Cerebral Blood Flow Autoregulation: 
Essential Physiology in Neurocritical Care

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Disclosures: None
I think that there is too much "permissive hypotension" in our adult practice of anesthesia.
( "Pressure" = Mean Arterial Pressure )
1. The capacity of the cerebral circulation to maintain a constant CBF in the face of widely varying MAP.

2. Autoregulation is “myogenic”, i.e., it is mediated by the smooth muscle of pial arteries/arterioles.

3. Physiologically very fragile.
The lower limit of CBF autoregulation

"Pressure" = Mean Arterial Pressure
Misunderstandings

1. The lower limit of adult CBF autoregulation (LLA) is probably a MAP that is greater than you were taught.
Changes in CBF caused by independent alterations in PaCO2, PaO2 and blood pressure. “Anesthesia” (Ed., RD Miller) 1\textsuperscript{st}, 2\textsuperscript{nd}, 3\textsuperscript{rd}, 4\textsuperscript{th} editions.
The effects of blood pressure reduction on CBF in non-anesthetized volunteer subjects

Morris et al., Surg Forum 4: 140-3, 1953

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Mean 104 → 62 57 → 39
The Lower Limit of Autoregulation: Time to Revise Our Thinking?

Table 1. Data Regarding the Lower Limit of Autoregulation in Nonanesthetized, Normotensive Adults

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Anesthesiology 86: 1431-2, 1997
PaCO₂, PaO₂, MAP (mmHg)
“I’ve had lots of patients who were OK after MAPs in the 50’s and 60’s.”
We “get away” with MAPs < the LLA because there is a substantial CNS blood flow reserve in most adults.
The effects of blood pressure reduction on CBF in non-anesthetized volunteer subjects
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Mean 104 → 62  57 → 39
Question: So what?  
Answer: Erosion of the physiologic reserve.

The “reserve” protects patients in the event of hypotension.
Misunderstandings

1. The lower limit of adult CBF autoregulation (LLA) is probably a MAP that is greater than you were taught.

2. We “get away” with MAPs < the LLA because there is a substantial CNS blood flow reserve in most adults. But, many clinicians are not aware of that reserve and fail to recognize situations in which it may not be present.
Trouble occurs when the reserve has already been compromised by:

1. Reduced resting flow/Impaired autoregulation
   e.g., head injury, SAH, spinal cord injury

2. Raised local tissue pressure
   e.g., spinal stenosis, retraction, ↑ICP, ↑intraocular pressure

3. Unrecognized hypertension

4. CNS vascular disease; Collateral loss or variation

5. Anemia
Autoregulation is physiologically very “fragile”.

![Graph showing CBF (ml/100g/min) against CPP (mmHg). The graph has a linear relationship between CBF and CPP up to a certain point, after which CBF remains constant, and then increases again. There is a dashed line indicating a “Pressure-passive” state.]
Insertion of a Tracheostomy Cannula

ICP (torr)

BP (torr)

Pentothal 150 mg
CBF (ml/100g/min) vs. CPP (mmHg)
Cerebral circulation and metabolism after severe traumatic brain injury: The elusive role of ischemia

Bouma et al., (MCV / Neurosurg), J Neurosurg 75: 685-93, 1991

• “During the first 6 hours after injury, CBF was low (23 ± 5)”

• “Focal CBF was <18 in 1/3 of patients studied within 6 hrs of injury”
Ishii, J. Neurosurg, 1979

See also: Hattingen et al., (Perf Weighted MRI)
A Prominent Theme in Contemporary Neurologic Care:

Maintain Cerebral Perfusion Pressure

Because of:

Low post-insult CBF

Absent autoregulation
The effect of changes in cerebral perfusion pressure upon middle cerebral artery blood flow velocity and jugular bulb venous oxygen saturation after severe brain injury

(Edinburgh) J Neurosurg 77: 55-61, 1992


Conclusion: TCD/SjvO2 may be used to define the optimal CCP for management of severe TBI pts.

