1
Prepartum and Intrapartum Fetal Monitoring

Ramon Martin

Anesthesia for the obstetric patient is an integral part of labor and delivery. For routine, normal deliveries, anesthesia usually involves providing pain relief with an epidural technique. In pregnancies complicated by either maternal or fetal disease, the role of anesthesia is more central to patient care and can involve close monitoring with invasive lines during labor, fluid management, and discussion with the obstetricians about the timing and type of anesthesia.

Equally important in the dialogue with the obstetricians is an understanding of the techniques used to assess the fetus. During labor and delivery, the fetus is evaluated primarily by fetal heart rate (FHR) monitoring, either electronically or with intermittent auscultation. This technique is only one of several methods to monitor the fetus from the midfirst trimester through birth. As pregnancy progresses, the prenatal record contains a wealth of information not only about the parturient but also about the fetus.

The monitoring of the mother and the fetus during this period of development has evolved considerably as a result of biochemical and technical advances that have yielded a better understanding of the fetus. Most pregnancies proceed and end with no complications. Monitoring techniques are used not only for diagnostic purposes, thereby serving a preventive role, but also are possibly useful in treatment when the fetus is stressed. Stress to the fetus is defined in this chapter as either hypoxia or asphyxia, because the supply of oxygen to the fetus is crucial. Any diminution or cessation of oxygen results in an immediate change in acid–base status, affecting all organs, particularly the heart and the brain. There are compensatory responses by the fetus, but fetal reserves are limited. It is therefore important to recognize the fetal response to stress and, if possible, to identify the cause of the stress and treat it.

This chapter reviews the relevant aspects of fetal respiratory and cardiac physiology to define the fetal response to stress (i.e., asphyxia or hypoxia). The techniques used to monitor the fetus during pregnancy, labor, and delivery are discussed in relation to their effectiveness in determining whether a fetus is stressed.

Fetal Cardiovascular System

Fetal gas exchange occurs via the placenta. Because the fetal lungs are nonfunctional, several shunts in the fetal circulation allow oxygenated blood to pass from the placenta to the systemic circulation. Streaming or laminar blood flow keeps oxygenated blood separate in the venous system and assumes great importance in preferentially supplying oxygenated blood to organs such as the heart, brain, and adrenal glands during periods of hypoxia.

Venous Flow from the Placenta to the Fetal Heart

Approximately 40% of fetal cardiac output goes to the placenta, with a similar amount returning to the right heart via the umbilical vein (Figure 1.1). The blood in the umbilical vein has the highest oxygen saturation in the fetal circulation, so its distribution is important for the delivery of oxygen to fetal tissues. Half the umbilical venous blood enters the ductus venosus, which connects to the inferior vena cava; the rest enters the hepatoportal venous system.[1]

Streaming, which is the separation of blood with differing oxygenation saturations as it flows through a single vessel, is an important determinant of oxygen delivery to fetal tissue. This effect is seen when the more highly saturated umbilical venous blood passes through the ductus venosus into the inferior vena cava to meet the desaturated venous drainage from the lower trunk. In the liver, umbilical venous return is directed toward the left lobe and then portal venous return to the right lobe, so that there is a marked difference in oxygen saturation (higher in the left hepatic lobe than the right).[2,3] Although both hepatic veins enter the inferior vena cava, the left hepatic vein streams preferentially with the blood flow from the ductus venosus[3] whereas the right hepatic vein flow follows the same route as that from the abdominal vena cava.

Preferential flow of the umbilical venous return to the left atrium occurs because of the crista dividens, which splits the

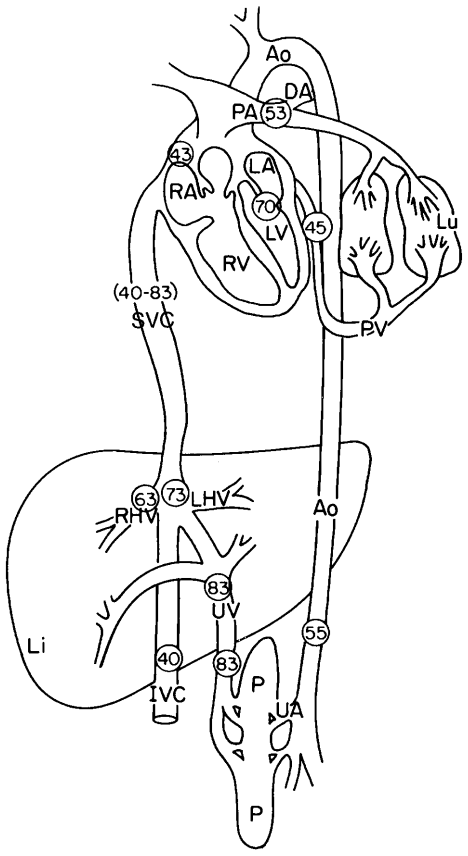

FIGURE 1.1. Normal fetal circulation with major blood flow patterns and oxygen saturation values (*circled numbers* indicate percent saturation). *IVC*, inferior vena cava; *P*, placenta; *Li*, liver; *RHV* and *LHV*, right and left hepatic veins; *SVC*, superior vena cava; *RA* and *LA*, right and left atria; *RV* and *LV*, right and left ventricles; *DA*, ductus arteriosus; *PA*, pulmonary artery; *Ao*, aorta; *Lu*, lung; *DV*, ductus venosus; *PV*, pulmonary vein; *UV*, umbilical vein; *UA*, umbilical artery.

inferior vena cava blood flow into two streams. One stream includes the oxygenated blood from the umbilical vein that is directed toward the foramen ovale and into the left atrium; the other stream consists of deoxygenated blood from the lower extremities and portal vein that enters the right atrium, resulting in a higher oxygen saturation in the left atrium than in the right. Blood flow through the superior vena cava is also preferentially streamed along with blood flow through the coronary sinus via the tricuspid valve. The desaturated blood from the right heart is directed toward the placenta for reoxygenation. The left heart supplies oxygenated blood for the brain.

Cardiac Output

Because of intracardiac and extracardiac shunts, the two ventricles do not work in series, as in adults. Therefore, they do not have the same stroke volume. The right ventricle ejects approximately two-thirds of fetal cardiac output (300 mL/kg/min), and the left ventricle ejects about one-third (150 mL/kg/min). Of the right ventricular output, only a small fraction (8%) flows through the pulmonary arteries. Most of the output crosses the ductus arteriosus and enters the descending aorta, allowing deoxygenated blood to return preferentially to the placenta. The left ventricular output enters the ascending aorta, and most of the output reaches the brain, upper thorax, and arms.[4–6]

TABLE 1.1. Distribution of cardiac output in fetal lambs.

Organ	Blood flow (mL/kg/min)	Cardiac output (%)
Heart	180	2
Brain	125	2
Upper body	25	16
Lungs	100	8
Gastrointestinal (GI) tract	70	5
Kidneys	150	2.5
Adrenals	200	0.1
Spleen	200	1.2
Liver	20	1.5
Lower body	25	20
Placenta	20	37

This distribution of cardiac output to individual organs is shown in Table 1.1. Because flow to the organs below the diaphragm is derived from both ventricles, flow is expressed as a percent of the combined ventricles.

Myocardial Function

The fetal myocardium, relative to the adult myocardium, is immature in structure, function, and sympathetic innervation. Although the length of the fetal sarcomere is the same as that in the adult,[7] the diameter of the fetal sarcomere is smaller, and the proportion of noncontractile mass to the number of myofibrils is less, 30% in the fetus versus 60% in adults.[8] Active tension generated is less than that in the adult heart at all lengths of a muscle along a length–tension curve. Passive or resting tension is higher in fetal myocardium than in the adult, suggesting lower compliance for the fetus.

A study of volume loading by infusion of blood or saline solution in fetal lambs showed that the right ventricle is unable to increase stroke work or output as much as that in the adult.[9] Cardiac output varies directly with heart rate, so an increase in rate from 180 to 250 beats/min will increase cardiac output 15% to 20%. Conversely, a decrease in heart rate below basal levels causes a decrease in ventricular output. Histochemical staining of the sympathetic nervous system demonstrates delayed development. Compared with the adult, isolated fetal cardiac tissue has a lower response threshold to the inotropic effects of norepinephrine, which is presumed to be secondary to the incomplete development of the sympathetic nervous system.[8] As a result, the fetal heart appears to operate at or near peak performance normally.

Control of the Cardiovascular System

The cardiovascular system is controlled by a complex interrelationship between autoregulation, reflex effects, hormonal substrates, and the autonomic nervous system. Although many organs in adults are able to maintain fairly constant blood flow over a wide range of perfusion pressures, the placental circulation does not exhibit autoregulation.[10] As a result, blood flow changes directly with changes in arterial perfusion pressure. Papile et al. demonstrated in fetal lambs that the cerebral circulation is autoregulated.[11] The baroreflex has also been shown to exist in fetal animals. In adults, it functions to stabilize heart rate and blood pressure, but in the fetus it is relatively insensitive. Marked changes in pressure are required to produce minor responses, so that the function of the baroreflex is probably minimal in utero.[12]

The chemoreceptor reflex is governed by receptors in either the carotid body or in the central nervous system (CNS) and causes hypertension and mild tachycardia with increased respiratory activity. Chemoreceptors in the aorta cause bradycardia with a slight increase in blood pressure. The former are less sensitive than the latter, so that bradycardia and hypertension are seen with hypoxia because of the overriding response of the aortic chemoreceptors.

The autonomic nervous system is fully developed in the fetus, as demonstrated by the presence of receptors and acetylcholinesterase and its response to cholinergic or adrenergic agonists. The renin-angiotensin system is also important in regulating the normal fetal circulation and the response to hemorrhage. Angiotensin II exerts a tonic vasoconstriction on the peripheral vasculature to maintain systemic arterial blood pressure and umbilical blood flow.[13] Vasopressin, although detectable in the fetus, probably has little regulatory function. Stress, that is, hypoxia, elicits an increase in vasopressin secretion and results in hypertension and bradycardia.[14] In the presence of decreased cardiac output, the renin-angiotensin system maintains the flow to the brain, heart, and placenta, while flow to the splanchnic bed decreases.[15] Circulating prostaglandins are present in high concentrations in the fetus[16,17] and are produced by both the placenta and the fetal vasculature. Prostaglandins (PGEs) have diverse effects on the cardiovascular system. Infusions of PGE_1, PGE_2, PGF_2, and thromboxane constrict the umbilical–placental circulation,[18,19] whereas prostacyclin has the opposite effect. Prostaglandin E_1, PGE_2, PGI_2, and PGD_2 cause pulmonary vasodilation in the fetus, and PGF_2 produces vasoconstriction.[20,21] Prostaglandins also relax smooth muscle in the ductus arteriosus so that it remains patent in utero.[22,23]

Placental Respiratory Gas Exchange and Fetal Oxygenation

Although fetal viability is seen at earlier gestational ages, a significant amount of morbidity results from the underdevelopment of the respiratory system. After the embryonic period, the airways proliferate and branch from 8 to 16 weeks gestation. Vascular channels appear from 17 to 27 weeks and approximate the potential air spaces; this is when effective gas exchange becomes possible. Surfactant appears and enhances adequate surface tension to keep the alveoli open. Type I and II epithelial cells are also identified. From 28 to 35 weeks gestation, the interstitial spaces thin and the peripheral air spaces develop. There is a gradual increase in the surface area for gas exchange. From 36 weeks on, the number of alveoli rapidly increases, and there is further differentiation of specific cell types.

The passage of oxygen from the atmosphere to the fetus can be described in a sequence of six steps. These steps alternate bulk transport of gases with diffusion across membranes. The first three steps are primarily maternal and the last three are fetal (Figure 1.2).

Transport of oxygen starts from the atmosphere to the maternal alveoli through the large airways by the respiratory muscles, in exchange for carbon dioxide. The pressure of oxygen in the alveoli is regulated by several mechanisms that respond to changes in the levels of the partial pressures of oxygen (P_{O_2}) and carbon dioxide (P_{CO_2}), and the pH of maternal blood. Arterial P_{CO_2} in the parturient is regulated at a lower level than in the nonpregnant woman, secondary to the effects of progesterone.[24]

With the second step, oxygen diffuses rapidly across the alveoli to maternal erythrocytes. The PO_2 of maternal arterial blood is slightly less than that in the alveoli because of shunting and inequality of ventilation and perfusion throughout the lung fields. In the pregnant woman, the gradient of oxygen in the arterioles and alveoli is dependent on position and widens

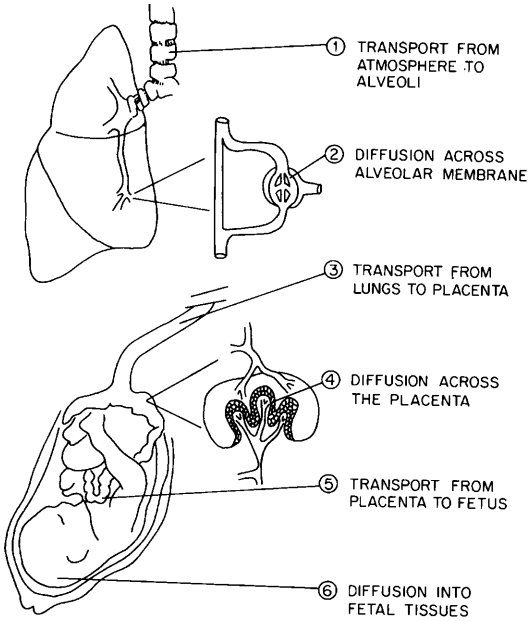

FIGURE 1.2. Six steps in the transport of oxygen from the atmosphere to the fetal tissues.

when she moves from the upright to the supine position. Maternal blood transports oxygen to the placenta in two forms, free and bound to hemoglobin. These two forms are in a reversible equilibrium.

