Neonatology

Respiratory Therapy

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INTRODUCTION

There are several reasons why we ventilate foals. But one of the most common reasons is lack of central respiratory control. The central respiratory receptors are very susceptible to damage by hypoxia and sepsis (a common manifestation of Neonatal Encephalopathy). The effect of hypoxia or sepsis is to decrease the receptor's sensitivity so that a higher $\mathrm{Paco_2}$ or a lower $\mathrm{Pao_2}$ is required to stimulate respiration. Thus these foals will be hypercapnic and hypoxic but at the same time not realize they are. They will not have an increased respiratory effort or other signs of respiratory distress, despite this respiratory compromise.

Other foals will realize that they are hypoxic or hypercapnic however will be unable to respond because they are weak and hypotonic. They try to breathe but cannot. These foals may be weak from hypoxic neurologic disease or from sepsis. While they may initially have an increase respiratory effort with nasal flare eventually they become fatigued, as they cannot respond further. Initially these foals will have an increased respiratory rate, as many of them have stiff lungs and it is easier for them to take rapid shallow breaths rather than deep, long breaths. They will have tachypnea and have a worried expression with nasal flare. As their respiratory muscles fatigue they will rely more on their diaphragm to assist them because their lungs are stiff and their ribs are soft. Once there intercostal muscles become fatigued they will not be able to splint their chest as the diaphragm contracts. This results in a respiratory pattern where during inspiration their chest wall will move inward as their diaphragm moves down. The downward motion of the diaphragm will cause displacement of the abdominal viscera resulting in an outward movement of the flanks. This respiratory pattern has been called a "wave chest" or "paradoxical respiration" and heralds complete fatigue and respiratory failure. As these foals become tired, their desperate attempts at maintaining their blood gases will fail. As they become significantly hypercapnic they will experience central respiratory depression. They will appear not to be breathing so desperately. This appearance is deceiving. Bystanders may feel that the foal is doing better where as he is actually suffering from severe hypercapnia and will soon arrest. If these foals are to be saved, they need to be ventilated before they reach this state.

Another group of foals that require respiratory support occasionally extending to ventilation are foals with upper airway obstruction. These foals are usually Neonatal Encephalopathy cases that lack pharyngeal tone and also may simultaneously have dysphagia leading to aspiration pneumonia complicating the picture. The lack of pharyngeal tone is not a problem with the foal at rest but if the foal begins to take deep breaths (because of exercise or when startled) the resulting negative airway pressure pulls the flaccid pharyngeal walls inward causing respiratory obstruction. The obstruction results in increased inspiratory effort leading to more extreme negative airway pressure leading in turn to further obstruction. Without an airway stent (e.g. endotracheal tube) the obstruction won't be relieved and the resulting hypoventilation may lead to exhaustion and respiratory followed by cardiac arrest. Some foals will require ventilation as the recover from the exhaustion and secondary asphyxia.

The last group of foals that requires ventilation is those with pneumonia (aspiration pneumonia, ARDS) or other primary chest disease (e.g. pulmonary hypertension or primary cardiac disease). These foals may be very difficult to ventilate. They will present much like the weak foal because decreased compliance from pneumonic or otherwise abnormal lungs will eventually result in fatigue. Before they become fatigued they will be tachypneic and generally in respiratory distress. The presence of lung disease makes ventilation of these patients a significant challenge.

NORMAL PHYSIOLOGY

CHEMICAL CONTROL OF RESPIRATION

We breathe to get rid of CO_2. The high affinity of hemoglobin for oxygen insures that we receive enough oxygen in the process. This arrangement works okay until things go wrong. Respiratory failure is the inability to maintain gas exchange at a rate that matches metabolic demand. This failure may occur because of inadequate alveolar ventilation, mismatching, or abnormal perfusion.

The respiratory receptors which regulate minute-to-minute ventilation are located in the Medulla Oblongata. These receptors are primarily responsive to CO_2 and H^+ however there is a modulating response to oxygen. Minute to minute changes in blood CO_2 change these receptors response which in turn orchestrates respiratory rate and depth. Breathing causes small cyclical changes in Pao_2 and $Paco_2$. These changes are important in setting the pattern for respiration.

