Endometriosis
from A to Z

ENDOMETRIOSIS HANDBOOK
Endometriosis affects 200 million people around the world. Too many not to be heard, too many to be ignored. Endometriosis is not rare. It is real, it is painful; it ruins careers, relationships, lives, dreams, self-esteem, fertility, financial security and the list goes on. Endometriosis patients deserve proper medical care, faster diagnosis and better appropriate standardised treatment.

Many thanks to those who shared their stories with us and to the ones who took part in our photo collage. Special thanks go to Amy, I, M and L.

An handbook containing up to-date and factual based information about endometriosis.

Warning: It contains surgical photos pages 120-127
Disclaimer:

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Dr Gabriel Mitroi, 2019

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Facts & Figures

178,000,000+
people around the world
have endometriosis

Endometriosis is as common
as asthma and diabetes

18%
of hysterectomies in the U.S. are
performed due to endometriosis

Pregnancy
is not a cure

30–50%
of women with
endometriosis
are infertile

Endometriosis creates
its own estrogen

9 years old
the youngest case
report of endometriosis

The stage does not
correlates with the level
of pain

70–80%
recurrence rate with ablation

Endometriosis
is not rare

78 years old
the eldest case report of endometriosis

Menopause
is not a cure

70.9 bil euro
annual cost of endometriosis in USA

10%
of all women of reproductive age have
endometriosis

Hormonal medication
does not cure

€6,298 lost
in work productivity
per woman annually

Excision
has a low recurrence rate

€3,113
health care costs per woman annually

Endometriosis
surgery requires
specialist treatment

keep fighting

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Forewords

Education is the most powerful weapon which you can use to change the world.
Nelson Mandela

As a disease that affects an estimated 200 million people around the globe, endometriosis and its effects on one’s life are not appropriately acknowledged in society. Despite a large number of people affected by endometriosis, 320 years later, after the first clinical description, endometriosis is still underdiagnosed and undertreated. Many patients with endometriosis have their social, personal and professional lives comprised by the disease and in many cases, those patients cases are managed poorly and improperly.

Endometriosis has various presentations, from mild to severe, and it takes between 7-10 years from the onset of symptoms until diagnosis. For endometriosis patients, educating themselves on endometriosis is the key to changing their lives. There are also endometriosis patients, charities and online groups who are contributing enormously to make endometriosis well known among the general public, by sharing their stories or creating educational materials about this illness.

At the same time, progress has been made in the last few years, with patients being better informed about endometriosis, with doctors’ dedicating their time to treat this illness as well as providing information for patients and doctors alike. As a disease that has an unknown cause, endometriosis can affect people of all ages, with patients being diagnosed with endometriosis from a very young age. Excision surgery is the state-of-art treatment of endometriosis, supported by intensive cohort studies and both doctors’ and patients’ experiences.

Endometriosis is a complex pathology, which frequently surprises even those for whom endometriosis treatment is one of their main activities. This guide contains information from various sources, and it covers all aspects of endometriosis in all its varied forms and symptoms, from its origins to methods of treatment.

Our primary purpose in writing this guide is to provide information about endometriosis for endometriosis patients, general public and healthcare practitioners. We hope that with the information presented in this guide, endometriosis patients will educate themselves on endometriosis and the treatment modalities, as they stand at the moment of publication. This will allow them to make informed decisions on the most effective care and to manage the way endometriosis impacts their lives.

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Forewords

Have you heard of endometriosis? If you have, do you know all of the facts?

7-10 years for diagnosis is appalling. Why does it take so long for people to be diagnosed with endometriosis? Is it because medical professionals don’t know about endometriosis? Is it because endometriosis is seen as a career woman’s disease? Is it because endometriosis is said to be just painful periods? All of these are terrible reasons for people suffering with endometriosis to be dismissed and misdiagnosed for years.

Endometriosis is not just painful periods, a womb disease, or a woman’s disease. There are many misconceptions and myths that surround endometriosis. Myths include: pregnancy cures endometriosis, hysterectomy cures endometriosis, endometriosis is endometrial cancer, endometriosis is an STD; and many others.

The only way to truly diagnose endometriosis is through laparoscopic surgery, and the tissues need to be sent off to pathology for testing (with the results correctly documented and sent to the patient).

Endometriosis does not always show up in imaging, or could be misrecorded by an untrained eye. As of this publication, there is not a definitive blood test that comes back positive for endometriosis if a patient has the disease. Laparoscopic surgery is invasive for the patient, yes, but patients need a confirmed diagnosis so they can move forward in finding a treatment option that works best for them for the illness they have. So it’s important that it’s scheduled and performed properly - by a team trained to recognise all the forms of the disease - for the patient to have the least number of interventions and the best quality of life possible.

The health care system is failing endometriosis patients and the community. Patients have to endure test after test, procedure after procedure, doctor after doctor to try to find some type of relief.

Excision surgery is the gold standard for endometriosis treatment and laparoscopic surgery technique, yet it’s not easily accessible to all endometriosis patients. It’s more expensive, isn’t always covered by medical insurance, and patients have to pay for travel expenses because endometriosis specialists are not everywhere. Excision surgery has the highest success rate/lowest rate of endometriosis reoccurrence. And as such, should be a viable treatment option for all in order to limit the impact this disease has on the lives of patients and their families.

Gynecologists are not fully equipped to handle endometriosis, yet they are operating on endometriosis patients. Medical students don’t even have an entire class on endometriosis; they may have a few lectures, which isn’t enough. Instead of operating, gynecologists should refer endometriosis patients to an endometriosis specialist to receive the best care possible.

Doctors from different specialties should be working together to provide each of their patients with proper standard of care. Patients should not have to endure multiple laparoscopic ablation surgeries (which is burning of the disease) in a short amount of time or cyclical fashion throughout their lives to try to get symptom relief. Nor should they be left with (or without) a lifetime of pain medications and arguably ineffective treatments, and all the detrimental effects that come with them and long term use. Earlier diagnosis and excision surgery with a specialist could drastically lower the number of surgeries, interventions and medications a patient will need in their lifetime.
Why is this a global problem that needs to be taken seriously? Because at least one out of ten people have endometriosis. This means your mother, sister, aunt, grandmother, daughter, niece, cousin, partner, friend, co-worker, or others could be impacted by this awful disease. Teenagers are missing their education; adults their chosen careers and family opportunities. This disease does not discriminate against race, color, creed, gender, weight, or location; and there is no cure.

Every single person who learns about endometriosis is helping the millions worldwide who suffer with this disease, daily.

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Living with Endometriosis: The Complete Guide to Risk Factors, Symptoms, and Treatment Options
An award-winning book by: Samantha Bowick, MPH
Foreword by: Ken Sinervo, MD
Forewords

Enigmatic Endo and Collaborative Consideration

This foreword is written with hope for the future, and dedicated to the memories and voices of all those* who have lost their lives.

I’m so so sorry that advances didn’t come soon enough for you.

Amy Jane Melhuish xXx

Readers: please make use of this resource, and those mentioned within it. Please share it amongst fellow practitioners, patients & their entourage, and fellow advocates as a ‘handbook with signposts’ to pop in your pocket and refer to for experience-based and evidence-based* knowledge as you decide (or help people to know) what’s best given their individual circumstances, and to manage expectations of all involved.

What’s with the *...? That ‘1 in 10’ and other statistics that get used are, I believe, more than likely incorrect. We - the global endo community - are woefully lacking in truthful, realistic, centralised data AND information.

When presented with statistics, it would be wise to consider how (for what purpose and on what scale) and by whom (with what training or financial backing) they’ve been compiled, presented or used in the decision making process for patient ‘care’. Data and information are NOT the same thing.

You’ve all heard of asthma and diabetes, right? Well endometriosis is as common. Yup! Shocking.

You’ve all heard of cancer too ...Well, endometriosis can be described as “the most aggressive benign disease”. There is currently no cure.

(Please note: I am not in any way saying one is worse / better / easier than the other...my heart goes out to anyone finding themselves dealing with any health problems and all that that can entail. And note to anyone who isn’t: please be grateful and attempt empathy towards others, and take heed of your own daily choices so that it may forever stay that way for you. In either scenario, words I live by are "what can we learn from this?" and "how can I ..." rather than what I can't do at that time ...)

Endometriosis (end-oh-mee-tri-osis) can / does affect multiple organs and, whilst every case is unique, endometriosis is a body-wide disease and is most certainly NOT “just a bad period”. I’ve literally heard it all over the years (nearly three decades), as have many others on their journeys.

Here are some actual comments made directly to me and/or written in my notes, by doctors from whom I was seeking help for a debilitating condition, some of which have been more or less detrimental to my mental as well as physical wellbeing along the way, and include amongst many others:

... go have a baby THEN come back to me (whilst single & unemployed)...no don’t be dramatic, you don’t need to freeze your eggs at your age (during a meeting with my then partner for whom his own children was nonnegotiable) ...well you are one of those career women aren’t you (whilst being self-employed because I was "unreliable" in the workplace due to my health)...are you sure you’re not just imagining this, you don’t look ill (I’d purposefully not even worn makeup nor brushed my hair that day)...you’re just a bit stressed (I have techniques)....
...you've had a hysterectomy, so you're all fixed (during discussions regarding other body parts failing me)... oh hello AGAIN (so sorry to be a bother)... what on earth have you got that trolley for? (to maintain a level of independence and be able to leave the house on the days I can move, how about some empathy rather than judgement?)... why haven't you gone back to work? (you've obviously not read my notes then)

...oh that bump...Congratulations ! (you've DEFINITELY not read my notes then)... it's just a little procedure, you'll be back at work in a couple of weeks (I still wasn't after a year, and after two, I'd lost my house as well as my job)... it's just constipation (that's only one of many symptoms)... no this examination doesn't hurt (when I just said that it did) ...nothing showed up you're all fine (no I'm not, which is why I'm here & hoping you'll be able to help me)...

Some of the above were during the thirteen years it took me to get a diagnosis (eventually back in 2005), others were since, as in WITH a surgically-confirmed diagnosis, and ongoing health problems.

We - patients, practitioners, the media - have a duty of care to stop and correct the spread of misinformation. Endometriosis tissues are similar to but not the same as endometrium that lines the womb. It has been scientifically proven so, repeatedly, for a long time now! …rather unfortunately the name given to the disease ‘back in the day’ most certainly does not help this common misconception!

Perpetuating the misconceptions will continue to drive incorrect and incomplete assessments, ‘care’ plans and the peddling of ‘treatments' that often mask symptoms whilst disease silently progresses. It will continue to cost countries in lost annual GDP and miss spent health and research budgets. And it will continue to cost lives.

It is a body-wide disease (different patients have it in different locations & combinations), it is NOT confined to those with a womb (men also have it, women who've had hysterectomies for whatever reason or are in menopause can / still have problematic endometriosis) and one doesn’t have to be a certain age (as you’ll see documented herein)...

These still far too common misconceptions are NOT helping true progress when it comes to the likes of classification of this disease, treatment pathways & national guidelines, debates highlighting the need for cross departmental involvement (health AND Social), more money for (broader) research, the correct (financial and otherwise) support for those with it and so on and so on... Though these ongoing misconceptions are understandable when a journalist Googles endo quickly for an article that millions will then ingest, as even some reputable medical organisations define endo incorrectly; or if a practitioner simply abides by the short hours or few lectures they had on it whilst at Med School.

We’re in this together:
if ‘we’ continue to not look, ‘we’ will continue to not find nor document it appropriately and 'rare' will remain rare even if it's, in fact, not... And, as such, practitioners and legislators will continue to rely on or refer to and quote incorrect data as 'evidence-based' decision-making, whilst patients continue to be misinformed & misguided. Most of us (from years of observing numerous groups) do have coexisting pathologies. However, what diagnoses we end up with depends on what practitioner is seen on what day, for how long, and what was documented where & how (what training/experience have they & their support staff had, and are they all having a good or bad ‘day at the office’; as well as where the patient is at in their cycle/flare at the time of the appointment and if the tone of the consultation has lead to PTSD shutting them down or to feeling confident and safe enough to open up).
Endometriosis - historically & currently - hasn’t been considered as a primary source of many symptoms. It should be, and likely is. I wonder, when further much needed research and training across all medical disciplines is carried out, how these diagnoses statistics will change, how much will be attributed to endo itself when the disease is better understood scientifically, documented across the lifetime of patients and the correct referrals made? 'The system' for scheduling and referrals as currently stands in most countries is adding to unreliable data for practitioners, to patients not feeling heard nor taken care of, and to the suicide rate.

Collectively, we can change that haphazard rhetoric.

Ignorance isn’t bliss, actually.

Ignorance is an opportunity to learn, to share, and to change lives for the better.

When it comes to endo, I can say from experience that ignorance is dangerous.

And it’s costly. Both to healthcare providers and to patients.

It’s costing people:

Organs, bodily functions, relationships, careers, schooling, financial security, homes, their mental health, dignity and their ability to dress as their personality may wish (just ask anyone with ‘endo belly’!)

…I could go on, but I won’t.

You get the picture.

These are all often unmerited side effects of a broken system and lack of training / empathy.

That’s avoidable!

Now in my forties, I can’t tell you how many times I’ve said “but nobody told me”.

Had I known, how many different life choices would I have made?

I honestly can’t answer that.

But what I can say, is that those choices should have been made clear and were mine to make.

Well this, right here, is your chance to know a little or a lot more than you may have known yesterday.

Your chance to bring more up-to-date collated knowledge to the table in order to arrive at more informed decisions – be you practitioners guiding or patients deciding; all of whom are doing their best (one would hope) to navigate enigmatic endometriosis.

We don’t know what we don’t know, but chances are somebody else does. Follow the signposts.

After countless (literally in the hundreds) of consultations and conversations with medical professionals (specialists, radiographers, consultants & educators, general practitioners, pharmacists, physiotherapists, midwives, nurses, care assistants, support staff).

…across many organisations and disciplines (endometriosis affects multiple organs and bodily functions so ‘we’ get divided-up…)
…over the decades I’ve had it (it’s a chronic condition that CAN be improved, but one that also needs to be recognised officially and globally as the disability that it is / can be)

…in multiple countries (I’ve lived in UK, Australia, and France; and attended medical conferences and support group meetings across the globe over the years)…

…after all that …and multiple surgeries and multiple ‘treatments’ and countless side effects and/or progression of the disease (still undecided amongst the medical community), I can say with experience, hindsight and conviction that:

Everybody needs to know endo.

Ignorance is a choice (with or without reason).

Knowledge is power (that should not be abused), and ignorance no longer an excuse for inaction.

Whilst research data* gets presented at AAGL, Congresses and beyond, and debates are finally being heard in parliaments (some governments sooner and more willing than others), and the ACOG and NICE guidelines (and the equivalent in each country globally) continue to be questioned at multiple ‘levels’ by grassroots patient-led organisations as well as by some national charities; there is the harsh reality of how long these amendments take to trickle through ‘the system’ (years) and how many more lives are lost or negatively impacted in the meantime (I refer to practitioners’ stress levels as well as patients’ quality of life here! Modern Medicine is currently being taught a newly titled discipline that should warn all to take heed, and not just when it comes to endo or the pelvis!).

‘Thanks’ to increased media attention over these past few years, endometriosis may seem like a current epidemic*.

It isn’t. Yes, some ’modern day’ factors may or may not have exacerbated the prevalence of symptomatic disease, but it remains that it is one disease that has been underfunded and incorrectly dealt with for centuries. Whilst the subject matter remains unsexy for marketing organisations, and often taboo amongst societies: time’s up.

People continue to join forces and raise their voices. We WILL be heard.

Together we can. Together we will. Together we must. If there’s a problem, there’s a solution.

Solutions can and should be shared (please & thank you). We can individually decide if we want to be a part of the collective problem or collective solution.

Scientific debates regarding enigmatic endo are rife - and ‘should’ be respectfully encouraged in order to truly progress with the quest for a cure for this very common disease and everything associated with it. Egos and vendettas or personal mishaps aside (I don’t mean to belittle what I myself nor anyone else has gone through in phrasing it as such. I sincerely mean ‘each to their own’ with how individuals choose to react and proceed), there ARE still collective solutions that can and ‘should’ be put in place NOW in order to help those currently navigating the journey.

Our collective objective ‘should’ be to help people today to make INFORMED decisions and find what works best for them from the options currently available; whilst simultaneously collectively paving a brighter and clearer path for the footsteps that follow …may their journeys have fewer “what the f*ck !?!” and “but nobody told me” moments than has been and continues to be the case for millions upon millions of people globally.
Though this publication is comprehensive and broad, there are some other treatments not listed herein at the time of publishing that are currently being researched or advanced, or that are already in use in some countries (though patients there may not even know of it!). And many deemed as ‘alternative’ to Medicine that may also help (some) patients.

I don’t have regrets, life’s too short. Believe me when I say that I’ve worked on myself a LOT to get to this point (and self-development never stops!): to be able to share whilst vulnerable and to search for solutions rather than focus on blame. But, dang, I sure wish I’d had this and the other resources mentioned within it decades ago! So please do your bit to ensure that others now do!

In the meantime, I, like others, will keep working on plans to bridge gaps. Through evidence-based advocacy + evidence-based medicine, may we move forward. Globally. Together.

May each patient get to form their own pathway that’s right for them, based on informed decisions made with and referred by their team.

And may each patient have access to an educated team with which to do so. Hindsight 20~20 vision in 2020 and beyond. We’ve a lot that we CAN learn from to propel us forward.

So let’s do it!

Amy Jane Melhuish
Independent patient mentor, global advocate and award-winning entrepreneur drawing on her professional and personal experiences to help the collaborative efforts for positive change

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a global social enterprise of experience-based and evidence-based knowledge for 20~20 vision

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Table of Content

Chapter 1 About Endometriosis........ 14
Endometriosis History .................. 14
Definition of endometriosis ............ 14
Difference between the endometrium and endometriosis ........... 15
Pathophysiology .......................... 15
  Retrograde menstruation theory ...... 15
  Mülleriosis/ Embryologic origin of endometriosis ........... 16
  Homeobox genes ......................... 17
Other causes ................................ 17
Symptoms .................................. 18
  Endometriosis signs and symptoms .. 18
  Break down of the endometriosis symptoms ......................... 19
Endometriosis pain ...................... 19
  Types of pain ................................ 19
  Pain with minimal endometriosis ...... 20
Menstrual cramping and abnormal periods ........................................ 21
Diagnosing endometriosis .............. 21
  Methods of diagnosis .................... 22
  Anamnesis ................................ 23
Physical examination .................... 23
Imaging ................................ 23
Laparoscopy ................................ 23
Biomarkers/lab tests ...................... 24
Why such a long delay in diagnosis? .. 24
Endometriosis categories ............... 24
  Superficial peritoneal endometriosis... 24
  Endometriomas cysts ..................... 24
  Deep infiltrating endometriosis ....... 25
Histopathology .......................... 25
Location of endometriosis .............. 25
Colours & appearance of endometriosis 26
Types of endometriosis lesions ........ 27
The role of imaging in endometriosis .... 27
  MRI by Dr Livia Stanciulescu ........... 28
  Colonoscopy ............................... 29
Endometriosis staging ................... 29
  Revised American Society for Reproductive Medicine classification.. 30
  Enzian score .............................. 31
Adhesions ................................... 32
Frozen pelvis .............................. 33
Kissing ovaries ............................ 33
Pain management ........................ 33
  Medical therapies ....................... 33
  Hormonal contraceptives ............... 34
  Progestin therapy ....................... 35
  Visanne .................................. 35
Gonadotropin-releasing hormone therapy ........................................ 36
  GnRH side effects ....................... 38
Use of hormonal medication prior to and after surgery ......................... 39
Pregnancy effects on endometriosis ...... 40
  Estrogen- phytoestrogens- xenoestrogens ........................................ 40
Chapter 2 Endometriosis by sub-type and location .................. 42
Ovarian endometriosis .................... 42
  Symptoms .................................. 42
  Diagnosis ................................ 42
  Treatment ................................ 43
Gastrointestinal endometriosis ........ 43
  Diagnosis ................................ 44
  Symptoms ................................ 44
  Treatment ................................ 44
Rectovaginal and utero-sacral ligaments endometriosis ..................... 45
Urinary tract endometriosis (UTE) ....... 46
Endometriosis from A to Z

Bladder endometriosis .......................... 46
Symptoms ........................................ 46
Diagnosis ......................................... 46
Surgical Treatment ............................ 47
Ureteral endometriosis ........................ 47
Diagnosis ......................................... 47
Symptoms ........................................ 47
Surgical treatment ............................ 47
Urethra endometriosis ........................ 48
Renal endometriosis ......................... 48
Thoracic and Diaphragmatic endometriosis ........................................ 48
Surgery ........................................... 49
Endometriosis of the peripheral nervous system ....................................... 50
Endometriosis of the autonomic nervous system ........................................... 50
The somatic nervous system .......... 51
Endometriosis of the sacral nerve roots .......................................................... 51
Endometriosis of sciatic nerve ...... 52
Symptoms ........................................ 52
Diagnosis of sciatic nerve endometriosis ......................................................... 53
Treatment of sciatic nerve endometriosis ....................................................... 53
Cutaneous-abdominal wall endometriosis ......................................................... 53
Forms of very rare endometriosis ...... 54
Liver endometriosis ............................. 54
Pericardial endometriosis ................. 55
Umbilical endometriosis ................. 55
Inguinal endometriosis ................. 55
Pancreatic endometriosis ............... 55
Perineal endometriosis ................. 55
Invisible/occult microscopic endometriosis ..................................................... 55
Endometriosis by age ....................... 56

Endometriosis in teenagers .......... 56
Endometriosis in menopausal patients... 57

Chapter 3. Surgical Interventions ......... 59
Laparoscopy .................................... 59
Laparotomy .................................... 59
Hysterectomy .................................. 60
Video-Assisted Thoracoscopic Surgery (VATS) ............................................. 60
Robotic Surgery ................................ 60

Chapter 4. Surgical Treatment .......... 63
Excision ........................................ 63
Excision technique- Wellborn Centre.. 63
Thermal ablation techniques ............. 66
Excision vs ablation ......................... 66
Cystectomy .................................... 68
Hysterectomy and oophorectomy ...... 68
Presacral Neurectomy (PSN) ............. 69
Adhesiolysis .................................... 70
Intestinal Surgical Procedures ........ 71
Rectal shaving ................................ 71
Disc resection .................................. 72
Segmental resection ......................... 72
Urinary Tract Surgical Procedures ...... 74
Ureteral surgical procedures .......... 74
Ureterolysis (Ureteral shaving) ......... 74
Ureteroneocystostomy ..................... 74
Uretero-ureteral-anastomosis .......... 75
Bladder Surgical Techniques .......... 75
Surgery outcomes ............................ 76

Chapter 5. Endometriosis and Infertility ......................................................... 78
Tests for the female partner ............ 78
Tests for the male partner ............... 78
Endometriosis and reproductive treatments ................................................. 78
AMH, AFC and FSH .......................... 79
Methods of Assisted Reproductive Technology (ART)............................. 80
The effects of endometriosis surgery on fertility ........................................ 80
Pregnancy after surgery ...................................... 81
Medical therapies ........................................... 81
Ovarian reserve- excision vs ablation ........................................ 81
Endometriosis effects on pregnancy ........................................... 82

Chapter 6. Other Info ........................................ 83
Adenomyosis ........................................... 83
   Symptoms............................................ 83
   Diagnosis............................................ 84
   Treatment ........................................... 84
Adenomyosis and fertility ........................................ 84
Endosalpingiosis ........................................ 85
Endocervicosis ........................................ 85
Fibroids .............................................. 85
   Symptoms and signs .................................... 86
   Diagnosis ............................................ 86
   Treatment ........................................... 86
Endometriosis and PCOS ........................................ 86
   Sign and Symptoms .................................... 86
   Diagnosis ............................................ 87
Occult Hernias ........................................ 87
Recurrence in endometriosis ........................................ 89
Methods of preventing surgical adhesions ........................................ 89
Endometriosis surgery complications ........................................ 90
   Fistulas ............................................. 91
Anaesthesia-Wellborn ........................................ 92
Endometriosis and associated diseases ........................................ 93
   Endometriosis and cancer ........................................ 93
   Endometriosis and auto-immune diseases ........................................ 93

Endometriosis and thyroid diseases ........................................ 93
Endometriosis and depression ........................................ 94
Endometriosis and Fatigue ........................................ 94
Endo belly-bloating ........................................ 95
Brain fog- clouding of consciousness ........................................ 95
Other types of pain ........................................ 96
The role of surgery ........................................ 96
Conservative - medical treatment ........................................ 97
Endo pain-free- managing expectations ........................................ 98
Pelvic floor therapy ........................................ 99
Endometriosis specialist vs a regular obstetrician-gynaecologist (ES vs OG) ........................................ 99
Endometriosis centres ........................................ 100
How to prepare for surgery? ........................................ 101
   Bowel preparation ........................................ 101
Endometriosis surgery recovery ........................................ 102
Persisting pain after surgery ........................................ 102
Managing endometriosis symptoms ........................................ 103
Diet ..................................................... 103
Endometriosis patients- What do we all need to know? ........................................ 104
Endometriosis Summary - Dr Gabriel Mitroi ........................................ 105
Patients’ stories ........................................ 109
The Demon Within by Aimee Brown ........................................ 116
Endometriosis groups and information sources ........................................ 116
Surgery photos ........................................ 119
About Wellborn Endometriosis Centre ........................................ 128
Wellborn Centre-Case Reports ........................................ 129
Glossary ................................................ 131
References ............................................ 132
Chapter 1 About Endometriosis

Endometriosis History

In “Endometriosis: ancient disease, ancient treatments” by Nezhat et al., is noted that symptoms similar to endometriosis are documented in ancient medical texts dating back more than 4,000 years. Surgery made progress in the 18th century and became more advanced in the 19th century when endometriosis is described in more detail.

