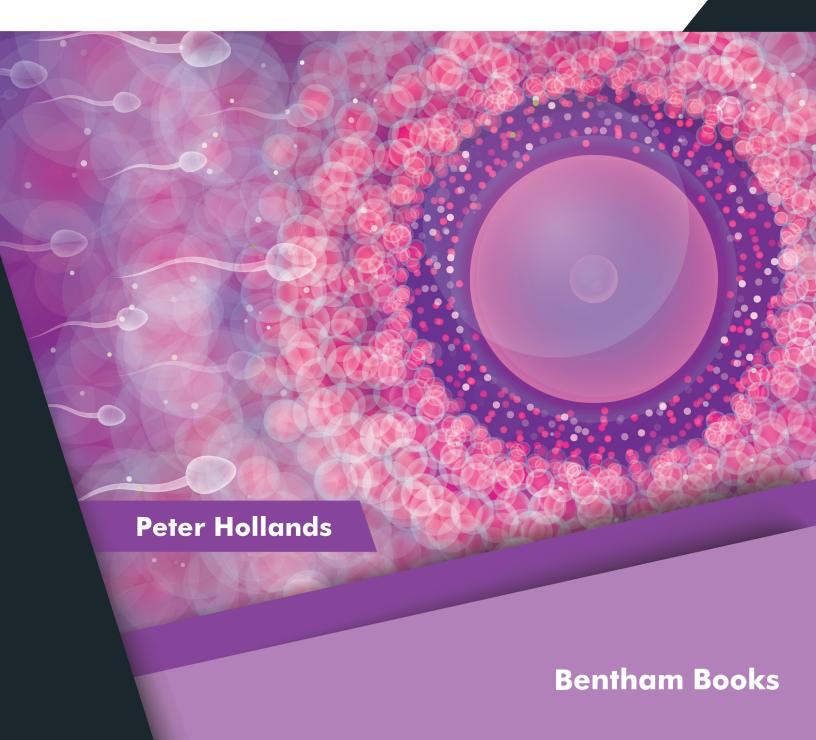
# THE FERTILITY PROMISE THE FACTS BEHIND IN VITRO FERTILISATION (IVF)



# **Medicine Demystified**

(Volume 2)

# The Fertility Promise: The Facts Behind in vitro Fertilisation (IVF)

Authored by

**Peter Hollands** 

Freelance Consultant Clinical Scientist Huntingdon, Cambs, PE26 1LB UK

# Ogf lelpg'Fgo {unltlgf

Volume #4

 $Vj \; g''Hgt \textit{vkrks} \textit{| 'Rt qo kug < Vj g''Hc ewi'Dgj kpf ''kp''xkst q''Hgt \textit{vkrkuc vkqp''*} KXH + \textit{| Market and weakly between the property of the prope$ 

Cwj qt: Rgvgt' J qmcpf u

ISSN (Online): 4959/7286

ISSN (Print): 4959/7278

ISBN (Online):; 9:/;:3/7262/4:/;

ISBN (Print):; 9:/;:3/7262/4;/8

ISBN (Paperback): ; 9: /; : 3/7262/52/4

 $\ensuremath{\mathbb{C}}$  2022, Bentham Books imprint.

Published by Bentham Science Publishers Pte. Ltd. Singapore. All Rights Reserved.

# BENTHAM SCIENCE PUBLISHERS LTD.

#### End User License Agreement (for non-institutional, personal use)

This is an agreement between you and Bentham Science Publishers Ltd. Please read this License Agreement carefully before using the ebook/echapter/ejournal ("Work"). Your use of the Work constitutes your agreement to the terms and conditions set forth in this License Agreement. If you do not agree to these terms and conditions then you should not use the Work.

Bentham Science Publishers agrees to grant you a non-exclusive, non-transferable limited license to use the Work subject to and in accordance with the following terms and conditions. This License Agreement is for non-library, personal use only. For a library / institutional / multi user license in respect of the Work, please contact: permission@benthamscience.net.