There are also peripheral receptors in the carotid and aortic bodies. These receptors play only a minor role in regulating respiration unless the oxygen falls

below 60 torr in the presence of hypercapnia or acidosis. When central depression results in ineffective regulation by the central respiratory receptors, and the animal becomes hypercapnic and hypoxic, with the Pao_2 falling below 60 torr, the peripheral receptors will begin to regulate respiration. When moderately severe central disease is present from hypoxic ischemic encephalopathy, peripheral receptors may play a central role in driving respiration. Foals with this problem will have a $Pao_2 < 60$ torr and be hypercapnic. If these foals are placed on intranasal oxygen, and their $Paco_2$ rises above 60 torr and in extreme cases they may even stop breathing because of a lack of respiratory drive. This situation requires immediate ventilation, since the alternative (allowing their Pao_2 to drop, so that hypoxic respiratory drive resumes) is not acceptable in these compromised patients. In this discussion I have used a magic number of 60 torr, however you should realize that the critical value depends on the pH and $Paco_2$ as well as the responsiveness of the receptors.

MECHANICAL PROPERTIES

(Why down foals should stay sternal)

To understand the importance of keeping a foal sternal we first need to review pulmonary gas exchange principles. The distribution of ventilation in the lungs of normal foals is uneven. One way to visualize this is to consider the Slinky (the spring toy of your childhood). If you hold one end of the Slinky up and let the other fall to the ground you will notice that the distance between the spirals of spring are further apart near the top than near the floor and finally at the floor the spring is compressed. Gravity pulls the spring open more at the top than bottom. This also occurs when the lungs are suspended in the chest. As the foal stands his front legs support his body from the side of his chest allowing his rib cage and the lungs inside to be suspended (rather than supported from below). The alveoli at the top of the lungs are pulled open more because they are pulled by the weight of the lung below them. So alveolar near the top of the lung are larger and open more than alveoli at the bottom. Alveoli at the very bottom are so small they are collapsed (resting on the sternum).

When the foal takes a breath, if all things are equal (let’s ignore surfactant), then an equal amount of gas may enter each alveolus. Because the alveoli are unequal in size, the effect of a breath will vary depending on the level of the lung. Those alveoli near the top will receive a smaller percentage (although the same absolute amount) of fresh air on each breath and expel a smaller percentage of gas on each expiration. Those alveoli near the bottom will receive a relatively larger percentage of gas on each breath (relative to their size) so each breath will change their gas composition more. So alveoli near the bottom will be ventilated

better with each breath. Of course those collapsed at the bottom of the lung will not be ventilated at all.

When surfactant is added to this system, the disparity in ventilation is increased. As you will recall, surfactant decreases surface tension allowing for the lung expansion with less resistance. Alveoli that are small have a thicker layer of surfactant, thus have lower surface tension and are more easily expanded. The smaller alveoli at the bottom of the lung will thus be more easily expanded and will accept more of each breath than the alveoli at the top of the lung. So both gravity and surfactant insure that the lung near the bottom of the lung is better ventilated than alveoli near the top.

Now let's consider perfusion. Gravity also works on perfusion to result in uneven distribution. If you look at the cross section of a foal's chest you will notice that there is a large dorsal to ventral dimension. The larger this dimension is, the more gravity will affect the lung. You will also note that the heart base (position of the pulmonary veins) is approximately in the middle of the chest. Thus part of the lung is above the heart base and part below. Because of this and gravity’s effect on blood flow, the top of the lung is not as well perfused as the bottom of the lung. At the top of the lung, the alveolar pressure may be greater than the capillary pressure, resulting in collapse of the blood vessels and no blood flow at all (alveolar pressure is the same throughout the lung but the venous pressure varies). The venous pressure at the bottom of the lung is higher and the blood flow increased because the heart base is above this level. In some areas the venous pressure will be greater than the alveolar pressure and collapse the alveoli. The result of this distribution of blood flow is that the alveoli at the bottom of the lung will receive the best perfusion.

