Liquid Ventilation

(Maybe not so Science Fiction…)

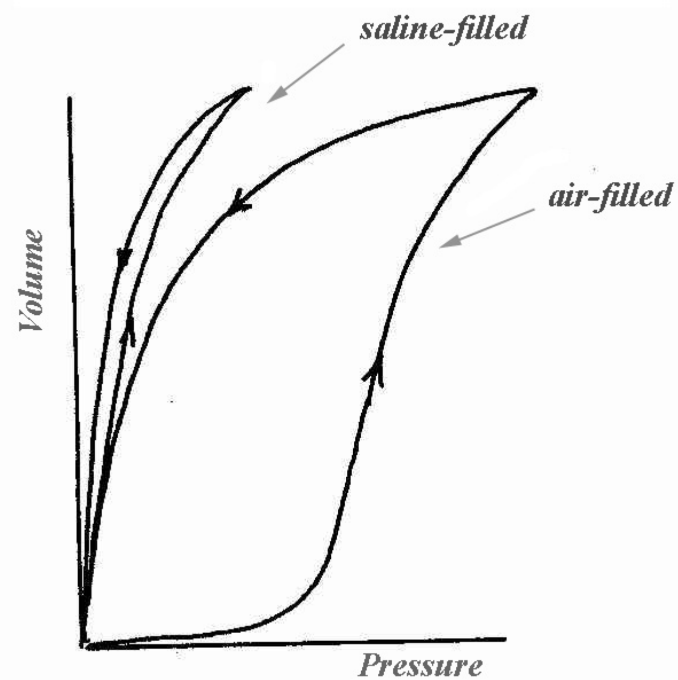
By: Kevin Lapeyre, Jessica (So Hyun) Ahn, and Michael Xu

First, a little review

- Ventilation in CAPS 422 is commonly known as Conventional Gas Exchange
- Involves movement of O_2 and CO_2 in and out of the lungs through mechanical ventilation
- Forces to overcome include frictional resistance and surface tension in the lungs

We know Surface Tension is a huge contributor to resistance (From our lectures on Surface Tension)

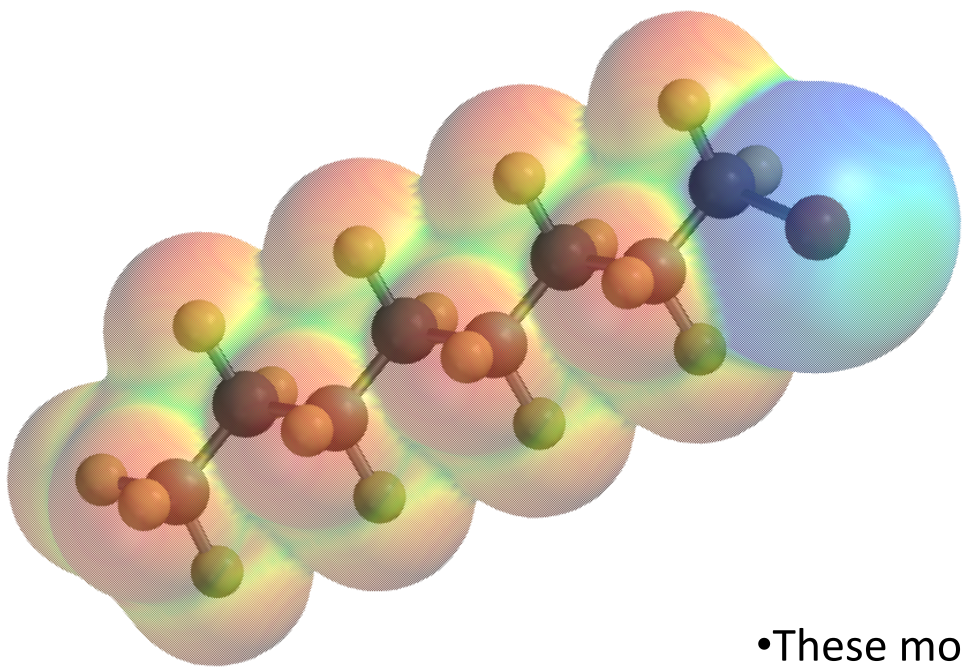
- P-V curves for lungs filled with air and then saline
- More force required to overcome surface tension in the alveoli
- Filling the lungs with saline eliminates surface tension, so less force is required!



