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The uterine tubal fluid: secretion, composition and biological effects

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Abstract

Gamete transport, sperm capacitation, fertilization, and early embryo development are all physiological events that occur in a very synchronized manner within the uterine tubal lumen. The tubal fluid that bathes the male and female gametes allows these events to occur *in vivo* much more successfully than *in vitro*. Collection of tubal fluid from domestic females has been performed by different methods. The amount of fluid secreted by the uterine tube increases during estrus and decreases during diestrus and pregnancy. The ampulla produces approximately two thirds of the total daily secretion, while the isthmus supplies the rest. Steroid hormones qualitatively and quantitatively modify the tubal fluid, through both a direct effect on epithelial cells and indirectly through their action on the vascular bed. Estrogen predominantly stimulates while progesterone inhibits tubal fluid secretion. The concentration of nutrients in tubal fluid is generally below plasma concentrations which suggests an overall transport of nutrients across the tube, mainly by diffusion. High potassium levels in the tubal fluid seem to be constant across species and is an important factor to consider when designing fertilization culture medium. The main energy substrates in tubal fluid are glucose and pyruvate derived from blood, although some sucrose and lactate are also present. In the rabbit tube, 25% of lactate is filtered from the blood and 75% is produced from vascular glucose by the tubal epithelial cells. Twenty-five free amino acids were present in the tubal fluid of cows, ewes, pigs, rabbits, and mice. Glycine was found in the highest concentrations in all the species studied, but levels of free amino acids varied across species and also during the estrous cycle. Protein concentration in the fluid is approximately 10-15% of that in serum. Albumin and immunoglobulin G, derived from the blood stream, are the most common proteins representing about 95% of the total protein of the tubal content. Tubal-specific glycoproteins produced by the epithelial cells have been identified and characterized in several species. Prostaglandins, steroid hormones, and growth factors have also been found in the tubal fluid and likely play important roles in tubal events. Continuous changes that occur in the secretory patterns throughout the estrous cycle and among the different regions of the tube indicate the existence of systemic and local controlling mechanisms of tubal fluid production.

Keywords: uterine tube, oviduct, fluid, composition, secretion, fertilization

Introduction

The uterine tube provides the appropriate environment for oocytes, spermatozoa transport, fertilization, and early embryo development. When attempts to reproduce any of these events outside the tubal lumen are made, dramatic drops in efficiency are consistently seen. This limitation is particularly strong in the mare, where a repeatable *in vitro* fertilization method has not yet been developed. Part of this problem may be due to the lack of knowledge of the tubal environment. Studies on physiology and fluid composition of the uterine tube, from very basic measurements (temperature, pH, osmolarity) to highly sophisticated techniques (e.g. growth factors gene expression), have been performed widely in the last 20 years. These studies revealed a great degree of complexity in the tubal physiology. Cyclical and regional variations in tubal secretion have been seen within species. This review will cover the major characteristics of the tubal environment of domestic, laboratory animals, and humans focusing on the collection, formation, regulation, composition, and biological effects of the tubal fluid.

Collection of tubal fluid

Collection of normal and physiologic tubal fluid has been performed in various ways for research purposes. The most frequently used technique is by means of a surgically installed cannula in the lumen of the tube *in vivo* which allows the collection of fluid from domestic females at different reproductive stages and for a long period of time. Another approach is by using *in vitro* preparations of tubes and perfusing them with medium through the ovarian artery. In this way, vascularly perfused tubes, which can be maintained viable for up to 3 hours, have been used to study the formation and composition of tubal fluid in rabbits and women (Leese and Gray, 1985; Dickens and Leese,

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1994, Dickens *et al*., 1995; Tay *et al*., 1997). Luminal tube samples have also been collected under anesthesia with a micropipette from the ampulla and ampullary-isthmic junction of pigs. In a series of experiments, the tubes of anaesthetized rabbits were cannulated at each end, and a fixed volume of saline solution was recirculated through the lumen for 4 h in order to study the movement of amino acids (Leese *et al*., 1979) and energy substrates (Leese and Aldridge, 1979) across the tubal epithelium.

Cannulation

Collection of tubal fluid *in vivo* has been performed over the years by a number of authors in different species. This technique involves the surgical installation and fixation of a cannula in the tube (generally at the ampullary end) to collect the fluid over a period of time. Installation of cannulae into the tubes of pigs (Engle *et al*., 1968; Rodriguez-Martinez *et al*., 1983; Archibong *et al*., 1989), cows (Roberts *et al*., 1975, Kavanaugh and Killian, 1988; Gerena and Killian, 1990; Wegner and Killian, 1991), ewes (Black *et al*., 1963; Iritani *et al*., 1969), rabbits (Mastroianni *et al*., 1961; Engle *et al*., 1968; Libersky and Boatman, 1995), mares (Engle *et al*., 1970; 1975; 1984; Campbell *et al*., 1979; Willis *et al*., 1994), monkeys (Mastroianni *et al*., 1961), and women (Lippes *et al*., 1972; Borland *et al*., 1980) has been repeatedly successful for the collection of tubal fluid *in vivo.* The patency of the catheters, in a study involving 23 cannulated cows, varied from 2 to 156 days with an average duration of 68.2 days (Kavanaugh and Killian, 1988). In that study, fluid flow ceased most commonly when a catheter was avulsed from the surgical site (58%) or became occluded with fibrin (14%). Collection of separated ampullary and isthmic fluid has been achieved by dual tubal cannulation in the cow (Kavanaugh *et al*., 1992; Grippo *et al*., 1992; 1994; 1995).

Tubes have been also cannulated for other proposes such as the transfer of oocytes and spermatozoa into the tube. The effect of the cannula on the physiology of the tube was studied in the rabbit. Tubes of recipient rabbit females were cannulated and embryos transferred to recipients several times. When embryos were transferred into cannulated tubes of 18 recipient does, eight of them (44.4%) showed implantation sites 12 days after transfer. A total of thirty-five embryos were transferred to the 8 recipients that had shown implantation sites and 21 of them (60%) had implanted (Sloan and Johnson, 1974b). In addition, a different study also demonstrated that the presence of a cannula in the fimbriated end of the rabbit tube did not alter the lipid and protein balance of the tubal fluid (Sloan and Johnson, 1974a).

The effect of cannulae on oocyte and/or embryo recovery from sheep tubes has been also evaluated (Ball *et al.*, 1979). In this study, three ewes were bilaterally cannulated at the uterine-tubal junction, spermatozoa injected through the cannulae, and fertilized oocytes (4 out of 8) were recovered after flushing. When cannulae were installed near the ampullary-isthmic junction of non-stimulated ewes (n=4), no oocytes were recovered from the tube. The authors suggested that cannulation reduced superovulatory response (measured by counting the number of ovulation points in the ovary by laparotomy) to exogenous gonadotrophins in sheep. This effect was also confirmed in rabbits: 8.6 ovulations in superovulated cannulated rabbits versus 25.6 ovulations in superovulated non-cannulated rabbits. In the same study, concentrations of LH and progesterone detected in blood plasma were not affected by the presence of the cannulae, and cannulated animals showed normal cycle lengths. The cannulae were still patent in animals sacrificed more than 6 months after their installation.

Similar studies cannulating tubes in the cow have been conducted. The tubes of a recipient cow were surgically cannulated into the ampulla (about 5 cm) through the ostium abdominale tubae, and 2 embryos were transferred to the uterus of the recipient through the cannula. The recipient female became pregnant and gave birth to a live, normal calf. After the birth, the cannula was found to still be patent (Jillella et al., 1977). In mares, cannulation of tubes was used successfully to collect tubal fluid, but its effect on the fertility has not been studied. These studies are summarized in Table 1. The studies described above demonstrated that although cannulation of the tubes may appear as an invasive technique and could alter the normal tubal environment; fertilization, cleavage, and subsequent implantation can still take place in females with cannulated tubes. In conclusion, tubal fluid collected by cannulation may be studied as a reliable representation of the *in vivo* tubal environment.

Table 1. Effect of cannulation on uterine tubal function.

Rabbit	Sheep	Cow
8 cannulated does	3 cannulated ewes	1 cannulated cow
21/35 (60%) implantation rate of embryos transferred through cannula	4/8 (50%) fertilization rate of oocytes inseminated through cannula	1 normal calf of 2 embryos transferred through cannula
Sloan and Johnson, 1974b	Ball *et al*., 1979	Jillella, *et al*., 1977

Formation and secretion rates

The tubal fluid is a complex medium formed by a combination of selective transudate from the blood and secretory products from the epithelial cells (Leese, 1988, Malayer *et al*., 1988). The concentration of nutrients in tubal fluid is generally below their plasma concentrations (Leese and Barton, 1984), which suggests that their overall transport across the tube occurs principally by diffusion (Leese and Gray, 1985). Components of the tubal fluid such as ions (Brunton and Brinster, 1971; Brunton, 1972), albumin (Glass, 1969), immunoglobulins (Parr and Parr, 1986), glucose, and pyruvate (Leese and Gray, 1985) are considered to be transferred from blood while a number of specific tubal proteins are known to be produced by the epithelial cells (Gandolfi *et al*., 1993).

The production of tubal fluid in the rabbit was measured by a transmural potential difference between the serosa (positive) and the lumen (negative). An increase in this potential difference was associated with a decrease in the production of tubal fluid, and this inhibition was mediated by cAMP (Gott *et al*., 1988). In humans, there is enough evidence to indicate that the major driving force for human tubal fluid formation is the trans-epithelial secretion of chloride ions into the tubal lumen, and that extracellular ATP is a potential modulator of this secretion (Dickens *et al*., 1996; Downing *et al*., 1997). It was proposed that adrenergic agonists and cAMP modulate rabbit tube fluid formation in part via trans-epithelial chloride transport. (Dickens *et al*., 1993). For a more detailed explanation on the mechanisms that underline tubal fluid secretion and the effect of some of its modulators see Leese *et al*. (2001).

