Normative values of electrical activity of the diaphragm in non-ventilated preterm infants

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The University of Toledo
2011
Acknowledgements

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Introduction

The electrical activity of the diaphragm (Edi) is a measure of diaphragmatic electromyography (EMG) and reflects the neural control of respiration. It is measured via transesophageal electrodes positioned at the level of the crural diaphragm, which record total action potentials propagated from the neural respiratory centers along the phrenic nerve to the diaphragm (Beck et. al, 2001). Edi peak correlates with inspiratory drive by measuring the amplitude of the electrical impulse needed to elicit a contraction of the diaphragm. Edi min correlates with the tonic activity of the diaphragm during rest between breaths and maintains functional residual capacity. A new type of mechanical ventilation known as neurally adjusted ventilatory assist (NAVA) provides positive pressure ventilation in proportion to Edi. Because the respiratory center and the ventilator are driven by the same signal, the level of ventilatory assistance can be modified on a breath-by-breath basis (Biban, Serra, Polese, Soffiati, & Santuz, 2010). Patient-ventilator asynchrony is a common problem caused by conventional modes of ventilation, and can result in complications such as diaphragmatic dysfunction, pneumonia, higher ventilator weaning failure, increased use of analgesics and sedation, and most importantly, tremendous patient discomfort (Rowley, Lowson, & Caruso, 2009). With the utilization of Edi, the ventilator delivered assistance from NAVA is matched to individual neural demands, thereby vastly improving synchrony.

In addition to its use in observing patient-ventilator interaction, Edi value comparison may also be useful in the assessment of respiratory drive, diaphragmatic fatigue, respiratory impairment, and neuromuscular pathology. Edi values provide a more comprehensive understanding of breathing patterns, the control of breathing, and the mechanisms underlying tidal breathing (Hutten, van Thujil, van Bellegem, van Eykern, & van Aalderen, 2009). To date,
most Edi data has been obtained from patients on mechanical ventilation with respiratory
dysfunction. There is currently no data existing on the normative values of Edi in healthy non-
ventilated preterm infants. Without a reference of data in healthy subjects, there is limited
utilization of existing Edi data as there is nothing for comparison. NAVA and Edi are novel
concepts that may improve patient comfort and outcomes from mechanical ventilation. Because
so many premature infants require mechanical ventilation, obtaining normative Edi values in this
population will help guide the practitioner to proved appropriate ventilatory support in sick
preterm neonates. The purpose of this study is to measure Edi values in non-ventilated preterm
non-ventilated to establish normative values.
**Definitions**

**Electrical Activity of the diaphragm (Edi):** Measurement of neural impulses (action potentials) propagated from the phrenic nerve to the diaphragm to elicit a breath.

**Electromyography (EMG):** Study of the electrical activity of a muscle.

**Esophageal EMG:** Measurement of electrical activity of the crural diaphragm by electrodes within a nasogastric tube centered at the level of the diaphragm (esophageal hiatus).

**Edi Min (aka tonic Edi):** Baseline electrical activity of the diaphragm; the degree of activation at rest between breaths.

**Edi Peak:** Highest electrical activity of the diaphragm; the degree of respiratory effort associated with the production of a single breath.

**Preterm neonate:** In this study, refers to a neonate delivered at 24-36 weeks gestational age.

**NAVA (Neurally Adjusted Ventilatory Assist):** A mode of mechanical ventilation that delivers assist in proportion to a patient’s neural respiratory demand, reflected by the Edi signal.
Literature Review

Electrical Activity of the Diaphragm

The act of breathing is a complex sequence of events. Electrical impulses start in the respiratory neurons of the brainstem, travel down the phrenic nerve to electrically activate the diaphragm, causing muscle contraction, a drop in airway pressure, and lung expansion (Beck, 2010). Due to the fact that phrenic nerve velocity cannot be directly measured, the best representation of neural respiratory drive is the electrical activity of the diaphragm (Edi) (Beck et al., 2001).

