Notes from the Chair
by Timothy R. Myers, BS, RRT

Now that summer is here, those of us working in children's hospitals across the country are preparing for the "trauma season." The kids are out of school, the weather is nice and warm, physical activities and car trips are increasing, and our beds are, unfortunately, filling up with accident victims and near drownings. Since school is out, surgical activity is on the rise as well. But despite these busy times, I need to remind you of two very important items that we will need to address:

1. Prior to the publication of the next Bulletin: the selection of a new Neonatal-Pediatric Section Chair and Specialty Practitioner of the Year (SPOY).

The AARC will be sending out ballots for the chair election in the next several months. Two former SPOY winners, Melissa Brown, from California, and Michael Tracy, from Ohio, will be on the ballot. The winner of this section-only election will serve one year as chair-elect (2004) and then a three-year term as chair (2005-07). If our section still has 1,000 or more members on December 31, the new chair will also serve on the AARC Board of Directors. As the last U.S. presidential election demonstrated, every vote counts, so please remember to cast your vote for one of the two candidates.

As many of you are aware, every year each of the AARC Specialty Sections presents a Specialty Practitioner of the Year award to a deserving member at the Awards Ceremony during the AARC International Respiratory Congress this year in Las Vegas, NV, December 8-10, 2003. As the nomination deadline approaches, I encourage all members to start brainstorming names of worthy candidates and preparing nominations for submission. The easiest way to nominate a peer is through the Neonatal-Pediatric Section continued on page 4

HFOV in the NICU: An Update
by Michael Tracy, RRT

True or False: HFOV reduces the incidence of air leak and cerebral bleeding in preterm VLBW infants in the NICU.

Before you jump on your buzzer, let's look at the literature and see what objective evidence there is to support your "true" or "false" answers.

In 2002 the Cochrane Database of Systematic Reviews, based at the University of Sydney in Australia, did a meta analysis of all the studies pertaining to preemies and HFOV in the NICU. Their stated objective was to "determine whether the elective use of HFOV as compared to CMV in preterm infants who are mechanically ventilated for RDS decreases the incidence of CLD without adverse side effects."

The Cochrane group found eight studies eligible for their meta analysis. The first study was the HIFI study published in 1989, which enrolled 673 infants weighing 750-2000 grams. Study protocol dictated the same P aw for the HFOV arm as the patients had been on for their CMV period, or started the P aw at 8-10 cm H2O if they went straight to HFOV. Enrollment was stopped at an interim analysis because there was no difference between the CMV and HFOV groups in the incidence of BPD. Additionally, the HFOV group trended toward a higher incidence of air leak. The rate of significant [grade III & IV] intraventricular hemorrhage (IVH) and periventricular leukomalacia cerebral bleeds was significantly higher in the HFOV group. This study has been criticized because it did not include methods to recruit lung volume.

The Provo Multicenter Trial enrolled 125 patients. The study protocol started the HFOV group P aw 1-2 cm H2O higher than the P aw on their CMV. Surfactant was administered while the patients were on CMV. This study concluded that when used early with a lung recruitment strategy, HFOV after surfactant replacement therapy resulted in outcomes consistent with a reduction in both acute and chronic lung injury. Two other noteworthy elements in this paper: (1) routine suctioning (Q4) was discouraged to prevent volume recruitment strategy, HFOV after surfactant replacement therapy resulted in outcomes consistent with a reduction in both acute and chronic lung injury. Two other noteworthy elements in this paper: (1) routine suctioning (Q4) was discouraged to prevent volume while the CMV group required more frequent suctioning and (2) this is the only study to HFOV. Enrollment was stopped at an interim analysis because there was no difference between the CMV and HFOV groups in the incidence of CLD. Clark et al. found no significant differences between the groups in the incidence of PIE, pneumothorax, or IVH. One noteworthy segment of the paper states, "Because of logistic factors, the time of initiation of HFOV (mean 8 hrs) was comparable with that used in the baboon HFOV 'rescue' trial. Therefore the clinical response would not be as dramatic as that seen with the immediate institution of HFOV. These observations support the hypothesis that the pattern of lung injury characteristics of hyaline membrane disease occur within a few hours of initiation of assisted ventilation and that optimal therapy would require early intervention at the time of birth." Clark comments that Lee and O'Brodovich suggest that "when collapsed units are reopened, airway epithelial surfaces that were adherent to the lung were injured. Protein leaks from these injured areas and inhibits the effectiveness of surfactant. A cycle can develop whereby injury necessitates the use of higher air pressure excursions which produces more injury."

