

Daniel T. O'Connor

Endometriosis

Daniel T. O'Connor

MB, BS(QLD), FRCOG, FRACOG

Visiting Gynaecologist, Royal
Brisbane Hospital, and Visiting
Gynaecologist, Cancer
Detection Clinic, Royal Women's
Hospital, Brisbane

Endometriosis

Series Editors

ALBERT SINGER AND JOE JORDAN

Churchill Livingstone 

EDINBURGH LONDON MELBOURNE AND NEW YORK 1987

CHURCHILL LIVINGSTONE
Medical Division of Longman Group UK Limited

Distributed in the United States of America by Churchill
Livingstone Inc., 1560 Broadway, New York, N.Y. 10036, and
by associated companies, branches and representatives
throughout the world.

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publishers (Churchill Livingstone, Robert Stevenson House,
1-3 Baxter's Place, Leith Walk, Edinburgh EH1 3AF).

First published 1987

ISBN 0-443-02995-4
ISSN 0264-5610

British Library Cataloguing in Publication Data

O'Connor, Daniel T.

Endometriosis.—(Current reviews in obstetrics and
gynaecology, ISSN 0264-5610)

1. Endometriosis

I. Title II. Series

618.1'4 RG483.E53

Library of Congress Cataloging in Publication Data

O'Connor, Daniel T.

Endometriosis.

(Current reviews in obstetrics and gynaecology,

ISSN 0264-5610)

1. Endometriosis. I. Title. II. Series.

[DNLN: 1. Endometriosis. W1 CU8093M/WP 390 018e]

RG483.E53025 1987 618.1'42 86-17153

Typeset by CCC, printed and bound in Great Britain by
William Clowes Limited, Beccles and London

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Foreword

This series aims to present one person's overview of a clinical problem and in this book Dan O'Connor presents a unique assessment of the problem of endometriosis. He has reviewed, comprehensively, the world literature and based his conclusions on an exhaustive review of 717 cases of endometriosis personally diagnosed and managed. Many will be surprised that he demonstrated endometriosis, usually by laparoscopy, in one in 10 of all new patients seen by him between 1968 and 1983 and that one in 20 sufferers were teenagers. This latter group highlights his plea for early diagnosis by laparoscopy and that any management plan must consider the place of long-term suppression of menstruation as well as conservative surgery. The place of medical management of pseudopregnancy and pseudomenopause is described. No treatment is totally free of side-effects and the author's disillusionment with danazol (Danol) is obvious. However, the prospect of medical oophorectomy by the use of a gonadotrophin releasing hormone agonist and luteinising releasing hormone agonist offers an exciting new possibility.

For long the relationship between endometriosis and infertility has been known even when there seems to be no obvious reason why minimal areas of endometriosis should prevent pregnancy, but Dr O'Connor describes how recent work into the effect of endometriosis on the immune system may provide the answer.

In presenting such a large personal series of patients the author has given us a refreshing insight into a problem, often difficult to manage, which faces all gynaecologists and his conclusions are particularly relevant in that they are based on a combination of an extensive knowledge of published work and an obviously compassionate attitude to his patients: commendably he shows us how

important it is that clinicians should never forget to treat the patient
and not the disease!

London
Birmingham
1987

Albert Singer
Joe Jordan

Preface

Dramatic progress in most areas of obstetric and gynaecological practice has occurred in the last 20 years. Diverse topics have occupied centre stage during that time including, intermittently, endometriosis. Longstanding problems concerning this disease still, however, persist. It is still difficult to explain with confidence the aetiology of endometriosis to its sufferers because there is no simple explanation. It is likewise difficult to prevent the disease, and the many therapeutic programmes advocated in the past have always seemed to produce a hard core of failures and recurrences, a distressing and depressing situation for sufferers and those who care for them.

This book resulted from a visit to Brisbane in May 1981 by Joe Jordan. During his stay he attended one of my routine elective, non-selective gynaecological operating lists in St Andrew's Hospital and was intrigued by the number of cases of endometriosis, a number not thought to be unusual by the surgeon. He and Albert Singer subsequently asked me to write this book, suggesting that I tell about endometriosis as I understand it.

