

THE INFERTILITY TRAP

A potential crisis in human fertility is brewing. As societies become more affluent, they experience changes that have a dramatic impact on reproduction. As average family sizes fall, the selection pressure for high-fertility genes decreases; exacerbated by the IVF industry which allows infertility-linked genes to pass into the next generation. Male fertility rates are low, for many reasons, including genetics and exposure to environmental toxins. So, a perfect storm of factors is contriving to drive fertility rates down at unprecedented rates. If we do not recognize the reality of our situation and react accordingly, an uncontrollable decline in population numbers is likely, which we'll be unable to reverse.

This book will address in a unique and multifaceted way, how the consequences of modern life affect fertility, so that we can consider behavioural, social, medical and environmental changes which could reduce the severity of what is about to come.

John Aitken is the highest ranked expert on sperm biology and fertilization in the world (Expertscape). In 2019 *The Australian* magazine named him as Australia's leading reproductive biologist while a recent ranking of the world's leading scientists by Stanford University ranked him in the top 5 in Obstetrics and Reproductive Medicine. He has won several major awards in reproductive science including the Carl G Hartman Award from the Society for the Study of Reproduction (USA) and the Distinguished Andrologist Award from the American Society of Andrology. In 2012 he was named as NSW Scientist-of-the-Year.





The Infertility Trap

Why Life Choices Impact Your Fertility and Why We Must Act Now

R. JOHN AITKEN





CAMBRIDGEUNIVERSITY PRESS

University Printing House, Cambridge CB2 8BS, United Kingdom

One Liberty Plaza, 20th Floor, New York, NY 10006, USA

477 Williamstown Road, Port Melbourne, VIC 3207, Australia

314–321, 3rd Floor, Plot 3, Splendor Forum, Jasola District Centre, New Delhi – 110025, India

103 Penang Road, #05-06/07, Visioncrest Commercial, Singapore 238467

Cambridge University Press is part of the University of Cambridge.

It furthers the University's mission by disseminating knowledge in the pursuit of education, learning, and research at the highest international levels of excellence.

www.cambridge.org Information on this title: www.cambridge.org/9781108940818 DOI: 10.1017/9781108935593

© R. John Aitken 2022

This publication is in copyright. Subject to statutory exception and to the provisions of relevant collective licensing agreements, no reproduction of any part may take place without the written permission of Cambridge University Press.

First published 2022

Printed in the United Kingdom by TJ Books Limited, Padstow Cornwall

A catalogue record for this publication is available from the British Library.

ISBN 978-1-108-94081-8 Paperback

Cambridge University Press has no responsibility for the persistence or accuracy of URLs for external or third-party internet websites referred to in this publication and does not guarantee that any content on such websites is, or will remain, accurate or appropriate.

Every effort has been made in preparing this book to provide accurate and up-to-date information that is in accord with accepted standards and practice at the time of publication. Although case histories are drawn from actual cases, every effort has been made to disguise the identities of the individuals involved. Nevertheless, the authors, editors, and publishers can make no warranties that the information contained herein is totally free from error, not least because clinical standards are constantly changing through research and regulation. The authors, editors, and publishers therefore disclaim all liability for direct or consequential damages resulting from the use of material contained in this book. Readers are strongly advised to pay careful attention to information provided by the manufacturer of any drugs or equipment that they plan to use.



Dedicated to my family





CONTENTS

List of Figures

List of F	igures pag	ge xi
Forewor	rd	xiii
CHAPT	ER 1	1
1.1	Prologue	1
1.2	Summary	10
1.3	References	10
СНАРТ	ER 2	11
2.1	A Journey into the Demographic Heart of the Matter	11
2.2	The Shape of World Population Growth	18
2.3	The Emergence of Infertility	19
2.4	Longevity, Population Momentum and Migration	22
	2.4.1 Longevity	22
	2.4.2 Longevity, Affluence and Infant Mortality	24
	2.4.3 GDP and Health: Mixed Blessings	26
	2.4.4 Population Momentum	29
	2.4.5 The Key Role Played by Migration	32
	2.4.6 Can China and India Save Us?	37
	2.4.7 Can Africa Save Us?	39
	Forecasting an Uncertain Future	45
	Summary	51
2.7	References	52
CHAPT	ER 3	54
3.1	in a sign and a sign a	
	the Search for Self-Fulfilment	54
	3.1.1 The Ascent of Affluence	54
	3.1.2 Affluence, Infertility and the Malthusian	
	Paradox	60
	3.1.3 Examples of Prosperity's Power	62
	The Demographic Transition	67
33	Socioeducational Factors and Fertility	71

