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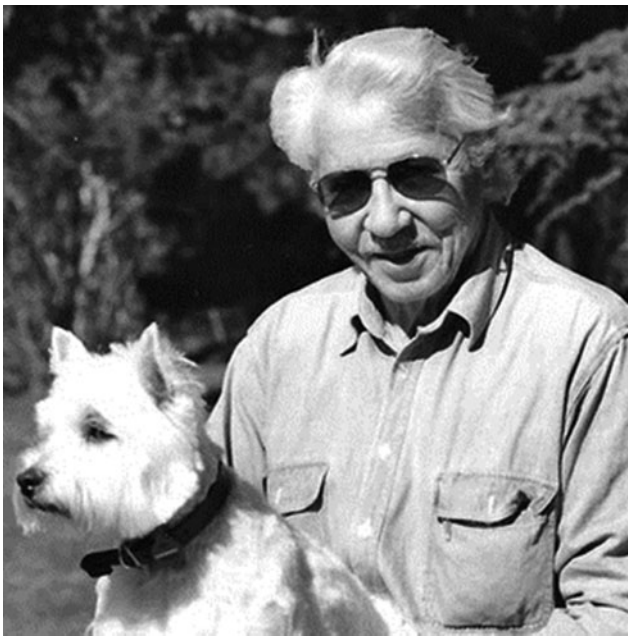
Recipient of the 2018 IETS Pioneer Award: David Thomas Armstrong, BSA, MSc, PhD



Dr David T. Armstrong was born in Kinburn, Ontario, in the Ottawa Valley, Canada, on 5 November 1929. He was raised on a farm and developed a great interest in animal reproduction from his early years. Dr Armstrong received his BSA major in animal husbandry from the Ontario Agricultural College, University of Toronto, in 1951, his MSc degree major in physiology; minors in biochemistry and endocrinology in 1956, and his PhD major in physiology; minors in biochemistry and endocrinology in 1959, both from Cornell University and under the mentorship of Dr William (Bill) Hansel. Dr Armstrong completed postdoctoral studies at Brookhaven National Laboratory in Upton, NY, from 1958 to 1960. From 1960 to 1968, Dr Armstrong was a research associate and assistant professor of Anatomy at Harvard School of Dental Medicine and Harvard Medical School, Boston. In 1968, he was appointed associate professor of Physiology and Obstetrics and Gynaecology at the University of Western Ontario ('Western'), London, Ontario, Canada. In 1969, he was promoted to professor at Western, a title he held until 1998, when he became professor emeritus. One university position was never enough for Dr Armstrong and his talents. For much of his career (1977 onward) he was also appointed as a visiting professor in Obstetrics and Gynaecology at the University of Adelaide, Adelaide, Australia.

Dr Armstrong's publication record extends from 1956 until 2012, and includes a total of 281 records in the Web of Science. These publications have been cited more than 10 000 times, providing Dr Armstrong with an h-index of 57. Over the years, Dr Armstrong has trained dozens of graduate students and postdoctoral fellows who have populated the Animal Science, and Obstetrics and Gynaecology departments of universities worldwide. Dr Armstrong's research interests were quite varied but he always kept up with times allowing him to make seminal contributions to many aspects of reproductive biology and embryo transfer right up to his actual retirement in 2012. These areas include:

1. Discovery, with Dr Hansel, of the luteolytic action of oxytocin (Armstrong and Hansel 1959). This was the first demonstration of the ability of a pharmacological agent to terminate corpus luteum function, thus providing the first method available for oestrous cycle regulation. It stimulated further research into methods of oestrous cycle synchronisation based on luteolysis, now widely used for artificial breeding programs in farm animals. The full physiological significance of this discovery did not emerge until ~25 years later with discoveries by others that the corpus luteum secretes oxytocin, and that oxytocin is a major regulator of prostaglandin secretion by endometrial and luteal tissues.
2. A major theme of Dr Armstrong's pioneering research focused on the use of *in vitro* techniques for studies of hormone actions on the ovary. His research on the actions of gonadotrophic hormones on glucose and cholesterol metabolism in the ovary provided the first evidence for the now widely accepted role of luteinising hormone (LH) in regulating ovarian steroid biosynthesis by influencing substrate availability to the rate-limiting mitochondrial steroidogenic enzyme(s) (Armstrong and Greep 1962; Armstrong 1963, 1967; Armstrong *et al*. 1963; Solod *et al*. 1966; Major *et al*. 1967; Jackanicz and Armstrong 1968; Behrman and Armstrong 1969; Behrman *et al*. 1970; Flint and Armstrong 1971, 1972; Robinson *et al*. 1975).
3. His work first demonstrated the role of LH in the regulation of progesterone secretion by the corpus luteum in rabbits (Kilpatrick *et al*. 1964) and rats (Armstrong *et al*. 1964; Armstrong 1967), and thus established the similarity of mechanisms of regulation of luteal steroidogenesis among mammalian species. These findings were of fundamental importance in shifting the thinking about corpus luteum regulation from prolactin (previously regarded as 'the luteotrophic hormone') to luteinising hormone.
4. He discovered, with Drs Grinwich and Kennedy, the essential role of prostaglandins in ovulation through local intraovarian action in rats (Armstrong and Grinwich 1972) and