Here are some historical findings about endometriosis:

• 1690, Daniel Shroen, a German physician, has mentioned “ulcers” on the surface of the bladder and intestines. Shroen is credited with describing umbilical endometriosis first;
• 1860, Karl von Rokitansky, an Austrian pathologist, has written the first detailed description of the disease in the scientific literature;
• Thomas Cullen is believed to be the first one to describe the full morphological and clinical pictures of endometriosis and adenomyosis. In 1908, he published his book “Adenomyoma of the Uterus”, and in 1919, he provided for the first time a list of possible sites of adenomyotic lesions;
• 1921, Dr John A Sampson, started describing ovarian endometrioma as “perforating hemorrhagic cysts of the ovary” and in 1927 he published a series of reports on endometriosis;

Definition of endometriosis

Endometriosis is a chronic condition that affects people of any age, including postmenopausal women, and it was found in men, animals and foetuses as well. Endometriosis, an inflammatory benign disease is the presence of tissues (glands &stroma) similar to the endometrium outside the uterus. In the earliest references of the disease in literature, endometriosis nodules in the rectum, ligaments, and bowel were described as adenomyomas.

The medical literature shows that endometriosis is commonly found in people of reproductive ages; however, endometriosis can affect people of all ages. Doctors have reported seeing patients as young as seven years old. The youngest case report is of a nine years old girl who had pelvic pain since her 8th year of life seen at an Endometriosis Research Centre in Berlin.

A possible case of infant endometriosis was found by Dr Redwine, using a magnifying glass, in the cul-de-sac of a 2-month-old infant who died of Sudden Infant Death Syndrome. Under the microscope, the small abnormal tissue had a glandular structure with questionable stroma surrounding, but since there is no information about how endometriosis looks in infants, he can’t say if what he found was endometriosis or not.
Geisinger Medical Center in Pennsylvania has reported a case of foetal endometriosis in an 18-year-old pregnant woman diagnosed with a large foetal pelvic mass at 35 weeks’ gestation. The mass was surgically removed by a paediatrician surgeon in day 2 of life, who performed an exploratory laparotomy and left salpingo-oophorectomy. The final pathology showed a 7.0 × 4.5 cm cyst-like structure consistent with haemorrhagic ovarian cyst wall and focal endometriosis. (Schuster M et al., 2015).

Endometriosis is a whole-body disease, (Nezhat C), and is associated with pelvic pain and infertility. Endometriosis tissues are often accompanied by fibrosis. Symptoms can range from mild to severe and in some cases, endometriosis can be asymptomatic. In this case, the disease is usually discovered either when the patients can’t conceive naturally and are seeking medical help, or during surgery for other indications. Due to the way it presents, endometriosis can have a serious impact on a person’s life.

Endometriosis is a benign medical condition believed to be oestrogen dependent; however, studies show that endometriosis tissues have progesterone receptors as well. It is a common disease affecting almost 200 million people around the world and due to some symptoms that correlate with other diseases, it is often misdiagnosed. It was included in the 20 most painful conditions by the NHS UK, and if it is not treated in time, it can potentially cause organ loss and disability.

**Difference between the endometrium and endometriosis**

Based on Sampson’s theory, endometriosis is misplaced endometrial tissues identical to the endometrium that responds to the ovarian hormonal cycle. Dr David Redwine searched to find if endometriosis is an autotransplant, using various words (endometriosis, endometrium, autograft, autotransplant). In his results, he noted that an autotransplant remains identical or very similar to eutopic tissues of origin.

Only a few studies have found similarities between endometrium and endometriosis. Other authors have found hundreds of differences between endometrium and endometriosis, showing that endometriosis is not normal endometrial tissues.

The many differences between the endometrium and endometriosis include histologic and morphologic characteristics, protein expressions, enzymatic activity, visual and microscopic appearances, hormone receptors and responsiveness, immune-histochemical as well as increased steroid and cytokine production, invasive properties, decreased apoptosis and biochemical.

**Pathophysiology**

The exact cause of endometriosis is not known so far. A few theories have been presented, and the pathophysiology is likely to be multifactorial. Since the exact cause of endometriosis remains unknown, excision surgery is the only curative method, in a single or a second surgery.

**Retrograde menstruation theory**

Sampson’s theory of reflux menstruation, also known as the implantation or transplantation theory, is one of the old theories about how endometriosis tissues develop. Each month the lining of the uterus is shed, resulting in what is known as menstruation.
Sampson’s theory suggests that the lining of the uterus (endometrial cells) rather than leave the body, are flowing back into the body through the fallopian tubes, where they can implant and attach to different areas and organs, causing the development of endometriosis. Once attached and implanted, these cells act as the endometrium during menstruation, they shed and bleed (internally).

This theory, though, does not match the fact that endometriosis was found in young girls, men, foetuses, and animals. Based on the history of endometriosis, when Sampson published his first data, the term endometriosis did not exist. In 1921, Sampson published a study done on 23 women, and only 9 cases were histologically proved endometrial type ovarian cysts.

Sampson believed that endometrial cysts once ruptured, the fluid would leak carrying endometrial cells that would implant on the pelvic surface. In cases where no chocolate cysts were found, he believed that then the endometrial cells are deposited directly onto the areas, through the fallopian tubes. Sampson thought that endometriomas cysts and endometriosis, which he refers to as the implantation of adenomyoma, are misplaced endometrial type tissues.

In 1922, he published another paper focusing on the content of the article published in 1921, where he pronounces his theory correct. He explains that the endometrial cells have either escaped from the tubes, the ruptured hematoma cyst, or both. Many years before his death, Sampson admitted that no explanation could be given for the origin of all cases of endometriosis. (Scott Robert, 1949).

Mülleriosis/ Embryologic origin of endometriosis

Mülleriosis, Dr David Redwine’s current and long standing theory of the origin of endometriosis, refers to a developmental defect in the differentiation or migration of any cellular component of the müllerian duct system, or of the coelomic epithelial anlage of the adult peritoneum, from which both the müllerian ducts and peritoneum arise. (Endopeadia). Dr Redwine mentions that Mulleriosis theory is different than Sampson’s Mullerianosis.

Based on this theory supported by foetal autopsy endometriosis forms during foetal development. The autopsy was done on 36 human female foetuses at different gestational ages, and four of them had misplaced endometrium in several sites such as the rectovaginal septum, cul-de-sac, and posterior wall of the uterus. This theory also explains the cases of endometriosis in males and animals and the presence of endometriotic tissues distant from the pelvis.

Mesoderm, which gives rise to specific tissues, can migrate outside the uterus, displacing Mullerian tissues in the body that can manifest as endometriosis. Mesoderm is one of the three primary layers of cells (ectoderm, mesoderm, and endoderm), and forms the coelom and its lining, bladder, kidney, uterus, ovaries, tubes, muscles, prostate. Based on this, endometriosis is, therefore, a manifestation of a defective mesoderm that was laid down during organogenesis.
Mulleriosis is a genetic-based process that refers to a developmental defect of the Mullerian ducts system during embryology. Mullerian ducts are the earliest development of the female reproductive tract and are initially formed regardless of genotypic sex. When the system is disrupted, malformation can occur.

Mulleriosis is an organoid structure formed in an embryo during organogenesis also known as chortistoma, a congenital anomaly, where normal tissue is incorporated within another normal organ during embryogenesis. Theory of Mulleriosis predicts that misplaced Mullerian tissue during organogenesis, results in the formation of 4 embryonic diseases:

- Endometriosis
- Adenomyosis
- Endocervicosis
- Endosalpingiosis

**Endocervicosis** is characterised by the presence of endocervical mucinous type epithelial inclusions outside the uterine cervix, and it primarily affects the bladder. **Endosalpingiosis** is characterised by the presence of tubal epithelium outside the fallopian tubes.

**Homeobox genes**

The genes that could play a role in the embryonic origin theory are the HOX genes, also known as the homeobox genes. Homeobox genes are a large group of similar genes, and their role is to direct the formation of many-body forms of many animals, including humans during embryonic development. They stay in the areas where they were laid down, and as a master regulator of embryonic development, mutations in these genes can cause genetic/developmental disorders.

HOX gene mutation or HOX gene expression can cause abnormalities in the reproductive tract development. The HOX genes can be changed by endocrine disruptors causing Mullerian defects. The HOX genes 9,10,11 and 13 are forming the female genital system, and HOX 12 and 13 form the sigmoid, the rectum and vagina. Endometriosis is caused by a problem with HHOX genes, which results in abnormal differentiation and migration of cells during the embryonic formation of the female reproductive tract.

**Other causes**

**Coelomic metaplasia** refers to the metaplasia of coelomic cells into endometriosis tissue as a result of chronic inflammation or irritation from the refluxed menstrual blood. The coelomic epithelium is the outermost layer of female and male reproductive organs. With this theory, coelomic cells are transforming into endometrial type glands in response to unknown stimuli. This theory also explains why endometriosis reoccurs after a total hysterectomy.

**Environment.** This theory suggests that the risk of developing endometriosis might be related to toxins in the environment, such as dioxin. Exposure to a toxic environment can affect the body, the reproductive and the immune systems. A study done in South Korea found that nickel allergy can be a risk factor for endometriosis.
Stem cell: Recent information shows the participation of endometrial stem and progenitor cells and bone marrow cells in the origin of endometriosis. This theory explains the possibility of finding endometriosis in remote areas from the pelvis. In a study done on a healthy uterus, a uterus with adenomyosis, excised endometriosis lesions and menstrual blood, the results suggest that ectopic endometrial lesions are caused by dislocation of the basal endometrium.

Immune dysfunction system: Endometriosis co-exists with other conditions, and some of them are autoimmune diseases. It has not been identified if an immune dysfunction is the cause of endometriosis or its results. Some research shows differences between the immune systems in patients with endometriosis and women with no health or fertility problems.

Genetic. Studies have shown that endometriosis runs in families, and the genetics is complex and remains unexplained. A population-based study done in Iceland in 2002, concluded that there is a raised risk for endometriosis, among close and distant relatives. The research was done on 750 patients who had endometriosis surgery from 1981-1993, and it looked at sisters and cousins. Sisters had a risk of 5.20% of developing endometriosis, and among cousins, the risk was 1.5%.

Symptoms
Pain is the main symptom of endometriosis. Endometriosis is a very complex disease, and the symptoms differ from person to person. Some symptoms of endometriosis correlate with other medical conditions, making diagnosis even more difficult. Endometriosis is felt differently from person to person, and the stage does not always correlate with the level of pain. Some symptoms are due to organs being affected directly or due to the irritation caused by endometriosis lesions.

Endometriosis can be symptomatic and asymptomatic, although, with the right questions/clinical investigations, an asymptomatic patient can become symptomatic. Also, in cases of asymptomatic (pain wise) endometriosis, if fertility is affected, then this becomes symptomatic, as infertility is a symptom of endometriosis. The pain can be cyclic or acyclic, and it gets worse during menstruation.

### Endometriosis signs and symptoms

| Pain before, during or after periods; Painful ovulation; Pain or bleeding with bowel movements; Pain during or after intercourse; Pelvic pain; Painful urination; Partial bowel obstruction; Leg and back pain; Right/left chest and shoulder pain; | Bloating and severe lower abdominal discomfort; Pain when breathing; Pain when sitting down; Infertility; Fatigue; Nausea and vomiting; Heavy periods; |
Break down of the endometriosis symptoms

Secondary **dysmenorrhea**- pain during menstruation, it may begin a couple of days before menstruation. The peak of pain can be during menstruation, and it can last after menstruation is finished.

**Dyspareunia**- painful intercourse, pain can occur during or after intercourse and can last for a couple of days. In some cases, bleeding can occur as well. Deep infiltrating endometriosis and recto-vaginal nodules can cause painful intercourse.

**Dysuria**- painful or difficult urination (bladder, urethral). In rare cases, patients will complain of painful or difficult urination.

**Dyschezia**- painful, bleeding or difficult bowel movement. When the terminal ileum is affected, the patient might have symptoms of partial bowel obstruction. Rectal wall endometriosis may cause pain with every bowel movement throughout the cycle.

**Endometriosis pain**

There are multiple mechanisms by which endometriosis produces pain, some of which are known, others are still being evaluated. The most common causes of pain in endometriosis are:

- organ compression/tension/nerve structures - in the case of ovarian endometriomas/nodules;
- the appearance of fibrous tissue, which can also compress, infiltrate nerve tissue;
- continuous discharge of inflammation mediators from nodules/lesions;
- the occurrence of angiogenesis and nervous reshaping processes in the affected areas;
- adhesions and fibrosis that may reduce organ mobility and ruptured cysts;

Some patients with mild forms of endometriosis have extremely high pains, and other patients with severe forms have minimal pain. Endometriosis pain is chronic is consistent, severe and is described as sharp, burning, stabbing, etc.

Depending on its location, endometriosis can produce different clinical signs and symptoms. Endometriosis is characterised by pain, located frequently to the pelvic area/organ affected by the disease either directly or by irritation. With estrogen levels rising (Mulleriosis), endometriosis glands secrete an unidentified paracrine product that destabilises nearby capillaries to bleed, irritating the tissue and causing pain.

A study done by Korotkova et al., 2014 in Sweden, had noted the association between muscle atrophy and weakness in patients with chronic inflammatory diseases caused by prostaglandins and leukotrienes resulting in muscular pain, and inflammation. Another study done by Sluka et al., 2010, from the University of Iowa, observed that fatiguing exercises enhance hyperalgesia.

**Types of pain**

Endometriosis pain can be multifactorial. **Somatic pain** is classified as pain in pelvic wall, skin, muscles, connective tissues or joints. Somatic pain is described as sharp, ache or cramps and is stimulated by movement, can be constant, confined locally or spread across larger areas of the body. Endometriosis can cause deep somatic pain (felt deeper in the body).
**Visceral pain** is a nociceptive pain and occurs when pelvic, thoracic and abdominal internal organs or tissues are damaged or irritated. The pain is vague, can be constant or intermittent and is described as pressure, squeezing or dull. Visceral organs have an autonomic innervation; thus, visceral pain can be accompanied by sweating, nausea and vomiting symptoms as well as emotional manifestation.

Visceral pain can radiate from the initial location affecting other areas of the body as well. Sometimes, pain from a specific organ or area can be felt in nearby organs/areas of the body. This is called referred pain. Surgery causes visceral pain. As opposed to somatic pain, visceral pain is difficult to pinpoint where it is coming from.

**Neuropathic pain** arises when pelvic nerves are affected/irritated by the disease. The patients will present with lower abdominal/pelvic pain that can be felt in the lower back. The pain is described as a burning pain that radiates down the leg, starting from the hip/glutes. A study done by Tokushige et al., found nerve fibres in peritoneal endometriosis that may play an important role in the mechanisms of endometriosis. Anaf V et al., have found a significantly increased number of nerve structures in endometriotic nodules which may contribute to the severe and neuropathic pain caused by these nodules.

Endometriosis can cause both precise and widespread pain, and it gets worse during periods. An observational study done by Mckinnon et al., shows that rectovaginal and peritoneal lesions are associated with nerve fibre, and are causing more menstrual pain than other lesions. Based on a pelvis map, the most common areas affected by the disease are the cul-de-sac and the ligaments that sustain/hold some of the reproductive organs. Common bodily functions and physical examination irritate these areas and cause pain.

**Pain with minimal endometriosis**

Endometriosis is a medical condition that causes pain; however, patients are often told because they have minimal disease they can't be in pain. Endometriosis patients can be divided into many categories including, patients with mild forms of endometriosis who have extremely high pain, and patients with severe forms who have minimal pain.

A classification of endometriotic implants by morphologic appearance and capacity to synthesise prostaglandin F (PGF) done by Vernon MV et al., found that PGF production of implants was higher in patients with mild and moderate disease. The implants from 14 patients were divided by authors in reddish, brown, powder-burn or black. The reddish implants produced twice the amount of PGF than brown implants which in turn produced more PGF than powder-burn implants.

Before the introduction of laparoscopy, laparotomy was used to locate and treat endometriosis surgically during which only typical lesions visible with the naked eye were removed. After laparoscopy was introduced, new lesions, red and white were identified, however, patients were still in pain after surgery. Hysterectomy was then offered to the patients who continued to be in pain after the surgery.

In cases of bowel involvement, the patients were diagnosed with IBS or were told that the pain is in their head. The peritoneum was identified as the cause of pain, and later on, due to unidentifiable lesions at that time and the recurrence of the pain, a pelvic pain map has been created. Surgeries were done under local anaesthesia, and the doctor was assisted by the patient to find the source of pain, and remove the lesions.
This approach showed that when the lesions were touched, the most visible and known endometriosis lesions, the black colour, were painful only in 11% of the patients, while the clear lesions were the most painful, in 32% of the patients. The red lesions in 37% of the patients and the white lesions in 20% of the patients were found to be painful. Another fact which shows that excision is better than ablation is that the pain is extending behind the visible border of the lesion, so to get rid of the pain, the lesion has to be excised.

Regarding the location of the pain, due to the patient assisted surgery, more information was found. Palpation of the uterus during mapping did not cause pain/cramps; the cramps were caused by palpation of the endometriosis lesions.

In patients who underwent a hysterectomy, cramps caused by palpation of the endometriosis lesions were still there. This has confirmed the findings that a hysterectomy is not a cure for endometriosis since the uterus is not involved in the endometriosis pain. In another study done on adolescents who presented with cyclic and acyclic pelvic pain, 58% of the patients who have been diagnosed with endometriosis had early and minimal stage disease.

**Menstrual cramping and abnormal periods**

Both menstrual cramping and abnormal periods are caused by different medical conditions such as adenomyosis, uterine polyps and fibroids. Hence why ruling out other symptoms generators plays an important part in diagnosis and treatment. In this case, surgery for endometriosis alone might not improve these two symptoms.

Abnormal periods include heavy menstrual flow, bleeding in between periods and prolonged periods. A normal period lasts between 2-5 days. In some cases, a period can last up to 7 days, and the flow is usually low in the last days.

Menorrhagia is characterised by long and heavy periods. Depending on the amount of blood loss during menstruation, one can’t maintain their daily activities. Soaking through a pad or clothes every couple of hours, passing big clots, changing pads every 30-60 minutes, using double or incontinence pads, anaemia, all are signs and symptoms of menorrhagia.

**Diagnosing endometriosis**

Clinical examination and anamnesis (discussion with the patient) often lead towards the correct diagnosis. Ultrasound examination and the MRI exam (with special protocol) can give important information about the degree of infiltration of the neighbouring organs. The most common infiltrated extra-genital organs are rectum, sigmoid colon, bladder, pelvic ureters, and the small intestine.

Other investigations that can give preoperative information are CT scan, urography and cystoscopy examination. They are very helpful in deciding the type of intervention so that the patient can be informed about possible surgical interventions (intestinal resections, bladder resection, etc.). Also, depending on the type of intervention, the patient can be adequately informed about possible postoperative complications.

**Note:** Endometriosis is not always visible on scans. The possibility of endometriosis should not be excluded if CT, MRI and ultrasounds show no endometriosis.
The CA-125 marker, so commonly associated with the disease in the past, has a limited role. It can be increased when the lesions are active - endometriotic cyst, but it often has normal values in deep lesions - endometriotic nodules.

Endometriosis is commonly associated with chronic pelvic pain and infertility. Despite some specific symptoms, the diagnosis of endometriosis is often delayed. Dr Mitroi says that when a patient presents to a specialist doctor with pelvic pain, and pain during menstruation, endometriosis should be considered as a cause.

This should be considered as a primary diagnosis, not the last one, the way it often happens. As a result, the diagnosis is delayed, and the disease will become more complex, infiltrating the pelvic organs. It can take up to 7 years or more from the onset of the symptoms until the final diagnosis is made.

Most patients with endometriosis will experience/report the onset of the symptoms during adolescence. A study done on 261 patients in Norway to find out the time difference between the start of pelvic pain symptoms and the final diagnosis, the results showed an average delay of 6.7 years and a medium delay of 5 years. The delay in diagnosis is a global issue. Barriers in diagnosis include high costs, selection bias, doctors’ experiences and abilities to recognise the disease, different presentation of the symptoms, etc.

Methods of diagnosis

The diagnosis of suspicion of endometriosis is based on cyclical pain; sometimes, patients do not have intense pain, but the clinical/ultrasound examination reveals the presence of deep lesions or ovarian endometriomas. In general, patients present to a doctor for two reasons: unbearable pelvic pain and infertility.

When a patient complains of chronic pelvic pain, cyclic (severe dysmenorrhea) the first problem to think about should be endometriosis. However, there are severe pelvic endometriosis patients with minimal pain, the main problem being intestinal transit disorders (constipation/diarrhoea), and sometimes the main symptoms are urinary disorders. What is important to remember is that regardless of the location of the pain, the menstrual character should play an important role in the diagnosis.

The European Society of Human Reproduction Embryology clinical practice guidelines of women with endometriosis published in 2013, states that endometriosis diagnosis is corroborated by the patient history, symptoms and signs, physical examination, imaging techniques, and finally proven by histology after laparoscopy.

Patient history, pelvic exam and imaging are methods of a presumptive diagnosis. Other European guidelines regarding the management and diagnosis of endometriosis are recommending that the possibility of endometriosis should not be excluded if the imaging tests are normal.
Anamnesis

The evaluation of the patient should start with a medical history discussion. This is an essential primary step in establishing the cause of the symptoms. By obtaining patient history about symptoms, and previous medical investigations, a presumptive diagnosis can be made. Based on the information collected, further investigations can be recommended if the diagnosis is not clear enough or to help with the treatment method.

Physical examination

When doing a pelvic exam, the doctor feels for any abnormalities and mobility of the pelvic organs. The bimanual exam consists of two fingers inserted into the vagina to evaluate the cervix, uterus and adnexa while pressing on the lower abdomen with the other hand. The exam can evidentiate pelvic masses, rectovaginal and uterosacral nodules, tenderness of the uterus, adhesions or frozen pelvis, and adnexal masses.

Imaging

Noninvasive methods\(^40\) of diagnosis such as MRI, abdominal and transvaginal scans can be useful in the diagnosis of retroperitoneal endometriosis and deep infiltrating lesions, however, they have limited utility in diagnosing adhesions, peritoneal and superficial lesions, due to the limited resolution.

Abdominal ultrasound can diagnose ovarian cysts while the transvaginal scan can help diagnose endometrioma\(^41\) and deep nodules. MRI\(^42\) is useful for assessing the extension of the disease, for planning a more appropriate surgical approach, and to have all the necessary specialists. Superficial lesions less than 5mm are often not visible on MRI either, as they are tiny or flat (no mass).