# **Usage Rules:**

- 1. All rights reserved: The Work is the subject of copyright and Bentham Science Publishers either owns the Work (and the copyright in it) or is licensed to distribute the Work. You shall not copy, reproduce, modify, remove, delete, augment, add to, publish, transmit, sell, resell, create derivative works from, or in any way exploit the Work or make the Work available for others to do any of the same, in any form or by any means, in whole or in part, in each case without the prior written permission of Bentham Science Publishers, unless stated otherwise in this License Agreement.
- 2. You may download a copy of the Work on one occasion to one personal computer (including tablet, laptop, desktop, or other such devices). You may make one back-up copy of the Work to avoid losing it.
- 3. The unauthorised use or distribution of copyrighted or other proprietary content is illegal and could subject you to liability for substantial money damages. You will be liable for any damage resulting from your misuse of the Work or any violation of this License Agreement, including any infringement by you of copyrights or proprietary rights.

#### Disclaimer:

Bentham Science Publishers does not guarantee that the information in the Work is error-free, or warrant that it will meet your requirements or that access to the Work will be uninterrupted or error-free. The Work is provided "as is" without warranty of any kind, either express or implied or statutory, including, without limitation, implied warranties of merchantability and fitness for a particular purpose. The entire risk as to the results and performance of the Work is assumed by you. No responsibility is assumed by Bentham Science Publishers, its staff, editors and/or authors for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products instruction, advertisements or ideas contained in the Work.

# Limitation of Liability:

In no event will Bentham Science Publishers, its staff, editors and/or authors, be liable for any damages, including, without limitation, special, incidental and/or consequential damages and/or damages for lost data and/or profits arising out of (whether directly or indirectly) the use or inability to use the Work. The entire liability of Bentham Science Publishers shall be limited to the amount actually paid by you for the Work.

#### General:

- 1. Any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims) will be governed by and construed in accordance with the laws of Singapore. Each party agrees that the courts of the state of Singapore shall have exclusive jurisdiction to settle any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims).
- 2. Your rights under this License Agreement will automatically terminate without notice and without the

- need for a court order if at any point you breach any terms of this License Agreement. In no event will any delay or failure by Bentham Science Publishers in enforcing your compliance with this License Agreement constitute a waiver of any of its rights.
- 3. You acknowledge that you have read this License Agreement, and agree to be bound by its terms and conditions. To the extent that any other terms and conditions presented on any website of Bentham Science Publishers conflict with, or are inconsistent with, the terms and conditions set out in this License Agreement, you acknowledge that the terms and conditions set out in this License Agreement shall prevail.

# Bentham Science Publishers Pte. Ltd.

80 Robinson Road #02-00 Singapore 068898 Singapore Email: subscriptions@benthamscience.net



# **CONTENTS**

PREFACE	
CONSENT FOR PUBLICATION	
CONFLICT OF INTEREST	
ACKNOWLEDGEMENTS	ii
DEDICATION	iii
CHAPTER 1 A BIT OF HISTORY	1
Peter Hollands	1
A CHILD IS BORN	1
CONTROVERSY	2
OTHER OPTIONS FOR FERTILITY PATIENTS?	3
THE FIRST FERTILITY TREATMENTS	3
The First Technology	
Fertility Treatment Today	
Global IVF	
Money!	
'Breakthroughs'	
Nobel Prize	7
Still Not A Cure	
Population Growth	8
ADOPTION	
PIONEERING TIMES	
BLACK MONDAY	10
INPATIENTS AND REGULATION	10
MORE RECENTLY	
INNOVATION	
PROFIT AND 'ADD-ONS'	
STAGNATION	
THE FUTURE	13
KEY POINTS OF CHAPTER 1	15
CHAPTER 2 THE FEMALE PATIENT	16
Peter Hollands	16
INTRODUCTION	16
FEMALE INFERTILITY	17
Blocked Tubes	17
Endometriosis	17
Polycystic Ovary Syndrome (PCOS)	18
Thyroid	
Premature Menopause	18
Surgical Damage and Fibroids	19
Sterilisation	
Medications	
Other Causes of Infertility	
Idiopathic Infertility	
Stress!	
'BACK-TO-BACK' TREATMENTS	
A FINAL PRAYER	
KEY POINTS OF CHAPTER 2	

