Biochemical shunt: where and how?

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Reply to G. Harutyunyan and co-workers:

G. Harutyunyan and co-workers, in their reply to our correspondence, introduce the fascinating concept of "biochemical shunt" to help explain some of the gas exchange abnormalities reported in patients with early coronavirus disease 2019 (COVID-19). In brief, they assert the plausibility that the oxyhaemoglobin dissociation curve (ODC), which may be normal in the arterial and venous blood, could be altered (*i.e.* reduced oxygen affinity) in the pulmonary blood flowing through diseased alveolar capillaries. It is not easy for us to understand which COVID-19-related factors, or metabolites, might alter the ODC specifically in the pulmonary circulation, and to what extent they involve the lung parenchyma (partially or totally, where and why). Let us suppose, for example, that the biochemical shunt occurs in the whole parenchyma (nearly fully ventilated in early COVID-19). Let us assume that these COVID-19 patients are treated with an inspiratory oxygen fraction of 40% and they are able to maintain an arterial carbon dioxide tension (P_{aCO_2}) of 40 mmHg. The lung capillary oxygen tension (P_{O_2}), in equilibrium with alveolar P_{O_2} (P_{AO_2}), will be around 235 mmHg (at a respiratory quotient of 0.8). Even assuming a dramatic right shift of the ODC (as may occur with a pH 7.0, a carbon dioxide tension (P_{CO_2}) of 40 mmHg, and 2,3-diphosphoglycerate of 1.6 mM, *i.e.* double the normal concentration), with a capillary P_{O_2} of 235 mmHg, the haemoglobin oxygen saturation would be 99.5% [1], 99.8% [2] or 98.7% [3], depending on which equation is used. It is even more difficult to accept the biochemical shunt if the alteration to the ODC occurs only, as an example, in 50% of the lung parenchyma.

We have also some problems in conceptualising the discussion of G. Harutyunyan and co-workers about the P_{aCO_2}–end-tidal carbon dioxide tension (P_{ETCO_2}) gap. Shunt or, more correctly, the venous admixture, does affect the alveolar–arterial P_{CO_2} (P_{ACO_2}–P_{aCO_2} gap), while the P_{ETCO_2}–P_{ACO_2} gap is a function of the alveolar dead space. Therefore, in the ideal gas exchanger, the P_{ETCO_2}/P_{aCO_2} ratio is an indicator of the overall gas exchange efficiency in the lung, which includes both shunt and dead space fractions [4]. A ratio of 1 would indicate the "perfect" gas exchanger, *i.e.* no shunt and no dead space. This is the physiological background of the paper from Lazzari *et al.* [5].

Finally, if we set aside the Riley's approach, more commonly used for the definition of shunt and dead space, and we refer to a continuous distribution of ventilation and perfusion and their mismatch, it is worth remembering that the ventilation–perfusion mismatch affects both oxygen and carbon dioxide exchange, which must always be considered together [6]. We remain, however, interested to learn about these local metabolic or endothelial factors that affect the ODC selectively in the alveolar capillaries, but not in the systemic blood, and their quantitative contribution to the gas exchange abnormalities seen in COVID-19.

Shareable abstract (@ERSpublications)
Response to Harutyunyan *et al.* "Hypoxaemia in the early stage of COVID-19: prevalence of physical or biochemical factors?" https://bit.ly/3K1NSKu

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Mattia Busana[1], Luigi Camporota[2] and Luciano Gattinoni[1]

[1]Department of Anesthesiology, University Medical Center Göttingen, Göttingen, Germany. [2]Department of Adult Critical Care, Guy's and St Thomas' NHS Foundation Trust, Health Centre for Human and Applied Physiological Sciences, London, UK.

Corresponding author: Luciano Gattinoni (gattinoniluciano@gmail.com)

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