

Critical Care News

Special NAVA Issue

NAVA - the latest
evolution in clinical
practice for critical care

PAGE 2

Experiences with
NAVA in pediatric
intensive care patients

Karl Erik Edberg, MD, PhD,
The Queen Silvia Children's
Hospital, Gothenburg, Sweden

PAGE 4

Paradigm shifts in
mechanical ventilation
— a NAVA session report

Christer Sinderby, PhD,
St. Michael's Hospital, Toronto,
Canada. Jennifer Beck, PhD,
Women's College Hospital NICU,
University of Toronto, Canada

PAGE 10

First impressions of
NAVA in adult patients

Carl-Johan Wickerts, MD,
PhD, Danderyd Hospital,
Stockholm, Sweden

PAGE 21



PAGE 4

Experiences with NAVA in pediatric intensive care patients

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Dr C-J Wickerts and patient, Danderyd Hospital, Stockholm, Sweden.

NAVA – the latest evolution in clinical practice for critical care

The modern intensive care environment as we know it evolved primarily with the introduction of modern mechanical bedside ventilators over thirty years ago. Ever since that time, clinical research and technological developments have led to continuing advancements in respiratory care. These advancements include the introduction of online CO₂ measurements in the late 70s, electronic PEEP in the early 80s, as well as an ever increasing number of ventilatory modes devoted to providing the physician the opportunity to deliver lung protective and synchronized ventilation therapy.

However, ventilation therapy during the past decades has primarily consisted of adjusting airway pressure, flow and volume in pneumatically driven mechanical ventilators. For the first time since the introduction of mechanical ventilation over thirty years ago, ventilation therapy can now be provided by means of the patient's own neural control, based on the physiological methodology of Neurally Adjusted Ventilatory Assist – NAVA.



Christer Sinderby, PhD at the Paradigm Shifts symposium in New York.

NAVA as a methodology is gaining increasing attention from the intensive care community. Research about NAVA has been published for a number of years, however studies in the area have expanded in recent years, and new developments in technology have now made the method available for use in bedside ventilation and monitoring in intensive care units. These exciting developments will contribute to new approaches and a new way of thinking in the critical care environment. That is why this special issue of Critical Care News is devoted entirely to NAVA.

Clinical experience opening new opportunities in pediatric intensive care

As former President of the European Society of Pediatric Intensive Care, Karl Erik Edberg, MD, PhD is an internationally known profile who has conducted and participated in pivotal ventilation research for many years.

He shares his experiences with the first series of pediatric patients that have been treated with NAVA at The Queen Silvia Children's Hospital in Gothenburg, Sweden, and his observations and ideas about new research and treatment opportunities that he believes that NAVA may provide.

Paradigm shifts in mechanical ventilation – a NAVA session report

Several hundred physicians and respiratory therapists had the opportunity to hear Jennifer



Nurses with pediatric patient treated with NAVA at the Queen Silvia Children's Hospital in Gothenburg, Sweden.

Beck, PhD, and Christer Sinderby, PhD present their latest research about NAVA in regard to patient-ventilator synchrony at the recent international symposium in New York, August 28-29, 2006.

A summary of the highlights of the NAVA sessions, with an interview with Jennifer Beck and Christer Sinderby regarding their latest research and ideas about NAVA is included as a feature in this special issue of Critical Care News.

First impressions of NAVA in the adult ICU environment

Carl-Johan Wickerts, MD, PhD has been involved in respiratory research for many years. He is chief of the ICU at Danderyd Hospital in Stockholm, Sweden, and shares his first impressions of the use of NAVA in adult patients, and his current experience of NAVA in COPD cases. ■



Jennifer Beck, PhD.



Karl Erik Edberg, MD, PhD with ten-month old NAVA patient and parents.

Experiences with NAVA in pediatric intensive care patients

The pediatric intensive care unit of The Queen Silvia Children's Hospital in Gothenburg, Sweden, is well known for applied clinical research in new therapies in Scandinavia. The PICU is one of the first clinics in Scandinavia to evaluate NAVA – Neurally Adjusted Ventilatory Assist as a new method of ventilatory assist of their small patients. Critical Care News was honored to observe this new generation of ventilation therapy on a ten-month old girl, who under post-operative sedation, was assisted by signals from a catheter to her diaphragm.

Critical Care News spoke with Karl Erik Edberg, MD, PhD, internationally known researcher and lecturer in regard to ventilation therapies, about the experiences with the first series of patients treated at Queen Silvia with this new generation of ventilation therapy.



Karl Erik Edberg is an internationally known research and lecture profile.

Can you tell us about the patient who was treated with NAVA while we were visiting today?

The patient weighs 8 kilos and has a ventricular septum defect, as well as a pulmonary stenosis and abnormal pulmonary circulation attributed to a MAPCA-vessel (major aorto pulmonary collateral artery). So the case has been quite complex, but in an otherwise healthy patient. She underwent surgery yesterday, and a Sanoshunt was placed between the right ventricle and the pulmonary circulation. More surgery will be needed in future, but these are the first surgical interventions. Post-operatively, there have been a few complications, as there may be in

more extensive heart surgery procedures, but since yesterday afternoon she has been doing well, and her lung x-ray this morning was good. I considered her a good candidate for NAVA, and informed her parents about the method and the study, and explained to them that she was a suitable candidate for weaning with NAVA. Prior to implementing the NAVA protocol, she was hemodynamically stable and on SIMV/PS, with 60-100% oxygen. During NAVA, she has been a model patient; she has generated her own breaths and Edi signals have been sensed in an exemplary manner and she was peaceful and calm throughout the procedure. We were even able to pull the chest tube aided by a small dose of alfentanil during NAVA. I anticipate that she will be extubated

shortly. (Editors note: This patient was extubated the same afternoon and was transferred from the PICU to a general ward the next morning.)

Before we speak more specifically about NAVA, can you give us a general description about your department, average number of patients and staff?

We have 10 ICU care stations, with the capacity of handling up to 13 patients if needed. We admit approximately 600 patients per year and our average ICU length of stay is less than 48 hours, which is remarkably short. The majority of our patients are under 1 year old, and a great majority of these are post-operative heart surgery patients. We take care of approximately 200 heart-lung patients per year, in addition to other surgical patients. In regard to staffing, we are about 20 physicians who share the responsibility, 24 hours a day and 365 days a year. In this group, there are 5 physicians who are working exclusively with intensive care, and the rest are bridging between the surgical theatre and the ICU. We try to specialize in the different areas of our rather broad spectrum of activities here. We work with 5-6 registered nurses per shift, and about the same amount of pediatric nurses and practical nurses per shift as well. We all work together in mixed teams.

Which types of patient situations do you most frequently encounter?

Primarily we see post-operative cardiac patients, but all sorts of pediatric intensive care patients as well; sepsis cases, encephalitis, meningitis. We have patients with renal insufficiency and failure in need of dialysis; we also have patients with congenital birth defects such as diaphragmatic hernias, oesophageal atresias and gastroschises in both newborns and premature infants. We also have patients with metabolic problems, severe seizure cases for diagnosis and treatment, trauma and accident cases such as poisonings, burn patients and drowning. For all cases here in general, the relationship between post-op patients and other ICU patients is 40/60%.

How are family member visits encouraged in your PICU environment?

