

## PRO:CON Debate

**ARDSnet vs. APRV**

**Inhaled Flolan vs. Inhaled Nitric Oxide**

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### Ventilator Induced Lung Injury

- The name of the game during mechanical ventilation is to reduce the damage done to the lung during ventilation.
- Though the arterial blood gas guides us through mechanical ventilation, VILI should be the primary focus of mechanical ventilation and not the ABG.
- Barotrauma, Volutrauma, Atelectrauma, O<sub>2</sub> toxicity, and Bio-Trauma are all preventable causes of ALI/ARDS

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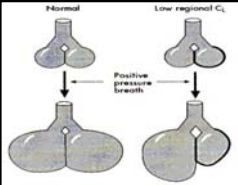
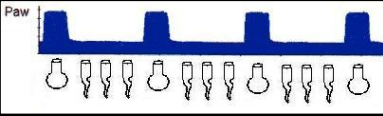
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- Atelectrauma
  - Injury to the lung parenchyma causes a loss of FRC, a decrease in lung compliance and an alveolar instability that results in alveolar derecruitment



- These characteristics of parenchymal lung injury are typically seen in a non-homogenous pattern

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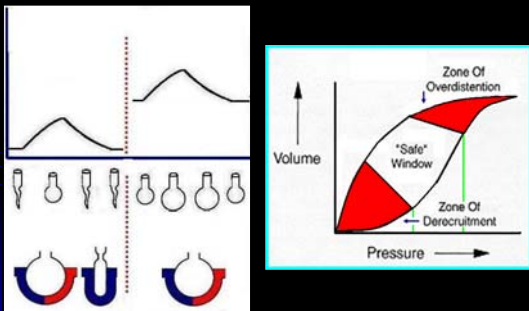
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• Atelectrauma

- These changes in lung characteristics require a management strategy that at first relies on an increased end-expiratory pressure to maintain alveolar recruitment




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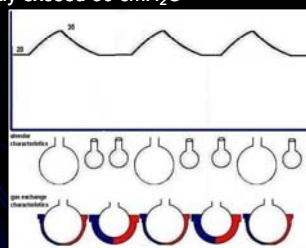
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• Atelectrauma ↔ Volutrauma

- However, in patients with severe disease, the end-expiratory pressure requirement to maintain alveolar recruitment continues to increase
- As PEEP is applied, the alveolar distending pressures required to maintain ventilation over and above the PEEP can quickly exceed 30 cmH<sub>2</sub>O




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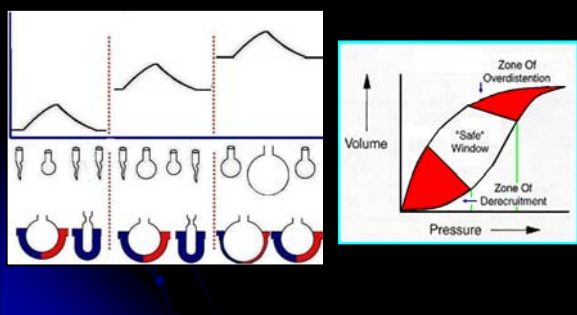
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• Atelectrauma ↔ Volutrauma

- As this occurs, the etiology of ventilator induced lung injury shifts from one of repetitive alveolar collapse and expansion to one of alveolar overdistention or volutrauma




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### ARDSnet ventilation – the PRO side

- The ARDSnet protocol is **simple-to-use and straightforward protocol that can be implemented for the majority of patients**
  - This ventilation strategy provides concise minute volume control which will lead to tighter control over the patient's ABG values.
  - The ARDSnet oxygenation provides a PEEP/FiO<sub>2</sub> titration table that is suitable for most patients
    - As the patient shows clinical indications of intrapulmonary shunt (FiO<sub>2</sub> requirement > 0.60) the titration table allows for increases in PEEP

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### ARDSnet ventilation – the PRO side