Thus there is a natural balance of perfusion and ventilation caused by gravity so that there is more perfusion to the best-ventilated lung at the bottom and less perfusion to the less well-ventilated lung at the top. In addition, in healthy foals, as in other animals, there is oxygen mediated vascular control. Areas with ventilated alveoli receiving oxygen will be better perfused because of oxygen mediated pulmonary vasodilatation. Other areas that are not ventilated and thus not receiving oxygen will have reflex vasoconstriction and less perfusion. So in healthy, standing foals there will be good matching of ventilation and perfusion.

This situation changes when the foal is sick. The foal lying in lateral recumbency no longer has gravity on his side. The lungs are no longer suspended but are supported from below. Thus the stretching of the lungs does not occur. Also a larger area of lung is ventral which tends to collapse and become atelectatic. When the foal tries to breathe, only the upper chest can move thus most of the ventilation occurs in the upper lung. With the foal lateral, the perfusion is primarily ventral, especially if the foal is hypotensive. With hypotension little blood may perfuse the upper lung. Increased perfusion to the bottom of the lung tends to favor edema formation as well. Thus there is significant mismatching with the

best ventilation occurring in the dorsal lung and the best perfusion occurring in the ventral lung.

This situation changes when we place the foal in a sternal position. It is important to prop the foal with support at his shoulder and not along the ribcage so that both sides of the chest can expand with each breath. Once the foal this placed sternal the matching improves dramatically. First, although the spring idea still does not apply, the area of lung that is directly supported (at the sternum) is a much smaller area, so the area of atelectasis is also smaller. With both sides of the chest expanding, both lungs will be ventilated. Although the best ventilation will no longer be at the bottom of the lung, the middle of the lung will be much better ventilated. And, although the bottom of the lung will continue to receive the best perfusion, the middle of the lung will receive enough to greatly improve the matching. The difference between the Pao2 of a foal in lateral recumbency and in sternal recumbency can be 20 to 30 torr.

Now you may be thinking that most healthy foals spend a good deal of time sleeping in lateral recumbency yet don't become hypoxic. One difference between the sick foal and the healthy foal is the presence of hypoxic vascular responsiveness. The healthy foal can get away with being in lateral recumbency, because the perfusion redistributes to match ventilation. It appears that the sick foal (especially the foal who has had hypoxic damage) no longer has this fine hypoxic vascular control of the pulmonary circulation. In reality, even very sick foals who have adequate perfusion, especially if they are on intranasal oxygen insufflation, will not have a significant gas exchange penalty when in lateral recumbency. But foals in metabolic jeopardy with marginal or abnormal cardiopulmonary gas exchange will benefit significantly from sternal positioning.

The situation also changes when positive pressure ventilation is used. As the alveoli pressure increases from the positive pressure, perfusion to those alveoli decreases. The pressure is essentially the same in all alveoli through out the lung. The increased pressure helps open some alveoli at the bottom of the lung where perfusion is good, resulting in better ventilation. However ventilation decreases perfusion to alveoli where alveolar pressure becomes higher than venous pressure (near the top of the lungs). The addition of PEEP will help hold open alveoli that were not open before, however if the PEEP is too high it again will decrease perfusion and exacerbate the situation.

GAS TRANSPORT

Efficient gas exchange requires matching of ventilation and perfusion. However throughout the lung there are a variety of ventilation/perfusion ratios. Although there are populations of alveoli which are not ventilated but are perfused

(shunting) and a population of alveoli that are ventilated but not perfused (alveolar dead space ventilation) and all the extremes in between, in the healthy lung the majority of the alveoli have good matching of ventilation and perfusion. When lung disease progresses to pulmonary failure, the average ventilation perfusion ratio is unchanged however more of the alveoli have V/Q ratios in the extreme range. Respiratory patients die of ventilation/perfusion mismatching. If shunting is present, the object of treatment is to ventilate the shunted blood (cases with intrapulmonary shunts, open the alveoli which are collapsed; cases with extra-pulmonary shunts, redirect the blood to pulmonary tissues). If alveolar dead space ventilation is present, the object of therapy is to increase perfusion to the ventilated (but not perfused) lung tissue. If mismatching is present the object is to increase the balance of ventilation and perfusion, either through redirecting blood or gas flow or enrich gas with oxygen to compensate for under ventilated, over perfuse areas.

