Effects on fetal and maternal body temperatures of exposure of pregnant ewes to heat, cold, and exercise

HELEN P. LABURN, ALIDA FAURIE, KATHLEEN GOELST;† AND DUNCAN MITCHELL

Brain Function Research Unit, Department of Physiology, University of the Witwatersrand, Parktown 2193, South Africa

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IN A PREVIOUS STUDY (16), we showed that, when pregnant ewes were exposed to mild heat and cold, deviations in body temperature were significantly less in the fetus than in the mother animal. Our findings have implications for human and animal reproduction; they imply that the fetus is granted thermal protection when the mother animal (or human) experiences thermal stress. Such protection would be particularly beneficial in the case of exposure to warm environments, considering the known teratogenic effects of heat; in early pregnancy, intrauterine hyperthermia is associated with a variety of congenital defects, particularly of the central nervous system (9), and in later pregnancy, intrauterine hyperthermia is associated with intrauterine growth retardation (8).

It is not known how fetal body temperature variations are attenuated when the mothers are subjected to thermal stress. We postulated that the fetus’ own thermal inertia and physiological mechanisms employed by the ewe during the thermal stress conspire to reduce the change in fetal body temperature when maternal body temperature rises or falls. Whatever the mechanisms, they appear to be present also during normal circadian variations in maternal body temperature (16) and during the hyperthermia associated with labor in sheep (15) but apparently are abandoned during maternal fever (16).

When fetal heat production and heat loss are in equilibrium, body temperature of the fetus is ~0.5°C above that of its mother in all species studied so far (3, 10, 12, 22, 26), including humans (32). The fetus produces large amounts of metabolic heat per gram of body mass (26) and relies on placental heat exchange for ~85% of heat loss (10, 26). Increases or decreases in umbilical and/or uterine blood flow, therefore, would increase or decrease, respectively, the rate at which the fetus loses heat via the placental route (27). We have postulated (14, 16) that active mechanisms attenuate excursions in fetal body temperatures when mother animals are thermally stressed, namely, an increase in uteroplacental blood flow during mild heat exposure and a decrease in that blood flow during mild cold exposure. However, it has been reported that maternal heat stress compromises uterine blood flow in sheep (1, 5, 8, 24), which in turn would compromise fetal heat loss. Indeed, our postulate may not hold during heat and cold stress more severe than that used in our previous studies. There also are reports that uterine blood flow is reduced during exercise in pregnant sheep (4, 17). If that is the case, then during maternal hyperthermia induced by exercise, fetal thermoregulation would also be compromised. Therefore, we have carried out experiments in which we have monitored fetal and maternal body temperatures in late-gestation pregnant sheep exposed to higher heat stress and exercise. Because of the anecdotal evidence that unexpected cold weather may precipitate fetal loss in some ungulate species (31), we also have exposed pregnant ewes to more severe cold stress than in our previous study. Our hypothesis is that, during greater environmental thermal stress and during exercise within the realm of
what pregnant sheep might encounter naturally, fetal thermal protection will persist.

As we did previously, we have used changes in the difference between fetal and maternal body temperature, the fetomaternal temperature gradient, as a gauge of changes in fetal heat loss. For a fixed fetal metabolic rate, a fall in the fetomaternal temperature gradient implies a greater rate of heat loss and a rise in the fetomaternal temperature gradient implies a lower rate of heat loss from the fetus. The most important cause of a change in the fetomaternal temperature gradient is a change in uteroplacental blood flow (27).

We again used radiotelemetry to measure fetal and maternal temperature. Radiotelemetry allows continuous measurement of body temperature in unrestrained animals over extended time periods limited only by the battery life of the telemeter.

**MATERIALS AND METHODS**

**Animals**

We used three groups of pregnant Dorper-cross ewes of average mass (60 kg). At ~110 days of pregnancy, in a sterile surgical procedure, the ewes were anesthetized using halothane (Fluothane, Hoechst; 2–8% to effect). After exposure of the uterus and hysterotomy, the fetal lamb was partially delivered. A sterile radiotelemeter was implanted into the abdomen of the ewe. The procedure has been described previously in detail (16).

The ewes were allowed ≥1 wk for recovery before they were subjected to experimental procedures. After surgery and for the duration of the study, the ewes were housed in indoor pens, where the ambient temperature varied between 21°C and 23°C and a natural circadian light-dark cycle prevailed. Water and hay were provided ad libitum, and commercial sheep concentrate pellets (1 kg/day) were provided once a day at ~1500. All ewes delivered normal healthy lambs at 145–150 days of gestation.

