Electronic Fetal Monitoring: A Primer on the Physiology of Fetal Heart Control

Understanding how the fetal heart reacts to labor is essential knowledge for clinicians who are responsible for the interpretation of heart rate tracings

Emily Hamilton, MDCM
Philip Warrick, Ph.D.

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Introduction

The clinical goal of electronic fetal monitoring is to identify fetuses with increased risk of hypoxic injury so that intervention can avoid adverse outcome without also causing excessive numbers of unnecessary interventions. Understanding the mechanisms of fetal heart rate control are important because they help us to infer the physiological state of the baby and gauge whether intervention is really necessary.

In adult cardiology, ECG changes are very helpful to diagnose myocardial infarction because there is a direct relationship, precisely defined by anatomy and electromagnetic physics, linking the presence of Q waves in the 12-lead ECG to the location of injured myocardium. In the fetal surveillance, the situation is very different. Standard monitoring provides only the heart rate, not the ECG. Clinicians depend upon the heart rate to infer the condition of another organ, namely the fetal brain. Although the fetal heart rate is related to fetal brain state, it is also affected by a number of other factors. The fetal heart rate results from the combined effect of several fluctuating influences mediated through extrinsic and intrinsic cardiac control mechanisms (sympathetic and parasympathetic nerves and circulating catecholamines), as well as intrinsic cardiac factors (myocardium and its conducting system). The following text describes the principal physiological pathways that control heart rate and influence heart rate variability.

What Regulates the Fetal Heart Rate?

The heart is a muscle with its own pacemaker, conducting system, numerous types of receptors (alpha and beta adrenergic) and direct neuronal connections to both the sympathetic and parasympathetic systems. Ultimately, any influence on heart rate is mediated by one or more of these structures. The basic anatomy and physiology of heart rate control are described in physiology textbooks. In the simple schematic diagram shown in Figure 1, factors which increase heart rate are shown on the left and factors which decrease heart rate are on the right. While this summary provides the basics for understanding heart rate regulation, it is important to remember that our understanding of this physiology continues to evolve.
Figure 1: Schematic outline of heart rate control mechanisms.

The cardio regulatory center in the medulla oblongata contains an acceleratory center and an inhibitory center. The cardio regulatory center receives input from the central nervous system, reflex pathways and circulating catecholamines. An example of central nervous system influence on the acceleratory response is seen with vibroacoustic stimulation. In response to sudden auditory stimulation, the central nervous system activates the cardioacceleratory center. The cardioacceleratory center increases heart rate directly via sympathetic cardiac nerves which interact with the sinoatrial node to increase the heart rate. The cardioinhibitory center slows the heart rate via the parasympathetic vagus nerve which can slow heart rate by modulation at various levels, including the sinoatrial node. Reducing cardioinhibitory activity increases heart rate.

Arterial baroreceptors, located in the aortic arch and carotid arteries, are sensitive to stretch or distension of a vessel caused by blood pressure changes. An increase in arterial blood pressure produces vessel distension and causes arterial baroreceptors to send neuronal messages to the cardioinhibitory center, which in turn causes rapid slowing of the fetal heart rate via the parasympathetic vagus nerve. A decrease in arterial pressure results in an increased heart rate.

The rapidity of heart rate change is determined by the conditions that trigger the change.
Arterial chemoreceptors located in the aortic arch and carotid arteries are sensitive to low pH and low oxygen saturation. When these chemoreceptors are activated, they cause the cardioacceleratory center to increase sympathetic impulses, resulting in an increase in the fetal heart rate. The α-adrenergic component of the chemoreceptor response causes vasoconstriction and hypertension. As will be described later, hypertension is an important part of the pathway producing fetal heart rate decelerations.

The catecholamines, epinephrine and norepinephrine, secreted from the adrenal, are both hormones and neurotransmitters. Norepinephrine binds to beta receptors in the heart causing an increase in heart rate, contractility and stroke volume. Catecholamines can also cause redistribution of blood flow by inducing vasoconstriction and vasodilation in different regions. Vasoconstriction is mediated through the α-adrenergic receptors in liver, kidney, skin and gut, and vasodilation is mediated through β adrenergic receptors in skeletal muscle. Catecholamine release is stimulated by the sympathetic nervous system and may be precipitated by stress conditions, such as loud sounds, fear or low blood sugar.

The rapidity of heart rate change is determined by the conditions that trigger the change. Central stimuli like a sudden loud sound or a quick increase in blood pressure cause rapid heart rate changes mediated by direct neuronal pathways to the sinoatrial node. Although chemoreceptor action on heart rate is also mediated neuronally (by the cardiac nerves), this influence tends to be slow because it is triggered by low pH and oxygen levels which tend to fluctuate slowly. Catecholamine mediated effects are relatively slow reflecting their half-life of 2 to 3 minutes.