In 1999 Thome et al enrolled 284 patients (>24 and <30 weeks gestational age) in a study that utilized a high volume strategy (HVS) where the P aw was 1-2 cm H2O above the CMV

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Paw. This trial is noteworthy because it utilized the Star 950 HFFI. This study was stopped
at an interim analysis point because there was no difference between the HFOV and CMV
groups, with a trend toward more lung injury in the HFOV group. Data analysis said that
the trend toward treatment failure in the HFOV group was solely contributable to air leak.
No difference was found in the frequency of cerebral bleed in the two groups. HFOV was
started within one hour of intubation. This study also utilized a sustained inflation maneu-
er after suctioning. Similar numbers of patients in both the HFOV and CMV groups
received surfactant. The authors were certain that surfactant was not a confounding factor.
Thome et al were the researchers criticizing the Provo Multicenter trial for their choice of
rate (<30) and higher PIPs. Thome et al close by quoting an A.H. Jobe7 editorial, “HFV
may not be better than optimal IPPV with a sufficient PEEP to achieve good FRC, low
tidal volumes, and PCO 2 targets that minimize hyperventilation. How well a mode is per-
formed seems to be more important than which mode is chosen.”

Moriette et al (2001) enrolled 273 patients (24-29 weeks gestation) using a lung
recruitment strategy and surfactant. Initial HFOV Paw was set at 14 cm H 2 O if the FIO 2
> 0.40 and 2 cm H 2 O above the CMV Paw if the FIO 2 < 0.40. Further optimization of the
lung was done using sigh breaths (T i < 1) with a pressure of 4 cm H 2 O greater than the Paw.
Improved oxygenation after the sigh breaths resulted in increasing the Paw x 2 cm H 2 O.
If the FIO 2 > 0.40, Paw was increased to 16, and as much as 18 cm H 2 O. The CMV arm
was also evaluated to allow increases in Paw.

Moriette et al concluded that, “HFOV in very premature infants decreases exogenous
surfactant requirements, does not improve the pulmonary outcome and may be associated
with an increased incidence of severe IVH. Exogenous surfactant is the undisputed first-
time treatment of respiratory distress syndrome.

Plavka et al enrolled 37 patients (<31 weeks, 500-1499 g) in a study design similar to that
of the Provo Multicenter Trial. The main differences were the start of the randomized ven-
tilator method within 20 minutes, use of surfactant after defined criteria were met, and a
significantly younger study population. Study design optimized lung volume by increasing
HFOV Paw 30% above that of CMV to obtain a CXR with nine ribs expanded. The
study concludes that, “HFOV applied early and when the clinical strategy of maintenance
of optimal lung volume is used, improves oxygenation in the acute stage of RDS, reduces
the need for surfactant and can decrease the injury to lung tissue even in extremely immu-
nature newborns.” No differences were found in the two arms for air leak or central nervous
system morbidity. Antenatal steroids were given to mothers with signs of premature labor
or with premature rupture of membranes at <32 weeks gestation. Approximately 50% of
each group received steroids

Rettwitz-Volk W et al enrolled 96 patients (gestation <32 weeks, 1/3 patients <1 Kg
equally divided in the two arms of the study). Paw and P were set to show good chest
movement. Entry to the study arm was 40 ±20 min for CMV and 70 ±30 min for HFOV.
Their conclusion was that after surfactant therapy, HFOV as a primary mode of ventila-
tion in premature infants with RDS is as safe and efficacious as CMV. Each group had
similar numbers of air leaks and cerebral vascular hemorrhage. Ogawa et al enrolled 92 patients in a multicenter trial. Patients weighed from 750 to 2000
grams. Patients were entered into their treatment arm by 60 minutes if they were inborn
and six hours if they were outborn. In the HFOV group, lung volume was recruited by
manual ventilation just before starting, and a high mean airway pressure was adopted.
Surfactant replacement therapy was used in this study when an RDS diagnosis was made.

This study found no significant differences in the incidence of air leak, pulmonary hern-
orrhage, IVH, pneumonia, or symptomatic PDA between the CMV and the HFOV arms
of the study. Patients receiving supplemental oxygen or mechanical ventilation at 28 days
were not statistically different in the two groups.

This study was designed to reevaluate the results of the HIFI study and observe the
major complications reported to be higher in HFOV. The authors write, “In this trial mean
airway pressure was significantly higher (the HIFI study kept mean airway pressure the
same in both arms) to attain lung volume recruitment.”

The study conclusion was, “HFOV improves oxygenation in preterm newborn infants
with respiratory failure but does not increase the risk of complications when used by expe-
CMV arm used V_t from 4-7 mL/Kg, with 5-6 mL/Kg preferred. PEEP was 4-6 cm H_2O.

Infants with air leak or CLD. Initial Paw was at least two times higher than on CMV. The lung expansion defined as expansion to 8.5 to 9.5 ribs for most infants but 7-8 ribs for emphasized lung recruitment and avoidance of atelectasis and over distension with ideal in the occurrence of other complications of premature birth.