MRI can visualise endometriosis lesion on the bladder, and it can also determine how much the lesion/nodule is infiltrating the wall of the intestines, the distance from the anus and the length of the affected area.

Laparoscopy

History and physical findings are a strong suspicion of endometriosis; however, the correct diagnosis\(^43\) requires surgery with histological verification of endometrial glands and/or stroma. Considered the gold standard in the proper diagnosis for endometriosis, laparoscopy is the most used method at the moment.

The ESHRE\(^44,45\) guide for clinicians and patients for the management of endometriosis, states that laparoscopy is the final and correct diagnosis. In the guide is noted that diagnosis during laparoscopy is dependent on the ability of the surgeon to recognise the disease in all its different appearances.

The following organisations consider laparoscopy as the correct diagnosis method for endometriosis: American College of Obstetrician and Gynaecologists\(^48\), (UK) National Institute for Health and Care Excellence\(^39\), Royal College of Obstetricians and Gynaecologists\(^46\), National German Guidelines\(^47\), France, CNGOF/HAS\(^49\).
Endometriosis from A to Z

Biomarkers/lab tests

The lab tests have very little or no role in the likely endometriosis diagnosis. The most known marker is CA125, and unfortunately, it has neither sensitivity nor specificity in the diagnosis of endometriosis.

Why such a long delay in diagnosis?

As a worldwide issue, the answers to this question vary. Dr John Lue, an author of the most recent practice bulletin on endometriosis from the American College of Obstetricians and Gynaecologists, says that the main challenge in diagnosis is the presentation of the disease that mimics other causes of chronic pelvic pain.

A study done in England concluded that the delay occurs at both individual and medical level. Symptoms are normalized by both patients and doctors, symptoms are suppressed through hormones, long or delay in referring the patient to an endometriosis specialist, doctors not recognizing endometriosis as a cause of the pain, women being embarrassed to admit the severity of their pain during menstruation, are some of the most encountered reasons in the diagnosis delay.

A study done in the USA found that the delay is much shorter in patients who presented with infertility than the ones who presented with pelvic pain.

Endometriosis categories

In the early 1960s, when laparoscopy was introduced, endometriosis was divided into three different clinical presentations: peritoneal, deep adenomyotic and ovarian cysts. Dr Donnez J and his colleague, Prof Nisolle noted that there are similarities between the red peritoneal lesions and eutopic endometrium, suggesting that these lesions are the first stage of early implantation of endometrial glands and stroma. The study concluded that superficial peritoneal, ovarian and rectovaginal lesions are separate entities with different pathogenesis.

Superficial peritoneal endometriosis

The peritoneum is a thin membrane that covers the organs in the abdomen and pelvic cavity. Superficial lesions are typically located on the pelvic organs or the peritoneum. Dr Redwine noted that at first the lesions are colourless or clear and in time they may become what is the most known appearance of endometriosis tissues, blue-black colour, known as powder burn or cigarette burn.

Allen and Masters have described a defect in the pelvic peritoneum, known as a window where endometriosis can be found. A study done by Chatman Dl on 635 cases of laparoscopy for primarily pelvic pain, 68% had associated endometriosis, suggesting that the defect might be related to endometriosis, with the disease either attacking an altered peritoneum or causing scars to the peritoneum.

Endometriomas cysts

Endometriomas are dark, dense filled fluid cysts, also known as chocolate cysts. They are most common in the ovaries and vary in size. They are associated with deep infiltrating endometriosis and affects 17-44% of patients with endometriosis. The cause of endometrioma is not known, but there are some theories; invagination of the ovarian cortex with endometriosis (pseudocyst), is one of them.
Deep infiltrating endometriosis

When endometriosis tissues are found deep within a tissue or organ, deep infiltrating endometriosis occurs. Although considered to be rare, deep infiltrating endometriosis is quite common. These lesions can be found in the rectovaginal septum, cul-de-sac, between the bladder and the uterus, on the uterosacral ligaments and in other extraperitoneal pelvic sites. Deep endometriosis presents as lesions/nodules larger than 5mm and is commonly associated with adhesions, dysmenorrhea, dyspareunia, pelvic pain and infertility.

Philippe Koninckx et al., have classified the deep infiltrating lesions in three types:

- **Type I** lesions are conically shaped rectovaginal septum nodules and are located between the posterior and anterior walls of the vaginal mucosa and rectal muscularis, respectively.
- **Type II** lesions are deeply located and form from the posterior fornix to the rectovaginal region. They are typically covered by extensive adhesions causing retraction.
- **Type III** lesions are composed of spherical nodules. The largest dimension of these lesions is located under the peritoneal fold of the rectouterine pouch of Douglas.

Histopathology

Under a microscope, if a tissue outside the uterus has endometrial stroma and epithelium present along with glands, it is defined as endometriosis. The gland and stroma have similar features to the tissue lining the uterus. While glands do not contribute to the growth of the disease, they secrete chemicals that can trigger inflammation and irritate the surrounding tissues/area and can cause scarring.

The characteristics of endometriosis lesions are quite varied both during surgery and under a microscope. Superficial and deep endometriosis lesions look different under the microscope. Deep endometriosis lesions are surrounded by scar tissue (muscle tissue changed into fibrotic tissue), so individual glands cannot be seen. The pathology report will describe muscular and/or fibro conjunctive tissues with endometrial type glands next to stroma or surrounded by stroma.

Location of endometriosis

Endometriosis is not limited to the pelvic region only; it can be located in different parts of the body. After Sampson had published his chocolate cysts paper in 1921, ovaries were considered and are still considered the most common site for endometriosis. Further research established that the ovaries are the 7th and 9th as places where endometriosis is most commonly found.

In his final version of his theory in 1927, he mentioned that the statement made in his initial version that the ovary is the primary if not the only source of peritoneal implantations, was because he only saw a few peritoneal lesions without endometrial tissues in the ovary.

In 1940, Sampson mentioned that blood with bits of Mullerian mucosa is escaping during menstruation through the fallopian tubes into the peritoneal cavity. These tissues under favourable conditions will implant on any structure and are most frequently found in close proximity to the distal ends of the tubes (ovaries, posterior surface of the uterus, the broad ligaments, the bottom of the cul-de-sac).
Dr David Redwine, wanting to know if Sampson’s theory is correct, decided to do a map of the pelvic cavity with the affected parts. He also wanted to see, if, based on Sampson’s theory, the older is the patient, the more endometriosis is found. He divided the pelvis into anatomic regions and based on surgery findings; he added a mark in the area where endometriosis was found.

The most common sites where endometriosis is found based on a study done on 132 patients age 16-52 are the cul-de-sac, broad ligaments, uterosacral ligaments, bladder, left ovary, fundus, sigmoid, right ovary, tubes, round ligaments. Endometriosis was also found on the exterior of the uterus, appendix, peritoneum, ileum, rectum, the torus uterinus and posterior fornix, peritoneum packets.

Less common areas where endometriosis can also grow are blood vessels, the cervix, diaphragm, lungs, nerves, ureters, vagina, and inside of caesarean or other surgical scars. In very rare cases, endometriosis can even invade other vital organs and structures such as the eyes, bone, kidneys, liver, pancreas, brain, heart, skin and nasal cavity.

**Colours and appearance of endometriosis**

Endometriosis presents as a variety of colour manifestations, mostly nonblack, and easily missed during surgery unless a meticulous inspection is done to identify small or nonhemorrhagic lesions. The diagnosis during laparoscopy is dependent on the ability of the surgeon to recognise the peritoneal disease in all its different appearances (ESHRE, Sep 2013). Therefore, if the surgeon is not familiar with the visual appearance and the places where endometriosis occurs, it will result in misdiagnosis and/or partial treatment, especially in cases of deep endometriosis where the lesions can hide beneath peritoneal surfaces/pockets and adhesions.

Starting with 1980 when researchers have begun to write about the subtle manifestation of the disease, the most common sign of the disease has become the least common. Although the subtle manifestation of endometriosis can be recognised during surgery, there are still lots of surgeons who have not been trained to identify atypical, subtle, non-hemorrhagic forms of the disease.

Based on the embryonic origin theory, the tracts which are colourless at the beginning and are laid down during organogenesis, they either contain rests of actual endometriosis or, with rising of estrogen levels during puberty, these tracts may undergo metaplasia. Due to an unknown substance secreted by the glands, that irritates the tissues and causes pain, the healing process results in angiogenesis, neovascularity, and overlying fibrosis.

The colourless or clear lesions may become reddish, then yellow or whitish due to fibrosis, then blackish when trapped blood degenerates. Some patients can have superficial colourless disease forever.

The substance secreted by the glands is causing bleeding to the nearby blood vessels resulting in subtle fibrosis of the peritoneum. In time, more fibrosis and new blood vessels can form obscuring the peritoneal endometriosis lesions. In stages 3-4, the disease can be identified due to the distorted anatomy caused by adhesions, while in stage 1-2, the disease can be identified based on the colour of the lesions.
Types of endometriosis lesions

In his articles about endometriosis, Sampson described chocolate cysts and endometriosis tissues as "red, purple and blueberry raspberry" due to recent or old haemorrhage. This description has led to believe that all endometriosis lesions are, therefore, pigmented, and the typical endometriosis lesions are a dark colour.

The embryonic origin theory shows that lesions are at first colourless and in time they become pigmented and typical dark colour lesions are predominant in older patients. A few biopsy studies have demonstrated the subtle and non-pigmented appearance of endometriosis.

In a study done on 137 nonpigmented specimens, 73 showed endometrial like glands and stroma, 12 showed only stroma and 10 had no histologic features of endometriosis. Six patients had developed pigmented endometriosis within 6-24 months after first surgery. The non-pigmented lesions were white opacified peritoneum, red flame-like, and glandular lesions.

Another study done in 1980 on adolescents who underwent laparoscopic surgery at Boston Children’s Hospital, showed that endometriosis was found in 66 out of 140 patients and 13 patients had unrecognized but morphologically confirmed disease.

Studies have shown that a large number of patients have multiple types of disease while some have only subtle types; therefore, in these patients, misdiagnosis and mistreatment is highly likely to happen. A study done on 133 patients who underwent laparoscopic surgery with lesions sent for biopsy showed that endometriosis is not limited to a single colour. 75% of the lesions have a mixture of colours and 283 of 553 lesions tested, were subtle. The most common area histologically confirmed was cul-de-sac.

From the subtle ones, 58% contained histologically confirmed endometriosis, and in 30 patients, the only lesions identified were red or white with 18 of them having confirmed endometriosis. The authors concluded that 16% of the subjects would have been excluded if the diagnosis of endometriosis would have been based solely on the appearance of these lesions. Dr Redwine found that the black lesions were outnumbered by lesions of other colours. 82 patients had black lesions, and 91 had different colours.

In the Laparoscopic Appearance of Endometriosis, the authors concluded that endometriosis can change frequently or easily (protean) which can be confused with other pelvic pathologies. The identifiable endometriosis lesions included puckered black lesions (typical), white scars, red polyloid lesions, clear papules, brown vesicles, adhesions, yellow-brown patches, yellow lesions, deep nodules and peritoneal pockets.

The role of imaging in endometriosis

Endometriosis can be diagnosed after the biopsy of the lesions following laparoscopic surgery. A presumptive diagnosis can be made based on imaging findings, which can be useful in the differential diagnostic process, in assessing the involvement of the internal organs before surgery, in planning the operation and informing the patient.

The radiologic examination can be used to find out the location, the size and the number of nodules as well as to check for endometriosis foci in pelvic organs that are often affected by the disease. As mentioned in the diagnosis part, imaging can only detect deep endometriosis, lesions smaller than 5mm can’t be seen on the imaging.
Pelvic MRI with gel instillation

The pelvic MRI for endometriosis in addition to helping the surgeon to organise the team and to inform the patient about the possibility of organ loss/resection, it can also be used for disease staging, using the Enzian score. However, to be able to get a clear image of the affected organs, the MRI for endometriosis should be done with vaginal and rectal gel instillation.

The T1- and T2-weighted images are used to assess the uterine and vaginal cavity and to evaluate the rectum. Once the walls of these structures are distended, by using different types of water-soluble rectal and vaginal gels such as the ultrasound gel which has better distention stability and high contrast, the types, size and locations of the endometriosis tissues can be easily evaluated. Based on the authors' experience and the experience of the Wellborn Endometriosis Centre Medical team, distention of the vagina using gel is increasing detection of small lesions, while the rectal distension of the rectosigmoid colon allows clear delineation of the bowel lumen and the wall.

Although there is no international consensus regarding prior patient preparation, some clinics/radiologists doing the MRI with the vaginal and rectal distention for endometriosis might require prior bowel cleansing and/or fasting for a few hours before the MRI. Also, an antispasmodic agent is generally administered intravenously or intramuscularly, to slow down the intestines. The amount of gel used for vaginal and rectal filling varies based on the Tesla used, and the doctor’s knowledge and experience with endometriosis and can be from 50ml to 100ml for vagina and 10-150ml for the rectum.

MRI by Dr Livia Stanciulescu

The examination of MRI in endometriosis is dedicated mainly to the preoperative evaluation of deep endometriosis and complements the clinical and ultrasound examinations. A qualitative examination should provide the surgeon with a more detailed map of the lesions, and begins with good communication between the gynaecologist and the imaging doctor and continues with a more detailed discussion between the imaging doctor and the patient.

Knowing the patient's symptoms is of real use in guiding the examination protocol. Intravaginal and intrarectal gel instillation relax the cavities, thus leading to better visualisation of the walls and possible endometriosis nodules, with the possibility of evaluating the depth of the infiltration zone. By contrast, offered by the gel, a better delineation of the peritoneal recesses (recto-vaginal and bladder-vaginal recession) is obtained. Also, the presence of gel reduces peristaltic artefacts.

The MRI ovarian endometriomas appearance is that of the cyst in the hypersignal in the T1 weight (bright white) and the hyposignal in the T2 weight (different shades of grey, determined by the presence of haemoglobin degradation products, in various stages).

Endometriotic nodules appear as a mass with infiltrative characters, spiked contour, with very low signal in T2 weighting, frequently with hyperintense cystic inclusions in T1 weighting, causing adhesions and retracted effect on the adjacent structures. The recto-vaginal septum requires special attention; lesions at this level are frequently underdiagnosed.
For intestinal endometriosis, the role of the MRI exam is to preoperatively evaluate the depth of endometriotic infiltration, nodules that affect the muscularis propria and have an indication for resection. The distorted appearance of the digestive wall is a good indicator for infiltration of the muscular layer. The degree of stenosis is approximately appreciated, the rectal ampulla is a cavity organ whose maximum degree of repletion cannot be reproduced only with the help of gel instillation. An almost circumferential arrangement of the lesion is a criteria for a high degree of stenosis.

For urinary tract endometriosis the MRI examination, apart from detection, aims to assess the depth of endometriotic infiltration. If the pelvic ureters appear dilated, it should be mentioned in the written report, which may be a consequence of direct endometriotic infiltration or pelvic adhesion syndrome. The uterus-bladder recess is another frequently missed localisation, often due to a maximal replenishment of the bladder or an excessive anteversion of the uterus, which may mask any lesions.

Uterine adenomyosis is a pathology commonly associated with endometriosis, and it may also accompany the presence of leiomyomas, hyperplasia or endometrial polyps. It has an MRI expression a thickening above the accepted standard limit (12 mm) of the myo-endometrial junction, frequently with included microcystic glandular dilations and irregular contour. It may have a diffuse or focal nodular appearance, sometimes polypoid, procident in the uterine cavity. The junctional area is influenced by the period of the menstrual cycle. It increases considerably in thickness during the menstrual period. To avoid a false-positive diagnosis, the time indicated for examination is the late proliferative phase.

**Colonoscopy**

A colonoscopy is considered to be an invasive technique, and it has a minimal role in the diagnosis of bowel endometriosis. A colonoscopy uses a telescope to examine the inside of the intestines for any abnormalities and obstructions. The intestines have four layers, and endometriosis affects from the outer to the inner layers. Nodules or endometriosis implants rarely penetrates through the bowel walls to be seen during a colonoscopy.

A study done by Marco Milone et al., to evaluate the accuracy of colonoscopy in the diagnostic work-up of bowel endometriosis concluded that as an invasive procedure, a colonoscopy should not be routinely performed in the diagnostic work-up of bowel endometriosis. From the 76 patients with surgically confirmed bowel endometriosis who underwent colonoscopies before surgery, only 6 of them had intestinal endometriosis detected during colonoscopy. The cases of intestinal endometriosis detected were two mucosal, three submucosal and one serosa involvement.

**Endometriosis staging**

Classification of the endometriosis stages has been done mainly to predict fertility outcome and is based on the lesions appearance, adhesions, anatomic location of the disease and pelvic adhesions. Endometriosis is classified in 4 stages, mild, minimal, moderate and severe. In 2017, the World Endometriosis Society published an international consensus on the classification of endometriosis.
The WES concluded that for all patients who are undergoing surgery the r-ASRM score and stage to be used, for patients with deep endometriosis the Enzian score to be used, and for the staging of fertility, the EFI score to be used and documented in the medical reports.

Revised American Society for Reproductive Medicine classification

The r-ASRM current classification of endometriosis stages 1 to 4 is the most used and accepted staging system. The classification is done using point scores depending on location, extent and depth of endometriosis implants; the presence and severity of adhesions, and the presence and size of ovarian endometriomas. The staging of endometriosis does not always correlate with the severity of symptoms.
Enzian score

The Enzian score is a new tool for the classification of deep infiltrating endometriosis with the system focusing primarily on the retroperitoneal part of the severe endometriosis. The system classifies the disease by disease on the organs or other locations such as intestinal (FI), uterine (FA), intrinsic ureteral (FU), or bladder disease (FB), or disease at other locations (FO).

The Enzian score is made of capital letters, numbers and small letters. The F stands for external disease, E is used in cases of a tumour of endometriosis, the number is for the size of the lesion, the small letters are for the location or the affected compartment, and if they are double, signify bilateral disease.

Compartment a describes the disease affecting the Pouch of Douglas, the vagina including the spread of the disease in the entire vagina, the posterior wall of the uterus as well as invasion of the uterus. Compartment b includes the uterosacral ligaments to the pelvic wall. Compartment c describes lesions of the bowel.
Adhesions

Endometriosis is one of the most common causes of adhesions unrelated to surgeries. Usually, tissues and organs in the body are prevented from sticking together by the slippery surfaces. When the tissues are irritated, the body repair mechanism responds by creating scar tissues, known as adhesions.

Endometriosis tissues cause inflammation to nearby area/organs, and in the healing process, the affected area can become stuck to another, creating a band of scar tissues. Symptoms caused by adhesions are pain, pain when walking, sitting or lying in certain positions, rectal bleeding, constipation, cramps, infertility, bowel obstruction, urinary issues.

The adhesions or scar tissues are a normal part of the healing process and vary in appearance from thin, transparent, and flimsy to dense, thick and opaque.

The pelvis and the abdomen are among the most common locations where adhesions can occur. Both cases of adhesions are a common complication of infection, surgery (C-section, hysterectomy) or trauma. The pelvic adhesions may involve any organ within the pelvis, and in cases where adhesions are affecting the fallopian tubes, fertility might be affected.

Adhesions can cause their own type of pain, and the pain is different from endometriosis pain. The pain is usually constant in intensity during the menstrual cycle. It can, however, increase in severity if the adhesions are around an ovary with a cyst. The patients are describing the adhesions pain as a tight, pulling, and stiff that is more noticeable during certain movements.
When adhesions are around organs, the patients are often describing feeling the organ as being “trapped.” In some cases, pelvic nerves are also involved, causing neuropathic pain (shooting or burning pain). Adhesions involving the uterus or the vagina might cause pain during intercourse. Studies show that almost 50% of patients who undergo pelvic or abdominal surgery will develop adhesions. When the symptoms caused by adhesions are affecting the quality of life or fertility, surgery is indicated. The procedure is called adhesiolysis, meaning the disintegration of adhesions.

Frozen pelvis

Frozen pelvis is one of the most advanced forms of endometriosis. The internal organs in the pelvic cavity should be flexible and separated from each other. With frozen pelvis, either partial or full, due to adhesions or internal scars, organs lose their mobility and are attached together.

A frozen pelvis is caused by surgery, infection, endometriosis, adenomyosis, and fibroids. A frozen pelvis can be felt during a pelvic examination and a transvaginal scan, as the organs have little or no mobility at all. The physical examination can be very painful due to the lack of flexibility of the organs, also due to the altered anatomy, usual functions such as bowel movements can be quite painful.

Kissing ovaries

The kissing ovaries sign seen on ultrasounds is associated with the presence of moderate to severe endometriosis. Due to the pelvic adhesions caused by endometriosis that forms between the ovaries, the ovaries are pulled towards each other in close proximity, or they touch each other, behind or above the uterus. Endometriomas, especially the large ones, can also make the ovaries stick to each other. The endometriomas lead to adhesions and adjacent para-ovarian scarring.

Pain management

As it has been said, endometriosis affects patients in different ways, and not all of them will experience the same symptoms or the same pain intensity, and as such, there is no treatment plan guaranteed to work. Some will find relief on a day to day basis with lifestyle changes such as healthy eating, physical activities, and/or home remedies, essential oils, Chinese medicine, over the counter and prescription medications.

The primary recommended method of treating mild to moderate endometriosis pain is a nonsteroidal anti-inflammatory drug (NSAID). If they do not work, then stronger painkillers might be prescribed. In addition to analgesics, contraceptive pills are also recommended. Heat pad, hot water bottle, TENS machines are also used to relieve the pain.

Medical therapies

The retrograde menstruation theory proposes that endometriosis is depended on the patient’s cyclic production of menstrual cycle hormones. Therefore, this theory suggests that by suppressing ovulation, it might slow down the endometrial tissue growth and reduce the likelihood of future implants. Studies have shown that endometriosis tissues have different supplies of estrogen, its own supply due to the intrinsic aromatase activity, the ovaries and the peripheral fat.
The assumption has been made that, if the symptoms of pain and infertility are responding to hormone therapy, then they are caused by endometriosis. Based on Sampon’s theory, the use of supplemental hormones to stop the ovarian function, is considered an effective method in reducing or eliminating the disease. Not all symptoms are endometriosis symptoms; in fact, endometriosis is not the only condition causing pain and infertility; uterine fibroids, adenomyosis, infections can cause pain and infertility. Amenorrhea will always improve painful menstruation symptoms.

When recommending the use of suppressive medications, it is most important to understand the actual effect of these agents and what they can do. The GnRH drugs work on the pituitary gland, an endocrine (hormone-producing) gland that sits just beneath the base of the brain. The pituitary gland takes the messages from the brain and uses them to produce hormones. Gonadotropins (LH and FSH) are secreted by the anterior pituitary gland. When the gland no longer produces the LH and FSH, the ovarian functions stop, and for the duration of the therapy, symptoms are quietened down.

Hormonal treatments, like almost any known drug, generally have severe side effects that are difficult to tolerate by many patients. Gn-RH analogues (Diphereline, Zoladex, Lupron, Orilissa) induce menopause, with all its adverse effects. Moreover, in young patients, these effects are felt more aggressive than in the patients who spontaneously enter menopause. The loss of ‘bone tissue’ from this period (6-9 months) is very difficult to recover by the patient; sometimes, it can last for years.

As of now, no studies have shown that hormones cure the disease. There is enough evidence showing that symptoms return once the medication is stopped. A study done at the Royal Free Hospital in London showed that patients with endometriosis treated with GnRH are highly likely to suffer a recurrence of their disease, particularly if their condition is severe at the outset. Fifth-year recurrence rates were 36.9% for minimal disease and 74.4% for severe disease.

This review shows that there is no evidence of benefit in the use of ovulation suppression in subfertile patients with endometriosis who wish to conceive, and due to the adverse effects commonly associated with these treatments, ovulation suppression cannot be recommended as a standard therapy for endometriosis-associated infertility.

Medications currently recommended include gonadotropin-releasing hormone (GnRH) agonists, progestins, oral contraceptive pills, and androgens. All these treatments have similar clinical efficacy in terms of reduction in pain-related symptoms and duration of relief.

