CALCULATION OF DEAD SPACE - RELEVANCE IN CRITICAL CARE

Kodati Rakesh
Dead space

• Dead space calculation
• CO2 measurement
• Effect of mechanical ventilation
• ARDS
• Recruitment & proning
• Pulmonary embolism
• Weaning
DEAD SPACE CALCULATION
Dead space

• Volume of the airways and lungs that does not participate in gas exchange

• **Anatomical dead space**
  - Volume of conducting airways
  - Upper airways, larynx, trachea, bronchi and bronchioles
  - Does not include respiratory bronchioles and alveoli

• **Physiologic dead space (VDphys)**
  - Total volume of the lungs that does not participate in gas exchange
  - Includes *anatomic* dead space plus a *functional* dead space in the alveoli
Dead space
Dead space

Difference b/w expected & actual composition of the effluent media
Basis for calculating dead space and shunt
Dead space

Rileys 3 compartment model

Alveoli groups according to V/Q ratios
A – normal perfusion, no ventilation (shunt V/Q of 0)
B – normal perfusion & ventilation (shunt V/Q of 1)
C – normal ventilation, no perfusion (shunt V/Q of infinity)

Physiological dead space (VD phys)
Airway dead space (VD aw)
Alveolar dead space (VD alv)

Riley RL et al, J App Physiol 1949
Dead space
Bohrs dead space

- Danish physiologist Christian Bohr in 1891
- Mass balance calculation dilution of the expired gas by the inspiratory gas filling the conductive airways

\[ V_T = V_A + V_D \]

\[ V_T \times F_{ECO_2} = V_A \times F_{ACO_2} + V_D \times F_{DCO_2} \]

\[ \frac{V_D}{V_T} = \frac{(F_{ACO_2} - F_{ECO_2})}{F_{ACO_2}} \]

\textbf{FACO}_2 - mean alveolar CO2 concentration
sample of gas collected late in exhalation

\textbf{FECO}_2 - fractional CO2 concentration in the total mixed exhaled breath

H. Thomas Robertson, Eur Respir J 2015; 45
Tusman G et al, Anesth Analg 2012
Bohr's dead space

- Fractions or partial pressures of CO2 are used interchangeably.
- $\text{FACO}_2$ is the mean value of CO2 within the alveolar compartment.
- $\text{FE CO}_2$ is calculated using formula:
  \[ \frac{V_{CO2}}{V_T} \times (P_b - P_{H2O}) \]

*H. Thomas Robertson, Eur Respir J 2015; 45
Tusman G et al, Anesth Analg 2012*
Bohrs dead space

• Direct measurement of \( \text{PACO}_2 \) has not been validated until volume capnography

• \( \text{PACO}_2 \) was replaced by its surrogate parameter end-tidal CO2 (PET CO\(_2\)) assuming both are same

• \( \text{PACO}_2 = \text{FACO}_2 = \text{PET CO}_2 \)

• \( \text{VD/VT} = (\text{PET CO}_2 - \text{PE CO}_2)/\text{PET CO}_2 \)

\( H.\text{Thomas Robertson, Eur Respir J 2015; 45} \)
Bohrs dead space

- $\text{PACO}_2 / \text{PET CO}_2$ used in Bohrs equation is determined by many factors
  - non-uniform $V/Q$ distributions
  - diffusion coefficients
  - tidal fluctuations in alveolar gas composition
  - alveolar expiratory time constants

H. Thomas Robertson, Eur Respir J 2015; 45
Tusman G et al, Anesth Analg 2012
Bohrs dead space

Draw backs

• End tidal CO$_2$ does not reflect the mean alveolar CO$_2$ in diseased lungs
• In exercise & hyperventilation the difference increases by more than 4-6 mm Hg
• Usage of ET CO$_2$ overestimates the true VDphys

H. Thomas Robertson, Eur Respir J 2015; 45
Tusman G et al, Anesth Analg 2012
Enghoffs modification

- Enghoff proposed the substitution of $\text{PaCO}_2$ by $\text{PACO}_2$ in Bohrs equation in 1938
- Difficulty in identifying mean $\text{PACO}_2$ is avoided
- Always be greater than classical Bohrs dead space as $\text{PaCO}_2$ is always greater than $\text{PACO}_2$
- It is sensitive to range of gas exchange abnormalities

