University of Dundee

Education, education, education

Andersen, Claus Yding; Kristensen, Stine G.; Mamsen, Linn Salto; Barratt, Christopher

Published in:
Molecular Human Reproduction

DOI:
[10.1093/molehr/gay028](https://doi.org/10.1093/molehr/gay028)

Publication date:
2018

Document Version
Peer reviewed version

[Link to publication in Discovery Research Portal](#)

Citation for published version (APA):

Andersen, C. Y., Kristensen, S. G., Mamsen, L. S., & Barratt, C. (2018). Education, education, education: now more than ever? *Molecular Human Reproduction*, 24(8), 426-429. <https://doi.org/10.1093/molehr/gay028>

General rights

Copyright and moral rights for the publications made accessible in Discovery Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from Discovery Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain.
- You may freely distribute the URL identifying the publication in the public portal.

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

1 **Education, education, education – now more than ever?**

2

3 **Yding Andersen Claus^{1,*}, Kristensen Stine G.¹, Mamsen Linn Salto¹, Barratt Christopher L.R.²**

4

5 ¹ Laboratory of Reproductive Biology, The Juliane Marie Centre for Women, Children and Reproduction,
6 Copenhagen University Hospital and Faculty of Health and Medical Sciences, University of Copenhagen,
7 Copenhagen, Denmark.

8 ³Reproductive and Developmental Biology, School of Medicine, Ninewells Hospital and Medical School,
9 University of Dundee, Dundee, DD19SY, UK.

10

11

12 *Corresponding author: e-mail: yding@rh.dk, phone: +45 3545 5822, fax: +45 3545 5824, Address:
13 Laboratory of Reproductive Biology, Section 5712, The Juliane Marie Centre for Women, Children and
14 Reproduction, University Hospital of Copenhagen, Faculty of Health and Medicine, University of
15 Copenhagen, Blegdamsvej 9, Rigshospitalet, DK-2100 Copenhagen, Denmark.

16 ORCID: <https://orcid.org/0000-0001-7681-253X>

17

18 **Running title:** Educating the next generation

19

20 **Disclosure summary:** The authors has nothing to disclose

21

22 **Key words:** Training, post-doctoral education, fertility and reproduction

23

24

25 **Introduction**

26 A whole generation of young scientists and medical doctors enthusiastically entered the field of assisted
27 reproduction and infertility treatment after the birth of the first *in vitro* fertilized (IVF) child Louise Brown in
28 1978. A new paradigm for treating infertility opened and created unprecedented room for research and
29 development. Indeed, the first years of the IVF era was characterised by a huge research effort
30 understanding follicular development including ovarian stimulation and developing robust methods in the
31 laboratory. Thus, many young clinicians and scientists found a significant career opportunity in the field.
32 Their efforts and successes resulted in a logarithmic increase in activity. The SART register in USA have
33 reported that the US had around 25 clinics performing a few thousands cycles annually in 1985, which
34 today has risen to a little less than 400 clinics doing more than 200,000 cycles (SART, 2015). It is estimated
35 that currently over 5 million IVF children have been born worldwide contributing significantly to the next
36 generation (Fauser et al, 2013). Several of the clinicians and scientists who entered the field in the 1980'ties
37 have been leading figures in IVF treatments but now 30-40 years later they have or are about to retire. This
38 implies that the profession faces a massive transgenerational transition. This in itself calls for a strong
39 educational effort of the new and coming generations, but a number of other factors also highlight the
40 need for continued and expanded education in the field of reproduction.

41

42 **The IVF era: Standardizing treatments**

43 Whereas initially the emphasis was on basic research and development of the IVF technology, focus has
44 during the past decades generally switched to optimising treatment outcome including standardisation and
45 consolidating of procedures used clinically (De los Santos et al., 2016). This has resulted in improved
46 reproductive outcome and more efficacious treatment modalities. The introduction of standardised
47 operation procedures has stabilised results for most fertility clinics and currently many clinics perform with
48 stable pregnancy rates. However, overall success rates have only shown modest increases in the last
49 decade suggesting that continued increase in successful treatments is unlikely to derive from new and

50 different stimulation protocols and further standardisation of protocols and laboratory procedures. The
51 above notwithstanding, success rates are still modest. According to recent ESHRE and ASRM reports a
52 delivery rate of ~35 percent per cycle depending on patient selection (Calhaz-Jorge et al., 2017; SART,
53 2015). There is a growing understanding that a continued and expanded research effort is mandatory to
54 continue an improvement of treatment outcome.