As we observed during the NAVA case today, parents are welcome and are considered part of the PICU environment. We welcome parents at any time, day or night, and encourage them

to participate and be close to their children, and to observe treatment and care here. We try to encourage the parents to sleep at night, preferably away from the patient care area, and if they are living outside of the city, we try to arrange for accommodation in a facility close to the ICU building. Both parents are usually present for most patients, and siblings are also welcome. The only time where we actively encourage parents to leave their children is a rest period between 12 and 1 p.m. each day. This traditional rest period is something we have established for many years, to offer the children a chance for as much quiet and as little disturbance as possible. During this period we dim the lights, and try to minimize procedures and traffic in order to provide peace and quiet.

When did you become familiar with the concept of NAVA, and what were the primary factors leading to the initiation and testing of this therapy at your center?

I became familiar with the concept of NAVA for the first time in Montreux 2004, when I heard Jennifer Beck speak about Neurally Adjusted Ventilatory Assist. I was aware of the ongoing research, and read the literature that was published on NAVA at that time. I became personally interested in this methodology, since I am an ICU physician who has always had a special focus on pediatric ventilation. My doctoral thesis focused on lung mechanics and ventilation of premature infants. I was actively involved in HFO research, and was one of the first to introduce the HFO concept here in Sweden a number of years ago. I have also been involved in early research in treating infants with surfactant, and was first to introduce natural surfactant treatments in infants in Sweden, before surfactant became commercially available. I was also among the first to research and implement nitric oxide therapy, as well as non-invasive ventilation therapy for infants in Sweden. So, when NAVA became available for investigational use, naturally my colleagues and I were quite eager to try it.

The ten-month old infant patient whom we observed today, is the thirteenth patient you have treated by means of NAVA. How would you summarize your general experience with the method this far?

Primarily, that this method works very well, and we see that the children are doing well with it. It has become easier to apply and initiate NAVA with each consecutive patient. One extra pleasant surprise we have experienced is that

over half of the children treated with NAVA have gone straight from NAVA to extubation. This surprise was a little unexpected, since the expectations we had when we started working with NAVA and traditional ventilation therapy were such that we thought we might expect that these children would be extubated within a day or so after the completed NAVA protocol. But when we have applied NAVA and observed that the pressures generated by the children have become so low that the children are basically breathing spontaneously, we have gone to extubation, without any complications.

In terms of the ventilator program with NAVA that we were using, the method works well for the patient, but there were some initial difficulties for us as caregivers with monitoring and alarm functions. These functions had been developed for traditional ventilation therapy, and not for NAVA, which means there have been a lot of redundant alarms, which were irritating at bedside. Our input has contributed to an improved algorithm. Our experiences helped contribute to tailor these functionalities. In regard to our specific experience with the NAVA patient you observed today, I would say she was a textbook case, in that her lungs were in good shape, she was lightly but adequately sedated without pain, and was quiet and peaceful, and very appropriate for NAVA as applied to the research protocol we are currently running.

Are there some specific patient experiences that are of special interest?

The youngest patient weighed 3.2 kilos and was just a couple of days old; however the age and weight of the patient are not critical in regard to NAVA. It is important to consider extremely premature infants with unstable breathing patterns and periods of apnea, where NAVA might be complicated. But for the great majority of our patients, maybe with the exception of babies with extremely sick lungs where our NAVA experience is too limited, NAVA can be an excellent method. I think for the majority of our post-operative cardiac patients, NAVA will be very beneficial and appropriate.

We have experienced NAVA with different patient cases with varying treatment times, from a couple of hours to one case that was treated up to 6 or 7 hours, and ended with extubation. In considering that we have had 13 patients so far, I think we have gained a broad experience with different situations. One of our patients weighed about 50 kilograms, and had

severe lung disease, but we treated her with NAVA, which went exceptionally well. The pressures that we determined for her in Pressure Support were about the same levels that she generated herself with NAVA, but it was she who was driving her ventilation therapy and it went extremely well, despite the fact that she had very sick lungs.

We had one especially interesting case with a patient with a diaphragmatic hernia, who had received surgery here two years ago. The child returned with a recurrence of the hernia in the same area and needed new surgery. Earlier, we have been a little skeptical if a child with a diaphragmatic hernia could be treated with NAVA. But the therapy worked extremely well in this patient. We have had some patients where we have been uncertain in regard to their diaphragmatic function, including one patient who underwent neurosurgery for a tumor located in a portion of the brain where the respiratory centers are located. We had concerns that the respiratory center and respiratory regulation would be affected, and we were uncertain how the effect of the neurosignal to the diaphragm was functioning. But we provided NAVA in this patient, and it worked excellently. In fact, it was like a receipt that the patient's connection from the respiratory center in the brain to the diaphragm was functioning normally.

In general, on the basis of our first experiences with NAVA, it is exciting to identify a number of research opportunities in the future. Previously, I have treated many extremely premature infants, often with surfactant, and for many years we have strived for the most gentle ventilation therapy possible, to avoid barotrauma and volutrauma. We have known for a long time that there are dangers associated with ventilating at high pressures, which we have tried to avoid. I see this as a potentially broad area for researching if NAVA can be used for children with different levels of IRDS; to determine if it will work, and if so, to see which pressures these very small children will generate to achieve their ventilation, and to see the significance of them directing their own breathing as much as possible. This is a large and exciting area that I am very curious about. I will be getting involved with our neonatologists who are working with ventilation of premature infants to see how we can utilize NAVA in these patients.

What is your practical experience with NAVA catheter positioning: in order to obtain the

best ECG/EMG signals, how it is placed, when, and who positions the catheter as well as your experiences of administering NAVA and using the catheter as a normal feeding tube?

My experience is that this has been easy. We have been extremely careful to measure from the tip of the nose and around the ear to the lowest tip of the chest bone. We have made markings by using a separate catheter or the NAVA catheter. Placement has been confirmed very quickly in each case, mainly by means of the ECG. The catheter itself is very easy to place; it is moistened at the surface and is easy to get it down the esophagus, and simple to verify by means of stethoscope when it is in place. As a feeding tube, it works excellently for us, we have had no problems with this causing signal disturbance, and it is easy to evacuate air out of it. For the course of the evaluation, myself or another physician has been placing the catheter, however I am firmly convinced that in time this will be a routine assignment to other staff members, such as our nurses. In time, there will need to be other markings to indicate the center of the electrode array, and the distance is longer from the lowest electrode to the tip, which is placed in the stomach.

How do you perceive the Edi curve?

We have had some positive and some less than positive perceptions. We have treated a few children where the Edi curve has been perceived as a great jumble, difficult to comprehend and with a lot of disturbance. We have tried to adjust in order to get the Edi curve to present itself as we expect it to. But even if it has been jumbled, it has provided information to the ventilator so that the patient has received even and good tidal volumes. We have not had any case where the Edi curve has disrupted therapy, and we have always been able to treat the patient. And in some children, we have seen beautiful, harmonious, disturbance free Edi curves. In general, the Edi curves have functioned well, but there have been a few occasions where disturbances have taken place that have been difficult to identify.

Which ventilation therapies would normally have been used in these NAVA protocol patients?

We have utilized most of the modes that are available at present. The majority of our patients have received SIMV with Pressure Support, but we have also administered

Pressure Control, PRVC, and Pressure Support with CPAP to some of our patients.

In terms of experience after these initial patients, what do you perceive as the benefits of NAVA?

Our most definite experiences have been when we have perceived that we have given as much Pressure Support or SIMV as the patient required, we now realize that we have been giving too much. When we switch over to NAVA, we see by the Edi signal that the pressures being generated by the patient himself are substantially less than the pressures we had predetermined. We have simply been a bit too generous with pressures in the past in Pressure Support mode, which is our consensus after experiencing NAVA. When we return from NAVA to conventional respiratory therapy, we utilize this knowledge of the patient-generated pressures in NAVA, and we have treated with the NAVA pressure levels, and it has worked excellently. In any form of ventilation therapy where you can reduce airway pressures, reduce oxygen concentrations during ventilation therapy; all of these components are beneficial for our patients.

