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Placental gas exchange during amniotic carbon dioxide insufflation in sheep

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# KJC and RJH share joint senior authorship

Short Title: Carbon dioxide insufflation and placental gas exchange

Keywords: carbon dioxide, amniotic insufflation, fetal therapy, placenta, gas exchange

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**Contribution:**

**What are the novel findings of this work?**

This is the first study to show that amniotic CO2 insufflation causes reductions in placental gas exchange irrespective of gas temperature and humidity. It also showed that heated humidified insufflation reduces fetal blood gas disturbances seen when using cold dry gas by reducing fetal CO2 absorption from the uterus.

**What are the clinical implications of this work?**

This study provides physiological support for the use of heated humidified CO2 and lower uterine distension pressures as a way of reducing the fetal effects of amniotic insufflation during fetal surgery.
Abstract:

Objectives: Insufflation of the amniotic cavity with carbon dioxide (CO₂) is used clinically to improve visibility during complex fetoscopic surgery. Insufflation with heated, humidified CO₂ has recently been shown to reduce fetal hypercapnia and acidosis in sheep, but the underlying mechanisms are unclear. We have investigated whether differences in placental CO₂ and oxygen (O₂) exchange could explain these findings.

Methods: Fetal lambs at 105 days gestation (term 146 days) were instrumented with an umbilical artery and vein catheter and common umbilical vein flow probe. Arterial and venous catheters and flow probes were also inserted into the maternal uterine circulation. Six ewes were insufflated with cold, dry CO₂ (22°C, 0-5% humidity) and seven with heated, humidified CO₂ (40°C, 95-100% humidity) at 15mmHg for 180 minutes. Blood flow recordings and paired arterial and venous blood gasses were sampled from uterine and umbilical vessels. Rates of placental CO₂ and O₂ exchange were calculated. Data are presented as mean±SEM.

Results: After 180 minutes of insufflation fetal survival was 33% (2/6) using cold, dry CO₂ and 71% (5/7) using heated, humidified CO₂. By 120 minutes, fetuses insufflated with heated, humidified CO₂ had lower arterial CO₂ levels and higher pH compared to those insufflated with cold, dry gas. Insufflation significantly decreased placental gas exchange in both groups as measured by rates of both (i) fetal CO₂ clearance and O₂ uptake and (ii) maternal O₂ delivery and CO₂ uptake from the fetal compartment.

Conclusions: Lower arterial CO₂ and higher pH levels in fetuses insufflated with heated, humidified, compared to cold, dry CO₂, could not be explained by differences in placental gas exchange. Instead, heated humidified insufflation appeared to
reduce fetal CO₂ absorption from the uterus supporting its use in preference to cold, dry CO₂.
**Introduction:**

Detection of congenital anomalies, such as myelomeningocele, during mid-gestation ultrasound provides a window of opportunity for surgical intervention to reduce infant morbidity and improve their long-term outcomes.\(^{(1)}\) To minimise the impact on the mother, many of these surgeries are performed under video-guidance through ports in the uterine wall (fetoscopy).\(^{(2-4)}\) Complex fetoscopic procedures require gaseous distension of the amniotic space with carbon dioxide (CO\(_2\)) to see clearly and manipulate the fetus during surgery.\(^{(4)}\)

Carbon dioxide is a logical gas for insufflation given its low cost and extensive use in laparoscopic surgery with minimal adverse effects. Additionally, its high solubility allows gas from the amniotic space to dissolve into fetal and maternal blood rather than forming gas emboli which are potentially fatal.\(^{(5)}\) However, this additional dissolved CO\(_2\) must be removed from maternal and fetal blood to avoid lowering blood pH (acidosis). The mother easily eliminates excess CO\(_2\) from her lungs, however the fetal lungs play no role in gas exchange.\(^{(6)}\) Instead, excess CO\(_2\) is eliminated from the fetal compartment in the placenta where it enters the maternal circulation (Figure 1).\(^{(6)}\) As fetal placental gas exchange is less efficient than maternal respiratory CO\(_2\) elimination, the fetus may be vulnerable to accumulating CO\(_2\) during insufflation, which is consistent with several animal studies.\(^{(7-12)}\)

Our recent sheep study showed that using heated, humidified CO\(_2\) for insufflation greatly reduces fetal CO\(_2\) levels and partially mitigates the associated acidosis compared to unheated, unhumidified (cold, dry) insufflation.\(^{(8)}\) While these findings are consistent with trends in small human case series, the mechanisms explaining the fetal benefits remain unclear.\(^{(13)}\) Understanding these mechanisms will
allow refinement of insufflation parameters to further minimise the fetal effects of amniotic insufflation during a time of significant physiological stress.