- The ARDSnet protocol is the **standard of evidenced-based medicine for the management of ARDS patient**
- The ARDSnet mechanical ventilation strategy specifically **addresses the issue of volutrauma** by limiting the flow and, more importantly, volume according to end-inflation pressures
  - Continuously monitors pressure and compensates for high pressure by lowering the tidal volume, thus attempting to prevent further damage to the lung
  - The permissive hypercapnic strategy provides an oxy-hemoglobin curve shift that provides superior tissue oxygenation

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### APRV – the PRO side

- APRV for this talk will be considered a spontaneous mode of ventilation with a single high CPAP setting and a secondary zero of pressure setting in which the time of the CPAP on phase will be significantly longer than the CPAP off phase
  - T<sub>HIGH</sub> between 4 – 8 seconds
  - T<sub>LOW</sub> setting based off of the EEf/PEf ratio
  - P<sub>HIGH</sub> 20-30cm H2O
  - P<sub>LOW</sub> 0 cm H2O
  - Limited Sedation

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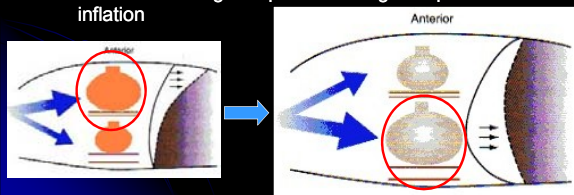
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### APRV – the PRO side

- Spontaneous breathing is superior to simple positive pressure breathing for many reasons
  1. Decreased need for sedation
  2. Patient has an active mucociliary escalator
  3. Patient maintains an active cough
  4. Negative pressure ventilation pulls gas to the dependent areas of the lung and promotes negative pressure re-inflation




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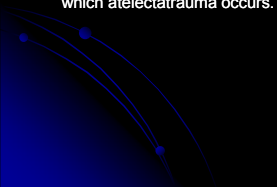
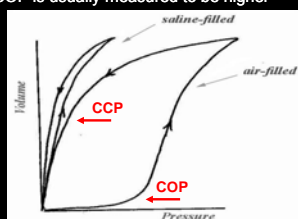
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### APRV – the PRO side

- APRV utilizes the critical closing pressure of the lung instead of the critical opening pressure of the lung (the reverse of normal PPV)
  - APRV does not start at a PEEP and force pressure above that level
  - Instead it starts at a  $P_{HI,GH}$  (which is greater than the Critical Opening Pressure) and permits the exhalation to occur down to the critical closing pressure.
    - In theory these two pressures should be the same, however due to airway resistance, the COP is usually measured to be higher
- The CCP is the pressure at which atelectrauma occurs.




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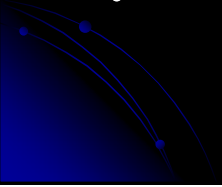
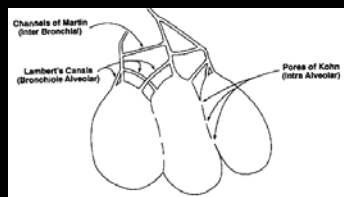
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### APRV – the PRO side

- Because pressure is applied for greater than 5 TC, intra-alveolar lateral wall pressure is created
  - This creates a pendelluft gas movement in the lung and promotes inflation and recruitment via collateral ventilation
- In addition, the prolonged elevated pressure promotes equal distribution and recruitment despite unequal inspiratory time/filling constants




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the CON side – ARDSnet ventilation

- A major pitfall is the fact that this is a protocol designed for the “average patient” and may eliminate critical thinking and assessment at the bedside
- Patient-ventilator dyssynchrony seen with low  $V_T$  and fixed inspiratory flow rates may require increased paralysis or sedation
- The use of sedation/paralytics can increase ventilator days & length of stay as well as morbidity and mortality