NAVA provides a potential to support bedside decision making, since in our experience, with support of the patient-generated pressure levels, it has contributed to early extubation of patients who we otherwise would not consider candidates for extubation. In these cases, we have been able to shorten the treatment time, as we have discovered that the patient was doing so well that we could discontinue ventilation treatment. Potentially, this means that lengths of stay in the ICU can be shortened, and costs can be reduced. I perceive NAVA as almost self-weaning for the patient. It functions in a manner where the less help a patient needs, the greater benefit the patient receives.

What, according to your experience so far, are the most important aspects for ICU staff to learn, prior to initiating NAVA?

First and foremost, it is important to truly understand the concept and with that, the realization that this type of ventilation therapy is very similar to the breathing patterns of children and adult patients when they are not on the ventilator, i.e. spontaneous breathing. There is variability in normal breathing which is rather large, and which is different from the very stereotypical conventional mechanical



Parents are welcome in the PICU at The Queen Silvia Children's Hospital.

ventilation, where you set the size, performance and frequency of each breath in a very standardized manner. This traditional mechanical ventilation results in beautiful curves and loops that all look similar. This is not the case with NAVA; there is a big variation that is similar to spontaneous breathing. The other important aspect for staff to learn is to be meticulous in placement and function of the NAVA catheter, which needs to be re-checked every now and then. It is important to monitor the catheter periodically to ascertain that the catheter has not moved, for example if the patient has coughed, vomited, or has rolled around in the bed. It is very important that the catheter maintains the same position throughout the course of therapy.

These are the two aspects I consider to be of most importance to learn, but otherwise this is a very simple and uncomplicated mode of breathing, since it is so self-regulating and patient-driven. I am convinced that this method will become very popular, when ICUs learn how simple it is, and see the benefits of it.

In a general ICU setting, what are the most significant initial pitfalls to be aware of or avoid in starting out with NAVA, with regard to your current experience?

It is important that the patient is somewhat stable, from a respiratory and circulatory

perspective, and that the patient has the capability of maintaining his own respiratory capacity with help of his diaphragm. But in starting out with the method, I would initially avoid patients who have muscular diseases or a neuromuscular disturbance of any kind, or patients with brain damage or apnea tendencies. I would avoid these groups to begin with, and become familiar with the method first, before attempting to treat them with NAVA.

Which types of initial patient categories would you recommend others to start with, in order to gain experience?

I would recommend gaining experience with patients who are relatively lung-healthy; post-operative patients are a good category when they have come through their muscle relaxants and are past the heaviest levels of sedation, and are stabilized. I think that this is an excellent patient category to begin NAVA

therapy with. I would start using NAVA in this category, and become more familiar with the therapy. After learning and becoming familiar with the therapy, it might be time to try it on other patient categories, such as muscular diseases, and diseases relating to the diaphragm, or brain. ■

Biography

Karl Erik Edberg, MD, PhD attended medical school at Umeå University during 1965-1972, and was employed as an anesthesiologist at Karlstad Hospital, Sweden in 1972. He specialized in anesthesiology and intensive care in 1977, and what was intended as a short stay at the Department of Pediatric Anesthesia and Intensive Care, Children's Hospital (later The Queen Silvia Children's Hospital) in Gothenburg, Sweden, is still ongoing. He was director of the department during the years of 1995 to 2004, and remains an ongoing consultant in pediatric intensive care at the institution.

Karl Erik Edberg was also appointed Clinical and Research Fellow at the Division of Neonatology, Department of Pediatrics at Vanderbilt University, Nashville, Tennessee during 1987-1988.

A major research interest in lung function in the newborn led to a thesis in 1991 entitled "Lung Function in Newborns with IRDS". Present research interests also include the clinical use of nitric oxide in neonatal and pediatric intensive care, and measurements of cardiac output in infants.

Karl Erik Edberg has served as organizer and invited speaker at numerous national and international meetings and congresses on pediatric intensive care. He was elected Vice President of the European Society of Pediatric Intensive Care in 1993, and was elected and served as President of the same society during 1995-1998. He served as Past President and member of the executive committee 1998, and was also member of the executive committee of the European Society of Intensive Care from 1995-1998. Karl Erik Edberg has also been a member of the board of the World Federation of Pediatric Intensive and Critical Care Societies from 1996 to 2004.

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[CLICK FOR ABSTRACT](#)

Ola Ingemansson, MD, works in the PICU at The Queen Silvia Children's Hospital.



Critical Care News also spoke with Dr. Ola Ingemansson of Queen Silvia Children's Hospital regarding his perceptions of NAVA during the clinical evaluation period:

What are your general perceptions of this new ventilation therapy at this point in the clinical evaluation?

During the NAVA sessions I have been involved in, I have observed that the majority of patients have been very calm and peaceful during NAVA, with the exception of one patient who had very sick lungs, and required very high pressures.

Based on these initial experiences, what do you think will be the advantages of NAVA,

compared to other traditional methods of ventilation therapy?

I believe NAVA will be a very good therapy for weaning, and I believe it may lead to earlier extubation in the future.

How would you practically advise other ICU's that are considering implementing NAVA as a new ventilation therapy?

Theoretically it is important to know how it works, the entire concept, before the institution initiates this new method of therapy. Secondly, you must be able to trust NAVA itself, which differs from other ventilation therapies. Our small patients are different, since spontaneously, they would like to

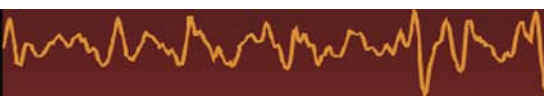
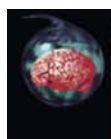
breathe more frequently and with fewer big breaths. You also must realize that the airway pressures are very low, and accept this fact, and not worry about it. This experience with NAVA has led us to the realization that we have probably had higher pressures on the other ventilation modes, before we have switched over to NAVA, where the patient has required much lower pressures. For ICU's that wish to start using NAVA, I personally would recommend starting out on post-operative patients who are hemodynamically stable and are close to extubation, since I believe this is the patient category where it is easiest to gain experience and confidence in the method.



Jennifer Beck, PhD, and Christer Sinderby, PhD at a lively Q & A session during the symposium.

Paradigm shifts in mechanical ventilation — a NAVA session report

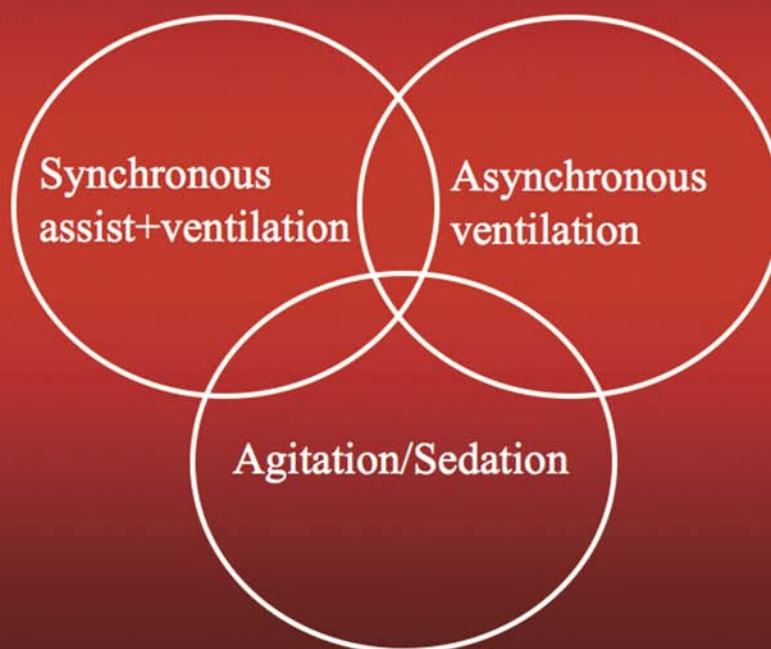
Research and practical implementation in regard to patient-ventilator synchrony was the focus of a four hour NAVA lecture session at the recent international symposium in New York August 28-29, 2006. Several hundred physicians and respiratory therapists had the opportunity to hear Christer Sinderby, PhD, and Jennifer Beck, PhD present their latest research about invasive and non-invasive NAVA in regard to different patient categories. Critical Care News also had the opportunity to interview Christer Sinderby and Jennifer Beck about their research in neonatal monitoring.