CHAPTER 3 THE MALE PATIENT	24
Peter Hollands	24
INTRODUCTION	24
THE MALE ROLE IN FERTILITY TREATMENT	24
THE 'MEN'S ROOM' PORNOGRAPHY AND SEMEN ASSESSMENT	25
Hot Pants!	27
Testicular Damage	
Vasectomy	
Ejaculation and Psychosexual Disorders	28
Hormonal and Genetic Disorders	
Medicines and Drugs	
Life-style Issues	
Stress	
A FINAL PRAYER	
KEY POINTS OF CHAPTER 3	_
CHAPTER 4 THE LGBT PATIENTS	
Peter Hollands	
INTRODUCTION	_
SAME SEX FEMALE PATIENTS	
Surrogacy for Same Sex Female Patients	
Female Partner Providing Eggs for Treatment	
SAME SEX MALE PATIENTS	
Egg Donation and Surrogacy	
Gender Re-Assignment	
KEY POINTS OF CHAPTER 4	
CHAPTER 5 IVF CLINICS	
Peter Hollands	
INTRODUCTION	
MONEY!	
PROFIT (OK, BUT NOT TOO MUCH!)	
PUBLIC PROVISION OF IVF SERVICES (DIFFICULT TO DELIVER)	
TREATMENT CYCLE NUMBERS (SIZE IS NOT EVERYTHING)	
'FAMOUS' (OR INDEED INFAMOUS) CLINIC STAFF	
IVF MARKETING (CAVEAT EMPTOR!)	
IVF CLINIC STATISTICS (IS THAT BLACK ACTUALLY WHITE OR IS IT GREY?)	43
SERVICE (GOOD, BAD OR INDIFFERENT)	45
FERTILITY CLINIC FACILITIES	
FERTILITY CLINIC STAFF	
FERTILITY CLINIC TECHNOLOGY	
QUESTIONS TO ASK A FERTILITY CLINIC	
KEY POINTS OF CHAPTER 5	49
CHAPTER 6 THE BASIC TREATMENT	50
Peter Hollands	50
INTRODUCTION	50
THE FERTILITY MEDICATIONS	50
FOLLICULAR GROWTH MONITORING	52
OVARIAN HYPER-STIMULATION SYNDROME	52
THE EGG COLLECTION	52
SEMEN PRODUCTION AND INSEMINATION	53

IVF FROM A LABORATORY VIEWPOINT	54
THE EMBRYO REPLACEMENT (TRANSFER)	
EMBRYO FREEZING AND REPLACEMENT	
THE PREGNANCY TEST AND THE DAY 35 SCAN	
A 'PRECIOUS' PREGNANCY	
DONOR GAMETES (DONOR SPERM AND DONOR EGGS)	
Donor Sperm	
Donor Sperm in IVF	
Donor Eggs in IVF	
KEY POINTS OF CHAPTER 6	
CHAPTER 7 THE 'ADD-ONS' SCANDAL	
Peter Hollands	
INTRODUCTION	
IVF TECHNOLOGIES AND WORK PRACTICE	
The 'Right' Patient	
'Wobbly' Evidence	
A 'Re-Boot' of IVF	
TREATMENTS OF MALE INFERTILITY	
'Catching Sperm'	
'Add-ons'	
Intracytoplasmic Sperm Injection (ICSI) and Related Technologies	
Intracytoplasmic Morphologically Selected Sperm Injection (IMSI)	
Physiological Intracytoplasmic Sperm Injection (PICSI)	
Sperm DNA Fragmentation Testing	
Time-Lapse Video Analysis of Embryonic Development	
Pre-Implantation Genetic Screening (PGS) and Preimplantation Genetic Diagnosis (PGD)	
Pre-Implantation Genetic Screening (Aneuploidy Screening)	
Pre-Implantation Genetic Diagnosis (PGD)	
Endometrial 'scratching' (Endometrial Injury)	
Assisted Hatching	
Embryo Glue	
Elective Freeze All Cycles	
Reproductive Immunology	84
Acupuncture	
CONCLUSIONS ON 'ADD-ONS'	85
MISLEADING	
COUNSELLING AND CLINICAL TRIALS	
STARTING FROM SCRATCH AND 'BLOBS'	
KEY POINTS OF CHAPTER 7	88
CHAPTER 8 THE REGULATORS AND PROFESSIONAL SOCIETIES	89
Peter Hollands	
INTRODUCTION	
POWER IS NOT ALWAYS A GOOD THING	
UK REGULATION	
THE ROLE OF A REGULATORY AUTHORITY	
What Does the Regulatory Authority Regulate?	
The European Society for Human Reproduction and Embryology (ESHRE)	
KEY POINTS OF CHAPTER 8	
CHAPTER 9 THE PATIENT 'JOURNEY'	
CHALLEN JUNIEL	20