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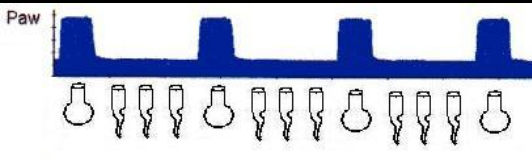
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the CON side – ARDSnet ventilation

- The PEEP/ $FiO_2$  titration table is an arbitrary table that does not address lung mechanics and the issue of atelectrauma in any one specific patient




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the CON side – ARDSnet ventilation

- Lung recruitment and distribution of ventilation
  - With fixed flow ventilation and an inspiratory time ( $T_I$ ) < 1.5 seconds, the ARDSnet strategy is completely affected by inspiratory time constants ( $T_c$ )
    - An inspiratory time constant is the relationship between the airway resistance and compliance
    - The inspiratory time constant for a normal healthy lung is approximately 0.2 seconds
    - One time constant equals a delivered volume of 63% of capacity
    - A filling capacity of 99% is accomplished via 5  $T_c$  (or  $T_I = 5 T_c$ )

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the CON side – ARDSnet ventilation

- Lung recruitment and distribution of ventilation
  - For most patient's receiving mechanical ventilation the  $T_c$  is usually elevated (~ 0.3-0.7 seconds) resulting in a necessary  $T_i$  of 1.5 – 3.5 seconds
  - If the  $T_i$  set on the ventilator is less than 5 times the patient's time constant the delivered breath will result in **un-equal filling of the alveoli and accinus.**
  - The gas follows the path of least resistance resulting in **over inflation in zone west I** and **under inflation in zone west III**

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the CON side – APRV

- APRV can be difficult to manage from a caregiver perspective for a number of reasons
  - APRV is a pressure limited mode of ventilation and therefore each individual volume as well as the accumulated minute volume is variable
    - This lack of direct control of volume can be extrapolated to ABG / arterial  $CO_2$  values
  - In addition, patients may be perceived to be "lung protective" because of a specific  $P_{HIGH}$  setting; however **the end-inflation or transpulmonary pressure of a spontaneously breathing patient may be much higher** than that which is set due to the variable volume and fluctuating pleural pressure

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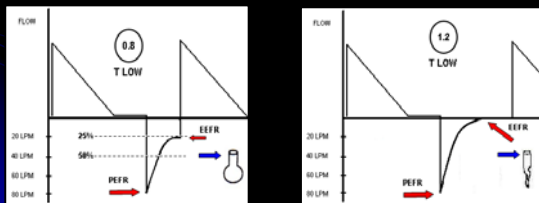
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the CON side – APRV

- APRV can be difficult to manage from a caregiver perspective for a number of reasons
  - The  $T_{LOW}$  is set so as to prevent complete emptying of the lung at end-expiration
  - Requires analysis of the end-expiratory flow and subsequent precision of the ventilator setting




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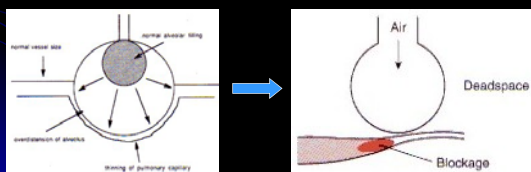
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### the CON side – APRV

- APRV can be difficult to manage from a caregiver perspective for a number of reasons
  - The practitioner must use careful physical assessment skills to determine/maintain optimal lung volume
    - Low lung volumes result in continued derecruitment, V/Q mismatch and an increased inspiratory work of breathing
    - High low volumes result in alveolar overdistension, V/Q mismatch, ↑ expiratory work of breathing, and cardiovascular derangements (↑ PVR & ↓ CI)




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### the CON side – APRV

- If APRV is used as a "rescue" mode of ventilation or a "last resort" there will be a delay in the alveolar recruitment seen with this mode of ventilation
  - Two things occur because of this difficulty in recruiting collapsed and flooded alveoli
    - The minute ventilation will be dramatically decreased at the initial switch from volume ventilation to APRV
      - As a result CO<sub>2</sub> elimination will diminish and the PaCO<sub>2</sub> will increase
    - The expected decrease in FiO<sub>2</sub> or pressure may not be realized
- Once the collapsed alveoli are re-recruited the blood gases should normalize

