Factice of Human Assisted Reproductive Technology

实用人类辅助生殖技术

主编 黄荷凤





实用人类辅助生殖技术

主 编 黄荷凤

副主编 乔 杰 陈子江 曹云霞 刘嘉茵 张 丹

图书在版编目(CIP)数据

实用人类辅助生殖技术/黄荷凤主编.—北京:人民卫生出版社,2018

ISBN 978-7-117-27228-5

I.①实··· Ⅱ.①黄··· Ⅲ.①试管婴儿-技术 Ⅳ.① R321 中国版本图书馆 CIP 数据核字 (2018) 第 182170 号

人卫智网 www.ipmph.com 医学教育、学术、考试、健康, 购书智慧智能综合服务平台 人卫官网 www.pmph.com 人卫官方资讯发布平台

版权所有, 侵权必究!



实用人类辅助生殖技术

主 编: 黄荷凤

出版发行: 人民卫生出版社(中继线 010-59780011)

地 址:北京市朝阳区潘家园南里19号

邮 编: 100021

E - mail: pmph @ pmph.com

购书热线: 010-59787592 010-59787584 010-65264830

印 刷:北京顶佳世纪印刷有限公司

经 销:新华书店

开 本: 889×1194 1/16 印张: 43

字 数: 1271 千字

版 次: 2018年8月第1版 2018年8月第1版第1次印刷

标准书号: ISBN 978-7-117-27228-5

定 价: 298.00元

打击盗版举报电话: 010-59787491 E-mail: WQ @ pmph.com

(凡属印装质量问题请与本社市场营销中心联系退换)



曹云霞(安徽医科大学第一附属医院)

陈子江(山东大学齐鲁医学院)

崔琳琳(山东大学附属生殖医院)

范建霞(上海交通大学医学院附属国际和平妇幼保健院)

黄荷凤(上海交通大学医学院附属国际和平妇幼保健院)

金 帆(浙江大学医学院附属妇产科医院)

金 丽(上海交通大学医学院附属国际和平妇幼保健院)

金 敏(浙江大学医学院附属第二医院)

李 蓉(北京大学第三医院)

刘嘉茵(南京医科大学第一附属医院)

罗琼(浙江大学医学院附属妇产科医院)

马 翔(江苏省人民医院)

马彩虹(北京大学第三医院)

钱羽力(浙江大学医学院附属妇产科医院)

乔 杰(北京大学第三医院)

秦莹莹(山东大学附属生殖医院)

曲 凡(浙江大学医学院附属妇产科医院)

舒 静(浙江省人民医院)

孙 斐(上海交通大学医学院附属国际和平妇幼保健院)

吴红萍(北京大学第三医院)

向卉芬(安徽医科大学第一附属医院)

徐键(浙江大学医学院附属第四医院)

徐晨明(上海交通大学医学院附属国际和平妇幼保健院)

许 泓(上海交通大学医学院附属国际和平妇幼保健院)

颜军昊(山东大学附属生殖医院)

叶英辉(浙江大学医学院附属妇产科医院)

张 丹(浙江大学医学院附属妇产科医院)

张峰彬(浙江大学医学院附属妇产科医院)

张润驹(浙江大学医学院附属妇产科医院)

章志国(安徽医科大学第一附属医院)

朱依敏(浙江大学医学院附属妇产科医院)

邹立波(金华市人民医院)





黄荷凤 中国科学院院士 上海交通大学医学院 附属国际和平妇幼保健院



乔 杰 中国工程院院士 北京大学第三医院



陈子江 教授 山东大学齐鲁医学院



曹云霞 教授 安徽医科大学第一附属医院



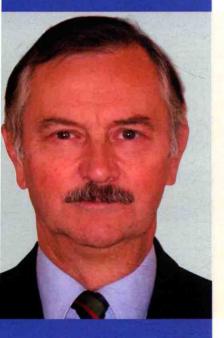
刘嘉茵 教授 南京医科大学第一附属医院



张 丹 教授 浙江大学医学院附属妇产科医院



序



Practice of Human Assisted Reproductive

Preface

Preface by Dr Peter R Brinsden MB BS FRCOG
Past Medical Director, now Consultant
Bourn Hall Clinic
Cambridge, UK