In the diffusion of oxygen across the placenta, the oxygen uptake by the gravid uterus is greater than that by the fetus; this is because, compared with the fetus, the placenta and uterus extract oxygen and consume a relatively large fraction. In chronic sheep preparations, this has been calculated with the Fick principle: uterine oxygen consumption is measured by the difference in oxygen content between the maternal arterial blood (A) and uterine venous blood (V). Multiplying the difference by uterine blood flow (F) yields uterine oxygen uptake:

$$(A - V)F = O_2 \text{ uptake by the gravid uterus}$$

In a sheep study, the umbilical vein was observed to carry the highest concentrations of oxygenated blood delivered to the fetus, but this is low when compared with maternal Po_2. Attempts have been made to explain the low fetal Po_2 with either a concurrent or cross-current model of placental oxygen exchange, but the placenta is probably more complex. Nonetheless, the umbilical venous Po_2 depends on and is not higher than the venous Po_2 of the uterine circulation.[25] In addition, three other factors might contribute to the inefficiency of the exchange process:

1. Shunting: the diversion of blood away from the exchange surface to perfuse the myometrium and endometrium
2. Uneven perfusion: differences in the ratio of maternal–fetal blood flow in portions of the placenta
3. Oxygen-diffusing capacity: defined as the product of the quantity of oxygen transferred from maternal to fetal circulation divided by the mean Po_2 difference between maternal and fetal erythrocytes; this is the result of the permeability of the placental membrane to oxygen transport and the reaction rate of oxygen with hemoglobin.[26]

Uterine venous Po_2, a primary factor that determines umbilical venous Po_2, is in turn influenced by a number of other factors (Box 1.1). Chief among these are the oxygen saturation and the oxyhemoglobin dissociated curve of venous blood. The oxyhemoglobin dissociation curve is shifted by pH so that Po_2 is inversely related to pH (Bohr effect). As a result, maternal alkalosis will shift the curve to the left, decreasing oxygen delivery to the fetus. Other factors that can shift the curve are temperature, hemoglobinopathies, and the 2,3-diphosphoglycerate (2,3-DPG) content of erythrocytes. Oxygen saturation of uterine venous blood (Sv) is a function of four variables: maternal arterial oxygen saturation (Sa), oxygen capacity of maternal blood (O_2Cap), uterine blood flow (F), and the oxygen consumption rate (Vo_2) of the gravid uterus (including placental and fetal oxygen consumption; this can be formulated as follows:

$$Sv + Sa - Vo_2(O_2Cap)$$

which is an application of the Fick principle. Anemic, circulatory, or hypoxic hypoxia will decrease uterine venous saturation, leading to a decrease in fetal oxygenation.

Box 1.1. Factors that determine uterine venous Po_2.

- Oxyhemoglobin dissociation of maternal blood
  - Hemoglobin structure
  - Temperature
  - Erythrocyte pH [2,3-diphosphoglycerate, (2,3-DPG)]
- Oxygen saturation in uterine venous blood
  - Arterial O_2 saturation
  - Uteroplacental blood flow
  - O_2 capacity
  - Placental and fetal O_2 consumption

Although umbilical vein Po_2 is less than that in the maternal circulation, there are compensatory mechanisms to ensure adequate fetal oxygenation. Fetal erythrocyte hemoglobin has a high affinity for oxygen. The rate of perfusion of fetal organs, compared with adult organs, is high in relation to their oxygen requirements. Physiologically, the low level of Po_2 in fetal arterial blood is a part of the mechanism that keeps the ductus arteriosus open and the pulmonary vascular bed constricted.

Supplemental oxygen increases the Po_2 of maternal arterial blood, but causes only a small increase in fetal arterial Po_2, because of the differences in the oxyhemoglobin dissociation curves between mother and fetus (Figure 1.3). Increasing the fractional inspired oxygen (Fio_2) to 100% causes a rise in maternal Po_2 from 90 to 500 Torr, or an increase of 1 mmol for the arterial oxygen content.[27] Because there is no change in uterine blood flow and presumably in uterine oxygen consumption rate, uterine venous oxygen content also increases 1 mmol. The resulting increase in uterine venous Po_2 is 11.5 Torr, which is not to say that supplemental oxygen for the mother has no effect; it probably is more important when the fetus is hypoxic.

As in the mother, carbon dioxide is one end product of fetal metabolism. Carbon dioxide from the fetus diffuses across the placenta from the umbilical circulation to the maternal side for transport to the lungs and excretion. The diffusion process requires that the Pco_2 of fetal blood be higher than that on the maternal side. In sheep, the umbilical venous blood is approximately 5 Torr higher than that in the maternal vein. As a result, perturbations in the maternal acid–base balance are quickly reflected in the fetus. Therefore, fetal respiratory alkalosis (low fetal Pco_2) is secondary to a low maternal Pco_2. Although fetal respiratory acidosis can be caused by a high level of maternal Pco_2, decreased placental perfusion resulting in an adequate gas exchange can also play a role.

Fetal Heart Rate

The average FHR decreases from 155 beats/min at 20 weeks gestation to 144 beats/min at 30 weeks gestation and is 140 beats/min at term. The variability is 20 beats/min in a normal

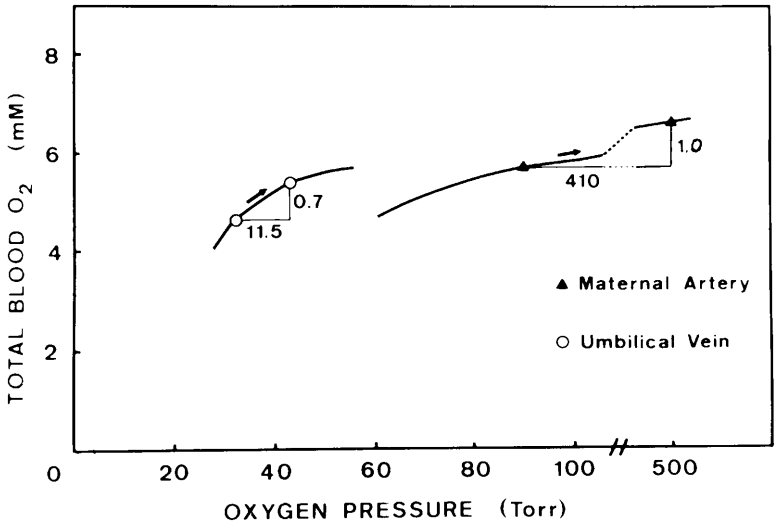

FIGURE 1.3. Relationship between oxygen content and Po_2 in maternal and fetal blood before and after maternal inhalation of 100% oxygen.

fetus. The sinoatrial (SA) and the atrioventricular (AV) nodes serve as intrinsic pacemakers, with the SA node setting the rate in the normal heart. Variability of the FHR is followed either beat to beat or over a longer period and is an important prognostic variable. Control of the FHR is the result of a number of factors, both intrinsic and extrinsic.

The parasympathetic nervous system contributes to cardiac regulation through the vagus nerve. It has endings in both the SA and AV nodes. Stimulation of the vagus nerve results in bradycardia through a direct effect on the SA node. Blocking the vagus nerve results in an increase in heart rate of approximately 20 beats/min,[28] so the vagus nerve exerts a constant influence to decrease a higher intrinsic rate. In addition, the vagus nerve transmits impulses that result in beat-to-beat variability of the FHR.[29]

The sympathetic nervous system has nerve endings throughout the myocardium at term. Stimulation of the sympathetic nerves causes release of norepinephrine and an increase in heart rate and contractility and therefore cardiac output. If the sympathetic nerves are blocked, there is an average decrease of 10 beats/min in the FHR.

The sympathetic and parasympathetic nervous systems are modulated by other factors. Chemoreceptors located in both the peripheral nervous system and the CNS exert their primary effect on the control of respiration, but they also have an effect on the circulation. With a decrease in arterial perfusion pressure or an increase in carbon dioxide content, a reflex tachycardia develops leading to an increase in blood pressure. Baroreceptors are located in the arch of the aorta and at the junction of the internal and external carotid arteries and are sensitive to increases in blood pressure. When pressure rises, impulses are sent via the vagus nerve to decrease the heart rate and cardiac output.

Of the possible hormones that can contribute to heart rate control, three have an effect during periods of stress. Epinephrine and norepinephrine are secreted by the adrenal medulla during stress. Their effects are similar to those caused by sympathetic stimulation: an increase in heart rate, contractility, and blood pressure. The adrenal cortex produces aldosterone in reaction to hypotension; this increases blood volume by slowing renal sodium output, leading to water retention.

Fetal Breathing and Body Movements

Fetal breathing and body movements are important functions during fetal life. The development of skeletal and diaphragmatic muscle is dependent on these movements in utero. Fetal lung development is also dependent on diaphragmatic motion. This movement does have its cost, consuming 15% to 30% of available fetal oxygen supplies.[30] Therefore, absence of either movement or breathing can be a sign of hypoxia.[31,32]

Fetal Breathing

Studies in lambs have demonstrated that breathing movements occur about 40% of the time during observation; this directly correlates with low-voltage electroencephalogram activity and electro-ocular activity.[33] Flow in and out of the trachea to the lungs occurs in conjunction with diaphragmatic motion.[34] In ewes, the frequency of fetal breathing movements decreases from 39% to 7% when hypoxia is induced.[31] Gasping movements occur with asphyxia in dying fetal animal preparations.[35] Two to 3 days before the onset of labor, fetal breathing movements decrease[36,37]; this is thought to be secondary to the rising concentration of PGE_2, which probably plays a role in the onset of labor.[38] Infusing PGE_2[39] or inducing labor with adrenocorticotropic hormone (ACTH),[37] with a subsequent rise in PGE_2, is associated with a drop in fetal breathing movements from 40% to 15% of the time.

A number of other factors can alter breathing activity (Table 1.2). The time of day is very important, particularly during the last trimester. In addition to circadian rhythms, 2

Table 1.2. Factors that alter fetal breathing.

Drug/condition	Effect
Hypoglycemia	Decrease
Glucose infusion	Increase
Ethanol	Decrease
Barbiturates	Decrease
Diazepam	Decrease
Catecholamines	Increase
PGE_2	Decrease
Indomethecin	Increase

PGE, prostaglandin.

to 3 h postprandial, fetal breathing movements increase significantly,[40–45] probably secondary to the increase in maternal blood glucose.[40–45] After either an oral[46] or an intravenous glucose[47] load to the mother, fetal breathing movements increase.[48] During the last 10 weeks of pregnancy, administration of carbon dioxide (5%) to healthy pregnant women results in increased breathing movements,[49] which is thought to represent maturation in the sensitivity of the fetal respiratory center. Maternal ingestion of drugs affects fetal breathing movements. After administration of ethanol[50] or methadone,[51] there is a marked decrease in breathing movements, whereas with maternal cigarette smoking,[52] there is a transient increase in the frequency of a fetal breathing activity. During the 3 days before the onset of spontaneous labor, fetal breathing movements decrease, and they are absent during active labor.[53]

Fetal Body Movements

Fetal body movements are considered significant when the body rolls and the extremities stretch. Isolated limb movement is not of any consequence. During the last trimester, fetal body movements occur on average 3 to 16 min in each hour during a 24-h period of observation.[54] The actual or mean number of fetal body movements ranges from 20 to 50 per hour, but up to 75-min spans of no movement have been recorded in healthy fetuses. Unlike fetal breathing movements, body movements are not influenced by maternal plasma glucose concentration[55] and maternal alcohol ingestion,[50] and they do not decrease during the last 3 days before onset of spontaneous labor.[56] Fetal body movements, however, are closely related to FHR accelerations. Reports show that from 91% to 99.8% of fetal movements are associated with FHR accelerations.[57]

Fetal Acid–Base Physiology

Fetal metabolism results in the production of carbonic and noncarbonic acids that require buffering. Carbonic acid is the hydration product of carbon dioxide, which in turn is the end product of the oxidative metabolism of glucose. Hemoglobin in the fetal erythrocyte buffers the carbonic acid and transports it to the placenta. Carbon dioxide is regenerated and diffuses quickly across the placenta. If maternal respiration and uteroplacental and umbilical blood flows are maintained, then large amounts of carbon dioxide can be eliminated rapidly. On a molar basis, the rate of fetal carbon dioxide production is basically equivalent to the oxygen consumption rate of the fetus.[58] The noncarbonic acids in the fetus include uric acid (from the metabolism of nonsulfur-containing amino acids), lactate, and keto acid (from the metabolism of carbohydrates and fatty acids). These noncarbonic acids are eliminated through the maternal kidneys, after diffusing slowly across the placenta. The maternal kidney regenerates bicarbonate from the excretion of the noncarbonic acids.

Box 1.2. Factors that affect fetal acid–base balance.

- Mother
  - Hypoxia
  - Hypoventilation
  - Altered hemoglobin
  - Metabolic acidosis
  - Decreased blood supply to placenta
- Placenta
  - Infarction or separation
  - Insufficiency
- Fetus
  - Obstruction of umbilical blood flow
  - Fetal anemia
  - Increased fixed acid production

A number of other factors that affect acid–base balance in the fetus disrupt either the supply of oxygen or the removal of the carbonic and noncarbonic acids through the placenta. The maternal, fetal, and placental factors listed (Box 1.2) can result in either respiratory or metabolic perturbations of fetal acid–base balance. Fetal respiratory acidosis is secondary to decreased carbon dioxide elimination, which is most commonly caused by either decreased minute ventilation or V/Q mismatch that results in maternal respiratory acidosis which is reflected in the fetus. As with primary fetal respiratory acidosis, rapidly reversing the cause in the mother restores fetal acid–base balance. Maternal respiratory alkalosis is caused by hyperventilation, which decreases the P_{CO_2}, increases the pH, and responds rapidly to reversal of the causes.

Fetal metabolic acidosis can result from either primary fetal or secondary maternal metabolic acidosis. The decreased pH is caused by loss of bicarbonate and is usually a result of chronic metabolic disorders. With prolonged fetal respiratory acidosis from cord compression or abruptio placentae, the accumulation of noncarbonic acids can result in a mixed respiratory-metabolic acidosis.

