Indirect Calorimetry
Resting Energy Expenditure (REE)

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RESPIRATION AND ENERGY PRODUCTION

Wasserman Gears

To see the effects of different variables, click the buttons below:

- Normal State
- Increased Demand
- Heart Disease
- Lung Disease

Muscle Activity
- CO₂ Prod.
- O₂ Consum.

O₂ & CO₂ Delivery
- O₂ Flow
- CO₂ Flow

Ventilation (Vₐ + V₅ = Vₑ)
- Expired
- Inspiration

Physiological Responses:
- ↑Qₐ₂
- ↑QO₂
- Dilate
- ↑SV
- Recruit
- ↑VT
- ↑f
Metabolism

- Metabolism is the generation of energy by consuming substrates (Carbohydrate, Fat, and Protein) producing heat.
- Each substrate produces a different amount of energy (kcal) and a different cost in terms of CO2 to be removed (octane in gas).
- The ratio of CO2 produced to O2 consumed is referred to as the Respiratory Quotient.

\[ RQ = \frac{V_{CO2}}{V_{O2}} \]

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Energy Balance Relationship

Intake = Expenditure

- Dietary Intake
- Stored Energy

- Dietary Thermogenesis
- REE

Energy required to digest food
Energy Balance Relationship

Intake = Expenditure

- Dietary Intake
- Stored Energy
- REE
- Dietary Thermogenesis
- Anabolism: Increase of endogenous fats and protein with buildup of tissues and energy reserve
- Catabolism: Energy Balance
Energy Balance Relationship

Intake
- Dietary Intake
- Stored Energy

Expenditure
- Major Surgery
- Sepsis/Burns
- Activity/Exercise
- Dietary Thermogenesis
- REE

Catabolism
Consumption of endogenous fats and protein with loss of tissue and energy reserve
Calorimetry

• Is the science of measuring the amount of heat generated (exothermic), consumed (endothermic) or simply dissipated

• Energy expenditure can be determined by measuring the heat production from consuming substrates (carbohydrate, fat and protein)
Calorimetry

• Respiratory Quotient or RQ, is the relationship between VO$_2$ and VCO$_2$ is determined by the substrate being consumed

• For example, consumption of carbohydrate would give

\[ \text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2 \rightarrow 6\text{CO}_2 + 6\text{H}_2\text{O} + \text{Kcal} \]

or an RQ = 1.0
Lipogenesis

- $\frac{V_{CO2}}{V_{O2}} > 1 \quad (V_{CO2}/V_{O2}=RQ)$
- Laying down fat
- Breathing required to get rid of CO2
Energy Expenditure is measured as Heat Production (kcalories/min)

Classically, this was accomplished by monitoring pressure changes in an enclosed chamber due to gas expansion caused by warming.

This is generally referred to as a “Bomb Calorimeter“.
Examples of direct Calorimeters
Relationship Between Heat Produced and Oxygen Consumption

- Weir Equation - describes this precise relationship
- \[3.94(VO2) + 1.11(VCO2)] \times 1.44 = 24 \text{ hr KCAL}\]
Gas Exchange Measurements

(Vt, O₂, CO₂, RR)

\[ V_E = Vt \times RR \]
\[ VO_2 = V_E \times FE_O2 \]
\[ VCO_2 = V_E \times FE_CO2 \]

Mixing Chamber (1 data point every 1-5 minutes, 10-20 minutes to assess Steady State)

\[ V_E = \text{Gas volume collected Gas over 1-5 minutes} \]
\[ FE_O2 = \text{Mixed Expired O}_2 \text{ from Chamber 1-5 minutes} \]
\[ VO_2 = V_E \times FE_O2\% \]

Breath by breath (Data point every breath, Faster Assessment of Steady State)

\[ V_E = \text{Gas volume each breath (Vt X RR)} \]
\[ FE_O2 = \text{Cross Product (O}_2\text{ waveshape)} \]
\[ VO_2 = \int \text{Flow} \times O_2\% \]
Measurement of Indirect Calorimetry