55 Since the field started in early 1980'ties, the business model for infertility treatment has dramatically
56 changed from being mainly a public-sector activity to more private sector involvement; in 2016 almost 60%
57 of all IVF and ICSI treatment in Denmark was performed in private clinics despite public funding for patients
58 below the age of 40 years (Sundhedsdatastyrelsen, 2016). This has necessarily resulted in an increased
59 focus on efficient clinical services and less focus on development of new techniques and improved
60 understanding of the underlying physiological processes (Spencer et al., 2016). However, an improved
61 understanding of the physiological and molecular requirements for successful follicular development,
62 oocyte maturation and sperm selection is widely acknowledged, but currently there is a limited effort to
63 secure knowledge transfer to the young generations and for continued education.

64 In this context it is interesting to notice that a wave of consolidation among fertility centres has taken place
65 in recent years in which many private fertility clinics are sold to larger consortiums usually comprising
66 several clinics in several different countries (Sydney Morning Herald, 2008; 2013; 2015). These consortia
67 often establish a central research and development unit to serve all member clinics. In the US, investors are
68 transforming an industry that has long been dominated by standalone clinics so much so that in the USA
69 the top five largest fertility chains now account for more than 16% of the marked share (SART, 2015).
70 However, as yet it is not clear to what extend these units will contribute substantially to the basic science
71 development required to advance new procedures with significant clinical impact. In addition, a lot of
72 smaller private fertility clinics contribute only to a minor extent to the education of new clinicians and
73 scientists, which with the increased development in the private sector potentially exacerbates the
74 educational gap.

75 Despite innovations in assisted reproductive technology (ART) such as intracytoplasmic sperm injection
76 (ICSI), preimplantation genetic diagnostic (PGD), and stem cell research the massive task of effectively
77 treating women at an advanced age is still unresolved. With the substantial postponement of childbearing
78 seen particularly in the European countries (Mills et al, 2011) and the increase in infertile couples seeking
79 help to have a child (Kupka et al., 2016; SART, 2015), the field of reproductive sciences is facing an
80 unprecedented challenge in developing new techniques to individualize and advance treatments for
81 infertility. Many of the potential new treatments that are to be developed will require a multidisciplinary
82 approach with several areas of expertise involved – often skills which do not normally participate in the
83 reproductive medicine arena. Examples of such new areas include *in vitro* follicle activation with activation
84 of specific intracellular signalling pathways (Kawamura et al., 2013), culture of human preantral follicles on
85 suitable scaffolds (Yin et al., 2016a; Laronda et al., 2017; McLaughlin et al., 2018), *in vitro* maturation of
86 immature human oocytes (Yin et al., 2016b), generation of artificial gametes from stem cells (Hikabe et al.,
87 2016), understanding *in vitro* meiosis, understanding and improving sperm quality (Barratt *et al.*, 2017) etc.
88 In order to facilitate an effective and orderly translational transition into the clinic a substantial educational
89 effort in broad areas of reproduction will be required.

90

91 **The missing links to a new generation of reproductive scientists**

92 Other medical professions may inspire our field on how to potentially improve and advance the educational
93 effort. For instance, in the area of neuropathology PhD students are required to follow 10 obligatory
94 courses and to pass an EU-course offered by the European Confederation of Neuropathological Societies
95 (Euro-CNS) in order to obtain their degree. Moreover, Euro-CNS has established several specialized
96 scientific and clinical programs to their European members on both junior and senior level to facilitate the
97 exchange of scientific information between members and to help clinicians and researchers to stay up to
98 date with the latest advances within their field. Further, the Federation of European Neuroscience Societies

99 (FENS) representing 42 European countries conducts courses and meetings to promote excellence in
100 neuroscience research (EAN, 2018).

101 Another initiative recently launched is the UK based Medical Research Foundation national PhD training
102 programme in anti-microbial resistance research. This innovative national programme will train 150 new
103 researchers to explore ways to tackle anti-microbial resistance, one of the greatest emerging threats to
104 human health and will provide a strong educational and networking platform, which will strengthen the
105 UK's research capacity overall during education. Importantly, an alumni platform for continued interaction
106 after PhD graduation is also included (University of Bristol, 2018).

107 These programmes are obviously expensive undertakings but perhaps international societies such as ESHRE
108 and ASRM could lead similar initiatives in our field and explore the options for a much more detailed and
109 comprehensive educational effort.