SjvO2 (%) (non-hyperemic pts)

CPP (mmHg)

Adult TBI; GCS ≤ 8 Sedated, ventilated.
Multimodality monitoring \([SjvO_2, TCD]\) as a guide to treatment of intracranial hypertension after severe brain injury

Chan et al. (Edinburgh), Neurosurgery 32: 547-53, 1993

“Cerebral perfusion pressure is the most important parameter to monitor during ICP therapy. It should be maintained > 70 mmHg with severe brain injury.”

\[(CPP = MAP - ICP)\]
Impact of Hypoxia and/or Hypotension* on Outcome after Closed Head Injury
(National Trauma Coma Data Bank)

(Chesnut, J Trauma 34: 216, 1993)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Good/Mod (%)</th>
<th>Poor/Dead (%)</th>
</tr>
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<tbody>
<tr>
<td>Total (GCS≤8)</td>
<td>699</td>
<td></td>
</tr>
<tr>
<td>Normoten/Normox</td>
<td>456</td>
<td>51</td>
</tr>
<tr>
<td>Hypotensive</td>
<td>113</td>
<td>24</td>
</tr>
<tr>
<td>Hypoxic</td>
<td>78</td>
<td>45</td>
</tr>
<tr>
<td>Hypox/Hypotensive</td>
<td>52</td>
<td>6</td>
</tr>
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</table>

(*At the time of hospital arrival)
Hypox = PaO2 < 60 mmHg; Hypotension = SBP < 90 mmHg
Cerebral circulation and metabolism after severe traumatic brain injury: The elusive role of ischemia

Bouma et al., (MCV / Neurosurg), J Neurosurg 75: 685-93, 1991

- “During the first 6 hours after injury, CBF was low (23 ± 5) but increased significantly during the first 24 hours.”
- “Focal CBF was < 18 in one third of patients studied within 6 hours of injury.”
- "... significant correlation between CBF in the first 8 hours and outcome."
Effect of cerebral perfusion pressure augmentation on regional oxygenation and metabolism after head injury*

Andrew J. Johnston, FRCA; Luzius A. Steiner, PhD; Jonathan P. Coles, PhD; Doris A. Chatfield, BSc; Tim D. Fryer, PhD; Peter Smielewski, PhD; Peter J. Hutchinson, PhD; Mark T. O'Connell, PhD; Pippa G. Al-Rawi, BSc; Franklin I. Aigbirihio, PhD; John C. Clark, DSc; John D. Pickard, FRCS; Arun K. Gupta, FRCA; David K. Menon, PhD

(Cambridge) CCM 33: 189-95, 2005
What should the target CPP* be in the adult head-injury patient?

* CPP = MAP - ICP
Multimodality monitoring [SjvO2, TCD] as a guide to treatment of intracranial hypertension after severe brain injury

Chan et al. (Edinburgh), Neurosurgery 32: 547-53, 1993

“Cerebral perfusion pressure is the most important parameter to monitor during ICP therapy. It should be maintained > 70 mmHg with severe brain injury. ”

(CPP = MAP - ICP)
Prevention of Secondary Ischemic Insults after Severe Head Injury

Robertson et al., (Baylor / Neurosurg), CCM 27: 2086-95, 1999

Does CBF / CPP targeted therapy improve outcome?

- Prospective; 189 adults
- CPP > 50 vs. CPP > 70
- Endpoints: Jugular desaturation, Intractable ICP, Outcome
Prevention of Secondary Ischemic Insults after Severe Head Injury

Robertson et al., (Baylor / Neurosurg), CCM 27: 2086-95, 1999

<table>
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<tr>
<th>CBF / CPP</th>
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<tr>
<td>CPP</td>
<td>&gt; 70</td>
</tr>
<tr>
<td>MAP</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>PaCO2</td>
<td>35 - 40</td>
</tr>
<tr>
<td>ICP</td>
<td>&lt; 20</td>
</tr>
<tr>
<td>CVP</td>
<td>5 - 8</td>
</tr>
<tr>
<td>PCWP</td>
<td>8 - 12</td>
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Sedation, temperature, CSF drainage, paralysis, mannitol: same for both groups (Prospective; 189 adults)
Prevention of Secondary Ischemic Insults after Severe Head Injury

Robertson et al., (Baylor / Neurosurg), CCM 27: 2086-95, 1999

Endpoints:

Primary: Frequency of jugular desaturation (< 50 % for > 10 min)

Secondary: Frequency of intractable ICP ( > 25 mmHg) requiring barbiturates or causing death.

Outcome at 3 and 6 months.
Prevention of Secondary Ischemic Insults after Severe Head Injury

Robertson et al., (Baylor / Neurosurg), CCM 27: 2086-95, 1999

Findings: Fewer episodes of jugular desaturation in the CPP-70 group.

