Influence of maternal dexamethasone administration on thermoregulation in lambs delivered by caesarean section

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Abstract

We have previously shown that lambs delivered by caesarean section 1 week prematurely become hypothermic due to reduced brown adipose tissue function in conjunction with low plasma concentrations of cortisol and thyroid hormones. The present study therefore aimed to determine whether maternal dexamethasone (a synthetic corticosteroid) administration could improve thermoregulation in premature lambs to the extent that they become similar to term lambs. Lambs were either delivered by caesarean section into a warm (30 °C; WD) or cool (15 °C; CD) ambient temperature at 140 days of gestation, 2 days after maternal dexamethasone treatment, or at 146 days for controls. During the first 30 min of life the decline in colonic temperature was greater in dexamethasone treated lambs compared with controls delivered into the same ambient temperature. All lambs then restored colonic temperature although this adaptation took longest in dexamethasone treated lambs CD but these subsequently attained highest plateau colonic temperatures. Oxygen consumption, breathing frequency and plasma free fatty acid concentrations were highest in dexamethasone treated lambs CD. There were no differences in plasma thyroid hormones between groups, but cortisol concentrations were lower in dexamethasone treated lambs irrespective of delivery temperature. Analysis of brown adipose tissue samples at 6 h of life demonstrated that dexamethasone treated lambs WD had more uncoupling protein and, in both dexamethasone treated and control lambs, uncoupling protein content was higher in lambs CD compared with those WD. An effect of ambient temperature on thermogenic activity was only observed in the dexamethasone treated group. It is concluded that maternal dexamethasone treatment can significantly improve thermoregulation after birth following premature delivery by caesarean section. As a consequence, dexamethasone treated lambs delivered 1 week prematurely do not remain hypothermic and have higher or similar colonic temperatures compared with untreated lambs born 1–2 days before term.


Introduction

During the transition from fetal to neonatal life it is necessary both to establish continuous breathing and to initiate independent thermoregulation in order to effectively adapt to the cool challenge of the extra-uterine environment. In lambs, premature birth and/or caesarean section delivery is known to compromise heat production by non-shivering thermogenesis in brown adipose tissue (BAT) (Alexander et al 1972, Clarke et al 1996a, 1997a). This may be due to reduced stimulation from endocrine factors including thyroid hormones and catecholamines. The ability of BAT to rapidly generate large amounts of heat is the result of the electron transport chain becoming uncoupled from adenosine triphosphate synthesis, an effect mediated by a unique uncoupling protein (UCP) (Cannon & Nedergaard 1985). During fetal life non-shivering thermogenesis in BAT does not occur as fetal body temperature is regulated by the mother (Gunn & Gluckman 1983). BAT therefore remains inactive due to a combination of placental inhibitory factors (e.g. adenosine, prostaglandin E2 (Gunn et al 1993, Ball et al 1995) and low plasma concentrations of stimulatory factors (e.g. thyroid hormones (Clarke et al 1997a)) that act to prevent lipolysis and maintain low abundance of mRNA for UCP and low thermogenic activity which then rise rapidly after birth (Casteilla et al 1989, Clarke et al 1997b).