**Temperature Measurements**

Radiotelemetry allowed continuous monitoring of fetal and maternal body temperature throughout the study period without the need for hard-wired temperature probes, which limit activity of the animal and increase the risk of infection. The temperature-sensitive radiotelemeters (Mini-Mitter or Datamed, Potchefstroom, Republic of South Africa) were connected to two 850 mA·h batteries connected in parallel and coated with an inert wax (Elvax, Mini-Mitter). They had a mass of ~30 g (telemeter + batteries) after waxing. The telemeters were calibrated against a high-precision quartz crystal thermometer (Quat 100, Heraeus Sensors, Hanau, Germany) by immersion in water at controlled temperatures over the anticipated range. The telemeters transmitted temperature-modulated frequencies in the 148- to 150-MHz range that were detected by a transceiver (model PT 290 R11, Yaesu Musen) connected to a desktop computer. The time taken for 30 beat-frequency pulses was averaged over three successive readings, and regression equations of pulse frequency vs. temperature were calculated for each telemeter and incorporated into the logging software. The radiotelemeters permitted measurement of body temperature to an accuracy of 0.1°C. During experiments, the receiver scanned each telemeter’s output every 15 min.

The telemeters, recovered from the animals using an abbreviated sterile surgical procedure similar to that used for implantation, were found most often deeply embedded in the abdominal cavity but could be found at various sites within that cavity. We previously observed that the temperatures measured in the ewe abdomen using two randomly implanted telemeters were not significantly different from each other (unpublished observations). Because the uterine artery supplying the placenta traverses the abdominal cavity, we considered that abdominal temperature was a reasonable reflection of the temperature of the blood delivered to the placenta and uterus.

**Experimental Procedures**

*Exposure to a hot environment.* Eight ewes were exposed once each to an isothermal climatic chamber in which dry-bulb temperature was 40°C and relative humidity was 60% (wet-bulb temperature = 32°C, water vapor pressure = 4.4 kPa). Mean radiant temperature was equal to dry-bulb temperature. During the procedure, the animals were confined to a trolley that allowed the ewe to turn around and lie down and free circulation of air. The ewe, in her trolley, was kept in an antechamber at 23°C for ≥1 h before being wheeled into the climatic chamber. Each ewe spent up to 2.5 h in the heat. Some animals whose body temperature rose >41°C before the end of the designated exposure time were removed from the heat after only 2 h of exposure. We continued to monitor body temperature of the ewes in their trolleys in the 23°C antechamber for another 2 h before returning them to their pens.

*Exercise.* Seven ewes were trained, over several weeks, to walk at increasingly faster pace on a motor-driven treadmill. On the day of the experiment, the ewe stood on the stationary treadmill for 1 h and then walked for 30 min with the treadmill set to a gradient of 5° or 10° and a speed of 2.1 km/h. Some animals whose body temperature rose >41°C during the procedure, the animals returned to the holding pens, during the procedure. Surprisingly, at the 10° gradient, body temperatures did not rise significantly more than at the 5° gradient, so we show only the results from the 5° gradient. All exercise was undertaken in a room, adjacent to the holding pens, where the ambient temperature was ~23°C. Relative humidity was not controlled.

*Exposure to a cold environment.* After ≥1 h in an antechamber at 23°C, nine ewes were exposed in the same trolleys to a temperature-controlled chamber with a dry-bulb temperature of 4°C and 90% relative humidity (water vapor pressure = 0.7 kPa) for 6 h. Mean radiant temperature was equal to dry-bulb temperature. After the cold exposure, the ewes were kept in the antechamber at 23°C for another 1 h.

**Statistical Analyses**

We used ANOVA with Dunnett’s post hoc tests and Student’s t-test with Student-Newman-Keuls correction for multiple comparisons where appropriate, to test for significant differences between the means of measured or calculated variables. $P < 0.05$ was considered significant.
Ethics

The procedures were approved by the Animal Ethics Committee of the University of the Witwatersrand under protocols 88/103/4 and 95/115/5.

RESULTS

Table 1 lists the body temperatures of ewes and their fetuses just before each of the experimental procedures. Confining the sheep to trolleys and moving them from their holding pens to the antechamber resulted in a significant rise in maternal and fetal temperature compared with the temperatures when the ewes were standing on the treadmill adjacent to their pens. The fetomaternal temperature gradient was not affected, however, and was in the range we observed previously for sheep in the same environment (16).

Figures 1–3 show effects of the experimental procedures on body temperatures of the ewes and fetuses and changes in the fetomaternal temperature gradient.

