low risk/high risk classification.

You are more likely to die on the first day of your life
than on any other, except the last.

An unattributed truism.

The Plymouth policy of continuous internal CTG monitoring for high risk pregnancies is consistent with current recommendations (FIGO, 1987). However, the incidence of birth asphyxia in the supposedly low risk group monitored externally or by intermittent auscultation was 2.44/1000, not significantly lower than the 2.47/1000 in the high risk group monitored internally. It is likely that some cases in the low risk group were, in reality, high risk, but the opposite is also true. A large proportion of cases were only monitored internally because they requested epidural analgesia and had no other risk factors.

The whole concept of deciding intrapartum risk, and therefore the method of monitoring, on the basis of antenatal events cannot be supported. As early as 1973 it was obvious that intrapartum events were far more significant in predicting outcome than antenatal risk factors (Hobel et al, 1973). In a summary of five risk assessment papers Wilson & Schifrin (1980) found that patients with low antenatal risk contributed 58% of perinatal mortality and morbidity cases compared to the 42% contributed by high risk groups. In Murphy's review of birth asphyxia 26 of 64 cases (40%) were low risk and had not been monitored by CTG (Murphy et al, 1990). A case-controlled study of intrapartum stillbirths in Western Australia failed to identify any antenatal risk factors which predicted these deaths (Alessandri et al, 1992). The only factors which are consistently associated with perinatal morbidity and mortality are low birthweight for gestational age and the presence of meconium liquor (Low et al, 1978).

Continued use of this unsafe distinction has important implications for the application of monitoring techniques, particularly the introduction of new techniques. Limitation of these techniques to 'high' risk cases will mean that a significant proportion of cases with poor outcome will never have the possible benefit of any improvements afforded by new technology.

The importance of the second stage of labour has also been highlighted by this review. Contraction frequency and strength increases in the second stage so that the time available for placental gas exchange is reduced and fetal hypoxaemia increases. This is also the time when fetal reserves may have been reduced by the events of the first stage. Obstruction of flow in a nuchal (or otherwise coiled) cord or in a very twisted cord (Collins & De Angelis, 1993) is also most likely in the second stage. This is the time that healthy babies are most at risk during labour, and therefore is the time when intrapartum monitoring is most important. The value of any method of intrapartum monitoring which is not practicable for use in the

second stage may be limited. Loss of signal or failure to monitor in the second stage were contributing factors in many asphyxia cases monitored by intermittent auscultation and external CTG. The deterioration of ECG waveform signal quality recorded by the STAN monitor in the second stage is therefore also of some concern.

CTG (mis)interpretation.

Previous studies have shown that the combination of CTG plus FBS resulted in a reduction in operative intervention compared to CTG used alone (Haverkamp et al, 1979, MacDonald et al, 1985). However, in this study, even with this combination, a significant number of unnecessary operative deliveries still occurred.

It is of more significance to note that the majority of birth asphyxia cases had what could be described as 'barn door' changes yet did not receive appropriate or timely management. Murphy et al (1990) found similar results in their review of birth asphyxia cases in Oxford. A recent audit of the labours of women (>37 weeks gestation, birth weight >2500g) whose babies required admission to SCBU in Manchester found the most common factor associated with avoidable perinatal morbidity was CTG misinterpretation (Hamilton & Maresh, 1992).

The most significant conclusion of this review is that the major problem with CTG monitoring is not that the CTG does not contain useful information, but that the available information is not interpreted correctly. Why is this?

The key to this problem lies in the use of the terms 'monitor' and 'monitoring' which imply a degree of automatic surveillance. In fact this is not the case. The surveillance or 'monitoring' is performed by the clinician or midwife who interprets the output of the machines which merely record FHR and uterine contractions.

In this country, most monitoring is performed by midwives, Senior House Officers and Registrars, usually in that order. It is salutary to note the level of training each receives. In Plymouth, in accordance with the national curriculum, midwives receive two hours teaching on CTG interpretation during their 18 months of training. One hour is provided by a midwife teacher who is unlikely to have worked on a labour ward for a number of years, and the other session is usually given by one of the registrars. Next in the line of command are the Senior House Officers (SHOs). In Plymouth they usually receive a 20 minute CTG session in the first week of their attachment but then are expected to receive guidance from midwives and Registrars. Registrars were once SHOs and their level of expertise varies enormously. This is in contrast to the Swedish situation, where consultants are always present on the labour ward during the day and frequently sleep in during the night (Lilja, personal communication). A comparison of Swedish and English perinatal mortality rates

made by Alberman in 1980 is shown in Table 4.5. Whilst the mortality rates for birthweights <2500g are comparable, there is a clear excess of deaths in larger birthweight babies in England.

Table 4.5 Perinatal deaths observed in England in 1978 compared with the expected deaths if Swedish birth weight-specific rates were applied (modified from Alberman, 1980).

Birthweight	Observed	Expected
<2500g	5984	5983.3
>2500g	3223	1905.9

It should be noted, in passing, that the neonatal paediatric medical staffing situation is very similar to obstetrics; i.e. the least experienced member of the team is the first called to an emergency. It is significant that Alberman's recommendations for improvement included the need for both on-site trained obstetric cover and on-site trained personnel skilled in neonatal resuscitation.

The Royal College of Obstetricians have recently recommended that consultants should cover labour ward on a regular basis and should make regular visits to the Labour Ward when on call to enable them to make a more formal contribution to the management of patients and the training of junior staff (RCOG, 1991). However, they also note that "in many units current staffing will not allow this at present". If it is difficult to provide trained (as opposed to training) obstetric cover during working hours in most units, then the ideal of 24 hour trained cover must be even further away.

The medicolegal implications of these conclusions are significant. A considerable proportion of litigation cases may be entirely justified - over 60% of 112 active litigation cases reviewed by Symonds were indefensible (Symonds, 1993). As has recently been pointed out by a High Court Judge, obstetricians cannot complain about the amount of litigation they face when labour wards continue to be staffed with inexperienced and inadequately trained personnel (Kennedy, 1993). As well as advocating changes to the present adversarial legal system, obstetricians need to do more to rectify contributory problems in their own discipline.

The implications of this conclusion for new methods of intrapartum fetal assessment are also important. Possible solutions to this problem are discussed in Chapter Six.

Chapter Five

The assessment of acid-base status at birth.

Introduction.

An assessment of acid-base status at birth can be made by analysis of umbilical cord arterial and venous blood. The cord vein carries oxygenated blood to the fetus whilst the two smaller arteries carry blood from the fetus to the placenta. Cord arterial blood therefore normally reflects fetal acid-base balance while venous blood reflect a combination of maternal acid-base status and placental function. The important defence mechanisms which enable the fetus to compensate for periods of reduced oxygen supply were reviewed in the introductory chapter. If cardiovascular and behavioural adjustments fail to maintain oxygen delivery to central organs anaerobic metabolism of glycogen and glucose to lactic acid occurs in order to provide the energy to maintain cellular and organ function. The presence of a metabolic acidemia in cord arterial blood is therefore indicative that significant oxygen deficiency has occurred and should provide important information about the effects of labour on the fetus. Despite the relative ease with which this information may be obtained, there is much debate about the value of umbilical cord blood sampling. A summary of the benefits and problems follows.

Benefits of cord acid-base assessment.

1. It provides an objective measure of neonatal condition at delivery and enables a group of fetuses at risk of neonatal morbidity to be identified by the presence of a metabolic acidemia (Low, 1988, Sykes et al, 1982, 1983, Goldaber & Gilstrap, 1993).

2. The percentage of cases born with a low pH or a metabolic acidemia can be used as an audit of the quality of intrapartum care (Eskes et al, 1983, Yudkin et al, 1987, Richards & Johnson, 1993).

3. Knowledge of acid-base status at delivery encourages a physiological approach to CTG interpretation and is useful for training and education and in litigation cases (Thorp et al, 1989, Gregg & Weiner, 1993, Goldaber & Gilstrap, 1993).

Problems with cord acid-base assessment.

1. There is a lack of consensus as to what levels of pH and/or BD constitute acidemia and metabolic acidemia.

2. There is a lack of correlation with measures of immediate neonatal outcome (Apgar scores, resuscitation, neonatal morbidity) in some studies (Dijxhoorn et al, 1985, Ruth & Raivio, 1988, Winkler et al, 1991) but not in others (Gilstrap et al, 1989, Low et al, 1988, 1990, Goldaber et al, 1991).

3. There is a lack of correlation with long-term neurological outcome (Low et al, 1983, Lauener et al, 1983, Dennis et al, 1989, Fee et al, 1990).

The key question is what levels of pH and BD indicate that significant hypoxia has occurred? The levels of cord artery pH used to define acidemia in a selection of studies in the literature are summarised in Table 5.1. In view of the wide range, it is not surprising that the value of the procedure remains a topic for debate.

Table 5.1 Levels of cord artery pH used to define acidemia in a survey of the literature.

Level of cord arterial pH chosen to define acidemia	Justification	References
< 7.20	?	Suidan & Young, 1985, Winkler et al, 1985, Page et al, 1986
<7.16	<2 SD below mean	Ruth & Raivio, 1988
<7.15	?	Lauener et al, 1983, Vintzileos et al, 1992
<7.12	<1 SD below mean	Sykes et al, 1982, 1983
< 7.10	? <2 SD below mean	Huisjes & Aarnoudse, 1979 Silverman et al, 1985, Thorp et al, 1989
< 7.05	relation to neonatal morbidity	Goldaber et al, 1991

Although not stated, the pH value of 7.20 used in many studies probably comes from the work of Bretcher and Saling, (1967). They derived the 'normal' range of fetal scalp pH during labour from repeated FBS in 306 labours which resulted in the birth of healthy, vigorous babies. They described a pH of less than 7.20 as 'acidotic' as this value was less than two standard deviations below the mean. Two interesting aspects of their study should be noted. Firstly, all fetuses with an FBS pH of less than 7.20 were excluded from the study and secondly, a pH of 7.20 was <2 SD below the mean **during labour** but not at delivery. The mean cord arterial pH at delivery was 7.27; two SD below the mean was 7.12. There would appear to be little justification for using a pH value of 7.20 to define cord arterial acidemia at delivery.

In some studies the mean of a highly selected subgroup of the population was used to define the normal range for cord pH at delivery (Thorp et al, 1989, Yeomans et al, 1985, Young 1989), whilst others used non-selected population data (Eskes et al, 1983, Low, 1988, Sykes et al, 1982, 1983, Yudkin et al, 1987).

The majority of workers define acidemia by pH only and do not distinguish between respiratory and metabolic components. A respiratory acidemia frequently occurs during

labour, particularly during the second stage, as a result of cord compression which can cause CO_2 accumulation without impairing O_2 delivery to vital organs. A metabolic acidemia, however, is much more significant as it indicates that O_2 delivery to the fetus has been insufficient for aerobic metabolism. The metabolic component of an acidemia can be assessed by examining the base deficit (BD), but relatively few studies do so. Only Sykes et al (1982) and Ruth & Raivio (1988) used both pH and BD to define metabolic acidemia whilst Low's group in Canada use another measure, the Buffer Base, calculated from a Buffer Base Chart (Low et al, 1974).

The BD value most commonly used is that calculated from the blood compartment of the whole of the extracellular fluid. This is the value calculated by most blood gas analysers and is suitable for use in adults but not in the perinatal period. The fetus and neonate have lower plasma protein concentrations and a relatively larger extravascular fluid compartment than adults so relatively more of their buffering capacity is outside the blood compartment. It is, therefore, more correct in the perinatal period to calculate the BD of the whole extracellular fluid (BDecf) rather than just that from the blood compartment (BDblood) (Siggaard-Andersen, 1976, Rooth, 1988). This is particularly important when pCO_2 levels are high, as calculations based on the blood compartment alone will result in erroneously high levels of BD and will thus overestimate the metabolic component of any acidemia (Rosén & Murphy, 1991).

Most studies report umbilical artery results but some have advocated using venous values because the artery can be difficult to sample (Huisjes & Aarnoudse et al, 1979). Occasionally, no vessel is specified (Halligan et al, 1992). Both artery and vein values are required to identify sampling errors (Silverman et al, 1985) but only two studies have specified a minimum acceptable venous-arterial pH difference (Huisjes & Aarnoudse, 1979, Eskes et al, 1983). In many studies where blood was only taken from the umbilical artery, it would have been impossible to identify erroneous results (Lauener et al, 1983, Page et al, 1986, Steer et al, 1989, Maclachlan et al, 1992).

In an attempt to understand these problems, a detailed analysis of the blood gas data from the randomised trial was performed. Data from both arms of the trial have been combined. The aims of the analysis were **firstly,** to address the specific practical problems related to umbilical cord sampling and to assess the reliability of the results, **secondly,** to determine the normal ranges for pH, pCO_2 and BDecf, **thirdly,** to investigate the relationships between BDecf and BDblood, BDecf and pH, and arterial and venous values and **finally,** to examine the relationships between Apgar scores and neonatal encephalopathy and blood gas values.

Methods.

In the first 400 randomised trial entries cord artery and vein cord blood samples were collected from selected patients (FBS during labour or any operative delivery) by research personnel. All of the next 2000 entries had samples taken by midwives and nursing auxiliaries.

A segment of cord (minimum recommended length 10 cm) was double clamped immediately after delivery. Extra cord clamps were included in all delivery packs to facilitate this. Cord segments were separated from the placenta, placed into a kidney dish and passed out of the delivery room for sampling. In this way the placenta did not have to be delivered before sampling so the third stage could continue without further interference. Blood was taken first from the artery and then from the vein using preheparinised syringes. Sampling within the first 10 minutes was recommended. If this was impossible the cord was placed on an ice pack until the samples could be withdrawn (blood does not clot while still inside the cord). Analysis was usually achieved within 30 minutes of delivery. Prior to the study serial analysis of cord specimens over a 60 minute period confirmed that no significant changes in cord blood gas parameters occurred during this time. Syringes were preheparinised on-site by adding one drop of liquid heparin (1:5000 units) from a 1ml tuberculin syringe into a 2ml plastic syringe and moving the plunger up and down before capping with a 21 gauge needle. All syringes were prepared by research personnel who were careful not to use more than one drop of heparin as changes in pCO_2 and pH can occur if heparin makes up more than 10% of the volume of any blood gas sample (Duerbeck et al, 1992). Results from non-heparinised and heparinised syringes were compared before the study and no difference in results was found.

A Corning 178 (CIBA Corning UK, Ltd) was used throughout the study. The machine is self calibrating (one point calibrations every 30 minutes and two point calibrations every two hours). During analysis, a reading is taken from each electrode (pH, pO_2 and pCO_2) twice a second for a maximum of 2½ minutes, or until 30 consecutive stable readings have been obtained. If stable readings cannot be obtained, two asterisks (**) are printed beside the value to indicate an unreliable result (CIBA Corning Diagnostics Corporation, 1981). The analyser was serviced daily by Medical Physics Department engineers. The sampling error was checked by analysing 110 pairs of consecutively introduced samples. The standard deviation of errors was the same as that reported in the Corning Manual; pH 0.002 units, pCO_2 0.55 mmHg, pO_2 0.4 mmHg (See Appendix 5).

The Corning Analyser provided BDblood calculations. During the trial BDecf was calculated manually from pH and pCO_2 using a Siggaard-Andersen Acid Base Chart

(Siggaard-Andersen, 1971) but once the results were entered into a database, a formula was used to automatically calculate BDecf from pH and pCO_2 (see Appendix 5).

The reliability of the results was checked by recording errors identified by the Blood Gas Analyser (BGA) and examining frequency plots of arteriovenous (A-V) differences. Once erroneous results had been excluded, histograms of the data were drawn and the normal range for pH, pCO_2, BDecf and BDblood for each vessel was determined. Both methods for BD calculation were compared and the differences assessed. The relationship between arterial pH and BDecf and arterial and venous pH and BDecf values were examined in various graphical presentations of the data. The relationship between arterial pH, pCO_2, BDecf and the A-V BDecf differences for one and five minute Apgar scores were determined. Finally the cord gas data for all cases of neonatal encephalopathy which occurred in trial entries were reviewed.

Results.

Reliability of cord blood results.

Errors identified by the BGA. Cord blood gas results were available in 2104 trial entries. A single vessel only was sampled in 65 of 2104 cases (3.1%). In another 28 pairs (1.3%) of results a reliable pH was only obtained from one vessel. This left 2011 paired results with a reliable pH in each sample. The lowest pH was always assumed to have come from the artery. Unreliable (**) pCO_2 readings were obtained in 18 pairs (0.9%); 17 from the artery and one from the vein (this was actually a printer error). Unreliable pO_2 results occurred in 75 pairs (3.7%); 47 in the artery, 15 in the vein and 13 in both.

A-V differences. In order to further identify erroneous results the A-V differences were examined. Figures 5.1-3 show the frequency histograms for venous-arterial pH and pO_2 differences, and the arterio-venous pCO_2 difference.

There were a number of paired samples in which the A-V differences were very small, absent or (for pCO_2 and pO_2) opposite to the expected values (i.e. arterial pCO_2 lower than venous pCO_2, arterial pO_2 higher than venous pO_2). It was difficult to provide a physiological explanation for these results, and it was most likely that the samples were either from the same vessel or that an unmarked error in analysis had occurred.

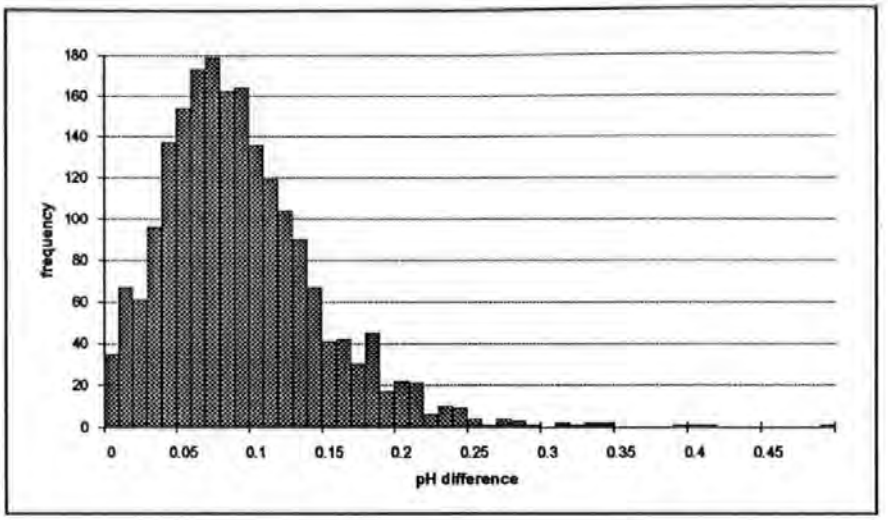


Figure 5.1 A-V pH differences, n=2011.

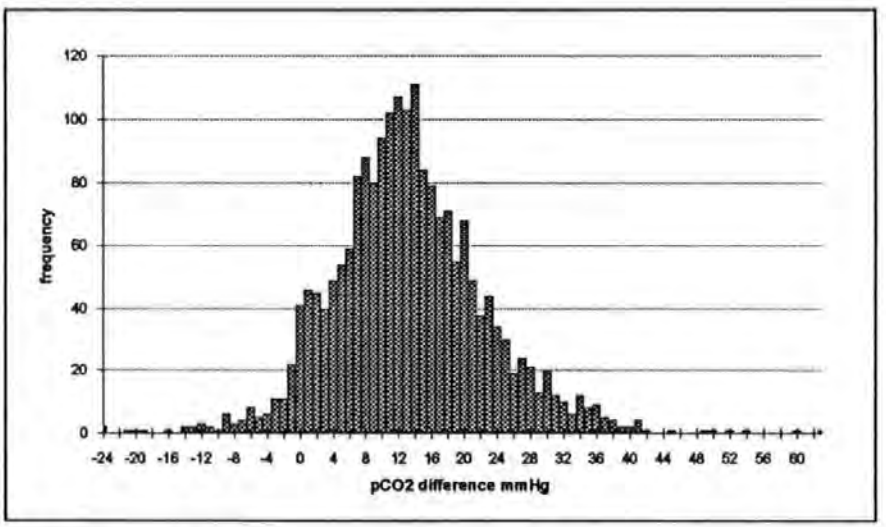


Figure 5.2 A-V pCO_2 differences, n=1993.

