Hypoxic Respiratory Failure in the Newborn

Question and Answer

Question: When administering nitric oxide to premature babies what is considered safe or common practice in terms of length of treatment?

Dr. Null: The Ballard study used NO for up to 24 days without evidence if complications. I older preterm infants with BPD > 2 months I have used it up to 35 days.

Question: Can you please clarify that nitric oxide can be used without the baby being intubated

Dr. Null: NO can be given by High flow nasal cannula or any CPAP setup. The flow requirement is 2 liters/min or greater. It can be used as a starting mode to avoid intubation or to facilitate earlier extubation.

Question: Is HFOV versus conventional ventilation preferred following iNO in preterm infant with PIE ?

Dr. Null: HFOV or jet ventilation would be preferred for patients with PIE as they are more lung protective

Question: Because of poor/ inadequate studies in extreme preterm infants, what gestational age would you not use nitric oxide, if any?

Dr. Null: Neither the Ballard study or the Kinsella study demonstrated problems with NO for patients 500 grams or higher. The neonatal network study suggested CNS problems but approximately 30% of the NO patients received NO for a very short time but were included in the NO group as intent to treat. It does not appear the NO poses a problem for the very preterm infant. I have used it in 23 to 24 week EGA patients. Since most of these patients have pulmonary hypertension due to sepsis the likelihood of complications are real.

Question: Is echo a must before starting nitric oxide?

Dr. Null: No but one should be done within 12 hours to insure that the patient does not have structural heart disease

Question: Does Inhaled nitric oxide have any effect on brain growth in preterm infants?

Dr. Null: Inhaled NO does not enter the circulation in any quantity and there has been no evidence of positive or negative effects on brain growth. One of John Kinsella's studies showed less IVH in his NO treated group.

Question: What type of sedation do you use with hfov and nitric oxide patients?

Dr. Null: Ativan or versed and for pain Fentanyl or morphine. If BP is OK in PPHN patients morphine would be preferred as it has pulmonary vasodilatory properties.

Question: What criteria would you use to declare a failure of iNO therapy?

Dr. Null: Evidence of adequate lung expansion and 6 hours of treatment with no improvement in PA pressures.

Question: Do you always increase iNO to 30-40ppm before considering ECMO?

Dr. Null: No but if PPHN remains I would consider adding Milrinone and Flolan before going to ECMO unless the RV is not working well.

Question: Is there a role for iNO in preterm infant with hypoxic respiratory failure with PPHN?

Dr. Null: NO should be considered and used in preterm infants with PPHN.

Question: What is the lowest gestational age infant you would use iNO with documented pulmonary hypertension?

Dr. Null: 23 weeks

Question: It seems as though we are getting away from obtaining methhemoglobin levels. What percentage of infants really develop methemoglobinemia?

Dr. Null: At 20 PPM of NO the number is very low at the most 1% but it still should be measures shortly after starting NO and at 24 hours.

Question: Recently, we used sildenafil as pulmonary vessels vasodilator obtaining a good response. What is your opinion?

Dr. Null: Sildenafil certainly will work. NO inhaled has some advantages such as being a bronchodilator, anti-inflammatory properties, avoiding worsening V/Q mismatch and no effect on Blood Pressure.

Question: In the presence of pneumothorax, is NO a good choice in hypoxic respiratory failure?

Dr. Null: Yes as it will improve V/Q along with PREVENTING HYPOXIC PULMONARY CONSTRICTION and reducing pulmonary artery pressures.

Question: With a baby with an unrepaired CDH with severe PPHN already on 20ppm and FiO2 at 100%, what do you recommend to help oxygenate the baby with the under-expanded lung from the CDH?

Dr. Null: The hypoplastic lung does not necessarily need to be expanded prior to repair. I use the HFOV what needs to be done is appropriate expansion of the normal lung. Typically these patients need a Paw of 12 to 14. The normal lung will need to be inflated to about 10 ribs. The problem usually is not adequately expanding that lung. If that is accomplished and still significant pulmonary hypertension then I add flolan IV starting at 4 ng/kg/min increasing by 2 every 10-15 minutes until the PaO2 improves or the blood pressure decreases. The usual good response occurs around 12-20.

Question: If the pt. that begins at 20ppm and is weaned to 5ppm in 4 hrs, was it necessary to start NO at all or you may have used other vent modes, such as HFOV as mentioned in the presentation?