H. Thomas Robertson, Eur Respir J 2015; 45
Tusman G et al, Anesth Analg  2012
Enghoff's modification
<table>
<thead>
<tr>
<th></th>
<th>Bohrs approach</th>
<th>Enghoffs approach</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Formula</strong></td>
<td>$V_D \text{ Bohr} = \frac{(PACO_2 - PECO_2)}{PACO_2}$</td>
<td>$V_D \text{ B-E} = \frac{(PaCO_2 - PECO_2)}{PaCO_2}$</td>
</tr>
<tr>
<td><strong>Type of V/Q analysed</strong></td>
<td>$V/Q$ of infinity (units C) High $V/Q &gt; 1$ but $&lt; \infty$</td>
<td>$V/Q$ of infinity (units C) High $V/Q &gt; 1$ but $&lt; \infty$ $V/Q$ of 0 (unit A) Low $V/Q &lt; 1$ but $&gt; 0$</td>
</tr>
<tr>
<td><strong>Type of measurement</strong></td>
<td>Noninvasive, continuous, breath by breath</td>
<td>Invasive, discontinuous provides information only when arterial blood samples are obtained</td>
</tr>
<tr>
<td><strong>Physiological factors influencing parameter</strong></td>
<td><strong>Alveolar overdistension</strong> by excessive PEEP or VT pulmonary embolism hypovolemia pulmonary hypotension</td>
<td>Idem Bohr’s approach plus all causes of <strong>shunt and low $V/Q$</strong> : atelectasis, pneumonia, COPD, asthma</td>
</tr>
</tbody>
</table>

* ENGHOFFS MODIFICATION REPRESENT GLOBAL INDEX OF $V/Q$ MISMATCH
Kuwabara’s correction of Enghoff equation

\[
\frac{V_d}{V_t} = \left( \frac{P_{vCO_2} - \left( \frac{P_{vCO_2} - P_{aCO_2}}{1 - Qs/Qt} \right)}{P_{vCO_2} - \left( \frac{P_{vCO_2} - P_{aCO_2}}{1 - Qs/Qt} \right)} \right) - P_{ECO_2}
\]

$P_{vCO_2}$ – partial pressure of CO2 in mixed venous blood
$Qs/Qt$ – right to left shunt
Dead space

- True dead space can only be determined by Bohrs equation
- Bohrs formula can't detect what is happening at the alveolocapillary membrane
- But Enghoff's approach is clinically useful – good global estimate of lung's state of V/Q

H. Thomas Robertson, Eur Respir J 2015; 45
Tusman G et al, Anesth Analg 2012
Fowlers dead space

• Ward Fowler calculated physiological dead space in late 1940’s
• It is now described as anatomical dead space
• Measurements of exhaled \( N_2 \) concentrations immediately following the inspiration of a breath of 100% \( O_2 \)
• Volume of the exhaled air was plotted against the exhaled \( N_2 \) concentration

Fowler WS, Am J Physiol 1948
Fowlers dead space

Phase I, contains no $N_2$
Phase II, progressively ↑ concentration of $N_2$
Phase III, $N_2$ concentration in alveolar gas

The vertical dashed line is positioned so that a and b subsume equal areas, and intersection of the dashed line with the exhaled volume axis defines “Vds”

Expired gas concentration vs tidal volume curve

Fowler WS, Am J Physiol 1948
Fowlers dead space

- Anatomical dead space in cubic centimetres roughly equalled a subject’s IBW in pounds
- Difference between measurements made at different end-inspiratory lung volumes (avg 100 cm$^3$ difference in dead space between the largest and smallest starting volumes)
- Measured dead space would decrease if a 20-s breath-hold preceded the exhalation

Fowler WS, Am J Physiol 1948
Fowlers dead space

Drawbacks

• Analysis by geometrical methods
• Doubtful results since the junction of the phases II and III is difficult to define in disease, especially during tidal breathing

Fowler WS, Am J Physiol 1948
Single breath test CO$_2$

- CO$_2$ can be substituted for expired N2 and plotted against tidal volume
- In contrast to the use of N2 washout in the it is not necessary to first ventilate with 100 % O2 because the “marker”, which in this case is CO$_2$, is already in the alveoli
- Basis for volumetric capnography

Fletcher R et al, Br J Anesth 1981
Single breath test CO₂
Langleys method

Volume of CO2 elimination per breath (ml)

Total expired volume (ml)
Re arranged alveolar equation

- Estimated VD/VT was calculated using re arranged alveolar gas equation for PaCO$_2$

- $\text{PaCO}_2 = 0.863 \times \frac{\text{VCO}_2}{\text{VA}}$

- $\text{VCO}_2 = \frac{\text{PaCO}_2 \times \text{VA}}{0.863}$

- $\text{VCO}_2 = \frac{\text{PaCO}_2 \times (\text{VE} - \text{VD})}{0.863}$

- $\text{VD} = 1 - \left(\frac{0.86 \times \text{VCO}_2\text{est}}{\text{VE} \times \text{PaCO}_2}\right)$
Re arranged alveolar equation

• VCO2est - estimated production of CO2 calculated from predicted resting energy expenditure equation (REE)

\[ VCO2est = \frac{(HBpred \times hf \times 0.8)}{6.8644} \]

• HBpred is gender specific

For females = 655.1 + (6.56 \times WtKg) + (1.85 \times Htc \text{m}) - (4.56 \times \text{age})

For males = 66.45 + (13.75 \times WtKg) + (5 \times Htc \text{m}) - (6.76 \times \text{age})

