



# PRACTICE BULLETIN

CLINICAL MANAGEMENT GUIDELINES FOR OBSTETRICIAN—GYNECOLOGISTS

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## Management of Intrapartum Fetal Heart Rate Tracings

*Intrapartum electronic fetal monitoring (EFM) is used for most women who give birth in the United States. As such, clinicians are faced daily with the management of fetal heart rate (FHR) tracings. The purpose of this document is to provide obstetric care providers with a framework for evaluation and management of intrapartum EFM patterns based on the new three-tiered categorization.*

### Background

In 2008, a workshop sponsored by the American College of Obstetricians and Gynecologists, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and the Society for Maternal–Fetal Medicine focused on updating EFM nomenclature, recommending an interpretative system, and setting research priorities (1). Nomenclature for baseline FHR and FHR variability, accelerations, and decelerations were reaffirmed (Table 1). New terminology was recommended for the description and quantification of uterine contractions. *Normal uterine activity* was defined as five or fewer contractions in 10 minutes, averaged over a 30-minute window. *Tachysystole* was defined as more than five contractions in 10 minutes, averaged over 30 minutes and should be categorized by the presence or absence of FHR decelerations. Tachysystole can be applied to spontaneous or induced labor. The terms hyperstimulation and hypercontractility were abandoned.

A three-tiered system for intrapartum EFM interpretation also was recommended (Box 1), with the nomenclature and interpretation described elsewhere (1). This second Practice Bulletin on intrapartum FHR tracings reviews the management of heart rate patterns based on the three-tiered classification system (Figure 1).

### Clinical Considerations and Recommendations

#### ► How is a Category I EFM tracing managed?

Category I FHR tracings are normal (Box 1). These tracings are not associated with fetal acidemia (2–6). Category I FHR patterns may be managed in a routine manner with either continuous or intermittent monitoring. Tracings should be periodically evaluated and documented during active labor by a health care provider (eg, this may include physician, nurse, or midwife) based on clinical

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**Committee on Practice Bulletins—Obstetrics.** This Practice Bulletin was developed by the Committee on Practice Bulletins—Obstetrics with the assistance of George Macones, MD, and Sean Blackwell, MD, in collaboration with Thomas Moore, MD, Catherine Spong, MD, John Hauth, MD, Gary Hankins, MD, and representatives from the Association of Women's Health, Obstetric and Neonatal Nurses—Audrey Lyndon RN, PhD, Kathleen R. Simpson, PhD RN, and Anne Santa-Donato, RNC, MSN, and the American College of Nurse–Midwives—Tekoa King, CNM, MPH. The information is designed to aid practitioners in making decisions about appropriate obstetric and gynecologic care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

