ENDOMETRIOSIS

Current Management and Future Trends

ENDOMETRIOSIS

Current Management and Future Trends

Juan A García-Velasco
MD PhD
Medical Director
IVI Madrid, Spain
Associate Professor
Rey Juan Carlos University
Madrid, Spain

Botros RMB Rizk
MD MA FACOG FACS HCLD FRCOG FRCS (C)
Professor and Head
Division of Reproductive Endocrinology and Infertility
Medical and Scientific Director
USA IVF Program
University of South Alabama College of Medicine
Alabama, USA

JAYPEE BROTHERS MEDICAL PUBLISHERS (P) LTD

St Louis (USA) • Panama City (Panama) • New Delhi • Ahmedabad • Bengaluru
Chennai • Hyderabad • Kochi • Kolkata • Lucknow • Mumbai • Nagpur

Published by

Jitendar P Vij
Jaypee Brothers Medical Publishers (P) Ltd

Corporate Office
4838/24 Ansari Road, Daryaganj, **New Delhi** 110 002, India, Phone: +91-11-43574357, Fax: +91-11-43574314

Registered Office
B-3 EMCA House, 23/23B Ansari Road, Daryaganj, **New Delhi** 110 002, India
Phones: +91-11-23272143, +91-11-23272703, +91-11-23282021,
+91-11-23245672, Rel: +91-11-32558559 Fax: +91-11-23276490, +91-11-23245683
e-mail: jaypee@jaypeebrothers.com, Website: www.jaypeebrothers.com

Branches

- 2/B, Akruti Society, Jodhpur Gam Road Satellite
  Ahmedabad 380 015 Phones: +91-79-26926233, Rel: +91-79-32988717
  Fax: +91-79-26927094 e-mail: ahmedabad@jaypeebrothers.com
- 202 Batavia Chambers, 8 Kumara Krupa Road, Kumara Park East
  Bengaluru 560 001 Phones: +91-80-22285971, +91-80-22382956
  +91-80-22372664, Rel: +91-80-32714073
  Fax: +91-80-22281761 e-mail: bangalore@jaypeebrothers.com
- 282 IIIrd Floor, Khaleel Shirazi Estate, Fountain Plaza, Pantheon Road
  Chennai 600 008 Phones: +91-44-28193265, +91-44-28194897
  Rel: +91-44-32972089 Fax: +91-44-28193231 e-mail: chennai@jaypeebrothers.com
- 4-2-1067/1-3, 1st Floor, Balaji Building, Ramkote Cross Road
  Hyderabad 500 095 Phones: +91-40-66610020
  +91-40-24758498, Rel:+91-40-32940929
  Fax:+91-40-24758499, e-mail: hyderabad@jaypeebrothers.com
- No. 41/3098, B & B1, Kuruvi Building, St. Vincent Road
  Kochi 682 018, Kerala Phones: +91-484-4036109, +91-484-2395739
  +91-484-2395740 e-mail: kochi@jaypeebrothers.com
- 1-A Indian Mirror Street, Wellington Square
  Kolkata 700 013 Phones: +91-33-22651926, +91-33-22276404
  +91-33-22276415, Rel: +91-33-32901926
  Fax: +91-33-22656075, e-mail: kolkata@jaypeebrothers.com
- Lekhraj Market III, B-2, Sector-4, Faizabad Road, Indira Nagar
  Lucknow 226 016 Phones: +91-522-3040553, +91-522-3040554
  e-mail: lucknow@jaypeebrothers.com
- 106 Amit Industrial Estate, 61 Dr SS Rao Road, Near MGM Hospital, Parel
  Mumbai 400012 Phones: +91-22-24124863, +91-22-24104532,
  Rel: +91-22-32926896 Fax: +91-22-24160828, e-mail: mumbai@jaypeebrothers.com
- "KAMALPUSHPA" 38, Reshimbag, Opp. Mohota Science College, Umred Road
  Nagpur 440 009 (MS) Phone: Rel: +91-712-3245220
  Fax: +91-712-2704275 e-mail: nagpur@jaypeebrothers.com

North America Office
1745, Pheasant Run Drive, Maryland Heights (Missouri), MO 63043, USA, Ph: 001-636-6279734
e-mail: jaypee@jaypeebrothers.com, anjulav@jaypeebrothers.com

Central America Office
Jaypee-Highlights Medical Publishers Inc. City of Knowledge, Bld. 237, Clayton, Panama City, Panama Ph: 507-317-0160