- Flow Sensor
  - $O_2$ Analyzer
  - $CO_2$ Analyzer
  - Computer
Gas Exchange Waveforms

\[ \text{VO}_2 = \int \text{Flow} \times \text{O}_2\% \]

\[ \text{VCO}_2 = \int \text{Flow} \times \text{CO}_2\% \]
Calculation of VO₂ & VCO₂

Gas Exchange Waveforms

VO₂ = \( \int \text{Flow} \times \text{O}_2\% \)

VCO₂ = \( \int \text{Flow} \times \text{CO}_2\% \)
Haldane’s Transformation Assumption

that

\[ \text{FIN}_2 = \text{FEN}_2 \text{ because N}_2 \text{ is inert} \]

and therefore

\[ \text{FIO}_2 + \text{FICO}_2 = \text{FEO}_2 + \text{FECO}_2 \]

However,

If we change \( \text{FIO}_2 \) then the \( \text{N}_2 \) in the Functional Residual Capacity as well as \( \text{N}_2 \) in the blood and tissue will shift to the new nitrogen level over time until it reaches steady state
Measurement of VO2 & VCO2

\[ \text{VO2} = (V_I \times F_{I\text{O}_2}) - (V_E \times F_{E\text{O}_2}) \]

\[ \text{VCO2} = (V_E \times F_{E\text{CO}_2}) - (V_I \times F_{I\text{CO}_2}) \]

OR

Using the Haldane Transformation Assumption

\[ F_{I\text{N}_2} = F_{E\text{N}_2} \text{ and that } F_{O_2} + F_{\text{CO}_2} + F_{N_2} = 1.0 \]

THEN

\[ \text{VO2} = V_E \times (F_{I\text{O}_2} - F_{E\text{O}_2}) \]

\[ \text{VCO2} = V_E \times (F_{E\text{O}_2} - F_{I\text{O}_2}) \]
VE increases linearly with VCO₂ so anything that increases VCO₂ will increase ventilatory requirements.
Measurement of Indirect Calorimetry

• Spontaneously Breathing
  – Mouthpiece
  – Mask
  – Canopy

• Ventilators
Spontaneously Breathing
Mask and Mouthpiece
Spontaneously Breathing Canopy
Canopy Measurements

For example: With a mask or mouthpiece,

\[ V_E = 10 \text{ L/min} \quad \text{FECO}_2 = 5.00\% \quad \text{FEO}_2 = 15.9\% \]

\[ \text{VCO}_2 = 10 \times (5.0\%) \text{ or } 500\text{ml} \quad \text{VO}_2 = 10 \times (20.9\% - 15.9\%) \text{ or } 500\text{ml} \]

In a canopy system, a fan pulls a larger “minute ventilation” through the canopy which captures all of the patients’ respiration mixed with air.

For example, a total volume of 25 L/min which contains 500ml CO₂ and 500ml O₂ exhaled by the patient mixed with a known amount of room air (Canopy Flow).

Canopy ventilation = 25 L/min which includes the patients 10L/min \( V_E \) within the total 25L/min so the dilution is 2.5 :1)

Therefore, \( \text{FECO}_2 = 2.0\% \ (5.0\%/2.5) \) & \( \text{FEO}_2 = 18.9\% \ ((20.9\% - 15.9\%)/2.5) \)

\[ \text{VCO}_2 = 25 \times (0.020 - 0.0) \text{ or } 500\text{ml} \quad \text{VO}_2 = 25 \times (0.209 - 0.189) \text{ or } 500\text{ml} \]
Fan speed must be adjusted to:

1. Maximize the CO2 waveform too fast will show smaller peaks while too slow will not clear the exhaled CO2 between breaths

2. Tracing should show a complete return to baseline between breaths which indicates all expired gas was captured
The unique aspect about the Face Tent is that the calculations are performed on actual patient breath by breath waveforms rather than averaging the data over a fixed time interval and assuming an FIO2.

