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Edited by Kevin Coward and Dagan Wells
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Edited by

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Foreword

It is a pleasure to pen the Foreword to this *Textbook of Clinical Embryology*. As someone who was in at the ‘ground floor’, it has always surprised me that it has taken so long to produce such a volume! After all, the basis for the body of knowledge produced here was first established in the 1940s and 1950s with the accumulation of the Carnegie collection of human embryos (Hertig *et al.*, 1956; Rock and Menkin, 1944; Rock and Hertig, 1948). However, the main stimulus to the explosive growth in studies on human embryos can be dated to a 1965 *Lancet* paper by Bob Edwards (1965), which described the maturation of human eggs *in vitro*. This paper was based on research spanning the previous ten years, during which time Bob had made many significant discoveries in developmental genetics, immunological contraception and embryonic stem cells, as well as in oocyte maturation – as witnessed in his 56 papers published by 1965 (Gardner and Johnson, 2011). However, his 1965 *Lancet* paper was a landmark trigger in that its Discussion set out the course for the next 20 years of what would become known as Assisted Reproduction. It also set the scene for his following papers proving the principle of PGD (Gardner and Edwards, 1968), the demonstration of IVF (Edwards *et al.*, 1969), and the development of morulae and blastocysts *in vitro* (Edwards *et al.*, 1970; Steptoe *et al.*, 1971). These papers made human embryos available for the first time in sufficient numbers for their study scientifically. They also brought to the fore a whole new set of ethical, legal and political questions about the status of the human embryo, how it should be treated and what control should be exercised over it – moving it from science fiction to science fact (Theodosiou and Johnson, 2011). Bob was at the forefront of public debate on these issues too, early key papers being Edwards and Sharpe (1971) and Edwards (1974).

However, although Bob provided the vision, the inspiration and much of the energy for driving this field forwards, progress would not have been

achieved without Patrick Steptoe. Bob originally believed that *in-vitro* matured oocytes from ovarian biopsies would be suitable for producing human embryos, and his motivation for contacting Patrick and initiating their collaboration was that Bob thought that Patrick could solve the sperm capacitation problem with which he had been wrestling since 1965 (Johnson, 2011), and which was, in fact, resolved in 1968 by the use of Bavister’s medium (Bavister, 1969). However, towards the end of 1968 Bob became less sure that the *in-vitro* matured eggs would produce viable embryos, despite their chromosomal maturity, and so he and Patrick turned to laparoscopic recovery of mature ovarian follicle eggs (Steptoe and Edwards, 1970). Patrick was a major pioneer in his own right, although as underappreciated at the time as was Bob (Johnson *et al.*, 2010). His book *Laparoscopy in Gynaecology* (Steptoe, 1967) is to keyhole surgery what Bob’s *Lancet* paper is to ART. These two professional outcasts formed a powerful partnership, known around Bourn Hall in later years as ‘Steppie and the Boss’.

There is a third player who often gets overlooked but whom it is particularly important to acknowledge in this book intended for ART practitioners, and that is Jean Purdy. Jean joined Bob in 1968 as his technician, one of her attractions being her nursing qualification, a sign of the increasing importance that his forays into use of clinical material was assuming. She worked with him and Patrick until her early death aged 39 in 1985 (Edwards and Steptoe, 1985). Jean was as hard-working and dedicated as both Steppie and the Boss, and had two attributes that were of key importance for the success of their partnership. Perhaps the most important, as has become clear from a recent analysis of a newly discovered set of Oldham notes and notebooks that Kay Elder and I are working through, is her organizational role – for it was Jean who methodically took all the notes made by Bob and Patrick on scraps of paper and entered, cross-checked and summarized

Foreword



Fig 0.1 Bob Edwards (1925–2013), Jean Purdy (1946–85) and Patrick Steptoe (1913–88) at Bourn Hall in 1981 (courtesy Bourn Hall Clinic).

them in the notebooks to give the detailed records on which they based their work over the period from 1969 to 1978 (and which we intend soon to publish). Bob and Patrick clearly relied on Jean to undertake this difficult and demanding task, which she appears to have performed meticulously. Less easy to evaluate is her role as the ‘oil’ in the relationship between these two strong-willed and determined men, between whom (despite, and perhaps even because of, their assigned roles as outcasts) sparks must have flown at times, both being under a lot of pressure – both internal and from outside.

Sadly, neither Patrick nor Jean were alive to share in the award or the joy of the Nobel Prize that went to Bob in 2010, and even Bob by then was too ill to attend in person, although delighted at the eventual recognition some 45 years after that *Lancet* paper that set the whole of ART in train. Were Bob alive today, I am sure that he would have been delighted to write this Foreword – although it would have taken a very different form – generous about the book’s scope and content but wagging that finger gently and with his rueful

smile (that says ‘it pains me to say this’) at what he thought was wrong and missing!

Professor Martin Johnson

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Preface

In the three decades since the birth of Louise Brown, the first child conceived using in-vitro fertilization (IVF), the field of clinical embryology has undergone remarkable growth and evolution. The discipline has come to embrace a wide-variety of specialized laboratory techniques, collectively falling under the umbrella-term *assisted reproductive technology* (ART). Worldwide, over 1 million ART cycles are carried out each year and over 5 million babies are estimated to have been born as a direct consequence. There is no doubt that ART represents one of the most successful interventions in any field of medicine. It has radically altered the way in which most forms of infertility are treated and brought hope to millions of infertile and sub-fertile couples around the world. However, it must be acknowledged that, despite the obvious successes, significant technical challenges still remain and scientific knowledge in some areas of clinical embryology is limited.

With the expansion of ART has come an ever greater emphasis on quality assurance and, in some countries, an increase in the extent to which treatments are overseen by independent or governmental bodies. In order to ensure that patients consistently receive optimal clinical care and the best chances of conception, meticulous training of new personnel in theoretical knowledge as well as practical skills is critical. However, it is equally vital that established doctors, nurses and embryologists constantly refresh their store of knowledge, keeping abreast of changes in the regulatory environment and understanding the benefits and limitations of new technologies – what is proven and what is, at least for the time being, hypothesis or conjecture.

This textbook was inspired by the M.Sc. in Clinical Embryology (University of Oxford), an intensive

one-year residential course that aims to motivate future leaders in clinical embryology and reproductive medicine, inspiring them to investigate the molecular and physiological mechanisms underlying human infertility. This course is now in its fifth successful year and continues to attract global interest, with student representation from 28 countries thus far. This textbook has been compiled by senior academic or clinical staff associated with the M.Sc. course, and aims to present a holistic approach to the treatment of human infertility and the biological mechanisms involved.

We would like to extend our special thanks to Nick Dunton at Cambridge University Press (CUP) for thoughtful and insightful discussion during the early phases of this project, and, above all, his patience during the extended period thereafter. We would also like to thank the following staff at CUP for their help and assistance during the copy-editing and production process: Jodie Hodgson, Lucy Edwards, Christopher Miller and Jane Seakins. Special thanks to Karen Verde at Green Pelican Editorial Services (NJ, USA) for copy-editing this large body of work in such a rapid manner. Special thanks also go to Mr Hamnah Bhatti (University of Oxford Medical School) for creating some of the illustrations provided in Chapters 8 and 32. Several members of the Nuffield Department of Obstetrics and Gynaecology (University of Oxford) provided key support, including Celine Jones, Junaid Kashir and Siti Nornadhirah Amdani. Finally, we would like to thank all of our authors for their support, dedication and patience.

We dedicate this textbook to the ever-lasting legacy of Professor Sir Robert Edwards.

Kevin Coward and Dagan Wells