UofT



Unloading by mechanical ventilation in spontaneously breathing patients



Can cerebral signaling be utilized for feedback in mechanical ventilation?

The problem of determining the patient's contribution or degree of inhibition to breathing was illustrated by Dr Sinderby in a series of patient examples. His point to the audience was that without the neural signal, it is very easy to be misled and to misinterpret the situation.

If synchrony is defined as including not only gas delivery, but also the degree of ventilation, this can only be achieved by a mode that allows the patient to control both cycling and volume, according to his/her receptor response. This indicates that respiratory muscles can only be efficiently unloaded by an inspiratory assist in full synchrony with the patient's own effort. Sensitivity of the respiratory center may be influenced by the administration of sedatives or opioid drugs. If the inspiratory assist is delivered in asynchrony with the patient's own effort, he may be adequately ventilated, but this does not constitute proof of respiratory muscle unloading.

During both conditions, the breathing pattern and resulting blood gases will be influenced by the administration of respiratory depressant drugs.

After a short review on the history of NAVA development, highlighting the progress of the development of the nasogastric (NG) catheter design, to the current electrode array (Edi catheter), Dr Sinderby proceeded by describing the reflex pathway and the mechanical coupling necessary to achieve respiration. He emphasized the necessity of catching the control signal early in the chain of events to avoid asynchrony and time delays.

Proper positioning of the Edi catheter can be easily achieved by using the standard measurement of nose-ear-xiphoid process as a first assumption. Final optimization of the position can then be determined by looking at the ECG progression, which is always recorded by the Edi catheter, provided that the patient is alive. If there is no Edi signal after proper placement of the catheter has been achieved

as determined by the ECG signal, the differential diagnosis of resulting functional apnea has to be determined. The most common explanations are hyperventilation or oversedation, according to Dr. Sinderby. In a severely ill patient it should be expected that the Edi amplitude is high, as a result of the mechanical impairment usually seen due to the disease process, resulting in a much weakened response by the respiratory muscle in spite of intense neural signaling. Experience dictates that the signal amplitude reflects that the Edi amplitude is dependent upon both respiratory drive and the expected mechanical response of the respiratory muscles.

As NAVA by design is a mode that works in synchrony with the diaphragm excitation, and the ventilator effectively uses the same signal as the diaphragm, Dr Sinderby was able to show how the "extra muscle" provided by the ventilator can unload all the inspiratory work, as proven by the abolishment of transdiaphragmatic pressure swing during a vital capacity maneuver in a

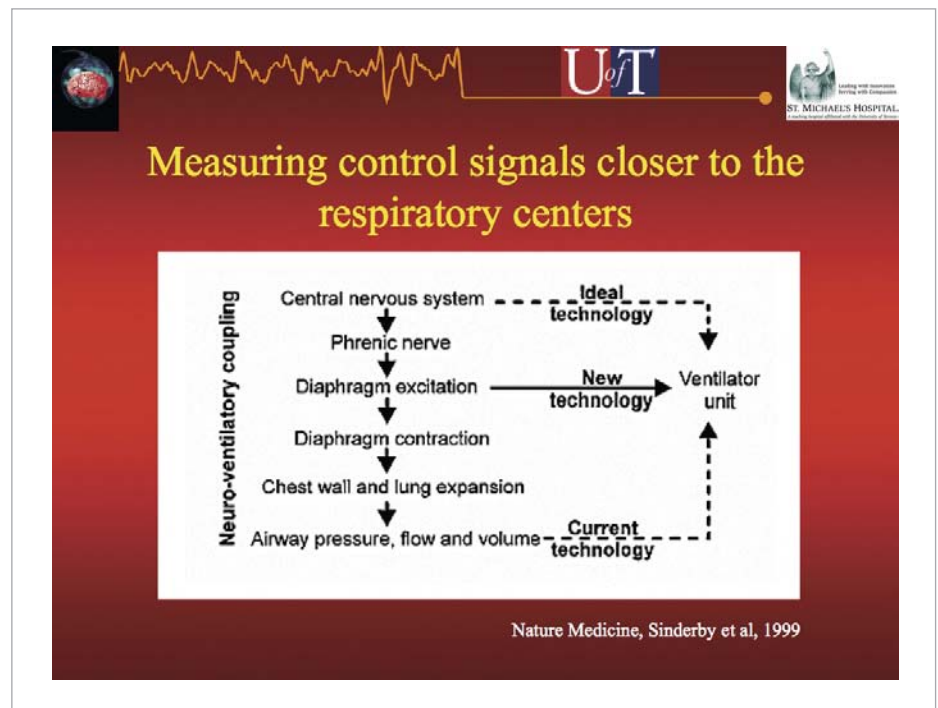
healthy subject (This study is now In Press in Chest, September 2006). Interestingly, the positive pressure delivered by the ventilator was essentially the same as the negative pleural pressure obtained without any assistance.

Dr Sinderby underlined that normal breathing is quite variable, even during resting conditions. It would seem logical to try to mimic this biological variability, by unloading the respiratory muscles in proportion to the extra load induced by the disease process, instead of imposing a breathing pattern that is strictly based on one pressure level or a fixed tidal volume. By delivering a proportional assist in synchrony with the patient effort, the amplitude of the Edi signal can be used to precisely titrate the amount of unloading required for the individual patient. A decrease in the amplitude of the Edi signifies less respiratory work for the patient, coupled with an increasing NAVA level, indicates that the extra muscle provided by the ventilator successively assumes a larger share of the respiratory work.

In summary, Christer Sinderby stated that if the electrode is positioned at the level of the diaphragm, if the patient is breathing, it must be possible to detect an Edi signal. If no diaphragmatic activity is detected and the ECG is still seen, the electrode is working. In the presence of diaphragmatic electrical activity, the diaphragm and ventilator receive the same signal and diaphragmatic and ventilator pressures are synchronously generated. To inflate the lungs in response to neural inspiratory drive, neural feedback will adjust the neural respiratory drive, which in turn will adjust the ventilator pressure generated to inflate the lungs.

Information captured from the EAdi signal

Dr Beck clarified that the electrical activity (Edi) of the diaphragm represents the respiratory center output for controlling rhythm, depth and duration of breathing. Depending on the response of the muscle, the signal will be modified as the feedback from the stretch receptors and chemoreceptors send back information to the respiratory centers. Since her research has been directed to the control of breathing in neonates and preterm infants, several distinguishing patterns have emerged, differentiating this patient population from adult patients. The research has been conducted by introducing a small-bore nasogastric (NG) feeding tube fitted



with an electrode array. The ECG has been used to determine correct positioning of the tube, with a prominent P-wave at the cranial electrode, and the disappearance of the P-wave at the caudal lead. She emphasized that X-ray was not necessary.