We hypothesised that cold, dry amniotic insufflation impairs fetal CO$_2$ elimination by reducing umbilical blood flow and placental gas exchange. Additionally, we hypothesised that heated, humidified insufflation mitigates the decrease in umbilical blood flow and, thereby explains lower fetal CO$_2$ and higher pH levels. Our aim was therefore, to compare rates of placental gas exchange during cold, dry and heated, humidified amniotic insufflation in sheep.
Methods:

Surgical Instrumentation:

The experimental protocol was approved by the Monash Medical Centre Animal Ethics Committee and followed a series of similar insufflation experiments in our laboratory. Thirteen pregnant, Merino-Border Leicester ewes (103-106 days gestation) were anaesthetized with Sodium Thiopentone (i.v. Pentothal, Boehringer Ingelheim, Warriewood, NSW, Australia) and intubated with an endotracheal tube. General anaesthesia was maintained with 1.5-2% inhaled isoflurane (Isoflow, Abbot Pty Ltd, North Chicago, IL, USA) in air/oxygen. The ewe’s ventilation rate and tidal volume were continuously adjusted to maintain arterial CO$_2$ levels between 35-45mmHg. Polyvinyl catheters (Internal Diameter (ID) 2.6mm, Dural Plastics, Sydney, NSW, Australia) were inserted into the ewe’s carotid artery and jugular vein. Ewes were administered a continuous infusion of saline solution throughout the experiment via the jugular vein.

Fetuses were partially exteriorised via a midline laparotomy and hysterotomy incision made near the tip of the pregnant uterine horn. During instrumentation the exteriorised fetus and uterus were covered with warmed Hartmans solution to prevent heat loss and vessel constriction. A flow probe (Transonic Systems, Ithaca, NY, USA, Size 4) was placed around the fetal common umbilical vein and a temperature probe inserted into the fetal oesophagus. Fetuses were then returned to the amniotic space and a cotyledon close to the placental origin of the umbilical cord was identified. Heparinised saline-filled polyvinyl catheters (internal diameter, 0.86 mm) where introduced into large branches of the cotyledonary artery and vein and the tips advanced into the common umbilical vessels within the cord (Figure 1). Insufflation tubing, a second temperature probe and an amniotic drainage catheter...
were inserted through the uterine wall into the amniotic sac. All catheters, temperature probes and flow probes were exteriorised and the hysterotomy incision closed in three layers to maintain an airtight seal of the uterus for insufflation as previously described.\(^8,12\)

A flow probe was placed around a large branch of the uterine artery supplying the pregnant horn and a polyvinyl catheter (internal diameter, 0.86 mm) introduced into the common uterine vein. The uterus was then returned to the maternal abdomen and the laparotomy incision closed to allow uterine insufflation within the abdominal cavity as previously performed in sheep and clinically in humans.\(^14-16\)

**Amniotic CO\(_2\) Insufflation:**

Paired maternal (carotid artery and uterine vein) and fetal (umbilical artery and vein) blood gases were sampled immediately after surgery and then after a 10-minute stabilisation period (post-operative and baseline samples). Maternal (ventilation rate, amniotic temperature, heart rate and uterine artery flow) and fetal (temperature, umbilical artery and vein pressure and common umbilical vein flow) physiological parameters were continuously recorded using LabChart and PowerLab data acquisition system (ADInstruments, Bella Vista, NSW, Australia).

The amniotic fluid was drained, and ewes were randomly allocated to cold, dry (22°C, 0-5% humidity) or heated, humidified (40°C, 100% humidity) amniotic insufflation. Intra-amniotic pressures were increased with an insufflator (40L High-Performance Insufflator, Stryker South Pacific, Australia) over five minutes to 15mmHg and maintained for 180 minutes with a flow rate of 0.5L per minute. This pressure and duration were chosen to replicate averages from human case series and our previous ovine study showing a benefit to heated, humidified insufflation.\(^8,\)
In ewes receiving heated, humidified insufflation, the gas was passed through a laparoscopic humidification system (MR860, Fisher and Paykel Healthcare, Auckland, New-Zealand) before entering the uterus.