Edi minimum (Edi min), or tonic Edi, refers to the baseline electrical activity of the diaphragm at rest between breaths. This maintained activity during expiration helps to regulate an infant’s reduced end-expiratory lung volume, and has been shown to decrease with the application of PEEP (Emeriaud, Beck, Tucci, Lacroix, & Sinderby, 2005). Edi peak refers to the amplitude of electrical activity associated with respiratory effort, and therefore diaphragmatic workload. The rate at which Edi approaches peak from baseline indicates how quickly the volume and pressure within the lungs must change in order to produce adequate air exchange to meet the current need (Binazzi, Lanini, & Scano, 2004). As the work of breathing increases, the neural signal sent to the diaphragm causes an increased Edi peak in order to maintain effective ventilation. As the work of breathing decreases, Edi will return to baseline, indicating the decrease in diaphragmatic workload (Rowley, Lowson, & Caruso, 2009). Changes in Edi over time can be used as an indicator of diaphragmatic fatigue.

Because the depolarization of a muscle fiber generates an electrical field outside of it, extracellular electrodes can be used to detect the diaphragmatic EMG signal. There are currently three types of electrode placement that can be utilized: intramuscular, surface, and
transesophageal. Intramuscular electrodes are inserted into the respiratory muscle of interest and provide the most precise sampling of Edi, allowing for the assessment of single motor units amongst respiratory muscles (American Thoracic Society/European Respiratory Society, 2002). These electrodes, however, lack the ability to provide an accurate assessment of global Edi, and are unsuitable for regular use in the clinical setting due to their invasiveness (Hutten, van Thuijl, van Bellegem, van Eykern, & van Aalderen, 2009). Surface electrodes are placed on the chest wall and are able to provide a global assessment of Edi. The disadvantage of these electrodes is that recordings are affected by muscle length during contraction, as well as body configuration, such as high amounts of adipose tissue and chest wall deformities. Esophageal electrodes are placed on a catheter, inserted via a nasogastric tube, and positioned at the level of the crural diaphragm. This is currently the most common type of electrode placement used to detect Edi, because not only does it assess global Edi, but it is less susceptible to changes in muscle length and chest wall configuration, and is less influenced by electrical “cross talk” from other respiratory muscles (American Thoracic Society/European Respiratory Society, 2002; Emeriaud et al., 2006). Many studies have confirmed that sampling a limited number of motor units in the crural diaphragm with esophageal electrodes provides an accurate assessment of global Edi, such as Beck et. al (2001) who demonstrated that the transdiaphragmatic pressure, a measurement of gross diaphragmatic activity, and Edi changed proportionally in the same direction with changes in pressure support ventilation. Because the cardiac pulse is stronger than respiratory muscle electrical activity, extra measures must be taken to subtract the ECG signal from the EMG signal to ensure accurate esophageal electrode recordings.

NAVA is a new type of ventilation that utilizes the Edi as its trigger to provide positive pressure ventilation. Unlike conventional ventilation, NAVA allows for the respiratory muscles
and the ventilator to be driven by the same signal. The level of assistance provided is proportional to Edi, and can therefore be adjusted on a breath-by-breath basis (Biban, Serra, Polese, Soffiati, & Santuz, 2010). Most importantly, the pressure delivered by the ventilator is stopped when the Edi signal is ended (Sinderby et. al, 2007), thereby avoiding patient-ventilatory asynchrony. Patient-ventilator asynchrony is present in approximately 25% of ventilated patients, and can result in such complications as diaphragmatic injury, pneumonia, longer duration of ventilation, increased need for tracheostomy and analgesics, higher weaning failure rate, extreme patient discomfort, and other morbidities associated with increased ICU time (Rowley, 2009). NAVA theoretically eliminates all asynchrony because the Edi controls the timing and magnitude of ventilator assistance based off the patient’s own respiratory center demand (Biban, Serra, Polese, Soffiati, & Santuz, 2010).

Currently very little data exists on the normative values of Edi of neonates. Without a reference, it is impossible to evaluate Edi signals in ventilated preterm neonates and determine the appropriate level of ventilatory support. In a study done by Stein, Burton, & Wilmoth (2010), normative Edi values were obtained in healthy term infants, and it was found that Edi min remained unchanged during feeding states, while Edi peak was found to be lower in the post-prandial state than the pre-prandial state (submitted data). This is most likely due to the fact that feeding resulted in an increased the intra-abdominal pressure and decreased the intra-thoracic volume, causing shallower breathes and a lower Edi peak.