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### the CON side – APRV

- Variable expiratory flow and time constants
  - The expiratory flow exits from portions of the lung at different flow rates or time constants
  - A diseased, or non-compliant, lung unit has a relatively strong recoil on exhalation
  - The flow exiting this non-compliant lung unit will thus be relatively fast and have a short time constant




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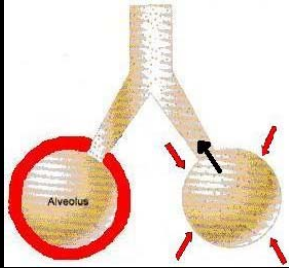
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the CON side – APRV

- Variable expiratory flow and time constants
  - The expiratory flow exits from portions of the lung at different flow rates or time constants
  - A healthy, or compliant, lung unit has a normal elastic recoil
  - The flow exiting the compliant lung unit will be comparatively slower and have a longer time constant




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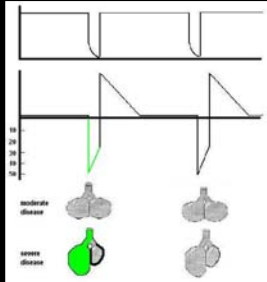
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the CON side – APRV

- Variable expiratory flow and time constants
  - The time frame, or  $T_{LOW}$ , required to trap an appropriate amount of flow in a healthy lung is therefore different than the  $T_{LOW}$  required to trap the appropriate amount of flow in a diseased lung
- In the example to the right, the  $T_{LOW}$  is set to trap the appropriate expiratory flow from a healthy lung unit




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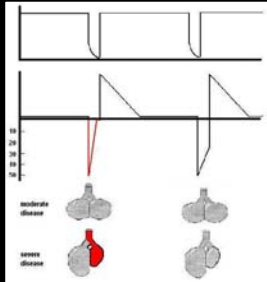
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the CON side – APRV

- Variable expiratory flow and time constants
  - The time frame, or  $T_{LOW}$ , required to trap an appropriate amount of flow in a healthy lung is therefore different than the  $T_{LOW}$  required to trap the appropriate amount of flow in a diseased lung
- If the  $T_{LOW}$  is set to trap flow exiting from the healthy lung unit, then the diseased lung unit will completely empty




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### the CON side – APRV

- Variable expiratory flow and time constants
  - The time frame, or  $T_{LOW}$ , required to trap an appropriate amount of flow in a healthy lung is therefore different than the  $T_{LOW}$  required to trap the appropriate amount of flow in a diseased lung
- This is what the graphic would look like if it were to display the expiratory flow coming from each type of lung unit
- The expiratory flow graphically displayed is essentially the average from the proximal airway

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### APRV vs. ARDSnet Synopsis

- Protocols, such as the ARDSnet, are developed, tested and implemented to do the most good for most of the patients
  - In this particular case, the ARDSnet protocol does exactly that for the "average" patient and is the standard for these patients
- However, any one design can not incorporate every demographic, etiology or specific clinical scenario
- The exudative phase of ARDS begins at the onset of injury and continues for approximately 72-96 hours; this is followed by a fibroproliferative phase
  - Sustained, and optimization of, lung recruitment is most likely to be achieved during this time frame
  - Determine failure of any modality and advance treatment in a timely fashion
  - The consideration and success of alternative modes of ventilation has been most successful if implemented early

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### APRV vs. ARDSnet Synopsis

- The key to remember is that both strategies are excellent, and precise clinical decisions must prevail for each individual patient
- Both ARDSnet and APRV protocols should be used in the critical care setting