But !!

No difference in outcome; 5 fold ↑ in ARDS
Principal's Editorial

Head Injury: Recent Past, Present, and Future


"The appropriate guideline for maintenance of CPP is still controversial. It is inappropriate to argue that a CPP level below 60 mm Hg is safe and appropriate in the adult [in the first 72 hours after TBI ]. "
Cerebral Perfusion Pressure Recommendations

Level 1: (“High degree of clinical certainty”) Insufficient data to support a recommendation

Level 2: (“Moderate degree of clinical certainty”) Aggressive attempts to maintain CPP > 70 mmHg should be avoided because of the risk of ARDS.

Level 3: (“Degree of clinical certainty not established”) CPP < 50 mmHg should be avoided. The CPP value to target lies within the range of 50-70 mmHg.
Ishii, J. Neurosurg, 1979

See also: Hattingen et al., (Perf Weighted MRI)
"Triple H" Therapy for Vasospasm: Hypervolemic Hemodilution & Hypertension

Awad et al., Stroke, 1987

("Triple H": Widely applied. Only the hypertension component has a well confirmed CBF benefit. See: Muench et al., CCM 35: 1844-51, 2008)
Trouble occurs when the reserve has already been compromised by:

1. Reduced resting flow/Impaired autoregulation
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2. Raised local tissue pressure
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   (Perfusion pressure = MAP - local pressure)

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A Prominent Theme in Contemporary Neurologic Care:

Maintain Cerebral Perfusion Pressure

Because of:

Low post-insult CBF

Impaired autoregulation
The *whole* truth and nothing but the truth . . . . .
Cardiac output is never a variable in autoregulation diagrams.

("Pressure" = Mean Arterial Pressure)
"Triple H" Therapy for Vasospasm: Hypervolemic Hemodilution & Hypertension

Awad et al., Stroke, 1987

("Triple H": Widely applied. Only the hypertension component has a well confirmed CBF benefit. See: Muench et al., CCM 35: 1844-51, 2008)
Which “H” really matters?

Kim et al., Neurosurgery 53: 1044-52, 2003

16 pt., vasospasm after SAH. CBF by XeCT

Phenyl: MAP $\uparrow$ 30 mmHg

Dobut: C.I. 4.1 $\rightarrow$ 6.0 (MAP unchanged)

Hypervol: 1.0 L colloid
4.0 L crystal

Hypertension (and cardiac output)
Kim et al., Neurosurgery 53: 1044-52, 2003
Cardiac output is never a variable in autoregulation diagrams.

I suspect, especially in low cardiac output states, that C.O. also influences CBF.

("Pressure" = Mean Arterial Pressure)
Clinicians who want to “push” cardiac output in this situation do have an evidence basis for the practice.
But, BP support should be part of the regimen.
CBF (ml/100g/min) vs CPP (mmHg)

- CBF (ml/100g/min)
- CPP (mmHg)

Graph shows a relationship between CBF and CPP with a red dot indicating a specific point on the graph.
PaCO₂, PaO₂, MAP (mmHg)
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Anesthesiology 86: 1431-2, 1997
Cerebral autoregulation following head injury

MAREK CZOSNYKA, PH.D., PIOTR SMIELEWSKI, PH.D., STEFAN PIECHNIK, PH.D., LUZIUS A. STEINER, M.D., AND JOHN D. PICKARD, M.CHIR., F.MED.SCI.

Conclusion: “Autoregulation was disturbed . . . . when ABP was too low (ABP < 75 mmHg).”
Cerebral circulation and metabolism after severe traumatic brain injury: The elusive role of ischemia

Bouma et al., (MCV / Neurosurg), J Neurosurg 75: 685-93, 1991

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2. Autoregulation is “myogenic”, i.e., it is mediated by the smooth muscle of pial arteries/arterioles.

3. Physiologically very fragile.
Two Themes

1. The lower limit of adult CBF autoregulation (LLA) is probably a MAP that is greater than you were taught.

2. There is a CBF (and spinal cord BF) reserve that protects most patients from hypotension. But, the failure to recognize situations in which that reserve is lost or reduced results in imprudent blood pressure management and neurologic injury.
A Prominent Theme in Contemporary Neurologic Care:

Maintain Cerebral Perfusion Pressure

Because of:

Low post-insult CBF

Impaired autoregulation