It is both an honour and a pleasure for me to write the preface to this magnificent textbook: "Practice of Human Assisted Reproductive Technology". Professor Huang Hefeng, Editor in Chief, is an Academician of the Chinese Academy of Sciences. Her renowned colleagues, the Deputy Editors in Chief are Professors Qiao Jie, of Peking University Third Hospital, Chen Zijiang of Shandong University, Liu Jiayin of Nanjing Medical University, Cao Yunxia of Anhui Medical University and Dan Zhang of Zhejiang University. They together have conceived and given birth to what must be the most comprehensive, authoritative and practical textbook ever to have come out of the People's Republic of China, possibly even the World.

As many of my friends and colleagues in China know, I am very proud to be the fourth generation of my family to have been born in China – born, in fact, in 1940 at The Peking Union Medical College! Having left China



in 1948, I started to visit again in 1989, when I was invited to a conference in Nanjing, since when I have visited regularly. Over the years I have been honoured with Visiting or Honorary Professorships at four Universities in China. Most recently I had the honour to be invited to lecture at the very important meeting organized by Professor Qiao and her Team from Peking University Third Hospital (PUTH) in March/April of 2018 to celebrate the 30th, anniversary of the birth of Zheng Mengzhu, China's first baby conceived by IVF. This momentous event was the result of the pioneering work of the celebrated Professor Zhang Lizhu, who had previously also invited me to attend and lecture at their 20th, anniversary celebration in 2008. It was a great honour for me to get to know Professor Zhang and her Team. In the same year Professor Huang invited me to a conference in Hangzhou— 'The International Seminar on ART Safety and the Health of Reproduction and Inheritance', at which I spoke on what was then the 'hot topic' of 'Single Embryo Transfer: The evidence for and against'. It was wonderful to visit Professor Huang and her Team in Hangzhou, not only for a great conference, but also because it is the city where my missionary family lived and worked for nearly forty years from about 1900.

It is entirely appropriate and not a mere coincidence, I am sure, that this major textbook is being published in this 30th. anniversary year. *In Vitro* Fertilization (IVF) and the associated Assisted Reproductive Technologies (ARTs) have now reached full 'gestation' and 'maturity' in China – the equal in quality of care and science in the best clinics to countries with the best outcomes in the world, and better than very many.

What has impressed me most during the last thirty years of my visits to China has been how rapidly and enthusiastically the technology has been adopted and adapted to the specific requirements of the people of China. In the most populous country in the World, it is estimated that some 40 million individuals (I believe this may now be a conservative figure) wishing to have children are infertile; of these some 6 million are likely

to require treatment with the advanced ARTs. There are approximately 450 IVF/ART clinics in mainland China now performing close to 700,000 cycles per year, with some of the major clinics performing some 20,000–30,000 cycles yearly—an amazing number by Western standards. And yet, as in many other countries, a large proportion of the infertile population of China are unable to afford to pay for the 'high tech' treatments they require.

The recent policy adopted by China in January 2016 allowing all couples to now have two children is likely to cause problems for fertility clinics. Women wanting their second child could make at least another 90 million women eligible, according to China's national Health Commission, many of whom will be aged 40 and above. If only 10% of these need IVF/ART, this could add another huge number of treatment cycles per year to the already overburdened clinics. Another issue adding to the likely future numbers requiring fertility treatment is the worrying decline in sperm quality and sperm counts of Chinese menas is occurring in many countries elsewhere. From an average count of 100 million/ml in the 1970s, the average was recently recorded as down to 20 million/ml. This has been blamed on urban living, pollution, stress, smoking, alcohol and later childbirth. If this trend continues it will contribute even more to the need for greater provision of IVF/ART treatment centres.