Fetal Temperature Regulation

Fetal temperature parallels that of the mother. Heat is produced as a by-product of metabolic processes that consume oxygen. Just as fetal oxygen consumption (approximately 6.8–8 mL/kg/min) is twice that of the adult (3–4 mL/kg/min), fetal heat production is also large compared to the adult. This

heat can be dissipated through either the umbilical circulation or the fetal skin; the former is the major source of heat loss. A decrease in uterine blood flow, as occurs during uterine contractions, might increase fetal temperature. Although this has not been shown directly, indirectly, the maternal and fetal temperature gradient does increase during labor.[59] Epidural anesthesia during labor has been associated with increased maternal temperature, but the mechanism has not been delineated, and there is no evidence so far of a detrimental effect on the fetus.[60]

Fetal Reaction to Stress

During labor and delivery, the main causes of stress for the fetus are hypoxia and asphyxia. Fetal hypoxia is caused by the mother breathing a hypoxic mixture of gases, which results in decreased oxygen tension. Asphyxia is secondary to a reduction of at least 50% in uterine blood flow. In addition to decreased oxygen tension there is also increased carbon dioxide tension, leading to both metabolic and respiratory acidosis. With prolonged asphyxia, the fetus switches to anerobic metabolism and produces a buildup of lactate. Metabolic acidosis subsequently develops. The fetal responses to hypoxia or asphyxia are as follows:

1. Bradycardia (due to increased vagal activity) with hypertension
2. Slight decrease in ventricular output
3. Redistribution of blood from the splanchnic bed to the heart, brain, placenta, and adrenals[61]
4. Decrease in fetal breathing movements (from 7% to 39% of the time)
5. Terminal gasping movements with asphyxia
6. Increased circulating catecholamine levels in fetal sheep
7. Increased alpha-adrenergic activity

In chronically instrumented sheep, fetal oxygen consumption drops by as much as 60% of control values with hypoxia[62]; this is accompanied, as already described, by fetal bradycardia, an increase in blood pressure, and progressive metabolic acidosis. The fetal sheep can tolerate this for approximately 1 h; these changes are rapidly reversed with restoration of oxygenation.[63] Fetal cerebral[64] and myocardial[65] oxygen consumption has been shown to remain constant. When hypoxia is prolonged or proceeds to asphyxia, these compensatory mechanisms are lost.

Transition from Fetus to Neonate

With labor and birth, the fetus becomes a neonate and undergoes a series of physiologic changes. Although these changes affect every major organ system, this section considers primarily the cardiovascular and respiratory systems. With the separation of the placenta, the changes that occur include the following:

1. Blood flow through the inferior vena cava decreases, with a resultant decrease in right atrial blood flow and pressure.
2. Pulmonary blood flow increases as pulmonary vascular resistance falls (secondary to lung expansion and vasodilation of the pulmonary vascular bed).
3. Venous return to the left atrium increases, as well as left atrial pressure.

These changes produce a "series" flow pattern from the fetal "parallel" flow pattern.

Closure of Fetal Shunts

The ductus arteriosus closes in response to a rise in oxygen tension and decreased levels of circulating prostaglandins. The former effect is age dependent, so that premature infants have a decreased response to a rise in P_{O_2}. Glucocorticoids, which are used in premature infants to accelerate fetal lung maturation, decrease this effect. The ductus venosus closes with the fall in partial venous and sinus pressures. Unlike the ductus arteriosus, the ductus venosus is not dependent on changes in P_{O_2} or endogenous levels of catecholamines. The foramen ovale closes because the pressure in the left atrium rises above that in the right atrium. Anatomic closure of all three shunts, although begun at birth, is not completed until 24 h to 3 months after birth.

Cardiac Output

Neonatal cardiac output is 600 to 850 mL/kg/min, a small increase over fetal cardiac output of 500 mL/kg/min. The left ventricular output increases to 2 to 2.5 times that of the fetal left ventricular output, whereas the output from the right ventricle remains basically the same. Neonatal heart rate decreases from fetal levels but can vary from 140 beats/min in the awake infant to 90 to 120 beats/min during sleep.

Respiratory Changes

The intermittent, rhythmic respiratory movements of the fetus become continuous after birth and ensure gas exchange. A number of factors exert an effect:

1. Changes in the physical environment (temperature, sound, and tactile stimulation)
2. Preconditioning changes during labor (increase in P_{CO_2} and a decrease in pH)
3. Increase in P_{O_2} secondary to the cardiovascular changes

With a vaginal delivery, the compression of the head and thorax during the passage through the vaginal canal followed by the sudden expansion with the delivery of the trunk results in an elastic recoil of the thorax and active contraction of the respiratory muscles. This change also stimulates two reflexes:

1. The Herring Breuer inflation reflex: lung inflation results in inspiratory inhibition, which causes a higher respiratory

rate in the neonate and may be important in maintaining a higher functional residual capacity (FRC).
2. Head's reflex: an increase in inspiratory effort with rapid lung inflation.

Reabsorption of amniotic fluid from alveolar air spaces, along with an increase in lung volume, results in a rise in lung compliance with birth that gradually continues to rise in the hours after birth. In premature infants, both lung volume and compliance are decreased and are further decreased in infants with respiratory distress syndrome (RDS). Airway and pulmonary resistance, although initially high at birth, decreases with age as the diameter of the airways becomes larger. FRC increases quickly after birth as amniotic fluid is reabsorbed. The respiratory rate, initially 60 to 80 breaths/min, gradually decreases to 30 to 40 breaths/min. Tidal volume is 5 to 7 mL/kg body weight. Minute ventilation ranges from 150 to 250 mL/kg/min.

During labor and delivery, uterine contractions decrease uterine blood flow, which in turn can decrease fetal gas exchange. This effect can also be produced by cord compression or partial separation of the placenta, resulting in relative hypoxia and hypercapnia at birth in neonates. These effects are transient in most neonates because the start of regular breathing improves oxygenation.

Perinatal Mortality

According to the National Center for Health Statistics,[66] the perinatal mortality rate (PMR) is defined as the number of late fetal deaths (>28 weeks gestation) plus early neonatal deaths (infants 0–6 days of age) divided by 1000 live births plus the fetal and neonatal deaths. In the United States, the PMR has declined by an average of 3% per year since 1965.[67] Over the past 6 years, fetal death rate alone has decreased 16%, and neonatal mortality has fallen 21%. Of all fetal deaths, 22% occur between the 36th and 40th weeks of gestation and another 10% occur beyond the 41st week of gestation.

Congenital anomalies account for 25% of perinatal mortality and are the leading cause.[68] Premature labor and delivery was the most common event leading to death in this group. Overall, prematurity with associated RDS was the next most common cause of perinatal death. Intrauterine hypoxia and birth asphyxia account for 3% of the PMR, and placenta or cord complications accounted for 2% of the PMR. Several associated factors identified by Lammer et al.[69] were race (African-American), marital status (single), age (>34 or <20 years), parity (>5), and lack of prenatal care. Multiple gestations were associated with 10% of all fetal deaths, giving a PMR of 50/1000, which is seven times that of singleton pregnancies. More than half of all fetal deaths were associated with asphyxia or maternal causes such as pregnancy-induced hypertension (PIH) or placental abruption.

If the first step to reducing the PMR further is recognizing the causes, then the next step is prevention. A study of perinatal mortality in the Mersey region of England showed that of 309 perinatal deaths, 182 or 58.9% were due to avoidable causes, primarily a delayed response to abnormalities of the progress of labor or FHR tracing during labor and delivery, maternal weight loss with a resulting growth-retarded fetus, and reductions in fetal movement.[70] Antepartum fetal monitoring is the means to decrease these fetal deaths; this is most useful when targeting specific groups of parturients who are at increased risk of perinatal mortality (Table 1.3).

TABLE 1.3. Parturients at increased risk of perinatal mortality.

Maternal disease	Fetal disease
Post-dates gestation	Neonatal asphyxia
Diabetes	Perinatal death
Previous stillbirth	Perinatal death
Pregnancy-induced hypertension	Fetal distress in labor
Maternal age >35 years	Congenital anomalies
Maternal weight loss	IUGR
Premature labor	RDS

IUGR, intrauterine growth restriction; RDS, respiratory distress syndrome.

Techniques of Fetal Assessment

Before 20 weeks gestation, tests are done to assess the fetus for fetal anomalies.

Amniocentesis

Performed before 15 weeks gestation, early amniocentesis is an alternative to chorionic villus sampling to obtain fetal cells for diagnosis of genetic or morphologic abnormalities. The indications for amniocentesis are listed in Box 1.3. Although the success of obtaining cells is the same as for chorionic villus sampling, the disadvantages are primarily those of withdrawal of amniotic fluid. The volume of fluid removed is a much greater proportion of the total fluid volume, which could increase fetal loss.

After 16 weeks gestation, midtrimester amniocentesis with ultrasound guidance is safe with a rate of fetal loss of 0.5% to 1.0%.[71,72] The amniotic fluid is used to grow fetal cells, which in turn are scanned for chromosomal aberrations. During the third trimester, amniocentesis is used to obtain fluid to assess fetal lung maturity.

Box 1.3. Indications for amniocentesis.

- Maternal age 35 years or older at delivery
- History of any chromosomal abnormality in a family member
- Birth of a previous child with Down syndrome or other chromosomal disorder
- Parents at risk for being carriers of X-linked disorders or inborn errors of metabolism
- History of recurrent spontaneous abortions
- Family history of neural tube defects

Chorionic Villus Sampling

Performed between 9 to 12 weeks of gestation, chorionic villus sampling allows early determination of chromosomal abnormalities. Under ultrasound guidance, this technique is simply the aspiration of villi through either the cervix or the abdomen. Because actual tissue is obtained, results from cells are available as early as 24 to 48 h and can also be analyzed for abnormalities in DNA or specific enzymatic reactions. Fetal loss was 2.3% to 2.5% in one randomized trial.[73] Limb reduction defects and oromandibular hypogenesis have been reported in a small number of infants after chorionic villus sampling,[74] but other studies[75,76] have not demonstrated any difference between the expected rates of appearance of these developmental aberrations.

Percutaneous Umbilical Blood Sampling

Starting at 18 weeks gestation, fetal blood can be obtained transabdominally under ultrasound guidance by needle puncture of the umbilical cord, a method useful in diagnosing a range of problems[77]:

1. Hematologic abnormalities, such as hemoglobinopathies, isoimmunization, thrombocytopenia, and coagulation factor deficiencies
2. Inborn errors of metabolism
3. Infections by viruses, bacteria, or parasites
4. Chromosomal abnormalities, especially mosaicism

The risk to the fetus is greater than other tests, with an increase in fetal loss of 2%.[77] As a result, this test is usually reserved for situations in which information cannot be obtained by other means.

Ultrasonography

During the past three decades, ultrasound has become an important method of antepartum fetal assessment. Useful throughout gestation, it gives an accurate measurement of gestational age and provides an assessment of fetal growth as well as developmental abnormalities. It is also an important guide in the performance of amniocentesis, chorionic villus sampling, and cordocentesis. Real-time ultrasound permits a dynamic assessment of fetal well-being by following, over time, fetal breathing activity, movements, and tone.

Despite its importance as a method of fetal assessment, there is still controversy about the routine use of ultrasound in pregnancy. In Helsinki, Finland, which like many other European countries advocates routine ultrasound screening, a randomized trial showed a significant decrease in perinatal mortality in the screened group compared to the control group,[78] primarily due to early detection of fetal malformations. A number of other studies have not found a benefit from routine ultrasound screening.[79,80] A recent large-scale study of 15,151 pregnant women demonstrated no difference in adverse perinatal outcome. Subgroups of women with post-dates gestation, multiple pregnancies, or infants who are small for gestational age did not differ in perinatal outcome between the control and study populations.[81] This controversy is also fueled by the desire to contain medical costs by decreasing unnecessary testing.

During the first trimester, ultrasonography, particularly transvaginal sonography, can help determine whether a fetus is viable, when there is vaginal bleeding, or determine the presence of other processes: ectopic pregnancy, uterine anomaly, or an adnexal mass. In addition, it can provide the first measurement of fetal crown-rump length as a measure of fetal age. During the second trimester, ultrasound assessment of biparietal diameter becomes an accurate measure of gestational age.[82] From 12 to 28 weeks of gestation, the relation between biparietal diameter and gestation is linear.[83] Ultrasound assessment of fetal growth, when continued into the third trimester, is important in diagnosing deviations from normal growth such as growth retardation, macrosomia, or developmental anomalies. Diagnoses of oligohydramnios or polyhydramnios are made by ultrasound. Real-time ultrasound measures variables that are the components of the Biophysical Profile (amniotic fluid volume, fetal breathing, limb movement, and tone). All these measurements can affect the course of labor and delivery.

Doppler Ultrasound Velocimetry

Blood flow in fetal and maternal vessels, particularly the umbilical artery, can be assessed by Doppler ultrasound velocimetry. The Doppler principle is the use of focused sound waves of a known frequency, directed at blood moving in a vessel. The sound waves that are reflected back have a different frequency and are converted to a visual displacement of blood velocity. This technique has been used since 1978 to measure fetal–placental circulation, particularly in high-risk disease states that result in vascular changes.

In a normal pregnancy, blood flows through the umbilical artery even during diastole because of decreased placental resistance. Increased placental vascular resistance, as seen with preeclampsia and resultant intrauterine growth restriction (IUGR), might result in decreased umbilical artery blood flow during diastole. Decreased diastolic flow results in an increased ratio of systolic to diastolic flows (S/D). Absent or reversed diastolic flow is considered potentially ominous and might be associated with either a fetal anomaly or severe IUGR. This finding usually indicates the need for further testing and possible delivery of a fetus. Several other blood vessels in the uterus and fetus have been studied but so far have had few useful clinical correlates.

Analysis of Maternal Serum

Maternal serum is routinely sampled during the first trimester to assess the possibility of neural tube defects and Rh sensitization. Neural tube defects are one of the most frequent con-

genital abnormalities, with an incidence of 1 to 2 per 1000 live births in the United States.

Alpha fetoprotein (AFP) is elevated in the fetal serum during the first trimester when the neural tube fails to close, resulting in anencephaly, meningomyelocele, or encephalocele. Alpha fetoprotein passes through the placenta into the maternal serum and can be measured with a radioimmunoassay. Alpha fetoprotein is also elevated in malformations of the gastrointestinal tract, as well as in fetal death, decreasing the specificity of the test. Despite this, it is still used as a general screening test; with any abnormal values, ultrasonography and amniocentesis are performed for confirmation.