The **only** requirements for are that you measure the FIO$_2$ and FICO$_2$, the Bias Flow captures all expired gas within the Canopy circuit

(\text{so O2 & CO2 must return to ambient levels between breaths})

and

the dilution is not so severe (\text{CO2 < 1.5%}) that the expired gas concentrations are too low to measure.
Mechanical Ventilation

• **General Contraindications for Indirect Calorimetry**
  – High Frequency Ventilation
  – Pressure Support
  – Bias Flow
  – Air Leaks in Patient or Ventilatory Circuit
    • Leaks most prone to occur @ the cuff of the ETT or trach
    • Chest tube

• **Measurement at the endotrachael tube overcomes errors associated with**
  – Pressure Support
  – Bias Flow
Location of Flow Measurement is Important During Mechanical Ventilation

• Flow measurement at the endotracheal tube
  – Eliminates issues related to the ventilator circuit and pressure support
  – Measures patient ventilation not ventilator activity

• Flow measurement at the ventilator exhaust
  – Patient circuit volume compression must be compensated
  – Bias flow must be turned off or isolated from the flow measurement
  – With pressure support, isolation valves are ineffective and become shutters
  – Pressure cycled optimum rather than flow cycled
Flow Measurement at the ET tube
Flow Measurement at Ventilator Exhaust
# Measurement of FIO₂/Effect of Errors

<table>
<thead>
<tr>
<th>FIO₂ (Read as)</th>
<th>VO₂ ml/min</th>
<th>VCO₂ ml/min</th>
<th>RER</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2093</td>
<td>250</td>
<td>200</td>
<td>0.80</td>
</tr>
<tr>
<td>@ 0.350</td>
<td>250</td>
<td>200</td>
<td>0.80</td>
</tr>
<tr>
<td>@0.345</td>
<td>218</td>
<td>200</td>
<td>0.92</td>
</tr>
<tr>
<td>% Error</td>
<td>-13%</td>
<td>0%</td>
<td>15%</td>
</tr>
<tr>
<td>@ 0.400</td>
<td>250</td>
<td>200</td>
<td>0.80</td>
</tr>
<tr>
<td>@0.395</td>
<td>166</td>
<td>200</td>
<td>1.20</td>
</tr>
<tr>
<td>% Error</td>
<td>33%</td>
<td>0%</td>
<td>50%</td>
</tr>
<tr>
<td>@0.600</td>
<td>250</td>
<td>200</td>
<td>0.80</td>
</tr>
<tr>
<td>@0.595</td>
<td>125</td>
<td>200</td>
<td>1.59</td>
</tr>
<tr>
<td>% Error</td>
<td>50%</td>
<td>0%</td>
<td>-99%</td>
</tr>
</tbody>
</table>
Correcting Fluctuating FiO₂

• Use an External Blender
  – Set Vent to FiO₂ to .6

• Use an External Gas Source
  – H cylinder
  – Set Vent to FiO₂ to .6

• Use an External Reservoir
  – Low Compliance
  – 1 – 1.5 Liters

OR

Make the Measurement at the Endotrachael Tube
Compensating for High or Changing FIO2’s

Basic Weir Equation for REE

\[
\left[ (3.94 \text{ VO}_2) + (1.106 \text{ VCO}_2) \right] \times 1.44 - 2.17 \text{ UN}
\]

What if...

\[
\left[ \left( 3.94 \left( \frac{\text{VCO}_2}{0.85} \right) \right) + (1.106 \text{ VCO}_2) \right] \times 1.44 - 2.17 \text{ UN}
\]

This equation assumes a RER of 0.85 which is centered between 0.7 (fat) and 1.0 (carbohydrate)

RER’s outside this range are non-physiologic
The error from this assumption is zero at actual RER= 0.85 and is 10% at an RER of 0.75 or 1.0
Response to step change in FIO₂

Change in FIO₂ from 21% to 60%

Impact of FIO₂ change persists until N₂ in Residual Volume stabilizes at new level
REE by CO₂ Substitution

