References

1. Kataja JHK, Kaukinen S, Viinamäki OVK, Metsä-Ketelä TJA, Vapaatalo H. Hemodynamic and hormonal changes in patients pretreated with captopril for surgery of the abdominal aorta. *J Cardiothoracic Anesth* 1989: **3**: 425–432.
2. McCarthy GJ, Hainsworth M, Lindsay K, Wright JM, Brown TA. Pressor responses to tracheal intubation after sublingual captopril: a pilot study. *Anaesthesia* 1990: **45**: 243–245.
3. Colson P, Saussine M, Séguin JR, Cuchet D, Chaptal P, Roquefeuil B. Hemodynamic effects of anesthesia in patients chronically treated with angiotensin-converting enzyme inhibitors. *Anesth Analg* 1992: **74**: 805–808.
4. Murphy JD, Vaughan RS, Rosen M. Intravenous enalaprilat and autonomic reflexes: the effect of enalaprilat on the cardiovascular responses to postural changes and tracheal intubation. *Anaesthesia* 1989: **44**: 816–821.
5. Coriat P, Richer C, Douraki T, et al. Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. *Anesthesiology* 1994: **81**: 299–307.
6. Sear JW, Jewkes C, Tellez J-C, Foex P. Does the choice of antihypertensive therapy influence haemodynamic responses to induction, laryngoscopy and intubation? *Br J Anaesth* 1994: **73**: 303–308.
7. Pasch T, Kleierl-Lindner C, Götz H, Pichl J. Untersuchungen über den überschießenden blutdruckanstieg nach kontrollierter hypotension und seine verhütung durch captopril. *Anaesthesist* 1986: **35**: 66–72.
8. Jacob L, Bonnet F, Sabathier C, Chiron B, Lhoste F, Viars P. Hormonal response to captopril pre-treatment during sodium nitroprusside-induced hypotension in man. *Eur J Anaesthesiol* 1987: **4**: 101–112.
9. Woodside J Jr, Garner L, Bedford RF, et al. Captopril reduces the dose requirement for sodium netroprusside induced hypotension. *Anesthesiology* 1984: **60**: 413–417.
10. Yates AP, Hunter DN. Anaesthesia and angiotensin-converting enzyme inhibitors. The effect of enalapril on peri-operative cardiovascular stability. *Anaesthesia* 1988: **43**: 935–938.
11. Tohmo HI, Karanko M, Scheinin M, Viinamäki O, Salonen M, Nieminen V. Enalapril premedication attenuates the blood pressure response to tracheal intubation and stabilizes postoperative blood pressure after controlled hypotension with sodium nitroprusside in neurovascular patients. *J Neurosurg Anesth* 1993: **5**: 13–21.
12. Boldt J, Knothe C, Schindler F, Stertmann WA, Hempelmann G. Isolated circulatory response to intravenous administration of the ACE inhibitor enalaprilat. *Br J Clin Pharmacol* 1994: **37**: 341–346.
13. The CONSENSUS Trial Study Group. Effects of enalapril on mortality in severe congestive heart failure. *N Engl J Med* 1987: **316**: 1429–1435.
14. Ambrosioni E, Borghi C, Magnani B. The effect of the engiotensin-converting enzyme inhibitor zofenopril on mortality and morbidity after anterior myocardial infarction. *N Engl J Med* 1995: **332**: 80–85.

Address:
Harri Tohmo, M.D.
Department of Anaesthesiology
Lounais-Häme District Hospital
FIN-30100 Forssa
Finland

HYPERLACTATEMIA ASSOCIATED WITH HYPOCARBIC HYPERVENTILATION

Sir,

I read with interest the article "Lactate metabolism and hypocarbic hyperventilation in piglets" by Karlsson et al. (1). They concluded that the increased concentration of lactate during hypocarbic hyperventilation was not caused by an increased peripheral release from the skeletal muscles of the pig but could be caused by an "altered splanchnic turn-over" of lactate. With the limitations of the experiment, it is premature to conclude that the hyperlactatemia is a result of an "altered splanchnic turn-over" of lactate.