It is established that, in order to maximise heat production after birth, lambs are able to utilise both non-shivering and shivering thermogenesis (Alexander & Williams 1968), although shivering is an inefficient method of increasing heat production (Alexander 1979) and is only recruited when BAT activity can no longer be increased. We have shown that, as is the case in infants (Christensson et al 1993), a critical factor determining body temperature...
after birth is route of delivery (Clarke et al. 1997a). Lambs delivered per vaginam therefore do not exhibit a decline in colonic temperature, due in part to high plasma thyroid hormone concentrations and increased sympathetic activity resulting in an enhanced ability to generate heat in BAT (Clarke et al. 1997a). If lambs are not subjected to the stress of normal parturition and delivered by caesarean section, colonic temperature rapidly declines and BAT function is impaired. Caesarean section delivered lambs are able to compensate for a reduction in BAT activity by increasing their recruitment of shivering thermogenesis as a result of enhanced adrenal activity (Clarke et al. 1997a). At 6 h of life caesarean section lambs delivered into a cool ambient temperature (15 °C; CD) have a higher body temperature than those born into a warm ambient temperature (30 °C; WD) or born vaginally. This is not the case when lambs are CD by caesarean section 5–7 days before term when they remain hypothermic, due to a low thermogenic activity of BAT and reduced plasma concentrations of cortisol and thyroid hormones (Clarke et al. 1996a). The present study therefore aimed to determine whether maternal dexamethasone (a synthetic glucocorticoid) administration would act to promote fetal maturation, thereby preventing hypothermia in lambs delivered 1 week prematurely by caesarean section. We hypothesised that, following antenatal dexamethasone treatment, thermoregulation would be similar between preterm and term lambs. This was assessed by comparing the effect of delivery temperature on adaptation after caesarean section birth with near-term lambs using a combination of in vivo recordings, measurements of the amount of UCP and its thermogenic activity (i.e. guanosine 5’-diphosphate (GDP) binding to mitochondrial protein), and circulating levels of thyroid hormones, cortisol and free fatty acids (FFA) during the first 6 h of neonatal life.

Methods

Animals and diet

Nine triplet-bearing North Country Mule ewes of similar age and background, and of known mating date, that had been confirmed as being pregnant with triplets using a real-time ultrasound echograph, were entered into the study. Four weeks prior to predicted lambing date, each ewe was individually housed and fed 0.4 to 0.6 kg concentrate and 1.2 kg hay, the combination of which contained sufficient energy and nitrogen to fully meet requirements for maintenance and pregnancy over this final period of gestation. The mean daily minimum and maximum temperatures recorded at 0900 h were 5.7 ± 1.9 (s.d.) and 16.5 ± 2.9 °C, respectively. Body weight and condition score (an index of body energy reserves) as assessed by the physical characteristics in the lumbar region, on and around the backbone in the loin area immediately behind the first rib (Russel 1984) were recorded on the day of caesarean section delivery. At 136 days of gestation (term is at 147 days) a jugular vein catheter was inserted into five randomly selected ewes and the following day blood samples were taken at 1 h intervals between 0830 and 1530 h. On day 138 of gestation 8 ml of dexamethasone (2 mg/ml Dexadreson, National Veterinary Supplies, UK) were administered intramuscularly. Jugular vein catheters were inserted in the four remaining ewes (controls) at day 138 of gestation and blood samples taken from all nine ewes on day 139 of gestation.

Experimental design

Caesarean section delivery was performed as described by Clarke et al. (1994) on day 140 of gestation in the five dexamethasone treated ewes and on day 146 of gestation in the four control ewes. Immediately prior to caesarean section delivery there was no difference in ewe colonic temperatures (control 39.8 ± 0.1 (n = 4): dexamethasone treated: 39.5 ± 0.2 °C (n = 5)). Paravertebral anaesthesia was administered by inserting spinal needles to allow blockage of the T13, L1, and L2 spinal nerves by surrounding them with 2% xylocaine, as the dorsal and ventral branches of these nerves pass above and below the transverse processes of the vertebrae. This was followed by jugular venous injection of 4–6 ml of ketamine (100 mg/ml in saline) into the ewe. A flank incision was made and the fetuses delivered, one of which was immediately placed in a warm ambient temperature (30 °C; WD) and its sibling in a cool ambient temperature (15 °C; CD). The remaining fetus was humanely killed by intravenous administration of barbiturate (100 mg/kg pentobarbital sodium: Euthatal, RMB Animal Health, UK) upon delivery. Before umbilical cord cutting a 5 ml umbilical venous blood sample was taken from each fetus. Both perirenal adipose tissue depots plus a liver and lung sample (20–30 g) and both thyroid glands were rapidly removed, placed in liquid N₂ and stored at −70 °C until analysed.