Step Change in FIO₂ from 21% to 60%

REE and VO₂ react strongly to FIO₂ change

REE by CO₂ continues unaffected at baseline level
REE Measurements using CO2 in High FIO2 Environments

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>VO2 (mL/min)</th>
<th>VCO2 (mL/min)</th>
<th>RQ</th>
<th>FIO2 (%)</th>
<th>RR (br/min)</th>
<th>Vt BTPS (mL)</th>
<th>VE BTPS (L/min)</th>
<th>REE (Kcal/day)</th>
<th>REE(CO2) (Kcal/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:26</td>
<td>511</td>
<td>417</td>
<td>0.82</td>
<td>20.42</td>
<td>11</td>
<td>1059</td>
<td>11.2</td>
<td>3567</td>
<td>3449</td>
</tr>
<tr>
<td>1:32</td>
<td>499</td>
<td>415</td>
<td>0.83</td>
<td>20.43</td>
<td>10</td>
<td>1073</td>
<td>11.2</td>
<td>3492</td>
<td>3432</td>
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<td>468</td>
<td>400</td>
<td>0.85</td>
<td>20.43</td>
<td>10</td>
<td>1066</td>
<td>11.0</td>
<td>3293</td>
<td>3308</td>
</tr>
<tr>
<td>1:45</td>
<td>431</td>
<td>417</td>
<td>0.83</td>
<td>20.42</td>
<td>10</td>
<td>1187</td>
<td>11.5</td>
<td>3144</td>
<td>3149</td>
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Predicting Energy Expenditure

Harris-Benedict Equation

- REE(kcal/24hrs) = [66.473 + (13.752xW) + (5.003xH)] - (6.755xA)
- REE(kcal/24hr) = [655.096 + (9.563xW) + (1.85xH)] - (4.676xA)

- Fundamental problems in applying the HB equation to the treatment of critically ill patients
  - The 239 subjects used in the HB study were healthy, and it assesses population means
  - When applied to individuals not resembling the original study population, the equations are inaccurate for 40-60% of hospitalized patients
Predicting Energy Expenditure Response to Clinical Stress

Energy Expenditure needs are estimated by combining:

- Basal Metabolism
- Dietary Induced Thermogenesis
- Physical Activity
- Stress Factors associated with disease, injury and pharmacological intervention
Effect of Activities on "Steady State"

Figure 1. A 220-minute segment of "raw data" of one of eight-hour studies, along with log of activity state of patient. *Horizontal line at VO₂ of 187 ml/min indicates mean steady-state VO₂ for complete study.*
How Does Measuring VO2 & VCO2 Provide Energy Expenditure?

Applying the Weir Equation

\[
\text{REE} = \text{Resting Energy Expenditure} = \text{KCAL} \\
\left[ \left( 3.94 \, \text{VO}_2 \right) + \left( 1.106 \, \text{VCO}_2 \right) \right] \times 1.44 - 2.17 \, \text{UN}
\]

Abbreviated equation does not require 24 hour Urinary Nitrogen (UN)

\[
\left[ \left( 3.94 \, \text{VO}_2 \right) + \left( 1.106 \, \text{VCO}_2 \right) \right] \times 1.44
\]
## Substrate Utilization

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Figure 1
Substrate Utilization

• At the cellular level, the Respiratory Quotient (RQ) is defined as \( \frac{\text{VCO}_2}{\text{VO}_2} \). Measurements of RQ made at the mouth are defined as Respiratory Exchange Ratio (RER).

• Ventilation and VCO2 can change significantly with small changes in VO2. (Readily available body stores: 20 Liters of CO2/600 mls of O2)

• RQ and RER are frequently used interchangeably but they are **only equal** if the patient is in a steady state.