In addition to the secretory properties of the tubal epithelium, it appears to have also some absorptive functions. Villin, a 95-kDa actin-associated protein considered to be a typical marker of absorptive cells (Bretscher *et al*., 1981), was detected in the proximal portion of the mouse uterine tube (preampulla, ampulla, and part of the isthmus) suggesting the possible absorptive function (Horvart *et al*., 1990). The idea of the bidirectional nature of molecular movement across the tubal epithelium had previously been proposed by Leese (1988).

Secretory rates

Steroid hormones qualitatively and quantitatively modify the tubal fluid, through both a direct effect on epithelial cells and indirectly through their action on the vascular bed (Jansen, 1984). Estrogen predominantly stimulates while progesterone inhibits tubal fluid secretion (Perkins, 1974). Commonly, the amount of fluid produced by the tube increases during estrus, and decreases during diestrus and pregnancy (Table 2). The amount of fluid secretion can dilute the concentration of certain components such as non-protein nitrogen and lactic acid (Iritani *et al*., 1971). In ovariectomized ewes, estrogen treatment increased tubal fluid secretion, whereas progesterone decreased and even antagonized the effect of estrogen (McDonal and Bellvé, 1969).

In a study conducted by Kavanaugh and Killian (1988) in cannulated cows, typical fluid volumes collected ranged from 0.1 to 3 mL per day depending on the estrus cycle stage. The secretory activity of the ampulla in cows and rabbits is more intense than that of the isthmus. The ampulla produces approximately two thirds of the total daily secretion, while the isthmus supplies the rest (David *et al*., 1969; Kavanaugh *et al*., 1992). Secretion rates of tubal fluid for some species are given in Table 2.

Table 2. Uterine tubal fluid secretion rates during estrus and diestrus (mL/24h).

Species	Estrus	Diestrus	References
Cow	4.46	1.43	Olds and VanDenmark, 1957a
Cow	1.54	0.77 [a]	Kavanaugh *et al*., 1992
Mare	5.08	2.82	Campbell *et al*., 1979
Pig	6.2 [b]	---	Archibong *et al*., 1989
Pig	2.7	---	Engle *et al*., 1968
Pig	1.19	0.35	Wiseman *et al*., 1992
Rabbit	0.89	0.07 [c]	Iritani *et al*., 1971

[a] Approximated value.
[b] Volume secreted during 4 days from both oviducts cannulated and ligated at the uterine-tubal junction.
[c] Pseudopregnancy.

Uterine tubal fluid composition

Ions

Concentrations of ions in tubal fluid tend to be similar to those in serum for the majority of the species, with some exceptions. Human tubal fluid had consistently higher concentrations of potassium and chloride than serum (Lippes *et al*., 1972; David *et al*., 1973; Borland *et al*., 1980). Similarly, potassium levels in cows were considerably higher in tubal fluid than in

plasma being the highest at or near estrus (Olds and VanDenmark, 1957a). High potassium levels in tubal fluid seem to be constant across species and it is an important factor to consider when designing fertilization culture medium. In a mouse *in vitro* fertilization (IVF) system, more pregnancies were obtained by using a medium formulated on the composition of human oviductal fluid (HOF) than with Tyrode's medium (which contains a lower concentration of potassium). Decreasing potassium content of HOF to that present in Tyrode's decreased the number of developing mouse embryos (Quinn *et al*., 1985).

Calcium concentrations of cow isthmic tubal fluid were significantly higher than those in ampullary fluid, and increased over plasma levels at ovulation (Grippo *et al*., 1992). In contrast, calcium in human tubal fluid tended to be lower than in serum (Borland *et al*., 1980). In the cow, magnesium concentrations differed significantly according to estrous cycle stage but not by uterine tubal region and were consistently lower than in serum (Grippo *et al*., 1992). Surprisingly, magnesium concentration in mare tubal fluid was reported to be 2 to 5 times higher than the mean plasma concentration (Campbell *et al*., 1979) and is apparently much higher than in the other species (see Table 3). Table 3 shows the concentrations of ions in the tubal fluid of some evaluated species.

Table 3. Concentrations of ions in the uterine tubal fluid of various species collected from ampulla, isthmus, or the whole tube (mEq/L).

	Cow		Cow	Ewe		Rabbit	Rabbit	Human	Human	Human	Mare
	Ampulla	Isthmus	Whole	Ampulla	Isthmus	Whole	Whole	Whole	Whole	Whole	Whole
Na	140.9	159.3	86.1	135	141	127.8	189.7	130	145	139.5	129.5
Cl			112.7			115.4	332.2	132	119.5	118	
K	4.53	4.24	65.7	8.12	6.9	5.6	16.8	21.1	6.7	8.8	7.9
Ca	1.83	2.64	3.19	7.6	5.96	7.98	2.71	1.13		2.13	2.28
Mg	0.662	0.685		1.18	1.08	0.141	0.473	1.42		0.61	4.59
S								12.3			
P			3.0			0.193		8.69			0.366
Zn						0.099	0.0046				
Bicarbonate							16.55				
References	Grippo *et al*., 1992		Olds and VanDenmark, 1957b	Restall and Wales, 1966; 1968.		David *et al*., 1969	Hamner and Williams, 1965	Borland *et al*., 1977	David *et al*., 1973	Lippes *et al*., 1972	Campbell *et al*., 1979

Energy substrates

Glucose, pyruvate, and lactate have been found in the tubal fluid of all the species that have been examined so far (Nichol *et al*., 1992). The purpose of glucose, pyruvate, sucrose, and lactate in the tube is to nourish the oocyte, spermatozoa, and early embryo as they travel through the tube (Leese and Gray, 1985). The main energy substrates in tubal fluid are glucose (Brewis *et al*., 1992) and pyruvate derived from blood although some sucrose and lactate are also present. In the rabbit tube, 25% of lactate is filtered from the blood, and 75% produced by the tubal epithelial cells from vascular glucose. Also, pyruvate can be synthesized by the tubal epithelium from glucose or lactate (Nichol *et al*., 1992).

Pyruvate, lactate, glucose, and sucrose were transported into the rabbit tubal lumen at different rates and a proportion of lactate entering the lumen was synthesized within the tube from vascular glucose (Leese and Gray, 1985). Facilitated diffusion moves glucose across the epithelium (Leese and Jeffries, 1977), and chloride ions have been shown to be involved in mediating the secretion of tubal fluid (Dickens and Leese, 1994). All segments of the tube appear to have slightly different percentages of fluid composition (Nichol *et al*., 1992). The levels of glucose, pyruvate, and lactate were 1.8 times higher in the ampulla than in the isthmus due to the greater surface area of the ampulla (Leese, 1983). The ampullary-isthmic junction is thought to be the site of fertilization. The ovulated oocyte or early embryo spends the majority of its tubal stay in this middle region of thetube, the ampullary-isthmic junction (Nichol *et al*., 1992). The greater output of glucose by the ampulla is therefore able to sustain the embryo until it passes into

the uterus.

The levels of lactate and glucose in human tubal fluid also varied depending on the day of the estrous cycle (Gardner *et al*., 1996). Glucose levels in the pig tubal fluid were found to decrease dramatically after ovulation (Nichol *et al*., 1992, 1998). In addition, the presence of embryos did not affect the glucose, pyruvate, and lactate concentrations in fluids from the ampulla or ampullary-isthmic junction of unilaterally ovariectomized pigs. Consequently, the levels of these energy substrates in the tubal fluid of pigs appear to be regulated by systemic mechanisms (Nichol *et al*., 1998). In contrast, the pH profile of the tube seems to be controlled by both systemic and local mechanisms such as the presence of embryonic factors (Nichol *et al*., 1997).

Similar to what was observed in the pig, a decrease in glucose concentration in rabbit tubal fluid occurs at three days after mating which coincides with the embryo's entrance into the uterus. Thus, the time when the need for glucose in the tube is no longer present (Edwards and Leese, 1993). Table 4 shows the concentration of glucose, lactate and pyruvate in the tubal fluid of some species.

Table 4. Concentration of energy substrates in uterine tubal fluid of some species (mM).

	Mouse	Ewe	Sow		Human	Cow	Mare
			Ampulla	Isthmus			
Glucose	3.4	1.57-1.76	0.25-097	0.17-1.65	0.53	0.02-0.04	2.84-5.92
Lactate	4.7	1.67-2.51	3.86-6.83	4.93-6.48	8.58		
Pyruvate	0.37	0.15	0.17-0.22	0.17-0.22	0.17		
References	Gardner and, Leese, 1990	Hamner, 1973	Nichol *et al*., 1992		Dickens *et al*., 1995	Carlson *et al*., 1970	Campbell *et al*., 1979

Amino acids

A total of 20 free amino acids were found in bovine tubal fluid (Stanke *et al*., 1974), but a later study showed that 25 free amino acids were present in the tubal fluid of cows, ewes, pigs, rabbits and mice (Guérin *et al*., 1995b). In mare tubal fluid only 17 amino acids were measured, and their concentrations were greater than in either plasma or follicular fluid (Engle *et al*., 1984). Glycine was found in highest concentrations in all the species studied, but levels of free amino acids varied across species and also during the estrous cycle (Guérin *et al*., 1995b, Engle *et al*., 1984, Moses *et al*., 1997, Menezo and Laviolette, 1971). A study by Nancarrow *et al*. (1992) demonstrated that most of the amino acids (methionine, leucine, phenylalanine, lysine, aspartic acid, glycine, alanine, taurine, tyrosine) in tubal fluid of sheep were higher than in plasma, while others (threonine, serine, ornithine) were at lower concentrations. In *in vivo* studies with anesthetized rabbits, Leese *et al*. (1979) found that 23 amino acids appeared in increasing concentrations during the time fluid was recirculating through the tube until reaching the average 27% of that in the plasma with glycine and alanine present in the greatest amounts. In addition, the movement of 6 neutral amino acids appeared to be enhanced relative to their plasma concentrations following ovulation.