Amplitude of the signals was referred to as phasic electrical activity of the diaphragm, and this phasic activity represents a progressive increase in inspiratory effort. When the signal begins to decline, it indicates that the brain has informed the diaphragm to stop the inspiratory effort. In adults, the signal usually goes back to 0 as there is a pause between breaths. However, in babies, a shift in the baseline represents the presence of diaphragmatic activity during expiration, which is called tonic activity of the diaphragm.

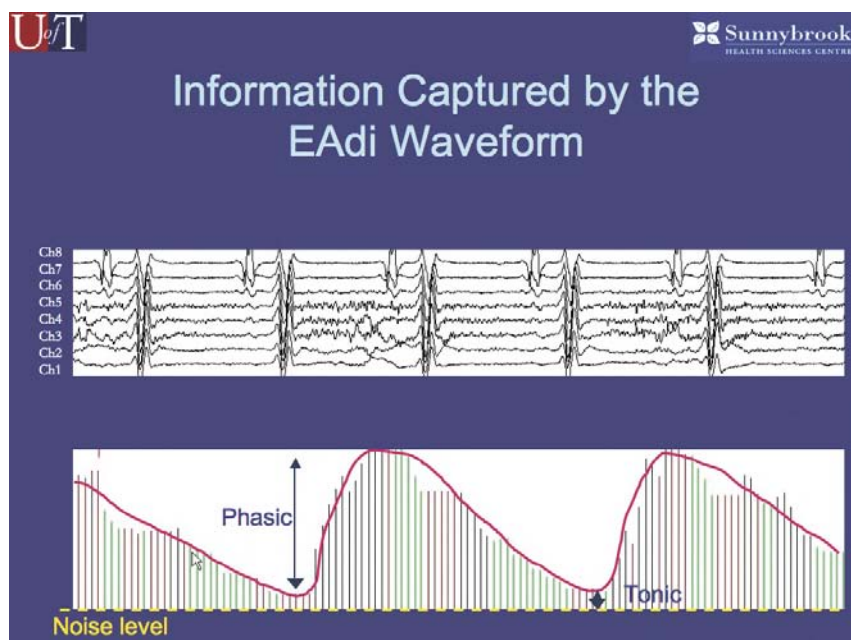
She proceeded to show examples of phasic diaphragm activity in adults, with tonic diaphragm activity. Dr Beck also showed examples of how increasing pressure support leads to a continuous decrease in transdiaphragmatic pressure and Edi amplitude, up to a point where the increase in pressure leads to increasing asynchrony and an increase in Edi amplitude.

On the other hand, with NAVA there is a linear relationship of continuous unloading as the mode does not induce asynchrony. SIMV is a commonly employed mode for neonates. The spontaneous neural inspiratory time for this population is 250-300 ms. In Dr Beck's example, SIMV time had been routinely set at 700 ms,

which resulted in grave respiratory asynchrony. As the average delay for the pneumatic trigger was 100 ms, patient-ventilator synchrony on inspiration resulted in 30% of neural inspiratory time spent trying to trigger the ventilator. When combining the inspiratory and expiratory asynchrony, 50% of the delivered assist was delivered out of phase with patient demand (Published in Ped Res 2004 Beck et al). Dr Beck commented on the paradox that SIMV stands for Synchronized Intermittent Mandatory Ventilation, when in fact it is not a synchronized mode.

Tonic diaphragm activity is nearly always present in neonates as their pliable chest wall is inefficient in maintaining lung expansion. In a situation where no PEEP is administered, there is a risk that the baby has to work continuously as he is not able to rest during expiration, possibly leading to frequent apnea and recruitment periods. Dr Beck elegantly showed how PEEP can more or less abolish this energy consuming and stressful breathing pattern. (Emeriaud et al, 2006 Ped Res).

An example of monitoring apnea and bradycardia in a pre-term baby was also presented. ECG signals were plotted as well as the diaphragm electronic activity. The pre-term infant had a typical chaotic breathing pattern, with a heart rate of 150 and satisfactory saturation one minute, and no diaphragm activity the next. During apnea indicated by absence of diaphragm activity, the heart rate fell to 66 and saturation to 82. When aroused, the baby made a large inspiratory effort and



breathed phasically on top of tonic activation (spontaneous recruitment maneuver), then became apneic again. According to Jennifer Beck, this example shows that monitoring the diaphragm electrical activity in neonates can provide the opportunity of evaluating the impact of the respiratory pattern on the entire organism.

In summary, Jennifer Beck stated that phasic Edi can provide information about changes in respiratory drive, and that the timing of diaphragm activity in relation to mechanical ventilation can provide information about patient-

ventilator interaction. She also stated that tonic diaphragm activity can provide information about the diaphragm's role in maintaining FRC, and that monitoring EAdi can provide insights into mechanisms of apnea of prematurity.

Practical implementation of NAVA in invasive ventilation

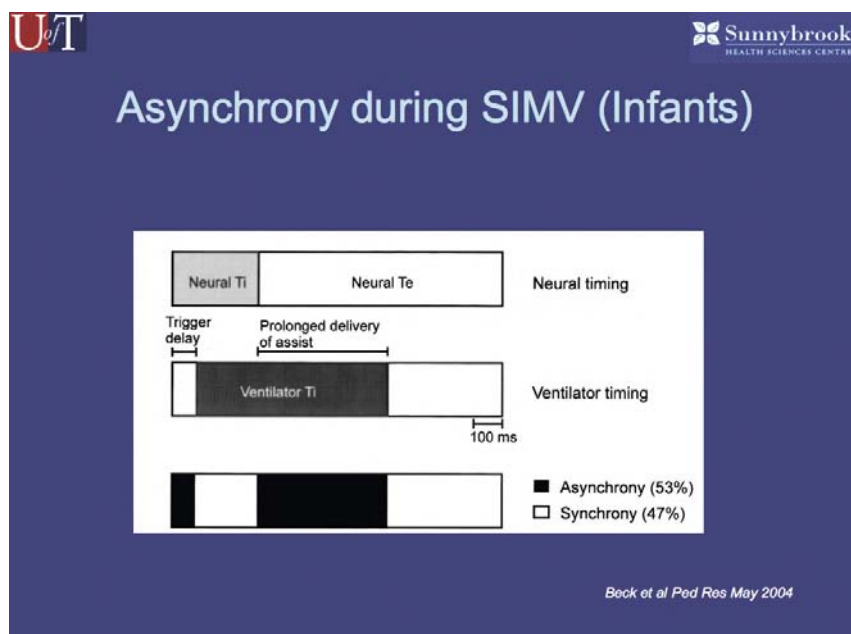
Christer Sinderby presented aspects of lung protection in relation to NAVA, as research available so far shows much promise. He showed a graph representing three maximum



Jennifer Beck during the NAVA lecture session.

inspirations, with no assist, with NAVA at medium level gain, and with NAVA level at maximum. Pressures were recorded, with peak pressure up to 60, or total lung capacity in that patient. The diaphragm activity went down to only 40% of the initial value. According to Christer Sinderby, this illustrates that you cannot fully suppress neural drive during NAVA. You may suppress it, but cannot remove it. Volumes are minimally affected, since the Hering-Breuer inspiratory inhibiting reflex prevents overinflation. He went on to present unloading with NAVA, by plotting mean airway pressure against mean esophageal pressure to identify the mean transpulmonary pressure. In the example a maximum inspiration created a mean inspiratory pressure of 15 cm H₂O esophageal pressure with a diaphragm activity of 100%. When increasing the NAVA level the same transpulmonary pressure was maintained. The system can be controlled within the whole range of volumes, but maintains proportionality. (In Press Chest 2006, Sinderby et al).