While all of the mechanisms described above modulate heart rate, it is important to recall that the overarching mission of the cardiovascular system is to deliver sufficient oxygen to key organs. Heart rate is an important determinant of this mission but only one, along with other cardiovascular compensatory mechanisms, which include redistribution of blood flow and changes in blood pressure, cardiac stroke volume or oxygen carrying capacity and hemoglobin-oxygen dissociation in the blood stream. The medulla oblongata contains the vasomotor center that responds to baroreceptors, chemoreceptors and catecholamines. It also regulates peripheral blood vessel dilation and constriction to help maintain normal blood pressure and distribution of blood to vital organs.

How Did Scientists Discover How the Fetal Heart Rate Was Regulated During Labor?

Fetal Heart Rate Decelerations
For a concise review of the extensive experimental work elucidating the mechanisms of fetal heart rate decelerations and response to hypoxemia, the reader is referred to excellent descriptions by Martin et al 2008 and Freeman et al 2012. 1, 2
Animal research has elucidated how the fetal heart behaves under artificially created hypoxemia or acidemia and what mechanisms are at play with fetal umbilical cord compression and *uteroplacental insufficiency*. Umbilical cord compression has been created in research environments by actually compressing the fetal cord with implanted mechanical devices that could be manipulated to compress the cord to different degrees and durations. Decreased uteroplacental oxygen delivery was generally simulated by compressing the arteries supplying blood to the uterus or controlling the levels of oxygen inspired by the experimental animals. Pharmacological blocking agents were added to inhibit the effects of the sympathetic and/or parasympathetic systems. Some experiments even used *vagotomy* to eliminate the effects of the vagal system. Inserted sensors measured blood pressure, heart rate and acid base status during the experiments.

**Variable Decelerations**

Figure 2: Three pathways are involved with variable decelerations, adapted from Freeman et al.²

Brief hypertension from compression of the umbilical artery developing during umbilical cord compression was not accompanied by hypoxemia or pH changes sufficient to activate other pathways. Only the stretch-sensitive baroreceptors were activated causing rapid modulation of the heart rate mediated through the vagus nerve. Thus the onset and end of the deceleration
was abrupt when the deceleration was caused by cord compression without hypoxemia or lowered pH.

As low pH and hypoxemia developed, the heart was exposed to the modulating influences mediated by the chemoreceptor pathway. When hypoxemia and pH changes were gradual, the chemoreceptors mediated changes in heart rate were gradual, mirroring their stimulating factors. However, acute falls in oxygen induced an abrupt fall in heart rate mediated through the chemoreceptors. 1, 4

With severe hypoxemia and fetal acidosis, there was a delayed deceleration component due to intrinsic myocardial effects.

**Late Decelerations**

Figure 3: Two pathways are involved with late decelerations, adapted from Martin 19791 and Freeman et al. 2

To simulate decreased uteroplacental oxygen delivery, Martin applied repeated hypogastric artery occlusions in sheep. These occlusions resulted in fetal hypertension which was followed by vagally mediated decelerations. The degree of hypertension and the amount of deceleration were closely related, although some deceleration remained when the transient hypertension was prevented by alpha-adrenergic blockade. The timing of the onset, nadir and end of the deceleration was delayed with respect to the occlusion and mirrored the timeline of the hypertensive response. Vagal blockade eliminated these decelerations in the non-acidemic sheep. Thus, “intermittent placental insufficiency” can cause decelerations and its effects are mediated by the vagus nerve. These “late” decelerations were not associated with fetal acidosis. 1, 3

When the occlusions were extended to produce fetal acidosis, the fetal hypertensive response lost its progressive character, reaching a plateau early after the beginning of the occlusion, while the deceleration continued to fall with its nadir occurring at or after the end of the occlusion. With progressive acidemia the decelerations became deeper and longer. In the

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presence of very severe acidemia (pH=6.96) they could not be eliminated by vagal blockade. With complete vagal and alpha and beta adrenergic blockade, the decelerations persisted. The fetal heart, devoid of any sympathetic and parasympathetic influences, showed decelerations suggesting that intrinsic myocardial depression was the deceleration mechanism in the presence of severe acidosis and hypoxia.³

Although the individual pathways described above cover the major mechanisms of fetal heart rate decelerations, the actual situation is more complex. Even in the sheep experiments using precisely controlled conditions, consistent fetal heart rate decelerations could not be produced equally in all animals despite 2 hours of repetitive maternal vascular occlusions.³

How Do These Discoveries Affect the Clinical Interpretation of Tracings?