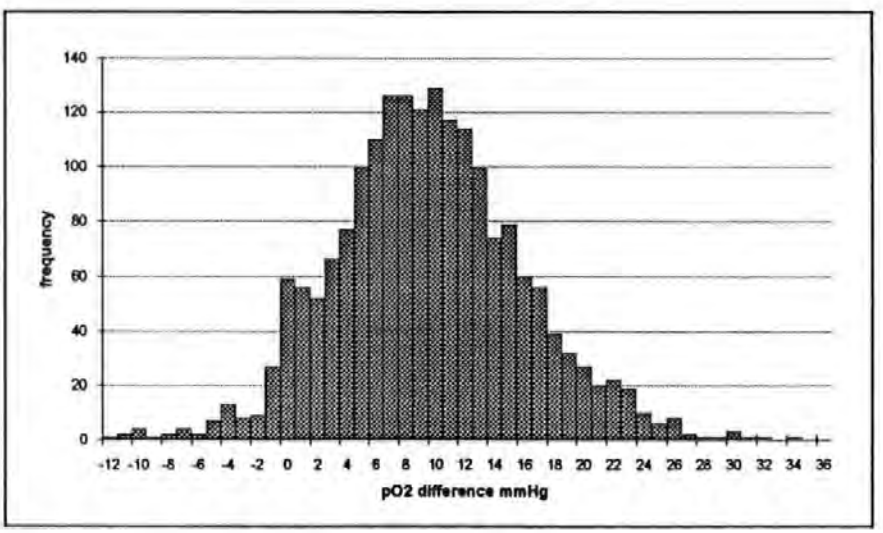


Figure 5.3 A-V pO_2 differences, n=1936.

Closer examination of Figures 1.1-3 revealed that the frequency distributions were bimodal; as smaller A-V differences were approached, each frequency distribution rose to a second modal point around or just above an A-V difference of zero. There was no obvious statistical test to separate out real from erroneous results (D. Wright, Principal Lecturer, Department of Mathematics & Statistics, University of Plymouth, personal communication). As a result, the minimum allowable AV difference was chosen from the nadir between the two modal points. The value obtained for the pH A-V difference was 0.02, for the pCO_2 difference 3.5 mmHg and for the pO_2 difference 2 mmHg.

Paired results from the same vessel would have similar pH, pCO_2 and pO_2 readings so all three differences could be examined when attempting to identify results from the same vessel. However, the accuracy of measurement of these variables was not comparable. pH and pCO_2 measures were most reliable with only 0.8% and 0.5% unreliable results (**) respectively. In comparison 2.3% of all pO_2 results were unreliable and a further 47 (1.1%) had pO_2 values > 50 mmHg which were clearly erroneous. In view of these findings, only pH and pCO_2 A-V differences were used to identify results from the same vessel.

Of the total 2011 paired samples, 101 (5%) had an A-V pH difference of <0.02, of these 91 (90%) had an A-V pCO_2 difference of <3.5 mmHg and 6 (6%) had an A-V pO_2 difference <2 mmHg. Three of the 4 remaining cases had low A-V pCO_2 differences (3.5, 4.0, and 4.3 mmHg), and the final case had a pCO_2 difference of 10.5 mmHg but a pH difference of 0.

189 cases (9.3%) had a pH difference of ≥0.02 but a pCO_2 difference of <3.5 mmHg; of these, 113 (60%) also had a pO_2 difference of <2 mmHg and 16 (8%) had very low arterial pCO_2 (values <35 mmHg). The majority of pH values from these 189 cases were probably reliable but, in order to examine pH and BD values and their relationships in both the artery and vein, all paired samples which did not meet both the pH and pCO_2 difference criteria were excluded from further analysis. This left 1719 pairs of results with an A-V pH difference ≥0.02 and an A-V pCO_2 difference ≥3.5 (and excludes 2 pairs with no venous pCO_2 result due to printer errors). However, on a final examination of the data, 3 cases had venous pCO_2 values which were very low and gave rise to very large venous BDecf values so were excluded from further analysis. A summary of the exclusions made is shown in Figure 5.4.

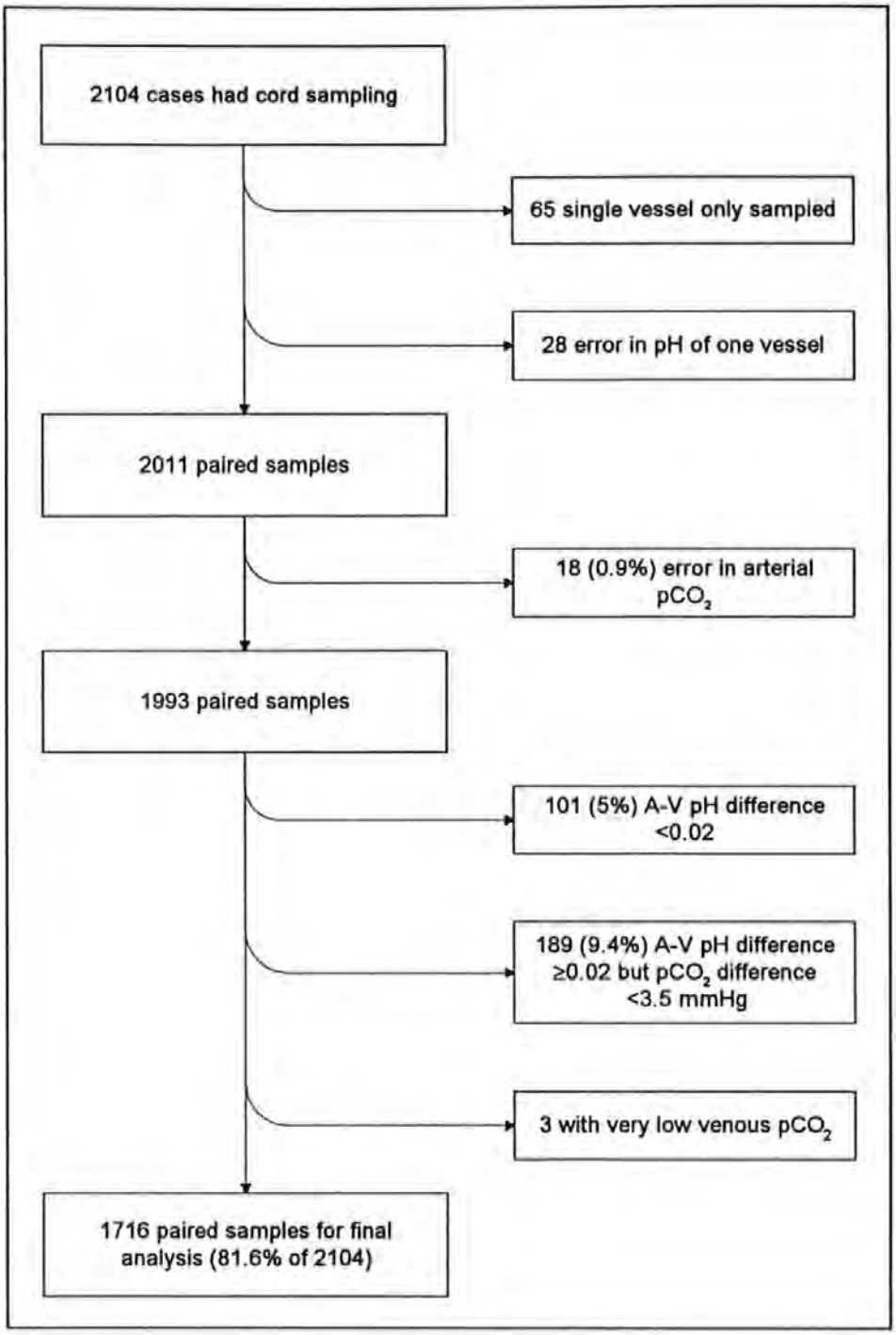


Figure 5.4 A summary of the exclusions made to identify reliable paired artery and vein cord data.

pCO_2 errors. Most of the samples rejected on the basis of a low A-V pCO_2 difference had unusually low arterial pCO_2 values. Why was this? The answer lay in the BGA. The 178 Analyser does not have automated sampling from either syringe or capillary. Syringe samples had to be injected by the operator and as a result two errors occurred. Firstly, air bubbles formed if the sample was injected too rapidly and produced an unreliable (**) result. The second error occurred as a result of back flow of blood once the syringe was removed from the injection port. If insufficient blood had been injected, the pCO_2 electrode (the last of 3 electrodes in series - pH, pO_2 and pCO_2) was no longer covered

with blood. As long as there were no gas bubbles in the fluid over the electrode, a stable reading for pCO_2 was obtained which was therefore not marked as unreliable by the analyser. However, the pCO_2 result obtained was invariably low (20 to 35 mmHg) and resulted in a falsely elevated BDecf value. CIBA Corning report that this problem has been obviated by the introduction of automatic sample aspiration in later models of their BGAs.

Identification of 'normal' ranges for pH, pCO_2 and BD.

The frequency distributions for pH, pCO_2, BDecf are shown in Figures 5.5-7.

The frequency distributions are markedly skewed and therefore any statistical description of the results should use the median and centile values. This is important because use of the mean and standard deviation (SD) is not only statistically incorrect but will also result in an underestimate of the lower limit of 'normal' for pH and an overestimate for the upper limit of 'normal'. For example, the mean arterial pH for the data shown in Figure 5.5 is 7.24, 2 SD below the mean is 7.08. However, the median pH is 7.26 and the lower 2.5th centile pH is 7.04. The same will apply to the pO_2 'normal range' and the reverse to pCO_2.

The cumulative frequency distributions are shown in Figures 5.8-10. The 'normal' range as defined by the median and 2.5th to 97.5th centiles is shown in Table 5.2. The results for BDecf and BD blood are given for comparison.

Table 5.2 The median and 'normal' range (2.5th to 97.5th centiles) for cord artery and vein pH, pCO_2 and BD.

	artery, n=1716 median & (2.5th -97.5th centiles)	vein, n=1716 median & (2.5th -97.5th centiles)
pH	7.26 (7.04-7.38)	7.35 (7.16-7.47)
pCO_2 (mmHg)	55.0 (37-81)	40.0 (27-59)
BDecf (mmol/l)	2.3 (-2.8-9.4)	2.9 (-1.4-8.8)
BDblood (mmol/l)	3.7 (-1.7-12.4)	2.9 (-1.5-9.6)

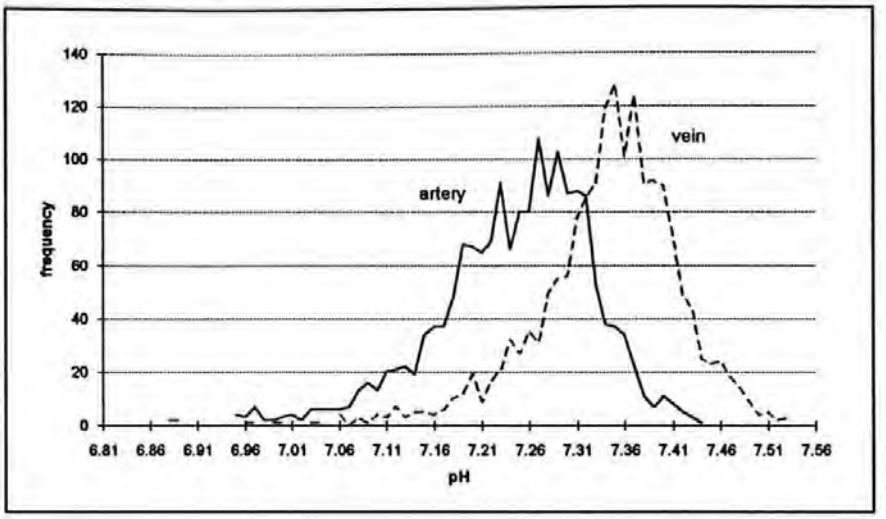


Figure 5.5 Frequency distribution of cord artery and vein pH, n=1716.

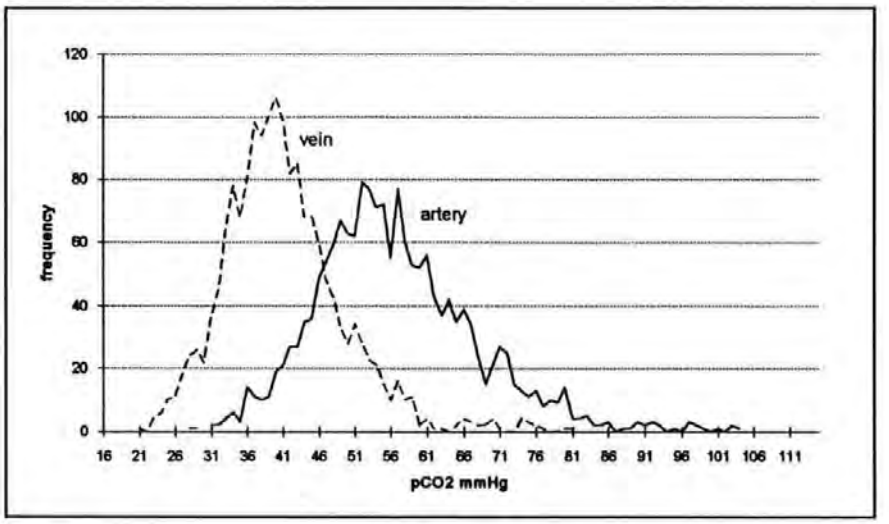


Figure 5.6 Frequency distribution of cord artery and vein pCO_2, n=1716.

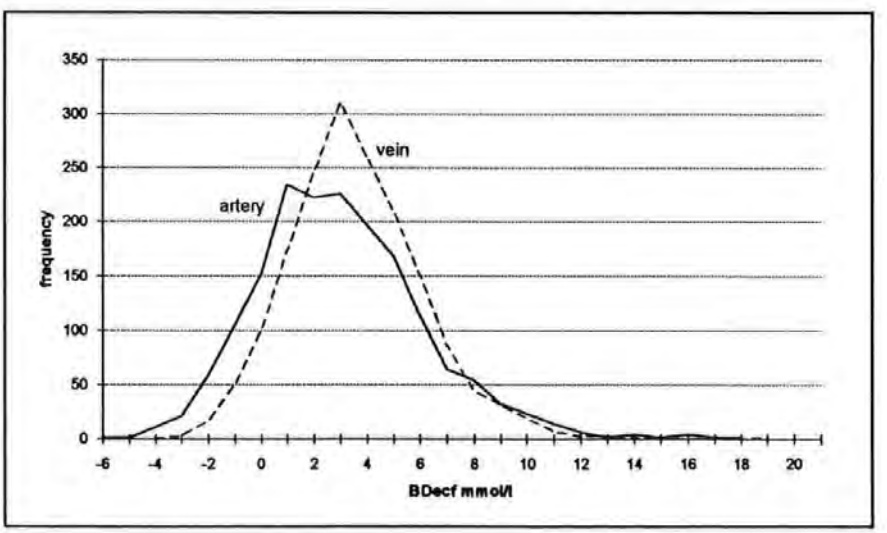


Figure 5.7 Frequency distribution of cord artery and vein BDecf, n=1716.

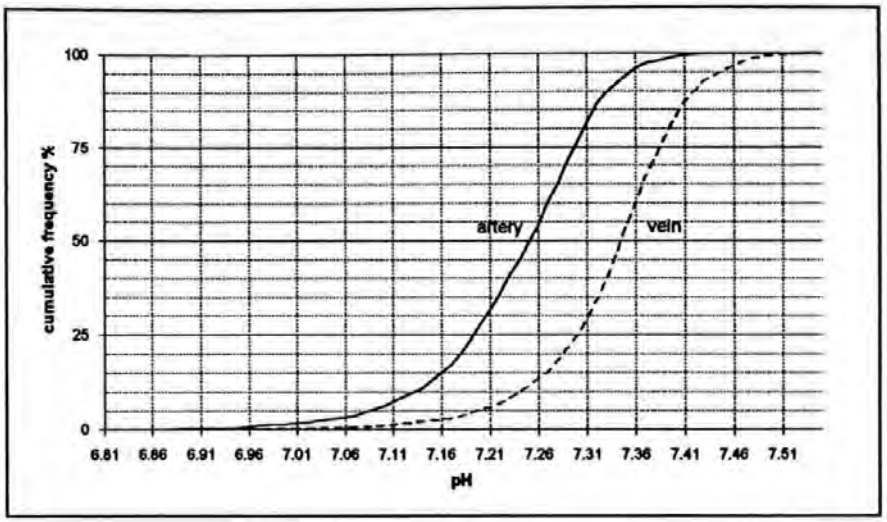


Figure 5.8 Cumulative frequency of cord artery and vein pH, n=1716.

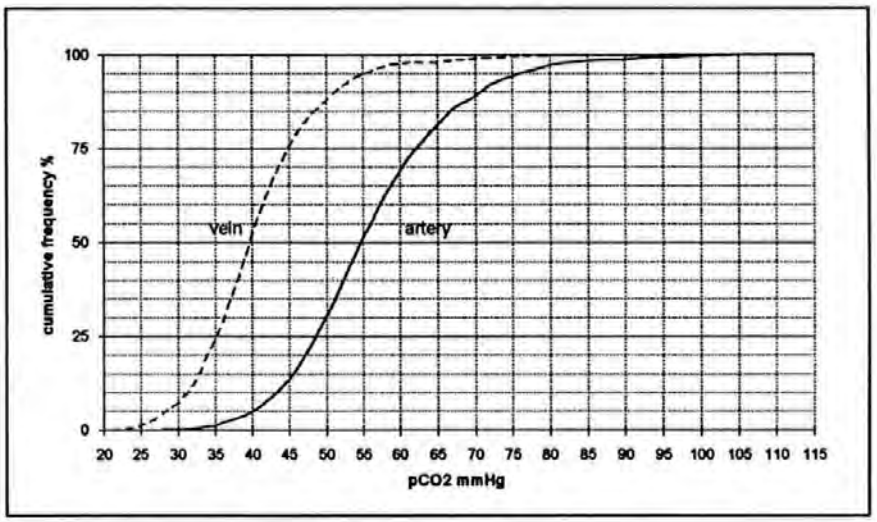


Figure 5.9 Cumulative frequency of cord artery and vein pCO_2, n=1716.

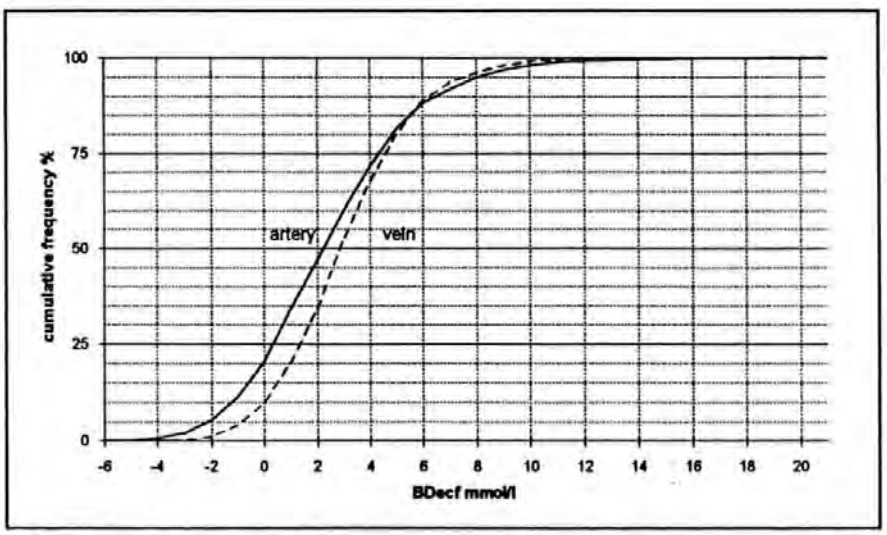


Figure 5.10 Cumulative frequency of cord artery and vein BDecf, n=1716.

