



## Using the fetal oxyhaemoglobin dissociation curve to calculate the ventilation/perfusion ratio and right to left shunt in healthy newborn infants

Theodore Dassios<sup>1</sup> · Kamal Ali<sup>1</sup> · Thomas Rossor<sup>2</sup> · Anne Greenough<sup>2,3</sup>

Received: 25 March 2017 / Accepted: 31 May 2018 / Published online: 6 June 2018  
© Springer Nature B.V. 2018

Oxygenation impairment can be non-invasively assessed by the degree of right-to-left shunt and ventilation/perfusion inequality. The relative rightwards displacement of an individual's oxyhaemoglobin dissociation curve (ODC) can be used to determine the reduction of the ventilation to perfusion ratio and the degree of depression of the ODC can be used to quantify the level of right to left shunt (Fig. 1). Using paired samples of peripheral oxygen saturation and fraction of inspired oxygen, a computer software can analyse and fit the data and derive a curve which represents the best fit for each infant and calculate the shunt and  $V_A/Q$ . These indexes have been described in sick newborn infants with pulmonary failure [1] and bronchopulmonary dysplasia [2–4].

We have recently reported normative values for these indices in healthy term infants which are essential to determine the magnitude of the abnormality [5]. We studied 145 infants with a mean (SD) gestation of 39 (1.6) weeks at a median (range) postnatal age of 3 (1–8) days and reported a mean (SD) rightwards shift of the ODC of 5.5 (1.1) kPa,  $V_A/Q$  ratio of 0.95 (0.21). None of the infants had a right-to-left shunt [5].

As with previous studies in sick newborns [1, 2, 4] we used the adult ODC as a reference curve. This curve however is positioned to the right compared to the fetal oxyhaemoglobin curve. The presence of fetal haemoglobin shifts the

fetal ODC to the left, reflecting the higher affinity of fetal haemoglobin to oxygen [6]. Thus, had we utilised a fetal curve we would have reported relatively higher values of shift and lower values of  $V_A/Q$  (Fig. 1). We chose the adult haemoglobin because the relatively rapid rate of decline of fetal haemoglobin after birth [7], would mean the neonatal curve would be shifting to the right during the first weeks, constituting a moving reference curve. The fetal ODC [8] for newborns is likely to be more accurate for use in neonates than the adult ODC, which is found after approximately 6 months [7]. We, therefore, reanalysed our data using the fetal curve as a reference curve. Differences of  $V_A/Q$  and shift calculated with the adult or the fetal ODC were assessed for significance using the Mann–Whitney U rank sum test. The mean (SD) rightwards shift of the ODC was 7.9 (1.5) kPa using the fetal curve compared to 5.5 (1.1) kPa using the adult ODC ( $p < 0.001$ ). The mean (SD)  $V_A/Q$  was 0.84 (0.18) using the fetal curve compared to 0.95 (0.21) using the adult ODC ( $p < 0.001$ ). The mean (SD) right-to-left shunt was 5.0 (5.4)% using the fetal curve compared to 0% using the adult ODC ( $p < 0.001$ ).

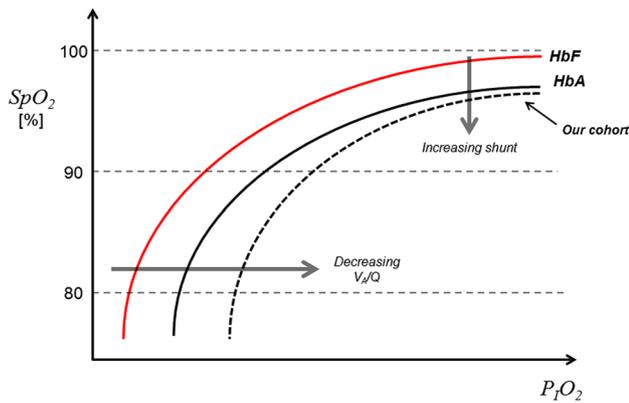
Using the fetal rather than the adult curve as a reference to calculate the  $V_A/Q$  ratio and the right-to-left shunt in healthy newborns, leads to lower values of  $V_A/Q$  and a detectable right-to-left shunt.

✉ Theodore Dassios  
theodore.dassios@kcl.ac.uk

<sup>1</sup> Neonatal Intensive Care Centre, King's College Hospital NHS Foundation Trust, 4th Floor Golden Jubilee Wing, Denmark Hill, London SE5 9RS, UK

<sup>2</sup> Division of Asthma, Allergy and Lung Biology, MRC-Asthma UK Centre in Allergic Mechanisms of Asthma, King's College London, London, UK

<sup>3</sup> National Institute for Health Research (NIHR) Biomedical Research Centre Based at Guy's and St Thomas' NHS Foundation Trust and King's College London, London, UK



**Fig. 1** The oxygen haemoglobin dissociation curve: haemoglobin saturation ( $SpO_2$ ) versus pressure of inspired oxygen ( $P_iO_2$ ). Increasing shunt displaces the curve downwards and decreasing  $V_A/Q$  shifts the curve to the right. The relative position of our cohort using the adult and the fetal haemoglobin dissociation curve as a reference curve is schematically presented

**Funding** The research was supported by the National Institute for Health Research (NIHR) Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust and King's College London. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. Dr Ali was supported by the King's College Hospital Research Initiative Grant.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

**Ethical statement** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

### References

1. Smith HL, Jones JG. Non-invasive assessment of shunt and ventilation/perfusion ratio in neonates with pulmonary failure. *Arch Dis Child Fetal Neonatal Ed.* 2001;85(2):F127–32.
2. Bamat N, Ghavam S, Liu Y, DeMauro SB, Jensen EA, Roberts R, et al. Reliability of a noninvasive measure of  $V_A/Q$  mismatch for bronchopulmonary dysplasia. *Ann Am Thorac Soc.* 2015;12(5):727–33.
3. Dassios T, Curley A, Krokidis M, Morley C, Ross-Russell R. Correlation of radiographic thoracic area and oxygenation impairment in bronchopulmonary dysplasia. *Respir Physiol Neurobiol.* 2016;220:40–5.
4. Dassios T, Curley A, Morley C, Ross-Russell R. Using measurements of shunt and ventilation-to-perfusion ratio to quantify the severity of bronchopulmonary dysplasia. *Neonatology.* 2015;107(4):283–8.
5. Dassios T, Ali K, Rossor T, Greenough A. Ventilation/perfusion ratio and right to left shunt in healthy newborn infants. *J Clin Monit Comput.* 2016;31(6):1229–34.
6. Bard H, Prossmanne J. Postnatal fetal and adult hemoglobin synthesis in preterm infants whose birth weight was less than 1000 grams. *J Clin Invest.* 1982;70(1):50–2.
7. Bard H. The postnatal decline of hemoglobin F synthesis in normal full-term infants. *J Clin Invest.* 1975;55(2):395–8.
8. Kasinger W, Huch R, Huch A. In vivo oxygen dissociation curve for whole fetal blood: fitting the Adair equation and blood gas nomogram. *Scand J Clin Lab Invest.* 1981;41(7):701–7.