• hf is hyper metabolic factors (1.13 per °C over 37°C, 1.2 for minor surgery, 1.35 for major trauma and 1.6 for severe infection)
Re arranged alveolar equation

• Rapid bedside estimation
• Uses only routine clinical data
• Shown to be predictor of mortality in ARDS

Draw backs
• No studies comparing it with actual Vd/Vt
• REE by Harris Benedict equation in critically ill not evaluated

Siddiki et al. Critical Care 2010, 14:141
Blanch et al. Critical Care 2016, 20:214
MIGET

- Multiple inert gas élimination technique
- Characterises gas exchange abnormalities
- Quantify the ventilation perfusion inequality, shunt and dead space fractions
- Partial pressures of six intravenously infused inert gases are measured in arterial and mixed venous blood and mixed expired gases
- MIGET software program used for calculation

The fraction of inert gas that is not eliminated is a simple function of the partition coefficient ($\lambda$) and the VA/Q ratio.

Retention of inert gas, $R = \frac{P_a}{P_v} = \frac{\lambda}{[\lambda + \frac{VA}{Q}]}$

Similarly excretion of inert gas is also measured.

VA/Q distributions are measured either from the excretion or the retention solubility curves.
MIGET

Retention (and excretion)/solubility curves and corresponding distributions of ventilation and blood flow

H. Thomas Robertson, Eur Respir J 2015; 45
MIGET

• Research tool rather than a clinical test
  – Operational complexity
  – Not evaluated as a clinical tool
  – Provides more information than we can currently use clinically in patient management and therefore is difficult to justify

Dead space

• Relationship b/w shunt and physiological dead space is nonlinear
• Effect of shunt on dead space increases as the shunt fraction exceeds 50 %, importance of shunts of < 30% is not great
• Many perturbations commonly seen in ICU influence the effect of shunt on calculated dead space like low cardiac output, metabolic acidosis, anemia and hyperventilation

Niklason L et al, Critical Care 2008, 12:R53
Dead space

\[ \frac{V}{Q} \] inequality generally is a cause of greater physiological dead space than shunt.
CO2 MEASUREMENT
CO2 measurement

- Douglas bag – measures PE CO₂
- Calorimeter method - measures PE CO₂
- Volume capnography – measures both PE CO₂ & PA CO₂

*Bohrs dead space – only by Vcap
  Enghoffs dead space – Vcap, Dbag, calorimeter
CO2 measurement

**Douglas bag**

- Expired air was collected during 2 to 3 minutes into a non permeable rubber bag of 50 to 100 L capacity
- PECO2 was determined using a sample taken from bag
- Time consuming & laborious
- Prone to handling errors
CO2 measurement

Fig. 17.—Douglas's respiration apparatus. From "Journal of Physiology" (Cambridge University Press).
CO2 measurement

Metabolic monitor

• Measure pulmonary O2 uptake and CO2 production (VO2 & VCO2)

• Used for measuring resting energy expenditure and dead space
CO2 measurement

• In both the methods of CO2 measurement, the expired gas is diluted by the compressed air within the ventilator circuit and bias flow

• Leads to overestimation of true VD/VT due to lowering of PECO2

• Requires correction factor based on circuit compliance and peak inspiratory pressure
CO2 measurement

**Volume capnography** - Standard now for dead space measurement

- Fast CO2 sensors and pneumotachographs
- Measures flow and CO2 with mainstream or side stream sensors placed at the airway opening
- $V_{cap}$ determined on a breath to breath basis
CO2 measurement

The slope of Phase III (SIII) - exclusively by gas from the alveolar compartment. Always positive and reflects the different time constants of emptying alveoli and the continuous influx of CO2 from the pulmonary capillaries.
CO2 measurement

- $PCO_2$ (mmHg)
- $V_{Daw}$
- $V_{TALV}$
- Mean $PaCO_2$
- $P_{ETCO}_2$
- V/Q Heterogeneity
- Normal physiology
CO2 measurement

• PACO2 was the main limitation in calculating true dead space initially
• PACO2 could theoretically be obtained from the midportion of phase III of the Vcap, resulting in reliable measurements of true VDPhys from Vcap
• This concept has been validated against the MIGET studies
**CO2 measurement**

- PECO2 and VD/VT measured by calorimeter and Vcap were compared
- 90 readings in 23 ARDS subjects

<table>
<thead>
<tr>
<th></th>
<th>Uncorrected Delta trac</th>
<th>Corrected Delta trac</th>
<th>NICO monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>PeCO2 (mm Hg)</td>
<td>15.7 ± 4.7</td>
<td>18.5 ± 5.7</td>
<td>17.5 ± 5.5</td>
</tr>
<tr>
<td>VD/VT</td>
<td>0.64 ± 0.11</td>
<td>0.58 ± 0.14</td>
<td>0.60 ± 0.12</td>
</tr>
</tbody>
</table>