The relationship between BDecf and BDblood.

Figure 5.11 shows the frequency distribution for BDecf and BDblood in both artery and vein.

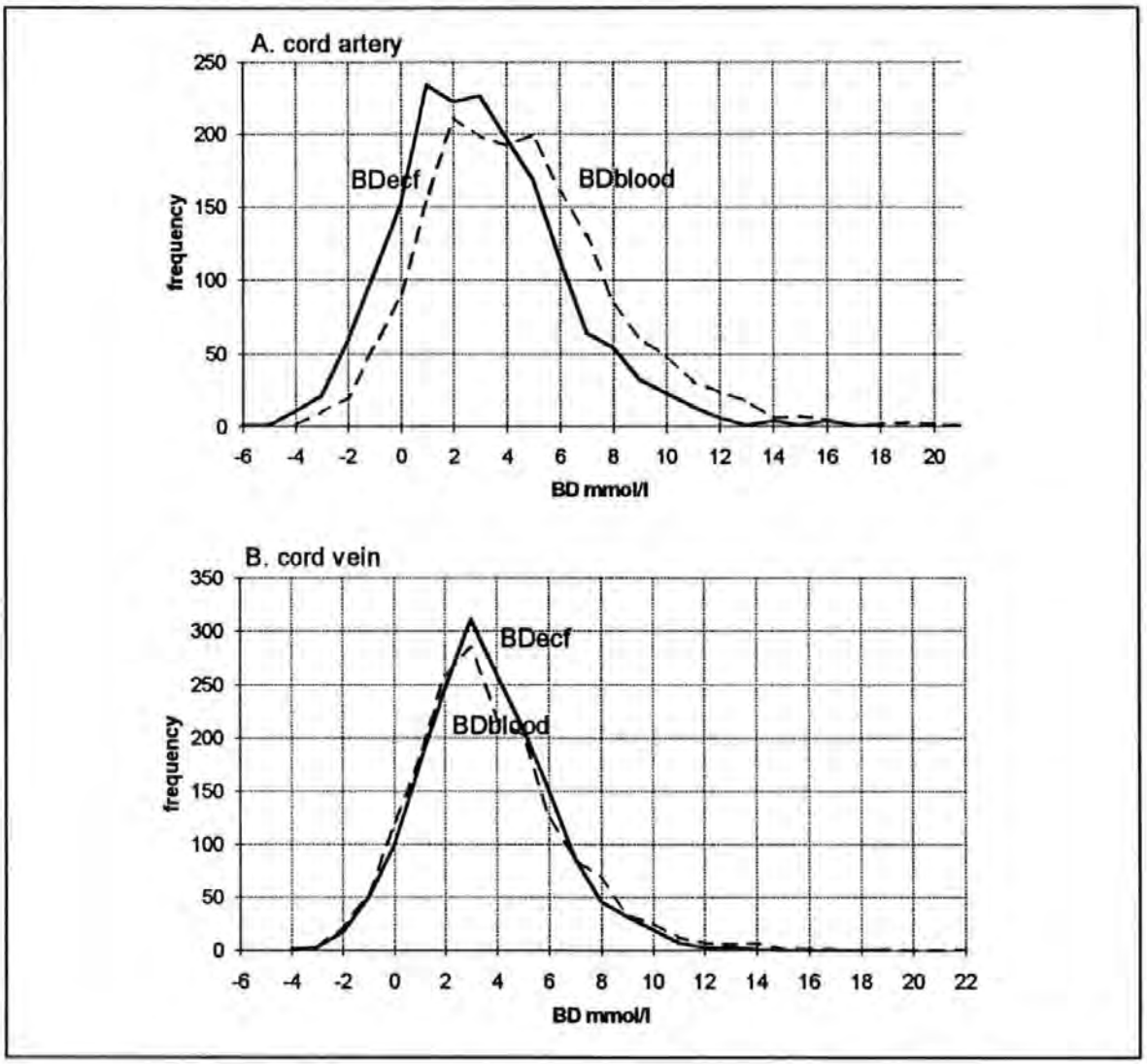


Figure 5.11 The relationship between BDecf and BDblood for A. cord artery and B. cord vein. n=1716.

The BDecf and BDblood values were very similar in the vein but different in the artery. Why was this, when the only difference between the two BD calculations was the concentration of haemoglobin (Hb) used in the formulae (see Appendix 5)? In an attempt to explain this the relationship between BD and pH at different pCO_2 levels was examined graphically (Figure 5.12). The BD values were calculated from the formulae given in Appendix 5.

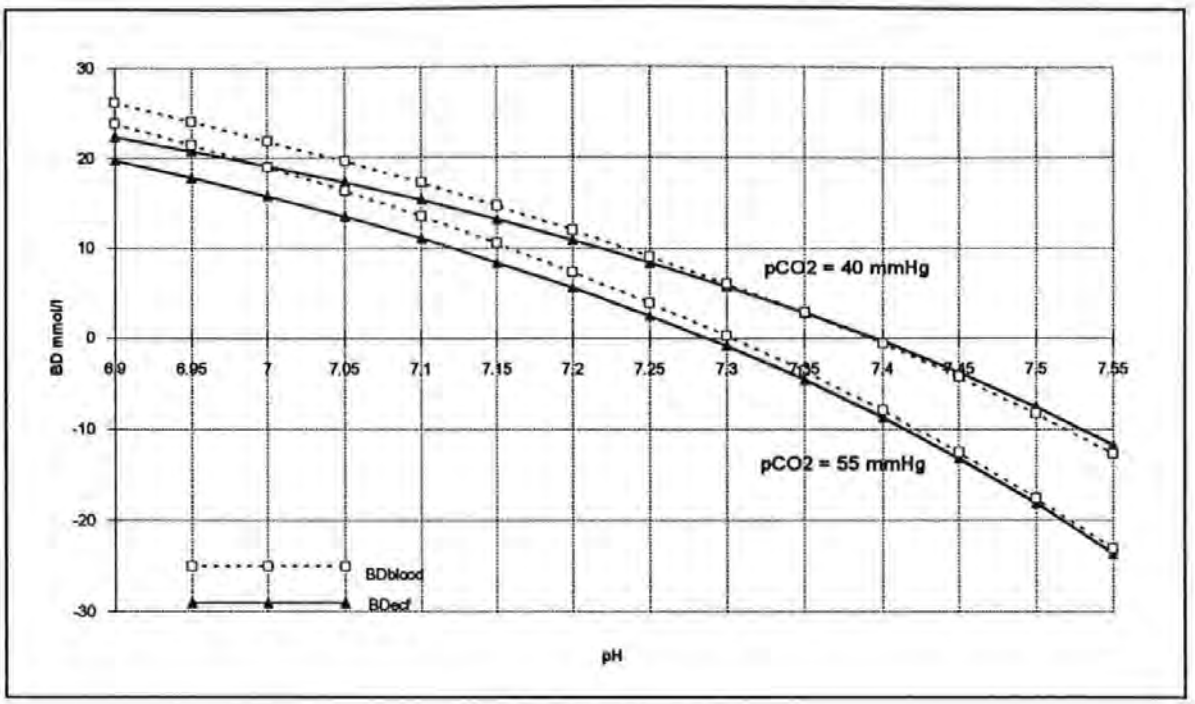


Figure 5.12 Comparison of BDecf and BDblood values for two different pCO_2 levels.

There was little difference between the BDecf and BDblood values at a pCO_2 of 40 mmHg (median venous pH) over the range of pH values commonly seen in the vein (7.25 -7.50). However at a pCO_2 of 55 mmHg (median arterial pH) the BDblood was higher than the BDecf over the range of pH values commonly seen in the artery (pH 7.10-7.30). Because BDblood is calculated from just the blood compartment, as pCO_2 rises, BDblood increases more than BDecf which is calculated from the whole extracellular fluid volume. This can be explained further in the following figures (Figures 5.13 & 5.14).

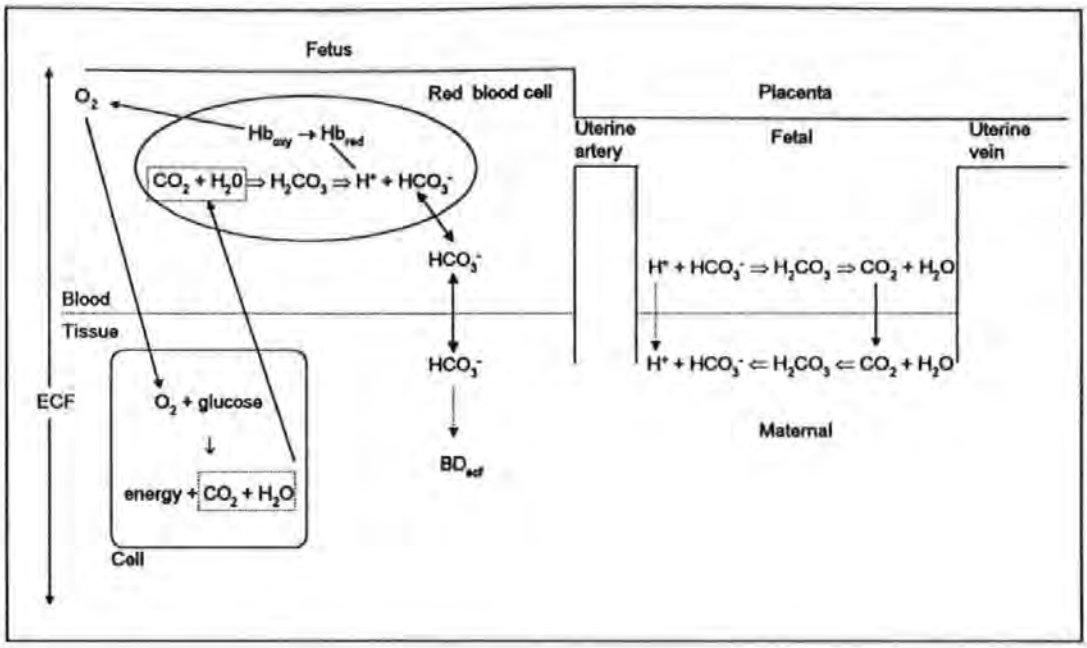


Figure 5.13 Normoxia. Glucose is metabolised aerobically to produce energy and carbon dioxide and water. This produces a large amount of carbonic acid (H_2CO_3) which must be excreted. The H^+ is buffered by reduced haemoglobin in red blood cells and is carried to the placenta in the umbilical arteries. In the placenta, CO_2 rapidly diffuses into maternal blood (whereas the transport of H^+ ions is much slower). Bicarbonate (HCO_3^-) is distributed throughout the extracellular fluid compartment and largely determines the base deficit of the extracellular fluid. Modified from Westgate & Rosén, 1993.

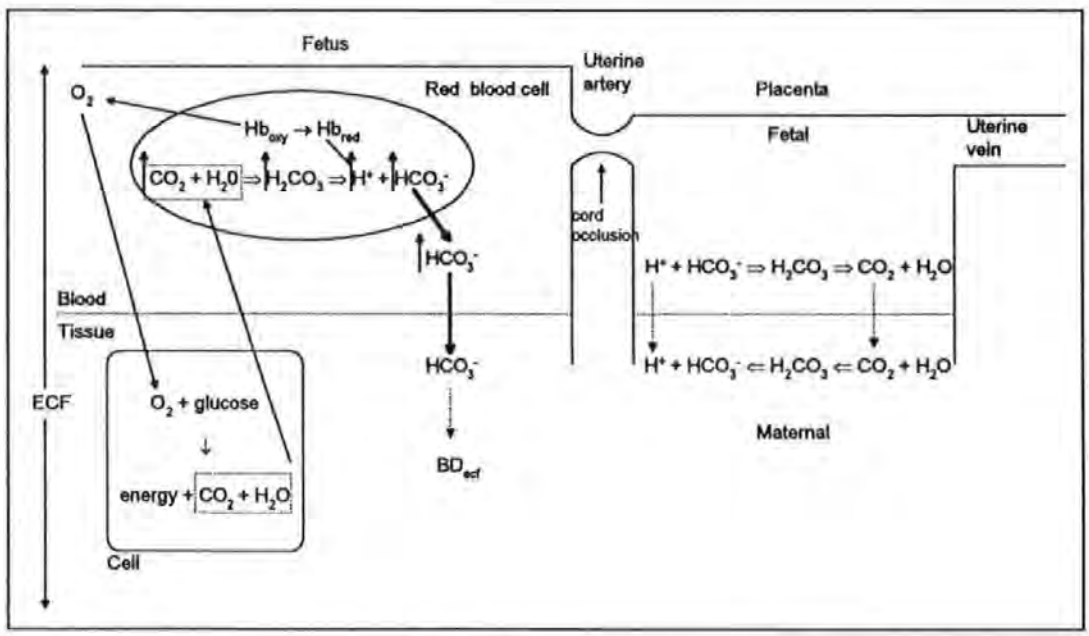


Figure 5.14 Respiratory acidemia. In this example cord occlusion has reduced the amount of CO_2 returning to the placenta resulting in an increase in blood CO_2 levels. This in turn increases H_2CO_3 concentration and results in more HCO_3^- leaving the red blood cells to enter the blood compartment. HCO_3^- then leaves the blood compartment to equilibrate with the interstitial fluid. There is a relative loss of HCO_3^- from the blood compartment (thus BDblood will rise) but no change in HCO_3^- or buffering capacity in the whole extracellular fluid compartment (thus BDecf remains unchanged). Modified from Westgate & Rosén, 1993.

The relationship between pH and BDecf.

In order to examine what level of arterial pH was associated with a significant elevation in BDecf, the relationship between the two was examined in the following scatter diagram.

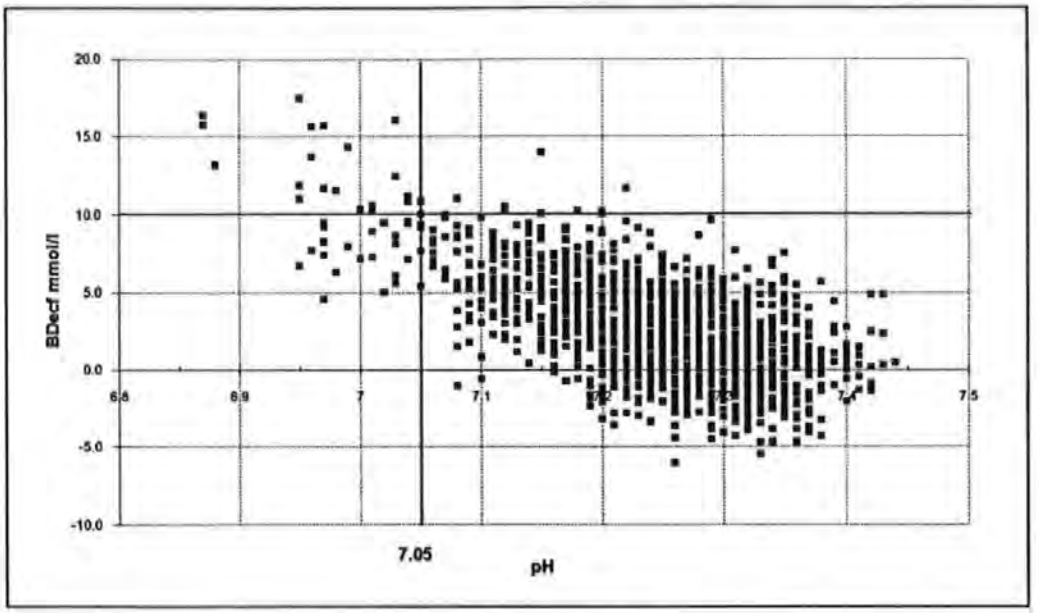


Figure 5.15 Scatter diagram of cord artery pH and BDecf (mmol/l), n = 1716.

The majority of results with a BDecf >10 mmol/l had a pH < 7.05 but not exclusively so. Nine values had an arterial pH well into the normal range but had high BDecf. Details of these cases are shown in the following Table.

Table 5.3 Blood gas values for cases with high pH and high BDecf divided according to size of A-V difference. (na = not available).

artery				vein			
pH	**pCO_2** mmHg	**pO_2** mmHg	**BDecf** mmol/l	**pH**	**pCO_2** mmHg	**pO_2** mmHg	**BDecf** mmol/l
large A-V BDecf difference (>3.5)							
7.12	54.5	19.1	10.2	7.33	47.3	23.3	0.6
7.12	53.4	na	10.5	7.31	39.6	31.8	5.4
7.15	37.5	28.6	14.0	7.44	26.5	34.9	5.2
7.18	44.8	22.0	10.2	7.32	36.4	25.8	6.3
7.20	42.4	na	10.1	7.32	34.4	24.7	7.3
7.20	42.0	30.0	10.2	7.37	33.0	42.0	5.3
7.20	35.3	15.5	11.7	7.42	30.8	23.9	3.7
small A-V BDecf difference (<1.5)							
7.08	59.0	18.8	11.0	7.18	39.3	30.8	12.1
7.15	49.9	19.6	10.1	7.21	41.5	27.3	9.9

There appeared to be three possible explanations for the 7 cases with large A-V BDecf differences.

1. The arterial pCO_2 results may have been erroneously low. However, the venous pCO_2 values were also low and the venous BDecf values were in the normal range. This suggested that the pCO_2 values were probably correct.

2. A period of obstruction in cord flow could have occurred immediately before delivery and caused a fetal metabolic acidemia. However, if this was the case the arterial pCO_2 values should have been high, and not low, as pCO_2 levels would have risen during cord occlusion.

3. The final, and most likely scenario was that a combination of maternal hyperventilation and fetal acidemia occurred prior to delivery. Maternal hyperventilation would have lowered both maternal and fetal pCO_2 levels but fetal hypoxia would have resulted in an increase fetal BDecf. Unfortunately maternal blood gas results at delivery were not available and knowledge of maternal analgesia was not helpful as epidurals were frequently left to wear off before pushing commenced. However, there was some evidence that fetal hypoxia may have been present; 4 cases had operative deliveries for fetal distress, 2 had a persistent bradycardia of 8 to 10 minutes duration prior to delivery and in the remaining case the FHR for the last 15 minutes before delivery was not recorded.

There were two cases with a small A-V BDecf difference where both arterial and venous BDecf values were high. Both venous pHs were less than the 7.5th centile. One case was in the ST+CTG arm of the trial and, interestingly, had meconium liquor and an abnormal CTG with a biphasic ST waveform in the second stage. The baby required 2 minutes of bag and mask ventilation following a normal delivery (Apgar scores 5^1 & 9^5). The other case was in the CTG arm and had an emergency LSCS under general anaesthetic for an abnormal FBS (FBS pH 7.14, pCO_2 38.7 mmHg, BDecf 14 mmol/l). Apgars were 6^1 & 9^5. Neither had any neonatal problems. Knowledge of maternal acid-base status would also have been helpful here. Both fetuses appear to have had a non-acute mixed acidemia, but neither had problems in the neonatal period.

The relationship between arterial and venous results.

Figure 5.16 shows the A-V BDecf differences grouped according to arterial pH.