Many people have helped in the compilation of the manuscript. In particular, my wife, Liz, and family, uncomplainingly provided the time, space and support necessary to put it all together, my loyal friend and secretary, Marjorie Bierne SRN, and my daughter, Susan, typed the manuscript; my good friend Margaret Mason provided help with the graphic art work; longtime colleague and friend Dr Lawrence Brunello supplied a photograph of tubal endometriosis; and the Director General of Health, Dr P G Livingstone of the Queensland Government Department of Health, gave permission for the use of the brochure concerning hysterectomy. The publishers of *Contemporary Obstetrics and Gynaecology* gave permission for the

use of a photograph illustrating Stage I endometriosis; Professor George Osbourne of the School of Veterinary Medicine at the University of Queensland advised on endometriosis in non-human primates; Mrs Elizabeth Drewe of the Australian Medical Association Queensland Branch Library kindly generated an extensive search of the literature; the enthusiastic and helpful staff of the Central Medical Library at the Royal Brisbane Hospital gave superb assistance; and Robert Hennig of Eldar Trading Company kindly provided the computer component.

Professor Robert Shaw of the Department of Obstetrics and Gynaecology in the Royal Free Hospital Medical School, London, most generously responded to a request from the publishers and kindly provided valuable information concerning a new medical approach in the management of endometriosis. He shared information obtained from his pioneering work concerning the use of gonadotrophin releasing hormone agonists in a series of patients with confirmed endometriosis that he has treated. This contribution has rounded out the text because I have had no personal experience with GNRH_A.

To all of the above a most heartfelt vote of thanks. The information in this book will, I hope, be useful not only in the educational situation but also when treating patients suffering from endometriosis. Meanwhile it is hoped that others will continue researching the many aspects of endometriosis that remain unclear so that the unanswered questions can be satisfactorily resolved for the benefit of patients with this vexatious disorder.

Brisbane 1987

D.O'C.

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Introduction

During a meeting of the Cambridge Medical Society on 14 April 1882, and reported in the *Lancet* of that year, Professor James Paget mentioned that many years before he had seen a young girl at Moorfields Hospital who, every month, had a small effusion of blood into the anterior chamber of her eye at the time of her menstrual period. This effusion was absorbed during the intervals between her periods.

Since this first record of the disease entity now known as endometriosis, interest and understanding of the disease have followed an erratic course with large gaps in our knowledge despite an increase in the volume of world literature.

This literature reflects many intriguing facets of this chameleon-like, ubiquitous disease process: the fact that there is no satisfactory single theory of aetiology; that this disease process affects not only human females and some males, but non-human primates as well; that no single therapeutic regimen suits all cases, and all stages of the disease, with equal expectations of success; that extended experience with conservative medical management seems so often to yield progressively less satisfactory results; and so on. One hundred years after the first somewhat offhand report of the disease entity, the omens suggest a much greater literature will need to accrue before the gaps in our knowledge of endometriosis are filled.

Twenty years ago, endometriosis was thought to be relatively uncommon, especially in public hospital patients, in Brisbane, Australia. While working in Guildford, England, during 1965 and 1966 the author was impressed by the fact that in Surrey at least, endometriosis was a relatively common disease amongst National Health Service patients and obviously there had to be other than geographic and ethnic factors operating to produce this disparity.

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On returning to Brisbane in February 1967, Professor Eric Mackay of the Department of Obstetrics and Gynaecology, University of Queensland, introduced the author to the laparoscope and the first diagnostic laparoscopy was performed in that centre in March 1967. Undoubtedly this diagnostic procedure has led to an increased awareness of the possibility of endometriosis, diagnosis of the disease at an earlier stage in its natural history, and a subsequent apparent increase in its incidence. This has led to an increasing interest in the disease, and has resulted in increased referrals of potential endometriosis sufferers by aware, conscientious general practitioners who know of the author's special interest, so that a self-generating influence has occurred.

In keeping with the philosophy of this book a current review of the relevant international literature to April 1984 on the subject of endometriosis has been carried out. A review of a personal series of cases of endometriosis treated in Brisbane from February 1967 to January 1983, allowing a minimum of 12 months follow-up before compilation of data on these patients, will also be presented.

The Brisbane series

During the years analysed—February 1967 to January 1983—6656 patients were seen in consultation by the author in his private practice. During this time 760 cases of surgically diagnosed endometriosis were discovered of whom 717 were documented with sufficient accuracy to be included in an in depth survey. These 717 patients will be referred to throughout this book as the Brisbane series for ease of comprehension. Since I am not aware of any other Brisbane gynaecologist who has published a similar series I do not believe this to be an unduly arrogant or proprietary attitude, and use the description merely for convenience.