Dr. Null: Some patients have a very rapid response and can be weaned to 5 PPM fairly quickly. While the ventilator may have played a roll the NO is likely to help extubating the patient to CPAP or HFNC with the NO faster than without it.

Question: Do you recommend checking the Met Hgb after 24 hours when using 20PPM or below?

Dr. Null: If you check it at 24 hours and it is <1 then there is no need to recheck it however most lab blood gas machines give a metHg level.

Question: What would you suggest if the term infant has all signs of PPHN including differential saturations, a cxr with a normal heart shadow, normal cardiac examination, but you have no echo readily available. Is it OK to try iNO?

Dr. Null: Yes but an ECHO should be done within 12 hours to look at cardiac structure and pulmonary artery pressures and R andL ventricular function

Question: Do you think about trialing iNO in infants < 35 weeks with documented PPHN? Infants with chronic lung disease and PPHN?

Dr. Null: Yes any preterm infant with PPHN NO should be considered. The same goes for the BPD patient

Question: Do you have an FiO2 where you would suggest iNO weaning can be initiated?

Dr. Null: Less than 60% but I prefer to have an ECHO that demonstrates that the PA pressure has decreased.

Question: We have never found an infant with high levels of methemoglobinemia. Is it OK to check a few levels early and then back off to once a day? What is your protocol?

Dr. Null: We check a few levels early and after 24 hours do not specifically check the levels after that unless we increase the dose

Question: Have you used iNO on HFJV?

Dr. Null: Yes one needs to follow their recommended set up.

Question: You mentioned starting iNO early. Is there an OI or clinical scenario that makes you consider iNO? Would you ever start prior to mechanical ventilation (i.e. CPAP)?

Dr. Null: A patient who requires FiO260% or greater who has episodes of desaturation when suctioning or handling should be considered irrespective of the OI. I have treated patients with NO and CPAP or NIPPV.

Question: In your case presentation and given the X-ray, is there any role for surfactant administration prior to nitric oxide?

Dr. Null: The problem is not will surfactant help, because it very may well help the patient. One of the difficulties is, as I think people know, when you give surfactant, the patient will be

transiently hypercarbic, will get more acidotic, and will be transiently hypoxic under those circumstances.

I think one of the things that I try to do is use a technique to get better inflation. One of the benefits of nitric oxide is that it blocks hypoxic pulmonary vasoconstriction. When I have a baby who has evidence of pretty severe pulmonary hypertension and I'm not sure I'm going to get a great response from surfactant, I would use the high frequency ventilator to improve lung inflation.

I would start the nitric and then I would give the surfactant to get a more rapid improvement, which frequently you can do. Because you have, then, the benefit of the nitric oxide being onboard and helping to reduce hypoxic pulmonary vasoconstriction and get the pulmonary vascular bed to relax rapidly once you get better inflation from that standpoint.

Question: How often would you do a methemoglobin level?

Dr. Null: Well, because babies can be deficient in methemoglobin reductase, which is what converts methemoglobin back to normal hemoglobin, one needs to do a methemoglobin level within an hour of starting the nitric oxide. If that level is normal, that means the patient is not severely deficient in methemoglobin.

It should then be checked again somewhere around 12 hours of age. If that level is normal, then unless you're increasing the nitric oxide dose, so maybe you started at 10 and now you go to 20, you don't really have to do a follow-up methemoglobin level because you've demonstrated that at the consistent nitric oxide level, the baby is able to manage that properly. Most of the studies done have shown that the normal neonate at levels of 20 parts per million, their methemoglobin levels are less than one with that.

Some people would get a methemoglobin level daily and most blood gases actually come with a methemoglobin level on it so you can look at that. But the real requirement is the initial one and one about 12 hours later to make sure that it's not increasing. Once that's demonstration is stable, unless you're increasing the nitric oxide dose there's not really a necessity to repeat that.

Question: Have you used PDE-5 inhibitor together with inhaled nitric oxide to improve responsiveness at initiation, since high levels of PDE were noted in PPHN?

Dr. Null: Yes, I have. I've frequently used milrinone with patients with that. That becomes a fairly standard management. Because not only do you get the inhibition with that, you get improvement. Can you use alternative drugs like sildenafil? The answer is yes, you can use sildenafil with that.

One of the things you want to remember, however, is that drugs like milrinone, sildenafil, Flolan, that are all pulmonary vasodilators will dilate the pulmonary vascular bed no matter what. The advantage that you have from nitric oxide is that it only dilates what it gets to.