110 On a practical level the professions attitude towards participation in congresses and educational activities
111 should be re-evaluated. Often young researchers are required to submit an abstract to a conference in
112 order to be supported financially. Most conferences understand this policy and accept most -- if not all --
113 abstracts. Unfortunately, this does not always result in a high-quality peer-reviewed paper and may serve
114 only as an entrance ticket for participation (Lensen *et al.*, 2017). Such a policy does not encourage senior
115 researchers to act as reviewers and may in the long term reduce the quality of the reviewing process.
116 Further, the abstract reviewing process is often not clear to neither those who submit an abstract and even
117 to those who evaluate abstracts. This strategy does not support a strong and thorough research
118 involvement from young clinicians and scientists and is in some aspects counterproductive to stimulate
119 new substantiated ground-breaking research.

120 Moreover, in the early years of the IVF era the pharma industry had minimal restrictions on supporting
121 participation in scientific conferences and symposia. Many young scientists and clinicians at that time
122 benefitted and received a significant training and education due to support from the pharma industry,
123 which to a large extent has disappeared today.

124 Additional challenges include the legal and regulatory structure for training in the field. For example, the
125 recognition of clinical embryology, which is now developing into an area of its own right with highly skilled
126 competences. This is not recognised in several countries, either educationally or legally and makes it less
127 likely that highly skilled persons will persuade a career in the field of reproduction (Kovačič et al., 2015).
128 These changes, amongst others, have led to a gap in the education of young scientists and clinicians. There
129 is a profound educational need to improve basic skills of the next generation to be able to take infertility
130 and treatment to the next level, improve clinical practise and widen the use of ART and make it more
131 accessible to larger population groups.

132

133 **Multi-disciplinary educational platforms are needed**

134 Although this educational challenge is widely recognised, it is interesting to appraise how we are currently
135 addressing it. . Large professional organisations like ESHRE and ASRM indeed undertake a lot of educational
136 activities including for example a one-and-a-half-day special interest group workshop that often dive into a
137 narrow area and provide an update on the current knowledge. Other arenas are well catered for. For
138 example, training of embryologists and nurses where there are a plethora of courses and an examination
139 system. However, in general these programmes are mainly centred on clinical activities and provide to a
140 lesser extent a broader knowledge base from which basic science-oriented research can benefit. A
141 fundamental question is how we best train our new MD/PhD students?

142 The ReproUnion network is an EU- and local funded multi-disciplinary collaboration between 14 public
143 fertility clinics and several basic science-oriented laboratories in the Capital Region of Copenhagen in
144 Denmark and the Skaane Region in Sweden. To date it has educated 25 PhD-students. This network has
145 provided 4 different PhD-courses centred on basic science in reproductive biology, ART procedures, male
146 fertility and epidemiological studies with reproductive medicine. ReproUnion support the ReproYoung
147 association – a network of young researchers working in the field of reproduction and infertility.
148 ReproYoung has facilitated inter-laboratory collaborations, and hosted several International ReproYoung

149 conferences, where all participants are required to present their work and have feed-back from other
150 young colleagues and senior researchers. These activities, together with monthly education seminars,
151 where the PhD-students present their work combined with senior lectures, provides a new type of
152 educational platform with a knowledge base that is able to sustain a larger collaborative effort within the
153 area of reproductive medicine. Another inter-sectorial and multidisciplinary network has recently been
154 established - 'GrowSperm' which aims to train and coach young scientists in the field of male reproduction,
155 and comprises several public and private EU partners.

156 However, the educational skills of hands-on laboratory training, where students learn specific procedures
157 by actually doing them are still missing in the educational programme of ReproUnion. In the US they have
158 overcome this hurdle with the Frontiers in Reproduction (FIR) course. FIR is a very successful and world-
159 renowned programme in reproductive biology held annually since 1998 at the Marine Biological Laboratory
160 (MBL) in Woods Hole, Massachusetts. The 6-week summer course represent a unique high-quality training
161 experience comprising daily laboratory exercises, informal seminars, one-on-one tutorials, and lectures in
162 the morning and evening by highly experienced faculty in the field. The FIR course is designed for scientists-
163 in-training who seek to improve their knowledge and experimental skills in order to pursue a career in
164 reproductive sciences, and a 10-year follow-up survey performed on former attendees has recently
165 confirmed the overall significant positive impact that the course has had on the training and upward career
166 trajectory of the participants (Ascoli et al., 2016). Moreover, the success of the course highlights the
167 excellent networking opportunities and research collaborations within and between attendees and faculty
168 which cannot easily be duplicated by any online e-learning system. The efficacy and impact of physical
169 interactions and personal communication should not be underestimated, and the inspirational and passion-
170 driven lessons from pioneers in the field are fundamental to these learning experiences.