Endometriosis: Current Management and Future Trends

First Edition: **2010**

ISBN 978-81-8448-808-1

Typeset at JPBMP typesetting unit
Printed at

To

Carmela, Maria and Jaime,
my strongest supporters and
my greatest motivation
—Juan A García-Velasco

My very dear wife and life partner
Mary for her love, support
and sacrifice
—Botros RMB Rizk

Contributors

A Schally
Veterans Affairs Medical Center and South Florida VA Foundation for Research and Education, Miami, and Department of Pathology and Division of Hematology and Oncology Department of Medicine, the Miller School of Medicne, University of Miami Miami, Florida, USA

Alka Prakash
University Department of Obstetrics and Gynaecology University of Cambridge United Kingdom

Anabel Salazar
IVI Madrid
Rey Juan Carlos University
Madrid, Spain

Andre van As
Repros Therapeutics Inc
The Woodlands, Texas, USA

Andrea G Edlow
Department of Obstetrics and Reproductive Biology, Brigham and Women's Hospital; Harvard Medical School, Boston, Massachusetts, USA

Andrew Prentice
University Department of Obstetrics and Gynaecology University of Cambridge United Kingdom

Anjali Chandra
Center for Reproductive Medicine, Glickman Urological and Kidney Institute and Obstetrics-Gynecology and Women's Health Institute; Cleveland Clinic, Cleveland, USA

Anna Sokalska
Department of Obstetrics Gynecology and Gynecological Oncology, Karol Marcinkoswski University of Medical Sciences Poland

Antoni J Duleba
Department of Obstetrics and Gynecology, University of California Davis, Sacramento, California, USA

Antonio Pellicer
Fundación IVI
Instituto Universitario IVI
Valencia University, Valencia, Spain

Antoine Watrelot
Centre de recherché et d´Etude de la Stérilité, Lyon, France

Ashok Agarwal
Professor of Surgery and Director Center for Reproductive Medicine Infertility, and Sexual Function Glickman Urological and Kidney Institute and Department of Obstetrics and Gynecology, The Cleveland Clinic Foundation, Cleveland, USA

Attila Bokor
Leuven Unoversity Center
Dept of Obstetrics and Gynecology
UZ Gastthuisberg, 3000
Leuven, Belgium

Botros RMB Rizk
Professor and Head
Division of Reproductive Endocrinology and Infertility, Medical and Scientific Director, USA IVF Program
University of South Alabama
College of Medicine, Alabama, USA

Bruno Borghese
Université Paris Descartes
Service de Gynécologie Obstétrique II et Médecine de la Reproduction
Unité de Chirurgie Gynecologique CHU Cochin-Saint Vincent de Paul Paris, France

Carlos Simón
Fundación IVI
Instituto Universitario
IVI Valencia University
Valencia, Spain

Caroline E Gargett
Centr for Women's Health Research
Monash Institute of Medical Research and Monash University
Department of Obstetrics and Gynaecology, Monash Medical Center
Clayton, Victoria, Australia

Carolyn JP Jones
Maternal and Fetal Research Centre
School of Clinical and Laboratory Science, Univeristy of Manchester
UK

Chakib M Ayoub
MBA, Associate Professor
Department of Anesthesiology
American University of Beirut
Beirut, Lebanon
Clinical Assistant Professor
Department of Anesthesiology
Yale University School of Medicine
New Haven, CT USA

Charles Chapron
Service de Gynécologie Obstétrique II et Médicine de la Reproduction
Unité de Chirurgie Gynécologique
CHU Cochin-Saint Vincent de Paul
Paris, France

Charles Countant
Service de Gynécologie-Obstétrique
Hôpital Tenon, Assistance Publique des Hôpitaux de Paris, Université Pierre et Marie Curie, Paris, France

Christopher B Rizk
Rice University
Houston, Texas
USA

David Redwine
St. Charles Medical Center
Bend, Oregon
USA

David Smart
Enovapharma
London, United Kingdom

Deborah Eapen
Center for Reproductive Medicine
Glickman Urological and Kidney Institute and Obstetrics-Gynecology and Women's Health Institute
Cleveland Clinic, Cleveland, USA

Dominique de Ziegler
Université Paris Descartes, Service de Gynécologie Obstétrique II et Médecine de la Reproduction, Unité de Chirurgie Gynecologique, CHU Cochin-Saint Vincent de Paul, Paris, France

Donald P Brawn
Institute for the Study and Treatment of Endometriosis
Chicago, IL, USA