CO_2

With CO_2 transport mismatching does not result in changes in $Paco_2$ because alveoli that are over ventilated makeup for those alveoli that are under ventilated. Small shunts can also be easily corrected by increased ventilation of perfused areas. Alveolar dead space ventilation basically represents wasted effort with less ventilation of perfused lungs. These principles hold as long as the area of hypoventilation or shunting is small. But when the proportion of shunt or hypoventilation increases there will be a point when the perfused and adequately ventilated areas will not compensate. That is there will be a point when all of the available CO_2 is being extracted however the remaining CO_2 results in hypercapnia.

O_2

With oxygen transport, mismatching consistently causes hypoxemia. This is because the over ventilated areas cannot compensate for the under ventilated/over perfused area. With increased ventilation some of the under ventilated/over perfused areas will improve, thus there can be partial compensation however it is far from complete. However, increasing the FIO_2 (fractional inspired oxygen concentration) will result in more oxygen being delivered to the under ventilated areas.

Shunting always leads to hypoxemia. Even if the FIO_2 is increased to 1.O (100% O_2) in those areas that are being ventilated and perfused, this will have very little effect because the ventilated blood will not be able to pick up enough oxygen to make up for the lack of oxygen in the shunted blood. Increasing ventilation to a ventilated area of lung will add little O_2 in the face of a significant shunt. The only way to correct the hypoxemia caused by shunting is to redirect shunted blood to ventilated alveoli or in the case of an intrapulmonary shunt, increase ventilation

to the nonventilated lung (open up atelectatic alveoli or alveoli which are collapsed because of pneumonia or edema).

The presence of alveolar dead space ventilation has no direct effect on Pao_2. However it is an indication of uneven perfusion since the blood that should perfuse these alveoli are perfusing others.

PATHOPHYSIOLOGY

HYPOVENTILATION

CAUSES HYPOVENTILATION: Whenever hypoventilation occurs, by definition the $Paco_2$ will be elevated. Concurrently the Pao_2 will be low since hypoventilation will cause mismatching (unless intranasal oxygen enrichment is used). Alveolar hypoventilation may be caused by a number of things. The most common one recognized clinically is depression of the central respiratory center caused by hypoxic ischemic central damage as occurs with premature placental separation or dystocia. Other possible causes include phenobarbital overdose, increased intracranial pressure, and sepsis. Hypoventilation is also cause by diseases that interfere with neuromuscular transmission such as botulism, spinal cord disease, or peripheral neuritis. Respiratory fatigue can also cause hypoventilation. This may be secondary to primary lung disease, general depression from sepsis, or decrease compliance of the lungs for any reason. Limitation of movement of the thorax can also result in hypoventilation such as occurs with fractured ribs (pneumothorax, hemothorax), diaphragmatic hernia, etc. Primary pulmonary disease may also cause hypoventilation as it results in decreased compliance and ineffective ventilation. Atelectasis, pneumonia, hyaline membrane disease, obstructing lesions, and interstitial pneumonia may all result in decrease effective compliance of the lungs.

Increased Alveolar Dead Space Ventilation: Alveolar dead space ventilation may be increased by a decrease in pulmonary blood flow as can occur with pulmonary hypertension or decreased cardiac output. Alveolar over distension as in asthma will also increase dead space ventilation.

Progressive hypercapnia results in a predictable syndrome. Once the $Paco_2$ rises above 60 torr the there is a release of catecholamines which results in increased in cardiac output, blood pressure and respiratory rate, all in an attempt to reverse the hypercapnia. This catecholamine response is maximum at about 80 torr in horses. As the $Paco_2$ continues to rise, eventually the resulting severe acidosis causes CNS depression and myocardial depression. This results in a progressive decrease in respiratory rate and heart rate until respiratory arrest followed by cardiac arrest occurs. Thus the hypercapnic patient may initially be tachypneic and tachycardic with an appropriate response. But resolution of the tachycardia and tachypnea may indicate improvement or may indicate

deterioration in the patient's condition. These cases need to be examined closely to determine which is occurring so that if failure is likely, definitive emergency steps may be taken to prevent it.