The Triple Screen blood test attempts to predict whether a fetus is at higher risk of having Down syndrome, anencephaly, or neural tube defects such as spina bifida. This test, however, may miss 15% to 40% of fetuses with Down syndrome and has a false-positive rate as high as 8%. As a result, this test is of decreasing interest to both clinicians and patients. Other tests, such as fetal nucleated red cells and urinary hyperglycosalated human chorionic gonadotropin (HCG), are being studied.

Maternal Assessment of Fetal Activity and Uterine Contractions

Asking a parturient to count fetal activity over a period of time provides a simple and sensitive test of fetal well-being. It is based on the fact that from 28 weeks of gestation on, the fetus makes approximately 30 body movements each hour (about 10% of the total time), and the parturient is able to appreciate most of these.[84] Although fetal movement is reassuring, lack of movement can indicate either a quiet period, which can usually last 20 min (but can last as long as 75 min), or fetal compromise secondary to asphyxia. Factors that can decrease maternal appreciation of fetal activity are an anterior placenta, polyhydramnios, and obesity.[85] Several studies have demonstrated that when patients reliably count fetal movements according to a set protocol, there is a significant reduction in fetal death.[86–88]

Because premature labor with resultant delivery of a premature infant is a leading cause of neonatal morbidity and mortality, it was thought that monitoring uterine contractions might predict women at increased risk of preterm labor. Several studies have demonstrated that ambulatory monitoring of uterine contractions does not reduce the rate of preterm delivery.

Assessment of Fetal Lung Maturity

Because fetal chronologic age does not necessarily correlate with functional maturity, particularly in respect to the pulmonary system, methods of assessing fetal lung maturity are important adjuncts in clinical decision making. The majority of perinatal morbidity and mortality results from complications of premature delivery. The most frequently seen complication is the RDS. This disorder is caused by a deficiency of a surface-active agent (surfactant) that prevents alveolar collapse during expiration. Phospholipids produced by fetal alveolar cells are the major component of lung surfactant and are produced in sufficient amounts by 36 weeks gestation. The most commonly used technique measures the lecithin–sphingomyelin ratio (L/S). The concentration of lecithin, a component of surfactant, begins to rise in the amniotic fluid at 32 to 33 weeks gestation and continues to rise until term. The concentration of sphingomyelin remains relatively constant, so that the ratio of the two provides an estimate of surfactant production that is not affected by variations in the volume of amniotic fluid. The risk of neonatal RDS when the L/S ratio is greater than 2 is less than 1%. If the ratio is less than 1.5, approximately 80% of neonates will develop RDS.

Disaturated phosphatidylcholine (SPC) is the major component of fetal pulmonary surfactant. The technique that separates SPC from lecithin in amniotic fluid is complicated, and the results can be altered by abnormalities in amniotic fluid production and excretion (i.e., oligohydramnios or polyhydramnios). A value greater than 500 μg/dL for SPC concentration in amniotic fluid is consistent with mature fetal lungs and a small risk for RDS. However, in diabetic parturients, the SPC value should be 1000.

The disadvantages in measuring the L/S ratio include a long turnaround time, the use of toxic reagents, a lack of technical expertise, and the inability to standardize the test. As a result, few hospitals are able to perform the test. Another test, the TDx fetal lung maturity test, is automated and avoids the technical involvement of sample preparation and measurement. The test relies on the fluorescence polarization of a dye added to a solution of amniotic fluid that is then compared with values on a standard curve to determine the relative concentration of surfactant and albumin. The determined values are expressed in milligrams of surfactant per gram of albumin. With a cutoff of 50 mg/g for maturity, the TDx test was equal in sensitivity (0.96) and more specific (0.88 versus 0.83) when compared with the L/S ratio in one multicenter study.[89]

Biophysical Profile

The biophysical profile involves evaluation of immediate biophysical activities (fetal movement, tone, breathing movements, and heart rate activity) as well as semiquantitative assessment of amniotic fluid. The biophysical parameters reflect acute CNS activity and when present correlate positively with the lack of depression (secondary to asphyxia) of the CNS. Amniotic fluid volume represents long-term or chronic fetal compromise. Major indications for referral for biophysical profile include suspected IUGR, hypertension, post-dates gestation, and diabetes.

The biophysical evaluation of the fetus is done by ultrasound with the sole purpose of detecting changes in fetal activity due to asphyxia. Changes in fetal breathing movements, heart rate, and body movements are indicators of the state of fetal oxygenation. Superimposed on these factors are the nonrandom pattern of CNS output and the sleep state, with effects that might be mistaken for hypoxia. However, extend-

TABLE 1.4. Biophysical profile scoring.

Variable	Score = 2	Score = 0
Fetal breathing movements	One episode, 30-s duration in 30 min	Absent
Gross body movement	Three discrete body/limb movements in 30 min	More than two episodes in 30 min
Fetal tone	One episode of extension/flexion of hand, limb, or trunk	Absent or slow movement
Fetal heart rate (FHR)	Two episodes of acceleration with fetal movement in 30 min	More than two episodes
Amniotic fluid volume	One pocket, 1 × 1 cm	No amniotic fluid or a pocket <1 × 1 cm

ing the period of observation to find a period of normal recovery for the latter conditions helps to differentiate asphyxia from normal variants.

The scoring of the fetal biophysical profile is an assessment of five variables (Table 1.4), four of which are monitored simultaneously by ultrasound. The variables are said to be normal or abnormal and are assigned a score of 2 for normal and 0 for abnormal. The nonstress test (NST) is monitored after the biophysical evaluation. When the test score is normal, conservative therapy is indicated, with some exceptions:

1. Post-date gestation with a favorable cervix
2. Growth-retarded fetus with mature pulmonary indices and a favorable cervix
3. Insulin-dependent diabetic woman at 37 weeks gestation or more with mature pulmonary indices
4. Class A diabetic woman at term with a favorable cervix
5. Women with medical disorders (e.g., asthma, preeclampsia, PIH) that might pose a threat to maternal and fetal health

Table 1.5 lists recommendations for management of biophysical profile scores.

Several prospective studies (Table 1.6) have shown that the majority of women studied (>97%) have normal test results and delivery outcome. Perinatal mortality varies inversely with the last score before delivery. In 1981 and 1985, in large groups of patients, Manning et al.[94,95] found that the gross perinatal mortality rate decreased from 11.7 to 7.4 per 1000 and the corrected value decreased from 5 to 1.9 per 1000. In Manitoba, since the use of this testing, the stillbirth rate has decreased by 30%. A stillbirth occurring within a week of a normal test result is defined as a false negative; this ranges from 0.41 to 1.01 per 1000 with a mean of 0.64 per 1000.

The false-negative rate, although small, directly reflects the negative predictive accuracy of the test. Manning et al.[90] calculated from a study of 19,221 pregnancies a negative predictive accuracy of 99.224%, or the probability of fetal death after a normal test result as 0.726 per 1,000 patients.

Because the ideal testing method would result in no false-negative deaths, the biophysical profile is not perfect. The cause of the imperfection is the probability of change in the fetal status from either a chronic condition or an acute variable. Although more frequent testing of all patients would decrease the false-negative rate, this has not been attempted because of the increased workload. The proper selection of patients requiring more vigilant monitoring (those judged to be at risk, e.g., an immature fetus with growth retardation, preeclampsia, diabetes) would render this more feasible.

Nonstress Testing

Nonstress testing is the external detection of FHR and fetal movement in relation to uterine contractions, noting accelerations of FHR with fetal movement. These parameters are predictors of fetal outcome.

With the parturient recumbent in the semi-Fowler's position and left lateral tilt (to displace the uterus from the inferior vena cava and aorta), 20 min of consistent FHR tracing is followed, and a tocodynamometer is used to measure uterine contractions. Fetal movement is noted either in the mother by external palpation of the maternal abdomen or by spikes in the tocodynamometer tracing.

The test is usually interpreted as either reactive, nonreactive, or of uncertain reactivity[96,97]:

1. Reactive: at least two fetal movements in 20 min with acceleration of the FHR by at least 15 beats/min, with long-term variability of at least 10 beats/min and a baseline rate within the normal range (Figure 1.4)

TABLE 1.5. Interpretation and management of biophysical profile score.

Score	Interpretation	Recommended management
8–10	Normal infant	Repeat test in 1 week[a]
6	Suspect asphyxia	Repeat test in 4–6 h[b]
4	Suspect asphyxia	If >36 weeks, deliver
		If <36 weeks, repeat in 24 h
0–2	Probable asphyxia	Deliver

[a]Repeat test twice a week if diabetic or >42 weeks gestation.
[b]Deliver if oligohydramnios is present.

TABLE 1.6. Biophysical profile and perinatal mortality.

Study	No. patients	No. deaths	Perinatal mortality
Manning et al.[90]	19,221	141	1.92
Baskett et al.[91]	5,034	32	3.10
Platt et al.[92]	286	4	7.0
Schiffrin et al.[93]	158	7	12.6

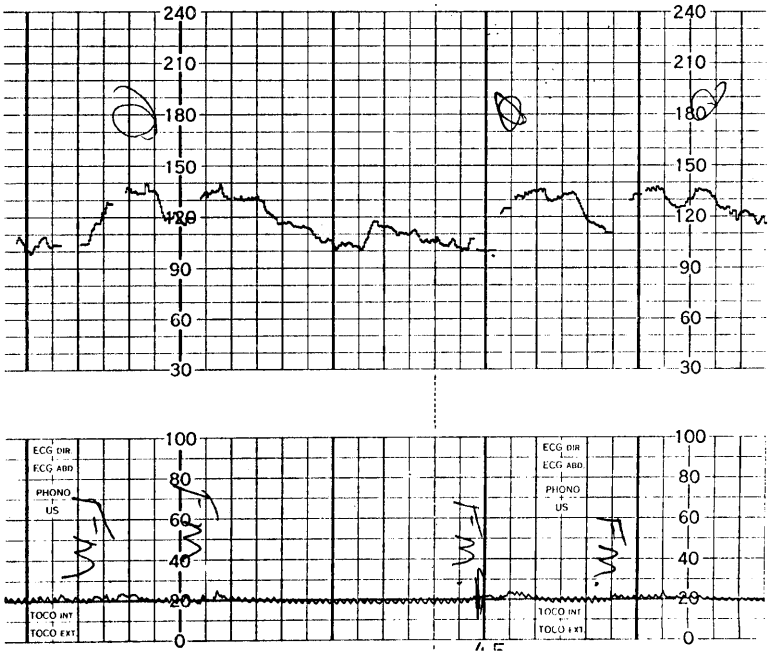

FIGURE 1.4. Reactive nonstress test, characterized by accelerations in the fetal heart rate (*FHR*) (top chart) with fetal movement (*FM*).

2. Nonreactive: no fetal movement or acceleration of the FHR with movement, poor to no long-term variability, baseline FHR may be within or outside the normal range (Figure 1.5)
3. Uncertain reactivity: fewer than two fetal movements in 20 minutes or acceleration of less than 15 beats/min, long-term variability amplitude less than 10 beats/min, baseline heart rate outside of normal limits

Fetuses have sleep or inactive cycles that can last as long as 80 min. The test administrator can either wait for a while or manually stimulate the infant.

A reactive test is associated with survival of the fetus for 1 or more weeks in more than 99% of cases.[96,98] A nonreactive test is associated with poor fetal outcome in 20% of cases.[99] Although the false-positive rate of this technique is high (80%), further evaluation is needed when a nonreactive result is obtained. The next step is usually a contraction stress test (CST). Similarly, an uncertain reactive pattern needs to be followed up with either another NST or a CST.

Contraction Stress Test

As its name implies, the CST assesses the fetal response (heart rate pattern) to regular uterine contractions. Using the same technique as the NST, the CST requires three adequate contractions within a 10-min period, each with a duration of 1 min. If there are not enough spontaneous contractions, augmentation with intravenous oxytocin is indicated. Beginning at a rate of 1.0 mU/min, the infusion is increased every 15 min until the requisite number of contractions is obtained. It is rarely necessary to exceed 10 mU/min.

Certain clinical situations present contraindications to CSTs: prior classical cesarean section, placenta previa, and women at risk of premature labor (premature rupture of membranes, multiple gestations, incompetent cervix, and women undergoing treatment for preterm labor).

CSTs are interpreted as follows:

1. Negative: no late deceleration and normal baseline FHR

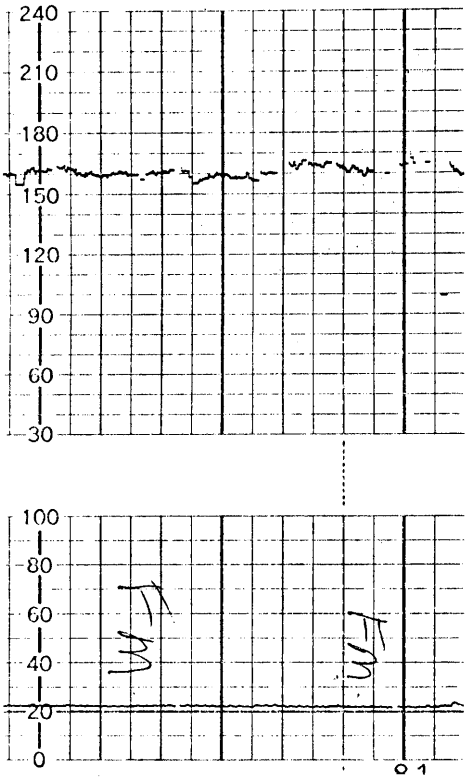

FIGURE 1.5. Nonreactive nonstress test, with no accelerations in fetal heart rate with fetal movement (*FM*).