rabbits (Grinwich *et al*. 1972). This work demonstrated that a prostaglandin synthase inhibitor modulated gonadotrophin action at intraovarian site(s) and provided the first evidence of the importance of prostaglandins in intraovarian paracrine regulation in the follicle. These studies defined a physiological role of PGE of ovarian origin as an intraovarian stimulus of follicular growth by exerting 'gonadotrophin-like actions on granulosa and theca cells which do not yet possess receptors for the gonadotrophic hormones' (Armstrong 1980). This prediction was borne out by findings of others that PGE is an essential mediator of the actions of an oocyte-secreted factor (GDF-9) in initiation of folliculogenesis.

5. Dr Armstrong, with Drs Dorrington, Moon, Papkoff and others, discovered the site of action of FSH in stimulation of oestrogen biosynthesis in Sertoli cells in the testes (Dorrington and Armstrong 1975) and ovarian granulosa cells (Dorrington *et al*. 1975; Armstrong and Papkoff 1976). This, together with discoveries with Fortune (Fortune and Armstrong 1977), of the stimulatory action of LH on androgen secretion by ovarian theca cells, provided definitive proof of the 'two cell, two gonadotrophin' theory of ovarian oestrogen biosynthesis and its regulation by gonadotrophins. This new concept resulted in re-evaluation of the follicle cells responsible for oestrogen secretion. The finding that the same cells can both secrete and respond to oestradiol provided crucial evidence for autocrine regulation within the follicle. Drs Armstrong and Tsang extended this concept and work to the human ovary (Tsang *et al*. 1979).
6. Dr Armstrong discovered, with Drs Leung, Dorrington, Daniel and others, the paracrine actions of androgens in follicle regulation by enhancing FSH actions on induction of progesterone synthesis (Armstrong and Dorrington 1976; Leung *et al*. 1979*a*, 1979*b*) and aromatase (Daniel and Armstrong 1980). This work provided definitive evidence for role(s) of ovarian androgens beyond that of substrate for aromatisation to estrogens, and foreshadowed research leading to the now well established importance of androgens in paracrine and autocrine regulation within the ovary.
7. Dr Armstrong's research covered the species model list, including, mouse, rat, sheep, porcine, bovine, monkey and human. He pioneered the investigation of *in vitro* maturation and fertilisation of rat oocytes with Drs Evans (Evans and Armstrong 1984) and Vanderhyden (Vanderhyden and Armstrong 1989), the use of bovine calf oocytes for embryo production with Dr Gandolfi (Gandolfi *et al*. 1998), investigated growth factor gene expression and signalling in oocytes and early embryos with Drs Xia, Tekpetey, Watson and Zhang (Xia *et al*. 1994; Watson *et al*. 1994; Zhang *et al*. 1994; Winger *et al*. 1997) and intraovarian growth factor signalling with Drs Gilchrist and Thompson (Gilchrist *et al*. 2004; Grupen *et al*. 2007; Albuz *et al*. 2010). His last published study featured effects of the ovarian reserve in women and appeared in 2012 with Dr Lane (Pacella *et al*. 2012).

As is expected for someone of his stature, Dr Armstrong has contributed much to the growth of his field. He served as the president of the Society for the Study of Reproduction (1976–77) and the IETS (1990–91), many editorial boards, scientific advisory boards, and national and international conference organising committees. Of note is his work on the Advisory Committee on Human Reproductive Technologies, Ontario Law Reform Commission (1983–85). This committee framed legal and ethical application and practise of Human ARTs in Canada. Among his many honours, Dr Armstrong was a Career Investigator of the Medical Research Council of Canada, a research Career Development Awardee of the NIH Institute of Child Health and Human Development, elected to fellowship of the Royal Society of Canada, an awardee of a Doctor of Science (*honoris causa*) from the University of Guelph, Guelph, Ontario, and was recipient of the Hartman Award from the Society for the Study of Reproduction.

Sadly, Dr Armstrong passed away on 1 August 2016 in the company of his family. Without question, his was a life well lived, full of meaning and impact. He is missed by many.

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