**Table 1. Electronic Fetal Monitoring Definitions**

| Pattern                | Definition  |
|------------------------|---|
| Baseline               | <ul style="list-style-type: none"> <li>• The mean FHR rounded to increments of 5 beats per minute during a 10-minute segment, excluding:               <ul style="list-style-type: none"> <li>—Periodic or episodic changes</li> <li>—Periods of marked FHR variability</li> <li>—Segments of baseline that differ by more than 25 beats per minute</li> </ul> </li> <li>• The baseline must be for a minimum of 2 minutes in any 10-minute segment, or the baseline for that time period is indeterminate. In this case, one may refer to the prior 10-minute window for determination of baseline.</li> <li>• Normal FHR baseline: 110–160 beats per minute</li> <li>• Tachycardia: FHR baseline is greater than 160 beats per minute</li> <li>• Bradycardia: FHR baseline is less than 110 beats per minute</li> </ul> |
| Baseline variability   | <ul style="list-style-type: none"> <li>• Fluctuations in the baseline FHR that are irregular in amplitude and frequency</li> <li>• Variability is visually quantitated as the amplitude of peak-to-trough in beats per minute.               <ul style="list-style-type: none"> <li>—Absent—amplitude range undetectable</li> <li>—Minimal—amplitude range detectable but 5 beats per minute or fewer</li> <li>—Moderate (normal)—amplitude range 6–25 beats per minute</li> <li>—Marked—amplitude range greater than 25 beats per minute</li> </ul> </li> </ul>  |
| Acceleration           | <ul style="list-style-type: none"> <li>• A visually apparent abrupt increase (onset to peak in less than 30 seconds) in the FHR</li> <li>• At 32 weeks of gestation and beyond, an acceleration has a peak of 15 beats per minute or more above baseline, with a duration of 15 seconds or more but less than 2 minutes from onset to return.</li> <li>• Before 32 weeks of gestation, an acceleration has a peak of 10 beats per minute or more above baseline, with a duration of 10 seconds or more but less than 2 minutes from onset to return.</li> <li>• Prolonged acceleration lasts 2 minutes or more but less than 10 minutes in duration.</li> <li>• If an acceleration lasts 10 minutes or longer, it is a baseline change.</li> </ul>  |
| Early deceleration     | <ul style="list-style-type: none"> <li>• Visually apparent usually symmetrical gradual decrease and return of the FHR associated with a uterine contraction</li> <li>• A gradual FHR decrease is defined as from the onset to the FHR nadir of 30 seconds or more.</li> <li>• The decrease in FHR is calculated from the onset to the nadir of the deceleration.</li> <li>• The nadir of the deceleration occurs at the same time as the peak of the contraction.</li> <li>• In most cases, the onset, nadir, and recovery of the deceleration are coincident with the beginning, peak, and ending of the contraction, respectively.</li> </ul>   |
| Late deceleration      | <ul style="list-style-type: none"> <li>• Visually apparent usually symmetrical gradual decrease and return of the FHR associated with a uterine contraction</li> <li>• A gradual FHR decrease is defined as from the onset to the FHR nadir of 30 seconds or more.</li> <li>• The decrease in FHR is calculated from the onset to the nadir of the deceleration.</li> <li>• The deceleration is delayed in timing, with the nadir of the deceleration occurring after the peak of the contraction.</li> <li>• In most cases, the onset, nadir, and recovery of the deceleration occur after the beginning, peak, and ending of the contraction, respectively.</li> </ul>  |
| Variable deceleration  | <ul style="list-style-type: none"> <li>• Visually apparent abrupt decrease in FHR</li> <li>• An abrupt FHR decrease is defined as from the onset of the deceleration to the beginning of the FHR nadir of less than 30 seconds.</li> <li>• The decrease in FHR is calculated from the onset to the nadir of the deceleration.</li> <li>• The decrease in FHR is 15 beats per minute or greater, lasting 15 seconds or greater, and less than 2 minutes in duration.</li> <li>• When variable decelerations are associated with uterine contractions, their onset, depth, and duration commonly vary with successive uterine contractions.</li> </ul>  |
| Prolonged deceleration | <ul style="list-style-type: none"> <li>• Visually apparent decrease in the FHR below the baseline</li> <li>• Decrease in FHR from the baseline that is 15 beats per minute or more, lasting 2 minutes or more but less than 10 minutes in duration.</li> <li>• If a deceleration lasts 10 minutes or longer, it is a baseline change.</li> </ul>  |
| Sinusoidal pattern     | <ul style="list-style-type: none"> <li>• Visually apparent, smooth, sine wave-like undulating pattern in FHR baseline with a cycle frequency of 3–5 per minute which persists for 20 minutes or more.</li> </ul>  |

Abbreviation: FHR, fetal heart rate.

Macones GA, Hankins GD, Spong CY, Hauth J, Moore T. The 2008 National Institute of Child Health and Human Development workshop report on electronic fetal monitoring: update on definitions, interpretation, and research guidelines. *Obstet Gynecol* 2008;112:661–6.

### **Box 1. Three-Tiered Fetal Heart Rate Interpretation System**

#### **Category I**

- Category I FHR tracings include all of the following:
- Baseline rate: 110–160 beats per minute
- Baseline FHR variability: moderate
- Late or variable decelerations: absent
- Early decelerations: present or absent
- Accelerations: present or absent

#### **Category II**

Category II FHR tracings includes all FHR tracings not categorized as Category I or Category III. Category II tracings may represent an appreciable fraction of those encountered in clinical care. Examples of Category II FHR tracings include any of the following:

##### Baseline rate

- Bradycardia not accompanied by absent baseline variability
- Tachycardia

##### Baseline FHR variability

- Minimal baseline variability
- Absent baseline variability with no recurrent decelerations
- Marked baseline variability

##### Accelerations

- Absence of induced accelerations after fetal stimulation

##### Periodic or episodic decelerations

- Recurrent variable decelerations accompanied by minimal or moderate baseline variability
- Prolonged deceleration more than 2 minutes but less than 10 minutes
- Recurrent late decelerations with moderate baseline variability
- Variable decelerations with other characteristics such as slow return to baseline, overshoots, or “shoulders”

#### **Category III**

Category III FHR tracings include either

- Absent baseline FHR variability and any of the following:
  - Recurrent late decelerations
  - Recurrent variable decelerations
  - Bradycardia
- Sinusoidal pattern

Abbreviation: FHR, fetal heart rate.