Hormonal contraceptives

When using a hormonal contraceptive, periods are lighter and shorter. Continuous administration of combined oral contraceptive pills helps avoid any menstruation and associated pain. There are two types of hormonal pills, the combined pill which contains estrogen and progestin and the mini-pill, which is progestin-only. A study done by Guzik et al., showed that both Lupron and continuous oral contraceptives appear to be equally effective in the treatment of endometriosis-associated pelvic pain. The hormonal contraceptives are used to mimic the presumed beneficial effects of pregnancy, based on assumptions that pregnancy cures the disease due to the decreased pain during pregnancy and breastfeeding.
During the menstrual cycle, the endometrium thickness range in size based on the phase of the cycle, and during ovulation the size goes up. When ovulation is suppressed either by pregnancy or menopause, the endometrium is regressing to normal
during pregnancy, the eutopic endometrial tissue is transformed into decidua, which later goes through necrosis and shrinkage. The induction of pseudopregnancy (continuous estrogen and progestin therapy) attempts to mimic the hormonal profile, and thus the endometrial changes that are seen in pregnancy.

Progestin therapy

Progestin, also known as gestogens or progestogens, is a synthetic form of progesterone causing decidualization and atrophy of the endometrium. It is available as intrauterine devices (Mirena), implants, injection (Depo-Provera) or pills. Progestin has been used since 1953 to treat endometriosis by Meigs, who after suggesting that early marriage and early pregnancy can be used as prevention for endometriosis, as a substitute he induced a state of pseudopregnancy in 12 of his patients by combining estrogen and two new progestin for seven months.

Progestational agents are better tolerated, however, estrogen is still required for the decidua necrosis seen in pregnancy and in cases where breakthrough bleeding occurs, a low dose of estrogen might be necessary to stabilise the endometrium. After withdrawing of the progestin injection, Depo-Provera, there is a prolonged delay in menstruation resumption; therefore, this method has a little indication in patients wishing to conceive soon after the therapy.

There is little research regarding the effectiveness of progestin agents in the endometriosis treatment. Some studies have shown that progestin agents are equally effective when taken continuously as other hormonal drugs, and they have fewer side effects.

Visanne

The active substance in Visanne is Dienogest, a selective progestin that has been investigated in a clinical trial programme for the treatment of endometriosis, and has the same beneficial effects on endometriosis symptoms as Lupron. A systematic review done by Andre Mde et al., to compare Visanne with other medical therapies, no studies were found comparing Visanne with first-line treatment, such as progestins and estrogen-progestogen combinations contraceptives, which are proved to be effective in the treatment of endometriosis symptoms, are less expensive, and also can be used for contraception. One study comparing Norethisterone with Visanne has found that Norethisterone is cheaper and is as effective as Visanne.

Visanne is a 19-nortestosterone derivative and when given continuously, induces a hypoestrogenic, hypergestagenic local endocrine environment, causing a decidualization of endometrial tissue followed by the atrophy of endometriotic lesions. Based on clinical trials with a duration between 12 and 24 weeks done in Europe and Japan, Visanne has received approval as a monotherapy for the treatment of endometriosis in Europe, Japan, Australia, and Singapore.
Dienogest/Visanne has been investigated as a long-term treatment of endometriosis in two large trials performed in Europe and Japan, which included assessments of efficacy, changes in the quality of life, safety, and tolerability.

The duration of the studies was 65 weeks in Europe and 54 weeks in Japan during which adverse effects occurred in 16.1% of patients, including breast discomfort (4.2%), nausea (3.0%), and irritability (2.4%). Mild to moderate side effects occurred in 92.5% of cases.

This study looks at the long-term treatment of endometriosis with Visanne on 37 patients for 60 months. The study concluded that Visanne reduced the endometriosis pelvis associated pain with adverse effects, and 15 patients were investigated for laboratory measures of lipid and liver metabolism, hemostatic and hormonal parameters. Also, from the trials, it is not clear if Visanne affects bone mineral density.

Provera is an oral progestin, and Depo-Provera is a long-acting injection. The acting ingredient in both of them is medroxyprogesterone acetate. Studies have shown that Depo-Provera treats endometriosis pain with same the efficacy as Lupron but with fewer side effects, according to the manufacturer of the medication.

There are two versions of Depo-Provera injection, the original Depo-Provera which must be injected into the muscle and the Depo-SubQ Provera 104 Injection, which is a new version approved in 2005 by the FDA, can be injected under the skin and has 30% fewer hormones than the original one.

According to the manufacturer, the Depo-Provera stabilises the hormone levels, halts menstruation, which results in thinner, more compact endometrial tissue. This, in turn, stops the growth of endometrial implants, relieving endometriosis-associated pain. The randomised controlled trial studies have been done by the manufacturer, Pfizer.

The Depo-Provera comes with a black box safety warning regarding bone loss for long term use (more than two years). The injection will also delay the return of periods, for up to 18 months, and can cause irregular bleeding, termination of periods (amenorrhea) and weight gain.

Gonadotropin-releasing hormone therapy

The GnRH is a releasing hormone of the FSH, LH from the anterior pituitary gland, an endocrine gland that regulates several psychological processes such as stress and reproduction. In postmenopausal patients, the atrophy of the endometrium is caused by the reduced/stopped ovarian secretion, and since endometriosis is believed to be oestrogen depended, and that endometriosis lesions are same as the endometrium, medical menopause is recommended as a treatment method. This can be done by using GnRH agonists to suppress gonadotropin release from the anterior pituitary gland, which mimics the menopause.
Studies have shown that efficacy is limited mainly to pain suppression, and this can be achieved with other types of medication, which are less expensive and with fewer side effects. Also, many doctors recommend add-back medication such as a low dose of estrogen or progesterone to reduce the side effects.

There is an element of bias in the results for the use of GnRH since all the clinical trial studies have been done either directly by the manufacturer, or they sponsored the organisations which have done the studies. Also, some of the results have been faked and the information, especially the side effects withheld from patients and doctors. The efficacy reports of the GnRH looked at the response of the endometrium and the resolution of the dysmenorrhea during treatment, not at the resolution of endometriosis.

GnRH is used before and after surgery and in quite a lot of cases is used as a diagnostic method. If symptoms such as painful or heavy periods are resolved during the duration of the treatment then the patient is diagnosed with endometriosis and no other causes of pelvic pain that are estrogen-responsive such as fibroids or adenomyosis will be considered.

All the GnRH agonists are very similar chemically, but they come in different forms:
- three-monthly injection
- monthly injection
- daily injection
- nasal spray

**Buserelin** comes as a nasal spray and daily injection. The clinical studies done have not mentioned the adverse effects, and most of them have focused on the treatment of pelvic pain associated with endometriosis. One study done by Fedele L et al., (1993 FertSter) on 35 infertile patients with stage 1 and 2, showed that improvement of pain symptoms persisted in approximately half of the patients for 12 months after the treatment was finished. In one-fifth, though, symptoms associated with endometriosis showed a spontaneous remission.

**Zoladex** under the generic name of Goserelin is a monthly or three-monthly injection and is used in men to treat prostate cancer and in women to treat certain breast cancers and uterine disorders such as fibroids and endometriosis. A study done by Pier Luigi Venturini et al., (1990, FertSer) in Italy showed that Zoladex provides good suppression of ovarian estrogen production and a decrease in symptoms.

**Leuprorelin** comes as monthly and three monthly injections under the brand name of Lupron Depot, Prostap, Enantone, Lucrin Depot and Trenantone gyn, and it is prescribed regularly for endometriosis, fibroids and non-diagnosable pelvic pain. Lupron is also used to diagnose endometriosis based on the results of one study done on 52 patients with endometriosis-associated pain.

According to the study, the small to moderate changes in a variety of laboratory parameters were not clinically significant. Andrew Friedman, who was hired by the pharmaceutical company to do research studies on Lupron, had committed scientific misconduct and admitted to falsifying or fabricating 80 per cent of the data in two published studies on Lupron.

The clinical studies filed with the FDA on the drug effectiveness at reducing endometriosis-related pain showed that most patients still required pain meds while on Lupron and some have taken narcotics at the same time. In 50% of patients, the pain went back to the baseline level, three months after stopping taking the drug.
In 2009, Dr. David Redwine did an assessment for the FDA on the original study done by the Lupron manufacturer, telling that the original data had been falsified. The assessment was hidden by the pharmaceutical company with a court order. Other GnRH injections drugs prescribed to treat endometriosis are Decapeptyl, Diphereline and Gonapeptyl.

**Note:** At the AAGL conference in Canada, 2019, Dr. Redwine talked about the side effects of Lupron and other hormonal drugs based on in-house studies results, the FDA reports and other studies. Following his talk, Dr. Redwine has submitted a couple of factual medical documents that will hopefully make some changes. More info on his page, David Redwine.

Elagolix sold under the brand name Orilissa, is an oral GnRH receptor antagonist that inhibits endogenous GnRH and it was approved by the FDA in July 2018 for management of moderate-to-severe pain associated with endometriosis. The approval was done on two double-blind, placebo-controlled trials of 16 premenopausal patients. The efficacy has only been demonstrated in placebo-controlled explanatory trials.

During the trial, the subjects reported improvement in 3 types of pain considered to be endometriosis pain; pain with sex, pain in between periods and painful periods. The pain with sex symptom was reduced with a double dose of 200 mg daily. In the placebo group, 36% of patients reported reduced pain in between periods, compared to 50% and 55% in the Orilissa group. Subjects have also used analgesics during the trial, such as hydrocodone and codeine.

The adverse reactions related to the drug include mild to serious side effects such as anxiety, depression, joint pain, amenorrhea, nausea, bone density loss, liver problems and mood swings, including suicidal thoughts.

During the trial, one subject committed suicide, two days after a 31 day course.

In a medical review done by drugs.com, the healthcare professionals have been informed about the genitourinary, hepatic, metabolic, nervous system, cardiovascular, gastrointestinal, hypersensitivity, musculoskeletal and psychiatric adverse reactions classified as common and very common, with an incidence of 1-10%.

On the manufacturer's site, it is noted that Orilissa causes a decrease in bone mineral density, and complete recovery may not occur. The effectiveness and safety of Orilissa have not been established in patients younger than 18 years old.

**GnRH side effects**

Some side effects of GnRH are usual menopause symptoms such as hot flushes, mood changes, anxiety, vaginal dryness, headaches, dizziness, nervousness, irritability and sleeplessness, depression and other mood disorders. Other side effects are more severe such as pain & fibromyalgia, musculoskeletal & articular disorders, memory and psychotic disorders, autoimmune thyroiditis, blood sugar rise, difficulty breathing, chest pain, liver function abnormality, vision abnormality and others.

A Cochrane review found that at present, there is no information on the effect of GnRH treatment on the incidence of ectopic pregnancy, multiple pregnancies or complications arising for the patients or their offspring. A new review is currently in preparation.
Drugs such as Zoladex, Lupron, Diphereline, were originally developed for prostate cancer patients and at the moment are used to treat patients with endometriosis and fibroids. In an expert report prepared by Dr Redwine in a Lupron liability lawsuit, he noted that the state of menopause with Lupron is unnatural due to the artificial menopause induced by the drug and levels of FSH which are not elevated as they are in normal menopause.

In 1999, the FDA received adverse drug reports about Lupron from 4,228 women and 2,943 men, 325 of women required hospitalisation and 25 of them died. The original manufacturer, Takeda-Abbott Pharmaceuticals (TAP), had stated that the side effects are temporary and should stop six months after stopping the medication. Currently, there are tens of thousands of severe side effects reports and thousands of deaths.

A survey done by the Endometriosis Research Centre on patients who took Lupron showed that the side effects lasted longer than five years in some cases. The TAP researchers have submitted a report to the FDA about a third of the patients who were yet to show reversibility in bone mass, six months after stopping the drug.

A significant number of patients have suffered irreversible and permanent side effects and/or permanent severely disabling health problems. Lupron has substantial safety concerns as an antineoplastic agent, is harmful to both cancerous and non-cancerous cells. An expert report by Dr Gueriguan, a former medical officer for the FDA in a case of Lupron liability lawsuit, shows that cancer drugs such as Lupron can be highly toxic and stays in the bloodstream for a prolonged period of time.

TAP did not perform enough long-term studies to detect potential long-term and irreversible side effects of Lupron, and once the treatment is finished, endometriosis symptoms will come back. The administration instructions state that Lupron has no hazardous components; however, the National Institutes of Health and the Occupational Safety and Health Administration categorise Lupron as a "hazardous drug" and that healthcare workers should only handle Lupron when wearing protective gowns and gloves.

**Use of hormonal medication prior to and after surgery**

There are a few studies that compare the effects of hormonal medication on endometriosis tissues. A review done by researchers at the Cochrane Collaboration on the use of hormone therapy prior or after surgery, updated in 2017, shows that "there is no proof that taking hormone medication before or after endometriosis surgery improves the outcome of the treatment."

The opinions regarding the use of hormonal medication before surgery are divided. Some doctors recommend stopping the medication a couple of months before surgery, as lesions become invisible, therefore disease will be left behind. And other doctors, believe that lesions are modified and the GnRH may suppress the adjacent bleeding, which is a way of identifying the disease, resulting in "invisible" disease.

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1. Hormonesmatter/Lupron  
   FDable.com/Lupron  
   Lupron-What Does It Do To Women's Health?- National Women Health Network  
   Lupronvictimshub
Endometriosis from A to Z

Pregnancy effects on endometriosis

Many endometriosis patients all over the world are advised to become pregnant in order to manage their symptoms and cure the disease. Pregnancy, same as the medications that mimic pregnancy, may temporarily suppress the symptoms. Some patients have reported after giving birth that their symptoms have returned and are worse than before pregnancy. Some pregnant patients are still experiencing endometriosis symptoms.

Endometriosis affects fertility, therefore getting pregnant in some cases, can be difficult or impossible to achieve. The belief that pregnancy cures endometriosis had started more than a century ago. Olshausen and Amos are the first ones to describe the co-existence of endometriosis and pregnancy, in 1904 and 1905.

In Sampson’s study, some of the women who took part, have been pregnant, therefore, it was believed that pregnancy prevents endometriosis from forming. Meigs based on the higher frequency of endometriosis cysts in women who have not given birth stated that “is the author’s belief that avoidance of endometriosis through early marriage and frequent childbearing, is the most important method of prophylaxis”.

The effect of pregnancy on endometriosis—facts or fiction? article in the Human Reproduction Update concluded that based on the limited and poor-quality of evidence available, pregnancy does not seem to result in benefits for patients with endometriosis. While some lesions show regression, others remain stable or increase. Also, due to rare but severe complications, the few beneficial effects should be carefully balanced against potential harms. Moreover, patients should be advised not to discontinue periodic evaluations, and possibly medical treatment, after giving birth, in the conviction of having been cured by pregnancy itself.

Estrogen- phytoestrogens-xenoestrogens

Estrogens are a group of sex hormones that have an essential role in the sexual and reproductive development of women. They also play an important role in bone growth and maturation of bone in young people, and also have a role in the regulation of bone remodelling in adults. There are four types of estrogens:

• Estrone (E1), a weak hormone found in women after menopause;
• Estradiol (E2) is produced by the ovaries and is the strongest hormone, and it has many functions;
• Estriol (E3), the weakest of the estrogens; it can be found in significant amount during pregnancy;
• Estetrol (E4) a weak hormone that is detectable during pregnancy;

Studies have shown that endometriosis is estrogen-dependent and can also make its own estrogen. As described in the Mulleriosis theory, the tracts laid down during embryogenesis can undergo metaplasia with the rising of oestrogen levels. Although studies have shown that endometriosis lesions have both estrogen and progesterone receptors, the medical treatment focuses mainly on suppressing/reducing ovarian estrogen production.
In a majority of endometriosis patients, with hormonal imbalance, estrogen is the dominant hormone, and it aggravates the inflammation, growth and the symptoms associated with endometriosis\textsuperscript{199}. Endometriosis tissues are associated or believed to be similar/identical to the eutopic endometrium; however, estrogen receptor levels in endometriosis are >100 times higher than those in endometrial tissue\textsuperscript{199}.

Due to the progestin therapy causing the endometrium to become atrophic, the same treatment method is used to treat endometriosis tissues; however, this does not stop the endometriosis tissues from growing. Studies have shown that endometrium is different than endometriosis in terms of production of estrogen and clinical response to progestin, which seems to offer only temporary relief of endometriosis-associated pelvic pain\textsuperscript{200}.

**Phytoestrogens** a natural estrogen are plant compounds that can mimic estrogen and can be found in a large variety of foods, including the ones recommended in the endometriosis diet\textsuperscript{202} and plasma and urine\textsuperscript{203}. Phytoestrogens are considered to have weak estrogenic effects; they can interact with estrogen hormones and should be consumed in moderation.

**Soy** is high in isoflavones (genistein and daidzein) that can increase estrogen levels in humans and is found in different food products. Soy contains phytic acid in high quantity, a natural substance that impairs the absorption of iron, zinc and calcium, and it also contains a high level of aluminium.

**Xenoestrogens** are chemicals that mimic bad estrogen; it may act like estrogen and could interfere with the actions of endogenous estrogens\textsuperscript{204}. Xenoestrogens are found in plastic, chemical products, pesticides, parabens, water systems, commercial food products, children’ toys, microwave.
Chapter 2 Endometriosis by sub-type and location

Based on the location of the endometriotic tissues, endometriosis can be divided by sub-type/location such as cystic ovarian endometriosis, gastrointestinal endometriosis, urinary tract endometriosis, thoracic and diaphragm endometriosis, abdominal and subcutaneous endometriosis, rectovaginal and uterosacral ligaments endometriosis, sciatic nerve endometriosis and endometriosis in places considered a rare entity statistically.

Ovarian endometriosis

Based on Sampson’s publication in 1921, the ovaries are considered to be the most common site to be affected by endometriosis. Further authors have found that this is not the case, and Dr Redwine estimated that the ovaries are the 7th and 9th most common places where endometriosis can be found. Ovarian endometriomas, also known as chocolate cysts, can occur unilaterally or bilaterally. They contain dark brown fluid and are often accompanied by disease elsewhere. The chocolate cysts can affect ovarian function, and in some cases, they can prevent pregnancy.

Endometrioma can range from a few mm to 10-15 cm in size. Levent Yasar et al., have reported a case of a huge ovarian endometrioma in a 33 year old patient. The cyst was 5 kg in weight, 26 × 18 × 17 cm in dimension, and contained 3,250 ml of chocolate brown fluid. The medical team did not suspect the endometrioma preoperatively.

The diagnosis was confirmed by postoperative pathologic examination. Due to the adhesions that form, endometriomas are often adherent to the nearby structures (the peritoneum, fallopian tubes, bowel). The largest endometrioma cyst reported was found in a 51 year old woman, and it weighed 64kg, Sakpal et al.

Symptoms

Endometrioma cysts can cause chronic pelvic pain, painful ovulation, lower back, hip and leg pain, pain in the groin area, painful sex, (sub)infertility, painful menstruation. If the ovarian cortex and adhesions are stretched, then pain will occur, pain which radiates throughout the lower pelvic region. In some cases, endometriomas are asymptomatic and if the patient is suffering from other conditions that are causing similar symptoms it is difficult to establish if the endometrioma is responsible for the symptoms. Endometrioma cysts have a 1% risk of malignant transformation.

Diagnosis

Endometrioma cysts can be found during a pelvic examination. Imaging tests can identify cysts of any size and may also suggest the type if they are done by an experienced radiologist or gynaecologist. Endometrioma is often mistaken for haemorrhaging cyst due to similar-looking features. Histopathological confirmation provides the most accurate diagnosis.
**Treatment**

When it comes to the treatment of endometriomas, opinions are divided. Some will argue that surgery is severely affecting ovarian reserve, and as such, medical therapy should be used. Others will use a combination of medical therapy and surgery or surgery only. Izabela Nowak-Psiorz et al., noted that surgical treatment is the primary therapeutic option and cysts larger than 4 cm in diameter, should be treated surgically due to the risk of their rupture or torsion.

The surgical approach to treat endometriomas also remains controversial. Currently, the surgical procedures for the treatment of ovarian endometriomas are either excision of the cyst capsule or drainage and ablation of the cyst wall. During excision, a small amount of healthy tissue is often removed alongside the cyst. Conservative surgery (vaporisation or coagulation) has been suggested as a preferred treatment method. This method has a recurrence rate of 80-100%.

A review done by Hart Jr et al., comparing excisional surgery versus ablative surgery for ovarian endometrioma, concluded that excisional surgery for endometrioma provides for a more favourable outcome than drainage and ablation with regards to the recurrence of symptoms and an endometrioma.

This particular study shows that ovarian reserve evaluated with antral follicle is not reduced after surgical treatment of an endometrioma. This review done on eight meta-analysis studies suggests that excision of endometriomas harms ovarian reserve as evidenced by a significant postoperative fall in circulating AMH. Two one year follow up AMH in patients with cystectomy showed that the decrease in the serum AMH levels caused by cystectomy can be recovered. Other studies have concluded that surgery has a temporary detrimental effect on the ovarian reserve.

**Gastrointestinal endometriosis**

Intestinal endometriosis produces disturbances in the intestinal transit manifested by constipation, colon pain or lower abdominal pain as well as bloating. Bowel endometriosis is a sign of severe deep infiltrating disease, with other organs being affected (ovaries, pelvis, cul-de-sac, ligaments).

The symptoms can resemble those of the IBS, resulting in misdiagnosis for a large number of people. Bowel endometriosis can be superficial, affecting the surface of the bowel, and usually causes no symptoms, or deep when the disease penetrates the bowel wall, and can partially obstruct the bowel wall.

Bowel endometriosis affects both the large and small intestines but is commonly found in the lower part of the large intestine, the rectum. The large intestine is about 1.5 m long, and it starts around the right waist, the cecum is the first part, and it ends at sigmoid, rectum and anus.

The small intestine is about 6m long, and at the last part, the ileum attaches to the large intestine (near the cecum). Endometriosis foci are invading the bowel wall from the exterior, typically involving the serosa and the muscularis propria (smooth muscle layer). The inner layers, submucosa and mucosa are rarely affected.
The rectosigmoid colon is the most commonly affected area by deep pelvic endometriosis, and it occurs in 3-37% of cases. The sigmoid, rectum followed by the ileum, appendix and the cecum are the most affected parts. In some cases, patients have multiple nodules affecting different parts of the large intestine, such as the rectosigmoid, upper rectum, the sigmoid loop, as well as the appendix.

Also, there are cases when both the large and the small intestines are affected, and as seen in this case report by Dr Mitroi, the patient had one recto-sigmoid nodule, one sigmoid nodule and one ileum nodule. A double resection was performed.

An endometriotic nodule is a fibrous, dense, retractable tissue, containing multiple endometrial glands. This often makes it difficult to recognize by surgeons/gynaecologists who are not familiar with this pathology, and they confuse it with either "intra-abdominal adhesions" or pelvic tumours.

Diagnosis

Intestinal endometriosis can be diagnosed based on the symptoms (where present), during a pelvic examination if there is any nodularity, transvaginal ultrasound, MRI and/or CT. Surgery remains the most accurate method of diagnosis of intestinal endometriosis. During an operation, all areas can be examined, and any intestinal involvement can be seen.

Symptoms

Intestinal endometriosis symptoms are based on the affected area and the depth of the lesions. Superficial bowel wall endometriosis does not usually cause symptoms, and some bowel endometriosis cases are asymptomatic.

The symptoms can occur at any time throughout the cycle, and they get worse during menstruation. Rectal nodules infiltrating the large bowel wall cause pain with every bowel movement, rectal pain when sitting down or during sex. Constipation and diarrhoea, mainly during menses, are also symptoms of bowel endometriosis.

Painful bowel movements, particularly during menses, can be caused as well by disease on the uterosacral ligaments or endometriosis of the cul-de-sac. Depending on the size and the location of the nodules infiltrating the bowel wall, ileal and recto-sigmoid obstruction might occur.

Other symptoms are pain and/or cramps in the right lower abdomen where the cecum and the ileum are based. Left side abdominal pain or cramps before bowel movements are caused by recto-sigmoid nodules. Rectal bleeding with bowel movements during menses is also a symptom of intestinal endometriosis.