Doxapram (Dopram®) has been advocated by some to treat hypercapnia secondary to central depression. It stimulates both peripheral and medullary receptors, if the damage to the CNS is not severe. The down side of this drug is that it increases both the oxygen requirement and the work of the myocardium. If the central depression is severe or the hypoxia progressive, it may hasten death.

Another group of drugs that may be more useful are the methylxanthines. Aminophylline, theophylline and caffeine are all in this class. These drugs result in central respiratory stimulation. The safest is caffeine and it has been used frequently over the last few years in foals with depressed central receptors with good results in our practice.

Causes of Hypoxemia

Although low inspired oxygen is a potential cause of hypoxemia, it virtually never occurs clinically. Diffusion impairment occurs in several different forms. It is rare to see chronic fibrosis causing a diffusion block, but occasionally interstitial pneumonia’s do occur. Other less obvious causes of diffusion blocks include pulmonary edema, exudate in the alveoli, capillary dilatation resulting in an increased distance between alveoli and the red blood cell, changes in red blood cell shape or membrane and decreased area as with emphysema, or capillary hypoplasia which again is extremely rare in clinical medicine.

Inadequate alveolar ventilation (hypoventilation) will also cause hypoxemia. Of course this will always be accompanied by hypercapnia. This can be caused by obstructive or restrictive disease but more commonly is caused by central neurologic depression or septicemia resulting in weakness and inability to effectively ventilate.

Another common cause of hypoxemia is venous admixture which may be from mismatching or shunting. This may be caused by widespread atelectasis, consolidation, persistent fetal circulation, right to left shunting, decreased blood flow (hypovolemia or right sided cardiac insufficiency), increased blood flow (not enough time for full equilibration), pulmonary edema, exudate in the airway, or uneven blood flow.

Mismatching

Mismatching (low ventilation/perfusion ratios) can be thought of as the middle ground between shunting (blood that bypasses all gas exchange areas) and

alveolar dead space ventilation (gas that never comes in contact with blood). The lungs are made of billions of alveoli which all have their own ventilation/perfusion (V/Q) ratios. The V/Q ratio at the top of the lungs is high (3.0). As you travel down the lung blood pressure increases faster than ventilation decreasing the ratio (0.6 near the bottom). The average V/Q ratio in normal individuals is about 0.8. However the average ratio in patients dying of respiratory disease because of extreme V/Q abnormalities is also usually 0.8. This is an instance where the physiology gets mixed up and does not follow common sense rules in the pathophysiology of lung disease. In essence the V/Q ratio does not change with severe disease because for any area of the lung which becomes over ventilated and under perfused, there is another part of lung which becomes over perfused and under ventilated. Thus respiratory patients die because more of their alveoli lie at the extremes of the V/Q ratio than near the ideal middle ground.

Mechanical ventilation may help correct mismatching since it can result in opening alveoli that have not been ventilated before, decreasing some intrapulmonary shunting. However mechanical ventilation may also over distend already opened alveoli resulting in compression of the capillary beds surrounding these alveoli and decreasing their blood supply, further disturbing the ventilation/perfusion matching. Obviously with billions of alveoli, some alveoli from both groups will be affected by ventilation. The success of ventilation in part depends on how many alveoli have an improved V/Q ratio and how many have a worse V/Q ratio as a result of ventilation. The art of mechanical ventilation is in adjusting ventilation to maximize the V/Q ratio.

Clinical diagnosis of V/Q abnormalities: Shunting can be differentiated from mismatching by a trial of 100% oxygen. Areas where mismatching is occurring will be corrected if the inhaled FIO_2 is 1.0 (as long as the mismatching is not extreme). In the usual case the Pao_2 will increase to 300-400 if mismatching is the only abnormality. If shunting is occurring then the Pao_2 will not rise as much. A clinical rule of thumb is that if cardiac shunting (as apposed to intrapulmonary shunting) is occurring then the Pao_2 will not rise above 100 mm Hg despite having an FIO_2 of 1.0. In most cases with cardiac shunting (this is right to left shunting) the Pao_2 will be between 40 and 60 mm Hg when the patient is on an FIO_2 of 1.0.