Free amino acids in the tubal fluid seem to be important for gamete unction and embryo survival. Synthetic oviductal fluid (SOF) supplemented with amino acids at *in vivo* oviductal fluid concentrations allowed the development of a higher percentage of ovine blastocysts compared with SOF with 2% human serum or SOF with bovine serum albumine (Walker *et al*., 1996). The total concentration of amino acids found in human serum and follicular fluid were about one-third to one-half of the concentrations present in two conventional media used for IVF Ham's F-10 and MEM. The use of a modified human tubal medium, containing amino acids at concentrations found in human follicular fluid, was more effective for culturing mouse embryos than the other two commercial media (Nakazawa *et al*., 1997). Hypotaurine, a sulfonic amino acid, is known to have protective effects against peroxidative cellular damage (Aruoma *et al*., 1988, Baker *et al*., 1996, Green *et al*., 1991). In addition, taurine and hypotaurine seem to be important compounds for sperm survival, capacitation, fertilization, and embryo development and are present in both sperm and genital secretions (Guerin and Menezo, 1995). Hypotaurine and taurine are secreted by cow, sow, goat, and rabbit tube epithelial cell monolayers (Guerin and Menezo, 1995). The enzyme cysteine sulfinate decarboxilase, identified in cow and goat tube epithelial monolayers, seem to be responsible for their production of the amino acid cysteine via the cysteine sulfinic acid pathway (Guérin *et al*., 1995a). Concentrations of free amino acids in tubal fluid of various species are given in Table 5.

Table 5. Amino acid concentrations in tubal fluids of various species (μM/mL).

Amino Acid	Mouse	Rabbit	Rabbit	Ewe	Ewe	Pig	Cow	Mare
3-methyl histidine	0.000	0.020	ND	0.019	ND	0.000	0.017	ND
Alanine	0.506	0.475	0.469	0.241	0.440	0.171	1.263	0.140
Arginine	0.023	0.024	0.064	0.048	0.140	0.059	0.202	0.031
Asparagine	0.014	0.036	ND	0.016	0.020	0.011	0.012	ND
Aspartic acid	0.215	0.025	0.024	0.021	0.120	0.004	0.061	0.022
Citrulline	0.020	0.023	ND	0.035	A	0.015	0.048	ND
Cystine	0.002	0.015	0.015	0.0008	B	0.001	0.001	0.003
Glutamic acid	0.497	0.211	0.192	0.047	0.200	0.005	0.361	0.057
Glutamine	0.347	0.272	ND	0.058	0.190	0.034	0.143	ND
Glycine	0.586	2.889	2.766	2.288	2.300	0.875	2.601	0.263
Histidine	0.021	0.070	0.067	0.031	0.070	0.019	0.152	0.020
Hypotaurine	0.141	0.158	ND	0.350	0.350	0.196	0.155	ND
Isoleucine	0.024	0.053	0.069	0.036	0.130	0.024	0.179	0.025
Leucine	0.043	0.099	0.129	0.083	0.250	0.033	0.352	0.053
Lysine	0.093	0.060	0.165	0.090	0.210	0.066	0.417	0.053
Methionine	0.029	0.032	0.022	0.014	0.050	0.007	0.075	0.014
Ornithine	0.028	0.015	ND	0.022	B	0.018	0.098	ND
Phenylalanine	0.033	0.051	0.065	0.030	0.180	0.013	0.154	0.026
Proline	0.141	0.102	C	0.047	0.300	0.001	0.200	0.048
Serine	0.136	0.201	0.318	0.024	0.040	0.050	0.121	0.051
Taurine	2.000	0.074	0.123	0.047	0.040	0.236	0.091	ND
Threonine	0.187	0.154	0.125	0.013	A	0.020	0.081	0.038
Tyrosine	0.032	0.066	0.079	0.032	0.150	0.014	0.123	0.041
Tryptophan	0.001	0.008	Undetectable	0.002	0.070	0.000	0.016	ND
Valine	0.104	0.169	0.172	0.079	0.250	0.036	0.250	0.041
References	Guerin *et al*., 1995b	Guerin *et al*., 1995b	Iritani *et al*., 1971	Guerin *et al*., 1995b	Moses *et al*., 1997	Guerin *et al*., 1995b	Guerin *et al*., 1995b	Engle *et al*., 1984

ND: not determined
A: Citrulline + Threonine: 0.140
B: Cystine + Ornithine: 0.050
C: Cystine + Proline: 0.086

Proteins

Protein concentration in tubal fluid is approximately 10-15% of that in serum Leese 1988). Albumin and immunoglobulin G, derived from the blood stream, are the most common proteins representing about 95% of the total protein of the tube content (Oliphant *et al*., 1978).

Oviduct-specific glycoproteins (OGP) have been identified and characterized in several species such as the mouse (Kapur and Johnson, 1985; 1986), hamster (Leveille *et al*., 1987; Oikawa *et al*., 1988; Abe *et al*., 1992), rat (Abe and Abe, 1993), sheep (Sutton *et al*., 1984a; 1986), pig (Buhi *et al*., 1989), cow (Malayer *et al*., 1988; Boice *et al*., 1990a; Gerena and Killian, 1990), goat (Gandolfi *et al*., 1993; Abe *et al*., 1995a), baboon (Fazleabas and Verhage, 1986; Verhage and Fazleabas, 1988; 1989), and humans (Verhage *et al*., 1988; Wagh and Lippes, 1989). Although no biological function has been demonstrated for these proteins, some of them have been found to be associated with the zona pellucida or cytoplasm of ovulated oocytes, early embryos (Brown and Cheng 1986; Hedrick *et al*., 1987; Kapur and Johnson, 1988; Kan *et al*., 1988; 1989; Gandolfi *et al*., 1989; 1991, Abe and Oikawa, 1990; Boice *et al*., 1990b; 1992; Wegner and Killian, 1991; Abe *et al*., 1995a; Staros and Killian, 1998), or the spermatozoa surface (Sutton *et al*., 1984b; Lippes and Wagh, 1989; McNutt *et al*., 1992; King and Killian, 1994; King *et al*., 1994; Abe *et al*., 1995b). The amount of tubal glycoproteins varies with the stage of the estrous cycle with higher concentrations during the periovulatory period. Estrogen stimulates synthesis and secretion of oviduct-specific glycoproteins in the golden hamster whereas progesterone seems to have little effect (Abe *et al*., 1998).

Protein secretion in the tube varies by region. The ampulla and the isthmus secrete many similar proteins; however, they each have different characteristics (Abe, 1996). The origin of proteins found in the tube is from two sources: 1) most are filtered from the blood and 2) the rest synthesized from the

epithelium. Although the exact function of tubal proteins remains unknown, it is speculated that these regional proteins have a specific role in the support of each region of the tube. Most of the oviduct-specific glycoproteins originate from the non-ciliated secretory cells in the tubal epithelium. Immunochemical studies have located glycoproteins in the secretory granules of secretory cells. Regional differences in the localization of these glycoproteins have been shown repeatedly (Kapur and Johnson, 1986; 1988; Abe and Oikawa, 1991; Abe, 1996; Gandolfi *et al*., 1991), indicating an important degree of regional specificity in glycoprotein synthesis. A very thorough review on the characterization and biological roles of oviduct-specific, oestrogen-dependent glycoprotein in the mammalian uterine tube was published by Buhi (2002).

Binding of bovine spermatozoa to glycoproteins in the tubal fluid has been shown to induce capacitation (McNutt *et al*., 1992). The binding of sperm cells to isthmic tubaric epithelial cells *in vitro* changed the types and quantities of proteins secreted by the tubal cells (Ellington *et al*., 1993). It has been hypothesized that another function of the tubal fluid proteins is associated with the release mechanism of the spermatozoa, which are bound to the epithelial cells of the tubal lumen (Gandolfi, 1995). Exposure of *in vitro*-matured pig oocytes and/or spermatozoa to porcine OGP (pOGP) decreased polyspermy and sperm binding to the zona pellucida but maintained high penetration rates of pig oocytes fertilized *in vitro*. In addition, pOGP showed an embryotrophic effect by enhancing cleavage and blastocyst formation when added to the embryo culture medium of *in vitro*-produced porcine embryos (McCauley *et al*., 2003).

High-density lipoproteins (HDL) of the tubal fluid from the follicular phase of the estrous cycle have a sperm capacitating effect *in vitro* (Ehrenwald *et al*., 1990). HDL are thought to be involved in sperm capacitation as an acceptor of sperm cholesterol efflux from the plasma membrane (Ehrenwald *et al*., 1990).

In a study in the golden hamster, an oviduct-specific glycoprotein designated as hamster oviductin-1, was localized in the putative secretory granules of non-ciliated cells. This glycoprotein is transferred to the zona pellucida of the oocyte during transit through the tube and later appears to be internalized by the blastomeres of the embryo and further processed through the endosomal/lysosomal pathway (Kan *et al*., 1988; 1989; 1993). In cattle, a 97- kDa oviduct-specific glycoprotein was detected in the secretory cells of the ampulla and the isthmus (Boice *et al*., 1990a). In sheep, a very similar glycoprotein of 92- kDa was found only in non-ciliated secretory cells of the ampulla and not in the isthmus (Gandolfi *et al*., 1991). Since this glycoprotein was only found in the secretory granules of the secretory cells of the ampullary region, it indicates that this glycoprotein is produced exclusively by the region of the tube in which fertilization and early embryonic development take place (Abe, 1996).

