Acid-base management during hypothermic CPB
alpha-stat and pH-stat models of blood gas interpretation

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alpha-stat vs. ph-stat

For Dummies

Here’s what you need to know.
Mains issues

Stroke, cerebral & cardiac dysfunction common after
- complex cardiac surgery using hypothermic CPB
- cardiac surgery using deep hypothermic circulatory arrest (DHCA)

Hypothermic CPB induces changes of pH and pCO$_2$
- pH affects intracellular function & regeneration after ischemia
- pCO$_2$ affects cerebral blood flow, and speed & homogeneity of cooling
Neurological dysfunction after cardiac surgery

**Global ischemia**: global hypoxia & circulatory arrest

**Focal ischemia (stroke)**:
- embolization of atherosclerotic material from aorta or brachiocephalic vessels
- risk factors: age, diabetes, hypertension

Reduced CBF reduces risk of embolization, but increases risk of hypoperfusion
Physiology of the brain

- 2% of the total body weight
- 15 - 20% of the resting cardiac output
- 20% of total body oxygen consumption

CMRO$_2$:
- cerebral metabolic rate / oxygen consumption
- averages 50 ml/min in adults
- greatest in the gray matter
Neurological dysfunction after circulatory arrest

Normothermia: brain injury occurs after ~ 4 minutes

Hypothermia (18°-20°C): allows for much longer periods

- Most patients tolerate DHCA up to 30 (- 40) minutes without neurological dysfunction
- > 60 minutes, the majority of patients will suffer irreversible brain injury
Drop in cerebral metabolic rate with hypothermia
Cerebral autoregulation

- CBF tightly coupled to cerebral metabolic demands
- CBF constant over wide range of perfusion pressures
- Cerebral autoregulation maintained in moderate hypothermia
- Cerebral autoregulation impaired during profound hypothermia (< 22 °C)

Acid-base management during hypothermia: alpha-stat vs. pH-stat
First cardiac surgery in hypothermia

Dr. F. John Lewis & Richard Varco
(1952, University of Minnesota):

- Closure of ASD (5-year-old girl)
- Surface cooling
- Moderate hypothermia
- Inflow and outflow occlusion of 5½ min.

Acid-base management during hypothermia: alpha-stat vs. pH-stat
First cardiac surgery in hypothermia

Before the operation:
- Patient anesthetized & wrapped in refrigerated blankets until rectal temperature < 28 °C

Following the operation:
- Patient placed in hot water at 45 °C to increase rectal temperature to 36 °C

Acid-base management during hypothermia: alpha-stat vs. pH-stat
First open-heart procedure using hypothermia

Henry Swan (1953, University of Colorado):

- Excision of a stenosed pulmonary valve
- 7 ½ min. inflow-occlusion
- Considered to have the most surgical experience using hypothermia
- Hundreds of cases, very low mortality
- Particular interest: prevention of ventricular fibrillation
Henry Swan

- Small plane pilot
- 1958 - 1959: survived three plane crashes
- sustained several ankle fractures among other injuries
Figure 2. Open-heart surgery performed in 1955. The patient is currently submerged in an ice bath. Courtesy of the US National Library of Medicine.
First successful cardiopulmonary bypass operation

May 1953, John Gibbon:

- Introduced pump oxygenator in clinical practice
- As a consequence, the sole use of hypothermia decreased rapidly
Background

Sealy, Brown & Young (1958):

- Added a heat exchanger to oxygenator
- Hypothermia in conjunction with CPB
- Perfusion at reduced flow rates

Acid-base management during hypothermia: alpha-stat vs. pH-stat
Introduction of deep hypothermic circulatory arrest

Charles Drew (1959, Westminster Hospital in London):
- First successful repair of an atrial and ventricular septal defect

Drew operated on infants only a few weeks old using ‘profound hypothermia with circulatory arrest and limited cardiopulmonary bypass’.