He also presented data from a study of increasing NAVA levels in rabbits with acute lung injury. The spontaneously chosen tidal volume before lung injury was 3.5 ml/Kg. After injury, this volume was the same, respiratory rate increased initially, and at 100% unloading, tidal volume was only increased to 4 ml/Kg. He stated that after delivering 100% unloading and increasing the NAVA level as much as possible there was no work of breathing, very little diaphragmatic activity, and only 0.5 ml/Kg change in tidal volume. After four hours, there





The symposium was attended by over 275 clinicians from many different countries.

were normalized breathing patterns, indicating that after induced injury and application of NAVA, the animals were able to regulate themselves.

He reported from a study of 14 sedated patients with acute lung injury, where NAVA was titrated to assist levels where no changes in breathing frequencies, tidal volumes or airway pressures were observed. Recordings were made over three hours of ventilation with NAVA and compared to pressure support or pressure control settings prior to NAVA. It was interesting to note that the patients chose a tidal volume of about 6 ml/Kg, which was similar to the pressure control or pressure support initial settings, with similar respiratory rates recorded prior to NAVA and during NAVA. PCO₂ and pH ratios stayed the same over three hours. However, mean airway pressure decreased to 4 or 5 cm H₂O, and diaphragmatic activity increased to double. Christer Sinderby commented that it seems that the patients actually want to use twice as much activity as he was allowed to on pressure support or

pressure control, while using a lower pressure to breathe than was delivered. He believes this is due to the limitations of one level of assist in conventional ventilation to cover the peaks in respiratory demand.

With regard to patient-ventilator synchrony, Christer Sinderby referred to a study by Martin Tobin et al, indicating the start and stop of diaphragm activity and ventilator activity, with poor overlap between the two. He then presented information by Dr Spahija et al, showing pressure support levels before switching to NAVA, and after NAVA. After switch to NAVA, the diaphragm activity was totally correlated with flow and airway pressure, in synchrony during both inspiration and expiration.

Christer Sinderby also presented examples from the same study illustrating NAVA compared to pressure support in low and high levels of assist in ARF patients. Breathing frequency in pressure support went from 25 to 17, where in NAVA it stayed at 25 at all times. This is due

again to the Hering-Breuer reflex, according to Christer Sinderby. He stated that perhaps it is not generally known that respiratory rate is reduced by increasing levels of pressure support. He stated that this is a fundamental difference between NAVA and PSV.

Christer Sinderby summarized his take-home message by saying that NAVA appears to offer improved trigger/cycling off synchrony, which can be mixed with existing technologies and that NAVA offers an appropriate level of assist that can be indicated by the patient. He stated that there is no runaway aspect to NAVA, and that it appears to offer appropriate ventilation with guaranteed respiratory drive.

Practical implementation of NAVA in non-invasive ventilation

Jennifer Beck introduced her presentation with a film of a healthy subject with an Edi catheter sending diaphragm electrical activity signals to the ventilator, with lung model inflation. Chest

movement and inflation of the lung model were clearly seen, illustrating synchrony in a situation of 100% leak, according to Jennifer Beck. This means that the idea of using an electrical signal to control the ventilator opens up a whole new field of possibilities for non-invasive ventilation. She also illustrated how size does not matter by means of a similar film of a 350 gram anesthetized rat that was spontaneously breathing, with signal to ventilator and inflation of lung model. Tidal volume in this case was around 2 ml. She pointed out that this also was an illustration of synchrony in the presence of a 100% leak.

She presented the helmet as another type of non-invasive interface, with a video of a healthy subject breathing on NAVA with a helmet. She stated that normally this device is hard to synchronize since it is so large, which makes it difficult to detect flow or pressure changes for triggering. Diaphragm activity, pressure delivered and esophageal pressures were displayed.

A study comparing pressure triggering and neural triggering of the helmet device in pressure support mode was presented. During pressure triggering there was asynchrony, with delays between the start of diaphragm activity and the delivery of assist. Every second breath in this case was a wasted effort. When switching to neural triggering, diaphragm electrical activity signaled to the ventilator and an assist was delivered, and synchrony was restored.

She also presented data showing neural control and pressure support in healthy subjects, with inspiratory and expiratory delay times. Different pressure support levels of 5, 10 and 15 were studied, with different respiratory rates of 10, 20 and 30. Independent of which pressure support level or respiratory rate was used, the inspiratory delay between the time the diaphragm becomes active and the time the ventilator delivers an assist, is reduced when you use a neural trigger. Jennifer Beck stated that this is even more striking when considering that the expiratory delays when cycling off with neural activity are much shorter in neural control. Comfort was rated by the subjects, and when comparing pressure trigger to neural trigger, independent of the pressure support level that was used, in general the neural trigger was more comfortable.

She also presented preliminary data from a study implementing NAVA before and after extubation in a rabbit with lung injury. Diaphragm electrical activity was measured at intubation



Jennifer Beck, PhD and Christer Sinderby, PhD have conducted research in the area of neurally adjusted ventilatory assist for many years, and their research has been extensively published in peer review publications.

and when the injury was induced. At extubation, a tube was placed 2 cm into one nostril of the rabbit, with mouth open and other nostril free. When ventilating with NAVA using a single nasal prong, the tonic activity disappeared completely. With increased levels of NAVA, the assist was delivered in synchrony and in proportion to the diaphragm electrical activity, despite the fact, as Jennifer Beck pointed out, that only one single nasal prong was used. When increasing NAVA levels 4 times, the respiratory muscles were unloaded by means of synchronized non-invasive positive pressure ventilation. She also pointed out that after extubation, despite that PEEP was removed, the tonic activity was not present.

Jennifer Beck presented a graph that she thought would make neonatologists very happy, illustrating baseline gastric pressure during the non-invasive runs. Mean level of assist delivered was depicted during progressive increase of NAVA level, with no evidence of stomach inflation. Even at peak pressures of 40 cm H₂O, there was no effect on gastric distention, according to Jennifer Beck.

She also presented an example from her preliminary data of non-invasive pressure support compared to NAVA, which she hoped the audience would observe as an important take-home message. The graph displayed tracings from a rabbit breathing on pressure support with a single nasal prong, diaphragm electrical activity, ventilator delivered pressure, and esophageal pressure swings. With such a substantial leak, the animal could not trigger pressure support, with declining PO₂ levels and increasing PaCO₂. After switching to NAVA, there was an instantaneous continuous recording of synchronized, non-invasive positive pressure ventilation, with immediate reduction of work of breathing and diaphragm activity, resulting in improved blood gases. Jennifer Beck completed her presentation by summarizing the goals of NAVA: improved patient-ventilator interactions, reduced work of breathing, to provide improved and safer ventilation, to reduce the need for sedation and paralysis, to adapt to altered metabolic demand, prevent diaphragm atrophy, shorten weaning time and improve non-invasive ventilation.

Critical Care News had an opportunity to speak to Jennifer Beck and Christer Sinderby during the symposium:

You are introducing the concept of tonic activity of the diaphragm, is this essentially a reflex?

Jennifer Beck: That is exactly what it is; it is the Hering-Breuer deflation reflex. We did a study in intubated babies in Montreal in 2004, and we evaluated the interaction they had on the ventilator settings that were prescribed by the physicians and the respiratory therapists. We looked at the patient-ventilator interaction and found a severe amount of ventilator asynchrony. Two years later we published a paper in the same patient population, where we made an intervention when we removed the PEEP for a short period while the patients were on mechanical ventilation, and we evaluated the tonic activation of the diaphragm. The tonic activation of the diaphragm is the presence of diaphragm activity during the exhalation period. We were able to develop a method to quantify how much diaphragm activity there is during the expiratory phase, and to see how application or removal of PEEP affects that. This study has been recently published in *Pediatric Research* by Emeriaud et al.