Prostaglandins

Free prostaglandin (PG) F2 alpha was detected in the tubal fluid, in the epithelium and lamina propria of the fimbria, and in the ampulla of human uterine tubes (Ogra *et al*., 1974). Concentrations of prostaglandin F were measured in tubal fluid of the ewe, and no relationship was seen with the stage of the estrous cycle (Warnes *et al*., 1978). However in the pig, day to day fluctuations of PGF2 alpha were evident and a consistent pattern was found between concentration and the stage of the estrous cycle. The highest concentrations were detected on the second day of standing heat (Rodriguez-Martinez *et al*., 1983).

Prostaglandins E and F increased significantly in the fimbria of rabbit tubes immediately before ovulation indicating a possible role in the process of ovum pick up (McComb and Moon, 1985). In human uterine tubes, prostaglandins E and F concentrations increased along the tube, with lower concentrations in the utero-tubal junction and maximum in the fimbria. These PGs increased during the luteal phase about two times greater than during the follicular phase (Nieder and Agustin, 1986). Also in human tubes, the number of binding sites for PGE2 and PGF2 alpha was greater in the isthmus than in the ampulla and was higher during the luteal phase (Sato, 1988). Chorionic gonadotropin seems to stimulate the production of PGs from the tubal mucosa. PGE2 inhibits tube contractions and stimulates the ciliary beat frequency in the oviducts (Coutinho and Maia, 1971; Spilman and Harper, 1975; Nozaki and Ito, 1986) which may be necessary for fertilization and embryo uterine tubal transport. Increasing levels of hCG resulted in an increase in the mRNA and protein of cyclooxygenase-2 and a subsequent increase in PGE2 production by mucosa cells of human tubes (Han *et al*., 1996). On other hand, the production of PGF alpha from bovine tubal epithelial cells is under the inhibitory regulation of growth hormone (GH) and insulin like growth factor I (IGF-I) (Makarevich and Sirotkin, 1997).

Steroid Hormones

Concentrations of progesterone in the tubal fluid of hamsters close to ovulation were significantly lower than in follicular fluid but higher than in serum (Libersky and Boatman, 1995). Estradiol concentrations in rabbit tubal fluid during estrous and pseudopregnancy were similar to those in serum. In contrast, progesterone concentrations in tubal fluid were similar to that in serum during estrus but lower during pseudopregnancy (Richardson and Oliphant, 1981). The amounts of estradiol and progesterone receptors in the pig uterine tube were measured during the estrous cycle. Estradiol and progesterone receptors followed a similar pattern, increasing during estrus and decreasing thereafter, but

their concentrations varied significantly between the ampulla and isthmus (Stanchev *et al*., 1985).

Growth factors

Growth factors are multifunctional regulators of cellular proliferation, differentiation, and invasiveness (Simmen and Simmen, 1991). There is clear evidence that several growth factors are involved in early embryogenesis as well as in other reproductive processes such as trophoblast growth, endometrial cell differentiation, conceptus invasiveness, regulation of steroidogenesis, along with others (Simmen and Simmen, 1991). Several studies have demonstrated the presence of growth factors, growth factor receptors, and growth factor binding proteins in the uterine tubal tissue and/or fluid of human and other species. This information is summarized in Table 6.

Table 6. Growth factors present in tubal fluids of various species.

Growth Factor	Human	Bovine	Ovine	Porcine	Baboon	Mare
Activin β A		X				
Amphiregulin				X		
Acidic FGF		X				
Basic FGF		X	X			
EGF	X	X	N/D	X	X	
EGFR	X	X		X	X	
HB-EGF				N/D		
GM-CSF	X					
GM-CSF αR	X					
GM-CSF βR	X					
IGF 2R		X				
IGFBP1	X	N/D				
IGFBP2	X	X	N/D			
IGFBP3	X	X	X			
IGFBP4	X	X	X			
IGFBP5		X				
IGFBP6		N/D				
IGF-I	X	X	X	X		
IGF-IR	X	X	X			
IGF-II		X	X	X		
Insulin R		X	X			
NGF			N/D			
PDGF		X				X
TGF α	X	X	X	X	X	
TGF β1			X			

References. **Humans**: Chegini *et al*., 1994; Zhao and Chegini, 1994; Pfeifer and Chegini, 1994; Smotrich *et al*., 1996; Adachi *et al*., 1995. **Bovine**: Viuff *et al*., 1995; Makarevich and Sirotkin, 1997; Gandolfi *et al*., 1995 ; Xia *et al*., 1996 ; Winger *et al*., 1997; Modina *et al*., 1997. **Ovine**: Watson *et al*., 1994; Stevenson and Wathes, 1996. **Porcine**: Wiseman *et al*., 1992; Swanchara *et al*., 1995; Kennedy *et al.*, 1994; Wollenhaupt *et al*., 1997. **Baboon**: Schell *et al*., 1994. **Mare**: Eriksen *et al*., 1994.

FGF: fibroblast growth factor; EGF: epidermal growth factor; EGFR: epidermal growth factor receptor; HB-EGF: heparin-binding epidermal growth factor; GM-CSF: granulocyte macrophage colony stimulating factor; IGF: insulin-like growth factor; IGFBP: insulin-like growth factor binding protein; PDGF: platelet derived growth factor; TGF: transforming growth factor; N/D: not detected.

Contents of IGF-I and -II in pig tubal fluid were reported to be greater at estrus than at pre- or post-estrus, although concentrations at both stages remained similar (Wiseman *et al*., 1992). In the ovine tube, mRNA encoding for IGF-I showed a cyclical pattern, increasing sharply during the late follicular phase and then declining (Stevenson and Whates, 1996). The mRNA and proteins of IGF-I, IGF-II, and their binding proteins (IGFBP-2,-3,-4, and –5) were detected in intact bovine tubes as well as in cells cultured in a monolayer and in vesicles (Xia *et al*., 1996; Winger *et al*., 1997). IGF-I, IGF-IR, and IGFBPs 1-4 were detected immunohistochemically in the ampullary and isthmic regions of human tubes. Their intensity was cycle dependent, increasing during the late proliferative and early to mid secretory phases (Pfeifer and Chegini,

1994). EGF, EGFR (EGF receptor), TGF alpha, and Amphireguline (an epidermal growth factor- related peptide) were detected in the pig tube (Kennedy *et al*., 1994, Swanchara *et al*., 1995, Wollenhaupt *et al*., 1997). EGF followed a cyclical pattern of release, increasing in cyclic versus early pregnant pigs (Swanchara *et al*., 1995), and EGFR was higher at day 1 versus day 6 of the estrous cycle (Wollenhaupt *et al*., 1997).

EGF, EGFR (EGF receptor), TGF alpha, and Amphireguline (an epidermal growth factor- related peptide) were detected in the pig tube (Kennedy *et al*., 1994, Swanchara *et al*., 1995, Wollenhaupt *et al*., 1997). EGF showed a cyclical pattern, increasing in cyclic versus early pregnant pigs (Swanchara *et al*., 1995), and EGFR was higher at day 1 versus day 6 of the estrous cycle (Wollenhaupt *et al*., 1997). EGF, TGF alpha, and EGF-R appear to be regulated by estrogen in the baboon (Schell *et al*., 1994) and human tube, and the transcription of mRNA for these three proteins was induced by estrogen (Adachi *et al*., 1995). In the mare, only one study reported the presence of a growth factor PDGF in the tube (Eriksen *et al*., 1994). The presence of growth factors and their receptors in the tubal tissue and on the early embryo suggest the involvement of autocrine and paracrine mechanisms in the processes of fertilization and embryo development.

Biological effects

The uterine tube is generally considered to be the site where capacitation of spermatozoa takes place (Ehrenwald *et al*., 1990). Spermatozoa reside in the lower isthmus for 18-20 hours in cattle (Hunter and Wilmut, 1984), 17-18 hours in sheep (Hunter and Nichol, 1983), 36 hours in pigs (Hunter, 1984), and up to 126 hours in ferrets (Chang, 1965). During this period of time, spermatozoa are found deep in the epithelial folds of the tube (Hunter, 1988). It is thought that capacitation occurs while the spermatozoa are in such close association with the tube epithelial cells (Parrish *et al*., 1989). The binding of spermatozoa to monolayers of epithelial tubal cells or tubal explants have been studied by several investigators in different mammalian species (Gutierrez *et al*., 1993; Dobrinski *et al*., 1996; Sidhu *et al*., 1998). Apparently some glycoproteins are involved in the interaction between tubal epithelial cells and sperm cells. Ball *et al.* (1997) using a panel of 10 fluorescein-isothiocyanate-conjugated lectins, the predominant glycoconjugates found galactosyl residues on mare's tubes. Regional differences between ampullary and isthmic distribution of these galactosyl glycoconjugates were observed among stages of the estrous cycle. Another important process that occurs when the sperm are in the tube is the efflux of cholesterol from the sperm membranes (Eherenwald *et al*., 1988) and the resulting decrease in cholesterol to phospholipids ratio which is an early, key event in the capacitation process that allows the fluidity of the membrane to increase in preparation for the acrosome reaction.

The isthmus of the tube apparently has two functions: 1) a site for sperm storage during the preovulatory period, and 2) a filter to decrease the number of sperm reaching the site of fertilization (Smith and Yanagimachi, 1990). Binding of spermatozoa in the isthmus is dependent on a carbohydrate recognition system between tubal epithelium and sperm membrane lectins. The monosaccharide, fucose, has been found to be important to this recognition system (Lefebvre *et al*., 1997). However, it was concluded by Grippo *et al*. (2000) that bovine tubal fluid does not contain physiologically active levels of free monosaccharides (fucose, galactose, glucosamine, mannose and xylose). Therefore, the monosaccharide fucose may be polymerized or bound to membrane proteins or lipids of the tubal epithelial cells.