VD/VT measured by volumetric capnography was strongly correlated with uncorrected ($r^2 = 0.93$, $p < 0.0001$) & corrected ($r^2 = 0.89$, $p < 0.0001$) measurements made using the metabolic monitor technique

RH Kallet et al, Resp Care 2015
EFFECT OF MECHANICAL VENTILATION ON DEAD SPACE
Effect of mechanical ventilation

• Numerous pulmonary and extrapulmonary factors affect interpretation of dead space variation at bedside

• Mechanical ventilation makes it more difficult to understand

• Tidal volume, PEEP, inspiratory time, flow pattern all affect the calculation of dead space
Tidal volume

• In normal subjects, increasing tidal volume increases ventilatory efficiency, decrease dead space

• In ARDS, no much change in dead space was observed with increasing VT
  – VT in ARDS may not recruit lung areas effectively
  – recruited diseased alveoli may not contribute to alteration of dead space

Romero PV et al, Eur Respir J 1997
PEEP

With less PEEP: Collapse aka SHUNT

With optimum PEEP

With high PEEP: over distention aka DEAD SPACE
Increasing PEEP

- Recruits the collapsed alveoli
- Decrease the cardiac output
- Increase the airway dead space

Global effect on physiologic VD/VT varies with PEEP & amount of lung injury
Inspiratory time

- Mean Distribution Time - the portion of inspiration available for alveolar gas mixing and diffusion
- Optimal MDT causes a proximal shift in the fresh-gas: respiratory zone interface up to the point of minimal CO₂ diffusion
- Prolonging MDT (either by increasing Ti or EIP) had similar positive effects on VT CO₂

Astrom E et al, Intensive Care Med 2008
Inspiratory flow waveforms

• Square flow form is better than descending ramp
• Impact on CO$_2$ excretion distinct from MDT; thought to be related to the effects of flow oscillations on diffusion
• Abrupt flow cessation cause high frequency oscillations that may resonate down to the respiratory zone and enhance gas mixing

Astrom E et al, Intensive Care Med 2008
End inspiratory pause

Increase in EIP from 0 to 30% resulted in increased MDT from 0.2 to 0.8s
Significant increase in PACO$_2$ and VTCO$_2$

Inspiratory pattern

• Inspiratory pattern with long MDT and end inspiratory flow (abrupt cessation)
• Optimal inspiratory pattern minimises the dead space ventilation with enhanced CO2 elimination
• Results in reduction of tidal volume – facilitating lung protective ventilation

“Short insufflation followed by a long post inspiratory pause”

DEAD SPACE ARDS
Dead space ARDS

- Vascular lesions include thrombotic, fibroproliferative, and obliterative changes leading to pulmonary vascular destruction
- Pulmonary hypertension due to hypoxic vasoconstriction, vascular compression & parenchymal destruction
- Alveolar filling leading to increased venous admixture and shunt

Dead space ARDS

• Responsible for CO2 retention in severe ARDS
• Increase in minute ventilation requirement
• Lung regions with low V/Q usually coexist with high V/Q regions
• Correlate with severity of ARDS
Dead space ARDS

- Gas exchange in ARDS by MIGET studies
- Shunt
- Low V/Q regions
- Increased overall V/Q heterogeneity
- Isolated high V/Q regions are infrequent despite severe elevations in physiologic Vd/Vt

Main contribution - raised VDphys

H. Thomas Robertson, Eur Respir J 2015; 45
# Dead space ARDS

Over all dead space fraction was $0.58 \pm 0.10$

<table>
<thead>
<tr>
<th>179 subjects of ARDS</th>
<th>Survived (n=104)</th>
<th>Died (n=75)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO2 : FiO2</td>
<td>$163 \pm 63$</td>
<td>$123 \pm 51$</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Quasistatic respiratory compliance (ml/cm H2O)</td>
<td>$33.6 \pm 12.0$</td>
<td>$27.2 \pm 8.5$</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Lung-injury score</td>
<td>$2.2 \pm 0.6$</td>
<td>$2.6 \pm 0.6$</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Dead-space fraction</td>
<td>$0.54 \pm 0.09$</td>
<td>$0.63 \pm 0.09$</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Absolute dead space — ml/kg</td>
<td>$6.0 \pm 1.3$</td>
<td>$7.2 \pm 1.3$</td>
<td>$&lt;0.001$</td>
</tr>
</tbody>
</table>

*Dead space was calculated 10.9 hrs after insult using Enghoff modification of the Bohr equation, Metabolic monitor method of CO2 measurement*

TJ Nuckton et al, NEJM 2002; 346 : 1281-6
## Dead space ARDS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dead-space fraction</td>
<td>1.45</td>
<td>1.15 – 1.83</td>
<td>0.002</td>
</tr>
<tr>
<td>(per increase of 0.05)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAPS II</td>
<td>1.06</td>
<td>1.03 – 1.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(per 1-point increase)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Static compliance</td>
<td>1.06</td>
<td>1.01 – 1.10</td>
<td>0.01</td>
</tr>
<tr>
<td>(per ↓ of 1 ml/cm of H2O)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Variables independently associated with risk of death*