Peter Hollands	
THE JOURNEY	
First Things First	97
Time is Running Out!	98
The First Consultation	
The Second and Nurse Consultation	99
At Last! The Treatment is Starting!	100
The Day of Egg Collection	100
Fertilisation Day and Onwards	
Embryo Replacement (Transfer) Day	
It's Freezing in Here!	102
Pregnancy Test Day	
The Day 35 'Heart Beat Scan'	
KEY POINTS OF CHAPTER 9	
CHAPTER 10 ADVICE TO FERTILITY PATIENTS	
Peter Hollands	
INTRODUCTION	
MORE ADVICE ON ADVICE	
Optimism and Electronic Advice	
Clinic Counsellor	
Who to Tell?	108
Family?	
Friends?	109
Should I Tell People At Work?	109
Smoking, Alcohol, Obesity and Underweight	110
Smoking	110
Alcohol	111
Obesity	112
Back-to-Back Treatment Cycles	114
Egg Freezing: Good Idea, False Hope or Money-Making Machine?	11:
Add-ons	
Pregnancy, Birth and Parenthood	11′
Pregnancy	113
Childbirth (Labour)	118
Parenthood	
A Second Opinion?	
CHANGING FERTILITY CLINICS?	
INFERTILITY AND MENTAL HEALTH	
IVF MYTHS	
KEY POINTS OF CHAPTER 10	
CHAPTER 11 THE FUTURE OF IVF	124
Peter Hollands	
INTRODUCTION	
FUTURE TECHNOLOGY	
The Starting Point	
Innovations	
Profit!	
Stagnation	
A PROMISING FUTURE?	
Telemedicine	129

INVOcell-A Possible Cheaper Version of IVF?	130
Laboratory Automation	131
Artificial Intelligence	132
Quantum Biology and Quantum Physics	132
PRP and Stem Cells	133
Embryonic Stem Cells and Hybrids	
KEY POINTS OF CHAPTER 11	136
CHAPTER 12 A FINAL THOUGHT	137
Peter Hollands	137
INTRODUCTION	137
FERTILITY PATIENTS	137
PHYSICIANS	138
CLINICAL EMBRYOLOGISTS	139
FERTILITY NURSES	140
CLINICS	
CONCLUSION	
KEY POINTS OF CHAPTER 12	142
SUGGESTED FURTHER READING	143
USEFUL WEBSITES	143
GLOSSARY	144
SUBJECT INDEX	368

# **PREFACE**

My inspiration to write The Fertility Promise has been my experience in assisted reproduction (or IVF) since it was first introduced to me at Bourn Hall Clinic in the early 1980's. I was lucky enough to be one of the first Clinical Embryologists in the world. I have seen IVF move from the initial ideas of Bob Edwards, Patrick Steptoe and Jean Purdy, being carried out in a little village in rural Cambridgeshire, to a billion-Dollar (or Pound!) industry being delivered on a global scale. Many things have changed in IVF during that time. IVF technology has moved on to a certain extent (but with no tangible benefit to patients but with definite financial benefits to clinics and manufacturers) and regulation to ensure optimum quality and safety of all fertility treatments is now routine in most countries. Regulation is extremely important in an area such as IVF to protect both patient and societal safety. Patient expectations, in terms of what a fertility clinic can deliver, have undergone an exponential rise. Unfortunately, the technology in IVF and the people working in IVF have not really met these expectations. Without a change in mind-set these patient expectations will never be met.