Endometriosis of the appendix is rare and can cause right abdominal pain associated with nausea and vomiting. The symptoms may present as appendicitis.

Treatment

Same as with other types of endometriosis, the treatment methods for intestinal endometriosis symptoms is medical therapy or surgery. Roman et al., have noted that the medical treatment for deep endometriosis does not cure the disease, and surgery is required when the lesions are symptomatic, and they alter organs function. At the time of publication, in the article is also noted that there is no consensus regarding the choice of technique for intestinal endometriosis.
The specific techniques in laparoscopic management of intestinal endometriosis are:
- shaving
- disc excision
- segmental resection

Surgery involves in the majority of cases, a gynaecologist and a colo-rectal surgeon. A multidisciplinary team is often necessary to treat deep endometriosis in a single operation. Because there is no consensus regarding the technique, the decision is taken by the gynaecologist and the colorectal surgeon on a patient-to-patient basis. The method of treatment depends on how much the bowel is affected, as well as how deep the lesions are.

For superficial disease, the lesions can be removed with rectal shaving. Small nodules can be removed using disc excision with the hole sealed surgically. In cases of deep endometriosis or sigmoid nodule, a segmental resection might be required, followed by anastomosis.

Mario Malzoni et al., 2015, noted that a segmental resection followed by anastomosis should be considered in patients’ with large lesions or deeply infiltrating nodules with extensive circumferential involvement.

Complications such as lower anterior resection syndrome, infection, fistula or leakage might occur after bowel resection and anastomosis. Bowel functions may be altered following bowel endometriosis surgery, and the recovery time varies from person to person.

Bowel obstruction requires urgent surgery. **Appendiceal** endometriosis is treated by appendectomy. Small bowel endometriosis surgical treatment depends on the size and location of the lesion.

Small implants may be treated by excision, and in cases where bowel wall is affected, a segmental small bowel resection may be performed.

**Rectovaginal and utero-sacral ligaments endometriosis**

Classified as a severe form of endometriosis, rectovaginal endometriosis occurs when lesions are affecting the rectum, and the vagina wall and other structures in between such as the rectouterine pouch, rectovaginal septum and uterosacral ligaments. The cul-de-sac and ligaments are the most commonly affected parts. As a form of severe disease, rectovaginal endometriosis is associated with disease elsewhere such as ovarian endometriomas.

The uterosacral ligaments are fibrous structures interposed between the uterus and the sacrum. They are located near the large intestine and endometriosis that has infiltrated into the ligaments can irritate the intestine causing cramps.

Scar tissue known as adhesions can form between the ligament and the intestine, irritating or narrowing the intestine. Endometriosis of the uterosacral ligaments can cause the formation of nodules that may be felt during internal examinations and may be sensitive to touch.

Recto-vaginal and utero-sacral ligaments endometriosis can cause lower back pain, leg pain, constipation, painful intercourse, dyschezia, painful periods, abdominal pain, gas. When surgery is indicated, laparoscopic resection/shaving can be performed on rectovaginal endometriosis.
Urinary tract endometriosis (UTE)

Endometriosis of the urinary tract, also known as genitourinary, is considered to be rare, and patients can experience significant morbidity such as kidney(s) failure, if not treated in time. The urinary system consists of the kidneys, ureters, bladder, and urethra. Endometriosis of the urinary tract is estimated to affect 0.3-12% of the cases, but due to the lack of knowledge among medical practitioners, the condition may be underreported.

The ureter and bladder endometriosis can be extrinsic when the tissues are found on the surface, or intrinsic when the tissues invade the organ. The bladder and ureter are the most commonly affected, and the urethra or kidney are less often affected. The UTE therapeutic approach depends on the extent, depth, and location of these lesions. When dealing with UTE endometriosis, doctors should be aware of the possibility of renal failure.

Bladder endometriosis

Bladder endometriosis, also known as vesical endometriosis, is classified as rare, with less than 400 cases described in the literature. It can be superficial when the lesions are found on the surface of the bladder, or deep when the lesions are infiltrating the bladder lining or the wall. The lesions usually develop from the peritoneum towards mucosa, can be multifocal and can also invade the detrusor muscle and in rare cases, other layers underneath.

A case of vesical endometriosis after a C-section has been reported by Posner MP et al., 12 years after an uncomplicated c-section, the patient had presented with an isolated vesical endometrioma. The detrusor muscle was infiltrated by endometrial tissues from the disruption of the uterine incision.

Symptoms

Bladder involvement usually presents with irritative symptoms, and the symptoms vary depending on the location and size of the lesions. A review done by Maccagnano C et al., found that 30% of the bladder endometriosis cases have no symptoms at all, and the diagnosis was incidental. The bladder endometriosis is often diagnosed as interstitial cystitis/painful bladder syndrome due to similar symptoms. Haematuria (blood in urine) is a rare symptom of bladder endometriosis, and it can occur during menses or at any time.

Symptoms of bladder endometriosis are:
- urgent and frequent urination;
- pain when the bladder is full;
- burning or painful sensations when passing urine;
- blood in the urine;
- lower back pain (on one side);

Diagnosis

Surgery is the correct diagnosis for bladder endometriosis. Cystoscopy can be helpful in diagnosis in cases where the lesion is penetrating the bladder wall. MRI scan can also be used to diagnose bladder endometriosis; ultrasounds, both abdominal and transvaginal can diagnose bladder endometriosis in some cases.
Surgical Treatment

The trigone and the dome are the most frequently affected sites, and the surgical methods for bladder endometriosis depend on the type of the disease. The superficial bladder peritoneum lesions can be treated with local excision. Invasive bladder disease will require a partial resection/cystectomy\(^\text{104}\) and the bladder nodules infiltrating the bladder wall can be excised\(^\text{106}\) or dissected.

Ureteral endometriosis

Ureteral endometriosis is a rare and silent disease involving one, usually the left ureter or both ureters (10-20% of cases) resulting in renal failure. Due to the silence and non-specific symptoms presentation, ureteral endometriosis is quite challenging to diagnose and can result in uretero-hydronephrosis\(^\text{157}\) and silent kidney loss if it's not effectively managed.

Ureteral endometriosis can be extrinsic in 70-80% of cases when the ureter is surrounded by the endometriotic tissues, and intrinsic in 20-30% of cases when the endometriotic tissues are invading the muscular layer or the mucosa.

Extrinsic ureteral\(^\text{157}\) endometriosis is caused by the extension of the adjacent affected organs such as the uterosacral ligaments or the rectovaginal septum. Ureteral endometriosis occurs in 50% of the urinary tract endometriosis cases. The ureters can also be surrounded by the nearby fibrosis.

The ureters carry urine from the kidneys to the bladder. When the disease invades the ureter, and partial blockage occurs, the urine cannot drain out from the kidney leading to swelling of the kidney known as hydronephrosis\(^\text{108,109}\).

Diagnosis

Imaging tests such as MRI, CT, renal scans help to establish the extent of the disease and the ureteral damage.

Symptoms

Ureteral endometriosis is often silent, and when symptoms are present, the patient might complain of abdominal pain, or flank pain, especially in cases of hydronephrosis. The symptoms can be cyclic or around menstruation.

Surgical treatment

Surgical treatment of ureteral endometriosis aims to preserve the kidney function and remove as much as possible of the lesions. The surgical method depends on how much the ureter is affected, and can be ureterolysis\(^\text{110}\), which is the first initial step in cases of limited disease, uretero-neocystostomy (refers to re-implantation of the ureter into the bladder), ureteral resection and end-to-end anastomosis, and in case of ureteral relapses, auto-transplantation.

A study\(^\text{240}\) done by a University Hospital in France concluded that ureteral lesions iatrogenic or secondary to endometriosis can be treated by JJ stent, cystoscopy and laparoscopy. The exact number of kidney loss due to endometriosis is not known, but according to some studies, it has a rate of 23-47%.

Nezat et al., presented a 3 cases report of silent kidney loss due to ureteral endometriosis. A 36 year old known with hypertension and infertility, diagnosed with severe hydroureter and hydronephrosis, was offered a nephrectomy due to 15% left renal function. The patient refused, and she was treated with a stent and placed on Lupron. A year later, a new mass had formed, and another stent was placed. The patient lost her kidney, in the end, a few months later, after the second stent was placed.
Urethra endometriosis

There a few urethra endometriosis cases reported individually, and the information is mainly included in urinary tract endometriosis articles. Chowdry AA et al., reported a case of urethral endometriosis presenting as a urethral diverticulum. The patient presented with lower abdominal pain and had a history of urinary tract infection in addition to other symptoms. The imaging showed 1 cm lesion in the urethra believed to be urethral diverticulum, and the biopsy revealed that the lesion was endometriosis.

Renal endometriosis

Kidney endometriosis has an incidence of 4% of the urinary tract endometriosis. As in other types of endometriosis, endometriosis of the kidney can be symptomatic and asymptomatic and due to its rarity is often misdiagnosed. Giambelluca et al., 2017, reported two cases of renal endometriosis diagnosed incidentally during oncologic follow up for gastric sarcoma and melanoma. The initial diagnosis was hemorrhagic cysts, and the biopsy revealed renal endometriosis.

When symptomatic, the patient might complain of back pain or might have symptoms that mimic Renal Cell Carcinoma such as a palpable lumbodorsal mass, pain and hematuria. Although the symptoms are common in both pathologies, the difference is that renal endometriosis symptoms are becoming aggravated during menstruation.

A 37 year old woman underwent a radical nephrectomy after initially being diagnosed with renal tumor. The patient complained of a dull pain in the lower back that has been aggravated during periods of six months duration. The patient was previously diagnosed with hydronephrosis, and she was treated with calculus dissolving drugs. Urography and CT scan were used to obtain further information, and the patient was diagnosed with a renal tumour. The histopathology confirmed the final diagnosis of the case as endometriosis of the right kidney.

Thoracic and Diaphragmatic endometriosis

Statistically speaking thoracic and diaphragmatic endometriosis are considered to be two rare forms of endometriosis often found in moderate to severe cases of pelvic endometriosis. Due to gynaecologists not being familiar with these forms of the disease, thoracic and diaphragmatic endometriosis are often treated partially or not seen during surgery.

The diaphragm is a thin skeletal muscle that separates the abdomen from the chest and allows a person to breathe. It is divided into two parts, right and left, and the liver is beneath the right side, and one part of the right diaphragm is behind the liver. Because of this, endometriosis on the right side is not seen unless the liver is pushed out of the way. On the left side, the spleen that might also require mobilisation during surgery. Endometriosis on the right side is more common than the left side. Due to the thin size of the diaphragm, endometriosis lesions can easily infiltrate the skeletal muscle.

Both forms of endometriosis can be asymptomatic and symptomatic. The pain can be intense, getting worse when breathing or coughing and usually occurs around menstruation time.
Diaphragm endometriosis symptoms

- right/left chest pain;
- shoulder pain;
- pain under the ribs;
- neck pain;
- shortness of breath;

Diaphragmatic endometriosis can be initially diagnosed based on the symptoms if they exist. The most commonly affected part is the right side, and the lesions can be found behind the liver. Endometriosis can cause holes in the diaphragm allowing air and fluid to pass into the pleural space causing the lung to collapse. This may produce pneumothorax and/or hemopneumothorax.

Surgery

As a disease outside the pelvic cavity, the surgical treatments require collaboration with other specialists. A thorough investigation of the entire diaphragm and adjacent areas is necessary. An operational challenge is the visualisation of the entire upper abdomen and the diaphragm surface.

For a better visualisation, several techniques can be used such as modifying the patient’s position as well as the surgeon’s position, in order to have access to the upper abdominal floor: liver, stomach, diaphragm, resecting the falciform ligament, mobilization of the liver, a high placed port, in order to be able to inspect the entire diaphragmatic surface, and to excise the lesions located at this level.

A laparoscope inserted through the umbilical incision can only visualise anterior and mid-diaphragm, and a subcostal laparoscope port incision can visualise the entire diaphragm\(^{191}\). Superficial lesions require partial-thickness membrane resection, and for infiltrating nodules, a full-thickness diaphragmatic resection is necessary.

During surgery, the diaphragm is pulled away from the liver, followed by resection of the lesions and/or the affected part of the diaphragm. Complete removal of endometriosis is required. Mobilising the liver will also facilitate easy access in order to suture the defects caused by excision. When the lesions are large (> 5 mm), the diaphragm defects should be sutured to prevent the occurrence of diaphragmatic hernias.

Thoracic endometriosis (TE), is the presence of endometriosis tissues in the lung or/and on the pleura. The lesions are found mainly in the pleura and rarely in the lung parenchyma. Endometriosis of the lung was described first in 1938 by Schwarz, and it can be classified into pleural and bronchopulmonary (parenchymal)\(^{115}\).

Patients often present with the following clinical signs and symptoms:
- catamenial pneumothorax (air in the pleural space);
- catamenial hemothorax (blood in the pleural space);
- catamenial hemoptysis (coughing up blood);
- catamenial chest pain;
- pulmonary nodules;
- shortness of breath;
- pleural effusion (fluid in the pleural cavity);
- diaphragmatic hernia;
As in other forms of endometriosis, thoracic endometriosis incidence is unknown, and 50-80% of patients diagnosed with TE have pelvic endometriosis as well. Nezhat et al., mentioned that the disease affects mainly the right pleura in 92% of cases and the left pleura in 5% of cases. Bilateral involvement of hemithorax affects 3% of cases. As a clinical presentation, pneumothorax is the most frequent finding, followed by hemothorax, hemoptysis and nodules.

The clinical suspicion of thoracic endometriosis is given by the symptoms. When symptoms are present, thoracic endometriosis can be diagnosed with video-assisted thoracoscopic surgery, which is the gold standard modality for both the definitive diagnosis and surgical treatment of catamenial pneumothorax. CT scan, chest X-ray, abdominopelvic and diaphragmatic magnetic resonance imaging can also be used to diagnose thoracic endometriosis.

Muhammad Shabbir Rawala et al., have reported a case of endometriosis pleural effusion in a 28 year old female who complained of right-sided pleuritic chest pain, for five years, dyspnea and menorrhagia. The symptoms corresponded with the start of her menstruation and relieved after.

CT scan and chest X-ray showed large right pleural effusion. In a case report by Haindong Hunag et al., a 29 year old patient presented to their clinic complaining of catamenial hemoptysis during menses. The patient had no proven pelvic endometriosis, and the CT and chest X-ray showed findings associated with lung endometriosis. The patient underwent an exploratory thoracotomy, and the biopsy confirmed endometriosis in the lung.

Endometriosis of the peripheral nervous system (PNS)

The peripheral nervous system is divided into the somatic nervous system responsible for the voluntary control of body movements and autonomic nervous system, responsible for regulating body functions such as digestion, heart rate, etc. Endometriosis of the PNS can be found on or near the nerves.

The pelvic region is made up of quite a lot of crucial nerves with important roles, and injuries to these nerves can cause disorders (sexual, urinary, movement). The pelvic region is very rich in nerve fibres, second to the brain.

Endometriosis of the autonomic nervous system

The autonomic nervous system, also known as the vegetative system has the role of regulating the functions of the internal organs (viscera), such as the heart, lungs, sexual organs, digestive and urinary system. When their role is affected, they continue to function in a disorganised way. Deep endometriosis affects various organs in the pelvis, especially the areas/organs that are near the uterus, as well as pelvic nerves (vegetative and somatic systems).

The vegetative nerves form a network of small nerves (plexus) that are located in the ligaments supporting the uterus at the intersection of the bladder, genitals and rectum. These nerves transmit information from the brain to the organs responsible for urination, defecation, sexual activity, and vice versa, from these organs to the brain. Thus, deep endometriosis affecting the uterus, ovaries, peritoneum, uterosacral ligaments can cause visceral and vegetative symptoms.

2 Treatment of sciatic endometriosis, 15 years experience- Possover International Medical Centre

Endometriosis, the praying mantis within the pelvis- Marc Possover
Hypogastric nerves and inferior hypogastric plexus are the most common nerve structures affected by endometriosis due to their proximity to the pelvic area involved with endometriosis. The vegetative nervous system can be disturbed when the uterus is inflamed but also when the nerves are directly affected (irritation or inflammation), causing disorders in the affected organs.

Disorders caused by inflammation or irritation of the vegetative nerves:

- a sensation of frequent urination even if the bladder is not full, burning sensation, an urgency to urinate;
- urgent need to defecate, painful stool especially during menstruation, constipation, diarrhoea;
- low abdominal pain;
- pain with intercourse;
- tiredness and fatigue;
- emotional distress;
- bloating;
- sickness and nausea;

The somatic nervous system

The somatic nervous system transmits signals from the brain to the end organs such as muscles and is made of sensory and motor nerves. The spinal cord is a nervous structure, made of 31 pairs of nerves and is divided into 5 segments: cervical, thoracic, lumbar, sacral and coccygeal. The lumbar plexus is a network of intersecting nerves and is made of the first four lumbar nerves (L1-L4).

The lumbar plexus is made up of a branch of nerves, iliohypogastric, ilioinguinal, genitofemoral, obturator and femoral nerve, which is the largest nerve of the lumbar plexus. The lumbar plexus serves the groin, thighs, calves, knees, back and the abdomen.

The sacral plexus serves the pelvis, buttocks, genitals, thighs, calves, and feet and gives rise to the longest and the largest spinal nerve, the sciatic nerve. The sciatic nerve runs from lumbar and sacral plexuses in the lower back and innervates the glutes, thighs, calves and feet.

The pudendal nerve, a sensory and somatic nerve originates from the sacral nerve roots. The pudendal nerve is the main nerve of the perineum and supplies the area around the anus and rectum, vulva, labia and clitoris, perineum, and sphincters of the bladder and rectum.

Endometriosis of the sacral nerve roots

The sacral nerve is part of the plexus nerve providing sensory and motor moves for the posterior thigh, a big part of the lower leg and foot and a part of the pelvis. The sacral nerve roots, also known as sacral plexus is at the back of the pelvis in between a gluteal region muscle (at the back of the nerve) and the ureter and sigmoid colon, at the front. Thus, when deep endometriosis is affecting the ureter, the uterine ligaments, rectovaginal septum, the disease can irritate or compress the sacral nerve.
When endometriosis is infiltrating the surrounding tissues of the uterus, nodules on the uterosacral ligaments can infiltrate the parameter and/or paravaginal tissue causing pain in the paravertebral region that radiates down the posterior thigh.

In this case, report\textsuperscript{119} by Dr Gabriel Mitroi, the 37 year old patient had deep endometriosis affecting the urinary system and with infiltration of the anterior rectal wall and compression of the right sacral roots. The surgery revealed nodules on the left ureter, the right parameter and the umbilical arteries. The medical team performed excision and dissection of the nodules.

The sacral plexus endometriosis is mostly on the left side with the patient experiencing some of the following symptoms:

• pudendal areas pain, vaginal pain, pain in the tailbone;
• perineal pain;
• pain radiating to the lower limbs;
• pain radiating down the gluteus, lower back;
• urinary function sensitivity;

Endometriosis of sciatic nerve

The sciatic nerve is the largest single nerve in the body connecting the spinal cord with the legs and feet. Endometriosis of the sciatic nerve is rare and is mostly found on the right side. The Possover International Centre has treated 300 cases of sciatic and sacral plexus endometriosis cases in 15 years\textsuperscript{3}.

Endometriosis of the sciatic nerve is difficult to diagnose as it resembles typical symptoms of sciatica. The cyclic nature of the symptoms should be used to differentiate between sciatica and endometriosis of the sciatic nerve. The sciatic endometriosis pain is extreme.

If the nerve is compressed, damaged, or partially destroyed by the disease, the patient will experience shooting, tingling, or numbness anywhere from the hip to the lower leg or foot as well as motor deficits (unable to walk unaided, use of crutches) including numbness of the leg. The sciatic nerve is part of the somatic nerves, responsible for carrying information to and from the brain. Endometriosis of the sciatic nerve can occur without pelvic endometriosis. At the beginning, the pain occurs during menstruation, and in time it will manifest daily. The somatic nerves are divided into four categories, sciatic nerve, pudendal nerve, obturator nerve and femoral nerve.

Symptoms

Depending on the affected nerve, the patient can experience:

• motor deficits and muscle weakness;
• numbness in the lower back and lower extremity (buttocks, calves, medial thigh, feet, back/side of the leg);
• pain, tingling radiating into hips, soles, knees, heels, feet;
• leg pain/cramps;
• feelings of numbness in the genito-anal areas;
• weakness and a feeling of leg instability;
• foot drop;
• pain when sitting and relieved when standing;
• pain in the perineum;
• pain in the lower back;
• pain in the external genitalia;
Endometriosis from A to Z

Diagnosis of sciatic nerve endometriosis

Endometriosis of the sciatic nerve can be suspected based on the symptoms, and the diagnosis should start by determining which nerve is affected based on the symptoms. Neuropelveology, focus on injuries to the pelvic nerves, is a new discipline founded by Prof Marc Possover. During the examination, the neuropelveologist examines the pelvic nerves with ultrasound. Further information can be obtained with a neuro Magnetic Resonance Tomography; however, laparoscopy can provide the correct diagnosis.

Treatment of sciatic nerve endometriosis

Endometriosis within the sheath of the sciatic nerve is associated with progressive paralysis of the legs\(^{215}\). In 1965, a 35 year old complaining of pain in the right buttock and legs for 20 months, with a different diagnosis, had surgery confirming endometriosis of the sciatic nerve\(^{215}\). Due to the importance of the somatic nerves, once the disease is diagnosed or suspected, the patient should have surgery as early as possible. Prof Possover says that the somatic nerves endometriosis should not be treated with medication since it cannot be stopped by hormonal treatment.

DeCesare et al., have reported one of the few cases of sciatic nerve endometriosis treated with GnRH. BJ Richards et al., have reported a case of sciatic\(^{120}\) endometriosis treated with danazol. The 46 year old patient presented with a history of progressive painless, right foot drop as well as numbness and tingling in the sole of the foot.

The examination revealed severe flexion weakness of the foot and toes and moderate weakness of the hamstrings. The CT scan revealed a mass adjacent to the right sacroiliac joint and the patient was put on danazol daily for 11 months. Three months after treatment, some of the symptoms improved, 15 months after the beginning of the treatment, the mass was reduced in size and two years after the presentation to the hospital she was symptom-free with a normal neurological examination.

Cutaneous-abdominal wall endometriosis

The cutaneous endometriosis is endometriosis involving the skin, the umbilicus and surgical scars. Cutaneous endometriosis is classified as primary in patients without a prior surgical history and secondary, in patients with abdominal surgeries. In surgical scars, cutaneous endometriosis involves mainly the fascia and presents as a single painful lump that can grow slowly.

Abdominal wall endometriosis AWE is a rare site of the extra-pelvic location. It occurs most frequently in patients who gave birth by caesarean section. The two generally accepted theories for AWE are iatrogenic transplantation of endometrial tissues in surgical scars after uterine surgeries\(^{242}\) (Nominato et al) and tissues undergoing metaplasia into endometriosis related to the wound healing process. (Redwine D).

There are also endometriotic nodules located in the perineum, after vaginal birth. Abdominal wall endometriosis is often mistaken for other abnormal conditions (a suture granuloma, incisional hernia, lipoma, hematoma, desmoid tumour, sarcoma). The endometriosis nodules are commonly seen in the cutaneous and subcutaneous fat tissue; the intramuscular scar endometriosis is quite rare. When the lesions are larger (more than 1.5 cm), the patients can palpate them. The nodule can vary in size during the menstrual cycle, and some patients can put their own diagnosis to it.
The symptoms vary from person to person, and some are asymptomatic pain-wise, while others may have abdominal cyclical pain. During menstruation, the patient feels tenderness/pain at the anterior abdominal wall in the umbilical region. A careful history and physical examination can establish a clinical diagnosis. Diagnosis is confirmed by imaging, either abdominal wall ultrasound or MRI exam, which highlights the presence of the nodule and its location.

The surgical treatment of cutaneous endometriosis is wide local excision of the tissues, and the method will depend on the location and the depth of the lesions and the experience of the surgeon. The removal of the nodule must be completed with safety margins (excision to healthy tissue) to avoid local relapse. Surgical scar endometrioma develops in 0.1% of patients who have undergone C-section, and 25% of these patients have pelvic endometriosis as well.