Uterine tubal fluid affects gametes differently depending on the region of the tube and the stage of the estrous cycle. According to Grippo *et al*. (1995), the higher calcium concentrations found in isthmic tubal fluid at stages other than the luteal phase may increase the occurrence of the acrosome reaction in bovine spermatozoa. After 14-16 hours of co-incubation, more bovine oocytes were fertilized *in vitro* when spermatozoa were reincubated in isthmic tubal fluid and the oocytes pre-incubated in ampullary tubal fluid (Way *et al*., 1997). Similarly, incubation of ovine oocytes in heat-inactivated tubal fluid during the final period of the maturation process, increased the percentage of *in vitro*-produced embryos developing to live offspring after transferred to female recipients (Libik *et al*., 2002).

Increased oxygen consumption by spermatozoa may be an important part of the capacitation process (Hamner and Williams, 1963). Respiration rates of horse spermatozoa were greater in the presence of tubal fluid than in any other medium *in vitro* (Engle *et al*., 1975). A similar effect was observed when tubal fluid stimulated the respiration of rabbit spermatozoa five-fold *in vitro* (Foley *et al*., 1972). In humans, spermatozoa motility rates were higher when spermatozoa was cultured in the presence of tubal fluid than in follicular fluid or control medium (Zhu *et al*., 1994b). Uterine tubal fluid also prolongs survival of human spermatozoa under *in vitro* conditions (Zhu *et al*., 1994a). The motility and percentage of hyperactivated spermatozoa was higher when tubal fluid was present (Kawakami *et al*., 1998). In pigs, culturing oocytes in 30% of tubal fluid had an increased rate of zona hardening at the time of sperm penetration which may prevent polyspermy and also increase complete cortical granule exocytosis after *in vitro* fertilization (Kim *et al*., 1996).

In conclusion, the uterine tubal environment which creates the necessary conditions for fertilization is a very sensitive and complicated system. Variations in the composition of the tubal fluid among species,

stages of the cycle and tubal regions reveal a great degree of complexity in the tubal physiology. Continuous changes that occur in the secretory patterns throughout the estrous cycle and among the different regions of the tube indicate the existence of systemic and local controlling mechanisms of tubal fluid production.

There is a diversity of chronologically controlled events that occur in the tube: sperm storage, capacitation, sperm release and transport, oocyte pick up, final oocyte maturation, fertilization, early embryo development and embryo transport to the uterus. These sequential events require a very dynamic and well-synchronized support system by the tube in order to occur successfully. Several stimulus-response interactions (gametes-tube, tube-gametes, gametegamete) may be part of the complicated mechanisms that control the tubal physiology. It has been evident that increasing the amount of knowledge about the composition and functions of tubal fluid components has allowed significant advances in the efficiency of assisted reproductive technologies. Developing different media based on the specific composition of the tubal fluid at particular times of the estrous cycle and/or from specific tubal regions may resolve part of the major limitations for developing *in vitro* fertilization and embryo culture systems that allow the production of embryos at comparable rates as those that occur *in vivo*. Further research is necessary to continue advancing in understanding the complexity of the temporal and regional variations in the tubal fluid composition, as well as the physiological interactions among sperm cells, cumulus-oocyte complexes, tubal epithelium and early developing embryos.

References

Abe H. 1996. The mammalian oviductal epithelium: regional variations in cytological and functional aspects of the oviductal secretory cells. *Histol Pathol*, 11:743-768.

Abe H, Oikawa T. 1990. Ultrastructural evidence for an association between an oviductal glycoprotein and the zona pellucida of the golden hamster egg. *J Exp Zool*, 156:210-221.

Abe H, Oikawa T. 1991. Immunocytochemical localization of an oviductal zona pellucida glycoprotein in the oviductal epithelium of the golden hamster. *Anat Rec*, 229:305-314.

Abe H, Abe M. 1993. Immunological detection of an oviductal glycoprotein in the rat. *J Exp Zool*, 266:328-335.

Abe H, Onodera M, Sugawara S. 1995a. Immunological detection and characterization of an estrus-associated antigen in the goat oviduct. *J Exp Zool*, 272:134-141.

Abe H, Satoh T, Hoshi HJ. 1998. Primary modulation by oestradiol of the production of an oviduct-specific glycoprotein by the epithelial cells in the oviduct of newborn golden hamsters. *Reprod Fertil*, 112:157-163

Abe H, Ookata K, Abe M, Oikawa T. 1992. Immunological characterization of oviductal glycoproteins associated with the zona pellucida of the golden hamster egg. *J Exp Zool*, 262:209-218.

Abe H, Sendai Y, Satoh T, Hoshi H. 1995b. Secretory products of bovine oviductal epithelial cells support the viability and motility of bovine spermatozoa in culture in vitro. *J Exp Zool*, 272:54-61.

Adachi K, Kurachi H, Homma H, Adachi H, Imai T, Sakata M, Higashiguchi O, Yamaguchi M, Morishige K, Sakoyama Y. 1995. Estrogen induces epidermal growth factor (EGF) receptor and its ligands in human fallopian tube: involvement of EGF but not transforming growth factor-alpha in estrogen-induced tubal cell growth in vitro. *Endocrinology*, 136:2110-2119.

Archibong AE, Petters RM, Johnson BH. 1989. Development of porcine embryos from one- and two-cell stages to blastocysts in culture medium supplemented with porcine oviductal fluid. *Biol Reprod*, 41:1076-1083.

Aruoma OI, Halliwell B, Hoey BM, Butler J. 1988. The antioxidant action of taurine, hypotaurine and their metabolic precursors. *Biochem J*, 256:251-255.

Baker HW, Brindle J, Irvine DS, Aitken RJ. 1996. Protective effect of antioxidants on the impairment of sperm motility by activated polymorphonuclear leukocytes. *Fertil Steril*, 65:411-419.

Ball BA, Dobrinski I, Fagnan MS, Thomas PG. 1997. Distribution of glycoconjugates in the uterine tube (oviduct) of horses. *Am J Vet Res*, 58:816-822.

Ball PJH, Simkin ME, Foote RH. 1979. Effect of cannulae in the ampulla of the oviduct and in the tubo-uterine junction on reproductive phenomena in sheep. *Theriogenology*, 12:389-398.

Black DL, Dudy RT, Rusen J. 1963. Apparatus for the continuous collection of sheep oviduct fluid. *J Reprod Fertil*, 6:257-260.

Boice ML, Geisert RD, Blair RM, Verhage HG. 1990a. Identification and characterization of bovine oviductal glycoproteins synthesized at estrus. *Biol Reprod*, 43:457-465.

Boice ML, Mavrogianis PA, Murphy CN, Prather RS, Day BN. 1992. Immunocytochemical analysis of the association of bovine oviduct-specific glycoproteins with early embryos. *J Exp Zool*, 263:225-229.

Boice ML, McCarthy TJ, Mavrogianis PA, Fazleabas AT, Verhage HG. 1990b. Localization of oviductal glycoproteins within the zona pellucida and perivitelline space of ovulated ova and early embryos in baboon (papio anubis). *Biol Reprod*, 43:340-346.

Borland RM, Biggers JD, Lechene CP, Taymor ML. 1980. Elemental composition of fluid in the human fallopian tube. *J Reprod Fertil*, 58:479-482.

Borland RM, Hazra S, Biggers JD, Lechene CP. 1977. The elemental composition of environments of the gametes and preimplantation embryo during the initiation of pregnancy. *Biol Reprod*, 16:147-157.

Bretscher A, Osborn M, Wehland J, Weber JK. 1981. Villin associated with specific microfilamentous

structures as seen by immunofluorescence microscopy on tissue sections and cells microinjected with villin. *Exp Cell Res*, 135:213-219.

Brewis IA, Winston RM, Leese HJ. 1992. Energy metabolism of the human fallopian tube. *J Reprod Fertil*, 95:257-262.

Brown CR, Cheng WKT. 1986. Changes in composition of the porcine zona pellucida during development of the oocyte to the 2- to 4-cell embryo. *J Embryol Exp Morphol*, 92:183-191.

Brunton WJ. 1972. Beta-adrenergic stimulation of transmembrane potential and short circuit current of isolated oviduct. *Nature New Biol*, 236:12-14.

Brunton WJ, Brinster RL. 1971. Active chloride transport in the isolated rabbit oviduct. *Am J Physiol*, 221:658-661.

Buhi WC. 2002. Characterization and biological roles of oviduct-specific, oestrogen-dependent glycoprotein. A review. *Reproduction*, 123:355-362.

Buhi WC, Vallet JL, Bazer FW. 1989. De novo synthesis and release of polypeptides from cyclic and early pregnant porcine oviductal tissue in explant culture. *J Exp Zool*, 252:79-88.

Campbell DL, Douglas LW, Ramge JC. 1979. Cannulation of the equine oviduct and chemical analysis of oviduct fluid. *Theriogenology*, 12:47-54.

Carlson D, Black DL, Howe GR. 1970. Oviduct secretion in the cow. *J Reprod Fertil*, 23:549-552.

Chang MC. 1965. Fertilizing life of ferret sperm in the female tract. *J Exp Zool*, 158:87-100.

Chegini N, Zhao Y, McLean FW. 1994. Expression of messenger ribonucleic acid presence of immunoreactive proteins for epidermal growth factor (EGF), transforming growth factor alpha (TGF alpha) and ECG/TGF alpha receptors and 1251-EGF binding sites in human fallopian tube. *Biol Reprod*, 50:1049-1058.

Coutinho EM, Maia H. 1971. The contractile response of the human uterus, fallopian tubes and ovary to prostaglandins in vivo. *Fertil Steril*, 22:539-543.

David A, Serr DM, Czernobilsky B. 1973. Chemical composition of human oviduct fluid. *Fertil Steril*, 24:435-439.

David A, Brackett BG, Garcia C-R, Mastroianni L. 1969. Composition of rabbit oviduct fluid in ligated segments of the fallopian tube. *J Reprod Fertil*, 19:285-289.

Dickens CJ, Leese HJ. 1994. The regulation of rabbit oviduct fluid formation. *J Reprod Fertil*, 100:577-581.