One of the things that has impressed me most during my visits to China and my interest in following the rapid development of ART in China in the literature over the past thirty years, has been the amount and real quality of research, both scientific and clinical that is now being published in international journals. Every month, the most reputable journals in our specialty publish some really excellent peer reviewed papers by researchers from China; this is in addition to the huge number of excellent scientific papers that are published in Chinese journals, which the rest of the World seldom get to see.

In 2001, China's Ministry of Health (CMOH) issued their first decrees on managerial methods and technical standards, which required all ART programmes to be registered and monitored. These regulations were further developed in 2003 to include ethical principles in the document "Technical Standards and Ethical Principles" covering all ART, including sperm banking. This was a very important development by the Chinese Government, as it set the high standards of patient care, laboratory procedures and ethics that must be followed by all clinics.

The early pioneers of IVF/ART in China – Professors Zhang Lizhu, Lu Guangxiu and He Cuihua – all of whom I had the pleasure of meeting in the early 1990s – met very much the same problems and setbacks as did my colleagues and mentors who were responsible for the birth of the World's first IVF baby, Louise Brown, on 25 July 1978 and who founded Bourn Hall Clinic in Cambridge, UK – the World's first specialist IVF/ART clinic.

This new and comprehensive textbook: "Practice of Human Assisted Reproductive Technology" will be the textbook that every ART clinician, scientist, nurse and ethicist should have access to. It covers the whole spectrum of ART: history, anatomy and physiology, the management of the male and female partners of infertile couples, the specifics of treatment by insemination, IVF, ICSI, PGD/PGS, genetics and frozen embryo transfer. Importantly, it also covers in detail the complications of treatment and maternal and child safety, as well as the follow-up of the children born from the ARTs. There are chapters on the establishment and management of ART clinics and the vital issue of quality control and the necessity of developing standard operating procedures. The final chapters cover ethical issues and regulation in IVF/ART worldwide; and lastly a chapter dealing with the management of twenty specific problems encountered in ART, such as Mullerian Duct Anomalies, polycystic ovary syndrome, tuberculosis and repeated implantation failure, to name just a few – a most useful chapter to finish with.

I do believe that this major work, gestated and delivered by these most eminent practitioners in the field of IVF/ART in China today, together with contributions from many other colleagues from clinics and laboratories from throughout China, is the most significant and comprehensive textbook to come out of China. It will become the "must have" textbook to be held by every clinic and laboratory in China. It is my hope that it may one day also be translated into English so that others in clinics worldwide may be able to share with interest the knowledge contained within this excellent publication.

Peter R Brinsden

July 2018







连雨不知春去,一晴方觉夏深。

时序已来到夏至!在这个鸟语蝉鸣、万木葱茏的时节,幸蒙邀请作序,得拜读稿文,深感内容博大精深,实为一不可多得的 医学宝鉴。

医学知识和技术的进步,给人类的生命与健康带来了令人欣喜不已的伟大成就。近年来生殖医学更是蓬勃发展,辅助生殖技术日新月异,不断创新求变,人类积极掌握生殖编码的讯息,为众多的不孕夫妇解决了生育遗憾与困扰,开创孕育生命的新篇。自 1978 年世界第一例试管婴儿 Louise Brown 诞生以来,揭开了人类辅助生殖研究的序幕,承继此项生殖科技,中国大陆首例试管婴儿也于 1988 年在北京大学第三医院诞生,虽然国内生殖医学起步稍晚,但近年发展迅速,一日千里,国内各项辅助生殖技术与不孕症诊治水平已与国际接轨,在某些顶尖科学技术领域亦早已走在世界前沿。

贯古通今,生殖一直是物种繁衍的永续主题,对于身为生殖 医学的临床工作者及相关的基础研究人员而言,承载着为不孕患 者家庭及社会带来和谐幸福的重责大任,迫切需要生殖领域丰富 的专业知识,裨能勠力使自身的诊断、经验及技术水平更臻完善。 故编纂一本临床应用与科学理论并重的本土生殖医学教科书,实 刻不容缓。