171 The FIR course serves as a good example of what can be accomplished with this type of training platform
172 and is an approach that needs to be complemented and expanded with a potential European counterpart
173 to significantly impact the advances in the reproductive sciences.

174 Currently there is enormous interest in new educational methods and how best to educate future
175 generations of scientists and clinicians (Bosch et al., 2017). In reproductive biology we also need to take a
176 fresh look at our current programs and evaluate if they are fit for the education of a new generation of
177 PhD/MD in the field.

178

179 **Conclusion**

180 For half a century medical professionals have been trained and educated to standardize and streamline
181 ART, but current treatment has reached a plateau in success rates and costs. We are facing a new era in
182 which research and development is absolutely fundamental to advance reproductive sciences. A new
183 generation of reproductive scientists needs to be educated in a more structured, broader and purposeful
184 way than current platforms are providing. Multi-disciplinary educational platforms are required to advance
185 the research and provide a more fully equipped educational package for young researchers in the field.
186 Today's trends in society calls for 'thinkers' – not merely technicians/clinicians – and we need to take
187 responsibility for the next generation in more than one way.

188

189 **Authors' roles:** All authors participated in the designing the ideas of this article and all participated in
190 formulating the article. All authors have approved this article.

191

192 **Acknowledgements**

193

194 **Funding**

195 This work was supported by The ReproUnion network and the Novo Nordisk foundation (C.Y.A.) and MRC,
196 Chief Scientists Office (Scotland) Astra Zeneca and Bill and Melinda Gates Foundation (C.L.R.B). They had no
197 influence on this manuscript.

198

199 **Conflict of interest**

200 C.Y.A is the editor-in-chief of the Reproduction section of Frontiers in Endocrinology and has received
201 lecturing and consulting fees from Merck, Ferring, Merck-Serono and IBSA.

202 C.L.R.B is the editor-in-chief of Molecular Human Reproduction and Chair of the World Health Organisation
203 Expert Synthesis Group on Diagnosis of Male infertility (2012-2017). C.L.R.B. has received lecturing fees
204 from Merck and Ferring.

205 S.G.K. is chairman of ReproYoung and has received lecturing fees from Merck and IBSA.

206

207 **References**

- 208 Ascoli M, Mebane D, Fazleabas AT (2016) Frontiers in Reproduction (FIR): An Assessment of Success. *Biol*
 209 *Reprod* 95:27,1-6.
- 210 Barratt CLR, Björndahl L, De Jonge CJ, Lamb DJ, Osorio Martini F, McLachlan R, Oates RD, van der Poel S, St
 211 John B, Sigman M, Sokol R, Tournaye H. (2017) The diagnosis of male infertility: an analysis of the evidence
 212 to support the development of global WHO guidance-challenges and future research opportunities. *Hum*
 213 *Reprod Update* 23:660-680.
- 214 Bosch J, Maaz A, Hitzblech T, Holzhausen Y, Peters H (2017) Medical students' preparedness for
 215 professional activities in early clerkships. *BMC Med Educ* 17:140.
- 216 Calhaz-Jorge C, Geyter C De, Kupka MS, Mouzon J de, Erb K, Mocanu E, Motrenko T, Scaravelli G, Wyns C,
 217 Goossens V, et al. (2017) Assisted reproductive technology in Europe, 2013: results generated from
 218 European registers by ESHRE. *Hum Reprod* 32:1957–1973.
- 219 EAN (2018). <https://www.ean.org/>
- 220 Fauser BC, Serour GI (2013) Optimal in vitro fertilization in 2020: the global perspective. *Fertil Steril* 100:
 221 297-298.
- 222 De los Santos MJ, Apter S, Coticchio G, Debrock S, Lundin K, Plancha CE, Prados F, Rienzi L, Verheyen G,
 223 Woodward B, et al. (2016) Revised guidelines for good practice in IVF laboratories (2015). *Hum Reprod*
 224 31:685–686.
- 225 Hikabe O, Hamazaki N, Nagamatsu G, Obata Y, Hirao Y, Hamada N, Shimamoto S, Imamura T, Nakashima K,
 226 Saitou M, Hayashi K (2016) Reconstitution in vitro of the entire cycle of the mouse female germ line. *Nature*
 227 539:299-303.
- 228 Kawamura K, Cheng Y, Suzuki N, Deguchi M, Sato Y, Takae S, Ho CH, Kawamura N, Tamura M, Hashimoto
 229 S, et al. (2013) Hippo signaling disruption and Akt stimulation of ovarian follicles for infertility treatment.
 230 *Proc Natl Acad Sci USA* 110:17474-17479.
- 231