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status and underlying risk factors. Thus, during the first stage of labor the FHR tracing should be reviewed every 30 minutes and every 15 minutes during the second stage (7). Documentation of this review should include description of FHR category and overall pattern. Change in management may need to occur only if Category II or Category III features develop (Figure 1).

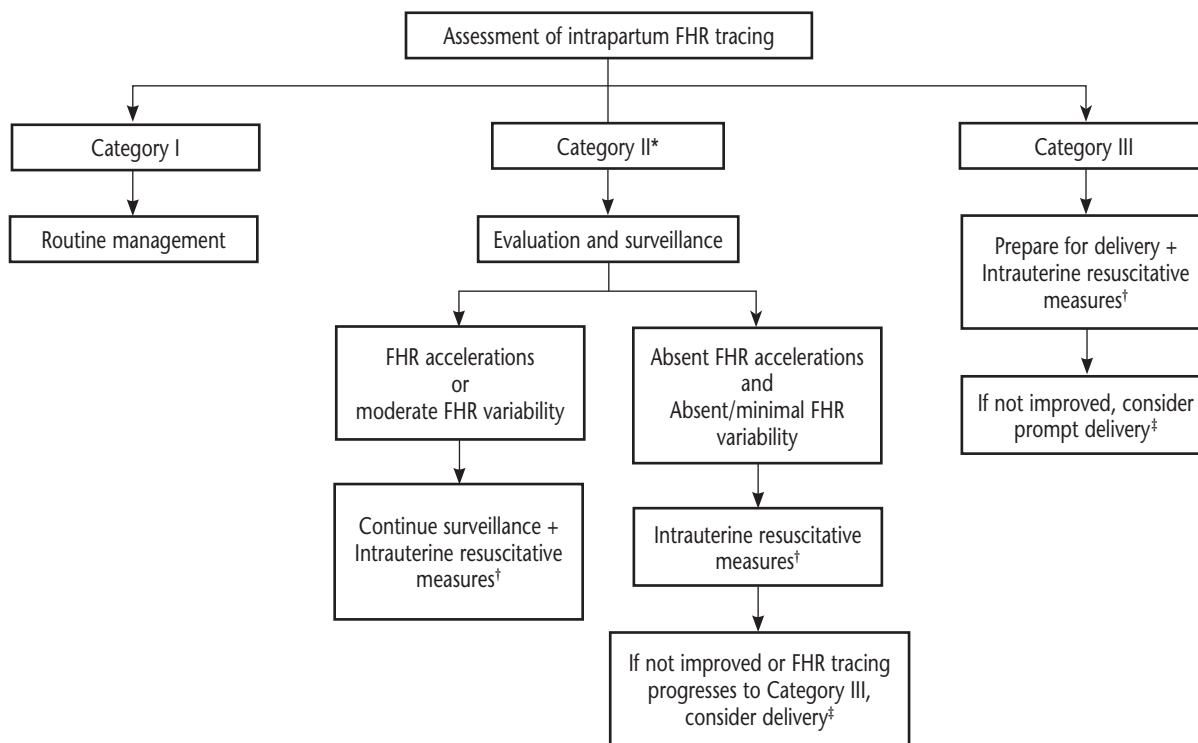
#### ► ***How is a Category II EFM tracing evaluated and managed?***

Category II FHR tracings include all FHR patterns that are not classified as Category I or Category III (Box 1). Category II tracings require evaluation, continued surveillance, initiation of appropriate corrective measures when indicated, and reevaluation. Once identified, these tracings may require more frequent evaluation, documentation, and continued surveillance, unless they revert to Category I. Given the diverse spectrum of abnormal FHR patterns in Category II, the presence of FHR accelerations (whether spontaneous or elicited by digital scalp or vibroacoustic stimulation) or moderate FHR variability or both are highly predictive of normal fetal acid–base status and, thus, may help guide clinical management (Figure 1) (8–12). The management of specific FHR abnormalities within Category II is discussed as follows.