During insufflation, paired maternal blood gases were sampled every ten minutes. Paired fetal gases were sampled every 10 minutes for the first 30 minutes and every 30 minutes thereafter. The uterus was desufflated after 180 minutes in surviving fetuses and monitoring continued for a further 20 minutes. Both the ewe and fetus were then euthanized using intravenous Pentobarbitone (Lethobarb, Virbac Pty Ltd, Peakhurst, Australia) and post mortem examination conducted.

Data analysis and statistics:
Maternal and fetal physiological parameters were assessed every five minutes by determining the mean of each parameter over twenty second epochs. Umbilical vein blood flow was adjusted for fetal bodyweight.

Total blood CO₂ and O₂ content was calculated from each blood gas sample to account for differences in bound and dissolved gas in arterial and venous blood (table 1, equations 1 and 2). Uteroplacental production of CO₂, the rate of CO₂ elimination from the umbilical circulation (fetal CO₂ clearance) and CO₂ uptake by maternal uterine blood (maternal CO₂ uptake) was calculated using equations 3-5 respectively. Similarly, the rate of O₂ loss from the uterine circulation (maternal O₂ delivery) and uptake by fetal umbilical blood (fetal O₂ uptake) was calculated using equations 6 and 7. These equations have been used extensively to calculate rates of placental gas exchange in sheep. Values are presented as mean ± standard error of mean (SEM). Blood gas and physiological data were normally distributed and compared at matched time points using a repeated-measures mixed analysis of
variance (ANOVA) with Sidak post hoc analysis. Analysis of variance was also used to compare each time point to baseline values within each group.

Linear regression and correlation analysis were used to assess the relationship between umbilical vein blood flow and fetal placental gas exchange as well as uterine artery blood flow and maternal placental gas exchange.
Results:
Of the thirteen pregnant ewes undergoing surgery and amniotic insufflation, six were insufflated with cold, dry CO\(_2\) and seven with heated, humidified CO\(_2\). Fetal weight and baseline blood gases values, physiological parameters and placental gas exchange data were similar between groups. Fetal survival over 180 minutes of insufflation was 33% (2/6) with cold, dry CO\(_2\) and 71% (5/7) with heated, humidified CO\(_2\) (Figure 2a.). 120 minutes was chosen as the timepoint for comparison because of limited survival in the cold, dry group beyond this point.

Fetal Effects
By 120 minutes of cold, dry and heated, humidified insufflation, the partial pressure of CO\(_2\) in the umbilical artery (PaCO\(_2\), Figure 2b), CO\(_2\) content in the umbilical vein (Figure 2c) and blood lactate level (Figure 2d) increased while the pH decreased (Figure 2e) from baseline. However, compared to cold, dry insufflation at 120 minutes, fetuses insufflated with heated, humidified CO\(_2\) had lower PaCO\(_2\) (99.5 ±14.6 vs.167.0 ±5.0 mmHg, P<0.01) and blood lactate (3.2 ±1.1 vs. 7.2 ±2.1 mmol/L, P<0.01) and higher arterial pH (pH 7.02 ±0.08 vs. 6.78 ±0.10, P<0.01). Within both insufflation groups, umbilical artery oxygen saturation decreased (Figure 2f) from baseline while the PaO\(_2\) remained stable (Figure 2g). During cold, dry insufflation, uteroplacental production of CO\(_2\) increased from baseline and was higher than the heated, humidified group after 120 minutes (Figure 2h).

During both cold, dry and heated, humidified insufflation, fetal temperature remained unchanged (Figure 3a.) while umbilical artery (Figure 3b) and vein (Figure 3c) pressure increased from baseline immediately after starting insufflation. Pressures remained elevated in the umbilical vein and gradually returned to baseline.
in the umbilical artery over 120 minutes. In both groups, the rate of umbilical vein blood flow (Figure 3d), placental CO\(_2\) clearance (Figure 3e) and O\(_2\) uptake (Figure 3f) decreased from baseline in response to insufflation. As there were no differences between groups, umbilical blood flow and fetal placental gas exchange data was pooled for linear regression analysis. This showed that rates of fetal CO\(_2\) clearance (r=0.43, P=0.01, Figure 3g.) and O\(_2\) uptake (r=0.64, P=0.01, Figure 3h.) were positively correlated with umbilical vein blood flow.