Can you tell us more about your research in monitoring of the diaphragm activity to evaluate the feasibility of using the signal in the neonatal patients?

Jennifer Beck: We just recently completed a study where we were monitoring the diaphragm activity in premature babies with respiratory distress. Most received surfactant at birth, and some of them also received mechanical ventilation. When we studied them they were all on room air, still being monitored for apnea due to prematurity. We used our methodology to monitor their diaphragm activity over several days. We were able to look at how much phasic activity they had, and how much tonic activity they had, and look at their apneas.

What were the sizes of these neonatal patients?

Jennifer Beck: The youngest was 28 weeks and they ranged up to 36 weeks gestational age, the smallest baby was one kilo. Most were being treated with caffeine for their apneas, and they were fed by feeding tube.

Can you give us a further differentiation between the phasic activity and tonic activity,



Christer Sinderby during NAVA lecture session.



Jennifer Beck during her session entitled Information captured from the Eadi signal.

and the types of responses you receive from physicians after hearing about your research?

Christer Sinderby: The breathing activity in itself is a waveform, where background diaphragm activity can occur during the exhalation period; for example you continue to expand the lungs to keep them open, to keep them from collapsing during the exhalation phase, and to keep the chest wall from collapsing. I think that this is something new here, that can actually be detected. The manner of ventilating these small patients is determined by the importance of synchronizing their ventilation, which can be a challenge with leakage from small cuffs. With the conventional ventilation technology, you have a problem to start and stop the ventilator, with the same

difficulties in obtaining synchrony in adults and neonates. So if the baby tries to breathe in, he might not get the breath he wants and he might not get assist at all. This system provides the neural feedback to start and stop the ventilator, and to see if the patient needs PEEP or not, or which level of PEEP is required from a recruitment perspective. The most interesting thing we have seen in excessive animal studies is that we can actually tell how much assist and PEEP there should be, and titrate these parameters based on the diaphragm electrical activity. It is to be emphasized that monitoring is not just treatment, but you get the feedback that might be of much value when tailoring the ventilatory treatment. The responses from neonatologists who have heard about our research are usually astonished.

Jennifer Beck: I am asked a lot of questions, like "does the feeding affect the signal"? So we have looked closely at that and have monitored the babies while they are being fed, and there are no artifacts on the signal. I am also asked if the position of the baby affects the signal, and as long as the electrodes in the feeding tube are positioned at the diaphragm, the signal is not affected.

Christer Sinderby: Two studies in neonates have been started and are ongoing in Toronto at Women's College Hospital at the present time, and we are expecting to see good results. The real challenge, which is already done was to establish that we can actually get signals in these small patients, and that the catheters are the right size for these babies.

What do you think will be the learning curve for clinicians in regard to NAVA?

Christer Sinderby: If you take a look at the set up we are using, for adults and infants, if you put the catheter down and don't see any signals, you will have to be very suspicious about what is going on, because if the electrode is in the right place you will get a signal. If the catheter is placed and you don't get a signal but you see that you are getting the ECG, the electrode is working but obviously the catheter is not in the right place and needs to be positioned.

As we find in a lot of patients, when we monitor the diaphragm activity, we can see

that they are not using the diaphragm, even though the ventilator is in a patient-triggered mode. Disuse of the diaphragm could potentially lead to problems with weaning.. When the patient is switched to NAVA, the diaphragm activity returned. The monitoring aspect that we should really emphasize is that you can flow, pressure and volume waveforms however, without Edi you cannot be sure what the diaphragm is doing.

We have heard from some of the researchers that have been utilizing NAVA, that after experiencing the neural drive and assist, they have come to the realization that they have generally been using much too high pressures

with pneumatically driven ventilation modes.

Think about it – the only development in spontaneous breathing that has occurred in the past 15-20 years is to improve the sensitivity of the pneumatic trigger to start a ventilator. It has improved to be more and more sensitive, but if you generate less than 1 cm of water in pressure you cannot feel it. The response with NAVA is every 16 milliseconds. The reflex response if I hit my knee is 60 milliseconds. So the neural ventilator response is 4 times as fast. From the neural perspective this gives us the power to have integrated information to make decisions faster, and continuously, and to avoid bad decisions. ■



Jennifer Beck and Christer Sinderby with symposium chairman Professor Arthur S Slutsky.

Biographies

Christer Sinderby, PhD is Assistant Professor at the Department of Medicine, University of Toronto, Canada, and Research Staff Scientist at St. Michael's Hospital, Department of Critical Care Medicine, Toronto. He received his MS degree from Karolinska Institute in Stockholm, Sweden, and Doctor in Medical Science degree at the Department of Neurosurgery, Sahlgrenska Hospital, University of Gothenburg, Sweden.

Christer Sinderby has won numerous academic committee assignments, including the University of Western Australia, as a peer reviewer for American Journal of Respiratory and Critical Care Medicine and Journal of Applied Physiology, and as a member of the American Thoracic Society/European

Respiratory Society task force for the ATS/ERS statement on standardization of respiratory muscle tests. He has won numerous research awards and grants including the Montreal Chest Hospital Research Institute Annual Award, the Parker B. Fellowship in Pulmonary Research and Fonds de la Recherche en Santé du Québec Chercheurs Boursier Scholarship. His research has been extensively published in peer review journals and monographies.

Jennifer Beck, PhD is Assistant Professor at the Department of Pediatrics, University of Toronto, Canada, and Associate Scientist, Clinical and Integrative Biology at the Sunnybrook Health Sciences Centre, Neonatal Intensive Care Unit, Women's College Hospital in Toronto, Canada. She received her MS degree and

Doctor of Physiology degree from McGill University in Montreal, Canada, and post-doctoral degrees from McGill University and the University of Montreal.

Jennifer Beck has won numerous research awards, including awards for scientific presentations from the Department of Physiology and the University of Miami, the MRC/Glaxo-Wellcome/Canadian Lung Association bursary in 1998, the FRSQ post-doctoral fellowship in 1999, and was also awarded in 2005 at the University of Toronto Critical Care Research Day. She was awarded an operating grant from the National Institute of Health for her work in Neural Control of Non-invasive Ventilation in the Preterm in 2003. Her research has been extensively published in a number of peer review journals.

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Dr. Wickerts and patient in the ICU.

First impressions of NAVA in adult patients

Carl-Johan Wickerts is head of a busy ICU ward at Danderyd Hospital in the city of Stockholm. He has been actively involved in respiratory research for a number of years, and was intrigued by the concept of Neurally Adjusted Ventilatory Assist.

Critical Care News recently met with Dr. Wickerts to discuss his early perceptions and experience of NAVA.

Can you describe the size of your department, average number of patients and staff here at Danderyd Hospital?

Our intensive care unit here is only about 3 years old, so the environment is quite modern and up-to-date. We currently have 8 ICU patient beds, but have recently expanded from 6 to 8 ICU beds. We operate a general ICU, treating primarily adult patients. We have two specialist physicians on staff on a daily basis, with additional interns and staff in training. Our total number of ICU personnel here is about 100, including physicians, nurses and licensed practical nurses. The length of stay is approximately 3 days, on average. Most patients are here for just one or two days, and a few patients may be here for much longer periods of care.