Dickens CJ, Southgate J, Leese HJ. 1993. Use of primary cultures of rabbit oviduct epithelial cells to study the ionic basis of tubal fluid formation. *J Reprod Fertil*, 98:603-610.

Dickens CJ, Comer MT, Southgate J, Leese HJ. 1996. Human fallopian tubal epithelial cells in vitro: establishment of polarity and potential role of intracellular calcium and extracellular ATP in fluid secretion. *Human Reprod*, 11:212-217.

Dickens CJ, Maguiness SD, Comer MT, Palmer A, Rutherford AJ, Leese HJ. 1995. Human tubal fluid: formation and composition during vascular perfusion of the fallopian tube. *Human Reprod*, 10:505-508.

Dobrinski I, Ignotz GG, Thomas PG, Ball BA. 1996. Role of carbohydrates in the attachment of equine spermatozoa to uterine tubal (oviductal) epithelial cells in vitro. *Am J Vet Res*, 57:1635-1639.

Downing SJ, Maguiness SD, Watson A, Leese HJ. 1997. Electrophysiological basis of human fallopian tubal fluid formation. *J Reprod Fertil*, 111:29-34.

Edwards LJ, Leese HJ. 1993. Glucose transport and metabolism in rabbit oviduct epithelial cells. *J Reprod Fertil*, 99:585-591.

Eherenwald E, Foote RH, Parks JE. 1990. Bovine oviductal fluid components and their potential role in sperm cholesterol efflux. *Molec Reprod Dev*, 25:195-204.

Eherenwald E, Parks JE, Foote RH. 1988. Cholesterol efflux from bovine sperm I. Induction of acrosome reaction with lysophosphatidilcholine after reducing sperm cholesterol. *Gamete Res*, 20:145-157.

Ellington JE, Ignotz GG, Ball BA, Meyers-Wallen VN, Currie WB. 1993. De novo protein synthesis by bovine uterine tube (oviduct) epithelial cells changes during co-culture with bull spermatozoa. *Biol Reprod*, 48:851-856.

Engle CC, Witherspoon DM, Foley CW. 1970. Technique for continuous collection of equine oviduct secretions. *Am J Vet Res*, 31:1889-1896.

Engle CC, Foley ED, Plotka ED, Witherspoon DM. 1984. Free amino acids and protein concentrations in reproductive tract fluids of the mare. *Theriogenology*, 21:919-930.

Engle CE, Foley CW, Witherspoon DM, Scarth RD, Goetsch DD. 1975. Influence of mare tubal fluids on the metabolism of stallion sperm. *Am J Vet Res*, 36:1149-1152.

Engle CC, Dunn JS, Hood RD, Williams DJ, III, Foley CW, Trout HF. 1968. Amino acids in sow and rabbit oviduct fluids. *J Anim Sci*, 27:1786. (abstract).

Eriksen T, Terkelsen O, Grondal C, Bruck I. 1994. The equine oviduct - histology and PDGF localization. *Theriogenology*, 41:191 (abstract).

Fazleabas AT, Verhage HG. 1986. The detection of oviduct specific proteins in the baboon (Papio anubis). *Biol Reprod*, 35:455-462.

Foley CW, Engle CC, Plotka ED, Roberts RC, Johnson AD. 1972. Oct. Influence of early pregnancy on proteins and amino acids of uterine tubal fluids in rabbits. *Am J Vet Res*, 33:2059-65.

Gabler C, Lauer B, Einspanier A, Schams D, Einspanier R. 1997. Detection of mRNA and immunoreactive proteins for acidic and basic fibroblast growth factor and expression of the fibroblast growth factor receptors in the bovine oviduct. *J Reprod Fertil*, 109:213-221.

Gandolfi F. 1995. Functions of proteins secreted by oviduct epithelial cells. *Microsc Res Tech*, 32:1-12.

Gandolfi F, Brevini TAL, Richardson L, Brown CR,

Moor RM. 1989. Characterization of proteins secreted by sheep oviduct epithelial cells and their function in embryonic development. *Development*, 106:303-312.

Gandolfi F, Modina S, Brevini TAL, Galli C, Moor RM, Lauria A. 1991. Oviduct ampullary epithelium contributes a glycoprotein to the zona pellucida, perivitelline space and blastomeres membrane of sheep embryos. *Eur J Basic Appl Histoch*, 35:383-392.

Gandolfi F, Modina S, Brevini TA, Passoni L, Petraglia F, Lauria A. 1995. Activin beta A subunit is expressed in bovine oviduct. *Mol Reprod Dev*, 40:286-291.

Gandolfi F, Passoni L, Modina S, Brevini TAL, Varga Z, Lauria A. 1993. Similarity of an oviduct-specific glycoprotein between different species. *Reprod Fertil Dev*, 5:433-443.

Gardner DK, Leese HJ. 1990. Concentrations of nutrients in mouse oviduct fluid and their effects on embryo development and metabolism in vitro. *J Reprod Fertil*, 88:361-368.

Gardner DK, Lane M, Calderon I, Leeton J. 1996. Environment of the preimplantation human embryo in vivo: metabolite analysis of oviduct and uterine fluids and metabolism of cumulus cells. *Fertil Steril*, 65:349-353.

Gerena RL, Killian GJ. 1990. Electrophoretic characterization of proteins in oviduct fluid of cows during the estrous cycle. *J Exp Zool*, 256:113-120.

G**lass LE**. 1969. Immunocytological studies of the mouse oviduct. *In*: Hafez ES (Ed.). *The mammalian oviduct*. Chicago: University of Chicago Press. pp.54-72.

Gott AL, Gray SM, James AF, Leese HJ. 1988. The mechanism and control of rabbit oviduct fluid formation. *Biol Reprod*, 39:758-763.

Green TR, Fellman JH, Eicher AL, Pratt KL. 1991. Antioxidant role and subcellular location of hypotaurine and taurine in human neutrophils. *Bioch Bioph Acta*, 1073:91-97.

Grippo AA, Way AL, Killian GJ. 1995. Effect of bovine ampullary and isthmic oviductal fluid on motility, acrosome reaction and fertility of bull spermatozoa. *J Reprod Fertil*, 105:57-64.

Grippo AA, Henault MA, Anderson SH, Killian GJ. 1992. Cation concentrations in fluid from the oviduct ampulla and isthmus of cows during the estrous cycle. *J Dairy Sci*, 75:58-65.

Grippo AA, Luo Y, Rougeau B, Wyatt Xv. 2000. Monosaccharides are not detected in whole or isthmic bovine oviductal fluid collected throughout the estrous cycle, as analyzed by HPLC. *Theriogenology*, 53:717-726.

Grippo AA, Anderson SH, Chapman DA, Henault MA, Killian GJ. 1994. Cholesterol, phospholipid and phopholipase activity of ampullary and isthmic fluid from the bovine oviduct. *J Reprod Fertil*, 102:87-93.

Guérin P, Menezo Y. 1995. Hypotaurine and taurine in gamete and embryo environments: de novo synthesis via the cysteine acid pathway in oviduct cells. *Zygote*, 3:333-343.

Guérin P, Tappaz M, Guillaud J, Menezo Y. 1995a. Demonstration of cysteine sulfinate decarboxylase (EC 4.1.1.29) in cultured oviduct epithelial cells in cows and goats. *C R Acad Sci III*, 318:523-528.

Guérin P, Gallois E, Croteau S, Revol N, Maurin F, Guillaud J. 1995b. Techniques de recolte et aminogrammes des liquides tudaire et folliculaire chez les femelles domestiques. *Rev Med Vet*, 146:805-814.

Gutierrez A, Garde J, Garcia-Artiga C, Vazquez I. 1993. Ram spermatozoa cocultured with epithelial cell monolayers: an in vitro model for the study of capacitation and the acrosome reaction. *Mol Reprod Dev*, 36:338-345.

Hamner CE. 1973. Oviductal fluid: Composition and physiology. *In*: Greep RO, Astwood EB. (Eds.). Handbook of physiology, endocrinology. Washington: American Physiologycal Society. pp.141-151.

Hamner GE, Williams WL. 1963. Effect of female reproductive tract on sperm metabolism in the rabbit and fowl. *J Reprod Fertil*, 5:143-150.

Hamner CE, Williams WL. 1965. Composition of rabbit oviduct secretions. *Fertil Steril*, 16:170-176.

Han SW, Lei ZM, Rao CV. 1996. Up-regulation of cycloogenase-2 gene expression by chorionic gonadotropin in mucosal cells from human fallopian tubes. *Endocrinology*, 137:2929-2937.

Hedrick JL, Wardrip NJ, Berger T. 1987. Differences in the macromolecular composition of the zona pellucida isolated from pig oocytes, eggs, and zygotes. *J Exp Zool*, 241:257-262.

Horvat B, Osborn M, Damjanov I. 1990. Expression of villin in the mouse oviduct and the seminiferous ducts. *Histochemistry*, 93:661-663.

Hunter RHF. 1984. Pre-ovulatory arrest and peri-ovulatory redistribution of competent spermatozoa in the isthmus of pig oviduct. *J Reprod Fertil*, 72:203-211.

Hunter RHF. 1988. Transport of gametes. *In*: The Fallopian tubes: Their role in fertility and infertility. Springer-Verlag, New York: pp 53-74.

Hunter RHF, Nichol R. 1983. Transport of spermatozoa in the sheep oviduct: Preovulatory sequestering of cells in the caudal isthmus. *J Exp Zool*, 228:121-128.

Hunter RHF, Wilmut I. 1984. Sperm transport in the cow: Peri-ovulatory distribution of viable cells within the oviduct. *Reprod Nutr Dev*, 24:597-608.

Iritani A, Gomes WR, Van Demark NL. 1969. Secretion rates and chemical composition of oviduct and uterine fluids in ewes. *Biol Reprod*, 1:72-76.