2. Positive: persistent late decelerations (even when the contractions are less frequent than three contractions within 10 min), possible absence of FHR variability.
3. Suspicious: intermittent late deceleration or variable decelerations, abnormal baseline FHR
4. Unsatisfactory: poor quality recording or inability to achieve three contractions within 10 min
5. Hyperstimulation: excessive uterine activity (contractions closer than every 2 min or lasting longer than 90 s), resulting in late decelerations or bradycardia

A negative CST is associated with fetal survival for a week or more in 99% of cases,[96,97] whereas a positive CST is associated with poor fetal outcome in 50% of cases.[99] As does the NST, the CST also has a high false-positive rate (50%), but the treatment, if delivery is indicated, can be a trial of induction of labor.

Fetal Heart Rate Monitoring

In conjunction with fetal scalp sampling and possibly fetal pulse oximetry to measure acid–base balance, FHR monitoring provides the main method of evaluating the fetus during the antepartum period as a part of nonstress testing, contraction stress testing, and biophysical profile and during labor and delivery. A review by Fenton and Steer[100] documented the historical use of FHR auscultation. FHR auscultation was first described by Marsac in 1650. A number of clinical studies have shown that perinatal morbidity and mortality are increased when the FHR is greater than 160 to 180 beats/min or less than 100 to 120 beats/min. Beginning in the 1940s, FHR was followed over a period of time as a more sensitive indicator of fetal well-being; this developed into continuous FHR monitoring, which charted beat to beat changes in the FHR.

Intermittent auscultation of the FHR is still a widely used means to monitor the fetus. In low-risk patients, this is done every 30 min, listening for 30 s during and after a contraction, when the parturient is in the first stage of labor, and every 15 min during the second stage of labor. In high-risk patients, the frequency of listening is shortened to every 15 min during the first stage of labor and every 5 min during the second stage. Auscultation with a fetoscope or Doppler can detect changes in basal heart rate, variability, and decelerations in relation to uterine contractions. When abnormalities are noted, either fetal scalp sampling or continuous FHR monitoring or both are indicated.

Continuous FHR monitoring entails measuring each fetal heartbeat as well as the interval between two beats, calculating the FHR, and then plotting each successive rate. This procedure can be done externally on the mother's abdomen with a Doppler ultrasound, a phonocardiographic monitor, or an electrocardiogram. An electrode attached to the fetal scalp after rupture of the amniotic membranes provides an internal or direct recording of FHR. Similarly, uterine contractions are measured either externally with a tocodynamometer or internally with a saline-filled catheter placed into the uterine cavity.

Fetal Heart Rate Patterns

The FHR pattern is characterized by its baseline between contractions and periodic changes in association with uterine contractions.[101] The baseline and periodic changes are further broken down into FHR and variability. This section considers the baseline FHR and its variants as well as variability.

Fetal heart rate from 120 to 160 beats/min between contractions is normal (Figure 1.6). Rates greater than 160

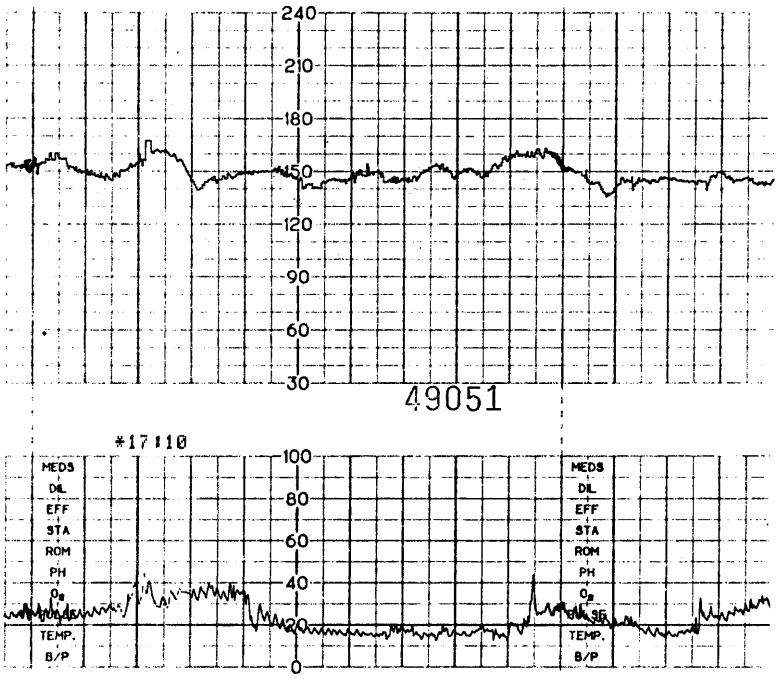

FIGURE 1.6. Normal fetal heart rate (*FHR*) pattern. The heart rate (140 beats/min) and short-term and long-term variability are normal. There are no periodic changes.

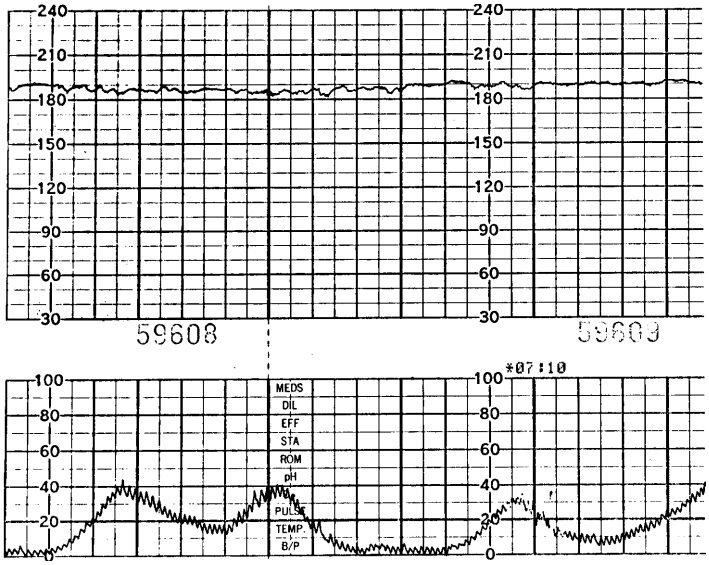

FIGURE 1.7. Tachycardia. In this case, there was a maternal fever secondary to chorioamnionitis.

beats/min are described as tachycardia (Figure 1.7) and those less than 120 beats/min as bradycardia (Figure 1.8). If the alteration in rate is less than 2 min in duration, it is called either an acceleration or a deceleration.

The usual, initial response of the normal fetus to acute hypoxia or asphyxia is bradycardia. A heart rate between 100 and 120 beats/min might either signify a compensated, mild hypoxic stress or be idiopathic and benign. When the heart rate falls below 60 beats/min, the fetus is in distress and requires either reversal of the cause of the bradycardia or emergency delivery. Other causes of bradycardia that are nonasphyxic in origin are bradyarrhythmias, maternal drug ingestion (especially beta blockers), and hypothermia. Tachycardia is occasionally seen with fetal asphyxia or with recovery from asphyxia, but is more likely seen secondary to these events:

1. Maternal or fetal infection, especially choriamnionitis
2. Maternal ingestion of beta mimetic or parasympathetic blockers
3. Tachyarrhythmias
4. Prematurity
5. Thyrotoxicosis

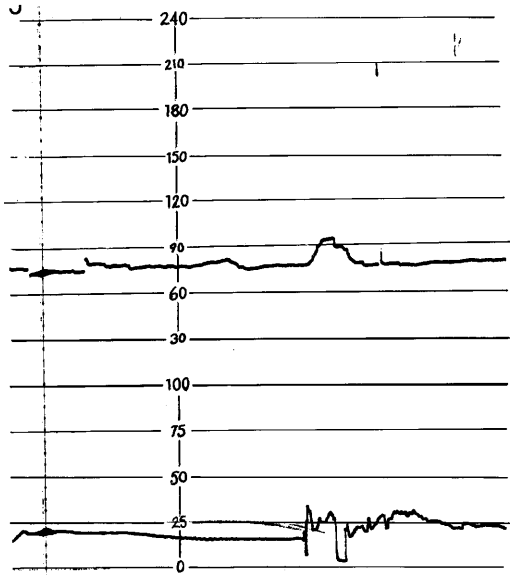

FIGURE 1.8. Bradycardia, accompanied by absence of FHR variability.

Variability in the FHR tracing describes the irregularity or the difference in interval from beat to beat. If the intervals between heartbeats were identical, then the tracing would be smooth (Figure 1.9). In most healthy fetuses, one notes an irregular line, thought to be secondary to an intact nervous pathway through the cerebral cortex, midbrain, vagus nerve, and the cardiac conduction system. It is thought that when asphyxia affects the cerebrum there is decreased neural control of the variability, made worse by the failure of fetal hemodynamic compensatory mechanisms to maintain cerebral oxygenation. With normal variability, therefore, irrespective of the FHR pattern, the fetus is not suffering cerebral anoxia.

Variability is described as being either short term or long term. Short-term variability is the beat-to-beat difference, and it requires accurate detection of the heart rate. Because this can only be obtained with the fetal electrocardiogram, external monitors cannot be used to describe short-term variability, which is characterized as either present or absent. Long-term variability looks at a wider window of the FHR, between 3 and 6 beats/min. It can be detected using either internal or external methods of FHR monitoring and is described by the approximate amplitude range in beats per minute as follows:

1. Normal: amplitude range 6 beats/min or greater
2. Decreased: amplitude range between 2 and 6 beats/min
3. Absent: amplitude range less than 2 beats/min
4. Saltatory: amplitude greater than 25 beats/min.

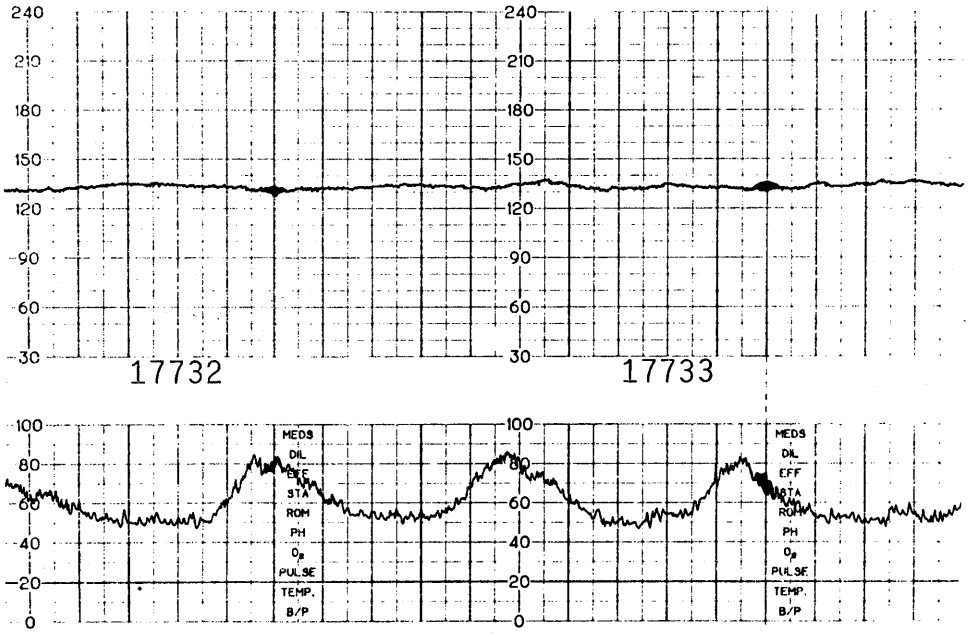

FIGURE 1.9. Decreased variability of the fetal heart rate (*FHR*).

In addition to asphyxia, other causes of altered variability include anencephaly, fetal drug effect (secondary to morphine, meperidine, diazepam, and magnesium sulfate), vagal blockade (due to atropine or scopolamine), and interventricular conduction delays (complete heart block).

Periodic changes in FHR occur in association with uterine contractions. Early decelerations that occur concomitantly with a uterine contraction have a smooth contour and are a mirror image of the contraction (Figure 1.10). The descent of the FHR is usually not more than 20 beats/min below the baseline. The cause is presumed to be a vagal reflex caused by a mild hypoxia but is not associated with fetal compromise. Late decelerations are also smooth in contour and mirror the contraction, but they begin 10 to 30 s after the onset of the contraction (Figure 1.11). The depth of the decline is inversely related to the intensity of the contraction.

Late decelerations have been classified as either reflex or nonreflex. Reflex late decelerations are caused by maternal hypotension, which acutely decreases uterine perfusion to an otherwise healthy fetus. A uterine contraction added to this insult further reduces oxygen flow, causing cerebral hypoxia, which then leads to deceleration. Between contractions, the FHR returns to baseline with good variability. The nonreflex late deceleration is the result of prolonged hypoxia that leads to myocardial depression. Cerebral function is also depressed, as is seen with preeclampsia, IUGR, and prolonged repetitive

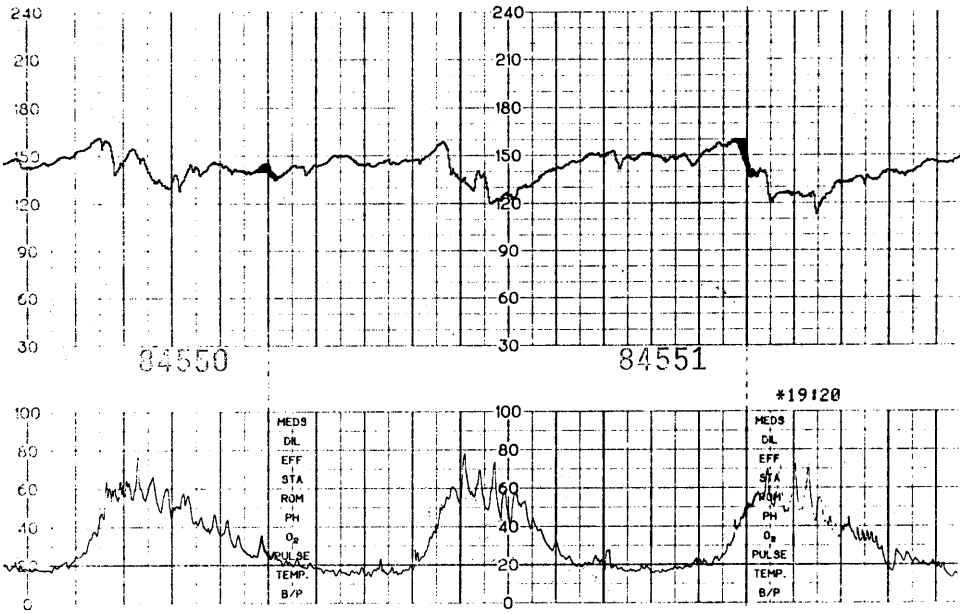

FIGURE 1.10. Early decelerations.