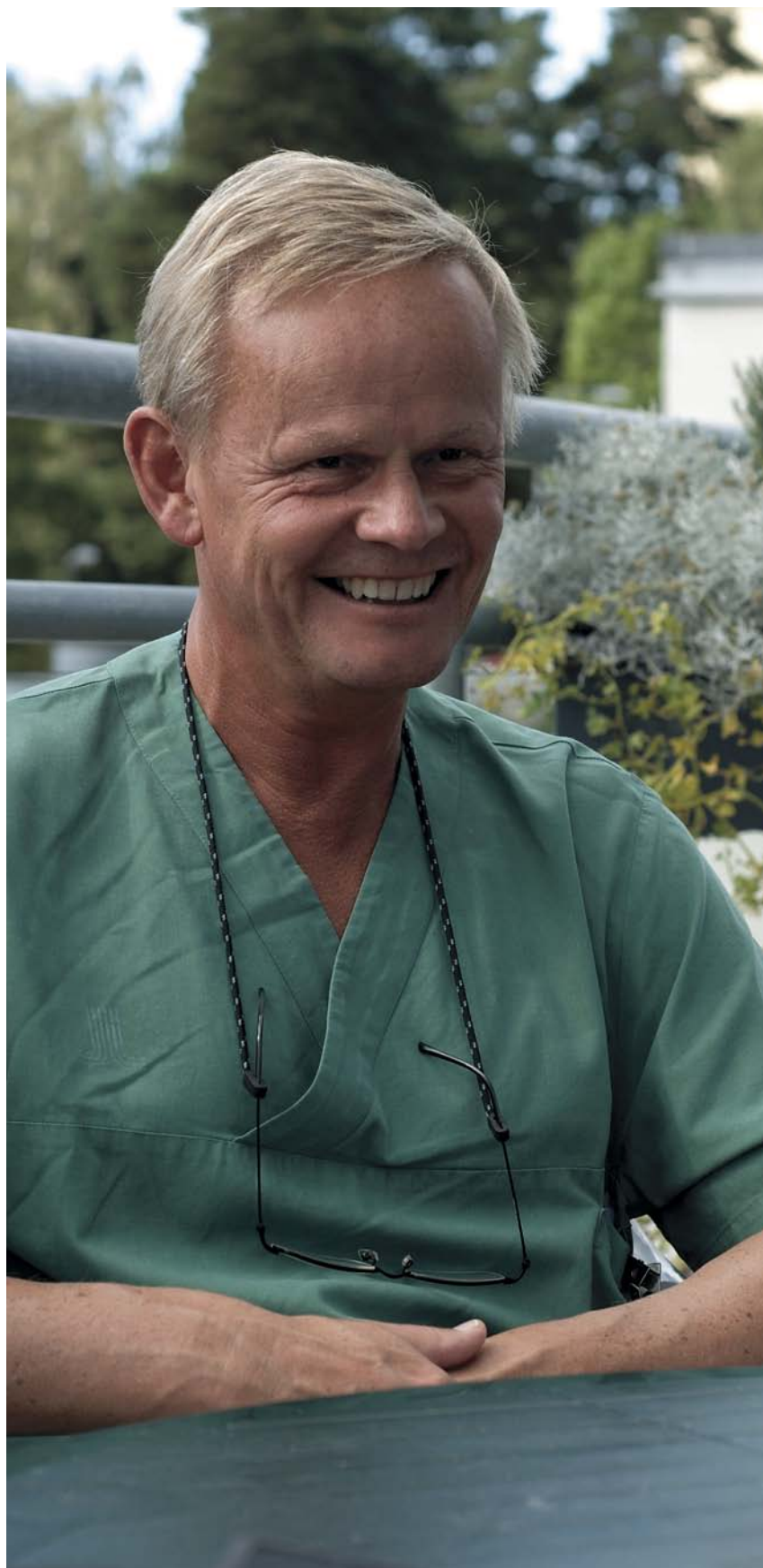
“We serve a population area of about 475,000 in this section of the city with some heavy industrial environments, and we have experienced increasing numbers of COPD patients and patients with other respiratory diseases in recent years.”

Which types of clinical situations and patient categories do you most frequently encounter?

Historically, we had a large infection clinic based here for the Stockholm area, so in the past, we had a large number of sepsis patients. Currently, we have primarily surgical cases, comprehensive surgeries, and post-surgical complications. We have a few trauma cases as well, but the other main patient category is chronic obstructive pulmonary disease patients. We serve a population area of about 475,000 in this section of the city with some heavy industrial environments, and we have experienced increasing numbers of COPD patients and patients with other respiratory diseases in recent years.

Which ventilation therapies do you normally use in these patient categories?

For the surgical patients, they are usually treated per-operatively with volume controlled ventilation, and post-operatively, if they remain intubated, we try to go over to pressure supported modes. We generally never use



Carl-Johan Wickerts, MD, PhD is head of the Intensive Care department of Danderyd Hospital in Stockholm.



Carl-Johan Wickerts has conducted research for many years within the field ventilation therapy.

volume controlled modes in the COPD patients, but primarily start out with non-invasive mask ventilation and pressure supported modes in these patients, to avoid intubation.

When did you become familiar with the concept of NAVA and what led to your interest to initiate and test this therapy at your hospital?

I first heard about NAVA at a lecture by Christer Sinderby at an international meeting several years ago. I have followed the development since then, and since I personally have been involved in respiratory research and development, as well as previous development projects for such things as ICU stations. I have a special interest for new and interesting generations of ventilation therapies, particularly those therapeutic developments that might reduce response times. But delays in triggering have always remained as a problem area. This is why NAVA as a concept was especially interesting to me. To have the possibility of ventilation without delay in response is an exciting opportunity

What are your first impressions of NAVA so far?

That it works. We had initial concerns, especially in COPD patients with very flat diaphragms, that the signals would have been too weak. The first two COPD patients I treated both had severe emphysema, and in one case the signals were a bit weaker, but in the other very strong signals were obtained. We were able to ventilate both of these cases with NAVA for long periods of time, up to 18 hours, without any difficulties. I want to continue to get more experience of NAVA in this particular patient category. NAVA also worked well in the other patients we have treated so far, post-op surgical and acute myocardial infarction with cerebral infarction.

What is your practical experience with placing and positioning the catheter?

Once the catheter is in place at the diaphragm, it has not been difficult to obtain a good Edi signal. However in a few cases, we initially

experienced difficulty to place and position the catheter through the esophagus, and we had a couple of experiences of the catheter doubling up on itself. Our experiences have contributed to the development of support tools to position and identify where the best signals can be obtained.

What is your perception of the Edi curve?

It has not been difficult to interpret these curves, once we have identified that the catheter is in the right place to obtain the signal. The curves have worked very well for us, so far.

What are your current perceptions of NAVA as a support in weaning?

We have been able to extubate most of our patients directly from NAVA, as a natural step in the weaning process. We have not experienced any difficulties in this respect; our experience so far is that NAVA works very well from a weaning perspective. ■



The Danderyd Hospital ICU has been recently constructed, with state-of-the-art equipment and windows reflecting the natural environment outside of the ICU.

Biography

Carl-Johan Wickerts, MD, PhD, is chief of the intensive care unit of Danderyd Hospital, Stockholm, Sweden. He received his medical degree in 1978, and specialized in anesthesiology 1982, with European Diploma in Intensive Care Medicine (EDIC) in 1994. He obtained his doctoral thesis in clinical physiology at Uppsala University in 1991, and was appointed Assistant Professor in Anesthesiology and Intensive Care in 1997 at Karolinska Institute, Stockholm, Sweden.

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