Edgardo Somigliana
Fondazione Hospédale Maggiore Policlinio, Mangiagalli e Regina Elena
Milan, Italy

Edurne Novella-Maestre
Valencia University
Valencia, Spain

Emile Daraï
Service de Gynécologie-Obstétrique, Hôpital Tenon, Assistance Publique des Hôpitaux de Paris, Université Pierre et Marie Curie, Paris, France

Engel, JB
Universitätsfrauenklinik Würzburg,
Würzburg, Germany

Eric S Surrey
Colorado Center for Reproductive Medicine Lone Tree, CO, USA

Felice Petraglia
Obstetrics and Gynecology
Department of Pediatrics
Obstetrics and Reproductive Medicine
University of Siena, Siena, Italy

Francisco Domínguez
Fundación IVI
Instituto Universitario
IVI Valencia University
Valencia, Spain

Friedrich Wieser
Department of
Gynecology and Obstetrics
Emory University School of Medicine
Atlanta, Georgia, USA

Gareth C Weston
Center for Women's Health Research
Department of Obstetrics and Gynaecology and
Monash Institute of Medical Research
Monash University Melbourne, Australia

Gil Dubernard
Service de Gynécologie-Obstétrique, Hôpital Tenon, Assistance Publique des Hôpitaux de Paris, Université Pierre et Marie Curie, Paris, France

Ioannis Vasilopulos
Université Paris Descartes Hôpital Cochin, Reprod Endocr and Infertility, Dept of Ob Gyn II, Paris, France

Irving M Spitz
Institute of Hormone Reseach and Ben Gurion University of the Neveg
Jerusalem, Israel

Isabelle Streuli
Department of Obstetrics and Gynecology, Hôpital de Morges
Switzerland

Jaques Donnez
Department of Gynecology
Université Catholique de Louvain
Cliniques Universitaires
St Luc, Brussels, Belgium

Jean-Christophe Lousse
Department of Gynecology
Université Catholique de Louvain
Brussels, Belgium

Jean Squifflet
Department of Gynecology
Université Catholique de Louvain
Brussels, Belgium

José Schneider
Department of Obstetrics and Gynaecology, Rey Juan Carlos University, Madrid, Spain

Juan A García-Velasco
Medical Director, IVI Madrid, Spain
Associate Professor, Rey Juan Carlos University, Madrid, Spain

Juan Balasch
Professor and Chairman, Institute Clinic of Gynecology, Obstetrics and Neonatology. Hospital Clinic
Institut d´Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS), Facultad of Medicine-University of Barcelona
Barcelona, Spain

Karamouti M
Department of Obstetrics and Gynecology, University of Crete
Greece

Lone Hummelshoj
Endometriosis.org
London, England

Luciano G Nardo
Department of Reproductive Medicine
St Mary's Hospital, Manchester, UK
Maternal and Fetal Health Research Centre, School of Clinical and Laboratory Science, University of Manchester, UK

Makrigiannakis A
Department of Obstetrics and Gynecology, University of Crete
Greece

Marc Bazot
Service de Radiologie, Hôpital Tenon, Assistance Publique des Hôpitaux de Paris, Université Pierre et Marie Curie
Paris, France

Marc Princivalle
Enovapharma
London, United Kingdom

Marc R Laufer
Chief of Gynecology, Department of Surgery, Children's Hospital; Division of Reproductive Endocrinology
Department of Obstetrics
Gynecology and Reproductive Biology
Brigham and Women's Hospital
Harvard Medical School, Boston
Massachusetts, USA

Marcos Ballester
Service de Gynécologie-Obstétrique, Hôpital Tenon, Assistance Publique des Hôpitaux de Paris, Université Pierre et Marie Curie, Paris, France

Marie-Madeleine Dolmans
Department of Gynecology
Université Catholique de Louvain
Brussels, Belgium

Marina Bellavia
Unité de medicine de la Reproduction, CHUV, Lausanne, Switzerland

Mary Lou Ballweg
President/Executive Director
Endometriosis Association (International)
USA

Michelle Nisolle
Gynecology-Obstetrics Department
CHR de la Citadelle
University of Liège, Belgium

Mohamed Aboulghar
Professor of Obstetrics and Gynecology
Faculty of Medicine, Cairo University
Egypt

Mohamed FM Mitwally
Reproductive Endocrinology and Infertility Specialist TCART (Toronto Center for Advanced Reproductive and Technology), University of Toronto
Toronto, Ontario, Canada