All lambs were monitored to ensure that continuous breathing was established, which normally occurred within 2–4 min of birth. Colonic temperature was recorded using an electronic thermometer (Type 3GID, Light Laboratories, Brighton, UK) and the lambs were dried with a towel. At 25–40 min after birth a jugular vein catheter was inserted into each lamb to allow blood sampling, plus three skin surface electrodes to record ECG for heart rate measurement. Local anaesthetic (10% xylocaine spray) was applied to each site several minutes before needle insertion. Each lamb was then placed in an indirect calorimeter maintained at the same ambient temperature into which it had been delivered. Continuous measurements of colonic temperature and breathing frequency and pattern using inductance plethysmography (Symonds et al. 1992) were made until lambs were 6 h old. Sleep state was determined from these respiratory pattern
measurements. Blood samples were taken hourly. Oxygen consumption and carbon dioxide production were measured continuously using indirect open-circuit calorimetry. The mean values presented represent values obtained during periods of non-rapid eye movement sleep in order to minimise variations due to animal movement, and were recorded using two identical indirect calorimetry systems based on that described by Symonds et al. (1992), with the modification that air flow was measured using a differential flow indicator (Perflow Instruments Ltd, Willesden, UK). All lambs were then humanely killed 6 h after birth to enable tissue sampling as described above for the fetus.

All operative procedures and experimental protocols had the required UK Home Office approval as designated by the Animals (Scientific Procedures) Act of 1986.

**Laboratory procedures**

Mitochondria were prepared from frozen perirenal adipose tissue as described by Symonds et al. (1992). The protein contents of homogenates and mitochondria were measured by the method of Lowry et al. (1951) and cytochrome c oxidase activity measured in order to assess the recovery of mitochondrial protein. The thermogenic activity of perirenal adipose tissue was assessed from the in vitro activity of the mitochondrial conductance pathway using GDP at a concentration of 2 µM, with non-specific binding measured using a 200 µM concentration of GDP. The amount of [3H]GDP trapped in extra-mitochondrial spaces was corrected for by measuring the trapping of [14C]sucrose (Symonds et al. 1992). UCP was detected in mitochondrial preparations following separation by sodium dodecyl polyacrylamide gel electrophoresis using immunoblotting and enhanced chemiluminescence (ECL, Amersham International plc, Bucks, UK). Antibodies used were raised against purified ovine UCP as described by Amersham International plc, Bucks, UK). All lambs were then humanely killed 6 h after birth to enable tissue sampling as described above for the fetus.

Antibodies used in immunoblotting and enhanced chemiluminescence (ECL, sodium dodecyl polyacrylamide gel electrophoresis using in mitochondrial preparations following separation by

**Results**

**Body weights and maternal plasma cortisol concentrations**

There were no differences in maternal body weight (controls: 88 ± 6 kg (n = 4); dexamethasone treated: 93 ± 4 kg (n = 5)) or body condition score (controls: 2·4 ± 0·2 (n = 4); dexamethasone treated: 2·3 ± 0·3 (n = 5)). Concentrations of cortisol in maternal plasma were significantly (P<0·01) increased following dexamethasone treatment (pre-treatment: 26 ± 11 nmol/l; post-treatment: 119 ± 21 nmol/l (n = 5)) and were therefore higher (P<0·01) than in controls (33 ± 11 nmol/l (n = 4)). Mean lamb body weight was lower (P<0·05) in the dexamethasone treated group (controls: 3·77 ± 0·20 kg (n = 12); dexamethasone treated: 3·21 ± 0·15 kg (n = 15)).

**Metabolic responses to warm and cool ambient temperatures**

Control lambs established continuous breathing more rapidly than those treated with dexamethasone, although this difference was only significant between CD groups (Table 1). Immediately after birth there was no influence of delivery temperature on colonic temperature in control lambs but dexamethasone treated lambs WD had a higher colonic temperature than those CD (Fig. 1). There was no difference between groups with respect to length of time after birth when shivering commenced, but the rate of decline in colonic temperature was greater in lambs CD than WD irrespective of dexamethasone treatment (Table 1; Fig. 1). All lambs were able to restore colonic temperature, an adaptation that took longer in CD than WD groups. This difference was only significant in the dexamethasone treated group (Table 1). By 6 h after birth there was no effect of ambient temperature on colonic temperature in controls but dexamethasone treated lambs CD had a significantly higher (P<0·05) temperature than all other groups.