**Maternal Effects**

No changes in amniotic temperature were observed during heated, humidified or cold, dry insufflation (Figure 4a). Maternal ventilation rates (Figure 4b) required to maintain maternal PaCO\(_2\) between 35 and 45mmHg (Figure 4c) were also similar between groups throughout the experiment.

Rates of uterine artery blood flow (Figure 4d), CO\(_2\) uptake (Figure 4e) and O\(_2\) loss (Figure 4f) from the uterine circulation decreased in both groups over 120 minutes of insufflation. As there were no differences between groups, uterine blood flow and maternal placental gas exchange data were pooled for linear regression analysis. This showed that both maternal CO\(_2\) uptake (r=0.44, P<0.01, Figure 4g) and O\(_2\) delivery (r=0.57, P<0.01, Figure 4h) were positively correlated with uterine artery blood flow.
Discussion:

This is the first study to simultaneously monitor fetal blood gases and rates of placental gas exchange during cold, dry and heated, humidified amniotic insufflation. Fetal PaCO$_2$ progressively increased and arterial pH decreased during cold, dry insufflation. These changes were partially mitigated by 90-120 minutes when the insufflated CO$_2$ was heated and humidified. Interestingly, we found that reductions in fetal and maternal placental gas exchange induced by insufflation were similar in both groups. Fetal and maternal placental gas exchange positively correlated with umbilical and uterine blood flow respectively.

These results confirm previous observations that fetal hypercapnic acidosis caused by cold, dry insufflation can be mostly mitigated over clinically relevant insufflation durations (120min) by heating and humidifying the CO$_2$. Like others, we observed a rapid (within 10min) and sustained reduction in fetal arterial oxygen saturation which was associated with a non-significant rise in fetal PaO$_2$. This was likely a pH-induced decrease in the affinity of fetal haemoglobin for oxygen. The slightly lower baseline fetal PaO$_2$ and pH values measured in this study, compared to our previous study, are simply due to the collection of fetal blood from a post-ductal artery (umbilical artery) instead of pre-ductal (carotid artery).

We suggest that increasing the amniotic pressure by 15mmHg caused the reductions in placental gas exchange. As ovine umbilical venous pressure is normally less than 15mmHg, amniotic insufflation would have compressed umbilical veins, potentially causing them to collapse. Vessel pressure must therefore increase during insufflation to re-expand the vessels and restore blood flow. This would explain the immediate increase in umbilical arterial and venous pressure during insufflation and the associated reduction in umbilical venous blood flow. Our data,
like others, has shown that umbilical blood flow is essential to maintain CO₂ and O₂ diffusion between the fetal and maternal compartments. As insufflation pressures were the same in both groups, this explains why reductions in umbilical blood flow and placental gas exchange were independent of CO₂ temperature and humidity.

These results provide a physiological explanation for ultrasound and histological findings in human fetuses undergoing amniotic insufflation suggestive of increased placental vascular resistance and fetal under-perfusion of the placenta. Additionally, they provide an important rationale for using insufflation pressures below human umbilical venous pressure (3-7mmHg) as a way to minimise the physiological effects of insufflation on the fetus. As such, ongoing efforts to avoid high insufflation pressures during human surgery by partially exteriorising the uterus appear physiologically justified. Future studies should investigate if lower insufflation pressures can maintain both placental gas exchange and adequate visualization during fetoscopic surgery.

Increasing amniotic pressure was also associated with lower uterine artery blood flow. Lower uterine artery blood flow appeared to decrease maternal CO₂ uptake from the fetus which likely contributed to progressive fetal hypercapnia. In both humans and sheep there is normally significant reserve in uteroplacental perfusion to avoid fetal blood gas changes during fluctuations in placental blood flow. However, this reserve may be reduced in the context of amniotic insufflation where fetal placental gas exchange is also compromised.

Contrary to our hypothesis we found no differences in umbilical venous blood flow or placental gas exchange to explain the fetal benefits of heated, humidified insufflation. This suggests that cold, dry CO₂ did not induce umbilical vasospasm like in vitro studies using temperatures <28°C. Although the entry temperature of
insufflated CO$_2$ was very different (22 vs 40°C), intra-amniotic temperatures were similar between groups. This similarity could be caused by the temperature probe lying against the fetus, uterine wall or residual amniotic fluid in both groups. This seems likely as there was little difference between the amniotic and fetal temperatures at all stages of the experiment. However, we also consider it likely that the insufflation gas was progressively heated within the uterus, particularly as insufflation flow rates were relatively low (0.5L/minute).