《实用人类辅助生殖技术》是以中国科学院新科院士、妇产生殖权威黄荷凤教授为首,联袂国内数十位生殖内分泌学及不孕专科领域的一流专家学者,共同编撰成册。本书作者以助推人类辅助生殖技术的应用与发展为神圣使命,帮助广大临床诊治医师

试读结束: 需要全本请在线购买: www.ertongbook.c

及相关科研人员扩展知识、开阔视野、提升专业素养及学术境界,以促进生殖学科发展、提高临床诊治及基础科研水平为终极目标。

本书内容翔实丰富,巨细靡遗,临床实用及学科理论并重,涵盖生殖医学发展史、生殖生理学、生殖内分泌学、生殖遗传学、男科学、生殖健康与安全、男女不孕症治疗策略、各种人类辅助生殖先进技术、实验室质控及规范、辅助生殖伦理、法律规章等广泛领域,概括多个交叉学科的专业知识,同时归纳国内外著名生殖中心所制订的临床指南和诊断治疗共识,荟萃若干特殊病例的诊治及辅助生育技术,并整理近年国内外生殖医学的最新进展、观念及学术研究。拙见此书乃海内外独树一帜的人类辅助生殖技术参考书,堪称是一部临床实用、学理并重、构思缜密、内容新颖、巨儒宿学、兼容并蓄的生殖医学权威专著。

值此盛夏,祝愿此书之出版,成为国内生殖医疗相关从业人员重要的参考准则,循途守辙,祈使生殖内分泌学专科日益精进,更上层楼,为国内外广大的不孕不育族群提供一帖良方。

Peter C.K.Leung
加拿大皇家学院(科学院) 院士
加拿大健康科学院 院士
加拿大不列颠哥伦比亚大学医学院 教授
谨序于 2018 年 7 月

前言





时光荏苒,生命如斯。从事人类生殖医学临床与科学研究工作近三十年,与国内外志趣相投的同道们亲历参与了辅助生殖历史激动人心的发展历程,深感生命之令人敬畏、医学之博大精深,也思考积累了一些临床心得体会,故会同乔杰院士、陈子江教授、曹云霞教授、刘嘉茵教授、张丹教授等生殖医学与多学科资深医者学者倾力编写此书。

生殖医学的快速发展为全球亿万生殖障碍夫妇及其家庭带来福祉,却也在医疗选择、生殖安全与子代健康、伦理与法律等多方面引发争议。这是一个充满未知魅力和发展潜力的学科。编者们在本领域知名专著基础上,以文献为鉴,以患者为师,结合临床实例、经验共识、国内外指南与最新研究,编撰此专著。

为了保证本书的实用性和广泛性,编委会组织了上海交通大学医学院附属国际和平妇幼保健院、浙江大学医学院附属妇产科医院、北京大学第三医院、山东省立医院、安徽医科大学第一附

属医院、江苏省人民医院等全国十余家医院生殖医学中心的学者参加编写。所有编者均为在临床、科研和教学一线,且具有高级职称的资深专家,并就其专长和特色领域进行相关内容编写。

期待本书可作为教科书和案头工具书,指导人类辅助生殖医疗实践;更力图体现生殖医学临床管理、技术发展、前沿研究、围辅助生殖处理、伦理等方面的新进展,希冀可令阅者翻卷有益。本书面向生殖专业医师、胚胎学家、专科护士、多学科同道、不同阶段研究生,以及对人类辅助生殖技术感兴趣的医学本科生及其他人群。阅读本书时,读者可逐章阅读,循序而渐进、熟读而精思,获得对当前人类辅助生殖技术的最全面系统认识;亦可根据临床工作需要翻阅查找,节选阅读,快速获得指导并协助解决临床实际问题。

攀折虬枝觅坦途,采得百花酿为蜜。感谢全体编写人员为本书投注的热忱和心血。在本书编写过程中,所有编写人员和审校人员均竭尽所能,力求准确,尽可能使本书体现当前人类辅助生殖技术的发展,并体现实用性和可读性。