Abdominal wall endometriosis at the trocar site of laparoscopy has been reported as well. Mojgan Akbarzadeh Jahromi\textsuperscript{196} have reported the 17th case of endometriosis on the trocar which was initially thought to be an incisional hernia.

Ahmet Kocakusak\textsuperscript{197} have reported a case of primary spontaneous abdominal endometriosis wall in a 37-year-old woman with an initial diagnosis rectus hematoma with no previous surgery. The medical team at Wellborn Endometriosis Centre has treated a case of symptomatic abdominal wall endometriosis in a patient with asymptomatic deep pelvic endometriosis.

Forms of very rare endometriosis

Due to the limited knowledge among medical practitioners and patients, it is not known if some of the endometriosis forms are a rare occurrence, or are misdiagnosed/not reported.

Liver endometriosis

The first case of liver endometriosis was described in 1986 by Finkel L et al., in a 21 year old patient with a history of epigastric pain. Prachi Rana et al., published a review\textsuperscript{121} of the literature and a case of endometrioma of the liver, believed to be the 29th case of liver endometriosis reported.

The authors\textsuperscript{121} are presenting the case of a 42 year old woman, initially treated for a presumed hydatid cyst that was later found to be endometriosis in the liver. The patient complained of episodic, severe right upper quadrant pain associated with nausea and vomiting. The patient had undergone a hysterectomy and left oophorectomy for unclear reasons. The CT showed cysts in the left, and the right hepatic lobes and the biopsy was unclear. Due to further imaging tests showing a new pericardial effusion, the patient underwent urgent surgery, and the biopsy confirmed hepatic endometriosis.

This review of the literature\textsuperscript{121} of the hepatic endometriosis shows ages ranged from 21 to 62, 6 patients were postmenopausal, 12 had a prior history of endometriosis, 90% had epigastric and right upper quadrant pain, 2 had characteristic cyclic pain, and three were asymptomatic, and 27 had surgery.
Pericardial endometriosis occurs in 2% of the patients with diaphragmatic endometriosis. Marcello Ceccaroni et al., have presented a case of pericardial, pleural and diaphragmatic endometriosis in a 28 year old patient with a clinical history of right upper quadrant abdominal pain radiating to the right shoulder which worsened during inspiration and supine.

J.M. Lund et al., have reported a case of pericardial, pleural and diaphragmatic endometriosis in a 31 year old patient with a history of three prior pneumothoraces who complained of right sided chest pain, orthopnea and dyspnea within 48h of onset of menses. The patient underwent a VATS during which suspicion of ectopic endometrial cysts were observed on the pericardium, the right diaphragm and the lung.

Umbilical endometriosis occurs in 0.5 to 1% of the endometriosis cases and is divided into two forms, primary when it appears spontaneous, described first by Villar in 1886, and secondary caused by a surgical procedure. It appears as an umbilical mass or firm nodule (blue, brown) of variable size, from a few millimetres up to 4-5cm and it can cause bleeding, swelling and cyclic pain.

Umbilical endometriosis has been diagnosed as an umbilical hernia, granuloma, and sebaceous cyst. Braunlich K et al., from the Largo Medical Centre in Florida, have reported a case of spontaneous umbilical endometriosis in a 30 year old patient who presented to their dermatology clinic with a nodule in her umbilicus.

Inguinal endometriosis presents in 0.3% - 0.6% of all cases of endometriosis, and it manifests as an inguinal mass, and the size can range from 1cm to 6cm. Battista Candiani G et al., reported inguinal endometriosis in six patients diagnosed initially with an incarcerated hernia. The biopsy after the surgery confirmed inguinal endometriosis and the round ligament was the most affected structure.

Pancreatic endometriosis was reported in a 72 year old woman with a preliminary diagnosis of pancreatic cancer. The patient underwent a hemipancreatectomy, and the biopsy revealed focal multicystic lesion with several endometriotic cysts.

Perineal endometriosis is an extremely painful condition, the same pathogenesis like abdominal wall endometriosis; occur after vaginal births. Patients experience unbearable perineal pain; sometimes, they can’t sit on a chair.

Invisible/occult microscopic endometriosis

Microscopic endometriosis is endometriosis tissues that can't be observed by inspection with the laparoscope or the naked eye. The first cases of microscopic endometriosis were reported in 1986 by Murphy et al., in 5 out of the 20 patients who underwent laparotomy. It is not clear if microscopic endometriosis exists as there are conflicting results regarding the incidence of not recognising all types and colours, and the existence of microscopic endometriosis.
In 1991, Nisole et al., have found microscopic endometriosis in 2 out of the 32 patients without endometriosis at laparoscopy. Nezhat et al., found one patient in the study who had a 1mm lesion underneath the normal-looking peritoneum. The authors of this study concluded that the results support the existence of unrecognized subperitoneal and microscopic surface endometriosis.

The incidence of microscopic endometriosis, according to Dr Redwine, seems to correlate with the distance between the laparoscope tip and the area excised/visualised. There are no studies to show if a microscopic tissue grows bigger in time or it becomes symptomatic.

Roman et al., have reported bowel occult microscopic endometriosis. The study was done on 103 patients who underwent bowel resection from 2009 to 2014. Bowel microscopic endometriosis was found in 14.6% of specimen resection margins, one year post-operatively the patients had no digestive or pelvic symptoms, and one patient had rectal recurrence five years later.

Endometriosis by age

Based on old authors' articles and theories and due to misdiagnosis, endometriosis is believed to affect mostly people ages late 20s to 40s. This is due to the delay in diagnosis from onset of the symptoms that can start at a young age and until the patient is diagnosed with endometriosis, which can be 8-10 years later. Based on the current facts, endometriosis has been reported in girls as young as 8-9 years old and in postmenopausal women.

Endometriosis in teenagers

Endometriosis symptoms are often ignored in people, especially in teenagers, since they are considered to be too young to have endometriosis. In some cases, the symptoms can start before the menarche, and they get worse after the first periods. Many of the teenagers who are experiencing endometriosis symptoms will miss school and daily activities because of pelvic pain.

Since some of the teens have pelvic pain during periods, they are often told by family, friends, teachers and doctors that symptoms are “normal period pain.” This, of course, will make the teenager accept painful periods as being a normal thing and that she/he will have to put up with the pain.

Endometriosis should be suspected and included in the differential diagnosis in young pre- or perimenarcheal patients with chronic/cyclic pelvic pain especially with no response to oral contraceptives and nonsteroidal antiinflammatory medicine. Marsh EE, has published a case series of five premenarcheal girls with chronic pelvic pain and negative gastrointestinal workup. All cases had laparoscopy with visual identification of clear, red, and/or white lesions.

Teenagers will start experiencing pelvic pain up to 1-2 weeks before menstruation. If they are sexually active, depending on the location of the lesions and the affected areas, then intercourse might be painful. Other symptoms include painful bowel movements, pain when sitting down, leg pain, back pain, etc. Some of the Wellborn Endometriosis Centre patients have had symptoms from the age of 12-13 years old.
Diagnosis of endometriosis in teenagers can be done mostly based on the symptoms such as pelvic pain since the disease might be superficial to be picked up by ultrasounds or MRI, or they are not sexually active. Erica Dun et al., had reviewed a series of 25 females ≤21 years of age with endometriosis diagnosed during laparoscopy for pelvic pain over eight years. The average age at surgery was 17 years old, stage 1, 2 and 3, had been identified in the patients during laparoscopy, and their symptoms were evaluated by an average of 3 doctors.

The treatment of endometriosis in teenagers is mainly based on the doctor's experience with endometriosis and the way he/she interprets the treatment. In most cases, the patients are started first on painkillers, followed by birth control pills. A review of publications relating to adolescent endometriosis done by Laufer MR concluded that if the pain does not respond to oral contraceptive pills and/or nonsteroidal anti-inflammatory agents, a laparoscopy surgery is indicated for diagnosis and surgical treatment at the same time. Furthermore, the gynaecologist should be familiar with the various presentations of endometriosis lesions as the clear, red, white, and/or yellow-brown lesions are more frequently than black or blue lesions.

Due to age, possible complications and the impact on fertility, surgery is offered quite rarely, despite the teenager being in pain. Some of them are instead put on GnRH drugs for long time use, which has been shown to have a high negative impact on bone density in this age category.

The ESHRE guidelines recommend clinicians to give careful consideration to the use of GnRH agonists in young people and adolescents, since they may not have reached maximum bone density.

Note: Special consideration is required when using GnRH in adolescents who are at a critical age for building up bone mineral density. The recurrent disease is more likely in teenagers as they are still forming their disease until mid-twenties.

Endometriosis in menopausal patients

Based on Sampson's theory, endometriosis is considered to be caused by retrograde menstruation, and it can be cured by menopause or pregnancy; therefore endometriosis patients are often told to have a baby, to have a hysterectomy or that after menopause, endometriosis will disappear. Studies have shown that none of the aforementioned is a cure for endometriosis since endometriosis grows outside of the uterus and by shutting down the uterus activity will not treat the illness.

Endometriosis symptoms may also occur in menopause. That's because there is also another source of estrogen in the body - adipose tissue - and also because at the time of menopause, patients already had endometriosis.

Because endometriosis symptoms tend to get worse with the onset of the menstrual flow, amenorrhoea might be a relief for some endometriosis patients. Wellborn Endometriosis Centre medical team has operated on patients who had a hysterectomy done previously to treat endometriosis. With the onset of menopause, symptoms related to the menstrual flow might decrease in intensity; however, symptoms associated with the digestive or urinary tract will remain the same.
Benjamin Snyder et al., have reported a rare case of bowel endometriosis in a 60 year old patient nine years after hysterectomy with bilateral salpingo-oophorectomy. A meta-analysis at the World Congress of Endometriosis in 2017 concluded that endometriosis can also occur in patients following surgical or natural menopause.

The analysis was done on 36 surgical menopause, four natural menopause plus a few other categories. A systematic review of the literature from 1997 to 2018, found that in 22 out of the 36 cases, the symptoms started ten years after menopause.

Manuel Garcia Manero reported a case of ovarian endometrioma in a 62 year old patient with no history of endometriosis and no previous hormonal therapy. The patient presented with acyclic pain, and she had entered menopause at the age of 47. The authors concluded that post-menopausal endometriosis confers a risk of recurrence and malignant transformation.

Edgar Heydon reported a case of menopausal endometriosis in a 78-year old woman and the medical team at St. Charles Endometriosis Treatment Program reported a biopsy confirmed endometriosis in a 74 yearold patient who underwent hysterectomy for endometriosis at the age of 73.

Dr Ken Sinervo from Centre for Endometriosis Care says that mild symptoms might get better after menopause, and in cases of severe disease, symptoms will persist. Also, in cases of a long history of painful symptoms, symptoms won't go away with menopause. According to some studies, the prevalence of postmenopausal endometriosis is between 2-5%; however the exact prevalence is not known.

A comprehensive retrospective study done in Germany by Haas D et al., on 42,079 patients with surgically confirmed endometriosis to find out if endometriosis is a disease that occurs only in premenopausal patients, the results showed a high prevalence of the disease in patients’ age over 40.

In the premenopausal group, age 0-45, 23 patients were younger than 15. In the perimenopausal group, age 45-55, the prevalence of endometriosis was 17%, in the postmenopausal group, age 55-95, endometriosis was found in 2.55% (1.074 cases), with eight cases in the 80-85 year and one case in the 90-95 years.

In an article by Umit Inceboz, Endometriosis after menopause, is noted that due to the high number of postmenopausal case reports, endometriosis is not a problem of “solely” reproductive years. In the article is also mentioned that surgery is the first choice of treating postmenopausal endometriosis mainly due to the risk of malignancy.
Chapter 3. Surgical Interventions

Laparoscopy

Laparoscopy is a minimally invasive procedure, performed under general anaesthetic, used to diagnose and treat abdominal and pelvic medical conditions, using a laparoscope to visualise the organs in the pelvic and abdominal cavities. Laparoscopic surgery offers a faster recovery, less postoperative pain, less post-op complications, less adhesions, better aesthetics, better visualization and shorter hospital stay. Dr Camran Nezhat is the inventor of the video laparoscopy in 1970-1980.

Patient preparation is required depending on the type of surgery being done. For gynaecological surgeries, a bowel preparation might be requested as well. Laparoscopy can be a one-day procedure or overnight/days stay.

For endometriosis surgeries, laparoscopy is the gold standard diagnosis and treatment procedure due to the use of a laparoscope which allows better magnification and visualization. The instruments needed are a laparoscope, a thin tube with a video camera and a light at the end, forceps, scissors, dissectors, hooks, uterine manipulator, and graspers.

The surgeon starts by inserting CO2 into the abdominal cavity, through a small incision near the belly button or left upper quadrant. After inflating the abdomen, the laparoscope is then inserted, which will play images to a TV monitor.

Depending on the condition treated, further key-hole incisions will be made for the use of the necessary surgical instruments. The surgical time depends on the illness treated and the procedure done. At the end, the gas is let out of the abdomen, and the incisions are closed using absorbable or removable stitches.

Laparotomy

Laparotomy is also known as open abdominal surgery. The surgery can be done with general or local anaesthesia, and it requires some pre-operative steps such as decompression of the stomach and the insertion of a catheter to empty the bladder.

The patient is placed in the dorsal decubitus position with the arms spread laterally. The incision is made with a scalpel and can be:
- the Pfannestiel horizontal cut known as bikini line cut;
- vertical cut from the pubic bone to the navel;

The surgeon starts by doing an incision in the tegument, followed by the section of the fat tissue until aponeurosis. Peritoneal fat and the peritoneum is highlighted, and the peritoneum is cut carefully. The incision is closed either with non-absorbable suture material or with delayed absorbable suture material.
Hysterectomy

Hysterectomy involves removal of the uterus. This intervention may or may not be accompanied by surgical removal of the ovaries and fallopian tubes (with or without anectomy).

There are several surgical approaches to hysterectomy:
• classic abdominal hysterectomy (technique rarely used nowadays);
• vaginal hysterectomy;
• laparoscopic hysterectomy / robotic hysterectomy - a rare indication;

Laparoscopic hysterectomy is done with the help of special surgical instruments that are inserted into the patient's abdominal cavity through small incisions. Three or one incisions can be used as well, but most gynaecological surgeons use four small incisions:
• one of 10 mm at the level of the umbilical scar through which the optical device is introduced;
• three incisions of 5 mm - two of them in the iliac fossa (right, left) and one at the suprapubic level;

Laparoscopic hysterectomy can only be performed under general anaesthesia and requires, in addition to the specific laparoscopy instrumentation, a uterine manipulator. The use of this is to facilitate surgical exposure and to reduce the operative time. Hysterectomy is indicated for fibroids, adenomyosis, cervical cancer, and can be subtotal, removal of the uterus only or total, removal of the uterus and cervix.

Video-Assisted Thoracoscopic Surgery (VATS)

VATS, a minimally invasive technique, is the current gold standard for the surgical treatment of endometriosis involving the thoracic cavity (lungs, pleura). The procedure was introduced 20 years ago to reduce the trauma of chest operations.

It is performed using a video-thoracoscope introduced into the chest and surgical instruments via separate small incisions called ports. Nezhat et al mention that postero-lateral thoracotomy position is a better approach than the axillary thoracotomy position since complete visualization of the diaphragm is difficult.

As a minimally invasive technique, VATS offers similar benefits as laparoscopy, faster recovery, less postoperative pain, better esthetics, short hospital stay. For VATS surgeries, the use of CO2 is not necessary due to the space needed for instrument manoeuvring created by collapsing the lung with one-lung ventilation. The patient is placed in the lateral decubitus position and the standard VATS pleurodesis procedure requires three ports.

Robotic Surgery

Robotic surgery is laparoscopic or endoscopic surgery, done using the Da Vinci system comprised of three components: a surgeon's console offering a close-up 3D view of the anatomy, patient-side cart, and a vision cart. When comparing the outcomes of how patients do after the traditional laparoscopy and robotic laparoscopy, there is no difference.
One study\textsuperscript{144} comparing the visualisation of endometriosis between the 3D robotic and 2D laparoscopic endoscopes showed that robotic visualisation resulted in detection of more confirmed lesions in all anatomic locations and for most appearances, including the cul-de-sac and atypical appearance.

Nezhat et al., have done a study\textsuperscript{145} to compare operative time, estimated blood loss, complication rate, and length of hospital stay between robotic laparoscopy vs conventional laparoscopy for advanced-stage endometriosis and the authors concluded that both methods are equally effective and the robotic platform is associated with increased operating time and might also be associated with a longer hospital stay.

Comparing robotic surgery with standard laparoscopy, a review\textsuperscript{146} done by Berland N, the authors concluded that the operative time was longer for robotic surgery and the major complications and laparotomy rates were higher in the robotic surgery group than standard laparoscopy.
Endometriosis from A to Z

Alexandra, 2nd laparoscopic surgery

Kristina, laparoscopy (diaphragm and pelvic endometriosis), her 4th surgery

Ruth, her first laparoscopic surgery and 5th surgery for endometriosis
Chapter 4. Surgical Treatment

Surgery for deep endometriosis is a complex surgery involving exposure of the pelvic and abdominal organs. Surgery remains the only method of establishing the exact extent of the disease, and the operative techniques for endometriosis are depended upon the size, location of the implants and most importantly, the surgeon's experience.

Various techniques and technologies have been described and used for the treatment of endometriosis. The techniques are divided into thermal ablation techniques and excision, using different tools, such as PlasmaJet, lasers, scissors, bipolar and monopolar electrosurgery, ultrasonic energy.

For endometriosis surgery, PlasmaJet\textsuperscript{146} can be used for both vaporisation and resection of the tissues at 100% power using high temperature and high gas flow. For vaporisation of superficial lesions, the probe is applied from 5mm distance from the tissue at a 45 degree angle.

When used in close proximity to the tissue and at a 90-degree angle, PlasmaJet can resect the lesions. Nezhat et al., have concluded on a study\textsuperscript{146} done on 18 patients that PlasmaJet can serve as a multi-functional device which has vaporization, coagulation and a degree of cutting capacities with minimal tissue destruction.

**Excision**

Excision is the act of removing implants by cutting them away from the surrounding tissues/structures. During excision surgery, the endometriotic tissues are removed down to the roots with organs being reconstructed and their functionality restored.

Excision surgery requires extensive training, and the diagnosis and treatment of endometriosis are depended on the surgeon's ability to recognise the disease in all its different manifestations\textsuperscript{44}. Therefore, if the surgeon does not recognise atypical lesions or he/she is not familiar with the places where endometriosis can be found, then the disease will be missed and left untreated.

Excision surgery can be done using sharp excision, using scissors to dissect the lesions, allowing a histological (biopsy) confirmation and avoiding the destruction of the surrounding tissues\textsuperscript{148}.

**Electrosurgery** or electroexcision is the most convenient method of quickly cutting the tissues using high-density electrical currents, and blunt dissection to separate the endometriosis from vital structures. Monopolar electrosurgery, is a widely used technique for cutting and deep coagulation of the lesions\textsuperscript{147}.

**Excision technique- Wellborn Centre**

A preoperative patient preparation is required, involving a light diet a few days before surgery and a bowel prep the day before surgery as deep endometriosis often affects the structures of the digestive tract. In cases of urinary tract involvement, a urological consultation is recommended, which may indicate, when there is compression/ureteral impairment, the preoperative installation of a ureteral catheter.
Endometriosis surgery is one of the most complex laparoscopic procedures, requiring meticulous exposure and dissection of the abdominal and pelvic organs. Therefore, it is necessary to use at least four trocars: a trocar placed at the level of the umbilical scar through which a laparoscope is inserted and three trocars operators placed at both iliac (right, left) and the suprapubic level. During operations for deep endometriosis, the patient is placed on the operating table in 'lithotomy position' (gynecology position). This facilitates access to the vagina and rectum, something that is necessary for this type of intervention.

Creation of pneumoperitoneum (introduction of CO2 to inflate the abdominal cavity) and the placement of trocars vary depending on the location of the disease and experience and habits of each surgeon. At Wellborn Centre, pneumoperitoneum is done through a mini-incision of 1-2 mm located at the left subcostal level (Palmer point), which has a very low risk of intraoperative complications.

When endometriosis affects both the pelvic organs and the diaphragmatic peritoneum or liver surface, the position of the trocars and the patient should be changed. After performing the pelvic surgical time, the surgeon’s position changes, s/he has to ‘work’ on the upper abdominal floor: peritoneal excisions, diaphragmatic excisions, liver resections (rare).

After the inspection of the entire abdominal and pelvic cavities and the trocars placements, recovering the pelvic anatomy, profoundly modified by endometriosis, the surgical intervention begins.

After the dissection of both ovaries on the pelvic peritoneum and, possibly, the drainage of the endometriomas, we carry out suspension of the ovaries to release the Pouch of Douglas. Later, we make the dissection of the rectum-uterine, recto-vaginal nodules, with the penetration into the normal recto-vaginal space that is below the level of the endometriotic lesion.

The uterine suspension is often necessary to facilitate the dissection of the rectum-vaginal space. We use this technique because in deep endometriosis surgery, at Wellborn Centre, we do not use the uterine manipulator; this facilitates access to the vaginal vault and highlights the degree of infiltration of the vaginal walls. Another important time is the dissection of the pararectal spaces and the highlighting of the hypogastric nerves, avoiding their damage.

When the lesions are more profound, with the infiltration of the parametric190 (lateral uterus) and paravaginal tissue, the dissection should be performed up to the level of the pelvic floor, the level of the obturator muscles. This type of injury can compress or infiltrate nerve structures such as the obturator nerve or sciatic nerve.

Excision of pelvic endometriotic lesions can be performed with different surgical instruments such as scissors, monopolar hook, ultrasound dissector, LigaSure calliper, Laser dissector, depending on the dissected tissues and the experience of each surgeon. As an Endometriosis Centre, the team practices extensive pelvic excision/resections (nodules, intestinal/bladder resections, diaphragmatic resections) with sutures of muscular defects, hepatic resections (when there is hepatic impairment), at the same time to avoid multiple surgeries.
Thermal ablation techniques

Thermal ablation technique\textsuperscript{147,148} also known as fulguration/ vaporization/ coagulation is a method whereby the endometriotic tissues are burned using heat, laser or cautery methods and can be done using different types of ultrasonic energy and laser.

The CO\textsubscript{2} laser vaporisation\textsuperscript{147} is considered the most effective technique for superficial endometriosis lesion. The tissues are entirely destroyed and can be used with minimal risks to the nearby organs. It produces lots of smoke, and it has high costs\textsuperscript{148}. Electrocoagulation is an operative technique whereby surgeons use high-frequency electrical currents to destroy diseased tissue with heat.

The monopolar electrocoagulation\textsuperscript{148} permits deep and complete coagulation of the nodules and may cause less haemorrhage. This method has numerous associated complications such as extensive destruction of surrounding and underlying healthy tissues, lack of biopsy and monopolar cautery hazard. The bipolar electrocoagulation\textsuperscript{148} permits superficial coagulation only, limited thermal injury to the surrounding tissues and haemorrhage is absent.

Regarding the effectiveness of thermal ablation techniques on endometriosis, the studies done on the use of these two methods focus on the reduction of the symptoms and not on disease eradication. Since endometriosis can be very invasive, during surgical treatment using thermal ablation, healthy tissues cannot be separated from diseased tissues. Furthermore, all the disease is considered to be superficial, and the surgeon has no means of ensuring that all endometriosis of any depth of invasion has been eradicated.

Excision vs ablation

Excision doesn't damage the tissues, therefore a biopsy of the excised tissues can be obtained, confirming the diagnosis. When it is done by an experienced endometriosis specialist, excision surgery has a low rate of recurrence, reducing the symptoms and improving fertility, thus having a positive impact on the patient's life.

The effectiveness of excising implants has been noted in clinical trials and through direct patients' observation\textsuperscript{155,156}. Both methods noted that excision of endometriosis resulted in fewer symptoms years after surgery in comparison with patients who underwent ablation surgery, and the symptoms returned within months. Cases of advanced disease experienced have a greater response to laparoscopic excision and a significant improvement in the symptoms of endometriosis.