  Hyperventilation or Mismatched Ventilator Parameters are the most common reason the assumption RER = RQ is not true.
Indications for Indirect Calorimetry

• Measurement of REE to guide appropriate nutritional support for mechanically ventilated patients

• Determine the REE and RQ to monitor adequacy, appropriateness and customization of nutritional support

• Determine O2 cost of breathing as a guide to selection of ventilator mode, settings and weaning strategies

• Assess the contribution of metabolism on ventilation
Indications for Indirect Calorimetry
Impact of Burn

- “Muscle protein degradation markedly decreased with administration of the high carbohydrate diet. Protein synthesis was unaltered”

- “Increased feeding relative to energy expenditure was associated with significantly lengthened total ICU stay and total percentage of time spent on a ventilator”

- “…declining energy expenditure was significantly associated with mortality, this correlation was particularly strong initially after burn and after the first month”
Indications for Indirect Calorimetry

Ventilatory Effects of Feeding

- “As expected, the respiratory quotient appeared higher in the high carbohydrate studies than in the high-fat group.” (0.88, 0.99)

- “Our results show that there was a statistically significant correlation between pre-albumin alterations and post operative complications (POC), as evidenced by the finding that 43.7% of the patients presenting POCs had low levels of pre-albumin”

- “The correlations between lung function impairments specific for the disease and FFMI emphasized the link between malnutrition and respiratory mechanical load irrespective of its aetiology”

Hypercaloric Feeding and Ventilatory Requirements

- “4 Weeks of Hypercaloric feeding may significantly increase VCO2 and RQ”
Nutritional and Metabolic Support are indicated for critically ill patients requiring mechanical Ventilation. Patients who fail weaning trials are unable to sustain spontaneous breathing

“In the absence of exogenous nutrition, glucose derived from liver gluconeogenesis is used for energy fuel by other organ systems and less is available for prompt repletion of respiratory muscle glycogen”


“These data indicate that prolonged under-nutrition causes deleterious effects in diaphragm muscle structure that impair its ability to generate force.”


“Ventilator-dependent patients who respond to nutritional support with an increase in protein synthesis are more likely to wean from mechanical ventilation than those who do not.”

- Larca Crit Care Med 10(5): 297-300, 1982
Indications for Indirect Calorimetry
Malnutrition and Subsequent Refeeding

“The interplay between adenosine 5’-triphosphate supply and demand, dictated by the degree of mitochondrial dysfunction and the level of metabolic shutdown….seems to be crucial in determining outcome.”
- Singer Crit Care Med 35[Suppl.] S441-S448 2007

“Allowing a patient’s nutritional state to deteriorate through the perioperative period adversely affects measureable outcome related to nososcomial infection, multiple organ dysfunction, wound healing, and functional recovery”
- McClave Chest 115: 64S-70S 1999

“Our study demonstrated significant reduction in whole-body protein turnover and synthesis only in patients with coexistent disease, whereas chronically undernourished patients without overt disease had values similar to healthy controls… The presence of disease in association with undernutrition appears to have a significant adverse effect on whole-body flux and synthesis.”
- Winter J Parenteral and Enteral Nutrition 29: 221-228, 2005
Indications for Indirect Calorimetry
Impact on Outcomes

- **Length of Stay/Costs**
  - “Patients who received early and Sufficient Nutrition had significantly shorter lengths of stay and charges”
    - LOS: 11.9 versus 13.3
    - Costs: $34,602 versus $38,578

- **Length of Stay/Costs**
  - “Patients who declined nutritionally ...had significantly higher hospital charges”
    - Costs $45,762 versus $28,631
    - Braunschweig J Am Diet Assoc 100:1316-1322, 2000

- **Length of Stay**
  - “Fat-Free Mass index is significantly associated with an increased length of stay”
    - Pichard Am J Clin Nutr 79: 613-618, 2004
Repeatability of Gas Exchange Testing
3 studies on a normal subject (29 year-old male)
6 months time difference and different equipment
Oxygen Uptake and work rate over time
3 studies on a normal subject (29 year-old male)
6 months time difference and different equipment
CO2 output and work rate over time
3 studies on a normal subject (29 year-old male)
6 months time difference and different equipment
Ventilation vs. CO2 output
Questions?