Between 1 and 2 h, oxygen consumption and carbon dioxide production were higher in lambs CD than WD, irrespective of treatment (Fig. 2). This effect of ambient...
Temperature was maintained throughout the study in the dexamethasone treated group, but not in controls, due to a greater decline ($P<0.05$) in both oxygen consumption and carbon dioxide production in lambs CD compared with those WD. Breathing frequency was greater ($P<0.05$) in dexamethasone treated lambs CD compared with both their siblings WD and controls (controls: WD $56\pm 5$ breaths/min, CD $50\pm 4$ ($n=4$); dexamethasone treated: WD $51\pm 6$ breaths/min, CD $75\pm 5$ ($n=5$)). Heart rate was not influenced by maternal treatment or ambient temperature (controls: WD $207\pm 33$ beats/min, CD $158\pm 32$ ($n=4$); dexamethasone treated: WD $213\pm 43$ beats/min, CD $192\pm 10$ ($n=5$)).

**Endocrine status**

Umbilical cord plasma concentrations of $T_4$ (controls: $98\pm 10$ nmol/l ($n=10$); dexamethasone treated: $123\pm 9$ nmol/l ($n=13$)), $T_3$ (controls: $2.01\pm 0.20$ nmol/l ($n=10$); dexamethasone treated: $1.79\pm 0.14$ nmol/l ($n=13$)), free $T_3$ (controls: $1.54\pm 0.44$ pmol/l ($n=10$); dexamethasone treated: $0.66\pm 0.13$ pmol/l ($n=13$)) and cortisol (controls: $59\pm 12$ nmol/l ($n=10$); dexamethasone treated: $98\pm 17$ nmol/l ($n=13$)) were similar irrespective of dexamethasone treatment. Plasma $T_4$, $T_3$ and free $T_3$ concentrations remained similar between groups after birth when cortisol levels were lower ($P<0.05$) in dexamethasone treated lambs (Table 2). In contrast, FFA levels were significantly greater ($P<0.05$) in dexamethasone treated lambs (Fig. 3).

**Perirenal adipose tissue composition and 15'D activity**

There were no differences in perirenal adipose tissue weight or protein and mitochondrial protein content between any groups of lambs (Table 3). Dexamethasone

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**Table 1** Time to commence breathing and shivering, and changes in colonic temperature, following caesarean section delivery into a warm (30°C; WD) or cool (15°C; CD) ambient temperature. The results are means ± S.E.M.

<table>
<thead>
<tr>
<th></th>
<th>Control ($n=4$)</th>
<th>Dexamethasone ($n=5$)</th>
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<tbody>
<tr>
<td></td>
<td>WD</td>
<td>CD</td>
</tr>
<tr>
<td></td>
<td>CD</td>
<td></td>
</tr>
<tr>
<td>Time to breathe (min)</td>
<td>$1.25\pm 0.95$</td>
<td>$0.25\pm 0.25$</td>
</tr>
<tr>
<td>Time to shiver (min)</td>
<td>$17.8\pm 3.3$</td>
<td>$17.3\pm 5.3$</td>
</tr>
<tr>
<td>Rate of decline in colonic temperature ($°C$/min)</td>
<td>$0.069\pm 0.012$</td>
<td>$0.087\pm 0.015$</td>
</tr>
<tr>
<td>Time to restore colonic temperature (min)</td>
<td>$81\pm 37$</td>
<td>$103\pm 21$</td>
</tr>
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* $P<0.05$, significant differences between control and dexamethasone treated group.
† $P<0.05$, significant differences between WD and CD groups in the same treatment group.