* TJ Nuckton et al, NEJM 2002; 346 : 1281-6
Dead space ARDS

- 80 patients of ARDS
- Vd/Vt in early (within 3 days) and intermediate phase of ARDS (8 – 10 days)
- PECO$_2$ measured by Douglas bag method for 5 min

<table>
<thead>
<tr>
<th>Dead-space fraction</th>
<th>Survived</th>
<th>Died</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early phase (n 45 vs 35)</td>
<td>0.53 ± 0.11</td>
<td>0.64 ± 0.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intermediate phase (n 31 vs 18)</td>
<td>0.50 ± 0.10</td>
<td>0.62 ± 0.09</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Raurich et al, Respir care 2010, vol 55 :3
Dead space ARDS

- Dead-space fraction of $\geq 0.60$ is associated with more severe lung injury
- Sustained dead-space elevation is characteristic in non-survivors

<table>
<thead>
<tr>
<th>Dead-space fraction (per increase of 0.05)</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early phase</td>
<td>1.59</td>
<td>1.18 – 2.16</td>
<td>0.003</td>
</tr>
<tr>
<td>Intermediate phase</td>
<td>2.87</td>
<td>1.36 – 6.04</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Raurich et al, Respir care 2010, vol 55 :3
Dead space ARDS

TJ Nuckton et al, NEJM 2002; 346:1281-6
Raurich et al, Respir care 2010, vol 55:3
<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Method</th>
<th>Survived vs dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cepkova et al, CHEST 2007</td>
<td>Prospective 42 ALI patients</td>
<td>Enghoffs equation Volume capnography Early phase of ALI</td>
<td>0.53 ± 0.10 (n=15) Vs 0.61 ± 0.09 (n=27) p = 0.02</td>
</tr>
</tbody>
</table>
| Kallet et al, Respir Care 2004 | Prospective 59 ARDS patients | Enghoffs equation Metabolic monitor Day 1, 2, 3 & 6 | **D1** 0.54 ± 0.08 vs 0.61 ± 0.09 (p < 0.05)  
**D2** 0.53 ± 0.09 vs 0.63 ± 0.09  
**D3** 0.53 ± 0.09 vs 0.64 ± 0.09  
**D6** 0.51 ± 0.08 vs 0.66 ± 0.09 (p < 0.001)  |
Dead space ARDS

- 109 pts in Mayo cohort, 1896 pts in ARDS-net cohort
- Estimated Vd/Vt - rearranged alveolar gas equation
- Both day 1 (OR = 1.07, 95% CI 1.03 to 1.13) and day 3 (OR = 1.12, 95% CI 1.06 to 1.18) estimated Vd/Vt predicted hospital mortality for 0.05 change
- Estimated Vd/Vt had weak correlation with PaO2/FiO2 and OI
- Independent predictor of poor prognosis

Siddiki et al. Critical Care 2010,14:141
Dead space ARDS

- VD/VT in early phase of ARDS is an independently predicts the mortality than oxygenation indices
- Sustained elevation of VD/VT in acute and subacute phases of ARDS was seen in non survivors
- VD/VT of 0.55 during first 6 days of ARDS was a/w significantly higher mortality risk
- It weakly correlates with P/F ratio & Oxygenation Index
DEAD SPACE – PEEP, RECRUITMENT & PRONING
PEEP and recruitment

**PEEP**
- Recruits atelectatic areas
- Increase FRC
- Increase compliance
- Increase arterial O2 concentration

**High PEEP**
- Overdistension of alveoli
- Increase in physiological dead space
- Decreased compliance
- Decrease in cardiac output

In ARDS, ideal PEEP titration achieves a balance between maintaining optimal alveolar recruitment and reasonably avoiding lung overdistension.
PEEP and recruitment

- Best PEEP - greatest O2 transport

VDalv
- Low levels of PEEP - VDalv decreased due to expansion of atelectatic areas
- Higher levels - VDalv increased due to more alveolar overdistension and under perfusion (raised intraalveolar pressure and decrease in cardiac output)