Hyperlactatemia is caused by a combination of increased production and impaired utilization (2, 3). Both pathways depend critically on oxygen. The intestine, receiving >20% of cardiac output, could be a major source of lactate production. The heart and brain may become lactate producers under pathological circumstances. Some studies have shown decreases in splanchnic, coronary and cerebral blood flow (hence, oxygen delivery) in response to hyperventilation (4, 5). Indeed, Johnson had demonstrated decreased mesenteric oxygen consumption and extraction (4). In addition, some workers suggested the hyperlactatemia was due to the stimulation of blood cell glycolysis (6). Although the liver has a large reserve capacity for lactate metabolism (2), the lactate metabolism could be compromised by the decreased total hepatic blood flow and oxygen delivery secondary to hypocarbia (4, 7). Therefore, the hyperlactatemia during hyperventilation may result from increased bowel lactate production, decreased hepatic utilization, or a combination of both, and possibly increased lactate production from other sources (e.g. heart, brain, blood cells) except from skeletal muscles. The placement of hepatic venous and portal catheters can address the changes in hepatic arterial, portal venous and total hepatic flow and oxygen metabolism, and splanchnic lactate production and utilization.

Interestingly, they showed an increased release of lactate from skeletal muscles without any significant effect on plasma lactate concentration in the normoventilated piglet. This probably reflects the increased hepatic utilization of the extra lactate load. Furthermore, the increased plasma concentration of epinephrine that may be related to the surgical stress could explain the increased release from skeletal muscles by direct β-adrenoceptor stimulation (3), because there were no significant effects on hind limb blood flow and oxygen delivery or extraction.

Po-Yin Cheung

References

1. Karlsson T, Stjernstrom E-L, Stjernstrom H, Wiklund L, Essen-Gustavsson B, Jorfeldt L. Lactate metabolism and hypocarbic hyperventilation: an experimental study in piglets. *Acta Anaesthesiol Scand* 1995: **39**: 109–117.
2. Madias NE. Lactic acidosis. *Kidney Int* 1986: **29**: 752–774.
3. Mizock BA. Lactic acidosis. *Disease-a-month* 1989, April.
4. Johnson EE. Splanchnic hemodynamic response to passive hyperventilation. *J Appl Physiol* 1975: **38**: 156–162.
5. Karlsson T, Stjernstrom E-L, Stjernstrom H, Norlen K, Wiklund L. Central and regional blood flow during hyperventilation: an experimental study in the pig. *Acta Anaesthesiol Scand* 1994: **38**: 180–186.
6. Zborowska-Sluis DT, Dossetor JB. Hyperlactatemia and hyperventilation. *J Appl Physiol* 1967: **22**: 746–755.

7. Berry MN, Scheuer J. Splanchnic lactic acid metabolism in hyperventilation, metabolic alkalosis and shock. *Metabolism: Clinical & Experimental* 1967: **16**: 537–547.

Address:
Department of Newborn Medicine
Royal Alexandra Hospital
10240 Kingsway
Edmonton
Alberta
Canada

REPLY

Sir,

We would like to thank Dr. Cheung for his comments on our article, and find them valuable. As we found the splanchnic area to be of great interest as a source of lactate during hypocarbic hyperventilation we have continued our experimental work in this area, following the lines suggested in his comments. We have placed portal and hepatic venous catheters and measured flow and substrate turn-over in the splanchnic area.

We have concluded from our work (1) that induced hyperventilation with large tidal volumes decreased the blood flow to most tissues, whereas hyperventilation with increased frequency keeping the tidal volume constant did not affect the cardiac output and the flow in the splanchnic area in the same way. We also found that the release of lactate from the splanchnic area during induced hyperventilation rather reflected release from its prehepatic portion than hepatic production (1).