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**Figure 1** Mean colonic temperature in premature lambs delivered by caesarean section into warm (WD) or cool (CD) ambient temperatures following maternal dexamethasone treatment and birth at 140 days or lambs that were born at 146 days of gestation. Values are means ± s.e. and $n=4$ or 5 per group.
treatment and ambient temperature had differential effects on the amount and activity of UCP. In control lambs, although there were no differences in thermogenic activity (i.e. GDP binding) between fetal lambs and those CD and WD, the latter group possessed significantly \((P<0.05)\) less UCP. There was no difference in UCP content between dexamethasone treated fetuses and lambs WD, but thermogenic activity was reduced \((P<0.05)\) in the group WD and more \((P<0.05)\) UCP was present in lambs CD compared with those WD. No differences were observed in I5'D activities between fetuses and lambs CD or WD in BAT (type I and II) or liver (type I) for control or dexamethasone treated groups (Table 4). Type I I5'D activity was greater in the thyroid glands of all dexamethasone treated groups although this difference was only significant \((P<0.05)\) between fetuses. A similar pattern was observed with respect to type II activity in the lungs which was significantly higher \((P<0.05)\) in dexamethasone treated fetuses.

**Discussion**

The present study’s primary finding is that, following maternal dexamethasone treatment, thermoregulation is substantially improved in preterm lambs to the extent that they are very similar to term lambs. This point is emphasised by the finding that body temperature was restored to similar or higher values in preterm dexamethasone treated lambs compared with term lambs delivered by caesarean section. A major factor further influencing adaptation after birth of dexamethasone treated lambs was ambient temperature, for which CD was beneficial. The significance of these results is emphasised from our earlier study when lambs delivered by caesarean section between 141 and 143 days of gestation remained hypothermic even when treated with a \(\beta_3\)-adrenergic agonist (Clarke et al. 1996a). These hypothermic lambs were characterised as having BAT with a reduced thermogenic activity and had low plasma concentrations of thyroid hormones and cortisol. Dexamethasone treated premature lambs in the present study had plasma thyroid hormone concentrations similar to control lambs at term despite having lower cortisol levels after birth. Cortisol is known to promote organ maturation prior to birth (Liggins 1994) although the full extent to which this is mediated directly or by changes in thyroid hormone secretion remains to be clarified. We have previously observed in both caesarean section and

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**Table 2** Jugular venous plasma concentrations of total \(T_4\), \(T_3\), free \(T_3\) and cortisol following caesarean section delivery into a warm (30°C; WD) or cool (15°C; CD) ambient temperature. The results are means ± S.E.M.

<table>
<thead>
<tr>
<th></th>
<th>Control (n=4)</th>
<th>Dexamethasone (n=4)</th>
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<tbody>
<tr>
<td></td>
<td>WD</td>
<td>CD</td>
</tr>
<tr>
<td>(T_4) (nmol/l)</td>
<td>110 ± 13</td>
<td>131 ± 21</td>
</tr>
<tr>
<td>(T_3) (nmol/l)</td>
<td>3.77 ± 0.65</td>
<td>4.35 ± 0.56</td>
</tr>
<tr>
<td>Free (T_3) (pmol/l)</td>
<td>3.00 ± 1.28</td>
<td>3.64 ± 1.51</td>
</tr>
<tr>
<td>Cortisol (nmol/l)</td>
<td>253 ± 77</td>
<td>363 ± 62</td>
</tr>
<tr>
<td></td>
<td>128 ± 5</td>
<td>123 ± 10</td>
</tr>
<tr>
<td></td>
<td>4.16 ± 0.47</td>
<td>4.33 ± 0.57</td>
</tr>
<tr>
<td></td>
<td>2.29 ± 0.68</td>
<td>3.27 ± 1.50</td>
</tr>
<tr>
<td></td>
<td>116 ± 24*</td>
<td>143 ± 12**</td>
</tr>
</tbody>
</table>

\(^{*}P<0.05, \ ^{**}P<0.01\), significant differences between control and dexamethasone treated groups.
vaginally delivered lambs that thyroid hormones have a critical role in the establishment of independent temperature control after birth (Schermer et al. 1996, Clarke et al. 1997a). In the present study an increase in plasma thyroid hormone concentrations in preterm lambs to values similar to those at term is therefore likely to play a primary role in improving thermoregulation after birth following maternal dexamethasone treatment.