Benefits of HFOV in terms of CLD appear to be outweighed by concerns about increased rates of pulmonary air leak and severe IVH. Until these issues are resolved HFOV cannot be recommended as the routine method of giving mechanical ventilation to preterm infants with RDS.”

Now which answer did you buzz in on?

After the Cochrane meta analysis was published in 2002, two additional studies and an editorial were published in the New England Journal of Medicine. Courtney et al enrolled 500 infants (601-1200 gms) where “strategies for ventilation for both groups emphasized lung recruitment and avoidance of atelectasis and over distension with ideal lung expansion defined as expansion to 8.5 to 9.5 ribs for most infants 7-8 ribs for infants with air leak or CLD.” Initial P_{aw} was at least two times higher than on CMV. The CMV arm used V_t from 4-7 mL/Kg, with 5-6 mL/Kg preferred. PEEP was 4-6 cm H_2O. All infants were treated with surfactant before entering the study.

No significant differences in the incidence of IVH or pneumothorax was found in either group. Pulmonary hemorrhage was less likely to develop and PIE was slightly more likely to develop in the HFOV group. They concluded, “There was a small (47% vs 56%) but significant benefit in terms of pulmonary outcome for VLBW infants without an increase in the occurrence of other complications of premature birth.”

The UKOS group trial (797 patients, 23-28 weeks) enrolled their HFOV arm to begin P_{aw} at 6-8 cm H_2O and increased by 0.5 to 1.0 cm H_2O Q 10-15 min until it was possible to decrease the FIO2. Nine ribs was optimal inflation. Infants received surfactant as soon as possible after birth. The primary outcome was death or chronic lung disease. Forty-one percent of each group had CLD and almost identical death rates (25% CMV, 26% HFOV). They concluded that CMV and HFOV do not differ in the early treatment of respiratory disease in VLBW infants.

Ann Stark wrote an editorial stating that, In 4 of 5 trials since surfactant replacement became available for the treatment of RDS, the choice of the mode of ventilation made no difference in the rate of survival without BPD. The one trial in which HFOV reduced the rate of BPD included few high risk patients and used relatively high vent pressures with CMV (The Provo Multicenter Trial)…Furthermore, in inexperienced hands, HFOV may confer additional risks for individual infants, including inadvertent over distension of the lungs, impaired cardiac output, and increased CVP that might lead to intracranial hemorrhage … HFOV [should be] used in the most experienced centers. However, for most preterm infants, CMV with low tidal volumes and reasonable ventilation goals remain the appropriate choice.

Notes from the Co-Editor
by Melissa K. Brown, RRT-NPS

In this Bulletin, you’ll find an excellent review article by Michael Tracy examining many of the studies published HFOV in the neonate, a topic interesting to our profession on several levels. Despite this modern era of evidence-based medicine, HFOV became a widely accepted therapy before there was scientific evidence of its clinical value and safety, for that matter. Indeed, the ten studies used for most recent Cochrane review were spread over 18 years period of time when obstetrics and neonatal practice had changed dramatically. The widespread use of intrapartum steroids and post-natal surfactant dramatically altered the clinical course of premature neonates. The early trials treating patients up to 34 weeks gestation and 2000 grams. Recent trials investigated HFOV in neonates less than 30 weeks and under 1200 grams. What’s more, intervention these studies were highly varied and featured different ventilators - not only different control ventilator types and modes, but also different high frequency ventilators. Of the ten trials in the review, four utilized the Sensormedics 3100a, one used the Infant Star 950, two used the Hummingbird, one used a French piston ventilator, and the used a variety. To top it all off, blinding was not possible in any of the studies, because as we all know, everyone can tell when a patient is on HFOV.

The NICU has a strong history of embracing therapies without evidence. For example, steroids to reduce ventilator days, hyperventilation for PPHN, and high-flow nasal cannulae for nasal CPAP. Adding to the irony is the historic for nasal CPAP. Adding to the irony is the historic reluctance of neonatologists to embrace new mechanical ventilation modes. How did HFOV become so entrenched? My guess is that it just made sense to most physicians that smaller tidal volumes would be better for our patients. Or, the companies that developed HFOV did a great job of selling it to us. (Food for thought: someone said to me recently that HFOV is the ventilator modes we use today in the ICU are the result of the crush, marketing, and marketing abilities of individuals and companies.)

This is an interesting time for facilities that utilize HFOV in the NICU. Here in San Diego, the discontinuation of the Infant Star ventilator is causing great discussion. What will we use in its place for HFOV? Will we purchase more Sensormedics 3100as? Will we re-embrace high frequency conventional ventilation with small tidal volumes a comparable therapy, as A. H. Jobe suggests? I tend to agree with Dr. Thome: it is most important to do what we know and do it well. This emphasizes the need for all clinicians, especially respiratory therapists, to be skilled clinicians and consultants, as well as skeptics and, most importantly, researchers!

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October 19-25, 2003
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