IVF has, in my opinion, stagnated in the past 25 years to the point where great change is needed to make further progress and improve the service provided to patients. There have been few effective innovations or new ideas and the live birth rate (which, by the way, is the *only* thing which really matters to all fertility patients) has not really changed since 1978. There are IVF clinics whose sole purpose is to maximise financial profit. There is little or no thought for the well-being of the patients involved or for their hopes, wishes and fears. There are some IVF clinics who deliberately mislead patients to ensure that their profit goals are met. This is not how medicine should be practised and is a very sad reflection on the current practice of IVF.

All physicians and healthcare professionals, in any speciality, have a duty of care to their patients which means that everything which is done to, or for, the patient is in the best interest of the patient. This is sadly not the case in the medical speciality of IVF which is a very sad and depressing reflection on the legacy which was left to us by Bob Edwards, Patrick Steptoe and Jean Purdy. It also means that fertility patients are not getting the care they deserve and need. This is a scandal on a global scale for which everyone involved in these poor practices should be ashamed.

In general terms, the highly vulnerable fertility patient will do anything to make their treatment a success. This is no different to any patient with any sort of problem but over the years I have seen this to be more pronounced in fertility patients. If I told a fertility patient to stand on her head for one hour every day and this will increase her chance of becoming pregnant then I am sure that this patient would do this. If I did this, I would be a very questionable healthcare professional because there is, of course, no evidence that standing on the head will improve fertility treatment outcome and it is therefore not in the best interests of the patient. The combination of vulnerable patients and corporate (sometimes even personal) greed leads us to the present situation in fertility treatment around the globe. There is hype, false promises, deliberately misleading information, false hope, false advice, false science and sometimes even deliberately false claims and marketing. This is destroying the reputation of IVF and seriously inhibiting those who seek to improve the technology with a true focus on patient care.

This book addresses all of these issues using clear, truthful, experienced and unbiased language so that fertility patients can see the true state of IVF. It is not easy reading. You may find some of it shocking. You may find some of it unbelievable but please remember that I

only describe what I have seen and know. I have no hidden agenda; my only agenda is to make fertility treatment better for patients. We can repair the damage which has been done to IVF and move forward in an ethical, truthful and professional way. In order to make these changes it will need co-operation from IVF clinics, the IVF equipment and reagent manufacturers, manufacturers of IVF related medication, the IVF regulators and anyone with a financial interest in IVF. These financial interests are often investors or financial giants with a clear vested interest in a fertility clinic or a group of fertility clinics. This is not intrinsically bad until financial interests overtake patient care, then we have a big problem. Staff who work in fertility treatments may well have to change the way in which they currently think to achieve progress. This means everyone in the clinic because if these changes in mind-set are not agreed upon across the clinic, then they will be ineffective. It will also need a clear understanding and critical analysis of IVF by fertility patients. This is a big challenge for fertility patients, because at present, it is very difficult for them to see who to trust. IVF patients need to move from being passive victims to becoming active, well informed people who have the knowledge and courage to challenge or question the activity or promises of their IVF clinic. If this book stimulates further debate and ultimate change, then it will be a success and IVF will become a trusted medical treatment once more. This is what I truly want to see, but at present, this is not where we are heading. We are heading towards more lies and profiteering in the name of IVF. The purpose for which IVF was invented, to give the opportunity of having a baby to infertile patients and not to generate excessive profit, will prosper. If not, IVF will continue to stagnate, patients will continue to be tricked and misled, and profits will continue to rise. I make no apologies for some of the hard truth and criticism of IVF in this book. I believe that the time is right for change and this book is the beginning.

#### **CONSENT FOR PUBLICATION**

Not applicable.

#### CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

#### ACKNOWLEDGEMENTS

Declared none.

Peter Hollands Freelance Consultant Clinical Scientist Cambridge, UK

# **DEDICATION**

This book is dedicated to my partner Louise Barrett for her love, dedication and support. I must also thank my cardiac surgeon, Mr Ian Wilson and everyone at Liverpool Heart and Chest Hospital without whom none of this would be possible!

# **CHAPTER 1**

# **A Bit of History**

#### **Peter Hollands**

(An Overview of the Historical Development of IVF from 1978 to the Present Day)

History will be kind to me for I intend to write it. Winston. S. Churchill

**Summary**: This chapter introduces the basic history of IVF and fertility treatment and sets the scene for the detailed information presented later in this book. It provides an initial overview of IVF technology from the first birth in 1978 to today and the alternatives to fertility treatment such as adoption. It also considers the growing population of Earth and the possible stagnation of fertility services.