Maternal dexamethasone treatment resulted in a pronounced increase in maternal plasma cortisol concentrations, although these were within the physiological range for pregnant sheep and were not higher than observed during parturition (Clarke et al. 1996b). The fact that lambs born vaginally have much lower plasma cortisol concentrations over the first few hours of life than those delivered by caesarean section (Clarke et al. 1997a) could indicate that, under normal birthing conditions, post-partum plasma cortisol concentrations may be predicted to rapidly decline, thereby enabling the newborn to have the capacity to adapt to any further physiological or pathological challenge. The extent to which lower plasma cortisol concentrations following caesarean section delivery are due to altered adrenal activity or effective adaptation clearly requires further study. Irrespective of the exact endocrine pathway by which dexamethasone treatment promoted fetal maturation, these lambs benefited from CD which resulted in higher rates of heat production that were associated with increased plasma FFA concentrations. This indicates an increased rate of lipolysis and may have enhanced non-shivering thermogenesis within BAT compared with their siblings WD.

The observation that dexamethasone treatment followed by WD was associated with a higher colonic temperature immediately after birth compared with

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**Table 3** Perirenal adipose tissue weight, composition, thermogenic activity and capacity. Tissue was sampled from fetuses or 6-hour-old lambs following caesarean section delivery into a warm (30°C; WD) or cool (15°C; CD) ambient temperature. The results are means ± S.E.M.

<table>
<thead>
<tr>
<th></th>
<th>Control (n=4)</th>
<th>Dexamethasone (n=5)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Fetus</td>
<td>WD</td>
</tr>
<tr>
<td>Weight (g)</td>
<td>16.3 ± 2.1</td>
<td>21.8 ± 0.7</td>
</tr>
<tr>
<td>Protein content (g)</td>
<td>2.09 ± 0.64</td>
<td>2.49 ± 0.69</td>
</tr>
<tr>
<td>Mitochondrial protein content (g)</td>
<td>1.08 ± 0.25</td>
<td>1.52 ± 0.31</td>
</tr>
<tr>
<td>Thermogenic activity (pmol per mg protein)</td>
<td>184 ± 36</td>
<td>141 ± 31</td>
</tr>
<tr>
<td>Uncoupling protein (% reference)</td>
<td>1.09 ± 0.32</td>
<td>0.44 ± 0.11*</td>
</tr>
</tbody>
</table>

*P<0.05, significant differences between WD and CD groups in the same treatment group.
controls is indicative of a lower thermal tolerance in lambs born to dexamethasone treated ewes. This could have contributed in part to the apparent decline in thermogenic activity within BAT observed in these WD lambs compared with dexamethasone treated fetuses or those CD and could also explain why plasma FFA concentrations only declined with time after birth in dexamethasone treated lambs WD. The observation of a greater effect of delivery temperature on thermogenic activity of BAT in dexamethasone treated compared with control lambs could indicate an increased sensitivity to any effects of temperature on sympathetic activity (Mitchell et al. 1992). Any effect of this type is likely to be mediated by changes in amount or sensitivity of β-adrenergic receptors and could result in enhanced responsiveness to exogenous β-adrenergic stimulation in order to further promote adaptation after birth in dexamethasone treated lambs.

It is of interest to note that triplet lambs used in the present study, with the exception of control lambs WD, all had BAT with UCP contents similar to that observed in vaginally delivered lambs. This contrasts with our earlier study using sheep of a different breed and lower maternal body weight that were predominantly twin bearing (Clarke et al. 1997a). It should be noted that, despite this difference in UCP content, all caesarean section delivered lambs were unable to maintain a constant body temperature after birth and their thermogenic activity at 6 h of life remained low compared with lambs born per vaginam (Clarke et al. 1997a). Furthermore, control lambs CD did not exhibit a higher thermogenic activity in BAT compared with their siblings WD, which is likely to be the main reason why body temperature was not higher in this group of lambs CD. This difference in lamb response to CD between studies may be explained by the fact that, in the current study, term lambs had a lower mitochondrial protein content and plasma T₄ and cortisol concentrations than previously observed (Clarke et al. 1997a) that may be linked to differences in breed of ewe. These contrasting results make the finding that dexamethasone treatment resulted in lambs CD having a higher colonic temperature, in conjunction with a greater thermogenic activity in BAT particularly striking. This response was observed although dexamethasone treated lambs had similar plasma thyroid hormone concentrations to controls despite lower cortisol levels and, as discussed above, emphasises the importance of additional endocrine changes in promoting BAT function in caesarean section delivered lambs.