P Cobos
Human Reproduction Unit
Department of Obstetrics and Gynecology, Cruces Hospital
País Vasco University
Baracaldo, Vizcaya, Spain

P Nervo
Gynecology-Obstetrics Department
CHR de la Citadelle
University of Liège, Belgium

Paola Vigano
AO Sant'Anna, Como and Center for Research in Obstetrics and Gynecology (CROG), Milan, Italy

Peter AW Rogers
Center for Women's Health Research
Department of Obstetrics and Gynaecology and
Monash Institute of Medical Research
Monash University Melbourne, Australia

Pascale Jadoul
Department of Gynecology
Université Catholique de Louvain
Brussels, Belgium

Rana Skaf
FACOG Active Staff
Greenwood OBGYN Associates
Greenwood, MS USA

Richard P Dickey
Clinical Professor and Division Head
Louisiana State University and
Medical Director, Fertility Institute of New Orleans, New Orleans
Louisiana, USA

Roberto Matorras
Human Reproduction Unit
Department of Obstetrics and Gynecology, Cruces Hospital
País Vasco University, Baracaldo
Vizcaya, Spain, IVI-Bilbao, Spain

Robert F Casper
Reproductive Endocrinology and Infertility Specialist TCART (Toronto Center for Advanced Reproductive and Technology), University of Toronto
Toronto, Ontario, Canada

Robert N Taylor
Department of Gynecology and Obstetrics, Emory University School of Medicine, Atlanta, Georgia, USA

Roman Rouzier
Service de Gynécologie-Obstétrique, Hôpital Tenon, Assistance Publique des Hôpitaux de Paris, Université Pierre et Marie Curie, Paris, France

Ronald D Wiehle
Repros Therapeutics Inc
The Woodlands, Texas, USA

Sajal Gupta
Center for Reproductive Medicine
Glickman Urological and Kidney Institute and Obstetrics-Gynecology and Women's Health Institute;
Cleveland Clinic, Cleveland, USA

Stefano Luisi
Obstetrics and Gynecology
Department of Pediatrics
Obstetrics and Reproductive Medicine
University of Siena
Siena, Italy

Shubbangi Kesavan
Center for Reproductive Medicine,
Glickman Urological and Kidney Institute and Obstetrics-Gynecology and Women's Health Institute;
Cleveland Clinic
Cleveland, USA

Sun-Wei Guo
Renji Hospital and Institute of Obstetric and Gynecologic Research
Shanghai Jiao Tong University
School of Medicine
Shanghai 200001, China

Thomas M D´Hooghe
Leuven Unoversity Center
Dept Obstetrics and Gynecology
UZ Gastthuisberg, 3000
Leuven, Belgium

Tony G Zreik
MBA, Associate Professor
Assistant Dean for Clinical Affairs
Dept OB/GYN, Lebanese American University School of Medicine
Beirut, Lebanon
Clinical Assistant Professor
Dept of Obstetrics, Gynecology and Reproductive Sciences, Yale University School of Medicine
New Haven, CT USA

W Paul Dmowski
Institute for the Study and Treatment of Endometriosis
Chicago IL, USA

Preface

Writing a book in the 21st century may seem outdated, when information flows quickly through the web, papers are read prior to being published as e-papers, abstracts are easily accessed through Internet and PDF files of books or journals sent by e-mail. Blogs and web pages may also offer a tremendous amount of information to the basic scientist of the clinician. However, still a book has many advantages over the other type of information, which undoubtedly is extremely useful now and in the future. But a book binds together judicious information from world-known experts, with not only longstanding deep knowledge of the disease—each one of them on different, specific areas—but also with a capacity to critically analyze the recent developments of this very enigmatic and frustrating disease, endometriosis.

In this book, we have tried to compile the most up-to-date knowledge on endometriosis, from sociological and epidemiological point of view to future treatments, covering the theories on the pathogenesis, current and future diagnostic methods, therapeutic alternatives, and side fields such as fertility preservation, cancer possibilities, and quality of life in these patients.

All together, this book offers you, the readers, a detailed and complete explanation of the disease in 2009 and hopefully, will help you not only understand but also provide a better management of this disease to your patients.

Front cover pictures are a courtesy of Dr Novella-Maestre and Dr Martinze-Salazar.