- Negative correlation with compliance

VDanat
- Increases due to distension of conducting airways

Suter et al, NEJM 1975
# PEEP and recruitment

Stefan Maisch et al, Anesth Analg 2008

<table>
<thead>
<tr>
<th>Participants</th>
<th>20 anesthetised patients, normal lungs undergoing maxillofacial surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>PCV mode of ventilation</td>
</tr>
<tr>
<td></td>
<td>Stepwise increase of PEEP/inspiratory pressures (0/10, 5/15, 10/20, 15/25 cm H2O, each level lasting for 20 min)</td>
</tr>
<tr>
<td></td>
<td>A recruitment manoeuvre (at 20/45 cm H2O for a maximum of 20 min) was performed, followed by a stepwise pressure reduction in similar way</td>
</tr>
<tr>
<td></td>
<td>At each level, FRC, compliance, Pao2, and dead space fraction measured</td>
</tr>
<tr>
<td>Results</td>
<td>All measured variables had <strong>better values after recruitment</strong> than before</td>
</tr>
<tr>
<td></td>
<td>At 10/20 cm H2O, compliance was highest with lower dead space</td>
</tr>
<tr>
<td></td>
<td>While paO2 and FRC were highest at the maximal pressure 15/25 cm H2O but deterioration of compliance and dead space worsened</td>
</tr>
<tr>
<td>Conclusion</td>
<td>FRC and Pao2 were insensitive to alveolar over-distension</td>
</tr>
<tr>
<td></td>
<td>Compliance and dead space fraction were indicators for efficient ventilation at an optimal PEEP</td>
</tr>
</tbody>
</table>
### PEEP and recruitment

<table>
<thead>
<tr>
<th><strong>Guo Fengmei et al, Respiratory Care 2012</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants</strong></td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
</tr>
<tr>
<td><strong>Results</strong></td>
</tr>
<tr>
<td><strong>Conclusion</strong></td>
</tr>
</tbody>
</table>
PEEP and recruitment

Guo Fengmei et al, Respiratory Care 2012
PEEP and recruitment

• In a decremental PEEP model after lung recruitment in 8 lung lavaged pigs
• Dead space variables during each PEEP level were correlated with CT aeration and oxygenation
• V\text{dalv}, V\text{Dalv}/ V\text{Talv}, and Pa-etCO2 showed a good correlation with PaO2 & normally aerated areas
• Monitoring of dead space was useful for detecting lung collapse and for establishing open-lung PEEP after a recruitment manoeuvre

Tusman et al, Intensive Care Med 2006
PEEP and recruitment

- VD/VT is a more global ratio is “contaminated” by the effect of PEEP on airway dead space.
- VDalv/VTalv is not influenced by Vdaw.
- Dead space portion of the alveolar gas provides more meaningful information than the classical VD/VT ratio when monitoring of the lung collapse-recruitment phenomena.

Tusman et al, Intensive Care Med 2006
# PEEP and recruitment

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>Methods</th>
<th>Results</th>
</tr>
</thead>
</table>
| Boyden L et al, Intensive care Med 2002 | 10 ALI patients | Stepwise increment of PEEP from zero to 15 cm H$_2$O  
Lung mechanics and Vd/ Vt were measured  
Vcapnography | VDalv does not vary systematically with PEEP in patients with various degrees of ALI  
Subjects in whom oxygenation improved with PEEP showed a concurrent decrease in VDalv and vice versa  
VD fractions are independent of compliance |
| Blanch L et al, ERJ 1999     | 8 normal 9 ALI 8 ARDS | Random change of PEEP (0, 5, 10 and 15 mH2O) at 4 levels  
Physiological measurements were made by volume capnography | VD/VT  
ALI patients > control patients  
ARDS patients > ALI patients  
PEEP had no effect on VD/VT in any group |
PEEP and recruitment

- VD/VT - no relation with PEEP in both the studies
- Few subjects in both the studies
- No recruitment was performed in both
- Different effect of PEEP in patients with various degrees of lung injury (or)
- in positive PEEP responders, the reduction in alveolar dead space compensated
- for the concurrent increase in airway dead space
PEEP and recruitment

- $\text{PaO}_2$ depends on hemodynamic and metabolic state as well, non specific for judging the recruitment
- $\text{PaO}_2$ determination is insensitive to the over-distension of alveoli, verified by reduced compliance and increased dead space fraction
- $\text{VD/VT}$ as a marker of $V/Q$ matching appears to be better suited for titrating PEEP than $\text{PaO}_2$
PEEP and recruitment

• Recruitment of lung results in better dead space fraction values as compared to pre recruitment
• Vd/Vt monitoring can be used to detect early lung collapse - derecruitment in decremental PEEP trial
• Can only be used in PEEP responders of ARDS
Response in proning

• Both PaO2/FiO2 and PaCO2 improve with prone positioning in ARDS
  — Decreased PaCO2 was inversely related to lung recruitment
  — PaCO2 responders had better survival than PaO2 responders

• VDalv may be the consequence of non perfused or poorly perfused lung areas in ventilated anterior areas, but also of a slow compartment partially excluded from ventilation

Gattinoni L et al, Critical care Med 2003
Protti et al, Intensive Care Med 2009
Response in proning

• Relevance of dead space measurement in proning in ARDS in 13 patients of severe ARDS (P/F <100)
• Persistent hypoxemia after 48 hr of ventilation
• PCO2, VD/Vt, P/F ratio, Crs were recorded in supine and 3, 6, 9, 12, 15 hrs after proning
• Responders to PP were defined after 15 hrs of PP either by an increase in PaO2/FiO2 ratio > 20 mmHg or by a decrease in PaCO2 > 2 mmHg
Response in proning