The arrest time varied between 38 and 67 min in his initial series from 1970 to 1973, and he lost only one out of 24 tetralogy cases.
Acid-base management during hypothermia: alpha-stat vs. pH-stat
Acid-base management during hypothermia - in vivo

Different strategies for animals that
- must remain active while hypothermic
- get hypothermic during hibernation
Thermoregulation: cold-blooded animals

Ectothermic / poikilothermic animals:

- body temperature closely follows ambient temperature
- optimal enzyme efficiency at hypothermia
- intracellular & extracellular pH allowed to increase at hypothermia (parallels pN of water)
- alpha-stat approach

Acid-base management during hypothermia: alpha-stat vs. pH-stat
Thermoregulation: cold-blooded animals

Ectothermic / poikilothermic animals:

- intracellular pH very close to neutral pH of water
- arterial blood pH more alkaline than intracellular pH
- constant $H^+$-gradient ($\Delta$ pH) over cell membranes at all temperatures
- helps to eliminate intracellular acids and $CO_2$
Hibernation (heterothermic mammals)

State of inactivity and metabolic depression

- low body temperature, slow breathing, slow heart rate
- low metabolic rate
- maintain arterial pH near 7.4 during hypothermia
- intracellular acidosis leads to depressed metabolism
- preserves intracellular substrates
- **pH-stat approach**
- active vital organs (heart & liver): **alpha-stat**
pH and pCO\textsubscript{2} in humans

Humans:
- Constant core temperature of 37°C

Blood and extracellular fluids:
- pH = 7.40
- pCO\textsubscript{2} = 40 mmHg
pCO₂ in humans
pH and pCO$_2$ in humans
Cerebral autoregulation: CO$_2$

- CO$_2$: potent, direct cerebral vasodilator
- alters cerebral autoregulation
- **hypercapnia** causes dilation of cerebral arteries and increased CBF
- **hypocapnia** causes constriction of cerebral arteries and decreased CBF
pCO$_2$-changes during hypothermia

Hypothermia:
- increases the solubility of CO$_2$ in blood
- decreases the partial pressure of CO$_2$ despite constant CO$_2$ content

Solubility of gasses during hypothermia
**pCO$_2$-changes during hypothermia**

Decreasing blood temperature:
- **increases** the solubility of pCO$_2$
- **decreases** the partial pressure of CO$_2$ (pCO$_2$)

Increasing blood temperature:
- **decreases** the solubility of pCO$_2$
- **increases** pCO$_2$
pCO$_2$-changes during hypothermia

Blood taken during hypothermia and warmed to 37°C:
- the CO$_2$ initially dissolved will contribute to pCO$_2$
- therefore: increased pCO$_2$

If estimated at the patient’s actual temperature:
- reduced pCO$_2$ despite similar arterial CO$_2$ content
- In addition, hypothermia decreases the metabolic rate and CO$_2$ production
pH-changes during hypothermia
pH-changes during hypothermia

(a) A strong acid such as HCl dissociates completely into its ions.

(b) A weak acid such as H$_2$CO$_3$ does not dissociate completely.
### pH-changes during hypothermia

<table>
<thead>
<tr>
<th>Temperature</th>
<th>[H⁺]</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>25°C</td>
<td>10⁻⁷ mol/l</td>
<td>7</td>
</tr>
<tr>
<td>&gt; 25°C</td>
<td>&gt; 10⁻⁷ mol/l</td>
<td>&lt; 7</td>
</tr>
<tr>
<td>37°C</td>
<td>10⁻⁶,8 mol/l</td>
<td>6,8</td>
</tr>
<tr>
<td>&lt; 25°C</td>
<td>&lt; 10⁻⁷ mol/l</td>
<td>&gt; 7</td>
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**Neutral water:** \[ [H^+] = [OH^-] \]

**Definition pH:** \[ \text{pH} = - \log [H^+] \]
pH-changes during hypothermia

Temperature vs. Neutral pH

[Graph showing the relationship between temperature (Celsius) and pH]
pH-changes during hypothermia

Blood neutrality:
- $[\text{H}^+] < [\text{OH}^-] = 1 : 16$
- at 37°C: pH = 7.40

Blood pH of various ectothermic species and the pH of neutral water as a function of body temperature
alpha-stat vs. ph-stat

Two schools of thought:

- alpha-stat strategy does not correct for pH and CO\(_2\) changes
- pH-stat does

Source of long-standing debate
Alpha-stat

Most centres changed to alpha-stat during mid 1970s - mid 1980s
Most widely used approach for acid-base-management during CPB in adults
Maintains normal pH (7.40) and pCO$_2$ (40 mmHg) measured at 37°C
Uncorrected for actual arterial blood temperature

- allows the pH to rise & pCO$_2$ to fall naturally with cooling
- relative (respiratory) alkalosis at the patient’s actual body temperature
- no CO$_2$ added to the circuit
Alpha-stat

alpha = ratio of protonated imidazole to total imidazole of histidine residues

At 37°C:
- normal intracellular pH 6.8
- alpha ≈ 0.55 optimal for intracellular enzyme structure and function
Alpha-stat - pros

- preserves cerebral autoregulation during moderate hypothermia
- extends the lower limit of autoregulation (mean arterial pressure 30 mmHg)
- avoidance of “luxurious” perfusion
- reduced CBF, decreased risk of microemboli
- preferable on cellular level, enzymatic function well maintained
- possibly preferable in adults
- may result in better neurocognitive outcome compared to pH-stat (adults)
Alpha-stat - cons

- May result in inadequate, nonhomogeneous brain cooling before circulatory arrest
- Might “steal” blood from cerebral to pulmonary circulation in congenital heart surgery (pulmonary circulation derived from arterial system)
- May result in cerebral dysfunction in children after cardiac surgery
pH-stat

- pH close to 7.40 at all temperatures
- Traditional acid-base management in the 1960s and 1970s:
  - Blood gas analysis performed at 37°C
  - Mathematically temperature corrected using a nomogram
  - CO₂ added to oxygen passing the oxygenator
  - Total CO₂ stores elevated
  - Marked respiratory acidosis at 37°C
**pH-stat**

Example:

- 17°C: pH 7.40  \(\text{pCO}_2\) 58 mm Hg
- 37°C: pH 7.06  \(\text{pCO}_2\) 156 mm Hg
- severe respiratory acidosis at 37°C
- increased CBF & loss of autoregulation
pH-stat - pros

Previously thought to be beneficial for

- cerebral vasodilation and
- maintenance of cerebral blood flow

- increased cerebral blood flow - quick and homogeneous brain cooling during the cooling phase of DHCA
- oxyhemoglobin dissociation curve skiftet to the right
- offers protection in neonatal and infant cardiac surgery
pH-stat - pros

- might inhibit cellular metabolism
- possibly better neurobehavioral development after DHCA in children
- particularly beneficial in cyanotic neonates and infants
- shifts more CPB flow toward the cerebral circulation
- improving cerebral cooling and oxygen supply
pH-stat - cons

- slightly greater complexity compared to alpha-stat strategy
- loss of cerebral autoregulation
- cerebral blood flow becomes pressure passive
- “luxury brain perfusion”: mismatch of CBF and CRMO$_2$
- increased risk of cerebral embolization & cerebral edema
Blood gas management during hypothermic CPB

More important in children:

- Greater degrees of hypothermia used, thereby
- More profound differences in blood CO\textsubscript{2} levels

Pediatric vs. adult cardiac surgery: differences in

- Brain neuroplasticity
- Presence of atheromatous aorta & cerebral embolic load
- Presence of multiple co-morbidities
Acid-base management during hypothermia: alpha-stat vs. pH-stat

In conclusion, there is evidence to suggest that the best technique to follow in the management of acid-base in patients undergoing deep hypothermic circulatory arrest during cardiac surgery is dependent upon the age of the patient with better results using pH-stat in the paediatric patient and alpha-stat in the adult patient.
Conclusion

- both alpha- and pH-stat management seems to work well
- physiologic differences appear to be subtle
- alpha-stat may be preferable for adults (protection from microemboli)
- pH-stat may be preferable for children (enhanced brain protection)
- evt. crossover-strategy during DHCA in adults
  - 10 min. cooling with pH-stat
  - followed by cooling with alpha-stat
  - rewarming with alpha-stat