232 Kovačič B, Plas C, Woodward BJ, Verheyen G, Prados FJ, Hreinsson J, De los Santos MJ, Magli MC, Lundin K,
233 Plancha CE. (2015) The educational and professional status of clinical embryology and clinical embryologists
234 in Europe. Hum Reprod 30:1755-1762
235

236 Kupka MS, D’Hooghe T, Ferraretti AP, Mouzon J de, Erb K, Castilla JA, Calhaz-Jorge C, Geyter C De, Goossens
237 V, (EIM) EI-MC, et al. (2016) Assisted reproductive technology in Europe, 2011: results generated from
238 European registers by ESHRE. Hum Reprod 31:233-248.

239 Laronda MM, Rutz AL, Xiao S, Whelan KA, Duncan FE, Roth EW, Woodruff TK, Shah RN (2017) A
240 bioprothetic ovary created using 3D printed microporous scaffolds restores ovarian function in sterilized
241 mice. Nat Commun 8:15261.

242 Lensen S, Jordan V, Showell M, Showell E, Shen V, Venetis C, Farquhar C (2017) Non-publication and
243 publication bias in reproductive medicine: a cohort analysis. Hum Reprod 32:1658-1666.

244 McLaughlin M, Albertini DF, Wallace WHB, Anderson RA, Telfer EE (2018) Metaphase II oocytes from
245 human unilaminar follicles grown in a multi-step culture system. Mol Hum Reprod (in press); doi:
246 10.1093/molehr/gay002.

247 Mills M, Rindfuss RR, McDonald P, Velde E te, ESHRE Reproduction and Society Task Force on behalf of the
248 ER and ST (2011) Why do people postpone parenthood? Reasons and social policy incentives. Hum Reprod
249 Update 17:848–860.

250 Mohr S, Koch L (2016) Transforming social contracts: the social and cultural history of IVF in Denmark.
251 Reprod Biomed Soc Online 2:88–96.

252 SART (2015). https://www.sartcorsonline.com/rptCSR_PublicMultYear.aspx?ClinicPKID=0

253 Sydney Morning Herald (<https://www.smh.com.au/business/lots-of-life-in-ivf-market-20080811-3t5n.html>;
254 <https://www.smh.com.au/business/investors-jump-into-virtus-float-20130611-2o1a8.html>
255 [https://www.ibisworld.com.au/media/2015/06/03/fertility-service-providers-adopt-differing-strategies-to-](https://www.ibisworld.com.au/media/2015/06/03/fertility-service-providers-adopt-differing-strategies-to-nurture-growth/)
256 [nurture-growth/](https://www.ibisworld.com.au/media/2015/06/03/fertility-service-providers-adopt-differing-strategies-to-nurture-growth/)

257 Spencer EA, Mahtani KR, Goldacre B, Heneghan C (2016) Claims for fertility interventions: a systematic
 258 assessment of statements on UK fertility centre websites. *BMJ Open* 6:e013940.

259 Sundhedsdatastyrelsen. Assisteret Reproduktion IVF-registeret - Tal og Analyse (2016) København.
 260 <https://sundhedsdatastyrelsen.dk/da/tal-og-analyser/analyser-og-rapporter/andre-analyser-og->
 261 [rapporter/assisteret-reproduktion](https://sundhedsdatastyrelsen.dk/da/tal-og-analyser/analyser-og-rapporter/andre-analyser-og-rapporter/assisteret-reproduktion)

262 University of Bristol (2018) <http://www.bris.ac.uk/cellmolmed/study/postgraduate/amr/>.
 263

264 Yin H, Kristensen SG, Jiang H, Rasmussen A, Andersen CY (2016a) Survival and growth of isolated pre-antral
 265 follicles from human ovarian medulla tissue during long-term 3D culture. *Hum Reprod* 31:1531-1539.

266 Yin H, Jiang H, Kristensen SG, Andersen CY (2016b) Vitrification of *in vitro* matured oocytes collected from
 267 surplus ovarian medulla tissue resulting from fertility preservation of ovarian cortex tissue. *J Assist Reprod*
 268 *Genet* 33:741-746.
 269
 270
 271