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### Pulmonary Vasodilators

- Pulmonary vasodilators are utilized clinically in the treatment of pulmonary hypertension and/or right ventricular dysfunction as well as refractory hypoxemia
- The use of systemically-administered vasodilators can be limited clinically because of their nonselectivity and the potential negative effects on blood pressure and oxygenation
  - Systemic vasodilation decreases mean arterial blood pressure and can result in hypotension
  - Nonspecific vasodilation in the lungs redistributes pulmonary blood flow to poorly ventilated lung regions, worsening V/Q matching and hypoxemia

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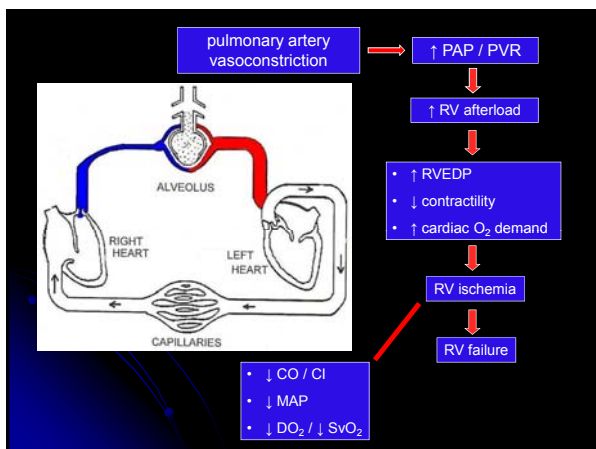
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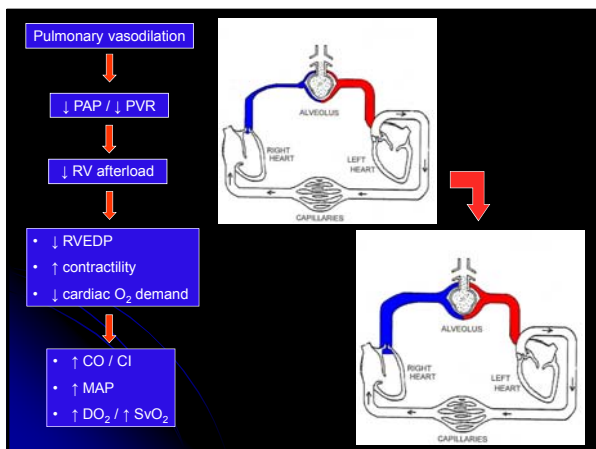
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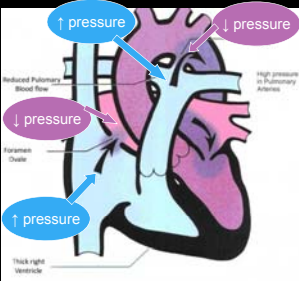
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- In neonates, increased pulmonary vascular pressures and afterload results in increased RVEDP
- The right-sided heart pressures become abnormally higher than the left-sided heart pressures
- Blood moves from high pressure to low pressure (right-to-left) through the previously closed shunts
- Deoxygenated, venous blood now mixes with oxygenated, arterial blood in the left heart and is then circulated through the arterial system to the tissues



The diagram shows a neonatal heart with a thick right ventricle. Labels include: '↑ pressure' (blue) pointing to the pulmonary artery, '↓ pressure' (purple) pointing to the pulmonary vein, 'High pressure in Pulmonary Arteries', 'Reduced Pulmonary Blood flow', 'Foramen Ovale', and 'Thick right Ventricle'.

