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REVIEW

# Temperature gradients in female reproductive tissues

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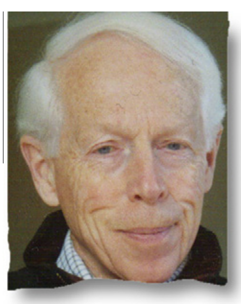

After training in Cambridge, England, and teaching in Edinburgh, Scotland, for some 16 years, RHF Hunter has been professor of veterinary physiology in Montreal, Göttingen, Copenhagen and Hanover. He has a long-standing interest in the events of fertilization and early embryonic development in domestic animals and man.

**Abstract** Deep body temperature in mammals is generally but incorrectly regarded as uniform. Alterations of temperature in oviducts and preovulatory Graafian follicles may play a vital role in gamete maturation, fertilization and early embryonic development. At a molecular level, the conformation of regulatory proteins is susceptible to changes in temperature. Deviation from physiological temperature during IVF procedures could thereby exert a profound influence on patterns of gene expression as the embryonic genome unfolds during early cleavage stages and act to generate specific anomalies. Systematic studies are urgently required.


**KEYWORDS:** embryo, fertilization, gametes, gene expression, oviduct

## Introduction

Most reproductive biologists have not reflected seriously on a potential involvement of temperature in the diverse processes that they study. Indeed, in the present author's experience, asking an audience of reproductive biologists to suggest spheres in which considerations of temperature might be relevant, there are usually just two responses: the cooling potential of scrotal testes and the mid-cycle elevation of body temperature in women. Seldom do such biologists recall the influence of ambient temperature during incubation of an embryo on sex determination in turtles, alligators, crocodiles and some lizards. This apparent lack of information or reflection is all the more surprising if one accepts that reproductive studies are now firmly established on a molecular stage.

A second reason for concern, especially in the case of domestic animal research, is the widespread assumption that deep rectal temperature is an accurate reflection of deep body temperature and that such temperature is uniform in and across the abdominal organs. As one consequence, studies performed in systems of culture, such as IVF and early development of the embryo, invariably use incubator settings that match deep rectal temperature and are held constant. Nonetheless, perusal of the literature on measurements of temperature in mammalian reproductive tissues gives guidance that should not be overlooked, not least in a context of gamete maturation and molecular embryology.

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Major questions remain concerning male mammals, such as the temperature of intra-abdominal testes and that of succeeding regions of the epididymal duct in scrotal mammals, but this short essay will focus on female mammals and their reproductive tissues. Temperatures have been measured in genital ducts and gonads by means of thermistor probes and/or infra-red sensing.

## Temperature gradients in the oviduct

Regional differences in temperature have been reported within the genital tract of three species and these are greatest in the oviduct of oestrous animals in the hours before ovulation. The caudal region of the isthmus may be 1–2°C cooler than the cranial portion of the ampulla (reviewed in Hunter (2009); **Table 1**). Sperm passage from warmer uterus through the uterotubal junction into cooler isthmus would contribute to reduced motility and a sperm storage function of the caudal isthmus during the preovulatory interval (Hunter, 2011; Hunter and Nichol, 1986; Suarez, 2007, 2008). The magnitude of the temperature gradient changes according to the stage of the oestrous cycle and, in particular, close to the time of ovulation. A peri-ovulatory increase in isthmus temperature would influence sperm activation and sperm surface architecture, not least by prompting the transmembrane migration of protein molecules. Even though spermatozoa may swim up an oviduct temperature gradient from cooler to warmer, this does not necessarily infer thermotaxis (Bahat et al., 2003). Indeed, such a putative role of thermotaxis has been challenged with a series of experimental observations (Hunter, 2009).

## Temperature gradients in the ovary

Temperature gradients have also been noted across ovarian tissues (**Table 1**). These may be accentuated at specific stages of an oestrous or menstrual cycle. In brief, preovulatory follicles were 1–2°C cooler than neighbouring ovarian tissues in rabbits and women (Grinsted et al., 1980, 1985). Preovulatory follicles in pigs were 1.3–1.7°C cooler than adjoining ovarian tissues (Hunter et al., 1997, 2000) and both ovarian compartments were cooler than rectal and jugular temperatures. There were no exceptions in a total of 73 observations. In cattle, Graafian follicles of 15–18 mm diameter were 1.5°C cooler than neighbouring ovarian tissues (Greve et al., 1996).

Despite shortcomings in the techniques employed to make the above observations, gradients in temperature clearly exist between different regions of the same oviduct and different regions of the same ovary. Their magnitude remains to be measured with precision, bearing in mind that the extent of such gradients may vary with the stage of the oestrous or menstrual cycle. As with other cyclic reproductive phenomena, variations in temperature in genital tissues are influenced by the pattern of ovarian steroid secretion (Hunter et al., 2006).

## Generation of gradients in temperature

Factors involved in generating temperature gradients deep within the abdomen include the relative distribution of blood flow, regional contractile activity of the myosalpinx and specific endothermic reactions (Hunter, 2009). Compared with the oviduct isthmus, the ampulla has an extensive capillary bed with marked dilatation of blood vessels late in the follicular phase as ovarian oestradiol secretion peaks. At this time, contractile activity of the ampulla exceeds that of the isthmus. Differences in the vascular bed and contractile activity could therefore contribute to temperature differences between the isthmus and ampulla. Countercurrent heat exchange mechanisms would underlie their maintenance (Einer-Jensen and Hunter, 2005).

More significant, however, could be the involvement of macromolecular secretions in the duct. As preovulatory follicles grow and mature and secrete increasing titres of oestradiol, viscous glycoproteins derived from the endosalpinx accumulate in the lumen of the caudal isthmus. If such secretions support endothermic reactions, as discussed below for ovarian macromolecules, they would offer a specific means of regional cooling. Such secretions are dissipated early in the luteal phase of the cycle, as oedema of the mucosa diminishes, the myosalpinx relaxes and the embryo progresses along the isthmus to the uterus.

**Table 1** The magnitude of temperature gradients recorded in female reproductive tissues around the time of ovulation.

| *Organ and location* | *Measurement method* | *Reference* | *Species* | *Overall difference in temperature (°C)* | *Comment* |
|---|---|---|---|---|---|
| Oviduct: isthmus versus ampulla | Indwelling probes | Bahat et al. (2003) | Rabbit | 0.8–1.6 | Isthmus always cooler than ampulla |
| | | Hunter and Nichol (1986) | Pig | 0.2–1.6 | |
| Ovary: preovulatory follicles versus ovarian stroma | Microelectrodes and/or acute thermosensing | Grinsted et al. (1980) | Rabbit | 1.4 | Mature follicles always cooler than stroma |
| | | Grinsted et al. (1985) | Human | 2.3 | |
| | | Greve et al. (1996) | Cow | 1.5 | |
| | | Hunter et al. (1997, 2000) | Pig | 1.3–1.7 | |