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Table 1. Maternal and fetal body temperatures before heat or cold exposure or exercise

<table>
<thead>
<tr>
<th>Condition</th>
<th>Maternal Temperature, °C</th>
<th>Fetal Temperature, °C</th>
<th>F-M, °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heat exposure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(40°C, 60% rh)</td>
<td>8</td>
<td>39.4 ± 0.13†</td>
<td>39.9 ± 0.12†</td>
</tr>
<tr>
<td>Exercise</td>
<td></td>
<td>7</td>
<td>38.4 ± 0.17</td>
</tr>
<tr>
<td>Cold exposure</td>
<td></td>
<td>9</td>
<td>39.3 ± 0.11†</td>
</tr>
</tbody>
</table>

Values (means ± SE) are maternal and fetal body temperatures and mean fetomaternal temperature difference (F-M) measured before start of experimental procedures. For heat and cold exposures, temperatures were calculated over 1 h with animals in the trolleys; for exercise, temperatures were measured over 30 min with animals standing on the treadmill. In all cases, ambient temperature was 23°C, rh. Relative humidity. Student’s t-test with Student-Newman-Keuls correction showed that maternal and fetal temperatures were significantly higher when sheep were in the trolleys than when they were on the treadmill (*P < 0.001, †P < 0.01), but F-M was not significantly different between the 3 preintervention conditions.

Fig. 1. Maternal (M) and fetal (F) body temperatures and fetomaternal temperature difference (F-M) before, during, and after (recovery) –2 h of exposure (horizontal bar) to 40°C and 60% relative humidity. Note interruption in time scale at end of period in the heat. Dashed line, zero body temperature difference between ewe and fetus. Each point is mean ± SE of 8 measurements. †Significantly different (Dunnett’s post hoc test, P < 0.01) from time 0. Value at 40 min of recovery for mother is significantly different from time 0 (P < 0.05). All values for fetomaternal temperature difference during heat exposure are not significantly different from zero.

Maternal and fetal body temperature declined to preexposure levels within the recovery period in the 23°C room.

The changes evident in Fig. 1 resulted from environmental heat load. Figure 2 shows the effects of a 30-min bout of treadmill exercise, that is, a metabolic heat load, on body temperature of the pregnant ewe and fetus. Ewe body temperature commenced its rise almost immediately after exercise commenced and was still rising when the treadmill was stopped. Fetal body temperature tracked the excursions in body temperature of the mother, except fetal temperature appeared to rise at a less rapid rate during exercise and to fall at a slower rate after exercise. Thus the fetomaternal gradient fell during the exercise but tended to rise after the exercise. Changes in the fetomaternal gradient were not as precipitous as at the beginning and end of environmental heat exposure.

Figures 1 and 2 reflect temperature changes in response to heat loads. Figure 3 shows the effects of 6 h of exposure of the pregnant ewes to 4°C. Cold exposure caused body temperature of the ewe to fall by ~1.5°C over the exposure period. Fetal body temperature fell as well, but by less than maternal body temperature, and there was a dissociation of fetal from maternal body temperature. The fetomaternal temperature gra-
dient doubled. In the recovery period following the cold exposure, all temperatures returned toward, but did not reach, their preexposure values within the hour.

Figure 4 consolidates the changes in maternal and fetal temperature during the three forms of thermal stress and explores their statistical significance. It shows the mean maximum changes in maternal and fetal temperatures and in the fetomaternal gradient for each experiment. Maximum changes were calculated by subtracting the highest (for heat exposure and exercise) or lowest (for cold exposure) temperature reached from the preexposure value. A zero change in the fetomaternal gradient would indicate that maternal and fetal body temperatures rose or fell in a parallel fashion, a rise in the fetomaternal gradient indicates a diversion in fetal compared with maternal body temperature, and a fall in the fetomaternal gradient indicates convergence of the two body temperatures. Increases in maternal and fetal temperature in response to the hot environment were highly significant. Nevertheless, fetal body temperature rose less than maternal body temperature, so there was a highly significant fall in the fetomaternal gradient of 0.54 ± 0.06°C. As during heat exposure, the body temperatures of ewes and their fetuses rose significantly during exercise, and again body temperature rose less in the fetus than in the ewe. Once again, we observed a significant fall in the fetomaternal gradient of 0.21 ± 0.08°C. During the cold exposure, the maximum declines in ewe and fetal temperatures were significant, as was the rise in the fetomaternal gradient.