All the patients in the Brisbane series have been cared for in a private practice environment having been referred by general practitioners or other medical specialist colleagues. Undoubtedly 'word of mouth' referral from other patients initiated many consultations, and the author's known interest in this disease process has probably led to a biased incidence in referred patients.

During the years under consideration, private medical practice and a form of socialist public hospital medical care had coexisted in the state of Queensland, in Australia, for nearly two generations. Patients have easy access to a full range of medical, hospital,

pharmaceutical, and diagnostic services in the public hospital system with no direct costs at the point of service. They are cared for, however, by a system, rather than by an individual as occurs in private practice, and the system includes medical and nursing undergraduates, postgraduate trainees, etc. During these years the medical, hospital, pharmaceutical and diagnostic costs of private patients were subsidized by voluntary private medical and hospital insurance schemes with a form of government subsidy covering some, but not all, of these services, with refunding of up to 85% of medical expenses. Private practice is entrepreneurial and competitive, and patients dissatisfied with the care, attention and results of treatment by individual gynaecologists can freely seek help elsewhere. About 50% of the population choose private medical care.

For 12 months during 1980–1981 the author was assisted by a postgraduate gynaecological trainee as part of an experiment to determine whether it was possible to train someone at a postgraduate level in a private practice milieu. This concept was accepted by the Royal College of Obstetricians and Gynaecologists and the experiment was, I believe, very successful. At no time did the trainee have sole unsupervised care of any of these patients but her interest and enthusiasm benefited all concerned. In all critical regards the patients in the series were under the sole and total care of the author.

Of the 717 patients in the Brisbane series 531 are classified as 'current attenders' having been seen in the last 2 years to January 1984. Sixty patients have not been seen during this time but have been traced at the general practitioner level, often in a distant part of the state of Queensland (for example 1200 miles away in the city of Cairns), or interstate. One hundred and twenty-six have been lost to follow-up and this group includes some 42 patients from such diverse places as Christmas Island in the Indian Ocean, the Kingdom of Tonga in the South Pacific Ocean, New Zealand, New Guinea, the Solomon Islands, Sweden and Vanuatu.

The population of Australia is polyglot with one-quarter born elsewhere, having voluntarily migrated to Australia in the last 30 years. Brisbane, a subtropical city with a population of one million (80 gynaecologists), services the state of Queensland which has a population of two million (a further 50 gynaecologists practising in non-metropolitan areas). It is also a port of entry for airlines from Papua New Guinea, New Caledonia, Vanuatu, the Solomon Islands, Fiji, New Zealand, Singapore, Hong Kong, Manila, and Tokyo as well as from the USA.

Aware that many of the traditional beliefs about endometriosis

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were liable to fall under close scrutiny in this current study, and having had the privilege of working in both the Kingdom of Tonga, and the Republic of Vanuatu (formerly the condominium of the New Hebrides), areas in the South Pacific populated by predominantly polynesian people and melanesian people respectively, the author knew that the belief that people from cultures regarded as unsophisticated by western standards rarely suffered from endometriosis, was just not true. Research into the countries of origin of the patients in the Brisbane series showed, not surprisingly (given the immigrant factor), that the 717 patients were born in Canada, Czechoslovakia, Denmark, Finland, France, Germany, Greece, Hungary, India, Indonesia, Iran, Ireland, Israel, Italy, Japan, Malaysia, Malta, Melanesia, Micronesia, The Netherlands, New Zealand, Norway, Poland, Polynesia, South Africa, Sri Lanka, Sweden, Switzerland, Thailand, UK, USA, Vietnam and Australia. It therefore seems reasonable to generalize that no ethnic group in this community seems particularly vulnerable, or immune, to endometriosis.

Records and record analysis

A very unsophisticated system of record keeping has been employed in the author's practice since its beginning and, prior to the invitation to write this book, there had been no pressing need to update the system. Colleagues at the medical school at the University of Queensland were consulted initially for help with information retrieval from patients' records and a system of retrieval using an unsophisticated method of data collection was organized and data painfully and tediously collected by systematically going through all patients' individual records, first to discover those surgically diagnosed as having endometriosis, and then to extract relevant information according to sets of relevant factors. Since, in the early years of the study, no attempt had been made to locate accurately or stage the disease, 43 patients' records were discarded as being inadequate for the survey. The medical school staff could not cope with the flood of information derived from the records reviewed, so after a frustrating delay and disappointment, help was obtained from a private company for data entry and analysis.