**Development of Respiration**

Respiration control beings with the neural respiratory drive in the brainstem, and is influenced by a variety feedback elements such as the upper airway, stretch receptors in the lungs, and chemoreceptors. Upper airway muscles must be intact to allow for airflow,
maintaining lung volume, and protecting the upper airway. Chemoreceptors located in the brain, aortic arch, and carotid arteries are sensitive to changes in arterial oxygen, pH, and CO₂ changes, and modify breathing on a second-to-second basis (Stokowski, 2005). The Hering-Breuer stretch receptors terminate inspiration in response to lung distention, and are especially important in maintaining the lung volume in the neonate, who is born with a highly compliant chest wall (Givan, 2003).

Migration of nerve cells to the respiratory center occurs at 10-20 weeks gestation. Rhythmic contractions of the diaphragm first appear in the fetus at 10 to 12 weeks gestation, and cause periodic and asynchronous fetal breathing movements. There are various stages of lung development including pseudoglandular (5 to 17 weeks gestation), canalicular (16 to 26 weeks gestation), saccular (24 to 38 weeks gestation), and alveolar (36 weeks gestation to 2 years). The fetal lungs are fluid filled with liquid secreted from the pulmonary epithelium and are not metabolically active. The volume and rate at which the liquid is secreted into the fetal lungs is controlled by fetal breathing movements and are the major determinants of normal lung growth (Sinha, Gupta, & Donn, 2007). Those infants born premature may experience difficulties dealing with these normal adaptive processes, and may require assisted ventilation.

The central chemoreceptors are active in the fetus and respond to CO₂ and blood pH levels (Givan, 2003). Carbon dioxide is the driving force for fetal breathing, where an increased PCO₂ will increase breathing and a decreased PCO₂ will decrease breathing. Oxygen status is also important, because a decrease in PO₂ will decrease respiratory movements. This response is unlike that of a matured respiratory center, in which the response to hypoxia should be an increased breathing rate, and demonstrates the inability of immature respiratory neurons to sustain activity in response to prolonged stimulation (Stokowski, 2005).
A neonate’s first breath results from a multifactorial process, most likely occurring due to the hypoxia created between separation from the placenta and decent down the birth canal (Givan, 2003). In order to transition to spontaneous breathing, a negative pressure change of 40 to 100 cm must be generated by the diaphragm in order to overcome the elastic and inertial properties of the respiratory system (Givan, 2003; Sinha, Gupta, & Donn, 2007). Breathing begins as rapid and irregular, with some grunting to aid in the clearance of fluid from the lungs. Respiration maturation is incomplete in all aspects at birth, including immaturity of chemoreceptors, respiratory reflexes, respiratory muscles, respiratory drive, and central neurons (Stokowski, 2005).

Many of the breathing patterns seen in premature infants resemble that of the fetus, such as periodic breathing, paradoxical breathing, and apnea. These are all the result of respiratory immaturity, including a poor respiratory drive, weak muscles, flexible ribs, surfactant deficiency, and impaired lung liquid clearance (Pas et. al, 2008). Periodic breathing involves sequences of respiratory pauses less than 20 seconds in duration mixed with intervals of normal breathing. It is normally considered a benign occurrence, but could lead to prolonged periods of oxygen desaturation (Stokowski, 2005). Paradoxical breathing occurs when the chest wall moves inward upon inspiration and outward upon expiration, and is the result of preterm infant’s highly compliant chest wall. The resulting chest wall distortions increase the volume of displacement of the diaphragm during inspiration, and can lead to diaphragmatic fatigue (Poets, 2009). The most common breathing difficulty by far is apnea, occurring in 54% of infants born at 30 to 31 weeks and nearly all infants born at less than 29 weeks (Stokowski, 2005). Apnea is a complete cessation of respiration greater than 20 seconds in duration, most commonly resulting from immature respiratory responses to hypercapnia and hypoxia (Miller, Martin, &Haxhiu, 2003).
These immature patterns of respiration decrease rapidly after 36 weeks gestation, and regular respiration increases dramatically (Parmelee, Stern, & Harris, 1972).