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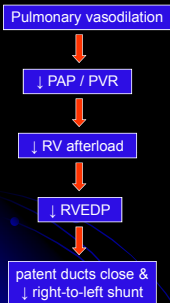
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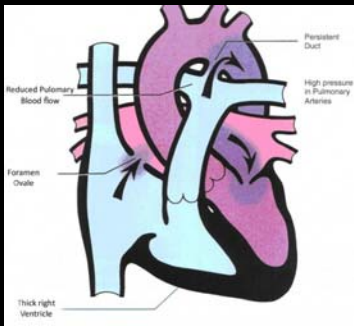
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    graph TD
      A[Pulmonary vasodilation] --> B[↓ PAP / PVR]
      B --> C[↓ RV afterload]
      C --> D[↓ RVEDP]
      D --> E[patent ducts close & ↓ right-to-left shunt]
    
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The diagram shows a neonatal heart with a thick right ventricle. Labels include: 'Reduced Pulmonary Blood flow', 'Foramen Ovale', 'Thick right Ventricle', 'Persistent Duct', and 'High pressure in Pulmonary Arteries'.

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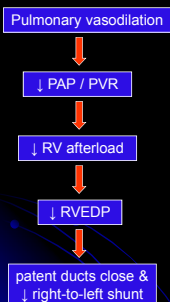
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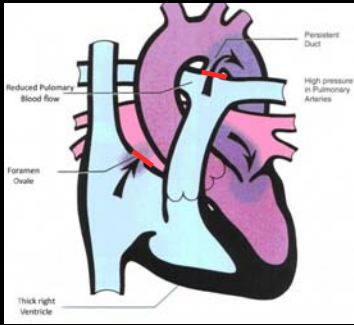
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The diagram shows a neonatal heart with a thick right ventricle. Labels include: 'Reduced Pulmonary Blood flow', 'Foramen Ovale', 'Thick right Ventricle', 'Persistent Duct', and 'High pressure in Pulmonary Arteries'.

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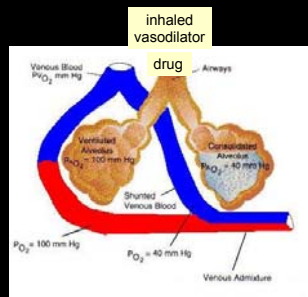
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- A vasodilator is inhaled into the lungs and travels through the tracheobronchial tree to only the well ventilated alveoli




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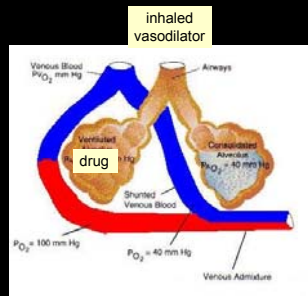
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- The gas or aerosol then diffuses across the alveolar capillary membrane and interstitial space, where it comes into contact with the pulmonary capillaries and arterioles




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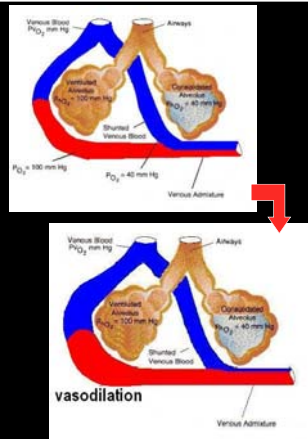
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- The inhaled drug then results in vasodilation
- This selective vasodilation redistributes and increases blood flow to that particular area
- Gas exchange in this area is theoretically, and relatively, good
- As a result of more blood flow participating in optimal gas exchange, the intrapulmonary shunt is decreased when venous admixture does occur




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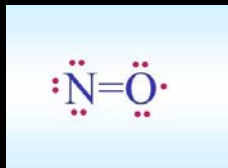
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### Pulmonary Vasodilators

- There are two widely-used vasodilators administered via inhalation in the acute care setting
  - Inhaled Flolan
  - Inhaled Nitric Oxide (iNO)



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### Inhaled Flolan

- Administration of inhaled Flolan
  - The drug is reconstituted in 50 ml of solution and administered via continuous nebulization
  - There are two different ways to deliver the drug via continuous nebulization
    - With an HEART jet nebulizer
      - Requires two infusion pumps for dose titration; one with the drug and one a diluent solution