#### ► ***How are intermittent and recurrent variable decelerations evaluated and managed?***

*Intermittent variable decelerations*, defined as occurring with less than 50% of contractions, are the most common FHR abnormality occurring during labor (13), most often do not require any treatment, and are associated with normal perinatal outcomes (3). Evaluation of recurrent variable decelerations includes their frequency, depth and duration, uterine contraction pattern, and other FHR characteristics such as FHR variability (14, 15). *Recurrent variable decelerations*, defined as occurring with greater than or equal to 50% of contractions, that progress to greater depth and longer duration are more indicative of impending fetal acidemia (2, 8, 14, 15). In FHR tracings with recurrent variable decelerations, the presence of moderate FHR variability or a spontaneous or induced acceleration suggests that the fetus is not currently acidemic.

Management of recurrent variable decelerations should be directed at relieving umbilical cord compression (Table 2). Maternal positioning as an initial therapeutic maneuver is a reasonable first step (16). Although there is limited evidence for improvements in short-term or long-term neonatal outcomes, amnioinfusion has been shown to decrease the recurrence of variable decelerations as well as the rate of cesarean delivery for “suspected fetal distress” (17). Adjunctive measures to promote fetal



\*Given the wide variation of FHR tracings in Category II, this algorithm is not meant to represent assessment and management of all potential FHR tracings, but provide an action template for common clinical situations.

†See Table 2 for list of various intrauterine resuscitative measures

‡Timing and mode of delivery based on feasibility and maternal–fetal status

**Figure 1.** Management algorithm of intrapartum fetal heart rate tracings based on three-tiered category system. Abbreviation: FHR, fetal heart rate.

oxygenation also may be useful depending on the severity and duration of the recurrent variable decelerations (Table 2).

► ***How are recurrent late decelerations evaluated and managed?***

Recurrent late decelerations are thought to reflect transient or chronic uteroplacental insufficiency (18). Common causes include maternal hypotension (eg, postepidural), uterine tachysystole, and maternal hypoxia. Management involves maneuvers to promote uteroplacental perfusion, which may include maternal lateral positioning, intravenous fluid bolus, maternal oxygen administration, and evaluation for tachysystole (Table 2) (16).

In Category II tracings with recurrent late decelerations, management includes intrauterine resuscitation and reevaluation to determine whether an adequate improvement in fetal status has occurred. Given the low predictive value of late decelerations for acidemia and their known false-positive rate for fetal neurologic injury (19–23),

evaluation for the presence of accelerations or moderate FHR variability or both may be useful to assess the risk of fetal acidemia (24). If despite intrauterine resuscitation measures late decelerations continue in the setting of minimal FHR variability and absent accelerations, the presence of fetal acidemia should be considered and the potential need for expedited delivery should be evaluated. If FHR variability becomes absent, then the FHR is now Category III and should be managed accordingly.

► ***How is intrapartum fetal tachycardia evaluated and managed?***

*Fetal tachycardia* is defined as a baseline heart rate greater than 160 beats per minute (bpm) for at least 10 minutes (Table 1). Fetal tachycardia should be evaluated for identifiable underlying causes such as infection (eg, chorioamnionitis, pyelonephritis, or other maternal infections), medications (eg, terbutaline, cocaine, and other stimulants), maternal medical disorders (eg, hyperthyroidism), obstetric conditions (eg, placental abruption or fetal bleed-

**Table 2. Various Intrauterine Resuscitative Measures for Category II or Category III Tracings or Both**

| Goal  | Associated Fetal Heart Rate Abnormality*   | Potential Intervention (s)†   |
|---|--|---|
| Promote fetal oxygenation and improve uteroplacental blood flow | Recurrent late decelerations<br>Prolonged decelerations or bradycardia<br>Minimal or absent fetal heart rate variability | Initiate lateral positioning (either left or right)<br>Administer maternal oxygen administration<br>Administer intravenous fluid bolus<br>Reduce uterine contraction frequency              |
| Reduce uterine activity   | Tachysystole with Category II or III tracing   | Discontinue oxytocin or cervical ripening agents<br>Administer tocolytic medication (eg, terbutaline)   |
| Alleviate umbilical cord compression                            | Recurrent variable decelerations<br>Prolonged decelerations or bradycardia   | Initiate maternal repositioning<br>Initiate amnioinfusion<br>If prolapsed umbilical cord is noted, elevate the presenting fetal part while preparations are underway for operative delivery |

\*Evaluation for the underlying suspected cause(s) is also an important step in management of abnormal FHR tracings.