Due to an infant’s low functional residual capacity (FRC), oxygen stores are diminished compared with metabolic needs. Compensation for this reduced FRC is accomplished via a prolonged end-expiratory phase (Givan, 2003). The appropriate hypoxic-ventilatory response does not develop until approximately 35 weeks gestation; therefore premature infants, like fetuses, respond to hypoxia with a decrease in ventilation. Preterm infants also have an impaired response to hypercapnia, exhibiting an increase in depth, but not frequency of breathing movements. These impaired responses demonstrate the premature infant’s strong tendency toward inhibition of breathing in response to stimulation of airway receptors (Stokowski, 2005).
Methodology

Research Design

This was a prospective observational study of non-ventilated preterm neonates in a resting state.

Population and Sampling Methods

The population for this study included neonates born between 24 to 35 weeks gestation who met the following criteria: were not on any form of mechanical ventilation, breathing either on room air (RA) or high-flow nasal cannula (HFNC) at $\geq 31$pm or regular nasal cannula (NC), free of any congenital anomalies, resolved or no respiratory problems, and have a nasogastric tube currently in place for routine use. This was a convenience sample of neonates born at The Toledo Children’s Hospital who meet the inclusion criteria. Information about participation in the study was provided to and informed consent obtained from the parents of the neonates. Study protocol was approved by the Institutional Review Board of The Toledo Children’s Hospital (IRB # 11-008).

Data Collection Methods

The infant had a NAVA nasogastric tube placed instead of the traditional nasogastric tube. Edi values were measured using electrodes embedded within the NAVA nasogastric tube that were positioned at the level of the crural diaphragm. Proper positioning was confirmed by on-line analysis on SERVO-i software. The nasogastric tube was connected to SERVO-i ventilator software for Edi recording. Data output included Edi peak and minimum, which was stored in minute increments in the SERVO-i software, downloaded to a flash drive, and imported into Microsoft Excel for data analysis. Data was collected for 4 hour increments and was performed weekly.
Variables Measured

Independent variables consisted of neonate gender, gestational age, weight, current respiratory support, oxygen saturation, and the presence of any apnea, bradycardia, or desaturation. The dependent variable was Edi, measured in microvolts (µV).

Statistical Analyses

Population means, standard deviations, and rangers of Edi peak and minimum were complied via Microsoft Excel to establish population normative values. Regression analysis was performed to compare Edi peak and minimum amongst each gestational age. Statistical significance was defined as p<0.05.
Results

A total of 17 neonates were enrolled in the study, 8 males and 9 females, all of whom met the inclusion criteria. A total of 97 studies were performed between gestational ages 26-38 weeks. Average birth weight was $1220 \pm 534$ grams, with a range of 628 - 2520 grams. Cumulative study time was 388 hours. There were a total of 28 studies done on HFNC, 25 studies on NC, and 44 studies on RA.

Overall Edi peak was $10.8 \pm 3.7 \, \mu V$ and Edi min was $2.8 \pm 1.1 \, \mu V$ and demonstrated no significant difference between gestational ages, as shown in Figure 1. There was no difference in Edi peak and min between the different types of non-invasive respiratory support (HFNC, NC, or RA). Average heart rate, respiratory rate, and oxygen saturation by gestational age are shown in Table 1 and are unchanged over gestational age.
Discussion

The purpose of this study was to establish Edi values in stable preterm neonates to determine a normative reference range so that these can be used to guide ventilator management and aide in the identification of respiratory pathology.

Edi peak and min remained unchanged over gestational age and were comparable to those previously reported in term neonates (Stein, Burton, & Wilmoth, 2010). The preterm neonatal population we studied all had to be off mechanical ventilation and breathing spontaneously. The Edi data supports the clinical picture that, neonates mature enough to have effective spontaneous respirations, should have a respiratory drive that is comparable to term neonates. Although preterm neonates are at risk for apnea, no apneic episodes were noted during the study periods. Due to data collection limitations, we were unable to assess periodic breathing, but predict that all our patients had some evidence of this during the studies.