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### Inhaled Flolan

- Administration of inhaled Flolan
  - There are two different ways to deliver the drug via continuous nebulization
    - With an AeroNeb ultrasonic nebulizer
      - Requires one infusion pump for dose titration



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### Inhaled Nitric Oxide

- Administration of iNO
  - iNO combined with oxygen is rapidly oxidized into toxic substances,  $\text{NO}_2$
  - Therefore it is combined with inert nitrogen in compressed gas cylinders available commercially from Ikaria
- iNO must also be delivered through a system with specific capabilities
  - The Ohmeda iNOvent and iNOmax DS are commercially available systems that, independent of ventilatory pattern, the is able to deliver a constant concentration of iNO



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### Inhaled Nitric Oxide

- Administration of iNO
  - The gas is introduced into the inspiratory limb of the ventilator circuit
  - A sampling line is placed at the distal end of the inspiratory limb just before the wye



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### Inhaled Nitric Oxide

- Administration of iNO
  - The gas can also be delivered non-invasively, however the delivered flow rate must be kept high
    - $\text{NO}_2$  builds up when delivering NO non-invasively through a nasal cannula, face mask or BVM.



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### Inhaled Flolan

- Monitoring of inhaled Flolan
  - The specific diluent used to reconstitute Flolan is known to crystallize
    - Additional modification of the ventilator circuit is required in that 2 (two) filters are placed on the exhalation valve to prevent the known possibility of exhalation valve malfunction



- The filters require changing approximately every four hours
- Diligent monitoring for signs of incomplete or retarded exhalation

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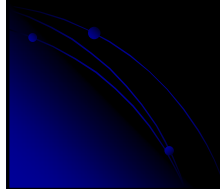
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### Inhaled Flolan

- Monitoring of inhaled Flolan
  - Flolan may cause a drop in both PVR and SVR resulting in a decreased mPAP and MAP



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### Inhaled Nitric Oxide

- Monitoring of iNO
  - Nitrogen dioxide (NO<sub>2</sub>) is produced spontaneously whenever iNO is exposed to oxygen
    - The clinical goal is to keep NO<sub>2</sub> exposure less than 2 ppm
- NO<sub>2</sub> can cause parenchymal lung destruction at concentrations as low as 2.0 PPM
- NO<sub>2</sub> is monitored by both the INOvent and the INOmax DS; thus the machine must be accurately calibrated and constant flow must be maintained



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### Inhaled Nitric Oxide

- Monitoring of iNO
  - NO is quickly bound to hemoglobin in the pulmonary vasculature and forms metHgb
    - metHemoglobin can cause organ damage with concentrations as low as 2% and can result in death with concentrations as low as 5%
    - Thus it must be continuously monitored through ABG with Co-oximetry
    - If metHbg > 5% attempt to decrease the dose of NO or dose with methylene blue or ascorbic acid.




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### Inhaled Flolan

- Indications / contraindications
  - Inhaled Flolan is contraindicated for
    - Post organ transplant
    - Neurological injured patient
    - Neonates
    - Severe hypotensive patient
      - Use must be closely calculated and titrated
- Efficacy
  - Administering Flolan via nebulization has been shown to have equal clinical efficacy as compared to iNO
- Acquisition
  - The cost of Flolan is substantially less expensive than that iNO

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### Inhaled Nitric Oxide

- Indications / contraindications
  - Nitric Oxide is safe to use with neonates
  - Nitric Oxide is safe to use with neurologically injured patients
  - Nitric Oxide works quicker than Flolan
  - Nitric Oxide has no effect on systemic blood pressure
  - Ease of use at the bedside is significantly easier with Flolan vs. Nitric Oxide

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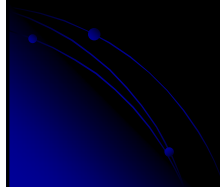
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Inhaled Flolan vs. Inhaled NO Synopsis

- The key to remember is that both drugs have their place in critical care it is not that one is superior to the other but when to use what, when.



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