†Depending on the suspected underlying cause(s) of FHR abnormality, combining multiple interventions simultaneously may be appropriate and potentially more effective than doing individually or serially (Simpson KR, James DC. Efficacy of intrauterine resuscitation techniques in improving fetal oxygen status during labor. *Obstet Gynecol* 2005;105:1362–8).

Data from Young BK, Katz M, Klein SA, Silverman F. Fetal blood and tissue pH with moderate bradycardia. *Am J Obstet Gynecol* 1979;135:45–7; Chauhan SP, Roach H, Naef RW 2nd, Magann EF, Morrison JC, Martin JN Jr. Cesarean section for suspected fetal distress. Does the decision-incision time make a difference? *J Reprod Med* 1997;42:347–52; Schaubberger CW, Chauhan SP. Emergency cesarean section and the 30-minute rule: definitions. *Am J Perinatol* 2009;26:221–6; and Schifrin BS, Hamilton-Rubinstein T, Shields JR. Fetal heart rate patterns and the timing of fetal injury. *J Perinatol* 1994;14:174–81.

ing), and fetal tachyarrhythmias (often associated with FHR greater than 200 bpm). In isolation, tachycardia is poorly predictive for fetal hypoxemia or acidemia, unless accompanied by minimal or absent FHR variability or recurrent decelerations or both.

Treatment for a Category II tracing with tachycardia should be directed at the underlying cause. In addition, other characteristics of the FHR tracing need to be evaluated in concert with the tachycardia, especially baseline variability. For example, a FHR tracing with tachycardia, minimal variability, and no accelerations cannot reliably exclude fetal acidemia.

► ***How are intrapartum bradycardia and prolonged decelerations evaluated and managed?***

*Fetal bradycardia* is defined as a baseline heart rate less than 110 bpm for at least 10 minutes (Table 1). *Prolonged decelerations* are defined as FHR decreases of at least 15 bpm below baseline that last at least 2 minutes but less than 10 minutes. Clinical intervention often is indicated before the distinction can be made between a prolonged deceleration and fetal bradycardia; thus, the immediate management of the two is similar.

Prolonged decelerations or fetal bradycardia should be evaluated for identifiable causes such as maternal hypotension (eg, postepidural), umbilical cord prolapse or occlusion, rapid fetal descent, tachysystole, placental abruption, or uterine rupture. Bradycardia due to these conditions often occurs in labor and usually is preceded by an initially normal FHR baseline. Rarely, bradycardia

also may occur in fetuses with congenital heart abnormalities or myocardial conduction defects, such as those associated with maternal collagen vascular disease. Most often the onset of bradycardia associated with congenital heart block occurs in the second trimester; it is extremely unlikely that new onset intrapartum bradycardia would be due to this condition.

Treatment for Category II tracing with bradycardia or prolonged decelerations is directed at the underlying cause (Table 2). Fetal heart rate variability during baseline periods should be evaluated in order to better assess the risk of fetal acidemia (25). If bradycardia with minimal or absent variability or prolonged decelerations or both do not resolve, then prompt delivery is recommended.

► ***How is minimal FHR variability evaluated and managed?***

As with other characteristics of the FHR tracing, baseline variability often changes with fetal sleep or wake state and over the course of labor, and it may transition from moderate to minimal and back again. Evaluation of minimal FHR variability should include evaluation of potential causes such as maternal medications (eg, opioid, magnesium sulfate), fetal sleep cycle, or fetal acidemia (26–28). For minimal variability thought to be due to recent maternal opioid administration, FHR variability often improves and returns to moderate variability within 1–2 hours. A fetal sleep cycle generally lasts 20 minutes but can persist up to 60 minutes, and moderate variability should return when the fetal sleep cycle is



complete. Thus, in these situations, continued observation and expectant management is appropriate. If minimal FHR variability is suspected to be due to decreased fetal oxygenation, then maternal repositioning, administration of oxygen, or intravenous fluid bolus may be considered (Table 2). If improvement in FHR variability does not occur with these measures and there are no FHR accelerations, additional assessment such as digital scalp or vibroacoustic stimulation should be done (12). Continued minimal variability (in the absence of accelerations or normal scalp pH) that cannot be explained or resolved with resuscitation should be considered as potentially indicative of fetal acidemia and should be managed accordingly.