When you have areas of atelectasis, those areas don't get vasodilated and so you improve your VQ mismatch with an inhaled drug, whereas an intravenous drug will dilate the whole bed. Yes, you'll get some improvement from the areas that are well inflated, but you will get blood flow going to areas that are not inflated and create problems with that.

Again, IV drugs are beneficial and I've used the PDE-5 inhibitor, which is sildenafil. Milrinone is actually a PDE-3 inhibitor. I've used both of those and used those in combinations with nitric, particularly in patients who are not as responsive as you would hope they would be.

Question: Do you feel that it's necessary to have the PPHN patient in a center that offers ECMO, in case inhaled nitric oxide does not work? We currently start patients on inhaled nitric oxide and then transfer them to a center with ECMO capability. I'd like to see us treat more aggressively with inhaled nitric oxide and keep those patients in-house.

Dr. Null: Because moving babies who have severe pulmonary hypertension is not always a pleasant experience for them, and often just moving them into a transport isolette or putting them in an ambulance or a helicopter and bouncing them around worsens their pulmonary hypertension. However, if the baby becomes very unresponsive and the right ventricle is not working, the baby can acutely need ECMO and you may not have time to transport the patient.

What I have dealt with, particularly people who have the capability of taking good care of the patient, is to start the nitric oxide and get your lung adequately inflated. If you see an improvement within the first three to four hours and you can wean the oxygen concentration down and you have the capability of looking at an echo and make sure that the right ventricle is working properly and your pulmonary vascular resistance is indeed falling, then I think it's very safe to manage the patient there and only consider moving them if they start to increase their need for support.

My answer would be you have about somewhere between two to four hours to see that you're getting a response. One of the keys is, is because sometimes your oxygen levels improve but your pulmonary hypertension does not change very much.

If your right ventricular pressure remains very high, the right ventricle will ultimately fail. If your nitric oxide's enabled you to wean the oxygen a little bit, but your right ventricular pressure is totally unchanged, then that baby should be moved to a center that has ECMO capability because the likelihood is that baby will need ECMO.

Question: How efficacious is nitric oxide in the extremely pre-term infant who is not oxygenating well on HFOV and a hundred percent FiO2? Should it be used as a last-ditch rescue?

Dr. Null: The question becomes why is the patient not responding? I think there are a couple of groups of babies that it's been proven to be very effective in, even in the very small pre-term infant. One of those is the baby who has pulmonary hypoplasia associated with prolonged

rupture of membranes in the mother's case. That baby typically will respond well to the nitric oxide.

The other is the infected baby. Obviously frequently the reason small preemies are delivered is because of the mother having severe chorio and the baby winds up being born with an infection, and those babies have pulmonary hypertension because of what's going on with the infection. Again, that group responds very well also. I think if you have babies in those categories, it is very clearly likely that it will benefit them.

Other babies, if you can't get the lung inflated and you've given surfactant and you still can't get the lung inflated, can you try nitric to see if you can improve the VQ and what part of the lung is open? The answer is it's worth a try. But the success would be less likely with that. The two groups I gave you are where it would be very likely to be successful.

Question: How does the presence of congenital diaphragmatic hernia change the initial inhaled nitric oxide respiratory management of HRF in a neonate?

Dr. Null: The issue with a congenital diaphragmatic hernia is they have two issues with pulmonary hypertension. One is the size of their vascular bed. If they have a really small lung on whichever side the hernia is on, they may have a very small contracted vascular bed. They have a degree of fixed pulmonary hypertension, so that no matter what you do they're still going to have an elevated pressure required.

They also have a reactive component. In a paper Reese Clark did, there was an issue with starting nitric oxide because a number of those babies had poor left ventricular function. One of the important parts with the diaphragmatic hernia is, is how is the heart functioning as part of this scenario?

If there's evidence that the left ventricle is not working, then giving nitric oxide will not only not help the patient it is likely to make them worse. Once they have an echo demonstrating, if you demonstrate good left ventricular function and evidence of pulmonary hypertension then I have used regularly and believe that nitric oxide can be very beneficial for that group of patients.

However, that is not a group of patients that should be kept in a non-ECMO center because they can deteriorate fairly rapidly and need to go on ECMO quickly. They should be in a center where ECMO is readily available.

Question: How is the dynamic use of nitric oxide, with and without HFOV different? Or is it not different? When we increase or decrease pulmonary volume only with the use of the ventilator, do we have to be more cautious with the use of nitric oxide?