**DISCUSSION**

Our study addresses the importance of fetal homeothermy in the context of the thermoregulation of the pregnant mammal. Fetal metabolic heat, arising from growth and maintenance processes, must be dissipated, and its immediate destination can only be the mother. For purely thermodynamic reasons, fetal temperature must be higher than maternal abdominal cavity temperature. How much higher it is, that is, the fetomaternal temperature gradient, is determined for any particular fetal metabolic rate primarily by the thermal conductance of the placenta and its associated...
blood vessels; almost all fetal metabolic heat is transferred via the placenta. If maternal temperature is disturbed, then fetal temperature will be disturbed as well, but its excursions can be attenuated by alterations in placental thermal conductance or fetal heat production. If maternal temperature rises, thermal conductance can be increased by increasing umbilical and/or uterine blood flow. Conversely, if maternal temperature falls, umbilical or uterine blood flow can be reduced. The modulation of blood flow carries a cost, however. Increases in flow require an increase in fetal or maternal cardiac output or diversion of blood previously destined for other tissues. Decreases in flow potentially compromise fetal and placental nutrition, oxygenation, and metabolic waste disposal. Thus a thermally stressed pregnant mother may protect her fetus by modulation of uteroplacental blood supply or may abandon fetal homeothermy and preserve other physiological functions. Similarly, a decrease in fetal metabolic rate during heat stress will reduce fetal hyperthermia but also compromise growth. An increase during cold stress will reduce hypothermia but increase energy demand.

Previously, we showed that fetal temperature changed less than maternal body temperature when ewes were exposed to warm and cool environments at rest (16). Here we have shown that in more severe hot or cold conditions the same phenomenon can be observed: body temperature rises less in the fetal lamb than in the mother during maternal heat exposure and falls less during maternal cold exposure (Figs. 1, 3, and 4). In the case of the hot environment, the conditions (40°C and 60% relative humidity) were more severe than those sheep are likely to encounter in natural climates. Therefore, resting sheep appear to attach high priority to maintaining fetal homeothermy.

A similar situation prevailed during the thermal stress imposed by our moderate exercise. We have measured, for the first time, fetal temperature in unrestrained exercising mammals, an achievement made possible by the use of fetal radiotelemetry. As shown in Figs. 2 and 4, during maternal exercise, fetal body temperature rose less than maternal body temperature. Again, the fetus was protected from the consequences of the thermal stress.

A quantitative index of the degree to which the fetus is protected from the consequences of maternal thermal stress can be derived by calculating the relative rates of change in fetal and maternal temperature once the stress is imposed. Figure 5 shows the result of such calculations. In the absence of thermal protection, the rate of change in fetal and maternal body temperature would be identical, and the ratio would be 1.0. Figure 5 shows that, during maternal hyperthermia and maternal hypothermia in our present study, fetal body temperature changed at a rate less than maternal body temperature. Calculations based on data from two of our earlier studies are also shown in Fig. 5. During the hyperthermia imposed by normal labor, as with treadmill exercise, the rate of rise of temperature was significantly less in the fetus than in the mother. The fetal thermal protection, however, appears to be abandoned during the special case of maternal fever, when fetal body temperature rose at a rate about one-third higher than that of the mother and by more than maternal body temperature (16).

We believe that the changes we have observed in the fetomaternal temperature gradient during thermal stress result from changes in uterine or umbilical blood flow. However, we did not measure blood flow. We are not aware of any technique for doing so in nonterminal experiments in unrestrained animals. Another theoretical possibility for the lag of the fetal temperature behind maternal temperature, namely, fetal thermal inertia, is eliminated by the events during fever, when fetal temperature changes faster than maternal temperature. Also, thermal inertia would protect the fetus during transients of maternal body temperature but not during sustained hyperthermia or hypothermia. Further evidence against passive thermal inertia as the source of thermal protection of the fetus is that the fetomaternal temperature gradient can increase in some circumstances of heat stress (6). A further theoretical possibility for the lag, namely, reciprocal change in fetal heat production, is eliminated by the measure-
ments of metabolic rate during fetal thermal stress; apparently, there is no reciprocal change in heat production (11, 28).

Umbilical and uterine blood flow have been measured by others, although only for short time periods, using hard-wired techniques in restrained mothers or using microspheres in terminal experiments. As we would have predicted, studies of ewes during environmental heat stress showed increases in umbilical blood flow (6, 30) and uterine blood flow (2). Lublin and Wolfenson (18) found a 50% increase in maternal blood flow to the placenta of pregnant rabbits during mild heat stress. On the basis of our observations of the fetomaternal temperature gradient, we would expect uteroplacental blood flow to increase during exercise as well. There is some evidence that it indeed does so in ewes (7, 25).