Neonates were studied as soon as they were off mechanical ventilation. Many of the subjects still required varying types of non-invasive respiratory support, reflecting some ongoing lung disease or prematurity. The amount of non-invasive respiratory support was determined to achieve a clinically stable patient with no respiratory distress. Heart rate, respiratory rate, and oxygen saturation were all within the normal range and physiologically appropriate for preterm neonates. This confirms that the subjects met the enrollment criteria and were clinically stable on all forms of respiratory support during all studies. There was no difference in Edi values between the various forms of respiratory support, suggesting that these Edi values may guide future clinicians on how much respiratory support is needed to facilitate the preterm neonate’s spontaneous respiratory effort. This data may also aide in the adjustment of NAVA ventilatory settings in those neonates requiring ventilation.
Conclusion

Establishing normative Edi values in non-ventilated preterm infants allows for a reference range for comparison in ventilated neonates. It appears that neural respiratory drive in the non-ventilated preterm neonates is comparable to term infants. Utilizing normative data will provide the clinician with values to work towards in the sick intubated preterm neonate. This may facilitate earlier extubation and decrease the incidence of chronic lung disease.
References


Table 1: Average heart rate, respiratory rate, and oxygen saturation by gestational age

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>Heart Rate (beats per minute)</th>
<th>Respiratory Rate (breaths per minute)</th>
<th>Oxygen Saturation (percent per minute)</th>
</tr>
</thead>
<tbody>
<tr>
<td>26, n=3</td>
<td>159.6 ± 15.6</td>
<td>55.8 ± 19.1</td>
<td>92.6 ± 3.8</td>
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<tr>
<td></td>
<td>Range 147-177</td>
<td>38-76</td>
<td>90-97</td>
</tr>
<tr>
<td>27, n=5</td>
<td>166.1 ± 5.7</td>
<td>50.4 ± 9.9</td>
<td>94.8 ± 5.2</td>
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<tr>
<td></td>
<td>Range 157-173</td>
<td>36-61</td>
<td>86-100</td>
</tr>
<tr>
<td>28, n=7</td>
<td>164.3 ± 4.3</td>
<td>55.7 ± 10.3</td>
<td>93.3 ± 2.8</td>
</tr>
<tr>
<td></td>
<td>Range 156-169</td>
<td>47-71</td>
<td>90-96</td>
</tr>
<tr>
<td>29, n=8</td>
<td>163.2 ± 12.1</td>
<td>51.2 ± 7.2</td>
<td>92.2 ± 4.8</td>
</tr>
<tr>
<td></td>
<td>Range 142-175</td>
<td>41-60</td>
<td>84-98</td>
</tr>
<tr>
<td>30, n=10</td>
<td>158.9 ± 6.5</td>
<td>50.2 ± 10.0</td>
<td>94.8 ± 3.2</td>
</tr>
<tr>
<td></td>
<td>Range 149-167</td>
<td>38-65</td>
<td>89-99</td>
</tr>
<tr>
<td>31, n=12</td>
<td>159.4 ± 7.7</td>
<td>52.9 ± 10.6</td>
<td>94.3 ± 2.9</td>
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<tr>
<td></td>
<td>Range 145-170</td>
<td>40-71</td>
<td>88-98</td>
</tr>
<tr>
<td>32, n=14</td>
<td>156.6 ± 17.5</td>
<td>51.0 ± 7.3</td>
<td>95.9 ± 2.7</td>
</tr>
<tr>
<td></td>
<td>Range 116-174</td>
<td>37-60</td>
<td>90-99</td>
</tr>
<tr>
<td>33, n=16</td>
<td>158.4 ± 11.5</td>
<td>52.8 ± 7.8</td>
<td>96.1 ± 3.0</td>
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<td>Range 136-173</td>
<td>42-74</td>
<td>89-99</td>
</tr>
<tr>
<td>34, n=11</td>
<td>157.3 ± 7.1</td>
<td>50.0 ± 6.3</td>
<td>96.7 ± 2.7</td>
</tr>
<tr>
<td></td>
<td>Range 143-167</td>
<td>38-58</td>
<td>92-100</td>
</tr>
<tr>
<td>35, n=5</td>
<td>160.0 ± 7.5</td>
<td>50.3 ± 5.0</td>
<td>95.0 ± 2.9</td>
</tr>
<tr>
<td></td>
<td>Range 151-171</td>
<td>45-55</td>
<td>91-98</td>
</tr>
<tr>
<td>36, n=4</td>
<td>165.2 ± 4.5</td>
<td>52.2 ± 8.5</td>
<td>93.4 ± 4.0</td>
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<td></td>
<td>Range 160-170</td>
<td>44-63</td>
<td>88-98</td>
</tr>
<tr>
<td>Term, n=2</td>
<td>167.0 ± 3.7</td>
<td>47.1 ± 1.7</td>
<td>91.1 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>Range 164-170</td>
<td>46-48</td>
<td>91-92</td>
</tr>
</tbody>
</table>
Figures