Ablation may vaporize the surface of a lesion and still leave active disease below, and it is particularly true for deeply invasive nodules of the uterosacral ligaments. With ablation, active disease can remain in the pelvis and continue to cause pain. This method can cause more scarring and tissue damage, deep implants cannot be reached, and there are no tissues for pathology to confirm the diagnosis.

With ablation there is a possibility of accidentally damaging the underlying tissue, such as the bowel, bladder or ureter; therefore implants that lie over vital organs, such as the bowel and large blood vessels are left untreated, resulting in higher recurrence more than 80% and further surgeries.
Very few studies have been done to observe the long term benefits between the two procedures. On a cohort study comparing the effectiveness of excision endometriosis vs ablation, the results showed that more than 80% of patients in the excision group reported improvements in symptoms vs less than 30% for the ablation group. A study done by Pundir J\textsuperscript{149} to observe the benefits between the two procedures, concluded that 12 months post-surgery patients undergoing excision showed a significantly greater improvement in symptoms compared with the ablation group.

A study done in the BSGE\textsuperscript{150} endometriosis centres in the UK, on 4721 patients with rectovaginal endometriosis concluded that when surgeries are done in specialist centres, the complication rate is low and excision surgery is effective in treating symptoms, and improving health-related quality of life.

A two year follow up study\textsuperscript{151}, shows coagulation to be better than excision. A three years follow up cohort study\textsuperscript{152} done in a private practice on 163 patients using electrosurgical excision of endometriotic implants, concluded that excision of endometriosis significantly reduces pain and improves quality of life, and only 32 patients underwent a second procedure.

A study\textsuperscript{153} observing the recurrence rate on 239 patients who underwent laparoscopic surgery from July 2010 to June 2015, 84.6% underwent laparoscopic excision, and 7.7% of the patients with endometriosis needed further surgical intervention. The study concluded that laparoscopic surgery for endometriosis had a low rate of reoperation and long-term improvement in pelvic pain, sexual function, quality of life and fertility outcomes, with a high satisfaction rate.

Photo source: Bloomin’ uterus, endometriosis excision vs ablation
Cystectomy

The two most used surgical methods to treat endometriomas are ablation and cystectomy/excision. A systematic analysis of the literature done by Alborzi et al. comparing laparoscopic cystectomy with laparoscopic drainage and coagulation of the cyst concluded that cystectomy was superior in terms of risk of recurrent symptoms, reoperation, and pregnancy.

Pre-surgical treatment with GnRH analogues is useless in ovarian endometriomas, it is not effective in reducing the size and volume of cysts, not even in terms of facilitating surgery. During excision of the endometrioma, some healthy ovarian tissue is removed as well. For endometriomas larger than 2 cm, the first step of the procedure involves ovarian adhesiolysis.

In most cases, the ovary is attached to the surrounding structures and in general, the cyst bursts during adhesiolysis, thus, the fluid needs to be drained immediately to prevent pelvic contamination. The cut is enlarged sufficiently to be able to examine the inner walls of the cyst in order to detect any suspected malignant lesions. At the same time, the capsule of the ovarian stromal cyst can be highlighted, and it should be removed entirely to prevent relapses.

Once the capsule is separated in an area, it can be dissected step by step. In general, the discovery of a good cleavage plane allows, through divergent traction with the help of two forceps grasper, the separation of the capsule from the normal ovarian tissue. Sometimes the stripping is very easy to do, other times it requires greater force or readjustment of the cleavage plane from time to time.

If the cyst is larger and/or the adhesions can be dissected without bursting the cyst, the extraction with the intact capsule can be tried. To enucleate the cyst with the capsule intact, a small incision is made with the monopolar electrode or the scissors.

From the edge of the incision, the ovarian cortex together with the stroma (usually very thin in these places) is grabbed with the grasper and the cleavage space between the cyst capsule and the ovary is highlighted. The dissection in this plane can be done with the cubed scissors, with the help of a bipolar (Maryland type), a spatula or the irrigation-suction rod. The blood vessels that supply the cyst are coagulated with bipolar forceps. The incision in the ovarian cortex is then expanded to allow removal of the intact cyst.

Following the extraction of the cyst capsule, ovarian tissue is exposed to bleeding areas. Hemostasis is done by bipolar electrocoagulation as not to affect the normal ovarian tissue. Also, the ovary can be sewed both for hemostatic purpose and to restore its shape. The hemostasis is rigorously checked, and the peritoneal cavity is washed in abundance, in order to limit the formation of postoperative adhesions.

Hysterectomy and oophorectomy

Endometriosis is one of the reasons that thousands of patients each year have menopause induced temporarily or permanently. Based on Sampson origin theory, endometriosis is considered to be a disease of the reproductive organs caused by reflux menstruation, and induced menopause (surgically or with hormones) is often recommended as a treatment method. Sampson hoped that once the ovarian function is stopped, it will possibly result in the atrophy of the endometriosis tissues in the pelvis.
By definition, endometriosis is disease outside of the uterus, therefore removing the uterus does not guarantee relief from endometriosis-related symptoms and will not treat the endometriosis, especially since endometriosis tissues can be found on different organs.

Attar E, demonstrated that endometriotic cells contain the full complement of steroidogenic genes for de novo synthesis of estradiol from cholesterol, meaning that they can make their own estrogen. If during the surgery, the uterus is removed, this may have little or no impact on the symptoms if, the disease in other places is not treated at the same time.

Endometriosis is not the only cause of pelvic pain and the exact mechanism by which endometriosis causes pain is unknown. Patients experiencing heavy and painful periods or with co-existing conditions such as adenomyosis or fibroids are likely to have an improvement or resolution of these symptoms following a hysterectomy.

Endometriosis produces its own estrogen and is responsive to estrogen, therefore by removal of the ovaries the nearby lesions will have less estrogen to respond to, resulting in a decreased activity and possibly less pain.

Removal of the uterus and ovaries only will not treat the symptoms caused by endometriosis on the bowel, or the urinary tract or in other parts of the body if the disease is left untreated, or if the surgeon does not recognise all endometriosis colours and areas where endometriosis occurs. A study done on 75 patients who underwent excision surgery following hysterectomy noted that endometriosis can remain symptomatic after castration, with or without estrogen therapy with a 33% frequency of intestinal involvement.

Clayton RD, have reported 5 cases of recurrent pain after hysterectomy and bilateral salpingo-oophorectomy for endometriosis. The main symptoms were general pelvic pain, dyspareunia and rectal pain, four patients had endometriosis which was not removed at the time of previous surgery, and one patient had hydrourerter and hydronephrosis caused by endometriosis surrounding the ureter.

**Presacral Neurectomy (PSN)**

Presacral Neurectomy is the surgical removal of the nerve fibres that innervate the uterus and results in a 75% pain relief. The procedure requires significant surgical skills and expertise. The presacral plexus is a group of nerves that conducts the pain signals from the uterus to the brain. This procedure may be the best option to alleviate pain for patients with adenomyosis, and severe dysmenorrhea wishing to preserve fertility.

The area where the resection of the nerves is done is near the sacral promontory, surrounded by major blood vessels, the ureters and intestines, so the surgeon should carefully resect the nerves without damaging the vital structures in the area.

The presacral nerve lies in between the right and left ureter, and the sigmoid is on the left as well. Vital structures that lie to the left and right sides such as common iliac veins and ureters can be injured during surgery. The left ureter is not easily visible during surgery as it is hidden by the sigmoid colon mesentery.

As part of the procedure, the sigmoid is suspended to the anterior abdominal wall or retracted from the operative site. The promontory, aortic bifurcation, ureters, common iliac arteries and veins, are then identified.

*Adenomyosis Presacral nerve resection Dr Gabriel Mitroi, Youtube, May, 2018
The peritoneum is elevated to move it away from the retroperitoneal vessels and incised at the promontory level. The retroperitoneal space is dissected in the triangle delimited by the right common iliac vessels, the inferior mesenteric artery and the left common iliac vessels; the upper limit is the bifurcation of the aorta.

After careful dissection, the presacral plexus is highlighted, and the nerve path is dissected from the bifurcation of the aorta to the anterior face of the sacrum at a distance of at least 6 cm; the lateral dissection is made until the right ureter (retroperitoneal) is seen. The excised portion should be at least 4 cm.

In a case study article in the Turkish Journal of Obs and Gyn regarding the efficacy of the PSN, the authors concluded that the pain decreased significantly at each follow-up visit. In another study done by Jedrzejczak regarding the efficacy of PSN, dysmenorrhea decreased at three months with patients reporting a significant decline in pelvic pain and dyspareunia unrelated to periods at 3 to 12 months follow up after the PSN.

The procedure is suitable for patients with midline pelvic pain as the main symptom. Lateral pelvic pain will not be improved. PSN denervates the uterus, therefore the resection of the presacral nerves will only reduce the pain connected to the uterus. Some complications include constipation and/or urinary symptoms.

**Adhesiolysis**

Adhesiolysis is a surgical procedure to restore normal anatomy and organ function, and involves cutting the bands of tissues that form between organs so painful symptoms can be relieved. Adhesions form in the abdomen after an infection, or after an abdominal surgery as part of the healing process. Adhesions can cause bowel obstruction, infertility and abdominal pain. In patients with endometriosis, adhesions are caused by the disease, and by previous surgeries. In moderate to severe cases, this is known as frozen pelvis.

Regarding surgery method, the lysis of adhesions can be done via laparoscopy or open surgery and can be done as part of other procedures (endometriosis, cysts) or as a procedure by itself. Due to the vital importance of the affected organs (intestines, bladder, nerves), laparoscopic adhesiolysis should be done by well-trained laparoscopic surgeons. Adhesions are encountered very often in endometriosis patients, and lysis of adhesions and/or organs dissection is one of the first steps done before proceeding with excision.

Laparoscopic approach for adhesiolysis compared with an open approach, offers a faster recovery, less pain and reduces the risk of developing post-surgical adhesions. As a single procedure, adhesiolysis is indicated in symptomatic patients with multiple surgeries, and in patients experiencing intestinal obstruction, chronic pain and infertility.

The procedure is done under general anaesthesia and can be done via 3-4 incisions, and extra care must be taken when placing the first trocar. As for instruments, the surgeon will need a laparoscope with a camera on the end, laparoscopic grasper, shears/scissors, and electrosurgery dissector. The dissection should be done with extreme care as not to perforate the bowel or cause any thermal injury.
**Intestinal Surgical Procedures**

Intestinal endometriosis is the most common form of extra pelvic endometriosis, and the surgical methods are dictated by the size, the location and the infiltration of the nodules. Superficial lesions can be shaved (rectal), while larger lesions and nodules require resection (sigmoid, rectal) followed by anastomosis. When nodules infiltrate the intestines, partial or total bowel obstruction can occur. It is important to know that even with thorough preoperative assessment, the surgical approach is made after the intraoperative assessment.

For multiple nodules affecting the same part of the intestine, an en-bloc resection can be done. A 30 year old patient with a previous endometrioma surgery, presented with multiple nodules affecting a large part of the intestine. The medical team at Wellborn Centre has performed an extensive intestine resection of 35 cm. When the nodules are affecting different parts of the intestine, shaving and single or double resection can be done.

In cases of bowel infiltration, between 80-90% of them are located on the sigmoid or the rectum, and it can be a single/multiple lesion or fibrotic looking nodules, thus most likely to require resection for deep infiltrating endometriosis. A PubMed and Cochrane review done to establish the surgical treatment for deep intestinal endometriosis affecting the sigmoid and the rectum concluded that a complete resection is required in order to achieve the best patient outcome. The surgical indication is given by the severity of the symptoms, or the presence of advanced disease.

Chapron et al., noted that lesions of the serosa without infiltration of the muscularis should not be classified as deep intestinal endometriosis, therefore do not justify any specific intestinal procedure from a surgical point of view.

For deep intestinal endometriosis, the two main characteristics are multifocality, the presence of other lesions within 2 cm area of the main lesion and multicentricity, the presence of other lesions beyond 2 cm from the main lesion.

**Rectal shaving**

Shaving defined as superficial peeling of the serosal and subserosal endometriosis is a conservative approach and can be performed using several techniques. The shaving technique is not well standardised; each surgeon/gynaecologist performs it according to his/her experience, and the type of surgical instruments s/he is most familiar with.

Rectal shaving is a technique used when the lesions do not infiltrate the muscular layer of the anterior rectal wall or infiltrate it on a very small surface. As the name implies, this type of excision can be performed only on lesions in the middle and upper rectum (endometriotic lesions rarely infiltrate the inferior rectum).

In this technique, various types of surgical instruments can be used to detach the nodule from the surface of the anterior rectal wall, depending on the surgeon's experience, and the degree of infiltration of the rectal wall (distance between the lesion and the intestinal muscular layer). When the distance is small, scissors are preferred, to avoid any distant thermal injury, and thus the appearance of a distal digestive fistula.

This type of excision cannot be performed at the level of the sigmoid colon, or the level of the recto-sigmoid junction due to the very thin wall at this level, and less vascularization. This would predispose the patient to an extremely high risk of digestive fistula.

*Endometriosis. Rectal nodule. Rectal shaving. Left parametrial nodule. Ureteral shaving, Dr Mitroi, Youtube, Oct 2019*
At any time, during rectal shaving, there is the possibility of damage to the entire intestinal wall. At this point, shaving is abandoned and replaced with another excision technique: disc excision or bowel resection, depending on the severity and extent of the lesions.

Of all the types of excision of endometriotic lesions, this type has the lowest risk of complications (fistulas, organic lesions, nerve injuries), but it also has the highest recurrence rate of the disease.

**Disc resection**

Laparoscopic disc excision (anterior discoid resection) involves complete removal of the endometriotic lesion, in a block with the anterior wall of the digestive segment (anterior rectum). This type of excision can be divided into two categories: discoid excision done with a circular stapler and normal excision of the endometriotic lesion followed by the laparoscopic suture of the parietal defect (detach and suture).

This procedure has fewer post-op complications than the segmental resection. The discoid resection has two parts; a laparoscopic one during which the lesion is shaved and a perineal part, during which the rectal lesion is excised using a circular stapler. For nodules infiltrating the low rectum, a new technique has been introduced by Roman et al., named Rouen technique using a special stapler called Contur.

In the past, the surgical approach was dictated by the size of the rectal lesion. Thus lesions larger than 3cm had an indication for segmental resection. At the time of publication, a discoid excision can be done on nodules bigger than 5cm using multiple staples. An essential fact in surgical planning is the distance between the nodule and the anal orifice. After the bowel is mobilized, and the lesion is isolated, full-thickness or disc excision is performed followed by the suture of the bowel defect.

Some studies show that full-thickness disc resection of bowel endometriotic lesion is often incomplete (V. Remorgida, 2005), which explains the higher recurrence rate compared with the segmental resection. At the end of the procedure, the bowel is checked for leaking with an air leak test. Complications can include recto-vaginal fistulas, possible bowel stenosis, bladder issues and conversion to a segmental resection.

**Segmental resection**

Segmental resection refers to the removal of the affected part of the intestine followed by anastomosis of the two intestinal segments. In performing these interventions, an important experience in laparoscopic colorectal surgery is required. The learning curve in performing this procedure is considered complete after at least 30 laparoscopic colorectal resections.

This procedure is indicated in the case of multifocal lesions, large lesions, lesions located at the level of the rectum-sigmoid junction or the sigmoid colon. Also, in the case of stenosis, and obstruction, the rectal-sigmoid segmental resection represents the best therapeutic option. Intestinal segmental resection can also be performed in cases of lesions of the small intestine (most commonly in the ileo-cecal region).
At the Wellborn Endometriosis Center, when the preoperative examinations confirm intestinal endometriosis (MRI exams, CT exam), a mixed surgical approach is programmed: gynaecologist surgeon, a colorectal surgeon. In cases of negative or minimal involvement, the colorectal surgeon is notified when, intraoperatively, it is found that the endometriotic lesions are more extensive, affecting the integrity of the digestive tract.

The surgical procedure begins with the dissection of the intestine from the surrounding organs and tissues. It is estimated that the limit of rectal resection distal (distant) from the endometriotic implant should be around 1-2 cm. The (near) juxta-rectal approach is preferred, which allows the preservation of the mesorectum and the mesosigmoid and implicitly of the vascularization and innervation of the colon and rectum, thus reducing the risk of postoperative complications.

For the correct / complete resection of the digestive system in a block with the endometriotic nodule/s depending on the affected intestinal part, mobilization of the small or large intestines is performed.

After detaching the nodule from the adjacent structures, the rectum is sectioned and sealed using a linear stapler, the proximal (near) segment carrying the endometriotic implants is extracted through a suprapubic minimal incision, where the resection will be completed.

This procedure must be performed carefully so as not to cause damage to the neighbouring structures. The resection can be done using a linear stapler (which cuts and seals) and the anastomosis can be end-to-end or end-to-side, intracorporeal or extracorporeal.

In situations where a low colorectal resection is required, a temporary stoma may be needed to protect the anastomosis and accelerate is healing. At the end, the quality of anastomosis is verified through various techniques such as the air test.

Complications of segmental resection can be rectovaginal fistulas, LARS syndrome, infections, postoperative bleeding and stenosis.
Urinary Tract Surgical Procedures

In order to evaluate the extent of the disease affecting the urinary tract, a cystoscopy or ureteroscopy might be recommended. Urinary tract endometriosis is considered to be rare, with the bladder being the most affected organ. The lesions can be superficial or deep, and the surgical approach is dictated by the size and the depth of the nodules/lesions. Left untreated, urinary tract endometriosis can cause, ureteronephrosis and hydronephrosis. In most cases, the injury to the ureters is caused by nodules on the uterosacral ligaments.

Ureteral surgical procedures

When endometriosis tissues affect the ureters, it can cause ureteral compression or stenosis; the results of such involvement can be hydronephrosis or organ failure. Depending on the extent of the disease affecting the ureters, several surgical procedures can be done starting with the resection of the affected tissues. The procedures might be accompanied by a cystostomy (surgical creation of an opening into the bladder).

Ureterolysis (Ureteral shaving)

Ureterolysis is the first approach to identify and free the ureters from the blockage caused by adhesions, and fibrotic tissues, before the resection of the nodules. It is a procedure indicated to treat extrinsic ureteral endometriosis and/or limited ureteral involvement with no urinary obstruction. The dissection of the pelvic ureters, most often infiltrated by endometriotic lesions, aims to relieve ureteral obstruction, is one of the most challenging times of surgery for deep pelvic endometriosis. This operative time is very difficult because the ureters are extremely delicate structures, with very thin walls, and can be easily injured during excision of the endometriotic nodules from the uterosacral ligaments.

Endometriosis surrounding the ureter, and fibrosis requires meticulous and long dissection. Ovarian endometriomas adherent to the ureters can impair the visualisation during dissection, making the process even harder. The dissection to free up the ureters can be done by using sharp and blunt dissection combined electro-surgery. Different surgical gestures (ligation/dissection of uterine arteries) might be required in order to completely free the ureters.

Ureteroneocystostomy

When ureteral involvement is suspected before surgery (ureterohydronephrosis, dilation of the ureter - MRI, impaired renal function), a presurgical cystoscopy, is recommended to place the double J catheter.

In cases of partial or complete ureteral obstruction, resection of a portion of the ureter is necessary. Ureteroneocystostomy refers to the re-implantation of the ureter into the bladder. This procedure corrects distal ureteral injuries or obstruction in close proximity to the bladder. Re-implantation of the ureter can be done by laparoscopy or laparotomy. The ureters carry urine from the kidneys to the bladder, at the proximal end of the ureter is the renal pelvis and at the distal end is the bladder. The most affected part is the distal one.

Dr Mitroi, Youtube, Ureteroneocystostomy, Nov 2019
Endometriosis. Bowel endometriosis, ureterolysis, Oct 2019
The procedure starts with the freeing of the ureters, which should extend behind the affected segment, so the distal ureter is visible. Before commencing the resection, a dye injection should be used to highlight portions of the urinary tract, which will alert the medical team if there is a urine leak or an obstruction following the resection.

This procedure should be done in a team with an urologist, who might also perform a cystoscopy with a double-J ureteral stent placement if it has not been done before the surgery. The stent will remain in place for a couple of weeks as per the urologist recommendation.

There are various approaches that can be used for ureteral reimplantation, depending on the preference and experience of the specialist physician. The resected ureter should be inspected to ensure the removal of all endometriosis.

**Uretero-ureteral-anastomosis**

This procedure refers to an end-to-end anastomosis of the segments of the same ureter. The operative approach depends on the affected part of the ureter such as upper, midline or lower ureter. Before starting the procedure, a ureteral catheter should be placed to aid the procedure. At the end of the procedure, a Foley catheter is left in for a period of time as per the surgeon’s instruction.

After the ureter is identified and freed, the ureter is transected, and the affected part is removed completely. The ureter requires careful mobilisation in order to prevent injury to its adventitia. Adventitia is the outermost layer of an organ or vessel.

After the removal of the affected part, the ureters are spatulated and the ends are linked (anastomosis) by using absorbable sutures as a mucosoa to mucosa technique. A JJ stent should be placed before completion of the anastomosis, in order to help the surgeon to identify the two ends of the ureter.

**Bladder Surgical Techniques**

Bladder endometriosis was described first by Judd in 1921 and refers to the full-thickness infiltration of the detrusor muscle (primary muscle of the bladder) of the trigone and the bladder apex (dome). When bladder endometriosis is suspected, a cystoscopy is recommended to obtain more information. Surgical procedures for bladder endometriosis depends on the size, and depth of the infiltration of the lesions into the bladder wall, and can be partial resection or partial cystectomy. The procedures can be done by laparoscopy or laparotomy, and intracorporeal suturing will be needed to repair the bladder.

A catheter is placed in the bladder and will be removed as per the surgeon’s recommendations. The procedure starts with the surgeon investigating the pelvic cavity, and the evaluation of the bladder and the vesicouterine space. During bladder surgery, care should be taken not to injure the ureters. For superficial lesions, peritoneal resection can be used, while for deeper lesions of the bladder muscularis, shaving of the nodule can be done.

Partial cystectomy of the bladder is used for total infiltration of the bladder muscularis or mucosa. The laparoscopic approach starts with the dissection of the vesicouterine space.
After the bladder is freed, and the nodule identified, the area next to it is dissected. The nodule is then entirely removed either by partial-thickness or full-thickness resection. After the resection, the bladder injury is repaired using absorbable suture, and a check-up is done using an irrigation type fluid.

**Surgery outcomes**

Charles Hammond noted in 1978 that before considering various forms of medication therapy, conservative surgery should be considered. The three primary outcomes of endometriosis surgery are:

- Pain reduction
- Fertility improvement
- Disease eradication

A systematic review done by Pundir et al., 2017 shows that at 12 months post-surgery, patients reported a significant improvement in symptoms of dysmenorrhea, dyschezia, and chronic pelvic pain. In 1975, Robert Kistner noted in the management of endometriosis in infertile patients, that, the conservative surgical procedure results in a subsequent pregnancy in 40 to 90% of patients.

A study done by William Andrews, 1975, showed a pregnancy rate of 58.9% in patients treated with surgery and 25.8% in the pseudopregnancy group. Out of 301 cases operated, 81 of them had a second surgery over a 14 year period.

A retrospective study done by Jamil Fayez et al., 1988, showed that pregnancy rate and disease resolution was higher in patients treated with surgery than in patients treated with danazol. A study done on 101 patients treated with surgery due to infertility, 52 patients conceived one year after surgery. A 15 year follow up study done by Wheeler JM et al., 1983 on 423 patients treated with conservative surgical procedures, showed a recurrence rate of 4 cases in the first postoperative year to 57 cases in the eighth postoperative year.

Another study done by Yeung et al., 2011, on 20 teenagers who underwent excision surgery followed up for 66 months, eight patients had a repeat surgery, and the rate of endometriosis (diagnosed visually or histologically) found at surgery was zero.

Sylvie Gordts et al reported symptoms recurrence in 6 out 74 patients who underwent surgery for deep infiltrating endometriosis, a year and a half after the surgery. Three patients underwent a second surgery, two of them had involvement of bowel serosa, and in one laparoscopy showed only recurrence of an endometriotic cyst.