Dr. Null: I don't think with nitric oxide you have to be a whole lot more cautious with it. Again, whatever mode of ventilation you're using, the goal should be to avoid atelectasis or avoid over-distension, because both of those create injury to the lung. I think one thing we forget about

is that atelectrauma is every bit as bad for the baby as volutrauma is. Avoiding particularly low lung volumes is important.

With nitric oxide, it's probably worse to go to low lung volumes than it is to high lung volumes because at low lung volumes the nitric oxide now is not getting to where it needs to reduce the pulmonary hypertension. Whereas high lung volumes, it's still helping, but you're creating some increased pulmonary hypertension due to compressing the small arteries in the lung with that.

One needs to be careful, but my argument would be you should always be careful in adjusting the ventilator to avoid high and low lung volumes.

Question: Is there any role for other inhalational agents like iloprost with or without nitric oxide?

Dr. Null: Yes. I have, because iloprost, getting it inhaled, which it does work very well, is difficult on high frequency. I've used Flolan in a number of patients and been very successful with Flolan, particularly in some babies where nitric oxide was not working very well. I've used intravenous Flolan.

I've used it intravenously, your blood pressure drops too much and that. I have found that it is very unusual for the patient to become hypotensive if you start it and slowly advance it because you get good improvement in pulmonary blood flow and so your coronaries get good improvements, so your left ventricular function continues to improve. That offsets any change you might have in the drop in peripheral vascular resistance.

Yes, inhaled iloprost has been demonstrated to work and that can be used as a front-line drug for severe pulmonary hypertension. Again, when you're using an inhaled it requires the same thing nitric oxide requires, which is you need to get the lung as uniformly inflated as possible to get it to be where it needs to be effective.

Question: Is there any contraindication for use of nitric oxide, specifically in some congenital cardiac diseases?

Dr. Null: Yes. Any cardiac issue that has left ventricular-sided problems, so total anomalous veins, severe coarch, interrupted arch, severe aortic stenosis or insufficiency, mitral stenosis insufficiency, severe left ventricular dysfunction nitric oxide is not a good choice for that because the problem is blood getting out of the lung, not blood getting into the lung under those circumstances.

Requirements, in any baby who requires, then, a ductus open, needing flow through the ductus, then that should not be utilized under those circumstances.

Question: What about the use of Nitrous Oxide and Sildenafil together?

Dr. Null: They certainly can be used together. As you know, Sildenafil is a PD5 inhibitor, and that assists in keeping the vascular bed dilated, the two together work effectively. One needs access, typically for these kinds of patients, to an intravenous dose of Sildenafil because of their severity of illness with that.

The combination is likely to improve the chances of getting the dilatation you need and certainly can be used. Often nitric oxide is all that you need by itself, but if things are not working well, certainly considering adding Sildenafil is an important option with that.

Question: How do you administer Surfactin without abruptly stopping the nitric to the lungs?

Dr. Null: When I was in San Antonio we did a study in looking at the administration of Surfactin during high frequency oscillatory ventilation. What we were able to demonstrate in the animal model was that you got better distribution when you gave the Surfactin while you remained connected to the high frequency ventilator rather than disconnecting and bagging it in or putting it in on a conventional device.

The way I do it is I put the patient right side down. I insert a catheter to the end of the endotracheal tube in a closed system and provide half of the dose of Surfactin. Sometimes you have to turn the amplitude up a little bit to keep the Surfactin going down into the lung. Keep the patient on that side for about three to five minutes, and then turn the baby to the other side and repeat the second half of the dose.

What I've found is that's a very effective way to do it. You do not have to get off of the oscillator when you do it. You do not have to disconnect from the nitric oxide source either, so you achieve all of the benefits.

Question: Can you speak to inhaled nitric oxide use in the preterm infant?

Dr. Null: As I think many of you know, multiple studies have been done looking at nitric oxide in preterm infants as a means to prevent chronic lunch disease. They have variable results. The Ballard study demonstrated very good protection.

Then there was the European study which showed no difference and the most recent study which did not really show a difference either. I think it's sort of out for that, but there are clearly preterm infants that benefit from nitric oxide.

That group of babies would be the acute pre-terms who have very high oxygen requirements, even when well recruited. Those babies often are infected or have hypoplastic lungs due to mothers with prolonged rupture of membranes.