Figure 1
Average Edi Peak and Min by gestation Age

Gestational Age
Appendices

RESEARCH INFORMED CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Title: Normative Values of Electrical Activity of the Diaphragm in Preterm Infants

Principal Investigator: Howard Stein, MD
Sub-Investigators: Keith Davis II, PA-SII, Rachel Hall, PA-SII

Why is this study being done?
You are being asked to give permission for your baby to participate in a research study of electrical activity of the diaphragm (Edi) in preterm babies. Edi measures the signal from the breathing center in the brain that goes to the diaphragm (the muscle that helps the lungs push air out). This signal is responsible for determining the size of the breath and the rate of breathing. The purpose of the study is to identify normal Edi in preterm neonates at rest. Data collection will benefit future patients in its application to identification of abnormal breathing function. Approximately 60-96 babies will participate in this study conducted at The Children's Toledo Hospital. Your baby was selected as a possible participant in this study because he or she was delivered between 24-35 weeks, is not on any form of mechanical breathing support, and has a feeding tube currently in place for routine use.

What will happen if you take part in this study? (Procedures and Duration)
If you decide to participate, your baby will have the regular feeding tube replaced by a specialized NAVA feeding tube. This NAVA feeding tube has electrodes imbedded in the wall to detect the Edi signal. This specialized feeding tube will be connected to a monitor that collects Edi data. Participation will last 3-4 hours and will occur in the baby's room. During this time your baby will remain in the isolette or crib but you will be able to remain with your baby the entire time. At the end of the study this tube can be used until it is time to replace it as normally done for routine care. This tube will be used weekly, instead of the regular feeding tube, to measure Edi until your baby reaches 35 weeks corrected age or no longer needs a feeding tube.

What side effects or risks could result from being in this study?
Feeding tubes are placed in babies frequently without complications. Possible complications, although extremely rare include esophageal perforation (a hole in the esophagus) or tissue trauma when the feeding tube is placed. This, however, is not an additional risk to your baby since the baby will require a feeding tube to be placed for
routine care. Over the past 19 years the complication rate per feeding tube placement in this NICU is 1 in 125,000. The feeding tube will be placed by an experienced doctor or nurse who will continue to be available throughout the study. We have been using this special nasogastric tube, to measure electrical activity of the diaphragm, for almost 3 years and have placed hundreds of these tubes without any complications. There are no long-term complications of this procedure.

**What are the benefits to participating and will you be paid to participate?**
There is no direct benefit to your baby and you will not be paid for participating in this study. The results of this study will benefit future babies, especially those requiring mechanical ventilation (help breathing) at birth and in the identification of abnormal breathing patterns.

**What other choices do you have if you do not take part in this study?**
You can choose not to participate in this study. Your choice not to participate will not affect your child’s care at The Toledo Children’s Hospital.

**Will your medical information be kept private?**
You and your child’s medical records will be maintained in accordance with federal and state laws. Efforts will be made to keep you and your child’s personal information confidential. The research investigator(s) cannot guarantee absolute confidentiality. Private identifiable information about you may be used or disclosed for the purpose of conducting this research project as described earlier in the consent form. The information that may be used or disclosed includes the following: physician/clinic records and hospital records.