本书出版之际,恳切希望广大读者在阅读过程中不吝赐教,欢迎发送邮件至邮箱 renweifuer @ pmph.com,或扫描封底二维码,关注"人卫妇产科学",对我们的工作予以批评指正,以期再版修订时进一步完善,更好地为大家服务。

黄荷凤 2018年7月

C NTENTS

总论篇

第一章 辅助生殖技术的历史、现状及展望 / 2

第一节 辅助生殖技术的历史 / 2

第二节 辅助生殖技术应用现状 / 6

一、辅助生殖技术的进展及现状 / 7

二、辅助生殖技术面临的挑战 / 8

三、我国辅助生殖技术的现状 / 9

第三节 现代生殖工程技术与辅助生殖技术展望 / 10

一、生殖克隆技术 / 10

二、线粒体置换技术 / 11

三、人胚胎干细胞技术 / 11

四、胚胎基因和线粒体 DNA 编辑技术 / 12

五、生殖干细胞技术 / 13

六、iPS 细胞诱导分化生殖细胞 / 13

七、孤性生殖技术 / 14

第二章 生殖生理 / 15

第一节 生殖系统的结构与发生 / 15

一、男性生殖系统结构 / 15

二、女性生殖系统结构 / 22

三、牛殖系统的发生 / 26

第二节 生殖内分泌的物质基础及调控 / 28

一、神经内分泌解剖与神经激素 / 28

二、促性腺激素与催乳素 / 31

三、性腺激素 / 41

四、其他激素 / 47

第三节 配子发生与发育 / 56

一、卵泡 / 卵子发育 / 56



二、精子发生与发育 / 57

第四节 受精与早期胚胎发育 / 61

第五节 胚胎植入 / 66

一、早期胚胎发育 / 66

二、植入 / 67

第三章 生殖遗传学 / 70

第一节 生殖遗传历史及概述 / 70

一、生殖遗传的概念及发展沿革 / 70

二、生殖遗传技术的发展及应用 / 71

第二节 遗传性出生缺陷及生殖遗传咨询 / 74

一、遗传性出生缺陷的种类及风险评估 / 74

二、生殖遗传咨询 / 76

第三节 重要生殖障碍疾病的遗传学背景及研究 / 79

一、与生殖相关的染色体异常 / 79

二、与生殖相关的基因异常 / 82

第四节 线粒体遗传与线粒体疾病 / 92

一、线粒体 DNA 及其遗传特点 / 93

二、线粒体遗传病 / 94

第五节 生殖遗传新兴技术与应用 / 99

一、基因编辑技术 / 99

二、生殖遗传技术在线粒体遗传病中的应用及展望 / 104

临床篇

第四章 女性不孕症的评估及治疗策略 / 110

第一节 女性不孕症的评估方法 / 110

一、病史 / 111

二、体格检查 / 112



三、辅助检查 / 114

四、不孕不育症的诊断流程 / 125

第二节 常见女性不孕症的治疗策略 / 128

一、输卵管性不孕症 / 128

二、子宫内膜异位症合并不孕 / 129

三、多囊卵巢综合征 / 132

四、不明原因不孕 / 135

第五章 特殊人群不孕症的治疗策略 / 140

第一节 高龄 / 140

第二节 卵巢储备不良 / 145

第三节 肿瘤 / 151

一、肿瘤患者的卵巢反应 / 151

二、肿瘤患者卵巢刺激方案的选择 / 152

三、肿瘤患者卵子受精方式的选择 / 153

四、肿瘤患者辅助生殖并发症的防范 / 153

第四节 复发性流产 / 154

一、病因 / 154

二、处理策略 / 156

第五节 胚胎反复着床失败 / 158

一、定义 / 159

二、病因 / 159

三、处理 / 160

第六章 男性不育症的评估及治疗策略 / 163

第一节 男性不育症的评估方法 / 163

一、病史 / 163