Instead of conveying acid base benefits by improving placental gas exchange, heated, humidified insufflation may slow fetal CO$_2$ absorption from the uterus. This is consistent with lower uteroplacental CO$_2$ production and the trend for lower umbilical vein CO$_2$ content during heated, humidified insufflation. Heating CO$_2$ gas from 22 to 40°C nearly halves its solubility and would reduce fetal absorption, but as discussed, this effect may be short lived. The addition of water vapour (humidification) lowers the partial pressure of CO$_2$ within the insufflated gas from ~740 to ~685mmHg.\textsuperscript{(34-36)} While this 7% reduction would also reduce fetal CO$_2$ absorption during heated, humidified insufflation, we do not believe it completely explains the fetal acid base benefits. We hypothesize that cold, dry insufflation damages the fetal membranes, increasing the rate of fetal CO$_2$ absorption. Indeed, we have previously shown that cold, dry insufflation increases neutrophil recruitment into the fetal membranes.\textsuperscript{(8)}

Although monitoring human fetuses during insufflation is technically challenging, human fetuses clearly tolerate insufflation better than sheep. Rates of human fetal survival are high and, reassuringly, post-surgical follow up has not identified neurological sequelae attributable to severe intra-operative acidosis.\textsuperscript{(13-16, 29, 37, 38)} On the other hand, fetal sheep clearly develop severe hypercapnic acidosis that impacts survival.\textsuperscript{(8)} These differences could be attributed to the cotyledonary
arrangement of the sheep placenta that may increase the surface area for fetal CO₂ absorption or the thinner sheep myometrium that may over-stretch and occlude uterine arteries when insufflated. Additionally, the partially keratinized skin of the 103-106-day sheep fetus may more readily absorb CO₂ from the uterus compared to the 24-26-week human fetus. While these differences suggest that human fetuses are not experiencing the same severity of disturbances, the principals of reducing fetal CO₂ absorption using heated, humidified CO₂ and avoiding high insufflation pressures to maintain placental gas exchange cannot be ignored. These principals should provide the rationale for future studies aiming to confirm the fetal safety of amniotic insufflation.

This study showed that amniotic insufflation reduced placental gas exchange in sheep, independent of CO₂ temperature and humidity. Interestingly, the fetal benefits of heated, humidified insufflation could not be explained by differences in placental gas exchange. Instead, heated humidified insufflation appeared to reduce fetal CO₂ absorption from the uterus.
**Acknowledgements:**

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**Disclosure statement:** The authors report no conflict of interest
References:

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Figure legends

Figure 1: Gas exchange in the placenta and instrumentation of the fetal and maternal placental compartments

Fetal blood is cleared of carbon dioxide (CO$_2$) and re-oxygenated by diffusion of dissolved gasses between the fetal and maternal compartments of the placenta. To measure rates of placental gas exchange in sheep the fetus was instrumented with an umbilical artery and vein catheter, umbilical vein flow probe and oesophageal temperature probe. The ewe was instrumented with a carotid artery catheter, uterine vein catheter and uterine artery flow probe. A temperature probe was also inserted into the amniotic space.

Figure 2: Fetal survival and blood gas changes

Fetal survival was 33% (2/6) with cold, dry CO$_2$ (■) and 71% (5/7) with heated, humidified CO$_2$ (▲) (a.). By 120 minutes in both groups, dissolved CO$_2$ in the umbilical artery (PaCO$_2$) (b), umbilical vein CO$_2$ content (c) and blood lactate level (d) had increased while the pH had decreased (e) from baseline. Umbilical artery PaCO$_2$ and lactate levels were higher and umbilical artery pH lower in the heated humidified group by 120 minutes. In both groups, umbilical artery oxygen saturation decreased (f) while dissolved oxygen levels remained stable (g). Uteroplacental production of CO$_2$ increased from baseline and was higher than the heated, humidified group by 120 minutes (h). Pre insufflation recordings were recorded immediately after surgery (post-surgery) and immediately before drainage of the amniotic fluid and insufflating the uterus (baseline). Data are presented as mean ± SEM. (*) represents p<0.05 vs. heated, humidified CO$_2$. (↑) and (↓) represent a
significant (P<0.05) increase or decrease compared to baseline values within each group.