vii



viii CONTENTS

	3.3.1 Educational Drivers for Female Infertility3.3.2 Female Education and Marriage	74 80
3.4	The Intersection of Education and Reproductive	
	Biology	84
	3.4.1 The Fundamental Biology of Female	
	Reproduction	84
	3.4.2 Age of Menarche	85
	3.4.3 The Reproductive Years: Over Before	
	You Know It	88
3.5	How the Immaturity of Human Infants Shapes Our	
	Reproduction	90
3.6	Reproduction and the Care of Our Offspring	92
	3.6.1 What is the Point of Granny and Grandad?	92
3.7	Marriage: Virtue or Vestige?	94
3.8	1	100
	3.8.1 'Why Have My Eggs Forsaken Me?'	101
	Chromosomal Abnormalities and Female Infertility	105
3.10	The IVF Industry and Maternal Age	109
3.11	Are There Any Solutions to Age-Dependent Female	
	Infertility?	113
	3.11.1 Oocyte Donation	113
	3.11.2 Oocyte Freezing	115
3.12	±	116
	3.12.1 Why Would Women Wed?	117
	3.12.2 A Role for Pro-Natalist Government	
	Policies?	121
3.13	· · · J	125
3.14	References	128
СНАРТ	ER 4	132
	What is Happening to the Human Male?	132
	Testicular Cancer	132
	Cancer and Opulence	137
	Other Defects of the Male Reproductive Tract	144
	The Vexed Question of Declining Sperm Counts	145
	Possible Causes of Declining Sperm Counts	152
1.0	4.6.1 Genetics	152
	4.6.2 Epigenetics	153
	4.6.3 Environmental and Lifestyle Factors	154
4.7	Environmental Pollution and Semen Quality	159



Contents		ix
	Falling Testosterone Levels and Semen Quality	165
	Summary	170
4.10	References	172
CHAPT	ER 5	180
5.1	The Miracle of Conception	180
	5.1.1 The Human Spermatozoon	180
	5.1.2 The Timing of Insemination	183
	5.1.3 The Ripening of Spermatozoa in the	
	Female Tract	186
	5.1.4 The Complexity of Fertilization	190
	Summary	200
5.3	References	200
CHAPT	ER 6	203
6.1	Why Are Men Infertile?	203
	6.1.1 Hamsters and Human Sperm Function	206
6.2	Oxidative Stress and the Infertile Male	211
	6.2.1 Reactive Oxygen Species	212
	6.2.2 Thaddeus Mann and Oxidative Stress	215
	6.2.3 Oxidative Stress and DNA Damage	219
	6.2.4 Oxidative Sperm DNA Damage	
	and Mutations in Our Children	220
6.3	Genetic Causes of Male Infertility	225
	6.3.1 Y-Chromosome Deletion	225
	6.3.2 Other Genetic Causes	229
	Summary	232
6.5	References	233
CHAPT	'ER 7	238
7.1	The Janus Faces of IVF	238
	7.1.1 Steptoe, Edwards and Purdy:	
	The Development of IVF	238
	7.1.2 ICSI and Male Infertility	245
	7.1.3 The rise of ICSI	247
	Consequences of ART When Conducted at Scale	254
7.3	Negative Impacts of IVF on the Mutational Load	
	Carried by Children	258
	Impact of Assisted Conception on Fertility	261
	Summary	262
7.6	References	264



X	C	CONTENTS
СНАРТ	ER 8	270
8.1	The Gathering Storm	270
	The Infertility Trap	278
	8.2.1 Demographic Factors	279
	8.2.2 Social Factors	280
	8.2.3 Economic Factors	283
	8.2.4 Environmental Factors	287
	8.2.5 Evolutionary Factors	291
8.3	Summary	299
8.4	References	301
СНАРТ	ER 9	305
9.1	How Do We Escape the Trap?	305
9.2	Sex Education	308
9.3	Remove Reproductive Toxicants	310
9.4	Counter Oxidative Stress	312
9.5	Elevate the Status of Reproductive Toxicology	316
9.6	Find Ways of Working With the IVF Industry	318
9.7	Engineer Social Change	322
9.8	Summary	325
9.9	References	327
Acknow	vledgements	330
Index	-	331



FIGURES

2.1	State of the global population.	page 17
2.2	Data provided by the World Bank on the major	
	factors impacting the size of the global population.	20
2.3	The benefits of affluence.	25
2.4	UN projections for future total fertility and total	
	population based on World Population Prospects	
	(2019).	30
2.5	UN projections for population change in individual	
	countries from 1950 to the end of the century.	35
2.6	Projected changes in the fertility of China and India.	38
2.7	Changes in fertility rate in sub-Saharan Africa.	40
2.8	Changes in the determinants of population growth	
	in the sub-Saharan African countries, indicating	
	the green shoots of a demographic transition.	42
2.9	The sub-Saharan story at a national level.	43
2.10	World population by fertility rate between 1950	
	and 2010.	47
2.11	Analysis of the ability of national populations	
	to self-correct as fertility rates fall.	50
3.1	Relationship between global fertility rate, wealth	
	as defined by GDP and global food production.	59
3.2	Examples of the powerful impact of socioeconomic	
	development on the status of human populations.	64
3.3	The demographic transition.	68
3.4	The relationship between female education	
	and fertility rate.	75
3.5	Examples of the impact of tertiary female education	
	on fertility rate, comparing the highly developed	
	nations of the EU with the developing	
	countries of sub-Saharan Africa.	77
3.6	The relationship between marriage and fertility rate	
	for four countries where detailed data exist: USA, So	uth
	Korea, New Zealand and the Netherlands.	82