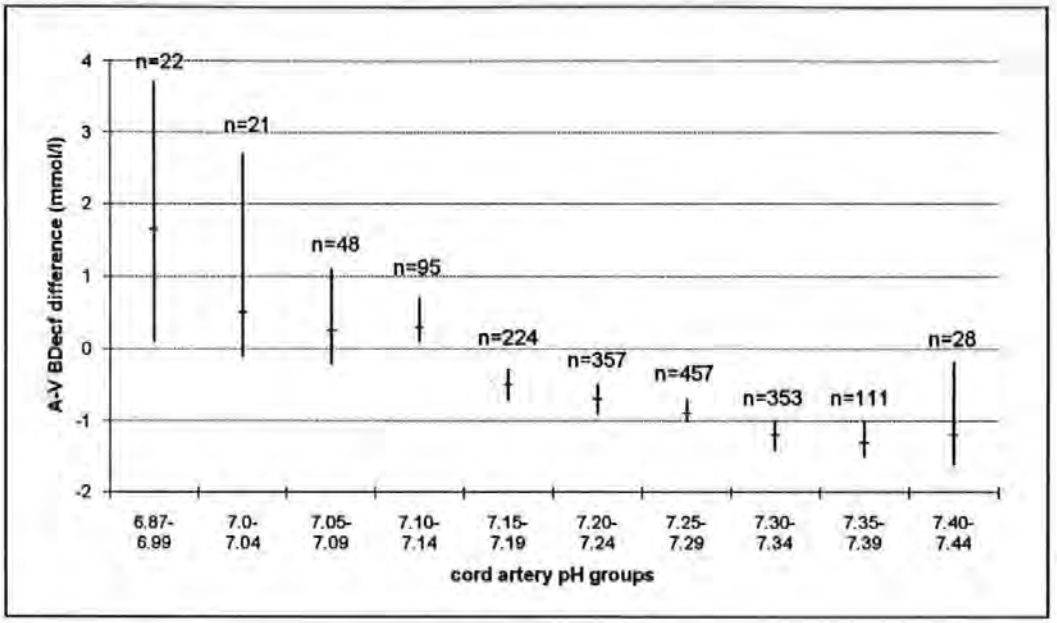


Figure 5.16 Median and 95% CI values for A-V BDecf differences by arterial pH groups, n = 1716

As cord artery pH decreased, BDecf difference increased. It is probable that large A-V BDecf differences (high arterial BDecf, low venous BDecf) reflect an acute onset of fetal metabolic acidemia as placental transfer of non-volatile acids is much slower than the volatile carbonic acid (CO_2). As a result it takes time for the placental extracellular fluid compartment to become saturated with lactic acid from the fetus. If both the artery and vein have a high BDecf the acidemia is not acute as equilibration has occurred with the fetal H^+ load being sufficient to saturate placental buffering capacity.

Large A-V BDecf differences are usually the result of cord entanglement (Rosén & Murphy, 1991) or a stasis of umbilical cord flow secondary to cardiac failure (Brar et al, 1988). The most notable example in the trial was one of the birth asphyxiated cases who developed severe variable decelerations and then a prolonged terminal bradycardia in the second stage as a result of a tight nuchal cord and unfortunately died (Case 1699, artery pH 6.88, BDecf 16 mmol/l, vein pH 7.38, BDecf 4 mmol/l). It is important to recognise that such large A-V differences are possible and that a normal venous pH and BDecf does not exclude the possibility of significant arterial metabolic acidemia.

An example of two cases from the trial which illustrate the significance of A-V differences are shown in Table 5.4 overleaf.

Table 5.4 An example of two cases with similar arterial results but different A-V differences. Case A (Trial number 1129) required resuscitation at birth, was ventilated for 48 hours and has a spastic hemiplegia at one year of age. Case B (Trial number 2009) had a 5 minute Apgar score of 8 with no neonatal problems.

	Case A		Case B	
	artery	vein	artery	vein
pH	7.03	7.10	7.04	7.32
pCO_2 (mmHg)	63.3	49.7	66.4	38.1
pO_2 (mmHg)	7.0	19.4	13.2	33.5
BDecf (mmol/l)	13	13	12	7

One other interesting observation can be made from Figure 5.16. When arterial pH was ≥ 7.15, the A-V BDecf difference was negative; i.e. the vein had a higher BD than the artery. There are two possible explanations for this; firstly, the venous BDecf may reflect placental metabolism which is only obvious when the fetus is not producing any lactic acid or, secondly, it may reflect the fact that reduced Hb in the umbilical artery has more buffering capacity than oxidised Hb in the umbilical vein.

Cord gases and Apgar scores.

The relationship between Apgar scores and cord artery pCO_2, BDecf and A-V BDecf difference are shown in the following figures.

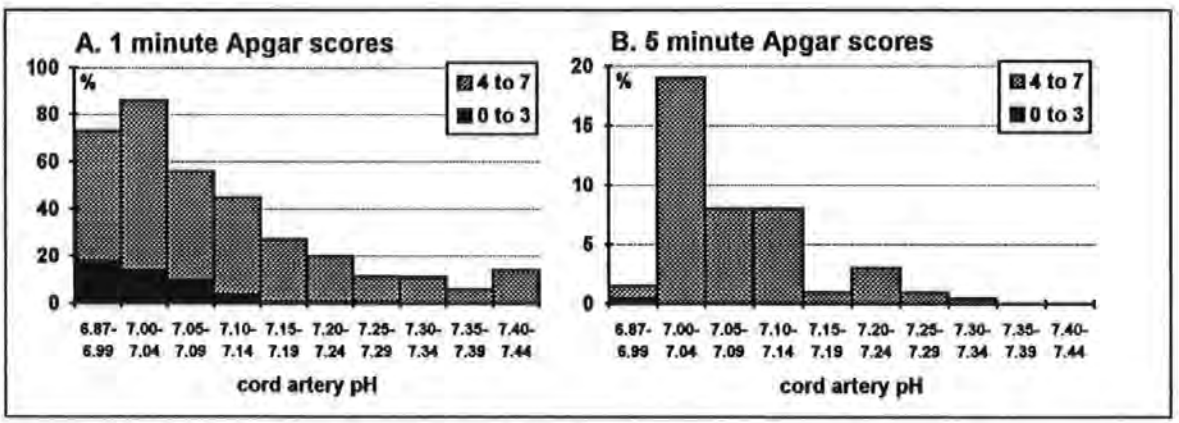


Figure 5.17 Percentage of 1 and 5 minute Apgar scores 0 to 3, and 4 to 7 by cord artery pH at delivery, n = 1716.

As cord artery pH decreased, a significantly higher proportion of babies had lower Apgar scores at both 1 minute (r = 0.39 [0.35-0.43], p<0.001) and 5 minutes (r = 0.45 [0.41-0.49], p<0.001, Spearman Rank Correlation). Although these correlations are statistically significant because of the large numbers involved, the relatively low r values show that the

correlations are not particularly strong. At a cut-off level for cord artery pH of 7.05, significantly more babies with a pH<7.05 had 5 minute Apgar scores <8 (χ^2 =23.64, p<0.001, OR 8.59 [3.38-21.8]).

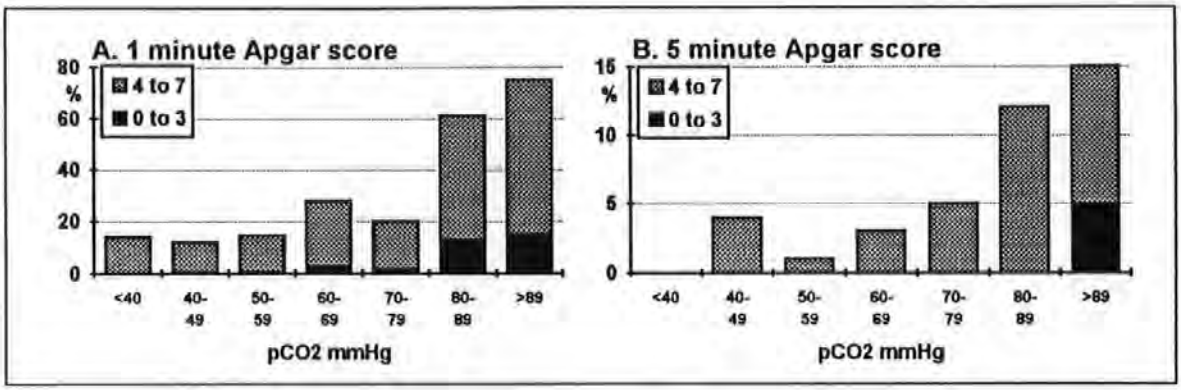


Figure 5.18 Percentage of 1 and 5 minute Apgar scores 0 to 3, and 4 to 7 by cord artery pCO_2 at delivery, n = 1716.

pCO_2 was poorly correlated with 1 minute (r = -0.08) and 5 minute Apgar scores (r = 0.29), but significantly more babies with an arterial pCO_2 >70 mmHg had a 5 minute Apgar score <8 (χ^2 =17.62, p<0.0001, OR 4.3 [2.02-8.92]).

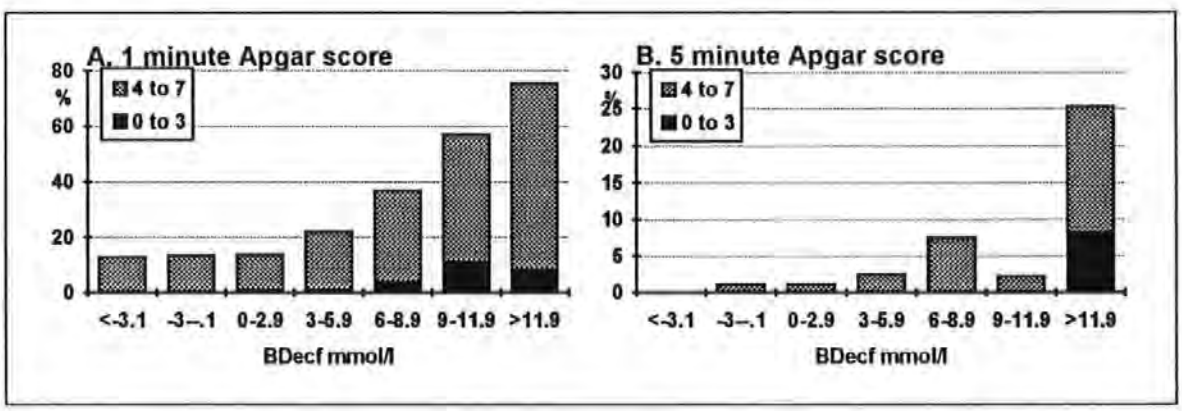


Figure 5.19 Percentage of 1 and 5 minute Apgar scores 0 to 3, and 4 to 7 by cord artery BDecf at delivery, n = 1716.

BDecf was also poorly correlated with 1 minute (r = 0.03) and 5 minute Apgar scores (r = 0.34) but significantly more babies with a BDecf >9 mmol/l had 5 minute Apgars score <8 (χ^2 =3.81, p<0.05, OR 3.81 [1.01-10.72]).

There was no obvious relationship between Apgar scores and A-V BDecf difference (Figure 5.20). However, this was not unexpected as the level of cord artery pH was not considered in the analysis so A-V difference was also examined for cases with arterial acidemia (pH<7.05) (Figure 5.21).

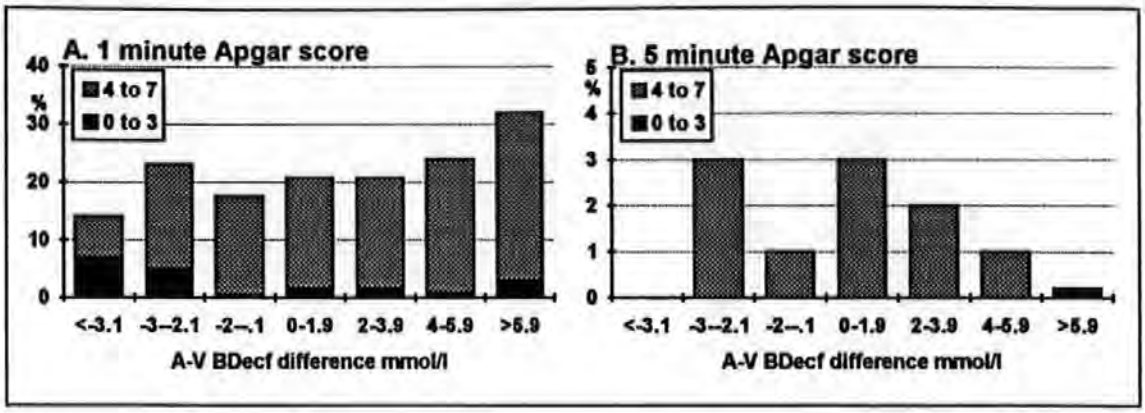


Figure 5.20 Percentage of 1 and 5 minute Apgar scores 0 to 3, and 4 to 7 by cord A-V BDecf difference at delivery, n = 1716.

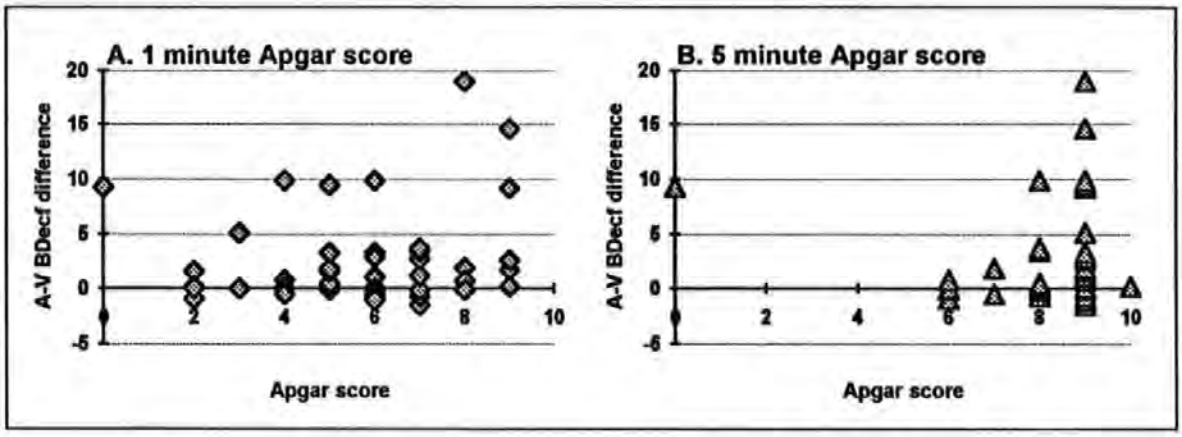


Figure 5.21 Scatter diagram of 1 and 5 minute Apgar scores and A-V BDecf difference for cases with arterial pH<7.05, n=44.

The numbers were small and the correlations were not significant (r = 0.14 for 1' Apgar and r = -0.4 for 5' Apgar). There was one outlying case, an asphyxiated baby (trial number 1699), who was stillborn with a large A-V difference. If this case was excluded from the calculations, the correlations became a little stronger and approached statistical significance (r = 0.26, p=0.09 for 1' Apgar and r = .24, p = 0.12 for 5' Apgar).

Cord gases and neonatal encephalopathy.

There were 5 cases of encephalopathy in the study (0.2%). The clinical details and cord gas data are shown in Table 5.5. Only one had a metabolic acidemia and fulfilled the requirements for the definition of birth asphyxia used in the randomised trial (case No. 1591, cord artery pH <7.05, BDecf >12, Apgar at 5 minutes <8, >4 minutes active resuscitation, neonatal problems). In one other case (case No. 1971) only a venous sample was obtained, so an arterial acidemia cannot be excluded, but the baby did not require any resuscitation at birth.

Table 5.5 Details of trial entries with neonatal encephalopathy.

Case No.	CTG	Meconium	Mode of delivery	Cord pH & BDecf	Apgar scores & Resuscitation	Neonatal details
682	Normal (CTG)	No	LSCS (GA) failure to progress	artery pH 7.29, BDecf 1.5 vein pH 7.32, BDecf 1.9	4^1, 9^5 4 mins active with intubation and IPPV. Naloxone given.	18h; right-sided fitting progressed to generalised fits. Abnormal EEG. Developed NEC and DIC. Ventilated. Died day 3. Peritoneal fluid grew *Clostridium perfringes*.
1586	Abnormal 100 mins second stage (ST+CTG)	yes	Vacuum extraction failure to progress	artery pH 7.15, BDecf 7 mmol/l. vein pH 7.26, BDecf 6 mmol/l.	8^1, 10^5. No resuscitation.	20h; right-sided twitching then right-sided and generalised fits for 4 days. Abnormal left hemisphere EEG. Moderately severe left hemiparesis at 18 months.
1971	Abnormal 5 hours first stage 3 x FBS (CTG)	yes	LSCS (GA) fetal distress abnormal FBS result (pH 7.13)	Artery not available (NA) vein pH 7.20, BDecf 1.1	6^1, 9^5. No resuscitation.	Symptomatic hypoglycaemia for 6 hours following delivery. Did not respond to oral carbohydrate feeds. Generalised fitting for 4 hours. At 14 months; height on 50th centile, weight on 3rd centile, global developmental delay, failed hearing tests, intermittent fits.
1591	Abnormal 120 mins (CTG)	yes	LSCS (GA) cord prolapse	artery pH 6.81, BDecf 12.2 vein pH 7.20, BDecf NA (printer error)	3^1, 7^5. 4 mins active resuscitation with intubation and IPPV.	8h; generalised fitting. Controlled on iv phenobarbitone. Discharged well. No follow-up.
2072	Normal (CTG)	yes	non-rotational forceps failure to progress	artery pH 7.30, BDecf 2.3 vein pH 7.39, BDecf 0.7	9^1, 9^5. No resuscitation.	24h; irritable, 27h; right sided fits. EEG showed bilateral irregularities. Normal at 3 months. No further follow-up.

Discussion.

This review was performed in an attempt to clarify some of the confusion about cord blood gas sampling and outcome. Perhaps, rather predictably, although some questions have been answered, many more have been raised.

Reliability of cord results.

Some of the confusion about the value of sampling must be related to erroneous results. It is imperative that samples are taken from both the artery and the vein and that the results are screened to ensure separate vessels have been sampled. Nearly 20% of all paired samples in this study were rejected. Research workers were far more accurate in sampling than midwifery staff. The first 144 cord samples were taken exclusively by research workers (one of whom was a midwife), a single vessel sample was obtained in 7 cases (5%), but in the next 1960 samples taken mainly by midwifery staff, 381 (20%) of samples came from a single vessel or had pCO_2 errors. Neither midwifery staff nor doctors were very good at identifying sampling or analysis errors. This was the first time that cord sampling had been performed in the hospital and success rates may have improved since then. Regrettably, lack of computerised labour ward records has not allowed this to be assessed. Others have reported 10% error rates with routine sampling by midwives (Riley & Johnson, 1993).

In this study the necessity for adequate BGA maintenance was recognised, and analyser function was checked before the study commenced. However, the unmarked error in pCO_2 values caused by back flow with small samples was only recognised during the study and was responsible for half of the rejected samples. Since then probable errors in pCO_2 values in other studies where the same BGA was used have been noticed (e.g. Newbold et al, 1991). It would not be unexpected to find similar (or additional) quirks in other BGAs and it has been impossible to find a recent comparison of currently available machines.

There is very little information on the normal range of A-V differences. The minimum A-V pH difference found by Rooth (1988) in his review of 4 studies was 0.04. Huisjes & Aarnoudse (1979) chose 0.03 units as a minimum allowable pH difference while Eskes et al (1983) used 0.02 units, but neither group provided support for the levels chosen. Egan et al (1992) accepted negative venous-arterial pH differences (i.e. venous pH lower that arterial pH) if the pCO_2 and pO_2 results were appropriate for each vessel (pCO_2 higher and pO_2 lower in the artery compared to the vein). It has been a surprise to find that these values have not yet been established and the most recent review of cord sampling managed to discuss sample collection and analysis without addressing this problem (Riley & Johnson, 1993).

There is some debate as to whether sampling should be routine (Thorp et al, 1989) or selective (Page et al, 1986, Duerbeck et al, 1992). Routine sampling occurred during most of the trial (2034 entries). Sampling was missed in 3.6% of cases either because staff forgot or were unable to take blood from the cord. During this phase, 27 (56%) of the 48 babies born with an arterial pH <7.05 had neither an FBS nor an operative delivery and would not have been detected by selective sampling. If cord gas data is to be used to identify neonates 'at risk' of neonatal morbidity or as a quality of care measure or for litigation defence, sampling will have to be routine.

Interpretation of results.

The main area of confusion lies in the definition of acidemia. Statistically low (or high) levels should be defined by centile values rather than mean and SD but only Eskes et al, (1983) have done so. Even then, are these the levels which are physiologically significant? In attempting to answer this question, several points have to be considered. **Firstly**, the relationship between pH and $[H^+]$ is not linear but logarithmic (Figure 5.22). A decrease in pH from 7.30 to 7.20 is only associated with a rise in $[H^+]$ of 13 nmol/l, but with a fall of pH from 7.00 to 6.90, $[H^+]$ rises by 26 nmol/l - a twofold increase. This means low pHs are more significant in terms of increased $[H^+]$ than the fall in pH units would suggest.