That group of babies will respond, typically, to nitric oxide. That should be utilized for them. Evidence of pulmonary hypertension in preterm infants is a reason to utilize nitric oxide and has been demonstrated to be beneficial.

I have had some success in treating babies with established chronic lung disease, meaning babies two to three months old who have worsened and are in high oxygen requirement. I have used nitric oxide in them and gotten a good response from the nitric oxide in those patients also. I think there clearly are babies who are preterm who will benefit from it, and it should be utilized in that group of babies.

Question: Would you start the baby on HFOV if the baby's PCO2 is in the 30 to 40 range and requiring 100 percent FiO2 and on 20 part-per-million?

Dr. Null: Yes I would, because high frequency enables to get the lung more uniformly inflated, which is very important for making the nitric oxide work best under the circumstances. What I will tell is, basically, virtually all of my babies who have hypoxic respiratory failure are on high frequency oscillatory ventilation, and it appears to be a successful way to treat it and get the nitric oxide to work well.

The only baby that I might not treat with high frequency would be the baby who has idiopathic persistent pulmonary hypertension, who has very clear lungs, because the pulmonary...that has been constricted, but there's absolutely no lung disease. Those babies could be treated very easily with conventional ventilation, because nitric oxide will get to where it needs to get to, because there's no real lung disease in that group of patients.

Question: Is it safe for a pregnant nurse or caregiver to give care to an infant on nitric oxide, and if not, what precautions are taken and what could happen to the caregiver if exposed to nitric oxide?

Dr. Null: When nitric oxide first came out, there was significant concern about how much nitric oxide would be in the exhalation limb of the ventilators and how close you had to be to the device. That was all looked at very, very carefully, and it turned out that you never exceed the parts-per-million that would be potentially problematic for anyone in the room from that standpoint, which is why we allow several nitric oxides running in the same room with other patients in the room.

There really is no risk to pregnant individuals from the nitric oxide, and they don't have to fear being there. We have lots of pregnant nurses in our nursery and we do not exclude them from managing babies with nitric oxides as there's never been any evidence, under the circumstances its given, that it would be problematic for them.

Question: How often do you see nitric oxide used with Vapotherm?

Dr. Null: We use Vapotherm sometimes, we use a Fisher & Paykel system sometimes, so basically a high-flow nasal cannula system, we frequently extubate from the ventilator prior to the patient being off of nitric oxide. In fact, I want babies to be extubated because they're ready and not continue to be intubated just because they're on nitric, very effective to be on a high-flow nasal cannula system.

Basically, if you're going to be running nitric oxide, and you want to know that it's given at the level that you're trying to give it at in parts-per-million, then you should be on about two liters of flow or more, or on CPAP, and in fact, I have two babies in my unit right now who are on nitric oxide, one on a high-flow cannula system and the other on CPAP.

Question: When treating a PPHN shunt by raising the system blood pressure, how high is too high?

Dr. Null: I've been through all of this since I started doing stuff in the late 1970s, where the way to stop the shunt was to raise the systolic blood pressure, and indeed you can do that, and you can stop the right-to-left ductal shunt, and the patient looks better.

What you're doing is you're putting an incredible stress on the right ventricle, which if you're not able to reduce the pulmonary vascular resistance, the right ventricle will fail, and if you don't have ECMO ready immediately, the child will die.

What is too much? Something that's super physiologic is too much, so a mean blood pressure that would be in the 80s would be about as high as I would ever raise the blood pressure to help the patient, but the key is to have an echo and make sure that the right ventricle under those circumstances is not dilating, because if all you're doing is causing the right ventricle to dilate, and you're not really reducing the pulmonary vascular resistance, then you're doing the patient a disservice and not helping them.

Transiently, it'll look good, but if you're not on call that night, your partner may be very unhappy with what happened.

Question: How frequently should a chest X-ray be performed to evaluate expansion when administering nitric oxide?

Dr. Null: Once you initiate the nitric oxide, if the patient does well, getting a film 24 hours later, remembering if you're on a high frequency device. You can examine the baby and find out where the liver is to determine whether you're getting over-inflated or not.

If you're not getting much response from the nitric oxide, then it's important to get a follow-up film at that point to see whether the problem is because you have not gotten the lung adequately expanded, and you may have to push your ventilator settings to get the lung adequately recruited to make the nitric oxide work properly.

Typically, we do X-rays on a once-a-day basis except under the circumstances I just talked about.

Question: What effect, if any, do you see on the respiratory distressed infant from the addition of infant cooling when nitric oxide is in use?

