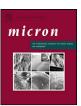


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# Micron





#### Invited review

# Ultrastructure of human gametes, fertilization and embryos in assisted reproduction: A personal survey

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#### ABSTRACT

This extensively illustrated review will cover the progression of recent research on the ultrastructure of human gametes, fertilization and embryos performed in collaboration with colleagues in In vitro fertilization (IVF) centers over the past three decades, in Australia, Singapore, India, England, Sri Lanka, Spain and Italy. It will also include some aspects of gametogenesis and embryogenesis, particularly in relation to the centrosome that activates embryonic development, and is inherited from the father at fertilization. Assessment of both normal and abnormal gametes and embryos and some clinical aspects of assisted reproduction will be discussed. Full reference will also be made to the contribution of other groups to the ultrastructure of reproduction, particularly in humans.

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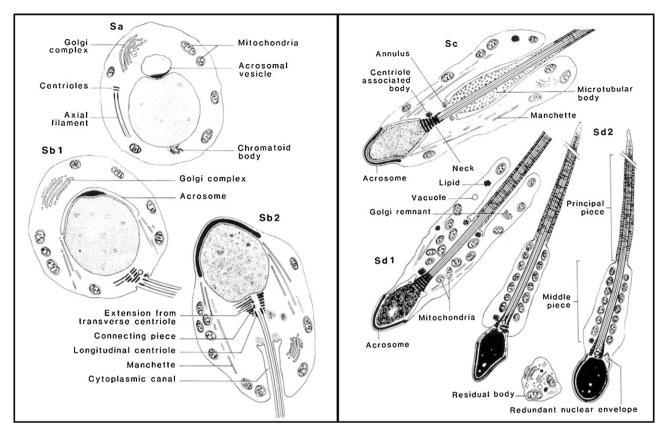
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## 1. Introduction

The electron microscope has been an invaluable tool in the study of the fine structure of cells and tissues through the past seventy-five years of biomedical research. This includes both transmission and scanning electron microscopy (TEM and SEM) in exploring the

internal and surface structure of cells and tissues at high magnification, well beyond the resolution of the light microscope (LM) and fluorescent microscope (FM). We have used TEM routinely in our studies of human sperm, oocytes and embryos in conjunction with our clinical IVF and assisted reproductive technology (ART) programmes at Monash University since 1977, also in collaboration with other groups overseas. Much has been published as research papers, atlases and CDs documenting our work aimed at developing and improving techniques of assisted reproduction,

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**Fig. 1.** Spermiogenesis: the final stages of sperm maturation. A round spermatid is transformed into an elongated sperm cell in the testis. Note formation of acrosome, nucleus and tail axoneme arising from the distal (longitudinal) centrosome. The proximal centrosome is transverse and adjacent to the nucleus. Courtesy De Kretser and Kerr (1994); reproduced from atlas, Sathananthan (1996).

trouble-shooting and above all assessment of the intricate processes of human gametogenesis, fertilization and embryogenesis, both normal and abnormal. TEM is laborious, time-consuming, expensive and sometimes boring, but ultimately rewarding. It is also an invasive procedure like FM and the materials used cannot be reused. However, TEM is ideally suited for studying single cells and early embryos and we developed rapid procedures for fixing, processing and flat embedding to facilitate orientation of multiple eggs and embryos; also serial ultramicrotome sectioning using glass and diamond knives, imaging with modern transmission and scanning electron microscopes and digital photo-microscopes for LM with expert laboratory support (see Sathananthan, 1996; Sathananthan and Nottola, 2007, for techniques). Dedication and patience was always the philosophy during our work.

The advent of IVF in 1978, pioneered by Professor Robert G. Edwards (Nobel Laureate for Physiology & Medicine in 2010), enabled us to explore the fine structure of gametes and embryos in vitro, Indeed, Robert Edwards has been a mentor of our research since 1980 (see Sathananthan, 2011). The late Professor Carl Wood was a pioneer of IVF in Australia, where IVF babies born to-date exceed 45,000. I joined his group in 1977, at the time Professor Geoffrey Burnstock left Melbourne for London. Carl Wood was also a great inspiration to in the IVF field. He passed away in Melbourne in late September 2011. This illustrated review is dedicated to him, acknowledging his great leadership and vision for the treatment of infertility by IVF and ART. For recent laboratory reports on sperm, oocyte and embryo assessments for ART (see Veeck, 1999; Elder and Cohen, 2007; Sathananthan and Gunasheela, 2007; Sathananthan and Osianlis, 2009; Trounson and Gardner, 2000; Gianaroli et al., 2000).

Our first paper on the human oocyte ultrastructure was published in Micron in 1980 (Sathananthan and Lopata, 1980). In the same year, we published the earliest images of human conception, 3 h after insemination, as shown by TEM (Lopata et al., 1980). This was followed by a paper on human embryos in (Sathananthan et al., 1982) and the publication of an atlas on the fine structure of human gametes and embryos by the Monash pioneers of IVF (Sathananthan et al., 1986a,b). It is now over 33 years, since we began our studies on human IVF, on gonads, gametes and embryos at Monash University, in collaboration with the Lincoln Institute of Health Sciences (now La Trobe University) and we would like to survey our published work in this pictorial presentation on the fine structure of human gametes and embryos (Sathananthan, 1996, 1997a,b, 2000, 2003, 2006, 2009; Sathananthan and Edwards, 1995; Sathananthan and Gunasheela, 2007; Sathananthan and Nottola, 2007; Sathananthan et al., 1986a, b, 1990, 1991, 1993, 1996, 1999a,b, 2000, 2003, 2004, 2006). We also cite the invaluable work of other leading groups involved in the microstructure of reproduction (Van Blerkom, 1989; Pereda, 1989; Motta, 1989; Schatten, 1994; Yanagimachi, 1994; Veeck, 1999; Munne, 2006; De Kretser and Kerr, 1994; Sutovsky and Schatten, 2000; Sundström et al., 1981; Lopata et al., 1983; Macchiarelli et al., 1998; Makabe et al.,

# 2. Review of early literature

The ultrastructure of sperm cells has been investigated for some time from ejaculated sperm and testicular biopsies by Fawcett (1981), Holstein and Roosen-Runge (1981) On the other hand, oocyte fine structure was investgated in follicular oocytes and

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