Iritani A, Nishikawa Y, Gomes WR, VanDemark NL. 1971. Secretion rates and chemical composition of oviduct and uterine fluids in rabbits. *J Anim Sci*, 33:829-835.

Jansen RPS. 1984. Endocrine response in the fallopian tube. *Endrocr Rev*, 5:525-551.

Jillella D, Eaton RJ, Baker AA. 1977. Successful transfer of a bovine embryo through a cannulated fallopian tube. *Vet Rec*, 100:385-386.

Kan FWK, St-Jacques S, Bleau G. 1988. Immunoelectron microscopic localization of an oviductal antigen in hamster zona pellucida by use of a

monoclonal antibody. *J Histoch Cytoch*, 36:1441-1447.

Kan FWK, St-Jacques S, Bleau G. 1989. Immunocytochemical evidence for the transfer of an oviductal antigen to the zona pellucida of hamster ova after ovulation. *Biol Reprod*, 40:585-598.

Kan FWK, Roux E, Bleau G. 1993. Immunolocalization of oviductin in endocytic compartments in the blastomeres of developing embryos in the golden hamster. *Biol Reprod*, 48:77-88.

Kapur RP, Johnson LV. 1985. An oviductal fluid glycoprotein associated with ovulated mouse ova and early embryos. *Dev Biol*, 112:89-93.

Kapur RP, Johnson LV. 1986. Selective sequestration of an oviductal fluid glycoprotein in the perivitelline space of mouse oocytes and embryos. *J Exp Zool*, 238:249-260.

Kapur RP, Johnson LV. 1988. Ultrastructural evidence that specialized regions of the murine oviduct contribute glycoprotein to the extracellular matrix of mouse oocytes. *Anat Rec*, 221:720-729.

Kavanaugh JF, Killian GJ. 1988. Bovine oviductal cannulations. *J Invest Surg*, 1:201-208.

Kavanaugh JF, Grippo AA, Killian GJ. 1992. Cannulation of the bovine ampullary isthmic oviduct. *J Invest Surg*, 5:11-17.

Kawakami E, Hori T, Tsutsui T. 1998. Induction of dog sperm capacitation by oviductal fluid. *J Vet Med Sci*, 60:197-202.

Kennedy TG, Brown KD, Vaugnan TJ. 1994. Expression of the genes for the epidermal growth factor receptor and its ligands in porcine oviduct and endometrium. *Biol Reprod*, 50:751-756.

Kim NH, Funahaashi H, Abeydeera LR, Moon SJ, Prather RS, Day BN. 1996. Effects of oviductal fluid on sperm penetration and cortical granules exocytosis during fertilization of pig oocytes in vitro. *J Reprod Fertil*, 1996:79-86.

King RS, Killian GJ. 1994. Purification of bovine estrus associated protein and localization of binding on sperm. *Biol Reprod*, 51:34-42.

King RS, Anderson SH, Killian GJ. 1994. Effect of bovine oviductal estrus-associated protein on the ability of sperm to capacitate and fertilize oocytes. *J Androl*, 15:468-478.

Leese HJ. 1983. Studies on the movement of glucose, pyruvate and lactate into the ampulla and isthmus of the rabbit oviduct. *Quart J Exp Physiol*, 68:89-96.

Leese HJ. 1988. The formation and function of oviduct fluid. *J Reprod Fertil*, 82:843-856.

Leese HJ, Aldridge S. 1979. The movement of pyruvate, lactate and lactate dehydrogenase into rabbit oviductal fluid. *J Reprod Fertil*, 56:619-622.

Leese JJ, Barton AM. 1984. Pyruvate and glucose uptake by mouse ova and preimplantation embryos. *J Reprod Fertil*, 72:9-13.

Leese HJ, Gray SM. 1985. Vascular perfusion: a novel means of studying oviduct function. *Am J Physiol Endocrinol Metab*, 248:624-631.

Leese HJ, Jeffries KS. 1977. Evidence for the facilitated diffusion of glucose into rabbit oviductal fluid. *J Reprod Fertil*, 51:93-97.

Leese HJ, Aldridge S, Jeffries KS. 1979. The movement of amino acids into rabbit oviductal fluid. *J Reprod Fertil*, 56:623-626.

Leese HJ, Tay JI, Reischl J, Downing SJ. 2001. Formation of Fallopian tubal fluid: role of a neglected epithelium. *Reproduction*, 121:339-346.

Lefebvre R, Lo MC, Suarez SS. 1997. Bovine sperm binding to oviductal epithelium involves fucose recognition. *Biol Reprod*, 56:1198-1204.

Leveille MC, Roberts KD, Chevalier S, Chapdelaine A, Bleau G. 1987. Uptake of an oviductal antigen by the hamster zona pellucida. *Biol Reprod*, 36:227-238.

Libersky EA, Boatman DE. 1995. Progesterone concentrations in serum, follicular fluid, and oviductal fluid of the golden hamster during the periovulatory period. *Biol Reprod*, 53:477-482.

Libik M, Slavik T, Schwarz T, Murawski M, Ciuryk S, Wierzchos E. 2002. Influence of oviductal fluid on ovine embryo viability. *Folia Biol (Praha)*, 48:145-148.

Lippes J, Wagh PV. 1989. Human oviductal fluid (hOF) proteins. IV. Evidence for hOF proteins binding to human sperm. *Fertil Steril*, 51:89-94.

Lippes J, Enders RG, Pragay DA, Bartholomew WR. 1972. The collection and analysis of human fallopian tubal fluid. *Contraception*, 5:85-95.

Makarevich AV, Sirotkin AV. 1997. The involvement of the GH/IGF-I in the regulation of secretory activity by bovine oviduct epithelial cells. *Anim Reprod Sci*, 48:197-207.

Malayer Jr, Hansen PJ, Buhi WC. 1988. Secretion of proteins by cultured bovine oviducts collected from estrus through early diestrus. *J Exp Zool*, 348:345-353.

Mastroianni L, Jr., Shah V, Abdul-Karim R. 1961. Prolonged volumetric collection of oviduct fluid in the rhesus monkey. *Fertil Steril*, 12:417-424.

McCauley TC, Buhi WC, Wu GM, Mao J, Caamano JN, Didion BA, Day BN. 2003. Oviduct-specific glycoprotein modulates sperm-zona binding and improves efficiency of porcine fertilization in vitro. *Biol Reprod*, 69:828-834.

McComb PF, Moon Y. 1985. Prostaglandin E and F concentration in the fimbria of the rabbit fallopian tube increases at the time of ovulation. *Acta Eur Fertility*, 16:423-426.

McDonal MF and Bellvé AR. 1969. Influence of oestrogen and progesterone on flow of fluid from the Fallopian tube in the ovariectomized ewe. *J Reprod Fertil*, 20 51-61.

McNutt T, Rogowski L, Vasilatos-Younken R, Killian G. 1992. Adsorption of oviductal fluid proteins by the bovine sperm membrane during in vitro capacitation. *Mol Reprod Dev*, 33:313-323.

Menezo Y, Laviolette P. 1971. Les constituants amines des secretions tubaries chez la lapine. *Ann Biol Bioch Biophys*, 12:383-396.

Modina S, Milanesi E, Baraldi-Scesi L, Brevini A, Acocella F, Lauria A, Armstong D, Gandolfi F. 1997. Comparison of the oviductal secretions of prepuberal and adult cows. *Theriogenology*, 47:335. (abstract).

Moses DF, Matkovic M, Fisher EC, Martinez AG. 1997. Amino acid contents on sheep oviductal and uterine fluids. *Theriogenology*, 47:336. (abstract).

Nakazawa T, Ohashi K, Yamada M, Shinoda S, Saji F, Murata Y, Araki H. 1997. Effect of different concentrations of amino acids in human serum and follicular fluid on the development of one-cell mouse embryos in vitro. *J Reprod Fertil*, 111:327-332.

Nancarrow CD, Hill JL, Connell PJ. 1992. Amino acid secretion by the ovine oviduct. *In*: Proceedings of the 71st Annual Conference of the Australian Society for Reproductive Biology, Adelaide. Adelaide: ASRB. pp.24.

Nichol R, Hunter RH, Cooke GM. 1997. Oviduct fluid pH in intact and unilaterally ovariectomized pigs. *Can J Physiol Pharmacol*, 75:1069-1074.

Nichol R, Hunter RH, Gardner DK, Leese HJ, Cooke GM. 1992. Concentrations of energy substrates in oviductal fluid and blood plasma of pigs during the peri-ovulatory period. *J Reprod Fertil*, 96:699-707.

Nichol R, Hunter RH, Gardner DK, Partridge R, Leese HJ, Cooke GM. 1998. Concentrations of energy substrates in oviduct fluid in unilaterally ovariectomised pigs. *Res Vet Sci*, 65:263-264.

Nieder J, Augustin W. 1986. Prostaglandin E and F profiles in human fallopian tubes during different phases of the menstrual cycle. *Gynecol Obst Invest*, 21:202-207.

Nozaki M and Ito Y. 1986. Menstrual cycle and sensitivity of human fallopian tube to prostaglandins. *Am J Physiol*, 251:R1126-R1136.

Ogra SS, Kirton KT, Tomasi TB Jr, Lippes J. 1974 Mar. Prostaglandins in the human fallopian tube. *Fertil Steril*, 25(3):250-255.

Oikawa T, Sendai Y, Kurata S, Yanagimachi R. 1988. A glycoprotein of oviductal origin alters biochemical properties of the zona pellucida of hamster egg. *Gamete Res*, 19:113-122.

Olds D, VanDemark NL. 1957a. Composition of luminal fluids in bovine female genitalia. *Fertil Steril*, 345-354.

Olds D, VanDemark NL. 1957b. Luminal fluids of bovine female genitalia. *J Am Vet Med Assoc*, 131: 555-556.