The rapidity of onset or end of the deceleration is an important clue to the inciting pathology. An abrupt or gradual onset is a defining characteristic of the NICHD definitions of Late or Variable decelerations.⁵ Cord compression does cause rapid fetal heart rate changes but so does a very rapid change in PO₂.¹,⁴

Slower changes are more likely to reflect the gradually changing pH and PO₂ or hypertension. Gradual decelerations with late times can be seen without acidemia.³

Late timing of the beginning or end of a variable deceleration with respect to an associated contraction may reflect simply the timing of the start and end of the umbilical cord compression. Late timing may also reflect the more slowly generated changes from waxing and waning hypertension seen with the chemoreceptor mediated changes or intrinsic myocardial effects.

The most recent NICHD classification divides decelerations into 3 distinct types -- Variable, Early and Late.⁵ Variable decelerations are characterized by an abrupt decrease in the fetal heart rate. Early and Late decelerations are characterized by a typically symmetrical gradual decrease and return of the fetal heart rate and then are named according to their temporal relationship to contractions.

Clinicians label decelerations types to help infer the underlying precipitating factors and fetal condition. But as we have seen, Variable decelerations from cord compression can lead to severe hypoxemia and Late decelerations can be present without acidemia. Thus, the mere classification of a deceleration does not equate to fetal condition. Furthermore, some decelerations can have shape aspects consistent with the definition of a Variable deceleration.
and some aspects characteristic of a Late deceleration. This is not surprising as the deceleration types share some common pathways. Irrespective of the precipitating cause of the impaired oxygen delivery, the development of hypoxemia and low pH and ultimately myocardial depression will produce similar effects on heart rate.

Underlying pathologies may also be mixed. Cord compression and uteroplacental insufficiency can coexist. Moreover the fetal heart rate can be affected by factors unrelated to cord compression or uteroplacental oxygen delivery, such as fetal head compression, medications, cardiac malformations and fetal maturity. Some examples of isolated and combined underlying pathologies are shown in Figures 4-7.

The classic example of uteroplacental insufficiency is that found with maternal hypertension and fetal growth restriction. This poorly functioning placenta was associated with repetitive Late decelerations. The tracing in Figure 3 was obtained prior to delivery by cesarean in a mother with severe preeclampsia, HELLP syndrome and oligohydramnios. Apgar scores were 0/4/7 at 1, 5 and 10-minutes. The umbilical artery pH was 7.03 and base deficit was 10 mmol/L.

Figure 4: This PeriCALM® Patterns™ tracing demonstrates classic Late decelerations

However, some babies may have a poorly functioning placenta and cord compression. A mixed pattern of Variable and Late decelerations is shown in figure 5. This tracing was obtained shortly before cesarean delivery. Amniotic fluid was meconium stained and a loose nuchal cord was found. Apgar scores at 1 and 5 minutes were 2/7, umbilical artery pH was 6.99 and base deficit was 14 mmol/L.

Figure 5: This PeriCALM Patterns tracing demonstrates both Late and Variable decelerations
A deceleration that is induced only by the baroreceptor mechanism with cord compression will have an abrupt onset and end. If the cord compression is relieved only at the end of the contraction the recovery may be late in timing, but still abrupt.

Figure 6 shows the portion of tracing just before forcep delivery of a term baby with a nuchal cord. The baby had 1 and 5-minute Apgar scores of 4/5, an umbilical artery pH of 6.99 and a base deficit of 13.0 mmol/L.

Figure 6: This PeriCALM Patterns tracing demonstration reveals Variable decelerations with rapidly increasing depth and duration

The tracing in Figure 7 shows an example of mixed deceleration types in a labor that is complicated by placenta abruption. Some of the late decelerations have onsets that are steeper or less symmetrical than others reflecting the net effect of superimposed physiologies. The baby continued to have a pattern of mixed deceleration types. The lower image shows the last tracing segment before birth by cesarean. The baby had 1 and 5 minute Apgar scores of 2/5, an umbilical artery pH of 7.15 and a base deficit of 8.4 mmol/L.

Figure 7: A PeriCALM Patterns tracing chronicles the progression of a mixed pattern of decelerations
Heart Rate Variability

Current clinical guidelines that classify tracings rely heavily on reduced baseline heart rate variability as an indicator of significant acidosis and/or need for intervention. Minimal variability, especially when it persists and is accompanied by decelerations, is associated with marked acidemia, low Apgar scores and hypoxic injury.

All of the mechanisms controlling fetal heart rate depicted in Figure 1 influence heart rate variability. Fetal behavioral states, breathing and movements affect heart rate variability acting though the central pathways to the medulla, and then to the heart via the sympathetic and parasympathetic systems. Fetal heart rate variability is suppressed by factors that depress fetal brain function.