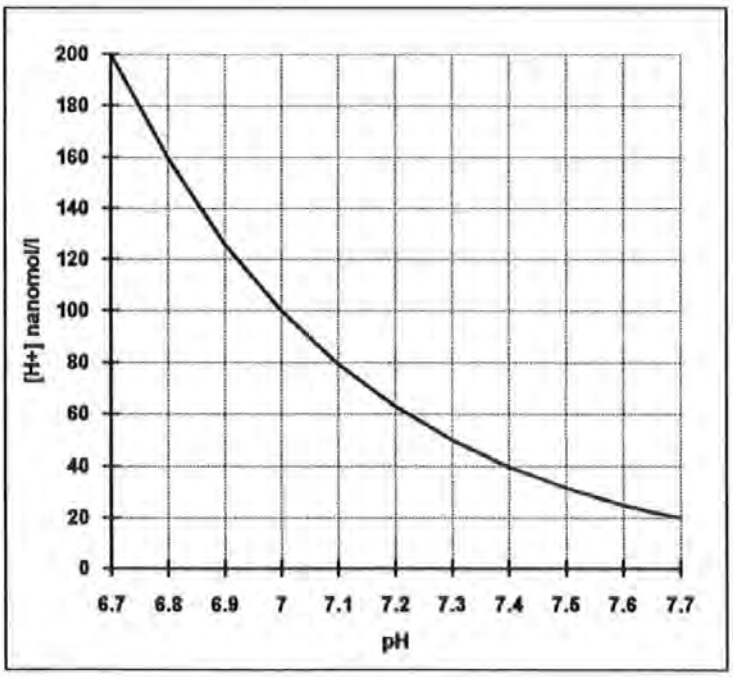


Figure 5.22 Relationship between pH and $[H^+]$.

It is clear that the level of pH chosen to indicate acidosis in many studies was far too high (Winkler et al, 1991, Gilstrap et al, 1989, Goldaber et al, 1991) so it is not surprising that no relationship has been found between pH and neonatal outcome. There is increasing

evidence from larger studies that the cut-off levels for a significant metabolic acidemia are a pH <7.05 and a BDecf >12 mmol/l. These figures are very close to those determined in this study on statistical grounds (pH <7.05, BD ≥10 mmol/l). Low et al, (1984) followed up 60 children with a metabolic acidosis (Buffer Base <34 mEq/l) at birth. At one year of age the degree of handicap was related (but not statistically significantly) to the degree of cord artery acidemia with key pH and BDecf values of 7.06 and 12 mmol/l respectively. Gilstrap et al (1989) found a significant increase in low Apgar scores at 1 and 5 minutes and a significant increase in neonatal morbidity with an arterial pH <7.00 in 2738 singleton pregnancies at term. Goldaber et al (1991) reviewed neonatal morbidity and mortality in 1270 term new-borns with an arterial pH <7.15 from a total population of over 30,000 cases. They found a significant increase in neonatal morbidity when pH <7.05, and particularly if pH <7.00. The neonatal death rate was increased when pH <7.05 (p=0.06). In their study two thirds of the new-borns with a pH <7.00 had a metabolic component to their acidemia with a BDblood >15mmol/l. This is comparable with a BDecf of 12 to 13 mmol/l. Seven of 8 babies with unexplained seizures had a metabolic contribution to their acidemia. Despite the statistical significance of these findings, the majority of babies with a cord artery pH <7.05 did not have poor neonatal outcome.

Secondly, a linear relationship between pH or BD at delivery and outcome should not be expected. The ability to mobilise glucose from glycogen and metabolise it anaerobically depends both on the availability of substrate and on the effectiveness of the beta-adrenergic mediated response to hypoxia. If substrate is lacking, as in growth retarded fetuses, or the appropriate response is affected by chronic hypoxic stress or infection, anaerobic metabolism may not be as effective at maintaining cell and organ function as in the healthy fetus. As a result pH may not fall and BDecf may not rise as much during hypoxia in the growth retarded or chronically stressed fetus. **But** that is not to say they do not display a metabolic acidemia at all. There is considerable evidence from cordocentesis studies that growth retarded fetuses have higher lactate levels and lower pHs than appropriately grown controls (Pardi et al, 1987, Soothill et al, 1987, Nicolaides et al, 1989, Ribbert et al, 1991). Low demonstrated some time ago that decreased weight for gestational age was the best predictor of metabolic acidemia (Low et al, 1981) and Lin et al, (1980) showed that the acid-base status of growth retarded fetuses with FHR decelerations deteriorated more quickly than appropriately grown fetuses. Schneider et al, (1988) have also reported an increased incidence of arterial pH<7.10 in fetuses who were small for gestational age (10%) compared to appropriately grown fetuses (1%). Finally, 5 of the 16 cases of birth asphyxia presented in this thesis were growth retarded with a metabolic acidemia. It is noteworthy that the lowest pHs (6.80, 6.82) were found in appropriately grown fetuses whilst the lighter babies tended to have pHs from 6.95 to 7.05.

Dennis et al, (1989) were unable to find a significant relationship between the degree of cord artery acidemia at birth and neurodevelopmental outcome at 4½ years of age. In fact,

the highest proportion of unimpaired children was amongst those with a cord artery pH <7.05 at birth. They suggested the ability to respond to intrapartum stress with a metabolic acidosis was a positive finding associated with good future outcome whilst babies who were not acidemic but had low Apgar scores at delivery were at most risk of poor outcome. Unfortunately, their conclusions are frequently interpreted to mean that some fetuses who become hypoxic during labour do not become acidemic but still suffer direct intrapartum cerebral damage. Physiologically, it is difficult to see how hypoxia would not result in metabolic acidemia, even in growth retarded fetuses, as has been discussed above. It may be that some fetuses have structural brain abnormalities which make them more susceptible to hypoxaemia so that they suffer neurological damage without major FHR abnormalities or acid-base disturbance (Hull & Dodd, 1992). It is known that chronic growth retardation affects brain development (Thordstein, 1991) so it would be of interest to know the birth weights and lengths of the children with poor neurodevelopmental outcome in Dennis et al's study.

Thirdly, the type and duration of acidemia are important. The scatter diagram of pH and BDecf (Figure 5.15) showed that half of the babies with a cord artery pH <7.05 had a BDecf <10 mmol/l, i.e. a respiratory acidemia. The respiratory and metabolic components of an acidemia will best be separated by BDecf, as it is less affected by high pCO_2 levels. In addition, the duration of metabolic acidemia is an important prognostic indicator (Low, 1988). Arterio-venous pH and BDecf differences can provide information about the time course of an acidemia which may be useful in future studies of long-term outcome. Although A-V BDecf difference and Apgar scores were not significantly correlated with pH in this study, Low has just reanalysed his data (over 30,000 paired cord blood gas results) using A-V Buffer Base differences and found a significantly poorer outcome with metabolic acidemia and narrow A-V differences compared to metabolic acidemia and large A-V differences (Low, et al, 1993). Chronic antenatal fetal acidemia is associated with poor subsequent neurological development. Soothill et al (1992) followed up 38 infants who as fetuses had cordocentesis for severe fetal growth retardation; 23 had normal acid base status and 13 were acidemic (pH < 2 SD below mean for gestation!). When the infants were examined at 12-52 months of age the Griffiths developmental quotient of the acidemic group was significantly lower than that of the normal pH group (mean 91.8 versus 100.3, p=0.011). One of the acidemic group infants had cerebral palsy. There was a weak correlation between the degree of fetal acidemia and the developmental quotient (r=0.41, p=0.012). In contrast, there was no significant correlation between the degree of growth retardation (weight for gestational age) and the degree of acidemia or the Griffiths score.

Finally, interpretation of cord gas results will be assisted by knowledge of the clinical situation, particularly maternal aid-base status. This is less easy to obtain than cord blood

and would require an extra (albeit minimal) invasive procedure for the mother. It may be more difficult to obtain these samples on a routine basis.

Cord gas results and Apgar scores.

In this study a weak relationship between cord gas parameters and Apgar score was found, in keeping with many other studies (Sykes et al, 1982, Silverman et al, 1985, Dijxhoorn et al, 1986, Ruth & Raivio, 1988, Gilstrap et al, 1989, Steer et al, 1989). Many have been confused by this. Silverman et al, (1985) went to great lengths to explain the finding of a low cord artery pH and a normal Apgar score as a result of a "maternal infusional acidosis". In fact, a strong association between the two should not be expected. The catecholamine surge which activates fetal defence mechanisms in response to hypoxaemia also has an affect on neonatal behaviour at birth. It is known that catecholamines are an extremely important part of the normal adaptation to extrauterine life and produce a general neonatal arousal (Lagercrantz & Slotkin, 1986). This arousal will affect most components of the Apgar score; a higher heart rate, stimulation of respiration, increased reflex irritability and tone, so it should be no surprise to find a high Apgar score where an appropriate response to hypoxia has occurred (Lagercrantz, 1982). Similarly, it is no surprise that the combination of severe metabolic acidosis and a one minute Apgar score <7 is associated with a significant increase in neonatal complications compared to those with acidosis and a normal one minute score (Low et al, 1993).

Cord gas results and neonatal encephalopathy.

The most recent proxy for birth asphyxia is neonatal encephalopathy. This is a clinically defined syndrome of disturbed neurological function in the earliest days of life in the term infant, manifested by difficulty with initiating and maintaining respiration, depression of tone and reflexes, subnormal levels of consciousness, and often by seizures (Leviton & Nelson, 1992). The severity of encephalopathy is a good predictor of both short and long-term outcome (Finer et al, 1981, Low et al, 1985, Levene et al, 1985, Robertson et al, 1989). The incidence of death and disability is not only increased in those who have had moderate or severe encephalopathy, but it has been shown that survivors of moderate encephalopathy without a motor deficit were more likely to have a lower IQ and poorer reading, spelling, and arithmetic skills than their peers at eight years of age (Robertson et al, 1989). Meta-analysis of all the randomised monitoring trials to date has found that use of the CTG during labour is associated with a significant reduction in neonatal seizures (Grant, 1991). In the light of the evidence from Robertson, et al (1989) this is likely to be an important benefit but one which is frequently dismissed as follow-up of cases from the Dublin randomised trial (MacDonald et al, 1985) revealed no difference in cerebral palsy rates at 4 years of age. However, the learning and behavioural disorders found by Robsertson et al may only become obvious in older children and probably require more extensive testing than the neurological examination which was performed on the Dublin children.

Neonatal encephalopathy has varying aetiologies; hypoxia, infection, inborn errors of metabolism, hypoglycaemia, trauma or structural abnormalities (Nelson & Leviton, 1991). The terms 'hypoxic ischaemic encephalopathy' (HIE, Sarnat & Sarnat, 1976, Finer et al, 1981) or 'post asphyxial encephalopathy' (PAE, Levene et al, 1985) are used to describe neonatal encephalopathy occurring as a consequence of 'birth asphyxia'. In these cases the diagnosis of asphyxia is usually made on clinical criteria (Levene, 1988). However examination of the 'clinical criteria' used by various workers reveals that they are somewhat non-specific (Table 5.6).

Table 5.6 Requirements for the diagnosis of new-born encephalopathy used in various studies. Modified from Nelson & Leviton, 1991. The italics have been added by the present author.

Reference	Terminology	Criteria: encephalopathy plus;
Sarnat & Sarnat, 1976	Neonatal encephalopathy	One of the following two - well defined episode of fetal distress *(not defined)* - Apgar score ≤4 at 1 or 5 minutes.
Volpe, 1976	Hypoxic ischaemic encephalopathy	Not defined.
Finer et al, 1981	Hypoxic ischaemic encephalopathy	One of three - abnormal FHR pattern *(not defined)* - Apgar score ≤4 at 1 or 5 minutes. - need for immediate resuscitation or intubation.
Amiel-Tison & Ellison, 1986	Hypoxic ischaemic encephalopathy	One of four - FHR <120 or >160 once if by auscultation or prolonged if by EFM - repetitive FHR decelerations *(not defined)* - presence of meconium - Apgar score <6 at 5 minutes.
Levene et al, 1985, Levene, 1991	Post asphyxial encephalopathy	One of five - abnormal CTG *(not defined)* - meconium staining - fetal scalp acidosis - low Apgar scores - delay in establishing respiration
Lipper et al, 1986	Post asphyxia score	Apgar score <6 plus one of the following - bradycardia *(not defined)* - variable or late FHR decelerations - loss of beat to beat variability - scalp or cord pH <7.20 - need for resuscitation - meconium aspiration.

Asphyxia with a metabolic acidemia only occurred in one of five cases of neonatal encephalopathy in the randomised trial. Others have found the same. In 1985 Low et al, reported that 78% of new-borns with severe encephalopathy had normal cord gas values. Neonatal respiratory complications and infection were significantly associated with

encephalopathy and they estimated that new-born hypoxia was twice as frequent as fetal hypoxia in cases with severe encephalopathy. Even Levene et al (1985) reported that 23% of infants with PAE had normal Apgar scores and, more recently, Hull & Dodd (1992) found 64% of infants with moderate or severe HIE had Apgar scores of >5 at 5 minutes and a number did not require resuscitation.

Use of terms like HIE or PAE which imply an aetiology should be avoided in favour of the more accurate descriptive term neonatal encephalopathy. Knowledge of umbilical acid base status will help to establish an aetiology for encephalopathy. Normal blood gas results may encourage paediatricians to search more vigorously for other non-asphyxial causes.

Is there a 'gold standard' measurement for neonatal outcome?

It is better to have absolutely no idea where one is, than to confidently believe that one is where one is not.

CF Cassini de Thury, 18th Century Surveyor.

Much of the confusion relating to the value of intrapartum fetal monitoring has been caused by the difficulty in assessing neonatal outcome. Initially Apgar scores were confidently used as a measure of 'birth asphyxia' until they were even more confidently replaced by 'hypoxic ischaemic encephalopathy'. Even the term 'birth asphyxia', confidently used by most (including the present author), has so many varied definitions it is not a useful term for general discussion and should be avoided in favour of descriptive statements about neonatal condition.

This imprecision in assessing outcome makes it very difficult for obstetricians to audit care and assess the value of monitoring techniques. When Murphy et al (1990) asked the neonatal staff to identify all cases of birth asphyxia during a 17 month period for their review of CTGs, they were initially presented with a list of 85 cases. However, when each case was reviewed in detail, paediatricians reversed their diagnosis of birth asphyxia in 25% of these. The important findings of their study may have been very different (or at least diluted) had these cases been included in the analysis.

Clinicians seem obsessed with finding **one** measure of fetal condition in utero and **one** measure of neonatal condition which accurately reflects preceding events, fetal responses to these events and future outcome. Given the complexity of the situation, this approach is somewhat naïve. The myth of the 'gold standard' should be laid to rest as soon as possible.

Full use of **all** available information should be made in assessing neonatal condition. Umbilical cord blood analysis provides an objective measure of fetal condition at birth,

which reflects fetal oxygenation prior to delivery and can be used in combination with more traditional measures such as Apgar scores. However, the information will only be valuable if it is both correct and correctly interpreted. Much of the confusion about the value of cord acid-base assessment lies in the use of erroneous data, inadequate definitions of acidemia which do not differentiate between respiratory and metabolic components and unphysiological expectations about its relationship to other measures of neonatal outcome.

It is important that this area of confusion is resolved as soon as possible, for without some consensus the value of intrapartum monitoring will be difficult to establish.

Chapter Six

Future approaches to intrapartum fetal monitoring.

Introduction.

The principle aim of this thesis was to validate a new technology for intrapartum fetal monitoring; analysis of the ST waveform of the fetal ECG. Whilst this has been achieved, a very important, rather fundamental point has been highlighted by the review of CTG and ST+CTG monitoring and cord blood gas analysis; it is the importance of accurate interpretation of data. The key question for the effective use of ST waveform analysis is whether the requirements for staff education and training will be recognised, met and maintained in every labour ward where it is used. It is salutary to realise that this has not yet been achieved for the CTG despite 25 years of clinical use. The addition of ST waveform analysis may make things more complicated and once other aspects of the ST waveform become available, e.g. waveform area or contraction-related changes, the situation may become impossible. Education is important but is unlikely to be the complete solution for, despite regular teaching sessions, suboptimal use of CTG and ST+CTG information occurred in many cases in the randomised trial. Educational attempts were hindered by the high turn-over rate of both midwives and junior doctors working on the labour ward and, of course, this is a national problem.

Currently, interpretation of CTG and ST+CTG recordings relies on a subjective assessment of the available information. There are many studies which highlight poor intra- and inter-observer variations in CTG interpretation (Trimbos & Keirse, 1978, Lotgering et al, 1982, Nielsen et al, 1987, Donker, 1991) although experienced active clinicians tended to agree more and interfere less than their junior colleagues (Lidegaard et al, 1992). The labour ward is a high stress area in which even experienced clinicians may have difficulty with decision making. More importantly, senior, experienced staff are usually only called to advise on cases when the midwife or junior doctors perceive there is a problem, and furthermore, they can only be in one place at one time.

Given the realities of staffing situations and levels of expertise available in hospitals throughout the country, it is most likely that consistent, optimal interpretation of the information in the CTG, the ST waveform, or any other new technology used, will only be achieved with some degree of automatic data processing and interpretation.

Computer Assisted Decision Support.

Background. The need for an objective, standardised interpretation of the CTG was recognised in the 1960s. The initial systems were expensive mainframe computers which performed their analyses from signals stored on magnetic tapes (Flowers et al, 1971, Crawford et al, 1975, Wade et al, 1976). The development of relatively inexpensive microcomputers allowed more sophisticated bedside analysis (Wickham et al, 1983) but

many workers chose to concentrate on the relatively simpler task of antenatal CTG interpretation (Searle et al, 1988, Dawes et al, 1982a, 1982b). Two systems have been specifically designed for intrapartum CTG analysis in Japan and Germany (Maeda, 1990, Krause, 1990). These systems are essentially aimed at overcoming the inadequacies of visual inspection of data. Maeda's system allocates scores to various CTG features and calculates a Fetal Distress Index every 15 minutes which classifies the CTG as either 'normal', 'requires further monitoring', 'suspicious' or 'diagnostic of fetal distress' (Maeda, 1990). Despite much descriptive information there are few reports of any observational studies (Parsons et al, 1985). Krause, from former East Germany, also extracts CTG features but combines them to calculate the discriminative function index (DF) based on a mathematical model. The CTG recording is not displayed but rather a plot of the DF with time is shown. A number of alarms are triggered by different heart rate patterns. In a multicentre study which compared 403 patients in labour monitored by this system and 393 by visual CTG analysis there were significantly more prepathological CTGs and FBS in the computerised group but no difference in operative intervention or neonatal outcome (Krause et al, 1988).

Expert systems. Further advances in computing technology have now produced computer programs which can simulate expert behaviour. These Expert Systems (ESs) use expert knowledge to attain high levels of performance over a narrow problem area or domain. The expert knowledge includes both **facts** - a body of information which is widely available, generally agreed upon by experts in the field and **heuristics** - private, little discussed rules of good judgement or intuition which characterise expert-level decision making in the field. In other words, ES aim to capture the 'art' of decision making in a specified area. They manipulate knowledge while most conventional programs manipulate data and they have solved complex tasks in many diverse areas where conventional computing approaches have failed (Waterman, 1986).

ES have wide applications in industry and manufacturing; the British Department of Trade and Industry has estimated that manufacturing industries could save £1.3 billion per annum by introducing ES techniques into maintenance procedures (Rada et al, 1991). Military and aeronautical applications are also extensive; e.g. the NASA space shuttles have three ES for navigation. The most famous medical precursor to modern ES was MYCIN, developed in the mid-1970s to aid physicians in the selection of the most appropriate antibiotics for patients with bacteremia and meningitis (Shortliffe et al, 1973). Since then a large number of medical ESs have been developed for both diagnosis and treatment for a wide range of conditions from chest pain to depression and glaucoma to lung disease (delightfully entitled PUFF). Most of these have reached the 'research prototype' stage (Waterman, 1986) and have yet to be introduced into routine practice.