In addition to the reports that show an increase in uteroplacental blood flow during maternal hyperthermia, several reports show that it is unchanged or even decreased. In one of these studies (5), ewes were exposed to conditions similar to those we used. However, in others, pregnant ewes had been exposed to much higher levels of heat stress (1, 8) or for longer periods of time (20) or had demonstrated more severe hyperthermia (6). Similarly, during intense exercise, uterine blood flow may be compromised in favor of flow to working muscles (4, 7, 17). We believe that the circumstances in which uteroplacental blood flow decreases, rather than increases, during heat stress are those in which the ewe’s own thermal status is so threatened that she abandons the homeothermy of her fetus. In a transition zone of maternal heat stress, uteroplacental blood flow may remain unchanged, as has been reported for sheep (30) and for human mothers (29).

If uteroplacental blood flow is enhanced during mild or moderate heat stress but diminished in severe heat stress, then one would expect the fetomaternal temperature gradient to decrease in mild or moderate heat, as we have found for ewes (16; present study) but to increase in severe heat stress. The decrease in the fetomaternal temperature gradient during heat exposure and the increase during more severe heat exposure have been observed by others in sheep (6, 24) as well as in pregnant baboons (21). Whether a similar pattern of fetal and maternal body temperatures occurs in exercise cannot be confirmed, because so few measurements have been made of fetal temperature in exercising pregnant animals. Lotgering et al. (17) also reported a fall and then a reversal of the fetomaternal gradient during exercise in pregnant ewes.

In the case of cold stress, rather than heat stress, the response preserving fetal homeothermy would be an increase in the fetomaternal temperature gradient, which we have found in mild and moderate cold stress in ewes (16; present study). In the only other study of which we know that has examined the effect on the fetomaternal gradient of heating and cooling of the pregnant animal, Morishima et al. (21) observed an increase to ~1°C in the fetomaternal gradient during cooling of pregnant baboons, a finding similar to our own. The widening of the fetomatal gradient during falling maternal body temperature brought about by cold exposure can be explained on the basis of maternal vasoconstriction of uterine vessels, for which there also is some evidence (3). No one has observed the decrease in the fetomaternal gradient during cold exposure that would occur if fetal homeothermy were abandoned to sustain other fetal or maternal functions, although sudden cold environmental stress is known to cause fetal death in certain species (31). Fetal animals may have access to other means of maintaining fetal homeostasis during maternal cold exposure, for example, vasoconstriction in skin vessels (13), which would reduce fetal heat dissipation via nonplacental pathways (10, 27).

In conclusion, using radiotelemetry, we have studied further situations of thermal stress in unrestrained pregnant ewes and have shown that, during exercise, as during moderate heat exposure, rises in fetal body temperature are attenuated and the risk of fetal injury due to hyperthermia is reduced. Similarly, during falls in maternal body temperature, fetal hypothermia is attenuated. In these contexts, fetal thermal inertia is an advantage for the fetus, but we believe that active thermal protection is conferred by appropriate maternal and/or fetal vascular responses that enhance or reduce fetal heat loss. Where maternal heat stress is so severe that maternal survival is threatened, changes in uteroplacental blood flow may occur that are counteradaptive for fetal homeothermy. We expect similar counteradaptive changes to occur in circumstances in which the demands of maternal muscles for blood take precedence over uteroplacental flow, but no one has measured fetal temperature in such circumstances. We predict that pregnant animals actively will defend the thermal welfare of their fetuses but not if doing so risks their own survival.

**Perspective**

At full term, the masses of the ewe and her lamb are similar to those of human mothers and infants, and, like humans, sheep usually carry one or two fetuses. On the basis of our observations, and those of others, on pregnant sheep, we may speculate about the consequences of thermal stress for human fetal welfare. If the cardiovascular responses of pregnant women are similar to those of sheep, the late-gestation human fetus is at greatest thermal risk during maternal fever (14, 16). We expect maternal cold exposure to be of little consequence, provided the mother has access to behavioral means to prevent hypothermia so severe that it might cause abortion. During mild and moderate environmental heat stress and exercise, fetal thermal inertia and uteroplacental blood flow changes are likely to protect fetal homeothermy, but, like ewes, we expect human mothers to sacrifice fetal homeothermy if the stress threatens their own survival. The threshold above which the human mother abandons the thermal welfare of her fetus may be lower than that of ewes, since, even during light exercise in pregnant

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**FETAL TEMPERATURE DURING MATERNAL THERMAL STRESS**

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women, uteroplacental blood flow is unchanged or decreased (19, 23).

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