• Maximal improvements in VD/VT and PaCO2 tended to occur earlier (6 and 9h respectively) compared to maximal improvements in PaO2/FiO2 (15 h)

• PaCO2 responders has greater decrease in VDav/VT ratio and in Pplat and a greater increase in Crs than P/F responders

• PaCO2 response is better associated with lung recruitability than PaO2
Response in proning

- Changes in dead space correlated with compliance and no correlation was found with oxygenation

Charron et al. Critical Care 2011, 15:R175
Response in proning

• Measuring dead-space may be a particularly expedient method for assessing the effectiveness of prone positioning in ARDS

• Using PaCO2 changes rather than PaO2/FiO2 changes to define the respiratory response to PP appeared more relevant

Charron et al. Critical Care 2011, 15:R175
DEAD SPACE - PULMONARY EMBOLISM
Pulmonary embolism

- Spatial differences in blood flow between respiratory units in the lung cause inefficient gas exchange that is reflected as increased alveolar VD.
- The mechanical properties may not be greatly affected, so these alveoli empty in parallel with other respiratory units with similar time constants.
- Because ventilation to the affected alveoli continues unabated, PCO$_2$ in these alveoli decreases.
- Exhaled dead space volume dilutes the amount of CO$_2$ in exhaled breaths relative to PaCO$_2$.

Nausherwan K Burki, Am Rev Respir Dis 1986
Pulmonary embolism

- Wide variety of pulmonary disorders in which VD/VT is increased - potentially less specific
- VD/VT < 40% makes the diagnosis of PE extremely unlikely
- VD/VT value > 40% in the presence of a normal spirogram is highly suggestive of PE and was comparable with lung perfusion scan
Pulmonary embolism

- Combination of D dimer assay and alveolar dead space fraction can be used as screening test for PE

<table>
<thead>
<tr>
<th>Subjects of suspected PE (n = 380)</th>
<th>Results of D dimer and VDav/Vt</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PE confirmed (n = 64)</td>
<td>40 both abnormal</td>
<td>Sensitivity 98.4 % (95 % CI 91.6 - 100)</td>
</tr>
<tr>
<td></td>
<td>20 abnormal D dimer</td>
<td>Specificity 51.6 % (95 % CI 46.1 - 57.1)</td>
</tr>
<tr>
<td></td>
<td>3 abnormal VDav/Vt</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 had both normal</td>
<td></td>
</tr>
<tr>
<td>No PE (n = 316)</td>
<td>26 both abnormal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>104 abnormal D dimer</td>
<td></td>
</tr>
<tr>
<td></td>
<td>75 abnormal VDav/Vt</td>
<td></td>
</tr>
<tr>
<td></td>
<td>163 both normal</td>
<td></td>
</tr>
</tbody>
</table>

Kline JA et al; REPE study, JAMA 2001
Pulmonary embolism

• Subjects with PE who died within a month had significantly higher dead space compared with who survived

• Dead space was significantly greater in subjects with high probability V/Q scan than other V/Q readings

Kline JA et al; REPE study, JAMA 2001
Pulmonary embolism

• End-tidal carbon dioxide tension (PET, CO2) is a physiological surrogate for vascular obstruction from PE and dead space ventilation

• 298 patients who underwent imaging for suspected PE were studied. PET, CO2 was measured within 24 after the imaging

A.R. Hemnes et al, Eur Respir J 2010
A PET CO2 of $\geq 36$ mmHg - a negative predictive value of 96.6%, which increased to 97.6% when combined with Wells score $< 4$

A.R. Hemnes et al, Eur Respir J 2010
Pulmonary embolism

- Prospective study - 53 subjects of suspected hemodynamically stable PE
- Confirmed in 33 subjects by V/Q scan or CTPA
- Correlation between perfusion defect and VDalv/Vt

<table>
<thead>
<tr>
<th></th>
<th>Confirmed PE (n = 33)</th>
<th>No PE (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perfusion defect</td>
<td>38 ± 22 %</td>
<td>-</td>
</tr>
<tr>
<td>VDalv</td>
<td>208 ± 115 mL</td>
<td>89 ± 66 mL</td>
</tr>
<tr>
<td>VDalv/Vt</td>
<td>43 ± 18%</td>
<td>27 ± 14 %</td>
</tr>
<tr>
<td>Mean SPAP</td>
<td>44 ± 17 mm Hg</td>
<td>34 ± 10 mm Hg</td>
</tr>
</tbody>
</table>

Kline JA et al, Acad Emerg Med 2000
Pulmonary embolism

Regression of VDalv/VT vs perfusion defect yielded $r^2 = 0.41$
Regression of VDalv/VT vs pulmonary artery pressures yielded $r^2 = 0.59$

* $P < 0.001$

Kline JA et al, Acad Emerg Med 2000
Pulmonary embolism

• 10 subjects had perfusion defect > 50% and mean VDalv/Vt was > 0.60 in that subgroup
• 7 subjects had VDalv/Vt > 0.60, 3 of them died
• PE increases the VDalv proportionately to the severity of pulmonary vascular obstruction
• Potential for VDalv to quantify the embolic burden of PE

Kline JA et al, Acad Emerg Med 2000
Lung embolism causes a difference between arterial and expired CO$_2$ even at the end of a long expiration (15% of pred TLC) while the normal lung & in airway disease it reaches PaCO$_2$ FDlate cutoff of 12% correlated significantly with the angiographic findings in PE.