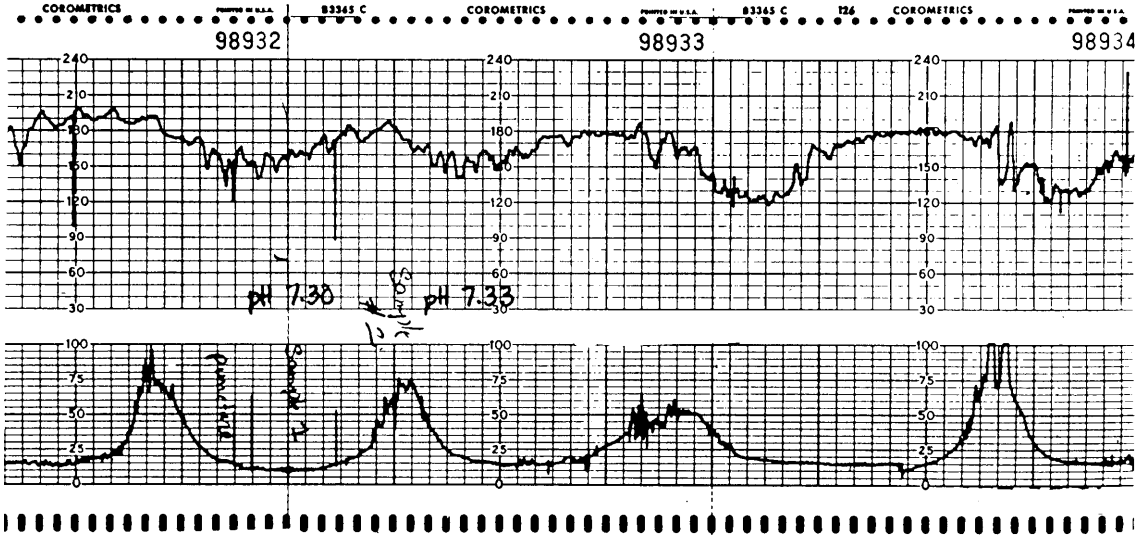

FIGURE 1.11. Late decelerations, with decreased variability of the fetal heart rate (*FHR*) between contractions.

late decelerations. Fetal heart rate variability is either decreased or absent.

Variable decelerations differ in duration, shape, and amount of decrease in FHR from contraction to contraction. The abrupt onset and cessation of deceleration is thought to result from increased vagal firing in response to either compression of the umbilical cord (during early labor) or dural stimulation with head compression (during the second stage of labor). The vagal activity causes bradycardia, which decreases cardiac output as well as umbilical blood flow. Variable decelerations are described as severe when they fall to 60 beats/min below the baseline FHR or last longer than 60 s (Figure 1.12). Otherwise, they are classified as mild to moderate (Figure 1.13). The normal fetus is generally able to tolerate mild to moderate variable decelerations for prolonged periods of time; however, severe variable decelerations eventually result in fetal compromise unless reversed.

Accelerations with uterine contractions represent the greater effect of sympathetic activity over the parasympathetic nervous system (Figure 1.14); these indicate a reactive, healthy fetus and have a good prognostic significance.

The components of FHR just described comprise a normal pattern of a baseline rate of 120 to 160 beats/min, which has a variability of greater than 6 beats/min. One can see either

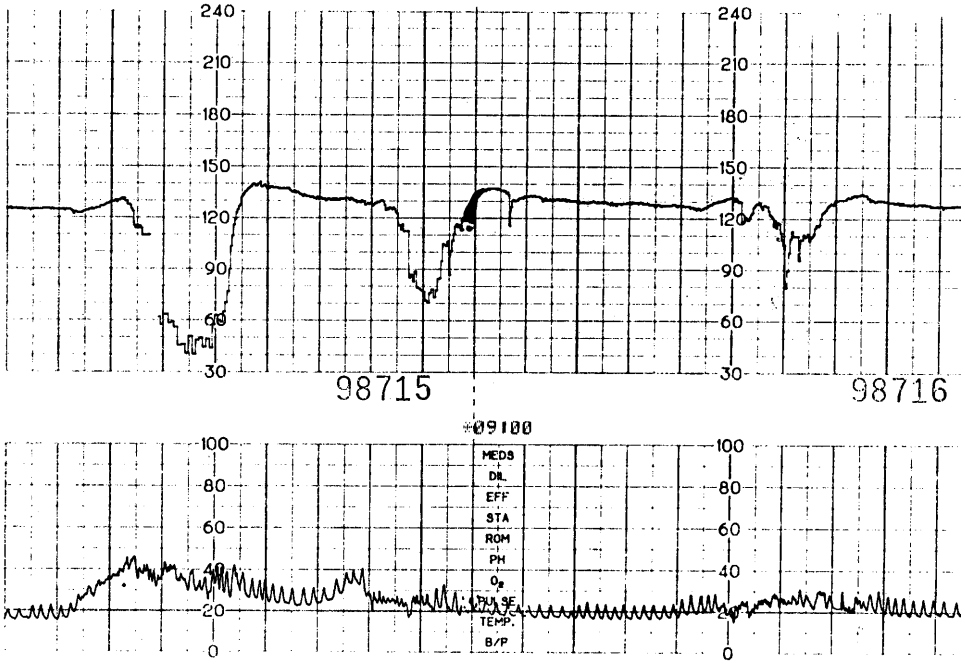

FIGURE 1.12. Severe, deep variable decelerations, with decreased variability of the fetal heart rate (*FHR*) between contractions.

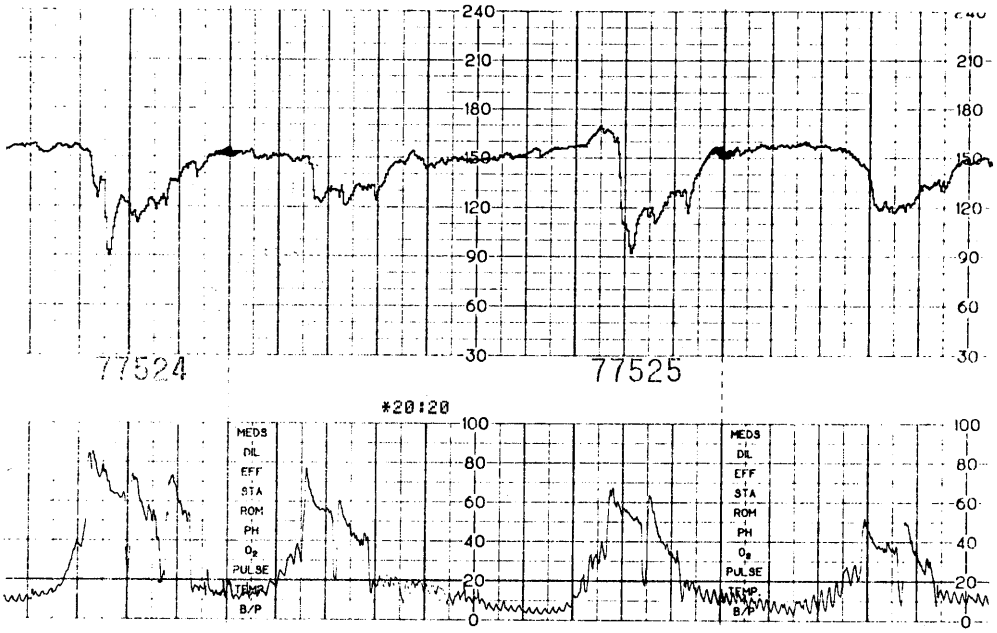

FIGURE 1.13. Mild to moderate variable decelerations with pushing during the second stage of labor.

no decelerations, early decelerations, or accelerations with contractions; this is associated with a good fetal outcome (i.e., Apgar score $>$ 7 at 5 min).[101,102] Depending on the severity and duration of the stress, other FHR patterns are seen.

The acute stress pattern is a compensatory reaction in an otherwise healthy fetus to a short-lived period of asphyxia or hypoxia. The FHR usually demonstrates bradycardia, although tachycardia is also seen, but the most important fact noted is that variability remains normal. There can be either late or variable decelerations. The fetal outcome is generally good,[103] because the impact of the asphyxia is brief, with possible depression from carbon dioxide narcosis, which is rapidly reversible.

When the stress persists, bradycardia is more profound and is associated with decreased variability as well as late or deep variable decelerations. This is a prolonged stress pattern that indicates mounting hypoxic damage to the heart and brain, resulting in the loss of compensatory mechanisms. Unless corrected, fetal death in utero can occur.

For a growth-retarded fetus, already compromised by a placenta with marginal function, persistent asphyxia results in a

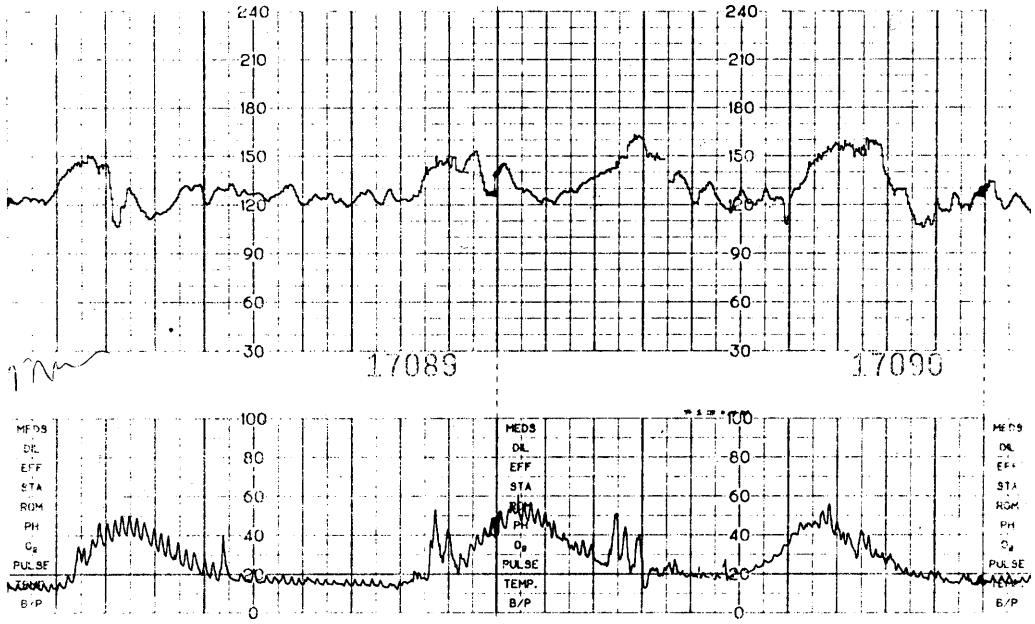

FIGURE 1.14. Accelerations with uterine contractions.

sinister pattern that is characterized by absent variability. The FHR displays severe variable or late decelerations with a smooth rather than abrupt decrease and recovery in heart rate. Persistent bradycardia without variability is also called sinister.

Nonreassuring Fetal Status

In an American College of Obstetrics and Gynecology (ACOG) technical bulletin on Fetal Heart Rate Patterns in 1995, it was pointed out that the term fetal distress is imprecise and inaccurate.[104] Instead of this general label, it was recommended that the term nonreassuring fetal status be used initially, followed by a description of the FHR pattern in terms of type and severity. This recommendation was reaffirmed in February 1998 with an ACOG Committee Opinion that fetal distress implies an ill fetus but has a low predictive value even in high-risk populations.[105] The preferred term, nonreassuring fetal status with a further description (i.e., fetal bradycardia, persistent late decelerations, etc.), imparts more information to the pregnant woman and other care providers. The implications of this are important to anesthesiologists because the description will affect the degree of urgency, mode of delivery, and type of anesthesia needed.

Treatment of Fetal Heart Rate Patterns

The first step in treatment is to recognize and describe an abnormal FHR pattern. The cause must then be identified, and it should be corrected as quickly as possible. Causes and treatment of FHR patterns are presented in Table 1.7. If the pattern does not improve with these measures, then one needs to acquire more direct evidence of the fetal status (i.e., fetal scalp sampling) or to deliver the fetus immediately.

Summary of Electronic Fetal Heart Rate Monitoring

Electronic FHR monitoring is now an important part of fetal assessment during the antepartum period. Its use to diagnose nonreassuring fetal status, whether acute or chronic, has directly affected labor and delivery practice in an attempt to decrease fetal morbidity and mortality. An analysis of the literature by Parer and King, however, suggests that electronic monitoring has poor sensitivity in identifying morbidity and limited sensitivity in predicting its absence.[106] To determine if neonatal neurologic damage could be correlated with FHR tracing, this review of 10 studies found the following:

1. There were several definitions of FHR patterns, making a comparison of data from various centers difficult.
2. Fetal heart rate patterns had a poor predictive value on outcome.
3. A significant number of neonates with poor outcome had no monitoring abnormalities.
4. Monitoring FHR did not lead to effective treatment that had a significant impact on neonatal morbidity.

Although electronic FHR monitoring has been used for more than 30 years, there is no standard associating brain damage with a specific FHR tracing. There has not yet been a study to demonstrate that FHR monitoring either predicts or prevents neurologic morbidity, but this does not deny that electronic FHR monitoring has merit. Rather, it needs to be further refined, standardized, and applied to particular clinical situations where physiologic correlations are possible.

In a technical bulletin,[104] ACOG reviewed the physiologic basis for monitoring FHR patterns, provided guidelines for performing the monitoring, and discussed interpretation and management; this is an attempt to provide standards so that FHR monitoring can be more useful. Despite the questions about its utility, FHR monitoring is still the predominate tool to monitor the fetus during labor and, as such, requires a basic understanding.