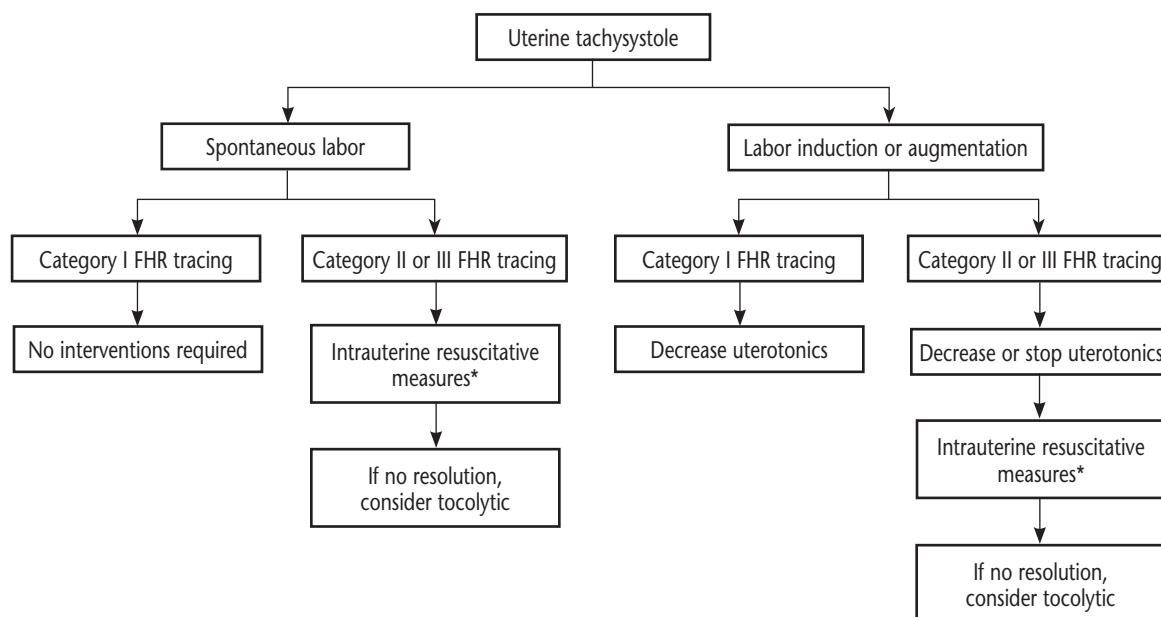
► **How is tachysystole with and without FHR changes evaluated and managed?**

*Tachysystole* is defined as more than five contractions in 10 minutes, averaged over 30 minutes. The presence or absence of associated FHR abnormalities is the key issue in management (Figure 2). For women with spontaneous labor, tachysystole coupled with recurrent FHR decelerations requires evaluation and treatment. Tachysystole occurring with less frequent FHR abnormalities may or may not require treatment, depending on the specific clinical situation and associated FHR characteristics such as variability and accelerations. In laboring women receiving oxytocin, management of tachysystole generally involves efforts to reduce uterine activity to minimize risk of evolving fetal hypoxemia or acidemia (29).

In labor induction or augmentation or both, a decrease in the oxytocin dose should be considered if tachysystole occurs in the presence of a Category I tracing. If there is a Category II or III tracing, oxytocin should be reduced or stopped in addition to intrauterine resuscitation (7). In addition, simultaneous initiation of multiple resuscitative measures may improve fetal condition more rapidly than the use of individual therapies (Table 2). If tachysystole induced FHR abnormalities do not resolve with these initial maneuvers, then tocolytic medications (eg, terbutaline) may be warranted (30, 31).