Eriksson et al, CHEST 1989; 96:357-62
FDlate

• Improves the specificity of the dead space measurement by separating patients with obstructive lung diseases from those with PE, both conditions being frequently associated with an increased Paco2-EtCO2 gradient

• It corrects for falsely positive CO2 gradient due to an incomplete diffusion time in patients with high respiratory rates or low VT values

Erikkson et al, CHEST 1989; 96:357-62
Pulmonary embolism

45 outpatients of suspected PE and high D dimer > 500 ng/ml
18 patients had confirmed PE

Verschuren et al, CHEST 2004; 125:841–850
Pulmonary embolism

• Dead space measurement can be used to exclude PE in conjunction with D dimer levels
• Can predict the severity of embolic burden
• FDlate had better diagnostic performance than P(a-ET) CO2 gradient or VD/VT in PE
• Not sensitive in cases of peripheral PE or in cases of adaptation of the V /Q ratio mismatches due to pulmonary infarction, atelectasis, or a potential hypocarbic bronchoconstrictive reflex
DEAD SPACE  WEANING
Success of extubation

- Vd/Vt in extubation success (n = 59) vs failure (n = 17) groups calculated prior to extubation 0.48 vs 0.65, p < 0.0001 in 76 adult extubated patients
- Significant association between the Vd/Vt and extubation failure, with OR = 1.52 (1.11 - 2.09, P = 0.008) for each 0.01 of Vd /Vt
- Vd/Vt of 0.58 - best sensitivity & specificity for predicting extubation failure

A. González-Castro et al, Medicina Intensiva 2011
Success of extubation

45 children in Paediatric ICU
Who met criteria for extubation
20 min on PSV to tidal volume of 6ml/kg – dead
space was calculated

<table>
<thead>
<tr>
<th>Vd/Vt</th>
<th>n</th>
<th>Successful extubation</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 0.50</td>
<td>25</td>
<td>24 (96%)</td>
</tr>
<tr>
<td>0.50 – 0.65</td>
<td>10</td>
<td>6 (60%)</td>
</tr>
<tr>
<td>&gt; 0.65</td>
<td>10</td>
<td>2 (20%)</td>
</tr>
</tbody>
</table>

## Success of extubation

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Subjects</th>
<th>Success vs failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ozylimaz et al, Tuberk Toras 2010</td>
<td>35 adults</td>
<td>25 (71%) vs 10 (29%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.54 vs 0.66 (p &lt;0.05)</td>
</tr>
<tr>
<td>Albert Bousso et al, Jornal de Pediatria - 2006</td>
<td>86 children</td>
<td>65 (76%) vs 21 (24%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.62 vs 0.65 (p = 0.4)</td>
</tr>
<tr>
<td>A. González-Castro et al, Medicina Intensiva 2011</td>
<td>76 adults</td>
<td>59 (78%) vs 17 (22%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.48 vs 0.56 (p &lt;0.0001)</td>
</tr>
</tbody>
</table>
Success of extubation

- Dead space was measured before and after tracheostomy in 42 patients in SICU
- No significant change of Vd/Vt was seen before and after the procedure (50.7 vs 51.9)
- No significant difference in Vd/Vt is seen b/w who were weaned within 72 hrs & who were weaned > 5 days post tracheostomy
- Change in dead space does not predict the weaning outcome

Mohr et al, J Trauma 2001; 51
Success of extubation

• Dead space measurement can predict the success of extubation

• Elevated VD/VT may be useful for predicting the need for NIV after extubation and therefore the potential for averting the need for re-intubation
VAE/VT – new variable

• Alveolar ejection volume
• Volume of the pure alveolar gas with minimum dead space contamination
• Represent an index of alveolar inhomogeneity
• It is unaffected by the variations in the tidal volume and set ventilatory pattern in acute lung injury

Vae/Vt

Normal

ARDS
VAE/VT

• Best correlated with mechanical alterations in ARDS (parallel inhomogeneity)
• Best predictor of outcome among all other capnographic indices (VD Bohr / VDPhys) in ARDS
Take home message

✓ Enghoffs approach - global gas exchange status
✓ Dead space calculated varies with the ventilator settings
✓ High dead space in ARDS predicts in hospital mortality
✓ Low dead space can be used for excluding PE along with D dimer values
✓ VD/VT as a marker of V/Q matching appears to be better suited for titrating PEEP than PaO2
✓ Better variable to detect response to proning and weaning from mechanical ventilation