The ability to incorporate expert knowledge into a computer system for intrapartum monitoring is an attractive idea. Computers work consistently 24 hours a day without becoming tired. If an effective ES could be designed, improved interpretation of CTG and ST waveform recordings and better management advice might increase the effectiveness of the CTG or ST waveform in clinical practice. This could also apply to any other combination of variables shown to be useful in the future.

In clinical practice, CTG changes are interpreted in context with labour-associated events (e.g. analgesia, uterine contraction frequency) and with knowledge of specific risk factors (e.g. growth-retarded fetus). An ES would allow these important factors to be incorporated into decision making. These systems can also explain the reasoning behind the advice they give and may also have a useful teaching role.

Several groups have investigated ES for antenatal CTGs with encouraging results (Becksaç et al, 1990a & b, 1991, Devoe et al, 1992). A large ES termed FOETOS with 5 separate components; antenatal CTG, fetal biophysical profile, contraction stress test, labour and neonatal diagnosis has also been described (Alonso-Betanzos et al, 1989) although preliminary assessment of its performance during labour in a small series of cases showed only 50% agreement with clinical experts.

The aim of the final two studies reported in this thesis were to assess the feasibility of an Expert systems approach to CTG interpretation. This work is one of the main research initiatives of the Plymouth Perinatal Research Group. It was performed in conjunction with a research engineer, Robert Keith, and forms part of his PhD Thesis (Keith, 1993). A patent for the system developed has been applied for.

Methods.

The requirements and design of an ES for CTG interpretation and labour management were established during structured and unstructured interviews between 3 experienced clinicians and the ES engineer over a three month period. A simple block diagram of the system is shown in Figure 6.1.

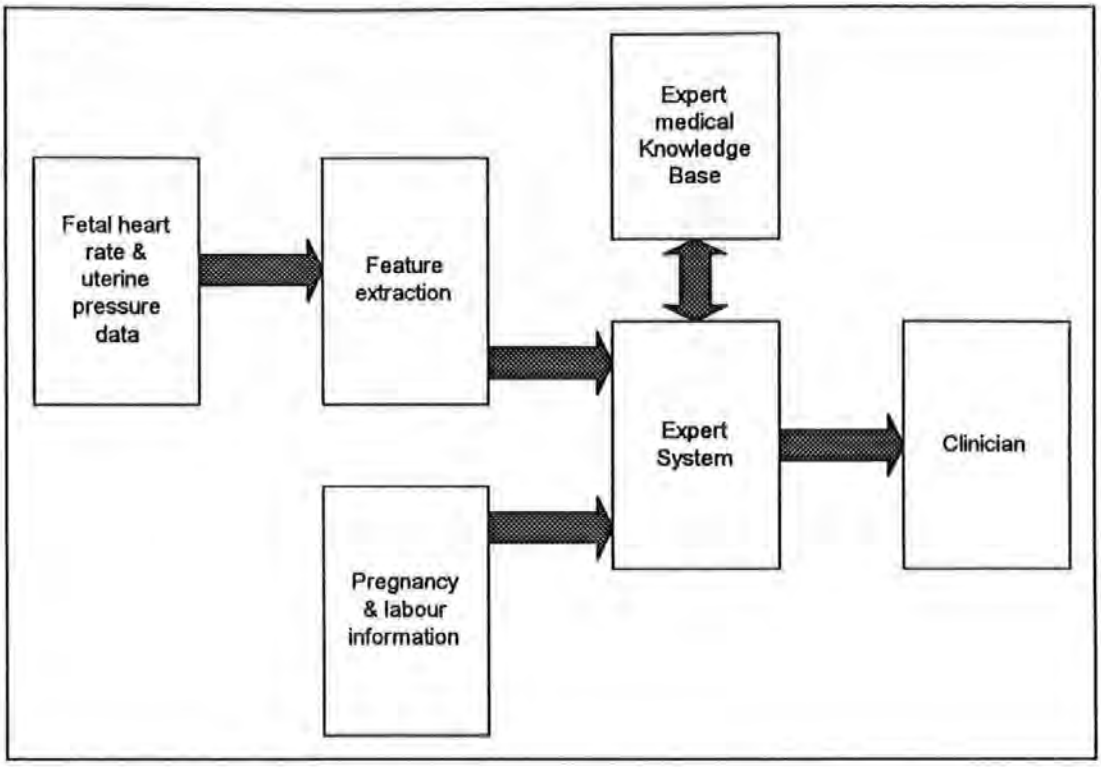


Figure 6.1 Simple block diagram of the Expert System designed for CTG interpretation.

Heart rate and uterine contraction signals are digitised and recorded from a standard CTG recorder. The important features (baseline, accelerations, decelerations [type and timing], contraction frequency and signal quality) are extracted using algorithms. Additional information relevant to each specific pregnancy and events during labour are combined with the CTG features and passed to the ES. The Knowledge Base contains long term information about CTG interpretation in the form of a series of rules which the ES applies to the dynamic knowledge to make an assessment of fetal condition which, along with any recommendations for action, is passed to the clinician.

Off-line assessment of the Knowledge Base.

Clinical assessment, interpretation and management of intrapartum CTG changes was represented in a series of decision tree diagrams. These flow diagrams were incorporated into a series of rules and conditions to create the Knowledge Base for the ES (see Figure 6.2 for an example). The ES was implemented in PROLOG on a 486 IBM compatible PC.

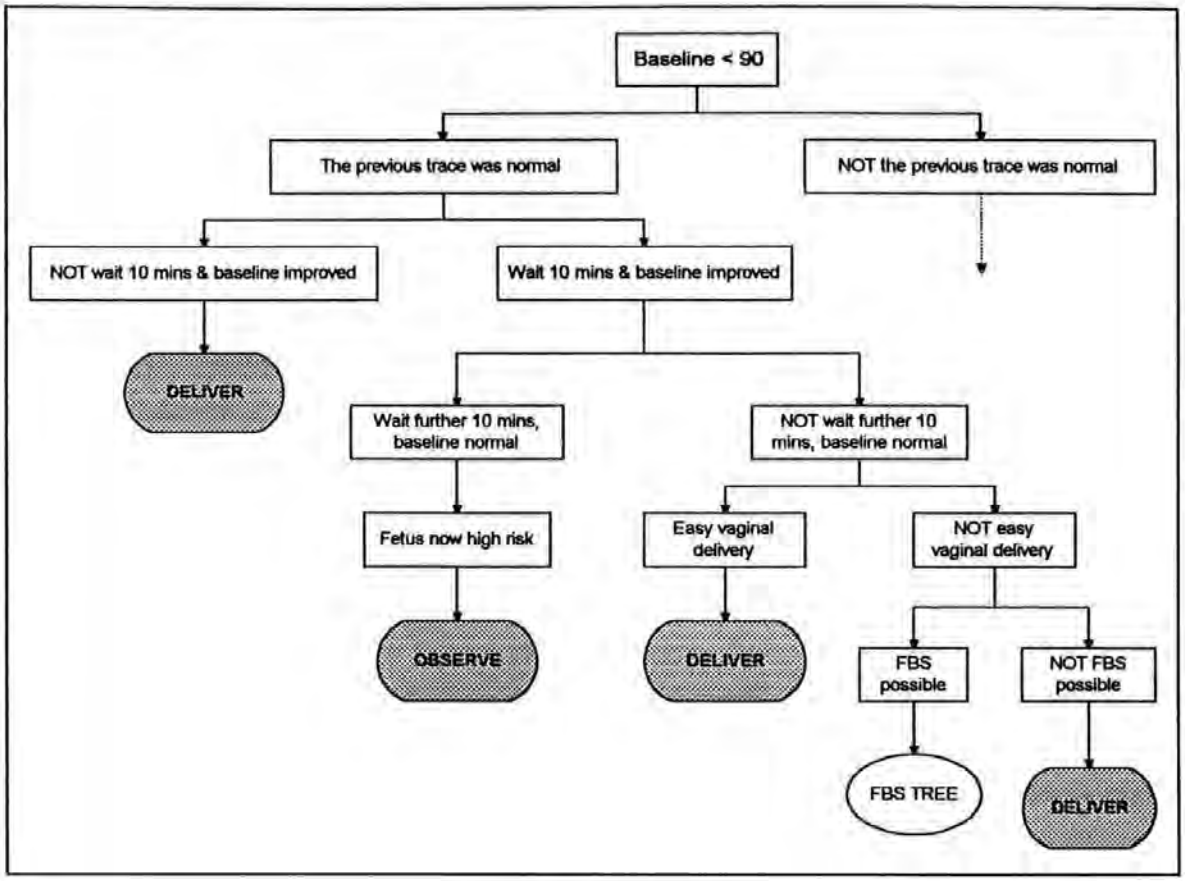


Figure 6.2 A section of the decision tree which makes up the Knowledge Base. Some of the rules derived from this tree are shown below. A rule is made of a series of *conditions* and has a **GOAL**. (Modified from Ifeachor et al, 1991).

Rule 34 IF *Baseline <90* AND
The previous trace was normal AND
NOT wait 10 mins & baseline improved THEN
DELIVER

Rule 35 IF *Baseline <90* AND
The previous trace was normal AND
Wait 10 mins & baseline improved AND
Wait further 10 mins & baseline normal THEN
Fetus now high risk
OBSERVE

Rule 36 IF B*aseline <90* AND
The previous trace was normal AND
NOT wait further 10 mins & baseline normal AND
Easy vaginal delivery THEN
DELIVER

At this preliminary stage information about CTG features was entered manually via the PC keyboard. This system was evaluated on recordings from 31 labours in the CTG arm of the randomised trial. These 31 labours were chosen randomly from the group who had an FBS during labour to ensure that a high percentage of abnormal cases were reviewed. All cases were reviewed retrospectively, blind to outcome by the author (JW) who acted as a 'clinical expert' and by a midwife using the ES (MW+ES). The midwife used a template which only allowed 10 minute sections of the CTG to be seen at one time. She described four features for each 10 minute epoch; baseline heart rate, variability, presence or absence of accelerations and the presence, absence and type of decelerations. The ES interrogated for additional information as required (e.g. progress of labour, drugs administered). The management recommended by the MW+ES was compared with that recommended by JW and with what actually happened in clinical practice (Ifeachor et al, 1991).

Preliminary on-line evaluation.

In the next phase techniques to automatically extract CTG features and present them to the ES were developed. Heart rate and contraction signals were obtained from the analogue output of a conventional Hewlett-Packard CTG recorder. The signals were digitised and the important features (baseline, variability, accelerations and decelerations) extracted using algorithms (Keith, 1993, Keith et al, 1993a).

During the randomised trial the CTGs from 300 patients were digitised and recorded onto Optical Discs. One hundred cases were used during development of the feature extraction algorithms. From the remaining 200 cases, the nine cases in which clinical intervention for 'fetal distress' (fetal blood sampling and/or operative delivery) occurred and 21 cases without intervention chosen at random were selected for a preliminary on-line evaluation of the ES.

The clinical decisions taken in these 30 cases were compared with those recommended from a retrospective review of the cases by the system and three experienced clinicians, (A, B and C). The reviewers assessed the cases independently, blind to outcome and with no knowledge of the system's recommendations or each others. The CTGs were exposed in 15 minute segments and each reviewer was asked to make an assessment of fetal condition based on the newly-revealed segment, the previous recording and the clinical information known at the time. They were then asked to specify an appropriate course of management; continue with the labour, obtain a FBS or request operative delivery. It was not possible for any reviewer to see future segments before the present segment had been assessed. Any additional information gained from actual clinical action was only revealed to the reviewers if they too had specified the same action.

The consistency of reviewer A was also assessed in a second assessment (A2) of the same cases five months later with the case order randomised. Reviewers B and C had helped compile the results of the first assessment and were thus too familiar with the cases to make their subsequent review useful.

Results.

Off-line study.

In each of the 31 cases reviewed at least one FBS had been performed in clinical practice. A comparison of the intervention and possible outcome made by JW and MW+ES is shown in Table 6.1.

Table 6.1 Comparison of FBS, operative delivery and outcome in clinical practice with that recommended in a review of 31 cases by a clinical expert (JW) and a midwife interacting with the Expert System (MW+ES).

	clinical practice	JW recommendations	MW + ES recommendations
FBS	31	16	13
Operative delivery for 'fetal distress'	15	12+1[1]	12+1[1]
Cord artery pH<7.15	8	4[2]	4[2]
5 min Apgar <8	6	2[2]	2[2]

1 Three fewer operative deliveries were recommended than were actually performed, and one additional was recommended but not performed in clinical practice.
2 Possible reductions due to earlier delivery.

There was good agreement between JW and MW+ES. Both would have reduced the number of patients having FBS by nearly 50%. Discrepancies occurred in only five cases (16%) and resulted from differences in visual assessment. In four cases the disagreement was in the type of deceleration present and in one case it was the baseline heart rate. The omission of an FBS would not have adversely affected the outcome in any case and would have prevented a forceps delivery in one of them. This FBS was performed within 15 minutes of a prolonged deceleration accompanying a tonic contraction. The pH was 7.17 but after a Keillands delivery 15 minutes later the cord artery pH was 7.28, Apgars 9 at one minute and 10 at five minutes. An extra FBS was recommended by both JW and MW+ES in 3 cases and may have reassured clinicians sufficiently to prevent two subsequent forceps deliveries for 'fetal distress' (cord artery pH 7.32 and 7.35).

JW and MW+ES both identified the same three cases for whom an operative delivery for 'fetal distress' was not required (cord artery pH 7.27, 7.28, 7.30, Apgar 8 at one and 9 at five minutes). However, both identified the same additional case where an operative delivery was indicated 20 minutes before a spontaneous delivery occurred (cord artery pH 6.95, BDecf 9 mmol/l, Apgars 6 at one and 9 at five minutes).

In seven cases both JW and MW+ES specified that action (FBS or delivery) was required 20 to 70 minutes earlier than actually happened. Three cases had low cord artery pH (7.01, 7.05, and 7.13) and required three to four minutes resuscitation at birth. Two of these were admitted to SCBU.

On-line study.

In 18 of the 30 cases studied, no action was taken clinically nor was recommended by any reviewer or the system. Neonatal outcome was good in every case with no metabolic acidemia and normal Apgar scores at five minutes.

The 12 remaining cases where intervention occurred clinically or was recommended by the system or a reviewer, are shown in Table 6.2.

Table 6.2 Details of cases where intervention was specified or occurred.

Case	Number of fetal blood samples						Operative delivery						Cord pH		Cord BDecf		Apgars	
No	ES	A1	B	C	A2	clin	ES	A1	B	C	A2	clin	artery	vein	artery	vein	1'	5'
1	2	1	2	2	1	2	cs	cs	cs	cs	cs	cs	7.21	7.31	6.1	7.1	7	10
2	1	1	1	0	1	1	cs	cs	cs	-	cs	cs	-	7.26	-	7.1	7	9
3	1	0	0	1	0	0	-	-	-	-	-	-	7.26	7.29	1.2	2.8	6	8
4	0	0	0	1	0	0	-	-	-	-	-	-	7.13	7.21	8.8	10	8	9
5	1	0	1	0	0	1	for	for	for	for	for	-	7.07	7.27	7.4	7.0	9	9
6	0	0	0	0	0	1	-	-	-	-	-	-	7.29	7.36	4.6	4.1	7	9
7	0	0	0	0	0	0	for	for	for	for	for	for	7.23	7.33	1.8	0.9	6	9
8	0	0	0	0	0	0	for	for	for	for	for	-	-	7.12	-	11.2	9	9
9	0	0	0	2	0	2	-	-	-	-	-	-	7.27	7.36	0.9	1.1	8	9
10	1	1	1	1	0	0	cs	cs	cs	cs	cs	cs	7.07	7.12	7.2	5.2	3	8
11	0	0	0	0	0	2	-	-	-	-	-	-	7.20	7.38	3.5	4.0	8	9
12	2	2	2	2	2	2	cs	cs	cs	cs	cs	cs	-	7.29	-	3.9	9	9

A1 first case review by A
A2 second case review by A
cs caesarean section
for forceps delivery

All actions recommended by the system were also recommended by at least one reviewer. All reviewers and the system recommended earlier delivery in the three cases with lowest cord pHs (cases 5, 8 and 10); in cases 5 and 8 a forceps delivery was recommended, 30 and 50 minutes respectively, before a spontaneous vaginal delivery occurred. In case 10, a FBS was recommended by all reviewers and the system (except A2) 40 minutes before the CTG severely deteriorated and an emergency caesarean section was performed. Further, operative intervention was recommended in the same seven cases by the system and all reviewers within 15 minutes, with one exception. The difficulty in this case (case 2) was with identification of the baseline heart rate. The system and reviewers A and B interpreted the recording as having a normal baseline with late decelerations and recommended a FBS, whilst reviewer C alone thought the baseline was low with accelerations. (Figure 6.3). It may be significant that C reviewed the cases for the study late at night whilst the others did so during daylight hours. In clinical practice an FBS was performed and the pH of 7.15 obtained precipitated immediate delivery by caesarean section. This case illustrates the importance of accurate identification of baseline heart rate for the correct classification of periodic changes.

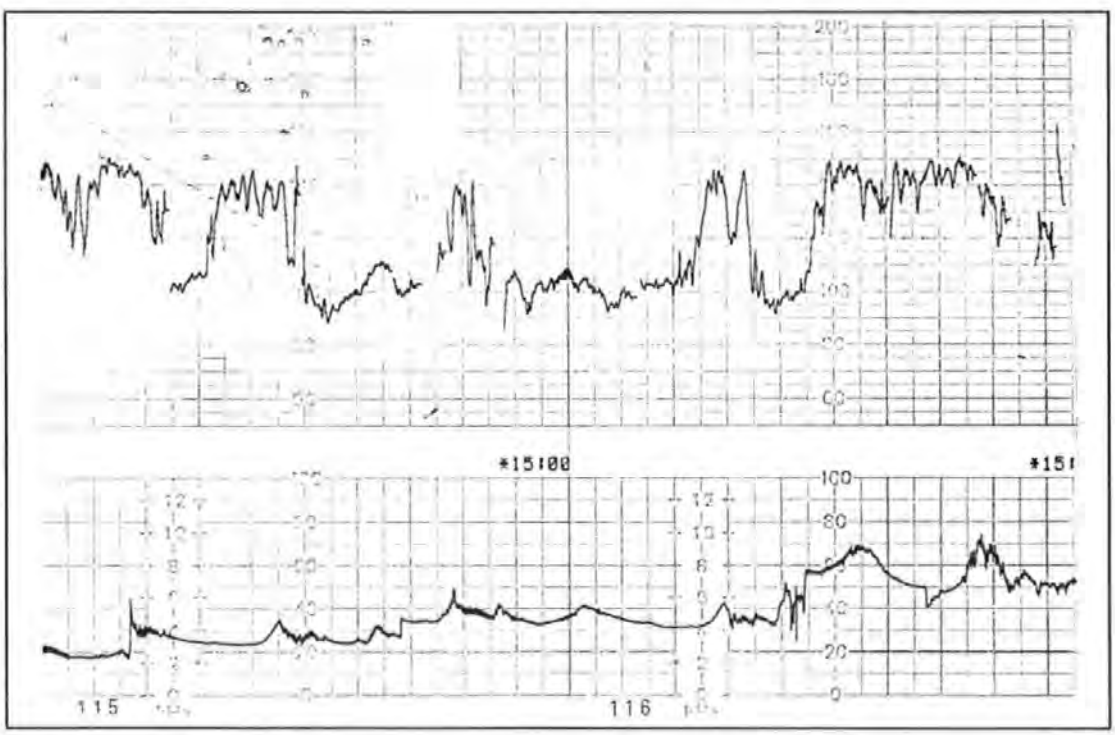


Figure 6.3 What is the baseline heart rate? CTG from Case 2 of the on-line study in which reviewers A and B and the Expert System thought the baseline was 140 bpm with prolonged decelerations to 100, whilst C thought the baseline was 100 bpm with accelerations to 140 bpm.