You have the right to access your child’s medical records. You may request that your child’s research medical record be released to your personal physician. Organizations that may inspect and/or copy your research medical records for quality assurance and data analysis include: Food and Drug Administration and ProMedica Health System Institutional Review Board. This information may be further disclosed if the recipient(s) described on this form are not required by law to protect the privacy of the information. Data from this study may be used in medical publications or presentations, but any information identifying you or your child will be removed.

The use and disclosure of your protected health information will conclude at the end of this study. If after you have entered this study and you wish to withdraw from participation, you have the right to change your mind about allowing the investigator to have access to this health information, although the investigator may use information already collected to maintain the completeness of the study. If you decide to revoke permission to use your child’s personal information, you should contact Dr. Howard Stein of Toledo Children’s Hospital at 419-291-8380.

**What are the costs of taking part in this study?**
There is no cost for participation in this study. You will not be charged for any of the study procedures.
What happens if you are injured because you took part in this study?
If your baby is injured as a direct result of participating in this study, treatment can be obtained at The Toledo Children’s Hospital. The costs of such treatment will be paid for by The Toledo Children’s Hospital. In the event of injury, contact Howard Stein, M.D. at 419 291-8380.

By signing this form you are not giving up any of your legal rights as a research subject.

Are any research team members being paid for conducting this study?
The investigators performing this study are not receiving any direct or indirect compensation to conduct this study. Dr. Stein is a speaker for Maquet, the manufacturer of the specialized nasogastric tube and monitoring device. All other investigators have no financial link to the makers of data monitoring devices used in this study.

What are your rights if you take part in this study?
Participation in this study is voluntary. If you decide not to participate in this study, your decision will not affect your future relations with any ProMedica Health System institution, its personnel, and associated hospitals. You have the right not to participate in this study, and refusing to participate will not affect the present or future medical care you receive and will not cause any penalty or loss of benefits to which you are otherwise entitled. If you withdraw from the study early, the research team may continue to collect follow-up information on your health status to be used as part of the study if you agree.

Who can answer your questions about the study?
Before you sign this form, please ask any questions on any aspect of this study that is unclear to you. You may take as much time as necessary to think this over. If you have any questions regarding your rights as a research patient, you may contact the Chairperson of the ProMedica Health System Institutional Review Board at 419-291-5362, during office hours Monday through Friday, 8 a.m. to 4:30 p.m.
**Signatures:**
You are making a decision whether or not to participate in this study. Your signature indicates that you have read and understood the information provided above, have had all your questions answered, and have decided to participate.

________________________
Printed Name of Subject (Your baby)

________________________
Printed Name of Mother

________________________  _______________________
Signature of Mother  Date

________________________
Printed Name of Father

________________________  _______________________
Signature of Father  Date

________________________
Printed Name of Person Obtaining Consent

________________________  _______________________
Signature of Person Obtaining Consent  Date

**YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP**

If you have any questions concerning this study or consent form beyond those answered by the investigator, including questions about the research, your rights as a research subject or research-related injuries, please feel free to contact the ProMedica Health System Institutional Review Board at 419-291-5362.
Abstract

**Background:** The electrical activity of the diaphragm (Edi) reflects neural respiratory effort. Edi peak correlates with inspiratory drive and Edi min correlates with the tonic activity of the diaphragm. Normative Edi values in preterm infants are unknown.

**Objective:** To establish normative Edi values in non-ventilated preterm neonates and to determine if these values vary between gestational ages.

**Methods:** Preterm neonates, off mechanical ventilation, were observed weekly for four hours until the neonate no longer required a NG tube. Edi values were measured via a nasogastric tube with embedded electrodes. Statistics were regression analysis with p <0.05.

**Results:** 97 studies were done between gestational ages 26 – 38 weeks. Overall Edi peak was 10.8± 3.7 µV and Edi min was 2.8± 1.1 µV. There was no difference in Edi peak and min between gestational ages.

**Conclusion:** In non-ventilated preterm neonates, Edi peak and min do not appear to vary over gestational ages.