**Figure 3: Fetal physiology and placental gas exchange**

Fetal temperature (a.) remained stable from baseline during cold, dry (■) and heated, humidified (▲) insufflation. Umbilical artery (b.) and vein (c.) pressure increased while umbilical vein blood flow (d.), fetal CO$_2$ clearance (e.) and fetal O$_2$ uptake (f.) decreased in both groups independent of CO$_2$ temperature and humidity. Umbilical vein blood flow negatively correlated with fetal CO$_2$ clearance (g.) and oxygen uptake (h.). Pre insufflation recordings were recorded immediately after surgery (post-surgery) and immediately before drainage of the amniotic fluid and insufflating the uterus (baseline). Data are presented as mean ± SEM. (*) represents p<0.05 vs. heated, humidified CO$_2$. (↑) and (↓) represent a significant (P<0.05) increase or decrease compared to baseline values within each group.

**Figure 4: Maternal physiology and placental gas exchange**

Amniotic temperature (a.), maternal ventilation rate (b.) and arterial CO$_2$ levels (c.) were the same during cold, dry (■) and heated, humidified (▲) insufflation and remained stable from baseline. Uterine artery blood flow (d.), maternal placental CO$_2$ uptake (e.) and placental O$_2$ delivery (f.) decreased in both groups independent of CO$_2$ temperature and humidity. Uterine artery blood flow negatively correlated with maternal CO$_2$ clearance (g.) and oxygen uptake (h.). Pre insufflation recordings were recorded immediately after surgery (post-surgery) and immediately before drainage of the amniotic fluid and insufflating the uterus (baseline). Data are presented as
mean ± SEM. (*) represents p<0.05 vs. heated, humidified CO₂. (↑) and (↓) represent a significant (P<0.05) increase or decrease compared to baseline values within each group.
Table 1: Calculations of blood gas content and placental gas exchange

<table>
<thead>
<tr>
<th>Name</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Total Blood CO(_2) Content (mmol/L)(^{(18)})</td>
<td>(PCO_2 \times 10^{(0.91 \times pH - 6.99)})</td>
</tr>
<tr>
<td>2. Total Blood O(_2) Content (mmol/L)(^{(17)})</td>
<td>(\frac{Hb \times SaO_2}{100} \times 0.62)</td>
</tr>
<tr>
<td>3. Uteroplacental CO(_2) production(^{(22)})</td>
<td>((UtV \ PCO_2 - UtA \ PCO_2) + (UmV \ PCO_2 - UmA \ PCO_2))</td>
</tr>
<tr>
<td>4. Fetal Placental CO(_2) Clearance (mmol/L/kg/min)(^{(19-21)})</td>
<td>(\frac{(UmV \ flow \times 0.95) \ (UmA \ TCO_2 - UmV \ TCO_2)}{UmA \ PCO_2 - UtA \ PCO_2})</td>
</tr>
<tr>
<td>5. Maternal Placental CO(_2) Uptake (mmol/L/Kg/min)(^{(19-21)})</td>
<td>(\frac{(UtA \ flow \times 0.84) \ (UtV \ TCO_2 - UtA \ TCO_2)}{UmA \ PCO_2 - UtA \ PCO_2})</td>
</tr>
<tr>
<td>6. Maternal Placental O(_2) Delivery (mmol/L/Kg/min)(^{(19-21)})</td>
<td>(\frac{(UtA \ flow \times 0.84) \ (UtA \ TO_2 - UtV \ TO_2)}{UtA \ PO_2 - UmA \ PO_2})</td>
</tr>
<tr>
<td>7. Fetal Placental O(_2) Uptake (mmol/L/kg/min)(^{(19-21)})</td>
<td>(\frac{(UmV \ flow \times 0.95) \ (UmV \ TO_2 - UmA \ TO_2)}{UtA \ PO_2 - UmA \ PO_2})</td>
</tr>
</tbody>
</table>

PCO\(_2\) – partial pressure of carbon dioxide, PO\(_2\) – partial pressure of oxygen, SaO\(_2\) – arterial haemoglobin oxygen saturation, TCO\(_2\) – total carbon dioxide content, TO\(_2\) – total blood oxygen content, UmA – umbilical artery, UmV – umbilical vein, UtA – uterine artery (maternal carotid artery blood samples have been used provide these values), UtV – uterine vein.