The actions recommended by the system, the reviewers, and the actual clinical management of the 30 cases were further compared. An agreement in management was said to occur when all recommendations for fetal blood sampling *and* recommendations for operative

delivery were specified within 15 minutes. The number of case agreements are shown below.

Table 6.3 Number of cases with complete agreement (maximum 30).

	Number of agreements				
	ES	A1	B	C	clinical
ES	-	27	29	25	22
A1	27	-	28	25	22
B	29	28	-	24	23
C	25	25	24	-	21
clinical	22	22	23	21	-

The actions recommended by reviewer A in his two reviews (A1 and A2) were entirely consistent in both action and timing in 28 out of 30 cases. Differences in fetal blood sampling occurred in cases 10 and 12, however operative delivery was still recommended in the same 15 minute segment in both reviews.

Discussion.

These studies have demonstrated the feasibility of an Expert Systems approach to CTG interpretation. The ES performed as well as clinical experts and better than clinical practice in both studies. In the on-line study, every action recommended by the ES was also recommended by at least one experienced reviewer. The highest level of agreement was with reviewer B (the author) whose knowledge had principally been incorporated into the system.

The on-line study also found that the experienced reviewers tended to agree on their interpretation of the CTG and subsequent management. These results are consistent with a larger study (Murphy et al, 1990), which obtained good inter-observer agreement (Kappa statistic 0.74, $p < 0.0001$) from a comparison of the recommendations of three experienced clinicians in a retrospective review of 158 cases. Many more studies have found poor agreement between reviewers (Trimbos & Keirse, 1978, Lotgering et al, 1982, Nielsen et al, 1987, Donker, 1991) but the true expertise of their reviewers could be questioned. The reviewers in this study and that of Murphy et al were active clinicians who regularly reviewed CTG recordings whilst those in Donker's study were heads of Department or Professors, many of whom were no longer active in intrapartum obstetrics.

The aim of an ES is not to replace experts but to guide inexperienced staff toward appropriate decision-making. Expert Systems can do this 24 hours a day, in every labour room and will not be affected by stress or tiredness. Because these systems can explain the reasoning behind their recommendations they can also contribute to staff education.

As yet no medical ES has achieved widespread acceptance but their increasing use in non-medical applications is sure to eventually have a 'knock-on' effect into medical areas. The acceptability of these 'expert' systems to clinicians, midwives and women in labour should be considered. Computer technology is now widely available in schools, homes and hospitals and many people are becoming more computer-literate. But the key question is whether clinicians and midwives accept advice from a machine? The impression gained during the studies reported in this thesis is that junior doctors and midwives find the labour ward a stressful place and would be grateful for all the help they can get. Of course, the acceptance of any computerised system must depend on the quality of the advice it provides, how robust it is and on evidence obtained from randomised trials that its use is appropriate in the clinical situation.

Future work.

Whilst these studies have confirmed the potential of an ES for CTG interpretation, a full validation procedure will need to be carried out before it is introduced into clinical practice. This work is now in progress and involves 17 clinical experts in 16 UK centres who are reviewing 50 complete labour records blind to outcome (Keith, 1993). Their recommendations for management will be compared with that of the ES and the actual clinical outcome. The user-interface will be developed and the system further tested in observational studies. Ultimately, the ES will be assessed in randomised clinical trials. In the future an ES for the interpretation of ST waveform changes will be developed and linked with the CTG system. An ES to aid clinicians in the interpretation of cord blood gas results is also under development by our group (Keith et al, 1993b).

In summary, staff training and education in the interpretation of intrapartum CTG changes has failed to provide a consistently high level of expertise in every labour ward 24 hours a day. The addition of other variables which reflect fetal condition may make training and interpretation more complicated. An Expert Systems approach to data processing and interpretation may be the only way in which the full potential of electronic fetal monitoring will be realised in clinical practice.

Chapter Seven

Summary and Conclusions

Summary.

- Dissatisfaction with the electronic recording of fetal heart rate and uterine contractions has resulted in a search for new techniques for monitoring the fetus during labour. It is important that each method has a sound physiological and pathophysiological basis, a model for the interpretation of changes and is thoroughly evaluated before introduction into clinical practice.

- Analysis of the ST waveform of the fetal electrocardiogram is the most advanced of the new techniques under investigation. Experimental studies have shown that elevation of the ST waveform occurs with a switch to myocardial anaerobic metabolism and that a negative waveform occurs during direct myocardial ischaemia. Human observational studies have suggested that a combination of ST waveform and CTG analysis may improve the specificity of intrapartum monitoring and reduce unnecessary intervention.

- A high quality FECG signal is necessary for waveform analysis; rubbish in, rubbish out. The FECG can be recorded from a fetal scalp electrode (FSE) during labour. The suitability of 5 commonly available FSEs for waveform analysis was compared. Single spiral FSEs had the most favourable physical and electrical properties and produced the best quality signals in a randomised clinical trial of 50 fetuses in labour.

- The on-line microprocessor system for ST waveform analysis (the ST ANalyser, STAN, Cinventa AB, Sweden) was validated before it was used in clinical studies. The filter characteristics of the system were appropriate for FECG waveform analysis. A number of adjustments to the STAN were recommended to improve signal quality and user-friendliness.

- Intervention rates and neonatal outcome in labours monitored with CTG alone were compared with those monitored with the combination of ST waveform analysis plus CTG (ST+CTG) in a randomised clinical trial of 2434 high risk labours over an 18 month period. There was a 46% reduction in operative intervention for fetal distress in the ST+CTG group ($p<0.001$, OR 1.96, [1.42 to 2.71]). There was a trend to less cord arterial metabolic acidemia ($p = 0.09$, OR 2.63 [0.93 to 7.39]) and fewer low five minute Apgar scores ($p = 0.12$, OR 1.62 [0.92 to 2.85]) in the ST+CTG arm.

- All recordings from the trial were reviewed retrospectively, blind to outcome and classified as normal, intermediate or abnormal according to the trial protocol. There was no significant difference in the proportion of recordings in each category between the trial arms. Operative intervention in the ST+CTG arm was significantly reduced in recordings classified as normal and intermediate by the review (12/1043 ST+CTG arm versus 48/1066 CTG arm, $p <0.001$, OR 0.25 [0.12 to 0.48]).

- Three patterns of ST+CTG change were identified.

1. Normal CTG, persistent stable ST waveform elevation. These fetuses had a good outcome and a significantly higher mean pH (7.29 [7.27-7.30]) and lower BDecf (1.1 mmol/l [0.3-1.9]) at delivery. The raised ST waveform may reflect sympathoadrenal stimulation from the general arousal of labour or a response to mild but compensated hypoxaemia and is in keeping with experimental data.

2. CTG abnormal, progressive elevation in ST waveform. All cases occurred towards the end of the second stage. These fetuses had a significantly lower mean pH (7.05 [7.02-7.08]) and higher base deficit (7.6 mmol/l [6.1-9.1]) than all other groups. This combination identified fetuses who were developing a metabolic acidosis as a result of significant hypoxia.

3. Abnormal CTG and a negative ST waveform. All cases with persistently negative waveforms were depressed at birth, required resuscitation and had low arterial pHs (where available); one died and one had transient neurological abnormalities. This high risk group probably had depleted myocardial glycogen reserves and suffered direct myocardial hypoxia, as seen in animal studies.

- These findings indicate that ST waveform analysis can discriminate CTG change during labour. The protocol is safe and depends upon adequate education and training of staff. The combination can result in a reduction in unnecessary intervention and has the potential to more accurately identify fetuses at risk of neonatal morbidity. Use of this technology also offers significant health care gain in terms of reduced morbidity and reduced delivery costs due to lower operative intervention rates. Further randomised trials in other units are required to confirm these findings and to provide further data to assess the possible effect on improved neonatal outcome.

- The retrospective review of trial recordings revealed significant difficulties with fetal blood sampling. Patient selection had been poor with 39% of FBS cases in each trial arm performed unnecessarily whilst 33% (CTG arm) and 23% (ST+CTG arm) of those who should have had a FBS did not have this done. The severity of CTG abnormality had no effect on the time from the onset of CTG change to FBS. Only 43% (CTG) and 53% (ST+CTG) of the emergency LSCS performed for fetal distress were preceded by a FBS. The use of FBS did not prevent subsequent poor outcome.

- FBS provides an intermittent variable which requires an extra invasive procedure which is inconvenient and uncomfortable for both mother and obstetrician and thus is infrequently used in clinical practice. FBS and the CTG are not independent variables. The decision to obtain a FBS depends upon interpretation of the CTG. If this is suboptimal, the value of FBS will be limited. Correct use of the information obtained at FBS requires an understanding of the events of labour and of the physiology of acid-base balance during labour.

- The second stage was identified as a crucial time for a fetus in labour. Half of the birth asphyxia cases studied in the review were associated with problems in the second stage. Most were well grown and supposedly 'low' risk. Cord problems were associated with the majority of cases. In the second stage contraction strength and frequency increase so there is less time for placental gas exchange and fetal hypoxaemia increases. Fetal reserves may have been depleted during the first stage, particularly if this has been long or associated with uterine hyperstimulation. The second stage is also the time when obstruction in a nuchal or very twisted cord is most likely to occur further impairing gas exchange.

- Despite the high level of training and education associated with the trial, the majority of birth asphyxia cases in this study had very obvious CTG abnormalities which should have precipitated intervention or more timely intervention. The term 'monitoring' implies a degree of automatic surveillance but this is not the case. Current intrapartum CTG monitoring relies on subjective interpretation of the available information, frequently by junior, inexperienced staff.

- The randomised trial also demonstrated the lack of appropriate measures of neonatal outcome with which to judge the effectiveness of fetal monitoring. The use of generic terminology such as 'birth asphyxia' or 'acidosis' which have varying definitions has caused much confusion and should be avoided. There is unlikely to be one 'gold standard' measure of neonatal condition at delivery.

- Analysis of cord artery and vein blood gas status at delivery can provide useful information about fetal oxygenation prior to delivery but currently the information is poorly used, if at all. Use of erroneous data, inappropriate measures of 'acidemia', failure to distinguish between respiratory and metabolic components and unphysiological expectations about relationships to other measures of neonatal outcome were some of the problems highlighted in a review of cord blood gas data from the trial.

- The importance of accurate interpretation of data was highlighted by the retrospective review. Given the realities of staffing situations and the levels of expertise available in hospitals throughout the country, it is most likely that consistent, optimal interpretation of the information in the CTG, ST waveform analysis, or any new technology, will only be achieved with a degree of automatic data processing and interpretation.

- The use of Expert Systems technology may allow the knowledge of expert clinicians to be incorporated into a computerised system which can support the decision making of junior or inexperienced clinicians. These systems can explain the reasoning behind their recommendations so may have a useful teaching role. The feasibility of representing expert clinical knowledge to provide consistent, accurate interpretation of the CTG has been demonstrated in two clinical studies.

Conclusions.

The work of this Thesis has attempted to place the clinical interpretation of electronic fetal monitoring on a more scientific basis. Intrapartum monitoring is a somewhat emotive subject so it is not too surprising to find that the CTG was first heralded as the key to preventing fetal death and handicap. Now the pendulum has swung almost as far in the opposite direction so that it is regarded as disappointing and unsatisfactory and is blamed for much unnecessary operative intervention. The truth of the matter probably lies in the old saying 'a poor workman blames his tools' - either because he has chosen the wrong tool for the job or because he is not using it as skilfully as is required.

The CTG is a useful, but rather blunt tool. This thesis has shown that ST waveform analysis of the fetal ECG provides the obstetrician with an additional and more specific tool which reflects the function of a vital central organ, the heart. Furthermore, it is a continuous variable which is available from the same signal source as the CTG. This has been the first time that a new concept for intrapartum monitoring has been tested in a randomised trial *prior* to introduction into clinical practice. The importance of ST waveform shape has been highlighted. Contraction related changes should be investigated further and the technology of the ST ANalyser should be updated.

The CTG and fetal blood sampling are currently used rather poorly in clinical practice. There is little point in providing clinicians and midwives with large amounts of complex information, be it CTG, ST waveform or acid-base status, if they are unable to interpret it correctly. Education and training in CTG interpretation have not produced satisfactory results despite 25 years of clinical use. Given the realities of labour ward staffing situations and the levels of expertise available in hospitals throughout the country, it is most likely that consistent, optimal use of the information provided by electronic fetal monitoring will only be achieved with some degree of automatic data processing and interpretation. The feasibility of a computerised expert system for the interpretation of CTG changes has been demonstrated. This work will be extended in further studies and eventually will include an expert system for ST waveform analysis.

There is a lack of appropriate measures of neonatal outcome with which to judge the effectiveness of electronic monitoring tools. Many of the current measures are inappropriate because they are used in isolation. Analysis of cord artery and vein blood gas status at delivery can provide useful information about fetal oxygenation prior to delivery but currently the information is poorly used, if at all. The use of generic terminology such as 'birth asphyxia' or 'acidosis' which have varying definitions has added to this confusion and should be avoided. There is unlikely to be one 'gold standard' measure of neonatal condition at delivery.

Appendices

Appendix One. **Summary of new and existing methods for intrapartum fetal surveillance.**

Modified from Greene & Rosén, Plymouth Perinatal Asphyxia Meeting, 1992.

Each method has been assessed according to three important requirements; the pathophysiology, available technology and potential clinical usefulness. A summary of how well each requirement is fulfilled is given by the symbol allocated in each category;

? - unknown, (+) - possibly, + - fulfils some requirements, ++ - fulfils most requirements and +++ - best fulfils the requirements.

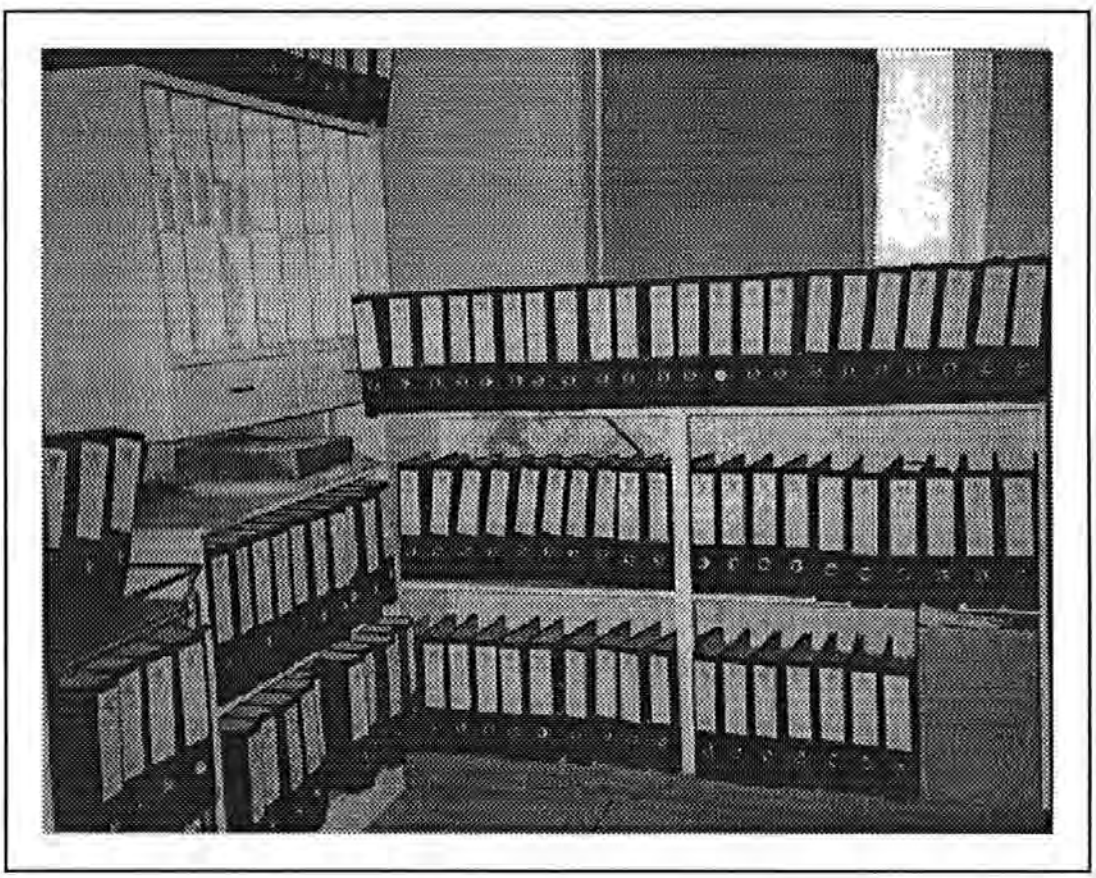
Method	Pathophysiology	Technology	Clinical usefulness	References
Continuous CTG	+ Empirical knowledge Limited experimental data Complex Primary variable	++ Robust Requires subjective interpretation	++ Long experience, routine use Identifies normal Randomised trials ? Quality of interpretation	Court & Parer, 1984 MacDonald et al, 1985 Parer, 1990 Murphy et al, 1990
ECG time constants	(+) Relationship of PR to RR intervals. Heart rate dependent	(+) Patented technology Not widely available	(+) ? Deceleration discriminator Limited observational data	Murray, 1986 Widmark et al, 1991
ST waveform analysis	+++ Reflects myocardial metab-olism; elevation- glycolysis & catecholamines; biphasic & negative- direct hypoxia	+(+) Available Improvements necessary	+(+) Observational data	Greene, 1987 Rosén et al, 1992

Fetal blood sampling	+(+) Reflects placental function Mixed variable	+ Intermittent Cumbersome Gives a figure	+(+) Not widely used ? Interpretation	Saling & Schneider, 1967 Beard et al, 1967 Clarke & Paul, 1985 Whebble et al, 1989
Continuous tissue pH	+ As above Does not distinguish metab-olic and respiratory acidosis	(+) ? Attachment ? Calibration	? Some observational data Tonsure effect ? Significant level ? Trend analysis useful	Weber & Hahn-Pedersen, 1979 Nickelsen & Weber, 1991
Continuous tissue pCO_2	+ Mixed variable Respiratory acidosis	(+) ? Attachment ? Calibration	? Tonsure effect, compression effect. ? Significant level ? Trend analysis	Hansen et al, 1984 Schmidt & Saling, 1987 Nickelsen & Weber, 1987
Pulse Oximetry	+(+) Reflects degree of hypoxaemia but not organ O_2 supply. ? equivalence of animal studies	(+) Patented technology ? Attachment ? Signal processing ? Signal quality	? Limited observational data ? Level of significance ? Trend analysis	Johnson 1991, et al, 1991 Jongsma et al, 1991 Swedlow, 1991
Near Infrared Spectroscopy	+? Measure of cerebral blood flow - high priority organ ? Level of significance	(+) ? Attachment ? Signal quality	? Neonatal use Scant observational data	Delpy, 1991 Reynolds et al, 1991 Peebles et al, 1992a & b

Appendix Two.

1. Raw data from randomised trial.

My supervisor was very anxious that I should include evidence of the raw data from the randomised trial in an Appendix. Due to the vast amount of data collected the only way this could be achieved was to include a photograph of the case record forms which are stored in 98 lever arch files in the Perinatal Research Group offices. Each patient record contains a completed case record form (see next page for a copy of this form), the original CTG or STAN recording and the printout of the cord blood gas results from the blood gas analyser.



Appendix Two.