Dr. Null: Infant cooling clearly will raise pulmonary vascular resistance, without question, so if a baby is on nitric oxide, and you then cool the baby, you are likely to see some alterations that

you will have some worsening of the pulmonary vascular resistance. That sometimes can be helped by adding a drug like Milrinone, which is a PDE3 inhibitor and does help offload the right ventricle a little bit.

There are other drugs that could be used, Sildenafil being one of them, Flolan being another IV preparation that you could give if the pulmonary hypertension is creating a problem, but most of the time, if the patient's responded well to the nitric oxide, while the cooling will raise the pulmonary vascular resistance, it won't raise it enough to create significant cardiovascular effects for the baby.

Question: What is your experience with inhaled nitric oxide and noninvasive ventilation? Do you see a benefit of this?

Dr. Null: Yes, I see a very important benefit with this, because we've gone more and more, as everyone has, to, I like to call it, less invasive ventilation, because if somebody stuck prongs up my nose and blew 10 liters up it, I wouldn't think it was not invasive.

In any case, for CPAP, for NIPPV, for high flow nasal cannula, you can stabilize the baby, and sometimes their oxygen requirement will go up, and if the baby has evidence of pulmonary hypertension, which sometimes is a clinical evidence, where if the prongs come out, the baby desaturates. You put the prongs back in. Instead of the oxygen level saturation coming immediately back up, it takes a couple minutes to come up.

That baby has pulmonary hypertension. If you start nitric oxide under those circumstances, you can, more likely than not, avoid intubating the baby and continue to wean the baby's support down significantly.

I think there really is a real role for nitric oxide in those kind of patients to enable us to not have to move forward with intubation, and also for the intubated baby, as I mentioned previously, to get them off the ventilator much more rapidly.

Question: In order to reduce right-to-left shunt, what inotropic support would be beneficial, because some of my colleagues will use dopamine with Milrinone, or would one inotropic support be sufficient to improve systolic blood pressure to reduce right-to-left shunt?

Dr. Null: I would use dopamine and Milrinone together also. The reason for that is that dopamine, once you exceed 10 mics per kilo per minute you have a significant risk of increasing pulmonary vascular resistance from the dopamine. The Milrinone offsets that and provides some improvement in right ventricle function, which then would more likely help you from the left ventricle point and blood pressure.

Now, if you're on both of those drugs and you still have significant hypotension, then two things could be utilized. One is many of these babies are cortisol deficient, so giving hydrocortisone in doses of 5 to 10 per kilo have been shown to be very helpful, and also it's interesting that they also help the nitric oxide work better.

Then, if you need another drug, the best other drug to use would be norepinephrine, and the reason for that is there was a couple studies done in France, both in an animal model and in a baby, which demonstrated that Norepinephrine improved pulmonary blood flow while also improving blood pressure.

When I was a younger person I always thought that Norepinephrine would significantly raise pulmonary vascular resistance while it raised blood pressure, but they were able to demonstrate that that's not true. When we need an extra drug, we go to the use of Norepinephrine for our patients.

Question: What criteria would you use to declare a failure of inhaled nitric oxide therapy?

Dr. Null: The studies demonstrate a statistical improvement within about 30 minutes. In my experience, that's true for a large number of patients, but it takes about two to three hours to say that nitric oxide is not going to work. Part of it has to do with have you made sure the left ventricle is working. Have you fixed that? Have you made sure the lungs are adequately inflated?

Once you achieve both of those, you have nitric oxide on board, and you've had it running for two to three hours, if it's not working at that point, it is not likely to work. You cannot just discontinue it at that point. You have to wean it off if you're going to stop it.

The reason you have to wean it off is if you abruptly discontinue it the patient who has got significant pulmonary hypertension will get even worse with that. One would have to wean it off. Those would also be patients that you might want to consider adding a drug like Flolan of Sildenafil or Prostacyclin being given inhaled. Any of those things would be considerations.

Question: What dose of inhaled nitric oxide do you use in CLD?

Dr. Null: I use 20 parts per million, and I keep them on that for a week. Then I go to 15 for a week, 10 for a week, 5 for a week, and then I wean them off over a week. It's a long process of getting them off. What I found was that if you tried to wean them off too quickly you lose the benefit you got.

The other thing is, do not expect them to respond in a very short period of time, meaning in an hour or two. There are babies that take several days before you see a significant response from it. One is going to use that for a longer period of time before you would say that it's not helping the patient.