# A CHILD IS BORN

On July 25<sup>th</sup>, 1978, a baby girl was born in Oldham General Hospital. This might not seem a terribly important event except, of course, for the parents and family who were welcoming a new baby into the world. This birth was, in fact, the start of a new era in science and medicine because that baby was Louise Joy Brown. Louise was the first ever baby to be born using technology called *in vitro* fertilisation (IVF).

1978 was an interesting year for other reasons, such as the introduction of the first email system and the first cellular mobile phone (which was the size and weight of a house brick). This communication technology has become pretty dominant in the 21<sup>st</sup> Century and has thankfully reduced in size and weight! It has also become important in the effective delivery of IVF. It was also the year that 'Space Invaders' hit the Earth and took over, Olivia Newton John and John Travolta were strutting their stuff in 'Grease' and the Bee Gees were 'Stayin' Alive'. On reflection, 1978 was a good year for me; I was studying in Cambridge and on a path which would lead me to being involved in the early days of IVF. I was destined to be involved in IVF for my whole career, along with my work in stem cell technology and regenerative medicine and being an academic in several Universities.

Peter Hollands All rights reserved-© 2022 Bentham Science Publishers Everything seemed a little more straightforward in 1978 than our complex, information laden lives in 2021, but it is often too easy to look back on the 'good old days' with rose coloured glasses. I know that it is important to live in the moment, not in the past. Despite this, we all naturally look back at what used to be, and this is perhaps part of what it is to be human and therefore very important. It is also how Historians make their daily bread!

# **CONTROVERSY**

The birth of Louise Brown following IVF resulted in a lot of controversy from many different people and organisations. Some people said it was just a coincidence and that Lesley Brown became pregnant naturally! Others threw their arms up in horror at the thought of 'test-tube babies', which was a terrible term invented by the newspapers. This is even more relevant when the importance of newspapers in 1978 is considered. Newspapers were very much more influential than they are today and what and how they wrote about any subject had a considerable impact on everyone. It is important to get one thing very clear from the start: The term 'test-tube baby' can and should be dismissed as irrelevant. IVF involves neither babies (these come much later in human development) nor test-tubes, so this term will not arise again in this book.

Controversy about IVF came from many directions, including from religious leaders, scientists, physicians, politicians and of course, some of the media harshly criticised the technology. Some surgeons (you know who you are!) claimed that IVF was nonsense, and that tubal surgery (re-opening of the Fallopian tubes by a surgical procedure) was the answer. It was not; tubal surgery has never worked. Vasectomy reversal is equally ineffective. Nevertheless, there were many people who had praise and admiration for the three pioneers who made this unusual birth possible. These three people were, of course, Bob Edwards, Patrick Steptoe and Jean Purdy. Jean Purdy was a nurse by training and became the second clinical embryologist (research assistant to Bob Edwards) in the world after Bob Edwards. Jean had fantastic attention to detail in her work and was critical in the development of the laboratory technology which enabled IVF to take place both for Louise Brown and in the early days of Bourn Hall Clinic. She worked with Edwards and Steptoe in both Oldham Hospital and Bourn Hall Clinic before her untimely death, resulting from malignant melanoma, in 1985. The ongoing legacy of Edwards, Steptoe and Purdy to the world is IVF and all of the related technologies. This admirable and essential teamwork should be admired and respected by everyone. It has to be said, however, that Jean Purdy has not been recognised for her important role in developing IVF until recently. She was on many of the early research papers as an author but interestingly was not an author on the 1978 paper in the medical journal, The Lancet, which



# **Peter Hollands**

Peter was trained at Cambridge University (Churchill College), and he completed his PhD under the supervision of Professor Sir Bob Edwards FRS, who was awarded the Nobel Prize for his work in IVF. Bob Edwards was the key inspiration for Peter to work in IVF, and Bob was his mentor and colleague for many years. Peter has worked as a Clinical Embryologist at Bourn Hall Clinic, the first-ever IVF clinic, and has been associated with IVF treatment for 40 years. Peter has also worked in IVF in Canada and Nigeria. He now lives in rural Cambridgeshire.