Juan A García-Velasco
Botros RMB Rizk

Contents

Section 1
Epidemiology

Section 2
Pathogenesis of the Disease

Section 3
Diagnostic Dilemmas

Section 4
Clinical Relevance and Treatment Options

Section 5
Surgical Treatment

Section 6
Classical Medical Treatments

Section 7
New Medical Treatments

Section 8
Future Trends

Introduction

"Even if peritoneal endometriosis arises from the implantation of endometrial and tubal tissue on the surface of the peritoneum, as I believe it does, this does not prove that all instances of endometrium-like tissue involving the peritoneum arise from this source."

—John A Sampson, 1927

In almost every textbook endometriosis is characterized as "*enigmatic*". Every woman, at every menstrual period shows some degree of retrograde menstruation. Menstrual debris reaches the peritoneal cavity every month. So, why do not all women develop endometriosis? After all, the viable regurgitated endometrial fragments constitute "self tissue" and they should not lead to activation of the peritoneal immune system. Still, that is exactly what happens. Peritoneal macrophages are activated, the menstrual fragments are digested, and the peritoneal cavity is cleaned month after month. Only if the menstrual reflux is too voluminous, or if the peritoneal defense system is too weak, does endometrium implant into the peritoneal lining and develop into endometriosis. Or, does it? In 1994, while reviewing the literature on occult endometriosis for Human Reproduction, I used the title *"Endometriosis does not exist, all women have endometriosis"* to stress that, apart from the many visible lesions, on purely theoretical grounds many more (as yet) invisible lesions can be expected to exist, waiting to develop into visible endometriosis.[1] So it depends on the definition you use and the meticulousness with which you scrutinize the peritoneal cavity whether endometriosis occurs frequently, always, or not at all.

Retrograde Menstrual Shedding of Viable Endometrial Tissue Fragments

What indeed is endometriosis? Is it always what we call a disease? Although the disease endometriosis can simply be defined as the presence of endometrial tissue, containing both glands and stroma, at locations outside the uterine cavity, emerging evidence indicates that to be pathologic, such tissue should not merely be there, it must persist and progress.[2] The simple existence of subperitoneal implants of endometrial tissue does not imply a pathologic condition as such. This suggests that attachment to, and subsequent invasion of the peritoneal lining by the refluxed endometrial tissue fragment is only phase I in the development of the disease. Phase II consists of the ensuing growth and proliferation of the seeded endometrium, interacting with the surrounding tissue of the peritoneal lining. If retrograde menstruation is a universal phenomenon in women,[3, 4] why do not all women develop endometriosis?[1] The puzzle of the sequence of events leading to the development of ectopic endometrial implants and eventually, in some women, to endometriosis, is gradually becoming unravelled. This book presents the state of the art of our knowledge of endometriosis. We have come a far way from the days of Karl Freiherr Von Rokitansky, who is often credited as the first one, in 1860, to describe the disease,[5] although Daniel Shroen, in 1690, already had mentioned typical "ulcers" on the surface of the bladder, intestines and broad ligament that gave rise to adhesions between the visceral organs.[6] The *magnum opus,* however, was written by John Sampson who presented in 1927, in his beautifully illustrated, 47 pages long paper *"Peritoneal endometriosis due to the menstrual dissemination of endometrial tissue into the peritoneal cavity"*[7] his regurgitation-implantation theory of endometriosis development, still the most widely accepted theory of the development of endometriosis today: Viable endometrial tissue fragments reflux during menstruation through the fallopian tubes into the abdominal cavity, where the first line of defence, the cellular and humoral peritoneal immune system is on the alert. A local, peritoneal inflammatory response occurs, the immune system is upregulated, and as a result individual tissue fragments are broken down into single cells to render them amenable to phagocytosis and subsequent digestion by the

hyperactivated peritoneal macrophages. If occasionally one or more intact tissue fragments escape this peritoneal garbage collection and disposal system (e.g. by their sheer numbers, or by innate defects of the peritoneal defence system), apposition, attachment and invasion of the peritoneal lining – although so far never having been observed *in vivo*[8] – must follow to allow for the development of (subperitoneally located) endometriotic lesions. The fragments then may grow until a critical tissue volume of about one cubic millimetre. Up to this size, oxygen and nutrients may reach the newly established implant by diffusion. Further growth and proliferation, however, require the development of a new vascular supply tree by angiogenesis.[9, 10] Only after it will have become connected to the host vascular system will the explant be able to grow beyond one cubic millimetre and become visible to the naked (laparoscoped) eye. Hence, in order for us to better understand the difference between the *disorder* 'endometrial explant' and the *disease* 'endometriosis', this critical tissue level of one cubic millimetre is pivotal. It is the maximum volume of tissue that is able to survive on diffusion alone, and it is at the same time the minimum volume of tissue identifiable at laparoscopy. In dealing with clinical endometriosis we will therefore have to realize that apart from the few visible lesions in early endometriosis, dozens, or may be even hundreds, of still-invisible submicroscopic lesions do exist that are not yet discernible to the naked eye. In fact, surgical pathology of blind biopsies of visually normal peritoneum in endometriosis patients has shown 14% occult endometriotic lesions.[11-13] The corresponding figure for blind biopsies of normal peritoneum in non-endometriosis patients is 6%.[12, 13] By extrapolation, if in every patient these authors would have taken 16 biopsies instead of a single one, all women with normal looking peritoneum would have shown evidence of endometriosis.