Animal experiments have shown that blockage of the parasympathetic system with atropine results in a reduction in short-term variability. A reduction in long-term variability occurs after sympathetic blockade. Fetal heart rate variability is more than the simple "push-pull" interactions between the inhibitory and acceleratory limbs of the autonomic nervous system. The heart itself contributes to variability. Even with complete double blockade of the sympathetic and parasympathetic systems, around 35-40% of fetal lamb heart rate variability persists. A clinical demonstration of the intrinsic rhythmicity of the heart is found in transplantation surgery. An excised heart continues to beat and demonstrate heart rate variability.

The association between variability and metabolic acidosis is less clear. This is important because all contemporary EFM classification methods place high reliance upon baseline fetal heart rate variability to exclude the presence of metabolic acidosis. The 2008 NICHD Update publication in which the Category I, II, III classification method was first described includes a statement that “moderate variability reliably predicts the absence of metabolic acidemia at the time that it is observed.” This concept was softened in the 2009 ACOG Practice Bulletin 106 with the statement “The data relating FHR variability to clinical outcomes, however, are sparse.” This practice bulletin endorsed the 3-level categorization of tracings where the third level required absent baseline variability.

The 2010 ACOG Practice Bulletin 116 presented a clinical management algorithm with high reliance on moderate variability. In this management algorithm, the recommendations for
tracings in Category 2 were continued surveillance and intrauterine resuscitation measures, as long as there was moderate variability. Only a failure to respond to intrauterine resuscitative measures in the presence of absent or minimal variability lead to the recommendation of “consideration of delivery” for Category II tracings.

There is a growing body of literature that does not support the statement that moderate variability reliably excludes the presence of metabolic acidemia.

In animal studies, vascular instrumentation allows for blood gas measurement at any specific time to be correlated with the coexisting fetal heart rate features. Martin demonstrated that in sheep the initial fetal heart rate response to sudden hypoxemia was a slowing of the heart rate with increased variability.1 Others observed similar changes in sheep and in monkeys.16-18 Field et al found initial decreases in heart rate variability with iliac occlusion in sheep, but variability returned to normal by 36 minutes despite worsening metabolic acidosis.19 These observations of normal variability in the face of acidemia led researchers to postulate that some aspect of variability control could be different in animals compared to humans.

In the human literature, four recent and independent studies using various definitions of acidosis and examining the last 30-60 minutes of the tracing reported that the percentage of babies with acidosis who had moderate variability ranged from 15% to 91%.20-23 Even with near lethal levels of uterine artery base deficit (>=16 mmol/L), a full 15 to 32% of these babies had moderate baseline variability in the tracing recorded just before birth.20,21 Another study examined baseline variability in term babies who required supplemental oxygen for more than 6 hours or mechanical ventilation.24 In this study, marked variability in the last 30 minutes was significantly associated with these respiratory morbidities. Minimal variability was not. This finding is in keeping with other direct observations on the correlation between increased heart rate variability and catecholamines concentration on non-acidotic term fetuses.25 It appears that marked variability may be a sign of activation of compensatory pathways.

Conclusions

In practice, clinicians must integrate clinical data with electronic fetal monitoring patterns in order to infer the condition of the baby, to project what is likely to happen and how quickly it might occur. As discussed throughout this article the relationship between heart rate and the underlying fetal condition is complex. This task is not simple. In fact, given complexity, one could consider that the substantial improvements in intrapartum-related neonatal encephalopathy seen in numerous regions around the world demonstrate a remarkable achievement. Several large jurisdictions with population-wide statistics have shown steady declines, often reaching reductions in the range of 40% per decade.26-34 One can only speculate on the reasons. Little has changed in the physical devices that record fetal heart rate and
contractions. On the other hand, clinical behavior has changed considerably. We have an increased understanding of fetal physiology, the natural evolution of fetal acidosis and the consequences of delayed intervention which in turn have led to better clinical practices.

We are entering a new phase in EFM research. Hospitals store vast amounts of clinical data and digital EFM tracings. We can now analyze these digital EFM signals directly, measure standard EFM features as well as new aspects of the tracing that are not readily visible to the human eye. In recent decades EFM research was stymied due to our inability to access and analyze the large data sets. As these impediments are overcome we are seeing a resurgence of research producing a better understanding of which standard EFM characteristics are truly associated with severe neonatal depression or metabolic acidosis. The next review in this series will describe some of these exciting advances as engineering mathematics and clinical sciences combine forces to address the challenges of fetal surveillance.

References


10. NICE Clinical Guideline 55. Intrapartum care 