► **How is a Category III EFM tracing evaluated and managed?**

A Category III FHR tracing is abnormal and conveys an increased risk for fetal acidemia at the time of observation. Category III tracings have been associated with an increased risk for neonatal encephalopathy, cerebral palsy, and neonatal acidosis. Nevertheless, the predictive value of Category III tracings for abnormal neurologic outcome is poor (32). If unresolved, Category III FHR tracings most often require prompt delivery. While intrauterine resuscitation measures are used, preparations for delivery should be considered and a time frame for proceeding to delivery should be determined if the FHR does not improve (Figure 1). As discussed previously potential interventions for intrauterine resuscitation are described in Table 2; these should be modified to the appropriate clinical circumstance(s) and specific FHR pattern.



\*See Table 2 for list of various intrauterine resuscitative measures

**Figure 2.** Management algorithm for uterine tachysystole. Abbreviation: FHR, fetal heart rate.

► ***If a Category III tracing continues and intra-uterine resuscitative measures are unsuccessful, over what time interval should delivery be accomplished?***

The acceptable time frame to accomplish delivery in the setting of a Category III FHR tracing has not been established. Historically, a 30-minute rule from decision-to-incision time for emergent cesarean delivery in the setting of abnormal FHR pattern has existed (7); however, the scientific evidence to support this threshold is lacking. In a study of 2,808 women who had cesarean deliveries for emergent indications, investigators found that more than 30% of the cesarean deliveries began more than 30 minutes after the decision to operate, yet adverse neonatal outcomes were not increased among those infants delivered after more than 30 minutes (33). Multiple other studies affirm the lack of association of increased adverse outcomes with this 30-minute decision-to-incision time frame (34–38). It also should be recognized that in some cases immediate delivery in a woman with an unknown duration of a Category III tracing may not improve outcome if the fetus has already experienced hypoxic ischemic injury (39, 40).

Nevertheless, when a decision for operative delivery in the setting of a Category III EFM tracing is made, it should be accomplished as expeditiously as feasible. The decision-to-incision interval and mode of delivery should be based on the timing that best incorporates maternal and fetal risks and benefits. For instance many of these clinical scenarios will include high-risk conditions or pregnancy complications (eg, morbid obesity, eclampsia, cardiopulmonary compromise, hemorrhage), which may require maternal stabilization or additional surgical preparation before performance of emergent cesarean delivery. These factors also may vary based on the institution and local circumstances. Preparation for impending delivery of a woman with a Category III tracing often requires assessment of several logistical issues depending on the setting and clinical circumstances (see Box 2).

## Summary of Conclusions and Recommendations

***The following recommendations and conclusions are based on good and consistent scientific evidence (Level A):***

- Category I FHR tracings may be managed in a routine manner because they are not associated with fetal acidemia.

### Box 2. Potential Logistical Considerations in Preparation for Operative Delivery in Setting of Category III Tracing

- Obtain informed consent (verbal or written as feasible)
- Assemble surgical team (surgeon, scrub technician, and anesthesia personnel)
- Assess patient transit time and location for operative delivery
- Ensure intravenous access
- Review status of laboratory tests (eg, complete blood type and screen) and assess need for availability of blood products
- Assess need for preoperative placement of indwelling foley catheter
- Assemble personnel for neonatal resuscitation

- A Category III FHR tracing is abnormal and conveys an increased risk of fetal acidemia at the time of observation.
- Amnioinfusion has been shown to decrease the recurrence of variable decelerations as well as the rate of cesarean delivery for abnormal FHR patterns.

***The following recommendations and conclusions are based on evidence that may be limited or inconsistent (Level B):***

- Intravenous fluid bolus, lateral positioning and oxygen administration, when used together, may improve fetal oxygenation during labor.
- Regardless of whether labor is spontaneous or stimulated, tachysystole accompanied by Category II or Category III FHR tracing requires evaluation and initiation of appropriate treatment.
- Category II tracings require evaluation, continued surveillance, initiation of appropriate corrective measures when indicated, and reevaluation. The presence of FHR accelerations (whether spontaneous or elicited) or moderate FHR variability or both are highly predictive of normal fetal acid–base status and, thus, may help guide clinical management.

***The following conclusion is based primarily on consensus and expert opinion (Level C):***

- The optimal time frame to effect delivery in the setting of a Category III FHR tracing has not been established.

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The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985–December 2009. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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