Table 1.7. Treatment of fetal heart rate patterns.

Pattern	Cause	Treatment
Bradycardia, late decelerations	Hypotension	IV fluids, ephedrine, change position
	Uterine hyperstimulation	Decrease oxytocin
Variable decelerations	Umbilical cord compression	Change position
	Head compression	Continue pushing if variability good
Late decelerations	Decreased uterine blood flow	Change position, O_2 for mother
Decrease in variability	Prolonged asphyxia	Change position, O_2 for mother

Effects of Epidural Anesthesia on Fetal Heart Rate

The definite effects of epidural anesthesia/analgesia on maternal blood pressure and uterine smooth muscle contractility have also raised concerns about the potential effects on FHR. In addition to local anesthetics (bupivicaine, lidocaine, and chloroprocaine), narcotics are also injected into the epidural space. A number of studies in humans[107–110] have demonstrated no deleterious effects on FHR. Studies[111–114] using Doppler velocimetry of umbilical and uterine arteries demonstrated that epidural anesthesia causes no change in the mean uterine and umbilical artery systolic–diastolic (S-D) ratios in normal parturients at term. In women with preeclampsia, epidural blockade caused a significant decrease in mean uterine artery S-D ratios without a change in the umbilical artery S-D ratio, indicating a decrease in uterine artery vasospasm. There were no changes in FHR. Alahuhta et al.[115] also used M-mode echocardiography to assess fetal myocardial function. Except for an increase in right ventricular end-diastolic dimensions, there was no effect on the fetal myocardial function.

Fetal Scalp Sampling

Since first introduced by Saling[116] in 1967, fetal blood sampling has become the final determinant in making a diagnosis of fetal hypoxia or asphyxia. The fetal blood sample is obtained from the presenting part (scalp or buttock) during labor. The instrumentation and technique of fetal blood collecting are described in many standard textbooks. In this brief discussion, mention is made of the indications for sampling as well as the prognostic significance of values obtained.

Although a full set of blood gas determinations (pH, P_{CO_2}, and P_{O_2}) can be done on as little as 0.25 mL of blood, most institutions obtain a minimal amount of blood for pH determination. The pH value alone does not allow differentiation between respiratory and metabolic acidosis. Treatments of the causes of acidosis are theoretically different. Metabolic acidosis requires immediate delivery, whereas respiratory acidosis should respond to standard resuscitation. In reality, the initial resuscitation measures (oxygen for the mother, uterine displacement, intravenous fluid bolus) are generally begun immediately with any severe deceleration. If a deceleration does not respond quickly to resuscitation, the clinical situation (stage of labor, presence of meconium, estimated fetal weight, gestation age, parity, etc.) will determine whether fetal scalp sampling is needed or if delivery is necessary immediately.

In human newborns, there is good correlation between the pH of scalp blood taken shortly before delivery and that of umbilical cord samples. Beard et al.,[117] correlating scalp blood pH and 2-min Apgar scores, showed that a scalp pH above 7.25 was associated with an Apgar score greater than 7 in 92% of infants. When the scalp pH was less than 7.15, the Apgar score was less than 6 in 80% of cases. Fetal heart rate deceleration has also been found to correlate with pH values (Table 1.8). This correlation is not always close, so fetal scalp sampling is used when there is any question about the FHR tracing.

Winkler et al.[119] evaluated the degree of umbilical artery acidemia with newborn morbidity. Comparing a group of 358 term infants with an umbilical artery pH below 7.20 to a matched control group, they found that only when the pH decreased to less than 7.00 did the incidence of complications increase. For 23 infants with umbilical artery pH less than 7.00, the average 1- and 5-min Apgar scores were significantly lower than the rest of the study and control infants. Only 2 of the 23 infants developed complications (seizures, persistent hypotonia, renal and cardiac dysfunction) secondary to asphyxia. Although both fetal scalp and umbilical artery sampling serve to indicate asphyxia, only the former allows one to alter the management of labor to either reverse the asphyxia or deliver the infant emergently.

TABLE 1.8. Correlation of fetal scalp pH and fetal heart rate pattern.

Deceleration pattern	Scalp pH
Early, mild variable	7.30 ± 0.04
Moderate variable	7.26 ± 0.04
Mild, moderate late	7.22 ± 0.06
Severe late, variable	7.14 ± 0.07

Source: From Kubli FW, Hon EW, Khazin AF, et al. Observations on heart rate and pH in the human fetus during labor. Am J Obstet Gynecol 1969;104:1190.

There are other FHR patterns that signal the need for fetal scalp sampling in addition to persistent late decelerations:

1. Absent or decreased short-term variability, which might be caused by CNS depressants given to the mother
2. Variable deceleration when combined with reduced or absent short-term variability
3. Severe, persistent, variable decelerations

The clinical situation provides indications for fetal scalp sampling, especially if there is decreased variability or severe decelerations.

Pulse Oximetry

Fetal pulse oximetry is being used increasingly as an ancillary test to FHR monitoring to measure fetal oxygen stores, particularly when there might be concern for hypoxia/asphyxia.

Reflectance pulse oximetry is a refinement of conventional pulse oximetry that requires transmitted light and provides a noninvasive method to assess fetal oxygenation. A study by Johnson and McNamara[120] demonstrated, in healthy parturients in labor, that when the sensor was placed between the cervix and the fetal presenting part, there was a significant correlation between fetal oxygen saturation and umbilical vein saturation and pH as well as umbilical artery pH. The relationship of umbilical artery pH and saturation to fetal O_2 saturation was not significant. The range of the values was large: for a fetal oximetry value of 60%, the umbilical vein saturation ranged from 30% to 70% and the pH from 7.25 to 7.38. Values for fetal pulse oximetry varied from 50% to 90% when, with delivery, the umbilical vein pH was generally greater than 7.24. Although there were statistical correlations, the wide range of values suggests a low specificity of the oximeter. Dildy et al. studied 73 healthy parturients in labor and was unable to obtain a reliable signal 50% of the time.[121]

In an ACOG Committee Opinion,[122] Federal Drug Administration (FDA) approval of a fetal pulse oximeter was noted, but the issue of reliability of readings remains an issue. A multicenter trial of fetal pulse oximetry and its usefulness in the management of nonreassuring FHR patterns resulted in an overall reduction (>50%) in the incidence of cesarean births due to nonreassuring fetal status.[123] There was, however, no overall difference in the rate of cesarean birth between the study and control groups because there was an increase in cesarean births secondary to dystocia in the study group.

These studies suggest that the use of the pulse oximeter shows promise, but more prospective, randomized control studies are needed.

Summary

The reduction of perinatal morbidity and mortality is the sole purpose of fetal assessment, which spans the three trimesters of gestation. Chromosomal and developmental abnormalities are the focus of first and early second trimester studies. During the late second and third trimesters, the emphasis shifts to detecting causes of asphyxia and hypoxia. These problems tend to occur more frequently in parturients who have underlying diseases such as diabetes, pregnancy-induced hypertension, drug addiction, malnutrition, and obesity. Although now no single technique can reliably detect asphyxia/hypoxia in a fetus, the potential usefulness and limitations of current monitoring techniques must be understood.

References

1. Edelstone DI, Rudolph AM, Heymann MA. Liver and ductus venosus flows in fetal lambs in utero. Circ Res 1978;42:426–433.
2. Bristow J, Rudolph AM, Itskovitz J. A preparation for studying liver blood flow, oxygen consumption in the fetal lamb in utero. J Dev Physiol 1981;3:255–266.
3. Bristow J, Rudolph AM, Istkovitz J. Hepatic oxygen and glucose metabolism in the fetal lamb. J Clin Invest 1983;71:1047–1061.
4. Rudolph AM, Heymann MA. Circulatory changes during growth in the fetal lamb. Circ Res 1970;26:289–299.
5. Peeters LL, Sheldon RE, Jones MD Jr, et al. Blood flow to fetal organs as a function of arterial oxygen content. Am J Obstet Gynecol 1979;135:637.
6. Peeters LL, Sheldon RE, Jones MD Jr, et al. Redistribution of cardiac output and oxygen delivery in the hypoxic fetal lamb. Am J Obstet Gynecol 1979;135:1071–1078.
7. Sheldon CA, Friedman WF, Sybers HD. Scanning electron microscopy of fetal and neonatal lamb cardiac cells. J Mol Cell Cardiol 1976;8:853–862.
8. McPherson RA, Kramer MF, Covell JW, et al. A comparison of the active stiffness of fetal and adult cardiac muscle. Pediatr Res 1976;10:660–664.
9. Heyman MA, Rudolph AM. Effects of increasing preload on right ventricular output in fetal lambs in utero. Circulation 1973;48:IV–37.
10. Berman W Jr, Goodlin RC, Heymann MA, et al. Pressure flow relationships in the umbilical and uterine circulations of the sheep. Circ Res 1976;38:262–266.
11. Papile L, Rudolph AM, Heymann MA. Autoregulation of cerebral blood flow in the preterm fetal lamb. Pediatr Res 1985;19:159–161.
12. Dawes GS, Johnston BM, Walker DW. Relationship of arterial pressure and heart rate in fetal newborn and adult sheep. J Physiol (Lond) 1980;309:405–417.
13. Iwamoto HS, Rudolph AM. Effects of angiotensin II on the blood flow and its distribution in fetal lambs. Circ Res 1982;48:183.
14. Drummond WH, Rudolph AM, Keil LC, et al. Arginine vasopressin and prolactin after hemorrhage in the fetal lamb. Am J Physiol 1980;238:E214–219.
15. Iwamoto HS, Rudolph AM, Keil LC, et al. Hemodynamic responses of the sheep fetus to vasopressin infusion. Circ Res 1979;44:430–436.
16. Challis JRG, Patrick JE. The production of prostaglandins and thromboxanes in the feto-placental unit and their effects on the developing fetus. Semin Perinatol 1980;4:23–33.
17. Mitchell MD, Flint AP, Bibby J, et al. Plasma concentrations of prostaglandins during late human pregnancy: influence of normal and preterm labor. J Clin Endocrinol Metab 1978;46:947–951.
18. Novy MJ, Piasecki G, Jackson BT. Effect of prostaglandins E2 and F2 alpha on umbilical blood flow and fetal hemodynamics. Prostaglandins 1974;5:543–555.
19. Berman W Jr, Goodlin RC, Heymann MA, et al. Effects of pharmacologic agents on umbilical blood flow in fetal lambs in utero. Biol Neonate 1978;33:225–235.
20. Cassin S. Role of prostaglandins and thromboxanes in the control of the pulmonary circulation in the fetus and newborn. Semin Perinatol 1980;4:101–107.
21. Cassin S. Role of prostaglandins, thromboxanes and leukotrienes in the control of the pulmonary circulation in the fetus and newborn. Semin Perinatol 1987;11:53–63.
22. Clyman RI. Ontogeny of the ductus arteriosus response to prostaglandins and inhibitors of their synthesis. Semin Perinatol 1980;4:115–124.
23. Clyman RI. Ductus arteriosus: current theories of prenatal and postnatal regulation. Semin Perinatol 1987;11:64–71.
24. Prowse CM, Gaensler EA. Respiratory and acid base changes during pregnancy. Anesthesiology 1965;26:381–392.
25. Rankin JHG, Meschia G, Makowski EL, et al. Relationship between uterine and umbilical venous PO_2 in sheep. Am J Physiol 1971;220:1688–1692.
26. Longo LD, Hill EP, Power GG. Theoretical analysis of factors affecting placental O_2 transfer. Am J Physiol 1972;222:730–739.
27. Meschia G. Transfer of oxygen across the placenta. In: Gluck L (ed) Intrauterine Asphyxia and the Developing Fetal Brain. Chicago: Year Book Medical, 1977:109–115.
28. Russell JC, Cooper CM, Ketchum CH, et al. Multicenter evaluation of TDx test for assessing fetal lung maturity. Clin Chem 1989;35:1005–1010.
29. Mendez-Bauer C, Poseirio JJ, Arellano-Hernandez G, et al. Effects of atropine on the heart rate of the human fetus during labor. Am J Obstet Gynecol 1963;85:1033–1053.
30. Vapaavouri EK, Shinebourne EA, Williams RL, et al. Development of cardiovascular responses to autonomic blockade in intact fetal and neonatal lambs. Biol Neonate 1973;22:1177–1188.
31. Rurak DW, Cooper CC, Taylor SM. Fetal oxygen consumption and PO_2 during hypercapnia in pregnant sheep. J Dev Physiol 1986;8:447–459.
32. Boddy K, Dawes GS, Fisher R, et al. Foetal respiratory movements, electrocortical and cardiovascular responses to hypoxaemia and hypercapnia in sheep. J Physiol (Lond) 1974;243:599–618.
33. Natale R, Clewlow F, Dawes GS. Measurement of fetal forelimb movements in lambs in utero. Am J Obstet Gynecol 1981;140:545–551.
34. Dawes GS, Fox HE, Leduc BM, et al. Respiratory movements and rapid eye movements in the foetal lamb. J Physiol (Lond) 1972;220:119–143.
35. Maloney JE, Adamson TM, Brodecky V, et al. Diaphragmatic activity and lung liquid flow in unanesthetized fetal sheep. J Appl Physiol 1975;39:423–428.
36. Patrick JE, Falton KJ, Dawes GS. Breathing patterns before death in fetal lambs. Am J Obstet Gynecol 1976;125:73–78.
37. Patrick J, Challis JRG, Cross J, et al. The relationship between fetal breathing movements and prostaglandin E_2 during ACTH-induced labour in sheep. J Dev Physiol 1987;9:287–293.
38. Thorburn GD, Challis JRG. Control of parturition. Physiol Rev 1979;59:863–918.
39. Kitterman JA, Liggins GC, Fewell JE, et al. Inhibition of breathing movements in fetal sheep by prostaglandins. J Appl Physiol 1983;54:687–692.
40. Richardson B, Hohimer AR, Mueggler P, et al. Effects of glucose concentration on fetal breathing movements and electrocortical activity in fetal lambs. Am J Obstet Gynecol 1982;142:678–683.
41. Patrick J, Richardson B, Hasen G, et al. Effects of maternal ethanol infusion on fetal cardiovascular and brain activity in lambs. Am J Obstet Gynecol 1985;151:859–867.
42. Boddy K, Dawes GS, Fisher RL, et al. The effects of pentobarbitone and pethidine on foetal breathing movements in sheep. Br J Pharmacol 1976;57:311–317.