xi



xii LIST OF FIGURES

3.7	J	
	ends of the demographic transition.	85
3.8	Childhood marriage, GDP and fertility.	87
3.9	The life cycle of a human egg and its contribution	
	to genetic aneuploidies responsible for conditions	
	such as Down syndrome.	103
3.10	Age, IVF and female fertility.	112
4.1	Increasing incidence of testicular cancer in all	
	developed nations of the world.	135
4.2	Affluence and testicular cancer.	136
4.3	Comparison of cancer rates in high and low HDI	
	(Human Development Index) countries.	138
4.4	Time-dependent trends in cancer incidence within	
	Australia.	140
4.5	Secular trends in human sperm counts in terms	
	of sperm concentration and total sperm count.	147
4.6	The process of spermatogenesis and sperm	
	maturation in the epididymis.	157
4.7	Secular changes in circulating testosterone levels.	168
5.1	The miracle of conception.	182
5.2	The complex process of fertilization.	188
6.1	General anatomy of the testes.	204
6.2	Sperm structure and function.	209
6.3	The 1992 Simpson Symposium on New Horizons	
	in Male Infertility.	218
6.4	Paternal age defines the mutational load carried	
	by the offspring.	221
6.5	The Y chromosome and male infertility.	226
7.1	The principles behind the in vitro fertilization	
	technology that won Bob Edwards a Nobel prize	
	for Physiology or Medicine in 2010.	239
7.2	An example of a genetic condition causing male	
	infertility is globozoospermia.	248
8.1	A map of India illustrating regional differences	
	in TV ownership fertility rate and infant mortality	273



FOREWORD

This is a very important book. I do not say this casually. If Professor Aitken's hypothesis is correct, the information he presents has significance not only for people currently living, but for future generations. Shall we be sceptical? By all means! That is the foundation of science. Does Professor Aitken have the credentials to address his subject? Few would be better prepared. I should know, having followed his work for decades. And this judgement goes beyond mere academic titles, which may not reflect one's true intellect. It is no exaggeration to say that John Aitken is at the pinnacle of his career, a highly respected scientist who has been a world leader in the field of human reproductive physiology. He has identified certain environmental factors that have the ability to impair fertilization and has proceeded to clarify the mechanisms by which they act.

I came of age in the 1960s, when Paul Ehrlich's *Population Bomb* awakened everyone to the Malthusian concern regarding overpopulation, the proposition that the growth of the world's population would exceed its ability to produce food, raising the spectre of famine. Years later, I travelled to New Delhi, India, for the World Health Organization, to speak about immune-contraception at their National Immunology Institute. The thesis presented in *The Infertility Trap* that the world was at risk of a devastating fall in population seemed counterintuitive. Yet I have come to believe that Professor Aitken's concerns are valid, and this is a first step towards action!

What then is Professor Aitken's thesis, which he now champions in this book and hopes to convince the reader of its urgency? Nothing less than a significant worldwide loss of human fertility that will lead to a devastating reduction in population of sufficient magnitude to be a threat to our species!



xiv FOREWORD

Can we believe him or is this a script for a grade B sci-fi movie? Are credentials enough? No, he would not want us to act on faith in his expertise alone, but rather be convinced by his argument.

And how does he convince us of the validity of this hypothesis? By a series of discussions, backed by data and presented to the reader in a logical sequence of chapters. Though well supported with graphs and tables, this is neither a dry book nor an incomprehensible academic tome. It is written in a conversational style, and we learn something of the man, his early life, his strivings that would later blossom into a leadership career.

The 'cast of culprits' in his hypothesis include the diminishing desire of couples to bear children as their livelihood improves, an increasing delay of women to seek to conceive, as they take the opportunity to pursue careers, a general lack of awareness amongst many women that fecundity falls a good decade before menopause, our increased exposure to environmental toxicants which impair reproduction in both men and women, and false expectations regarding laboratory-based treatments such as in vitro fertilization (IVF) to correct the problem of delaying plans to conceive.

In a prologue and eight additional chapters, we take a journey into the demographic heart of darkness, discover the miracle of fertilization, learn that female fertility is the hostage of affluence. We are alerted to the current trend toward impaired fertility of the human male and the mechanisms of how men can become infertile. We are made aware of the Janus faces of IVF, and given an assessment of the gathering storm. In his final chapter, Professor Aitken offers us guidance, not so much as a road map, but a prescription in broad terms on how we might escape the Trap. Most importantly, he has alerted us to this impending crisis, raised our level of consciousness so that many individuals, not a few pioneers, will begin to focus on the problem and the combined efforts of *Homo sapiens*, the 'thinking



Foreword xv

man', find a solution! Then, seeing how we are currently handling global warming, maybe not.

Professor Richard Bronson MD
Professor of Obstetrics, Gynecology and Pathology
Director, Division of Reproductive Endocrinology
Director of Andrology
Stony Brook University
August 2021