Oliphant G, Bowling A, Eng LA, Keen S, Randall PA. 1978. The permeability of rabbit oviduct to proteins present in the serum. *Biol Reprod*, 18:516-520.

Parr EL, Parr MB. 1986. Uptake of immunoglobulins and other proteins from serum into epithelial cells of the mouse uterus and oviduct. *J Reprod Immunol*, 9:330-354.

Parrish JJ, Susko-Parrish JL, Handrow RR, Sims MM, First NL. 1989. Capacitation of bovine spermatozoa by oviduct fluid. *Biology of Reproduction*, 40:1020-1025.

Perkins JL. 1974. Fluid flow of the oviduct. *In:* Johnson AD, Foley C W (Eds.). *The oviduct and its functions*. New York: Academic Press. pp.119-132.

Pfeifer TL, Chegini N. 1994. Immunohistochemical localization of insulin-like growth factor (IGF-I), IGF-I receptor, and IGF binding proteins 1-4 in human fallopian tube at various reproductive stages. *Biol Reprod*, 50:281-289.

Quinn P, Kerin JF, Warnes GM. 1985. Improved pregnancy rate in human in vitro fertilization with the use of a medium based on the composition of human tubal fluid. *Fertil Steril*, 44:493-498.

Restall BJ, Wales RG. 1966. The fallopian tube of the sheep III. The chemical composition of the fluid from the fallopian tube. *Aust J Biol Sci*, 19:687-698.

Restall BJ, Wales RG. 1968. The fallopian tube of the sheep V. Secretion from the ampulla and isthmus. *Aust J Biol Sci*, 21:491-498.

Richardson LL, Oliphant G. 1981. Steroid concentrations in rabbit oviductal fluid during oestrus and pseudopregnancy. *J Reprod Fertil*, 62:427-431.

Roberts GP, Parker JM, Symonds HW. 1975. Proteins in the luminal fluid from the bovine oviduct. *J Reprod Fertil*, 45:301-313.

Rodriguez-Martinez H, Petroni A, Einarsson S, Kindahl H. 1983. Concentrations of prostaglandin F2 alpha in the pig oviductal fluid. *Prostaglandins*, 25:413-424.

Sato N. 1988. [Cyclic changes in sex steroids, prostaglandins and oxytocin receptors of normal fallopian tube throughout the menstrual cycle]. *Nippon Sanka Fujinka Gakkai Zasshi*, 40:1432-1438.

Schell DL, Mavrogianis PA, Fazleabas AT, Verhage HG. 1994. Epidermal growth factor, transforming growth factor-alpha, and epidermal growth factor receptor localization in the baboon (Papio anubis) oviduct during steroid treatment and the menstrual cycle. *J Soc Gynecol Invest*, 1:269-276.

Sidhu KS, Mate KE, Rodger JC. 1998. Sperm-oviduct epithelial cell monolayer co-culture: an in vitro model of sperm-female tract interactions in a marsupial, the tammar wallaby (Macropus eugenii). *J Reprod Fertil*, 114:55-61.

Simmen FA, Simmen RCM. 1991. Peptide growth factors and proto-oncogenes in mammalian conceptus development. *Biol Reprod*, 44:1-5.

Sloan MH, Johnson AD. 1974a. The influence of a cannula in the rabbit oviduct. II Effect on embryo survival. *J Reprod Fertil*, 37:155-158.

Sloan MH, Johnson AD. 1974b. The influence of a cannula in the rabbit oviduct. I Oviduct fluid lipids and proteins. *J Reprod Fertil*, 37:149-153.

Smith TT, Yanagimachi R. 1990. The viability of hamster spermatozoa stored in the isthmus of the oviduct: the importance of sperm-epithelium contact for sperm survival. *Biol Reprod*, 42:450-457.

Smotrich DB, Stillman RJ, Widra EA, Gindoff PR, Kaplan P, Graubert M, Johnson KE. 1996. Immunocytochemical localization of growth factors and their receptors in human pre-embryos and fallopian tubes. *Human Reprod*, 11:184-190.

Spilman CH and Harper MJK. 1975. Effects of

prostaglandins on oviductal motility and egg transport. *Gynecol Invest*, 6:186-205.

Stanchev P, Rodriguez-Martinez H, Edqvist LE, Eriksson H. 1985. Oestradiol and progesterone receptors in the pig oviduct during the oestrous cycle. *Journal of Steroid Biochemistry*, 22:115-120.

Stanke DF, Sikes JD, DeYoung DW, Tumbleson ME. 1974. Proteins and amino acids in bovine oviductal fluid. *J Reprod Fertil*, 38:493-496.

Staros AL, Killian GJ. 1998. In vitro association of six oviductal fluid proteins with the bovine zona pellucida. *J Reprod Fertil*, 112:131-137.

Stevenson KR, Wathes DC. 1996. Insulin-like growth factors and their binding proteins in the ovine oviduct during the oestrous cycle. *J Reprod Fertil*, 108:31-40.

Sutton R, Nancarrow CD, Wallace ALC. 1986. Oestrogen and seasonal effects on the production of an oestrus-associated glycoprotein in oviductal fluid of sheep. *J Reprod Fertil*, 77:645-653.

Sutton R, Nancarrow CD, Wallace ALC, Rigby NW. 1984a. Identification of an oestrus-associated glycoprotein in oviductal fluid of the sheep. *J Reprod Fertil*, 72:415-422.

Sutton R, Wallace ALC, Engel H, Nancarrow CD. 1984b. Binding of sheep oviductal fluid proteins to spermatozoa. *In*: Lindsay DR, Pearce DT (Ed.). *Reproduction in sheep*. Canberra: Australian Academy of Science. pp.140-143.

Swanchara KW, Henricks DM, Birrenkott GP, Bodine AB, Richardson ME. 1995. Expression of epidermal growth factor (EGF) and EGF receptor in the porcine oviduct. *Biol Reprod*, 53:911-922.

Tay JI, Rutherford AJ, Killick SR, Maguiness SD, Partridge RJ, Leese HJ. 1997. Human tubal fluid: production, nutrient composition response to adrenergic agents. *Human Reprod*, 12:2451-2456.

Verhage HG, Fazleabas AT. 1988. The *in vitro* synthesis of estrogen-dependent proteins by the baboon (Papio anubis) oviduct. *Endocrinology*, 123:552-558.

Verhage HG, Fazleabas AT, Donnell K. 1988. The *in vitro* synthesis and release of proteins by human oviduct. *Endocrinology*, 122:1639-1645.

Verhage HG, Boice ML, Mavrogianis P, Donnelly K, Fazleabas AT. 1989. Immunological characterization and immunocytochemical localization of oviduct-specific glycoproteins in the baboon (Papio anubis). *Endocrinology*, 124:2464-2472.

Viuff D, Hytell P, Greve T, Ericksen T, Alexandersen S. 1995. Transcription and localization of growth factor mRNA in the bovine oviduct. *Mol Reprod Dev*, 42:28-34.

Wagh PV, Lippes J. 1989. Human oviductal fluid proteins. III. Identification and partial purification. *Fertil Steril*, 51:81-88.

Walker SK, Hill JL, Kleeman DO, Nancarrow CD. 1996. Development of ovine embryos in synthetic oviductal fluid containing amino acids at oviductal fluid concentrations. *Biol Reprod*, 55:703-708.

Warnes GM, Amato F, Seamark RF. 1978. Prostaglandin F in the fallopian tube secretion of the ewe. *Aust J Biol Sci*, 31:275-282.

Watson AJ, Watson PH, Arcellana-Panlilio M, Warnes D, Walker SK, Schultz GA, Armstrong DT, Seamark RF. 1994. A growth factor phenotype map for ovine preimplantation development. *Biol Reprod*, 50:725-733.

Way AL, Schuler AM, Killian GJ. 1997. Influence of bovine ampullary and isthmic oviductal fluid on sperm-egg binding and fertilization in vitro. *J Reprod Fertil*, 109:95-101.

Wegner CC, Killian GJ. 1991. In vitro and in vivo association of an oviduct estrus-associated protein with bovine zona pellucida. *Molec Reprod Dev*, 29:77-84.

Willis P, Sekhar KN, Brooks P, Fayrer-Hosken RA. 1994. Electrophoretic characterization of equine oviductal fluid. *J Exp Zool*, 268:477-485.

Winger QA, de los Rios P, Han VK, Armstrong DT, Hill DJ, Watson AJ. 1997. Bovine oviductal and embryonic insulin-like growth factor binding proteins: possible regulators of "embryotrophic" insulin-like growth factor circuits. *Biol Reprod*, 56:1415-1423.

Wiseman DL, Henricks DM, Eberhardt DM, Bridges WC. 1992. Identification and content of insulin-like growth factors in porcine oviductal fluid. *Biol Reprod*, 47:126-132.

Wollenhaupt K, Tiemann U, Einspanier R, Schneider F, Kanitz W, Brussow KP. 1997. Characterization of the epidermal growth factor receptor in pig oviduct and endometrium. *J Reprod Fertil*, 111:173-181.

Xia P, Han VK, Armstrong DT, Watson AJ. 1996. Expression of insulin-like growth factors in two bovine oviductal cultures employed for embryo co-culture. *J Endocrinol*, 149:41-53.

Zhao Y, Chegini N. 1994. Human fallopian tube expresses granulocyte-macrophage colony stimulating factor (GM-CSF) and GM-CSF and beta receptors and contain immunoreactive GM-CSF protein. *J Clin Endocrinol Metab*, 79:662-665.

Zhu J, Barratt CL, Lippes J, Pacey AA, Cooke ID. 1994a Human oviductal fluid prolongs sperm survival. *Fertil Steril*, 61:360-366.

Zhu J, Barratt CL, Lippes J, Pacey AA, Cooke ID. 1994b The sequential effects of human cervical mucus, oviductal fluid, and follicular fluid on sperm function. *Fertil Steril*, 61:1129-1135.