The amount of alveolar dead space ventilation can be estimated by comparing $ETCO_2$ with the $Paco_2$. For adequate explanation of why, you should see the discussion on capnography. Using the formula ($Paco_2$ - $ETCO_2$)/ $Paco_2$ the percentage of alveolar dead space ventilation can be estimated.

Functional residual capacity in weak foals

In healthy individuals the functional residual capacity (FRC) is maintained so that almost all alveoli are open and ventilated. In foals who are weak or debilitated,

the FRC can be significantly reduced resulting in poor ventilatory function. The FRC is maintained by the opposing forces of the rib spring which pulls the lungs outward and the elastic properties of the lungs which tends to make the lungs collapse. In newborn foals the chest wall is very compliant and does not have a good spring, resulting in less innate forces pulling the lungs open. Neonates can partially compensate for this by using their intercostal muscles to hold their chest wall out. Neonates also have lower lung compliance resulting in a stronger force pulling the lungs close. If the foaled is weak or fatigued, he no longer can maintain his FRC and the lungs began to collapse to a volume, where alveoli collapse during expiration and must be opened on each breath to receive ventilation. Alveoli that repeatedly close in this manner will tend to squirt surfactant into the airway each time it closes, resulting in loss of surfactant. As the amount of surfactant decreases it becomes more difficult to open these alveoli on inspiration and eventually they can no longer be opened and atelectasis results. This further decreases the compliance of the lungs and further tends to cause collapse of more alveoli. The sum affect of this is progressive atelectasis. Even in those alveoli which are being ventilated, the ventilation is less evenly distributed because alveoli not already open will not open until midway through inspiration. Other alveoli that are already opened will accept gas throughout inspiration. This results in maldistribution of ventilation and perfusion. Also alveoli that close during expiration only participate in gas exchange during inspiration.

The added work of opening alveoli during progressive atelectasis and the decreased compliance may result in fatigue of the respiratory muscles in the foal. Eventually the intercostal muscles will become so fatigued that they will no longer be able to hold the chest open during inspiration. As the diaphragm contracts producing a negative pressure in the thorax, the chest wall will tend to be pulled towards the lungs resulting in very inefficient ventilation. When these foals are observed, the chest wall will be seen to drop during inspiration as the abdomen expands secondary to the contraction of the diaphragm. This results in "wave chest" in which the thorax moves inward as the abdomen moves outward during inspiration. The abdomen moves inward as the chest moves outward during expiration. The development of " wave chest " heralds the onset of significant fatigue and respiratory failure which will lead to respiratory and cardiac arrest if not corrected.

Decreased FRC is most effectively treated through initiation of PEEP/CPAP. By increasing the airway pressure during expiration alveoli tend to stay open and on each new inspiration more alveoli may be recruited. Full recruitment using PEEP/CPAP requires 15-20 minutes. A full discussion of this ventilatory therapeutic modality is described elsewhere.

STATIC (EFFECTIVE) COMPLIANCE

= TIDAL VOL / PLATEAU PRESS-PEEP

This measure of compliance includes the compliance of the lung and the chest wall. It is a readily attainable, useful clinical parameter. It will decrease if there is an abnormality of the chest wall (a flail chest), decrease in functional alveolar numbers as with pulmonary edema, pneumonia or atelectasis and for other similar reasons. It may also be used to determine the best PEEP and best tidal volume if serial measurements are obtained at trial settings.

DYNAMIC COMPLIANCE

= TIDAL VOL / PEAK PRESS-PEEP

Dynamic compliance adds the effects of resistance to static compliance. Dynamic compliance will decrease with disorders of the airway, lung parenchyma, and chest wall. Dynamic compliance is less than static compliance when there is increased resistance such as with secretion in the airways or endotracheal tube, bronchospasm, or endotracheal tube kinking.