So what if we used a liquid to ventilate the lungs instead of a gas mixture!?

Image source: http://www.medicine.mcgill.ca/physio/resp-web/text3.htm

Perfluorocarbons



-Carbon backbone with surrounding fluorine atoms
-Common PFC used in ongoing research seen left,
-Perflubron (perfluoro-octyl bromide)

- These molecules have greater respiratory gas solubility than blood!

Total Liquid Ventilation

-Completely filling the lungs with PFC
-Ideally beneficial, but difficult to achieve and sustain – would need to move aliquots of PFC equal to tidal volumes, while keeping it heated, and ventilated with O_2 and CO_2 using a membrane oxygenator
-We do not have the current machinery capable of these requirements

Partial Liquid Ventilation

-Fill lungs with PFC only to a value of FRC, and mechanically ventilate with tidal breath volumes on top of the liquid
-Current research finds this more feasible and can utilize technology that is currently used in neonatal intensive care units

Oxygenated Perfluorochemical liquid

- Low surface tension
  - constant, unlike surfactant
- High solubility for oxygen and carbon dioxide
  - Oxygen carrying capacity can be more than 2 times that of blood
- Chemically and biologically inert, and undergoes no metabolism in kidneys and liver

Improvement in Acute Lung Injury

- Improvement in lung compliance
  - Eliminates the air-liquid interface
- Improvement in oxygenation
  - Because PFCs are dense liquids, they will gravitate to and reopen the collapsed regions of lung, acting as liquid end expiratory pressure

Current Applications

Severe respiratory failure due to

- Hyaline membrane disease
- Adult respiratory distress syndrome
- Meconium aspiration syndrome
- Pulmonary interstitial emphysema
- Congenital diaphragmatic hernia

Obstacles to Liquid Breathing

- High viscosity of PFC
  - Reduces CO_2 removal despite its high solubility in PFC
  - Imposes unrealistic demands on respiratory flow rates (need to breath approx. 10L/min; normal is 6L/min)

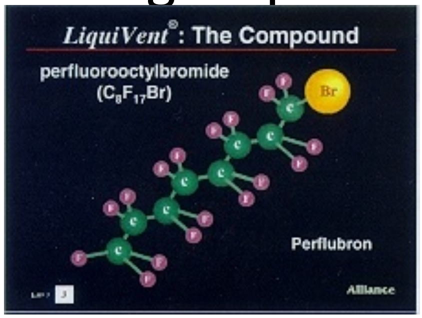
- Extremely difficult for lungs to move liquids compared to gases
  - PFC is dense!: 2000x more dense than air
  - greater mass means more work for respiratory muscles and longer transit time through airways
  - Increased metabolism → increase CO_2

Obstacles to Liquid Breathing (cont.)

- Pneumothorax
  - Alveolar collapse due to insufficient positive end-expiratory pressure causing alveolar shearing
  - Consequence of uncertain distribution of air in alveoli during PLV
- Effects on Pulmonary Circulation
  - Putative effect: density of PFC → pulmonary hypertension
  - Possible right heart failure

Clinical Status of Liquid Breathing

- Human studies on liquid breathing exist:
  - Late 1980s: liquid breathing in infants with severe respiratory distress
  - Mid-1990s: safety and efficacy study of PLV in mixed cohort of adults and pediatric acute respiratory distress symptom patients
  - Phase II and III trials for Perflubron as respiratory distress therapy
    - Showed little improvements compared to control group



Additional Applications beyond Respiratory Physiology

- Super-deep Diving: i.e. Marianas Trench
- Drug Delivery
- Space Travel