Dexamethasone lambs CD not only benefited from higher rates of heat production and greater colonic temperatures but also exhibited a faster rate of ventilation that would have the potential to enhance the rate of oxygen exchange across the lung. It is known that glucocorticoid treatment enhances lung maturation (Stein et al. 1994) which could be linked to altered thyroid status. The measurement of appreciable amounts of type II I₅'D activity in the ovine lung is particularly interesting as, to date, this has only been observed in fetal and neonatal rat pups (Obregon et al. 1991). Type II I₅'D activity has been suggested to be more important in providing an intracellular source of T₃ for subsequent binding to nuclear T₃ receptors in order to enable T₃ to influence gene transcription or translation within the cell (Wu et al. 1990). Studies in mice have shown nuclear T₃ receptors to be present in lung tissue (Gonzales & Ballard 1982) although their functional significance remains to be established (Liggins 1995). The observation of enhanced type II I₅'D activity, particularly in fetal lungs, could have an important role in mediating some of the beneficial effects of thyroid hormones and glucocorticoids on lung maturation.

It is noticeable that any increase in I₅'D activity following dexamethasone treatment was confined to the lung in which type I activity is absent and the thyroid glands in which type I activity is considerably lower than in liver and BAT. These contrasting responses between tissues could reflect altered ontogenic maturation with respect to any effects of cortisol on I₅'D activity. It is known that type I and II I₅'D activities in ovine BAT peak prior to birth whilst type I activity in liver peaks after birth (Clarke et al. 1997b) and in both tissues I₅'D activity is influenced by changes in maternal glucose metabolism (Clarke et al. 1996b). An increased understanding of the contrasting or additive effects of fetal glucose supply

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Control (n=4)</th>
<th>Dexamethasone (n=5)</th>
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<tbody>
<tr>
<td></td>
<td>Fetus WD CD</td>
<td>Fetus WD CD</td>
</tr>
<tr>
<td>BAT</td>
<td>164 ± 29 165 ± 29 183 ± 39</td>
<td>313 ± 164 149 ± 57 253 ± 101</td>
</tr>
<tr>
<td>Liver</td>
<td>0·21 ± 0·05 0·23 ± 0·10 0·14 ± 0·04</td>
<td>0·40 ± 0·21 0·20 ± 0·05 0·16 ± 0·03</td>
</tr>
<tr>
<td>Thyroid</td>
<td>30±3 317±1530 1833±585</td>
<td>1710±346 1156±91 1247±140</td>
</tr>
<tr>
<td>Lung</td>
<td>38 ± 1 31 ± 3 36 ± 4</td>
<td>76 ± 17* 60 ± 14 52 ± 9</td>
</tr>
</tbody>
</table>

*P<0·05, significant differences between control and dexamethasone treated group.

Table 4 Iodothyronine 5’monodeiodinase activity (pmol l⁻¹ released per mg protein per hour) in brown adipose tissue (BAT), liver, thyroid glands and lungs. Tissue was sampled from fetuses or 6-hour-old lambs following caesarean section delivery into a warm (30°C; WD) or cool (15°C; CD) ambient temperature. The results are means ± S.E.M.
and/or cortisol with respect to promoting T3 production within different tissues could be important with respect to improving our ability to maximise thyroid hormone secretion at birth. This could be particularly important for growth restricted or premature fetuses that are characterised as having low plasma thyroid hormone concentrations (Cabello & Levieux 1981, Thorpe-Beeston & Nicolaides 1992).

It is concluded that maternal dexamethasone treatment can significantly improve adaptation after birth following premature delivery of caesarean section delivered lambs. As a consequence, thermoregulation in dexamethasone treated lambs delivered 1 week prematurely by caesarean section is very similar to that in untreated lambs born 1–2 days before term. The magnitude of this effect is further influenced by delivery temperature for which maintenance in a cool environment has the potential to further improve thermoregulation in the newborn.

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