Where are we now?

This is where we are in 2009. The number of publications on endometriosis has rapidly risen, from 119 per year in 1968 to 131 in 1978, 334 in 1988, 408 in 1998, and to 715 in 2008. All have contributed to our increased understanding of the disease. We now know that viable endometrium reaches the peritoneal cavity during menses. We know that it activates the peritoneal immune system and that it elicits an inflammatory response. The next thing we know is that occult, microscopic endometrial implants have been found submesothelially in visually normal peritoneum, even in women without identifiable endometriosis. The phase in between these two stages of development, however, is still a black box: sophisticated *in vitro* experiments suggest that endometrial fragments rather than single cells have the capacity to remodel the mesothelium and bypass the peritoneal lining. This is how clinical endometriosis may start. But this represents only one of the many theories of endometriosis development. Some lesions may not depend on menstrual regurgitation and implantation of shed endometrium at all. They rather may result from coelomic metaplasia, from dedifferentiation of mesothelium, or from the late outgrowth of persisting embryonic rests. (Epi)genetic background and environmental factors play a role. In this book, internationally recognized experts in the field present their views on the development of endometriosis, on its pathophysiology, etiology and symptomatology, and on the most appropriate methods of (biomarker) screening, clinical diagnosis and treatment.

Johannes LH Evers
President, World Endometriosis Society
Professor, Department of Obstetrics and Gynaecology
Center for Reproductive Medicine and Biology
GROW, School for Oncology and Developmental Biology
Maastricht University Medical Center
P.O. Box 5800
6202AZ Maastricht
The Netherlands

References

1. Evers JL. Endometriosis does not exist; all women have endometriosis. Hum Reprod 1994;9:2206-09.
2. Holt VL, Weiss NS. Recommendations for the design of epidemiologic studies of endometriosis. Epidemiology 2000;11:654-59.
3. Liu DT, Hitchcock A. Endometriosis: its association with retrograde menstruation, dysmenorrhoea and tubal pathology. Br J Obstet Gynaecol 1986;93:859-62.
4. Eskenazi B, Warner ML. Epidemiology of endometriosis. Obstet Gynecol Clin North Am 1997;24:235-58.
5. Von Rokitansky K, Über uterusdrüsenneubildung. Z Gesellsch Ärtzte (Wien)1860; 16;577.
6. Shroen DC. Disputatio inauguralis medica de ulceribus uteri. Krebs publishers, Jena 1690, pp 6-17.
7. Sampson JA. Peritoneal endometriosis due to the menstrual dissemination of endometrial tissues into the peritoneal cavity. Am J Obstet Gynecol 1927;14:422.
8. Redwine D, Is "microscopic" peritoneal endometriosis invisible? Fertil Steril 1988; 50:665.
9. McLaren J. Vascular endothelial growth factor and endometriotic angiogenesis. Hum Reprod Update 2000;**6**:45–55.
10. Maas JW, Groothuis PG, Dunselman GA, De Goeij AF, Struijker Boudier HA, Evers JL. Development of endometriosis-like lesions after transplantation of human endometrial fragments onto the chick embryo chorioallantoic membrane. Hum Reprod 2001;16:627-31.
11. Murphy AA, Guzick DS, Rock JA. Microscopic peritoneal endometriosis. Fertil Steril. 1989;51:1072-74.
12. Nisolle M, Paindaveine B, Bourdon A, Berliere M, Casanas-Roux F, Donnez J. Histologic study of peritoneal endometriosis in infertile women. Fertil Steril. 1990;53:984-88.
13. Balasch J, Creus M, Fabregues F, Carmona F, Ordi J, Martinez-Roman S, Vanrell JA. Visible and non-visible endometriosis at laparoscopy in fertile and infertile women and in patients with chronic pelvic pain: a prospective study. Hum Reprod. 1996;11:387-91.