43. Piercy WN, Day MA, Neims AH, et al. Alteration of ovine fetal respiratory-like activity by diazepam, caffeine and doxapram. Am J Obstet Gynecol 1977;127:43–49.
44. Kitterman JA, Liggins GC, Clements JA, et al. Stimulation of breathing movements in fetal sheep by inhibitors of prostaglandin synthesis. J Dev Physiol 1979;1:453–466.
45. Patrick J, Natale R, Richardson B. Pattern of human fetal breathing activity at 34 to 35 weeks' gestational age. Am J Obstet Gynecol 1978; 132:507–513.
46. Lewis PJ, Trudinger BJ, Mangey J. Effect of maternal glucose ingestion on fetal breathing and body movements in late pregnancy. Br J Obstet Gynecol 1978;85:86–89.
47. Boddy K, Dawes GS. Fetal breathing. Br Med Bull 1975;1:3–7.
48. Natale R, Patrick J, Richardson B. Effects of maternal venous plasma glucose concentrations on fetal breathing movements. Am J Obstet Gynecol 1978;132:36–41.
49. Richie K. The fetal response to changes in the composition of maternal inspired air in human pregnancy. Semin Perinatol 1980;4:295–299.
50. McLeod W, Brien J, Carmichael L, et al. Maternal glucose injections do not alter the suppression of fetal breathing following maternal ethanol ingestion. Am J Obstet Gynecol 1984;148:634–639.
51. Richardson B, O'Grady JP, Olsen GD. Fetal breathing movements and the response to carbon dioxide in patients on methadone maintenance. Am J Obstet Gynecol 1984;150:400–405.
52. Thaler I, Goodman JDS, Dawes GS. The effect of maternal smoking on fetal breathing rate and activity patterns. Am J Obstet Gynecol 1980; 138:282–287.
53. Richardson B, Natale R, Patrick J. Human fetal breathing activity during induced labor at term. Am J Obstet Gynecol 1979;133:247.
54. Manning FA, Platt LD, Siopos L. Fetal movements in human pregnancies. Obstet Gynecol 1979;54:699–702.
55. Bocking A, Adamson L, Cousin A, et al. Effects of intravenous glucose injections on human fetal breathing movements and gross fetal body movements at 38 to 40 weeks' gestational age. Am J Obstet Gynecol 1982;142:606–611.
56. Carmichael L, Cambell K, Patrick J. Fetal breathing, gross body movements and fetal heart rates before spontaneous labor at term. Am J Obstet Gynecol 1984;148:675–679.
57. Timor-Tritsch IE, Dierker LJ, Zador I, et al. Fetal movements associated with fetal heart rate accelerations and decelerations. Am J Obstet Gynecol 1978;131:276–280.
58. Schiffrin BS. The rationale for antepartum fetal heart rate monitoring. J Reprod Med 1979;23:213–221.
59. Rooth G, Huch A, Huch R, et al. Fetal-maternal temperature differences during labor. Contrib Gynacol Obstet 1977;3:54–62.
60. Power GG. Fetal thermoregulation: animal and human. In: Poulin WW, Fox RA (eds) Fetal and Neonatal Physiology. Philadelphia: Saunders, 1998:671–676.
61. Cohn HE, Piasecki GJ, Jackson BT. Cardiovascular responses to hypoxemia and acidemia in fetal lambs. Am J Obstet Gynecol 1974;129: 817–824.
62. Parer JT. The effect of acute maternal hypoxia on fetal oxygenation and the umbilical circulation in the sheep. Eur J Obstet Gynecol Reprod Biol 1980;10:125–136.
63. Mann LI. Effects in sheep of hypoxia on levels of lactate, pyruvate and glucose in blood of mothers and fetus. Pediatr Res 1970;4:46–54.
64. Jones MD, Sheldon RE, Peeters LL, et al. Fetal cerebral oxygen consumption at different levels of oxygenation. J Appl Physiol 1977;43: 1080–1084.
65. Fisher DS, Heymann MA, Rudolph AM. Fetal myocardial oxygen and carbohydrate consumption during acutely induced hypoxemia. Am J Physiol 1982;242:H657–H651.
66. Friede A, Rochat R. Maternal mortality and perinatal mortality: definitions, data and epidemiology. In: Sachs B (ed) Clinical Obstetrics. Littleton, MA: PSG, 1985:1–33.
67. Vital Statistics of the United States, vol II. Mortality, section 4. Washington, DC: U.S. Department of Health and Human Services, Public Health Services, 1988, 1–7.
68. CDC. Contribution of birth defects to infant mortality—United States, 1986. MMWR 1989;38:633.
69. Lammer EJ, Brown LE, Anderka MT, Guyer B. Classification and analysis of fetal deaths in Massachusetts. JAMA 1989;261:1757.
70. Mersey Region Working Party on Perinatal Mortality. Perinatal health. Lancet 1982;1:491–494.
71. Working Party on Amniocentesis. An assessment of the hazards of amniocentesis. Br J Obstet Gynecol 1978;85(suppl 2):1–41.
72. Taber A, Philip J, Madsen M, et al. Randomised, controlled trial of genetic amniocentesis in 4606 low-risk women. Lancet 1986;1:1287–1293.
73. Jackson LG, Zachary JM, Fowler SE, et al. A randomized comparison of transcervical and transabdominal chorionic villus sampling. N Engl J Med 1992;327:594–598.
74. Burton BK, Schulz CJ, Burd LI. Limb anomalies associated with chorionic villus sampling. Obstet Gynecol 1992;79:726–730.
75. Monni G, Ibba RM, Lai R, et al. Limb-reduction defects and chorionic villus sampling. Lancet 1991;337:1091.
76. Mahoney MJ. Limb abnormalities and chorionic villus sampling. Lancet 1991;337:1422.
77. Shulman LP, Elias S. Percutaneous umbilical blood sampling, fetal skin sampling and fetal liver biopsy. Semin Perinatol 1990;14:56–64.
78. Saari-Kemppainen A, Karjalainen O, Ylostalo P, et al. Ultrasound screening and perinatal mortality: controlled trial of systemic one-stage screening in pregnancy: the Helsinki Ultrasound Trial. Lancet 1990; 336:387–391.
79. Ewigman B, LeFevre M, Hesser J. A randomised trial of routine prenatal ultrasound. Obstet Gynecol 1990;76:189–194.
80. Bekketeig LS, Eik-Nes SH, Jacobsen G, et al. Randomised controlled trial of ultrasonographic screening in pregnancy. Lancet 1984;2:207–211.
81. Ewigman B, Crane JP, Frigoletto FD, et al. Effect of prenatal ultrasound screening on perinatal outcome. N Engl J Med 1993;329:821–827.
82. Campbell S, Warsof S, Little D, et al. Routine ultrasound screening for the prediction of gestational age. Obstet Gynecol 1985;65:613–620.
83. Kurtz A, Wapner R, Kurtz R, et al. Analysis of biparietal diameter as an accurate indicator of gestational age. J Clin Ultrasound 1980;8:319–326.
84. Patrick J, Campbell K, Carmichael L, et al. Patterns of gross fetal body movements over 24-hour observation intervals during the last 10 weeks of pregnancy. Am J Obstet Gynecol 1982;142:363–371.
85. Srokin Y, Dierker L. Fetal movement. Clin Obstet Gynecol 1982; 25:719–734.
86. Neldam S. Fetal movements as an indicator of fetal well being. Lancet 1980;1:1222–1224.
87. Rayburn W. Antepartum fetal assessment. Clin Perinatol 1982;9:231–252.
88. Liston R, Cohen A, Mennui M, Gabbe S. Antepartum fetal evaluation by maternal perception of fetal movement. Obstet Gynecol 1982;60: 424–426.
89. Russell JC, Cooper CM, Ketchum CH, et al. Multicenter evaluation of TDx test for assessing fetal lung maturity. Clin Chem 1989;35:1005–1010.
90. Manning FA, Morrison I, Harmon CR, et al. Fetal assessment by fetal BPS: experience in 19,221 referred high-risk pregnancies. II. The false negative rate by frequency and etiology. Am J Obstet Gynecol 1987; 157:880–884.
91. Baskett TF, Allen AC, Gray JH, et al. The biophysical profile score. Obstet Gynecol 1987;70:357–360.
92. Platt LD, Eglington GS, Scorpios L, et al. Further experience with the fetal biophysical profile score. Obstet Gynecol 1983;61:480–485.
93. Schiffrin BS, Guntes V, Gergely RC, et al. The role of real-time scanning in antenatal fetal surveillance. Am J Obstet Gynecol 1981;140:525–530.
94. Manning FA, Baskett TF, Morrison I, et al. Fetal biophysical profile scoring: a prospective study in 1184 high-risk patients. Am J Obstet Gynecol 1981;140:289–294.
95. Manning FA, Morrison I, Lange IR, et al. Fetal assessment based on

fetal biophysical profile scoring: experience in 12,620 referred high-risk pregnancies. I. Perinatal mortality by frequency and etiology. Am J Obstet Gynecol 1985;151:343–350.
96. Schiffrin BS. The rationale for antepartum fetal heart rate monitoring. J Reprod Med 1979;23:213–221.
97. Keegan KA, Paul RH. Antepartum fetal heart rate testing. IV. The nonstress test as a primary approach. Am J Obstet Gynecol 1980;136:75–80.
98. Evertson LR, Gauthier RJ, Collea JV. Fetal demise following negative contraction stress test. Obstet Gynecol 1978;51:671–673.
99. Ott WJ. Antepartum cardiotachometry for fetal evaluation. South Med J 1981;74:310–314.
100. Fenton AN, Steer CM. Fetal distress. Am J Obstet Gynecol 1962;83:354.
101. Hon EH, Quilligan EJ. The classification of fetal heart rate. Conn Med 1967;31:779.
102. Schiffrin BS, Dame L. Fetal heart rate patterns: prediction of Apgar score. JAMA 1972;219:1322.
103. Krebs HB, Petres RE, Dunn LJ, et al. Intrapartum fetal heart rate monitoring. I. Classification and prognosis of fetal heart rate patterns. Am J Obstet Gynecol 1979;133:762.
104. ACOG Technical Bulletin. Fetal heart rate patterns: monitoring, interpretation and management. Int J Obstet Gynecol 1995;51:65.
105. ACOG Committee Opinion. Inappropriate use of terms fetal distress and birth asphyxia. Int J Obstet Gynecol 1998;61:309.
106. Parer JT, King T. Fetal heart rate monitoring: is it salvageable? Am J Obstet Gynecol 2000;182:982.
107. Lavin JP, Samuels SV, Miodovnik M, et al. The effects of bupivicaine and chloroprocaine as local anesthetics for epidural anesthesia on fetal heart rate monitoring parameters. Am J Obstet Gynecol 1981;141:717.
108. Abboud TK, Afrasiabi A, Zhu J, et al. Bupivicaine/butorphanol/epinephrine for epidural anesthesia in obstetrics: maternal and neonatal effects. Reg Anesth 1989;14:219.
109. McLintic AJ, Danskin FH, Reid JA, et al. Effect of adrenaline on extradural anesthesia, plasma lignocaine concentrations and the feto-placental unit during elective caesarean section. Br J Anesth 1991;67:683.
110. Loftus JR, Holbrook RH, Cohen SE. Fetal heart rate after epidural lidocaine and bupivicaine for elective caesarean section. Anesthesiology 1991;75:406.
111. Ramos-Santos E, Devoe LD, Wakefield ML, et al. The effects of epidural anesthesia on the Doppler velocimetry of umbilical and uterine arteries in normal and hypertensive patients during active term labor. Obstet Gynecol 1991;77:20–26.
112. Hughes AB, Devoe LD, Wakefield ML, et al. The effects of epidural anesthesia on the Doppler velocimetry of umbilical and uterine arteries in normal term labor. Obstet Gynecol 1990;75:809–812.
113. Lindblad A, Bernow J, Vernersson E, et al. Effects of extradural anesthesia on human fetal blood flow in utero. Comparison of three local anesthetic solutions. Br J Anesth 1987;56:1265–1272.
114. Turner GA, Newnham JP, Johnson C, et al. Effects of extradural anesthesia on umbilical and uteroplacental arterial flow velocity waveforms. Br J Anesth 1991;67:306–309.
115. Alahuhta S, Rasanen J, Jouppila R, et al. Uteroplacental and fetal haemodynamics during extradural anesthesia for caesarean section. Br J Anesth 1991;66:319–323.
116. Saling E, Schneider D. Biochemical supervision of the foetus during labor. J Obstet Gynecol Br Commonw 1967;74:799–811.
117. Beard RW, Morris ED, Clayton SE. pH of fetal capillary blood as an indicator of the condition of the foetus. J Obstet Gynecol Br Commonw 1967;74:812–822.
118. Kubli FW, Hon EW, Khazin AF, et al. Observations on heart rate and pH in the human fetus during labor. Am J Obstet Gynecol 1969; 104:1190–1206.
119. Winkler CL, Hauth JC, Tucker JM, et al. Neonatal complications at term as related to the degree of umbilical artery acidemia. Am J Obstet Gynecol 1991;164:637–641.
120. Johnson N, McNamara H. Monitoring the fetus with a sensor coverred with an irregular surface can cause scalp ulceration. Br J Obstet Gynecol 1993;100:961–962.
121. Dildy GA, Clark SL, Loucks CA. Preliminary experience with intrapartum fetal pulse oximetry in humans. Obstet Gynecol 1993;81:630–635.
122. ACOG Committee Opinion. Fetal pulse oximetry. Obstet Gynecol 2001;98:523–524.
123. Garite TJ, Dildy GA, McNamara H, et al. A multicenter controlled trial of fetal pulse oximetry in the intrapartum management of nonreassuring fetal heart rate patterns. Am J Obstet Gynecol 2000;183:1049–1058.