TREATMENT

Rx HYPERCAPNIA

MECHANICAL VENT

Hypercapnia must be treated with increased ventilation. This may be achieved by mechanical ventilation or in selected cases with chemical stimulants. If the cause of hypoventilation is central depression of respiratory centers, methylxanthines maybe utilize as respiratory stimulants. Caffeine is the safest and most effective metylxanthine for use in foals. It can be given orally or if there is GI intolerance as in necrotizing enterocolitis, it is also effective when given rectally.

When mechanical ventilation is used to treat hypercapnia, the tidal volume and respiratory rate should be adjusted to result in an acceptable $Paco_2$. A reasonable tidal volume to begin with is 8 to 10 mls /kg. An adequate tidal volume will open previously collapsed alveoli, but not over distend other areas of the lung. Extreme mismatching may result in hypercapnia. Ventilation can help correct this extreme mismatching at times. Another consideration in treating hypercapnia is in decreasing production of CO_2. This means avoiding treatment

with bicarbonate and preventing lipid metabolism by limiting intravenous lipid supplementation and excessive calories. The goal of treatment is to decrease the $Paco_2$ to below 60 mm Hg long as the pH is normal. It should be recalled that frequently foals have a significant metabolic alkalosis with respiratory compensation resulting in hypercapnia. This hypercapnia is an important compensatory mechanism which should not be undermined by ventilation. Hypercapnia secondary to metabolic alkalosis should be treated by correcting the cause of the metabolic component.

Treatment of hypoxemia

Hypoxemia should be treated when a Pao_2 is consistently below 60 mm Hg or the $Paco_2$ is > 60 mm Hg since on room air a $Paco_2$ of 60 - 70 will result in hypoxemia. Oxygen saturation can also be used as a guideline. Considerations of therapy should be given to any patient with an oxygen saturation below 90-94%.

Hypoxemia due to ventilation perfusion mismatching can be corrected by intranasal insufflation of oxygen. If high intranasal flows of oxygen do not significantly increase the Pao_2 than there may be significant shunting, atelectasis, consolidation, or persistent fetal circulation. Unless there is a large shunt, oxygen therapy will not only increase the Pao_2 but will also decrease the work of breathing necessary to maintain oxygen delivery (work of respiratory muscles and also myocardial work).

In rare cases, respiratory efforts will stop when oxygen therapy is applied. This will occur when there is significant damage to the central receptor or significant central receptor depression so that they are not sensitive to $Paco_2$ and the major drive for ventilation is hypoxemia. Most commonly this occurs with HIE but it can occur with phenobarbital overdose in seizing foals. Another potential problem of oxygen therapy is atelectasis secondary to complete absorption of high oxygen content gas in alveoli in poorly ventilated areas of the lung. Oxygen toxicity is also possible, however it is rare unless $FIO_2 > 0.5$ for more than 24 hours. Usually oxygen toxicity does not appear clinically unless $FIO_2 > 0.8$ for extended periods.

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Mismatching and intrapulmonary shunting can been reduced by manipulation of ventilation and perfusion. Mechanical ventilation may open alveoli that are closed resulting in better distribution of ventilation. However if the tidal volume is too large, over distension may not only cause volutrauma but also result in compression of alveolar capillaries resulting in poor matching of perfusion.

Addition of PEEP will result in better matching since the alveoli will remain open during the entire ventilatory cycle and gas exchange can occur throughout the cycle. Also the open alveoli more readily accept the breath resulting in much more even ventilation. Perfusion may also be increased in areas that have relative over ventilation. In alveoli that are being ventilated, decreasing a tidal volume or PEEP may encourage perfusion. Likewise, increasing perfusion pressure may result in better perfusion. The cardiac output may be increased by insuring proper volume loading and through the use of inotropes. Placing the foal in a sternal position may also increase matching dramatically. Decreasing pulmonary edema through the use of furosemide and decreasing inflammatory disease by treatment of pneumonia may also help improve matching. Surfactant therapy is also in theory a good idea, however in my hands it has not been very impressive.