2. Case record form used in randomised trial.

Date Y Y M M D D

Patient ID

Study number

Date of birth

Parity

1 Alive at 28 days
2 Neonatal deaths
3 Stillbirths

Best estimate of gestational age (completed weeks)

Confirmed by ultrasound between 16 and 24 weeks

1 Yes
2 No

Antenatal complications

1 Normal
2 Proteinuric pre-eclampsia
3 Diabetes
4 Suspected IUGR
5 Antepartum haemorrage
6 Others

Drugs in pregnancy (Specify generic names) _____

Presentation

1 Cephalic
2 Breech

Onset of labour

1 Spontaneous
2 Induced

Time of onset of labour D D H H M M

Rupture of membranes

1 Spontaneous
2 Artificial

Time of membrane rupture H H M M

Drugs

1 Oxytocin
2 PG
3 Both

Liquor

1 Clear
2 Meconium
3 None

Analgesia for labour

1 None
2 TENS
3 Pethidine

4 Epidural

5 Others (specify) _____

Time first given (D,D,H,H,M,M) ☐☐☐☐☐☐

H H M M

CTG record (time of onset) ☐☐☐☐

STAN record

Time begun ☐☐☐☐

Time ended ☐☐☐☐

FBS:	**First**	**Second**	**Third**
Time (H,H,M,M)	☐☐☐☐	☐☐☐☐	☐☐☐☐
Cx dil	☐☐☐	☐☐☐	☐☐☐
pH	☐☐☐	☐☐☐	☐☐☐
pCO_2	☐☐☐	☐☐☐	☐☐☐
pO_2	☐☐☐	☐☐☐	☐☐☐
BE (ecf)	☐☐☐	☐☐☐	☐☐☐

Time start second stage ☐☐☐☐

Time of delivery ☐☐☐☐

Mode of delivery ☐

1 SVD

2 Ventouse, for rotation

3 Ventouse, non-rotation

4 Forceps, for rotation

5 Forceps, non-rotation

6 Caesarian, epidural

7 Caesarian, general anaesthesia

Reason for operative delivery ☐

1 Abnormal CTG

2 pH

3 Failure to progress

4 Other

5 Abnormal ECG waveform (specify) _____

Complications of delivery (specify) _____

Birth weight, grams ☐☐☐☐

Birth weight-centile or S.D. ☐☐

SGA ☐

1 Yes

2 No

Sex ☐

1 M

2 F

Placental weight (if available), grams ☐☐☐☐

Cord Arterial

pH

pCO_2

pO_2

BE (ecf)

Cord Vein

pH

pCO_2

pO_2

BE (ecf)

Apgar scores

1 min

5 min

10 min

Time to first breath (min)

Time - Onset of regular breathing (min)

Paediatrician present at delivery?

1 Yes

2 No

Resuscitation

Time of onset (min after delivery)

Duration (min)

Method

1 Facemask only

2 IPPV

Drugs for resuscitation (specify) _____

Admission to SCBU?

1 No

2 Yes

Age when admitted to SCBU D D H H M M

Reason

1 Asphyxia

2 Hypothermia

3 SGA

4 Congenital abnormality - specify

5 Apnoea / Cyanosis

6 Others - specify

First neonatal blood gas

Time H H M M

Route

1 Capillary

2 Arterial

3 UA catheter

pH

pCO_2

pO_2

BE (ecf)

Respiratory support (day) 1 2 3 4 5 6 7

1 None

2 O_2 alone

3 CPAP

4 IPPV

Reason for respiratory support ☐

1 Apnoea

2 Cyanosis

3 Other (specify) _____

Sedation ☐

1 Yes

2 No

Neurology

Reactivity ☐

1 Normal

2 Apathy

3 Hyperexitable

Seizures ☐

1 None

2 Focal

3 General

Tonus ☐

1 Normal

2 Hypotonic

3 Hypertonic

Hypoglycaemia ☐

1 Yes

2 No

Lowest blood glucose _____

Main feeding pattern (day whilst in hospital) 1 2 3 4 5 6 7

1 Breast

2 Bottle

3 Tube

4 IV

Date of discharge from SCBU (M,M,D,D) ☐☐☐☐

Date of discharge from hospital (M,M,D,D) ☐☐☐☐

Diagnosis on discharge (specify) _____

Paediatric follow-up ☐

1 Yes

2 No

Post mortem requested ☐

1 Yes

2 No

Remarks...

Appendix Three.

Secondary analysis of randomised trial entries who recieved the allocated treatment.

Table 1. Randomisation details.

	CTG n=1212	ST+CTG n=1188	p value	Odds ratio (95%CI)
Maternal age (years) mean SD	26.5 5.4	26.3 5.3	>.05	(-0.23-0.63)[1]
Gestational age (weeks) mean SD	39.6 1.6	39.6 1.6	>.05	(-0.13-0.13)[1]
Primigravidae	821	805	.97	0.99 (0.84-1.19)
Antenatal complications Total - preclampsia - previous LSCS - growth retardation - antepartum haemorrhage - post dates (≥42 weeks) - others[2]	230 33 17 27 19 76 58	256 39 17 24 12 97 63	.13 .49 .91 .83 .30 .09 .63	0.85 (0.70-1.04) 0.83 (0.52-1.32) 0.99 (0.51-1.95) 1.11 (0.63-1.93) 1.56 (0.75-3.23) 0.75 (0.55-1.03) 0.90 (0.62-1.29)
Breech	25	270	.83	0.91 (0.52-1.57)
Inductions	393	437	.03	0.83 (0.70-0.98)
Epidural analgesia	663	689	.11	0.88 (0.74-1.03)
Meconium liquor	202	196	.96	1.01 (0.82-1.26)
Birth weight (grams) mean SD	3364 502	3386 517	>.05	(-97.3-53.3)[1]
Birth weight < 10th centile	43	36	.51	1.18 (0.75-1.85)

1. 95% CI for differences between means.
2. hypertension, diabetes, reduced fetal movements, urinary tract infection, asthma, polyhydramnios, anaemia.

Table 2. Fetal blood sampling by numbers of cases and number of samples.

	CTG n=1212	ST+CTG n=1188	p value	odds ratio	95% CI
Number of cases	114	90	.13	1.27	(0.95-1.69)
Number of samples	168	125	.02	1.37	(1.07-1.75)

Table 3. Indications for operative delivery.

	CTG n=1212	ST+CTG n=1188	p value	odds ratio	95% CI
Abnormal FBS pH	19	15	.65	1.25	(0.63-2.46)
Abnormal trace	92	45	<.001	2.09	(1.45-3.01)
Total deliveries for 'fetal distress'	**111**	**60**	**<.001**	**1.88**	**(1.45-2.60)**
Deliveries for 'failure to progress'	267	269	.76	0.97	(0.80-1.17)

Table 4. Mode of delivery for 'fetal distress'.

	CTG n=1212	ST+CTG n=1188	p value	odds ratio	95% CI
LSCS	30	15	.04	1.98	(1.06-3.710)
Rotational forceps	13	9	.55	1.42	(0.61-3.34)
Vacuum	10	5	.32	1.97	(0.67-5.78)
Non rotational forceps	58	31	.006	1.88	(1.20-2.92)
Total	**111**	**60**	**<.001**	**1.88**	**(1.36-2.60)**

Table 5. Neonatal outcome.

	CTG n=1212	ST+CTG n=1188	p value	odds ratio	95% CI
Cord artery pH<7.15	101	107	.61	0.92	(0.69-1.22)
Cord artery pH<7.05	25	22	.82	1.12	(0.62-1.99)
Metabolic acidosis; cord artery pH <7.05 & BDecf>12mmol/l	13	5	.11	2.57	(0.91-7.22)
Apgar at 5 min <7	32	20	.12	1.58	(0.90-2.79)
SCBU admissions	31	23	.41	1.33	(0.77-2.29)
Birth asphyxia	4	3			

Appendix Four.

Cases of birth asphyxia in babies of at least 34 weeks gestation who delivered during the trial period but who were not entered into the trial.

Parity & gestation	Intrapartum trace	Mode of delivery	Weight (grams)	artery & vein pH & BDecf (mmol/l)	Apgars at 1 5 & 10'	Resuscitation	Neonatal course
Primigravida, 36 W backache, unwell tense uterus	Antenatal CTG; absent variability, shallow late decelerations. ARM & synto, bradycardia 2hrs later.	LSCS	3100g	NA	stillborn	20 minutes failed	
Primigravida, 36 W absent fetal movements 24 hrs	Antenatal CTG; absent variability, shallow late decelerations. ARM & synto, bradycardia 10 mins later.	LSCS	1993g	6.85, NA 7.05, NA	0, 0, 3, 5^{15}, 5^{20}	20 min IPPV	Fitted, DIC, died day 6.
Multigravida, 38 W	Monitored by intermittent ausculation. Intrapartum abruption.	LSCS	2635g	6.93, 22 6.99, 18	0, 0, 3 5^{15}, 6^{20}	20 min IPPV	Fitted, DIC, spastic quadriplegia at 1 year
Primigravida. 37 W small APH at 37 W	External CTG normal 60 min, then sudden bradycardia.	LSCS	2615g	vein 6.98, 15	2, 6, 8	5 min IPPV	Hypoglycaemia
Multigravida, 41 W	Induction ARM, small APH. External CTG, record lost at second stage.FSE applied 30 min later, FHR 60/min.	forceps	3535g	NA NA	1, 5, 6	20 min IPPV	Ventilated, cardiovascular collapse, Hb 6g/L. Died at 6 hours.
Primigravida, 40 W	Spontaneous labour, first stage external CTG, second stage intermittent auscultation. 45 min decelerations & bradycardia, cord around neck.	SVD	2615g	NA NA	3, 5, 8	5 min IPPV	Hypoglycaemia.

Multigravida, 40 W raised BP, on methlydopa	Induced, external CTG, first stage normal, second stage poor quality, bradycardia, cord around neck.	SVD	3340g	7.04, 13 7.10, 10	3, 5, 6	5 min IPPV	Fitted and ventilated 2 days. Normal at 3 months.
Primigravida, 40 W	Spontaneous onset, first stage external CTG, second stage intermittent auscultation. 40 min bradycardia, cord around neck.	SVD	3180g	vein 6.82, 18	2, 5, 7, 8[15]	15 min IPPV	Ventilated, fitted 14 days. Spastic quadriplegia at 1 year.
Multigravida, 40 W	Spontaneous onset, intermittent auscultation. Bradycardia end first stage & second stage 35 min. Cord around neck.	SVD	3785g	vein 6.80, 20	3, 3, 6	15 min IPPV	Fitted for 8 days. Spastic quadriplegia at 1 year.

Appendix Five.

1. Blood Gas Analyser sampling error.

This was checked by analysing 110 pairs of consecutively introduced samples and comparing pH, pCO_2 and pO_2 results for each pair. The results are shown in Figures 1 A, B and C on the following page.

Estimation of the standard deviation of the sample errors was based on the following assumptions;

sample Y1 = X + E1 and
sample Y2 = X + E2

where Y1 and Y2 are the values given for sample 1 and 2 of each pair, X is the true value and E1 and E2 is a measure of the sampling error for each sample.

Therefore;

E1- E2 = Y1- Y2

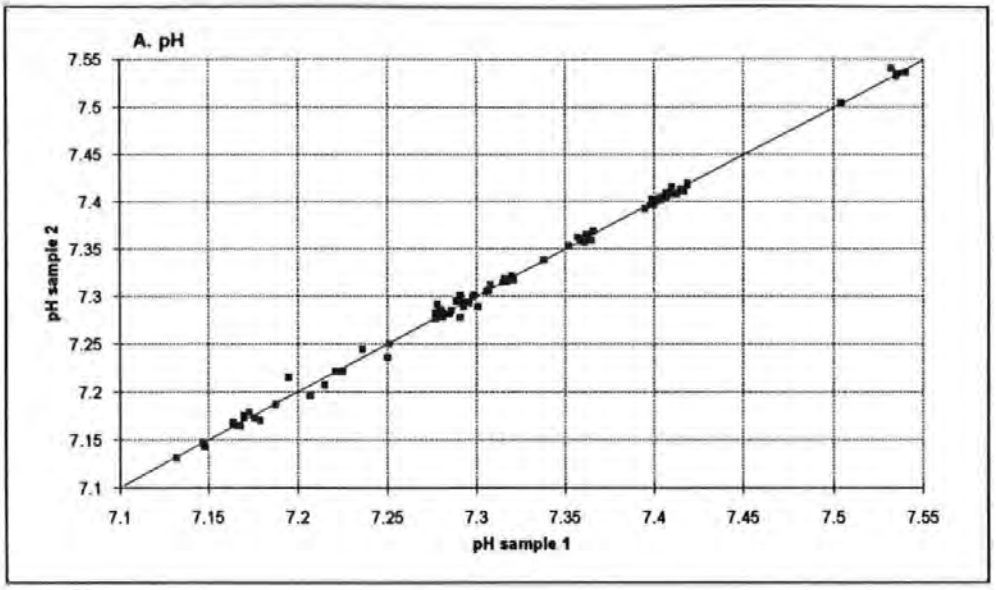
so an estimate of the standard deviation of the errors SDE = $\frac{1}{\sqrt{2}}(SD|Y1-Y2|)$.

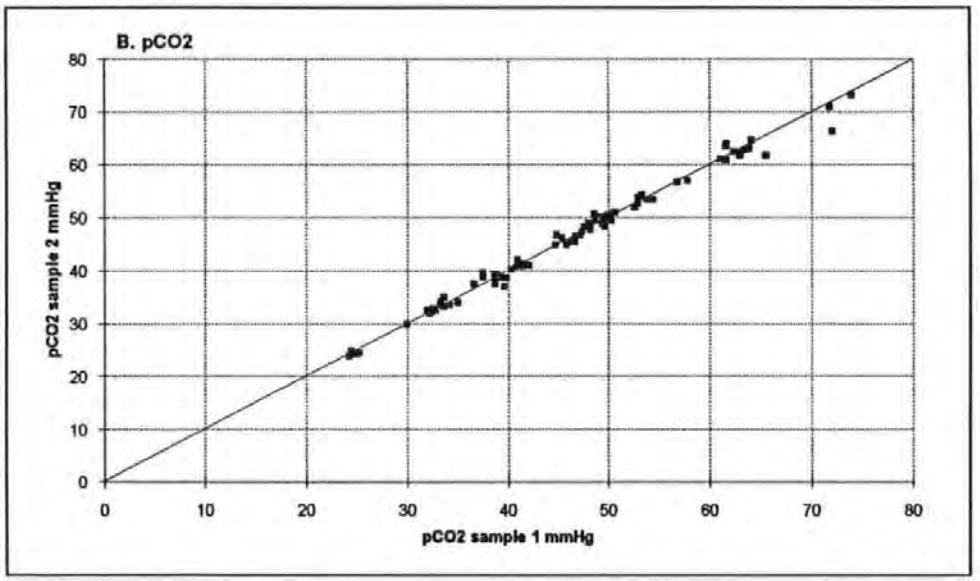
The values obtained from the 110 paired samples are comparable with those quoted in the Corning Manual as can be seen from the following Table.

	Plymouth SDE	**Corning Manual SDE**
pH	0.002	0.002
pCO_2 mmHg	0.55	0.5 to 0.6*
pO_2 mmHg	0.40	0.6 to 0.7†

* varies according to pCO_2 level, † varies according to pO_2 level.

The advice of Dr D Wright, Principal Lecturer, Department of Mathematics and Statistics, University of Plymouth in analysing this data is acknowledged.





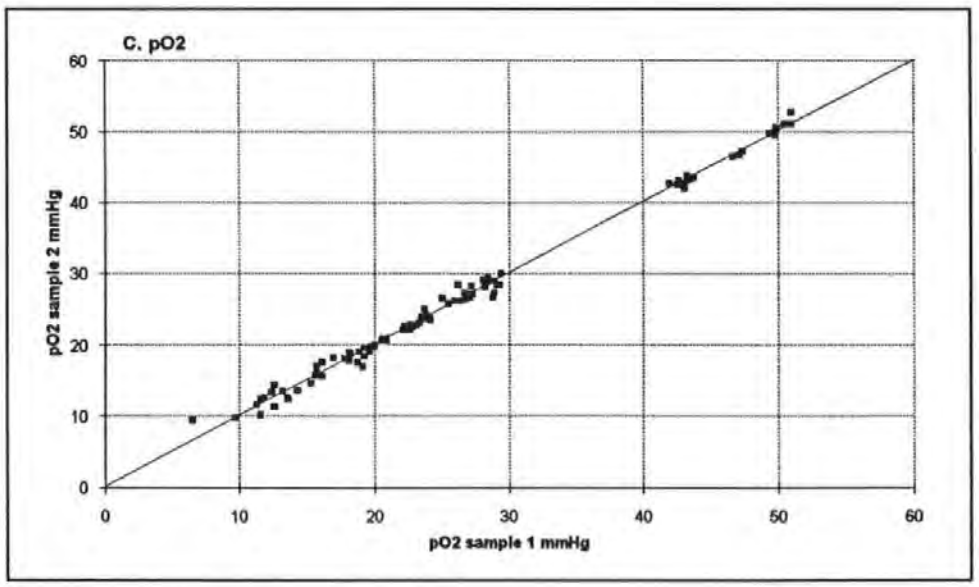


Figure A4.1 Relationship between A. pH, B. pCO_2 and C. pO_2 for results from samples 1 and 2 of consecutively introduced paired samples.

2. Formulae used for calculation of BDecf and BDblood.

A. BDecf.

$$BDecf = -(1-0.023\times Hb)(HCO_3^- - 24.1)+\left[(2.3\times Hb+7.7)(pH-7.40)\right]$$

where;

$$\log HCO_3^- = \log pCO_2 + pH - pK + \log S$$

and Hb = 3.7 g/dl, pK = 6.1 and S = 0.0303

so;

$$HCO_3^- = 0.0303\times pCO_2 \times 10^{(pH-6.1)}$$

and;

$$\boxed{BDecf = -0.9149\times\left[(0.031\times pCO_2\times 10^{(pH-6.1)})-24.1+16.21\times(pH-7.40)\right]}$$

Derived from Siggaard-Andersen, 1976, pages 32 & 32 and Siggaard-Andersen, 1971.

B. BDblood

$$BDblood = -(1-0.014\times Hb)\left[HCO_3^- - 24+(9.5+1.63\times Hb)(pH-7.4)\right]$$

where;

$$HCO_3^- = 0.031\times pCO_2\times 10^{(pH-6.1)}$$

and Hb = 15.0g/dl

so;

$$\boxed{BDblood = -0.79\times\left[(0.031\times pCO_2\times 10^{(pH-6.1)})-24.1+33.95\times(pH-7.40)\right]}$$

Obtained from CIBA Corning 178 pH/Blood Gas Analyser Instruction Manual. CIBA Corning Diagnostics Corporation, 1981, pages 6 & 7.

Appendix Six.

1. List of tables

2. List of figures

List of abbreviations

ADC	analogue to digital converter
ANOVA	analysis of variance
ARM	artificial rupture of the membranes
ATP	adenosine triphosphate
A-V	arteriovenous
BDblood	base deficit in the blood
BDecf	base deficit in the extracellular fluid compartment
bpm	beats per minute
CI	confidence interval
CTG	cardiotocogram
DHSS	Department of Health and Social Security
DF	discriminative function
DIC	disseminated intravascular coagulation
ECG	electrocardiogram
EEG	electroencephalogram
EFM	electronic fetal monitoring
ES	expert system
FBS	fetal blood sampling
FECG	fetal electrocardiogram
FHR	fetal heart rate
FIGO	Federation of International Obstetricians and Gynecologists
FSE	fetal scalp electrode
g	grams
GA	general anaesthetic
h	hour
H^+	hydrogen ion
HCO_3^-	bicarbonate ion
H_2CO_3	carbonic acid
HIE	hypoxic ischaemic encephalopathy
Hz	hertz
IPPV	intermittent positive pressure ventilation
IUGR	intrauterine growth retardation
iv	intravenous
K^+	potassium ion
LCD	liquid crystal display
LED	light emitting diode
LSCS	lower segment caesarean section
mmHg	millimetres of mercury
mmol/l	millimoles per litre
MW	midwife
NA	not available
NEC	necrotising enterocolitis
O_2	oxygen
OR	odds ratio
pCO_2	partial pressure of carbon dioxide
pO2	partial pressure of oxygen
PIB	patient isolation box
PAE	post asphyxial encephalopathy
RCOG	Royal College of Obstetricians and Gynaecologists
SCBU	Special Care Baby Unit
SD	standard deviation
STAN	ST ANalyser
SVD	spontaneous vaginal delivery
UK	United Kingdom

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