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Jugular Venous Hemoglobin Desaturation during Rewarming on Cardiopulmonary Bypass

What Does It Mean, What Does It Matter?

IN this issue of ANESTHESIOLOGY Hänel *et al.*¹ add interesting additional observations to the puzzling phenomenon of cerebral venous hemoglobin desaturation that occurs during the rewarming phase of cardiopulmonary bypass (CPB). This phenomenon is puzzling because (1) it is unclear whether it influences neurologic outcome after cardiac surgery; and (2) the mechanisms responsible for its occurrence are incompletely understood. Hänel *et al.* found jugular venous desaturation can be prevented by inducing mild hypercapnia ($\text{PaCO}_2 \cong 50$ mmHg) during CPB rewarming. Because brain oxygen consumption is not affected by such a small difference in PaCO_2 , the greater jugular venous saturation observed with hypercapnia was almost certainly a result of greater cerebral blood flow (CBF) (*i.e.*, greater cerebral oxygen delivery).

Why not measure CBF during rewarming to confirm this mechanism? The only methods currently available to measure CBF during human CPB are radioactive xenon clearance and inert gas washout.² Both techniques require at least 15-20 min to make a single CBF determination. Thus current clinical techniques do not have sufficient temporal resolution to demonstrate rapid CBF changes occurring during the rewarming phase of CPB. Although transcranial Doppler can provide a continuous measurement of cerebral blood flow velocity, two studies have clearly shown that, during CPB, changes in cerebral blood flow velocity do not correlate with

changes in standard measures of CBF.^{3,4} Thus clinical studies of jugular venous desaturation during rewarming are necessarily limited and conclusions are inferential because, in the absence of reliable CBF measurements, neither cerebral oxygen delivery nor cerebral oxygen consumption can be measured.

A series of studies from the Duke group have assessed the relationship between jugular venous desaturation and postoperative neuropsychologic outcome.⁵⁻⁸ Their first report found no association.⁵ Two subsequent reports, each derived from the same patient population, indicated that greater jugular venous hemoglobin desaturation at completion of rewarming (specifically, greater arteriovenous oxygen content difference) was associated with a greater incidence of postoperative cognitive deficits.^{6,7} Of note, patients who exhibited marked jugular venous desaturation at completion of rewarming tended to have lesser CBF, greater cerebral metabolic rate for oxygen (CMR_{O_2}), and greater brain oxygen extraction *before* the start of rewarming.⁶ This suggests patients who desaturated the most with rewarming differed from the rest of the study population *before* rewarming. Perhaps this preexisting difference was responsible for their greater postoperative cognitive impairment, not the jugular venous desaturation *per se*. This hypothesis is supported by a recent study by Goto *et al.*⁹ These investigators observed patients with greater abnormalities on preoperative brain magnetic resonance imaging (MRI) had greater degrees of jugular venous desaturation with rewarming.⁹ Thus patients with preexisting neurologic injury, even if subclinical, may have a limitation of cerebral perfusion reserves (see below). Both conditions may predispose to postoperative neuropsychological deficits. The most recent report from the Duke group finds jugular venous desaturation to have only a minor independent effect on neuropsychological outcome when baseline neuropsychological status, educational level, and age are factored.⁸ Thus marked jugular venous desaturation during CPB rewarming may occur more commonly in patients

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with preexisting subclinical neurologic abnormalities or abnormal cerebral perfusion reserves, but has only a minor independent effect on neurologic outcome in most patients.

If jugular venous saturation is an index of the relationship between global brain oxygen consumption and delivery, why does this relationship appear to "deteriorate" during CPB rewarming in virtually all patients, and markedly in some? Our group proposed that jugular venous desaturation could simply be the result of enhanced transfer of oxygen from warm (less oxygen avid) hemoglobin to a cold (more oxygen avid) brain.^{10,11} This proposal implies (1) that jugular venous desaturation should be greatest when blood-brain temperature gradients are greatest (usually at the start of rewarming), and (2) anaerobic metabolism should not occur. Although jugular bulb temperature is probably not a good indicator of brain temperature during rewarming, Hänel *et al.* convincingly demonstrate that maximum jugular venous desaturation does not occur when blood-brain temperature gradients are at their maximum, but rather occurs more toward the end of rewarming, when blood-brain temperature gradients are small.¹ Other human studies also show this pattern.^{12,13} In addition, recent work by Sapire *et al.* shows evidence of increased brain lactate production coincident with maximal jugular venous desaturation in some patients.¹³ Thus enhanced oxygen off-loading from hemoglobin to brain does not adequately explain jugular venous desaturation during clinical CPB, and it appears brain oxygenation may be compromised in some patients.

The marked hemodilution used during CPB may be partly responsible for compromised brain oxygenation. Although hemodilution increases CBF, the increases in CBF do not match the decrease in arterial oxygen content. As a result, brain oxygen extraction may need to increase to maintain aerobic metabolism. For example, in anesthetized normothermic dogs¹⁴ and rabbits,¹⁵ hemodilution from a hematocrit of 40% to 20% decreases cerebral venous hemoglobin saturation from its normal value of $\approx 60\%$ to 35–40%, whereas brain oxygen consumption does not change. During human CPB, decreases in jugular saturation with hemodilution and onset of CPB are not so marked, and during hypothermic CPB, jugular venous saturation usually increases to supranormal values (70–80%).^{12,13,16,17} During hypothermic CPB, these supranormal jugular venous saturations probably are the result of the combined effect of decrease CMR_{O_2} and alterations in hemoglobin oxygen affinity.¹⁰ With rewarming, these effects reverse, and

jugular venous saturations would be expected to decrease back to normothermic hemodiluted values, as they do. Jugular venous saturations at the end of CPB are the same regardless of whether CPB was continuously normothermic or hypothermic with terminal rewarming.^{16,17}

Although the normal brain tolerates marked hemodilution well, brains with preexisting injury and limited perfusion and extraction reserves may not. In penumbra regions, increases in CBF with hemodilution are not as great as in normal brains.¹⁸ As a result, greater than normal oxygen extraction is required to support tissue oxygenation.¹⁹ This may account for Goto's observation (discussed previously) that patients with preoperative MRI abnormalities had greater desaturation with rewarming.⁹

If we prevent venous hemoglobin desaturation during CPB rewarming using the technique described by Hänel *et al.*,¹ will neuropsychological outcome be improved? For most patients, probably not. However, there may be a subset of patients in whom outcomes might be improved on this basis. The challenge is to identify those high-risk patients and do the study.

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Choice of α -stat or pH-stat Management and Neurologic Outcomes after Cardiac Surgery

It Depends

IT has been slightly more than 10 years since Murkin *et al.*¹ reported that pH-stat management results in greater cerebral blood flow (CBF) during cardiopulmonary bypass (CPB) than does α -stat management. After this land-

mark study, numerous animal and clinical studies have addressed the question of which technique might be best for the brain during cardiac surgery. It appears we may now have the answer—it depends. In children undergoing deep hypothermic circulatory arrest (DHCA), pH-stat should be used. In adults undergoing routine cardiac surgery, α -stat should be used. Why the difference?

Two clinical studies, one retrospective² and a recent prospective randomized trial,³ find better neurologic outcome with pH-stat management in children undergoing DHCA. In this issue of *ANESTHESIOLOGY*, Kurth *et al.*⁴ provide important new insight into two mechanisms by which pH-stat management may be helping the brain during DHCA. First, their work shows that pH-stat management increases the rate of brain cooling, probably on the basis of greater CBF with pH-stat. Although the

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