Robert Hennig of Eldar Trading Company, knew nothing about endometriosis at the start of this project and the author knew nothing

about computers. Eventually they constructed a data bank system using the VACS data base on an ONYX 800 Z mini-computer. The work done was limited to the totalling and reporting utilities of the data base only as there was not enough time to carry out elegant statistical programming and analysis. The data base design consisted of a main record for each patient with an identifying code number so that anonymity was preserved, and all relevant personal data such as date of birth, marital status, parity, contraceptive history, past medical, surgical, gynaecological and family history, etc. were recorded. To these main records were hung sub-records covering such areas as diagnostic operations, medical treatment, etc., to which in turn were hung further sub-sub-records of such matters as operative complications, results of treatment, etc. The results are held on magnetic tape for re-use, re-evaluation and updating as needed.

Caught up in the promise of newfound success with synthetic hormone therapy in endometriosis, and with expectations of a new trend in the progression and management of this disease, in 1964 the author enthusiastically entitled his gynaecological commentary submitted in his book required for the MRCOG examination, 'The hormone treatment of endometriosis'. Since then there have been espoused a series of disappointing and disillusioning concepts relating to the aetiology and management of endometriosis, especially the non-surgical management. The concept of an induced 'pseudo-pregnancy' state with synthetic progestogens as found in the oral contraceptive preparations; the pseudomenopause treatment with danazol; the reports from China of the remarkable effects of gossypol acetate in the treatment of endometriosis and adenomyosis; the role of immunological factors in the aetiology of endometriosis and associated infertility; the significance of luteinized unruptured follicles; the role of prostaglandin levels in the peritoneal fluid in endometriosis; and now the new prospect of 'medical oophorectomy', have all paraded across the international literature, but none of these modalities has provided a total answer to endometriosis.

In addition to the introduction of laparoscopy into gynaecological surgery, undoubtedly the second most important factor in the conservative management of endometriosis has been the development of microsurgical principles and techniques. A further addition to microsurgery has been the very modern supplementary therapy using laser surgery.

Notwithstanding, there are still a number of recurring unanswered questions about endometriosis:

Endometriosis

Why does endometriosis persist and even progress in some patients during pregnancy and lactational amenorrhoea?

Why do neither pregnancy nor the oral contraceptive pill seem to protect patients against developing endometriosis?

What are the immune factors involved in the spread of this destructive disease process in individual patients?

Why do some males on oestrogen therapy in the course of treatment for prostatic disease produce tissue histologically identical with endometriosis?

Why is it that endometriosis and polycystic ovary disease seem to be commonly coexistent in Brisbane patients?

Why do so many adolescent females develop very significant disease after relatively few menstrual cycles?

Have altered attitudes in women and their expectations of normal feminine function influenced the apparent increase in the incidence of endometriosis?

Is physician orientated awareness responsible for earlier diagnosis?

Does infertility cause endometriosis or result from it?

Why, in the author's hands in Brisbane, does danazol seem to be little more than an expensive and disappointing disaster rather than an effective therapeutic aid?

Why does in vitro fertilization seem to be less successful for those who have suffered from and been treated for endometriosis, than for other infertility patients?

Perhaps by the end of this current review these questions and other puzzles may be answered.

Epidemiology

There are no complete epidemiological studies of endometriosis available but this review of the relevant literature, together with information retrieved from the Brisbane series, will add to the pool of epidemiological knowledge.

Ethnic factors

The diverse origins of the 717 patients in the Brisbane series have been previously mentioned. It has been suggested in the past that there should be a lower incidence of endometriosis in underdeveloped countries where prolonged lactation is maintained for both infant welfare and contraceptive purposes. The author's experience—gained from working for 5 years in two South Pacific nations, the Kingdom of Tonga and the Republic of Vanatu—suggests that this is not true and in these countries it is not at all uncommon to find high parity, a history of prolonged lactation, endometriosis, and fibroids or pelvic inflammatory disease coexisting in one patient. The introduction of diagnostic laparoscopy into all communities should certainly reveal a higher than anticipated incidence of endometriosis.

During a 3.5-year period in Nigeria, Ekwempu & Harrison (1979) found 27 negroid Nigerians with endometriosis, an incidence of 8.2%, but in their series the location of the disease was very different to that of the Brisbane experience, being rare in the pouch of Douglas and absent from the recto-vaginal septum. Chatman (1976) and Miyazawa (1976) have both written of a similar incidence of endometriosis in American black women and Japanese women respectively. It is possible that one reason why endometriosis has