CONTINUOUS POSITIVE ANYWAY PRESSURE

There are four methods of achieving CPAP:

1) endotracheal CPAP

2) nasopharyngeal CPAP (shortened endotracheal tube in posterior pharynx)

3) nasal prongs

4) negative end expiratory pressure (negative thoracic pressure)

Beneficial physiologic affects of CPAP are created by an increased transpulmonary pressure resulting in an increased FRC, stabilization of an unstable chest wall, and improvement in ventilation perfusion ratios. CPAP affects: pulmonary mechanics, cardiovascular stability, and pulmonary vascular resistance.

PULMONARY MECHANICS: CPAP is the major factor determining lung volume. At low CPAP (low volumes e.g. in diseased lungs), compliance is low; at higher volumes compliance increases; at high volumes (over distension) compliance again decreases. Optimum FRC results an optimum compliance and the lowest work of breathing. Optimum CPAP = optimum FRC. Lung volume is also related to airway resistance. At low lung volumes (insufficient CPAP) airway resistance is high and since atelectasis is not resolved, the work of breathing is high. At optimum lung volumes airway resistance is low. Thus CPAP can improve

distribution of ventilation to optimize FRC and therefore optimize both lung compliance and airway resistance.

CARDIOVASCULAR STABILITY: High CPAP can have a detrimental effect on the cardiovascular system, compressing right sided vessels, decreasing cardiac return which will result in decreased cardiac output. This may result in acidosis, tachycardia, decreased arterial blood pressure, etc. The amount of CPAP that is excessive and will produce this affect depends on the lung compliance. If the lung compliance is low, less intra-airway pressure will be transmitted to the plural space and cardiac compromise will be less. Hypovolemia will exacerbate the negative effect of high CPAP. Excessive CPAP may be detected by the development of acidosis, decreased dynamic lung compliance and increased CO_2 retention. A trial of lower CPAP or increased IV fluids will resolved the problem, however it should be recalled that too low a CPAP will also cause acidosis.

PULMONARY VASCULAR RESISTANCE: Over distension of the lung may cause direct pressure on pulmonary arterials and capillaries, increasing pulmonary vascular resistance and pulmonary artery pressure. Low levels of CPAP do not resolve atelectasis. Atelectasis results in shunting of blood away from collapsed alveoli and regional increase in pulmonary vascular resistance. Optimal CPAP will optimize the V/Q.

The affects of CPAP on renal perfusion have been controversial. However most are probably directly related to changes in cardiac output. CPAP's affects on cerebral pressure are directly related to the level of positive pressure applied to the airway and the lung compliance affecting blood flow. If the pressure is transmitted to the pleural space and the anterior vena cava, it may result in increased cerebral pressure.

Optimal CPAP can be found by producing a CPAP/PEEP grid: adjust CPAP to 1 cm above and 1 cm below current levels and after 10-15 minutes obtain Pao_2 or lung compliance depending on the goal of the CPAP.

NITRIC OXIDE THERAPY

The endothelium regulates vascular tone through its production of many vasoactive mediators, including endothelial-derived relaxing factor, prostaglandins, and endothelin which act on the underlying vascular smooth muscle. NO is constantly produced at a low level. It appears to be responsible for hypoxic vasoconstriction in the lungs. Patients with pulmonary hypertension appear to have low basal secretions of NO. In the endothelial cell L-arginine is converted by NOS to NO in a reaction that requires oxygen and calcium. NO

results an activation of soluble guantanyl cyclase which results in smooth muscle relaxation. NO is metabolized as it diffuses into the vascular lumen. It is quickly bound to hemoglobin, producing nitrosyl hemoglobin and methemoglobin. This rapid binding and metabolism of NO inactivates it, providing local regulation of vascular tone in the microcirculatory beds of the body without generalized systemic effects. Therapeutically, this inactivation allows for the use of inhaled NO gas to treat pulmonary hypertension without danger of systemic hypotension. In patients with pulmonary hypertension, adding 20-40 ppm NO to the inhaled gases will help vasodilate pulmonary vessels often leading to significant improvement. In patients with uneven ventilation/perfusion, treating with NO will tend to improve matching since where ever the gas is delivered (ventilated areas) vasodilatation will occur resulting in improved perfusion.