We did not find it possible to exclude the possibility that there could be a regional disturbance in oxygen availability in the preportal part of the splanchnic region as we found a decreased portal blood flow, a reduced preportal oxygen consumption and a release of lactate simultaneously after one hour of hypocarbic hyperventilation. We do agree with the point that alkalotic stimulation of glycolysis, especially in blood cells, can result in higher blood lactate levels, and that there is a certain degree of co-variation between blood pH and lactate concentration. In the alkalosis produced by infusion of sodium bicarbonate, we observed an increase in blood lactate concentration without reduction in splanchnic or portal blood flow, which indicates that pH in itself affects lactate production. We did not find any increased release from the splanchnic area after infusion of bicarbonate. Others have pointed out the relation between pH and blood lactate (3) and even described it as a means of acid-base regulation (2). We did not find any evidence of decreased liver lactate uptake. Furthermore, other organ systems have been directly or indirectly pointed out by others as low in blood flow, hypoxemic or directly as sources of lactate during hyperventilation (4–7).

With the aim of studying muscle content of lactate and by using microdialysis technique and contra-lateral muscle biopsies, we find that there was a small increase in interstitial lactate in the muscle during hyperventilation, perhaps more reflecting the afferent blood concentration than the intracellular concentration of lactate in muscle cells, as the biopsies did not show the same variation in lactate (1). We conclude that the skeletal muscle is not a major source of lactate during hypocapnic hyperventilation.

Further studies on lactate metabolism and its relation to oxygen supply during hyperventilation are necessary as hyperventilation is still used as a tool to reduce intracranial pressure in the clinic, and we are looking forward to opportunities to continue the discussion.

T. Karlsson

References

1. Circulation and turn-over of lactate during induced hypocapnic hyperventilation and metabolic alkalosis, an experimental study in the pig, Doctoral thesis, Uppsala University 1994.
2. Hood V, Tannen R. pH control of lactic acid and keto acid production: A mechanism of acid base regulation. *Miner Electrolyte Metab* 1983: **9**: 317–325.
3. Iles R, Baron P, Cohen R. Mechanism of the effect of varying pCO_2 on gluconeogenesis from lactate in the perfused rat liver. *Clin Sci Mol Med* 1979: **55**: 183–188.
4. van Rijen P, Luyten PR, van der Sprenkel J, et al. 1H and 31P NMR measurement of cerebral lactate, high-energy phosphate levels, and pH in humans during voluntary hyperventilation: associated EEG, capnographic, and Doppler findings. *Magn Reson Med* 1989: **10** (2): 182–193.
5. Cold GE. Does acute hyperventilation provoke cerebral oligaemia in comatose patients after acute head injury? *Acta Neurochir* (Wien) 1989: **96** (3–4): 100–106.
6. Wexels JC. Myocardial oxygen supply during hypocapnia and hypercapnia in the dog. *Can J Physiol Pharmacol* 1986: **64** (11): 1376–1380.
7. Semb BK, Hysing E, Mörkrid L. Effect of CO_2 on peripheral flow and central hemodynamics. *Eur Surg Res* 1984: **2** (133): 133–139.

Address:
Department of Anaesthesiology
Akademiska Sjukhuset
S-751 85 Uppsala
Sweden

COMMENT ON THE DESCRIPTION OF THE POLIO EPIDEMIC IN COPENHAGEN 1952

Dear Sir,

The comprehensive and thorough analysis by Wackers (1) of the events in Copenhagen calls for a comment.

The introduction of IPPV was probably not quite so important for the improved results as it is claimed in the article. It is hard to find theoretical reasons to believe that a principal difference exists between ventilation by means of positive pressure applied at the entrance of the airways and a negative pressure created in the alveoli by a body ventilator. In accordance with this, no major difference as to ventilation can be seen in clinical practice, provided the same pressures, pressure curves, frequencies etc. are used (which is usually not the case). It is obvious that IPPV made treatment of very ill patients easier. The tank was used several years after 1952 with acceptable results and is still used in selected cases at some places. As mentioned by Wackers, the good results reported by Bower et al. (2) were questioned in Copenhagen. But they were also doubted by most others with experience in polio treatment. However, it is possible that the results would not have differed much from those achieved, if a "Bower method" could have been implemented in Copenhagen instead of the manual IPPV-method.