Punnonen R et al., 1980, reported a recurrence of 132 cases out of 903 cases, over a period of 6-10 years. The re-operation was performed within 1 year after the primary operation for seven patients, within 1-5 years for 91 patients and more than 5 years after the primary surgery for 34 patients. The authors noted that Gestagen therapy after the primary surgery had no effect on the recurrence rate.

Nikkanen V et al., 1986, noted a recurrence in 120 cases out of 801 operated cases over a period of 7 years. The incidence of endometriosis was higher in postmenopausal patients than in young patients. Puolakka et al., 1980, noted symptoms improvement after surgery in 187 patients out of 208, over a period of 1-4 years.
Kristina 4 months after her excision surgery for diaphragm and pelvic endometriosis

Alexandra

Kristina after her 4th surgery for endometriosis
Chapter 5. Endometriosis and Infertility

Studies have shown that 30-50% of people with endometriosis have infertility. In a study done on 77 patients with nonpigmented endometriosis lesions, 70 of them were infertile. The authors concluded that the unexplained infertility is exclusive to the nonpigmented appearance of endometriosis. In addition to a gynaecological condition that affects fertility, other factors such as age, general health of both partners, malefactors, hormonal disorders, sexually transmitted diseases can affect a person's/couple's chances of conceiving.

Based on age, if a person/couple has not conceived naturally within 6-12 months of regular intercourse, medical help should be sought. To establish the cause/s of infertility, several tests are necessary:

Tests for the female partner:

• Tests to check FSH and LH levels
• AMH and AFC
• Chlamydia test
• Ultrasounds
• Tests to check tubal patency such as hysterosalpingogram and sonohysterogram
• Laparoscopy and hysteroscopy

Tests for the male partner:

• General physical examination
• Semen analysis
• Chlamydia test
• Hormones testing
• Scrotal ultrasound
• Specialised sperm function tests

Endometriosis and reproductive treatments

Endometriosis affects more or less the following:
• Ovarian reserve
• Quality of oocytes
• Maturation of oocytes
• Tubal function
• Fertilisation itself between oocyte and sperm cell due to a toxic pelvic environment in endometriotic lesions
• Embryo implantation

Once pregnancy occurs, spontaneously or assisted, its evolution will not be influenced by the endometriotic lesions. Conservative surgical procedures should be considered for patients that wish to preserve their fertility. Conservative therapy protecting fertility refers to laparoscopy and involves:

• excision of peritoneal implants
• resection of deep infiltrating implants
• excision of pelvic adhesions
• removal of ovarian endometriomas

Surgery for endometriosis, especially in patients of reproductive age, should be as conservative as possible and is better to be performed by a complex team, a gynecologist with surgical experience in endometriosis, general surgeon, urologist, and ideally, under the guidance of a specialist in assisted reproduction, which will always keep in mind the integrity of the ovaries and the best conservative approach for future fertility.
Hormonal medical management of endometriosis is intended to reduce estrogen levels and keep lesions quiet (oral contraceptives, GnRH analogues, etc.) Overall, studies have shown that there is no proven progression of endometriosis after IVF with no pregnancy.

Unfortunately, the stages III-IV of the disease produce infertility, and the only options to get pregnant remains ovarian stimulation treatments and IVF. In the case of ovarian stimulation treatments with no pregnancy, the lesions may continue to evolve with new active outbreaks or could remain stationary. Endometriosis itself is not a medical contraindication for ovarian stimulation treatments, which are often the only way to obtain a pregnancy.

**Ovarian stimulation** protocols for IVF can be adapted and customised for patients with advanced stages III-IV of endometriosis; according to endometriosis therapeutic protocols, these stages benefit postoperatively of 3-6 months of GnRH analogues (Zoladex, Dipherelin, Triptorelin, etc.) to produce ovulation suppression. Controlled ovarian stimulation for IVF will usually be added, as a long protocol in the last month of inhibitory treatment.

Also, studies show significant differences in the success of IVF treatments in advanced stages of endometriosis III-IV compared to mild stages I-II or tubal infertility; these differences are related to:

- higher doses of ovarian stimulation
- smaller number of oocytes
- lower rate of fertilization
- smaller number of embryos
- lower rate of implantation
- lower chance of clinical pregnancy per embryo transfer

Advanced stages III-IV, after surgery and IVF, will give the best chances of success to patients younger than 30-35 years old. Mild Stages I-II will have after surgery a good chance of pregnancy either with spontaneous conception or intrauterine insemination, depending on sperm count parameters.

**AMH, AFC and FSH**

AMH is a significant parameter in the evaluation of ovarian reserve, but it is not the only one. In order to evaluate the fertility of the woman in her biological evolution, there are several parameters, which provide essential information about both the ovarian reserve, practically the oocyte reserve, the functional reserve of the ovaries, the ability of the ovaries to respond to the ovarian stimulation treatments, and implicitly on the prognosis of both spontaneous pregnancy and in vitro fertilization procedures.

Women's fertility begins to decline naturally after 30 years of age, accelerated after 35, and after 40 years, fertility will be dramatically reduced or even absent. Along with AMH, the other three essential parameters are:

- FSH and Estradiol basal, tested between days 2 - 3 of the menstrual cycle; estradiol and basal FSH are closely related, and their correct interpretation is made with both values;
- AFC, that is, the number of antral follicles, ideally counted between days 2 - 5 of the menstrual cycle, by ultrasound examination;
**Methods of Assisted Reproductive Technology (ART)**

ART refers to treatments and procedures that aim to achieve pregnancy, an option for people who can't conceive naturally or who have not obtained a pregnancy through other infertility treatment options.

**In Vitro Fertilisation (IVF)** is a method of assisted reproduction which consists of obtaining embryos in the laboratory, by fertilizing an oocyte (egg) with a sperm, and then introducing the embryos into the uterus for pregnancy. The steps of IVF are:

- Ovarian stimulation
- Eggs retrieval
- Fertilization
- Embryo transfer

**Intrauterine insemination** is a simple method of assisted reproduction. It consists of introducing the semen sample, prepared in the laboratory, into the uterine cavity, when the female partner is ovulating. The processing of the semen sample in the laboratory aims to select the mobile sperm, the selection being made on the criteria: concentration and motility. The sperm is not selected on other criteria: quality, morphology, etc.

Intrauterine insemination can be performed both on the natural cycle and on the stimulated cycle. Intrauterine insemination can be done with:

- fresh sperm from the husband/partner prepared in the laboratory;
- sperm from an anonymous/known donor, from the sperm bank - recommended when the sperm sample in the couple does not have the appropriate parameters (azoospermia) or if the patient has no partner/husband;

**The effects of endometriosis surgery on fertility**

In cases when the patient has no symptoms, and s/he has been trying to conceive naturally for some time, in the absence of any visible abnormalities (fibroids, cysts, endometriosis) then exploratory surgery might be recommended. In cases when there is symptomatology, and the disease is clinically visible, depending on the stage, the methods of treatment for infertility can be medication and/or surgery.

The opinions regarding the effects of surgery on fertility are divided. Some studies show that surgery improves pregnancy rate, and other studies show that surgery has a negative impact on the Anti-Mullerian Hormone levels used to measure the ovarian reserve.

A scientific paper by the Royal College of Obstetricians and Gynecologists, The Effect of Surgery for Endometriomas on Fertility published in 2017, mentions that the current guidelines often rely on the evidence from either small and/or retrospective controlled studies, and the presence of endometrioma can cause a dilemma during the treatment.

The ovarian endometriomas are classified by the American Society for Reproductive Medicine as a moderate or severe stage, and they are often associated with disease elsewhere such as pelvic and intestinal disease. The inflammation caused by the ovarian endometrioma can affect the quality oocyte and ovarian reserve, especially if endometriomas occur bilaterally. A study done on 70 patients with unilateral endometriomas, concluded that ovarian endometrioma negatively affects the rate of spontaneous ovulation, and it may not be excluded that ovarian reserve is affected only by surgery.
Pregnancy after surgery

The ESHRE\(^{44}\) recommends that for stages 1 and 2, operative laparoscopy including adhesiolysis should be performed and in stage 3 and 4, clinicians can consider operative laparoscopy, instead of expectant management, to increase spontaneous pregnancy rates. Wellborn Endometriosis Centre has an increased pregnancy rate, naturally or assisted in patients undergoing endometriosis surgery, with patients conceiving a couple of months after the surgery.

A study done by Roman et al., shows that colorectal endometriosis surgery\(^{135}\) has a high postoperative fertility rate. The authors mention that deep endometriosis can affect fertility, and due to the symptoms caused, regular intercourse necessary for natural conception can be impeded. A study done on 43 patients\(^{136}\), the surgery revealed superficial lesions in 10 patients only, and the natural conception rate was 41.9% during the first year after surgery in infertile patients with endometriosis and no other factors.

Jason Abbot\(^{137}\) concluded that surgery for endometriosis might have dual effects; decreasing pain and enhancing fertility. The three options for endometriosis patients to become pregnant are: expectant management, IVF and surgery followed by one of the previous options. Surgery is known to improve the quality of life and symptoms, therefore is more likely for the patient to have regular timed intercourse.

Medical therapies

The NHS UK mentions that hormonal drugs have no effect on adhesions and do not improve fertility. A Cochrane review of 23 trials involving 3043 patients with endometriosis\(^{138}\) done by Hughes E et al., concluded that due to significant period of amenorrhea associated with ovulation suppression, fertility might be reduced; therefore, ovulation suppression cannot be recommended as a standard therapy for endometriosis-associated infertility in minimal to mild endometriosis.

Based on a Cochrane review, ESHRE\(^{44}\) recommends clinicians not to prescribe hormonal treatment prior to or after the surgery to improve spontaneous pregnancy rate, as suitable evidence is lacking, and they have severe side effects. Dominigue de Ziegler\(^{139}\) concluded that the use of oral contraceptive for 6 to 8 weeks prior IVF or ICSI (an IVF method) is beneficial in endometriosis. In severe endometriosis, including endometriomas, this method obtained a pregnancy rate similar to that of unaffected women of similar age.

At the time of producing this publication a review by Cochrane\(^{140,141}\) is currently in process to determine the effectiveness and safety of long-term GnRH agonist therapy versus no pre-treatment or other pre-treatment modalities, (such as long-term continuous combined oral contraceptive or surgical therapy) before standard IVF or ICSI in patients with endometriosis.

Ovarian reserve- excision vs ablation

The surgical methods of treating endometriomas considered to be effective based on cohort studies are excision and ablation of the cyst wall. ESHRE\(^{44}\) recommends that in infertile patients with ovarian endometrioma undergoing surgery, clinicians should perform excision of the endometrioma capsule, instead of drainage and electrocoagulation of the endometrioma wall, to increase spontaneous pregnancy rates.
Regarding the two surgical techniques for ovarian endometrioma, ESHRE mentions that both methods carry potential risks for ovarian reserve, either by removal of normal ovarian tissue during excision or by thermal damage to the ovarian cortex during ablation.

Studies have shown that excision of the cyst wall has better results in alleviating pain symptoms, recurrence of endometrioma, and spontaneous pregnancy than drainage or electrocoagulation of the cyst, which has a significant increase in the risk of cyst recurrence.

When comparing both techniques, stripping of the cyst wall vs ablation, some studies show that excision has a negative impact on the ovarian reserve, however, it is possible that the ovarian reserve was affected prior to surgery. Furthermore, other studies have shown that the lost ovarian reserve can be regained, and the recurrence rate is higher when ablation is used.

Endometriosis effects on pregnancy

Studies show that 60-70% of patients affected by endometriosis can conceive. Therefore, the coexistence of endometriosis with pregnancy will occur. This will lead to the mutual influence of the two conditions: pregnancy might influence the evolution of endometriosis, and endometriosis might affect or not the development of pregnancy.

A cohort study done by Nurses' Health Study II, showed that endometriosis was associated with spontaneous abortion, ectopic pregnancy, preeclampsia, and low birth weight. Also, endometriosis, due to the inflammatory and fibrous adhesions it develops, can create pain throughout pregnancy.

This is because the uterus, which is 'stuck' through these adhesive processes to the neighbouring structures (ovaries, uterine tubes, bladder, rectum, sigmoid colon) is greatly increased in size. Thus, the anatomical relations are altered, the uterus pulling the adjacent organs, creating tension and, implicitly, pain.

During pregnancy, endometriotic nodules in the recto-vaginal space may increase greatly, and vaginal birth should be contraindicated in terms of perineal laceration (tear) that may occur during the expulsion (2nd stage of birth, dilation, expulsion, placental). Also, pelvic pain may increase and may be confused with pain caused by uterine contractions.

When there is more advanced endometriosis, such as deep endometriosis, affecting the bladder or recto-sigmoid, handling of the uterus and the extraction of the fetus must be done with gentle care. This is necessary because the structures affected by the disease (endometriosis), and in the context of pregnancy, are very fragile and can be easily injured during these manoeuvres, whether the birth is vaginal or by caesarean.
Chapter 6. Other Info

Adenomyosis

Adenomyosis was described by Rokitansky in 1860 as adenomyoma, and in 1869 by Von Recklinghausen. Adenomyosis is the presence of endometrial glands or stromal tissues into the myometrium. The tissues are situated at least 2.5 mm below the endometrial-myometrial junction (Wang Ph et al., 2009).

Adenomyosis is similar to endometriosis, manifested by intense pelvic pain. During menstruation, these cells are stimulated by sex hormones and cause intense pelvic pain (menstrual cramps). Also, menstruation is more abundant than usual, and clots may appear in the menstrual blood.

Symptomatology, when present, is often ceasing during menopause. As opposed to endometriosis, the incidence of adenomyosis is not known. Kunz et al., 2005, have reported a prevalence of up to 90% using MRI, in patients with endometriosis. Adenomyosis co-exists with other pathologies such as endometriosis and fibroids, and it can also be the only pathology. The authors of “Adenomyosis, a neglected diagnosis” noted that during surgery in 65% of cases, adenomyosis was not recognised.

In medical literature, adenomyosis is described as a disease commonly found in patients age 30-50. This is mainly due to the fact that adenomyosis is diagnosed after hysterectomy; therefore, patients are most likely to have a hysterectomy from late 30s. Based on doctors and patients reports, adenomyosis affects people of all ages. The medical team at Wellborn Centre have seen a few patients age 25-30 with adenomyosis diagnosed during surgery for endometriosis.

Symptoms

The symptom of adenomyosis is variable, but it is dominated by pelvic pain. One-third of the patients have no symptoms, but for most of the patients, the pain and abnormal vaginal bleeding affect their daily lives.

The most common symptoms are:
- Extremely painful menstruation;
- Heavy menstruation/clots;
- Pain during intercourse;
- Chronic pelvic pain - "cramps" felt in the pelvic area of very high intensity;
- Pain radiating in the bladder,
- Pain during urination;
- Pain during bowel movements;
- Abnormal vaginal bleeding - metrorrhagia - bleeding between periods;

Adenomyosis can be diffuse - affects most of the endometrial wall and focal, which can be:
- adenomyoma (affected focal area, apparently encapsulated) characterized by epithelial glands associated with a stromal component; (Peterson M, 2009)
- cystic adenomyosis, a cystic structure lining the endometrium and covered with the uterine smooth muscle, containing old blood cyst fluid; (Yan-Yan et al. 2019)
- polypoid adenomyosis, a rare uterine endometrial polypoid, mesenchymal origin;
- endocervical adenomyosis, benign endocervical glands and smooth muscle typically located in the endocervix;
- retroperitoneal adenomyotic disease, adenomyotic disease of the retroperitoneal space; (Donnez J et al. 2001)
Diagnosis

In 1895, Thomas Cullen had reported his first case of adenomyoma of the uterus. Cullen has identified two main symptoms that can be used to diagnose adenomyosis; lengthened menstrual periods, and a great deal of pain (Benagiano et al., 2009). However, the two symptoms identified by Cullen are also symptoms of endometriosis and fibroids.

Transvaginal and MRI might be used as a diagnostic method. As a clinical sign, adenomyosis appears as a bulky/enlarged/asymmetric uterus.

Treatment

The only effective treatment that eradicates the disease is a hysterectomy. The first treatment line for adenomyosis mild to moderate symptoms is anti-inflammatory drugs, and hormonal medication in various forms and administration, to reduce the pain and abnormal bleeding. Temporary medical menopause might also be offered.

For moderate to severe symptoms, several methods can be used, such as:

- Uterine arterial embolization, tiny particles are injected into the blood vessels through a catheter in the groin. The particles aim to cut off the blood supply to the adenomyosis. This is less invasive than surgery and may help preserve fertility. It is likely to improve symptoms for a couple of years.
- Laparoscopic uterine nerve ablation (LUNA) involves the destruction of a small segment of the uterosacral ligament that carries nerve fibres within the pelvis (NICE UK).
- Presacral neurectomy is the surgical removal of the group of nerves that conducts pain signals from the uterus to the brain.
- Adenomyomectomy for focal adenomyosis, a procedure similar to myomectomy.

Adenomyosis and fertility

In a large number of patients, endometriosis and adenomyosis co-exist; therefore, due to limited available evidence, it is not clear how or if adenomyosis affects fertility. Studies and statistics show that adenomyosis is found in patients who have given birth multiple times. Adenomyosis can also affect nulliparous patients.

Adenomyosis may impair fertility by affecting the uterotubal transport, endometrial function and receptivity, and implantation. The uterotubal transport is impaired due to intrauterine anatomical distortion that can potentially block sperm migration and embryo transport. A higher density of macrophages and increased inflammatory response in adenomyosis patients can also affect fertility.
Endosalpingiosis

Endosalpingiosis is the presence of tubal type epithelium outside the fallopian tubes and is the result of misplaced Mullerian tissues during organogenesis (Batt RE, 2013). Due to its rare entity, endosalpingiosis is under-recognised and can be mistaken for an adenocarcinoma.

Endosalpingiosis may occur in ovaries, bladder, fallopian tube, uterine serosa, myometrium, pelvic peritoneum, axillary lymph node, omentum, bowel serosa and umbilicus. Although it is found mostly in premenopausal women, it has been found in postmenopausal women and in men as well.

Alexander Gallan et al., have reported 3 cases of benign müllerian-type glandular inclusions in men undergoing either prostatectomy or cystoprostatectomy. The authors concluded that the finding of Mullerian glands in men identical to endosalpingiosis in women supports the Mullerian theory.

A study done by Keltz MD concluded that endosalpingiosis may be found in association with chronic pelvic pain. Other symptoms include infertility, urinary symptoms, and in 1/3 of cases endosalpingiosis is associated with endometriosis and the two diseases have different clinical presentations. Endosalpingiosis is diagnosed only through surgical biopsy.

Endocervicosis

Part of the four Mullerian illnesses, endocervicosis is defined as the presence of endocervical-type mucinous glands outside the cervix, and affects the bladder, vagina and the cervix. Heretis J et al., have reported a case of bladder endocervicosis in a 67 year old woman with a history of left flank pain and dysuria. Ogah K et al., have reported the case of a 45-year-old woman presented with complaints of chronic pelvic pain, dysmenorrhea, irritative lower urinary tract symptoms and cyclical haematuria. The histopathology reported the presence of endometrial, endocervical and endosalpingeal tissues within the bladder mass.

Endocervicosis is considered the rarest of the Mulleriosis diseases; can be asymptomatic or symptomatic, causing pelvic pain, hematuria, urinary frequency and dysmenorrhea. Habiba M. based on the literature review concluded that endocervicosis and endosalpingiosis should be considered in the differential diagnosis of pre- and postmenopausal patients with pelvic pain, dyspareunia, lower abdominal pain or discomfort, dysuria, frequency or hematuria.

Fibroids

Fibroids, also known as myomas or fibromyomas, are benign (non-cancerous) tumours of the womb. They are growths of smooth muscle and fibrous tissue and varies in size from as small as a pea to a melon. At least one in five women develops a fibroid at some stage in their life, and uterine fibroids have an extremely low risk of malignancy (transformation into cancerous disease) - 1 / 3000-5000.

Type of fibroids
- subserosal fibroids - located on the external surface of the uterus;
- intramural fibroids - the most common - located in the thickness of the uterine wall, and may subsequently have a suberous or submucosal development;
- submucosal fibroids - present in the vicinity of the uterine cavity;
- cervical fibroids are found in the wall of the cervix (neck of the womb);
Symptoms and signs

The majority of women with fibroids show no symptoms. Many women are unaware that they have fibroids. However, if symptoms develop, you may experience one or more of the following:

• heavy bleeding during menstruation;
• painful menstruation;
• intermenstrual bleeding - especially submucosal fibroids;
• pelvic pain may be caused by compression of the neighbouring nerves or organs or in association with another pathology, adenomyosis, endometriosis;
• backache, or pain in the legs;
• discomfort, or swelling, in the lower abdomen, particularly if the fibroids are large;
• urinating frequently;
• constipation;
• pain or discomfort during sex;
• infertility;

Diagnosis

Fibroids are often found during a routine gynaecological examination. The most important imaging means for the detection of uterine fibroids is the ultrasound examination, because it provides accurate information on the location, number and size of the fibroids and sometimes also the therapeutic indication.

Treatment

Depending on the symptoms and age, the treatment can be medication to reduce the bleeding and the pain such as birth control, painkillers, tranexamic acid, Mrena coil, or hormonal medication to induce menopause.

Surgical treatment is based on the size and location of the fibroids and can be minimally invasive procedures such as endometrial ablation and uterine embolization, hysteroscopy and laparoscopic myomectomy. In cases of large fibroids, open myomectomy is performed. When fertility is not desired, a hysterectomy is performed.

Endometriosis and PCOS

Polycystic ovary syndrome (PCOS) is a hormonal disorder common among people of reproductive age. The exact cause is unknown; however, research has shown that PCOS is hereditary. PCOS is characterised by irregular periods, a higher-than-normal production of male hormones and polycystic ovaries (12 or more follicles on one ovary). The exact number of people affected by PCOS is unknown. In the USA, statistics show a prevalence of PCOS is 4-12%, and in some European studies, the prevalence of PCOS has been reported to be 6.5-8% in people of childbearing age.

Sign and Symptoms

- Menstrual dysfunction
- Anovulation
- Persistent acne
- Excessive hair growth on the face, chest, arms
- Thinning hair on the head
- Difficulty in getting pregnant
- Weight gain
- Sleep apnoea
- Enlarged ovaries
- Insulin resistance
Diagnosis

Patients presenting with two out of three of these symptoms, irregular periods, high androgen levels and multiple cysts, are diagnosed with PCOS. Blood tests and imaging can diagnose PCOS. Although PCOS affects fertility, many people diagnosed with PCOS can conceive.

Also, not in all cases, patients will experience symptoms. PCOS cannot be cured, but symptoms can be made manageable with lifestyle changes and medication to treat irregular periods, excessive hair growth, and fertility problems. Patients with PCOS have a higher risk of pregnancy complications, diabetes and high cholesterol.

Laparoscopic ovarian drilling is an option for patients' who are still not ovulating after losing weight and trying fertility medicines. The procedure involves puncturing the ovaries to correct the hormonal imbalance and to restore their normal function.

Occult Hernias

A hernia is when an organ pushes through an opening in the muscle, or tissue that holds it in place. An occult hernia is a very small hernia that is not palpable on physical examination.

Inguinal and pelvic floor hernias in women can cause chronic pelvic pain. Chronic pelvic pain is pelvic pain of a couple of months duration and is usually attributed to the reproductive tract. Because of this, many patients are undergoing hysterectomy and ovaries removal with no changes in their pain after the surgery. Hernias can be inguinal, incisional, umbilical and pelvic floor hernias (femoral, perineal, sciatica).

Michael Crade, from the Department of Obstetrics and Gynecology, University of California, have found 97 cases of unexpected hernias in patients sent for pelvic ultrasounds due to the pain. The authors’ recommend looking where the patient hurts and to include a pelvic hernia as a possible cause of female pelvic pain.

Hernias can cause pain with intercourse, and femoral hernias can cause pain radiating down the front of the leg. Inguinal hernias are hard to diagnose by palpation. Hernias same as endometriosis are considered to be rare; therefore, a gynaecologist might not consider hernia as a cause of pelvic pain.
Anatomy of the Female Pelvic Floor Muscles
Internal View

Pubococcygeus
Coxygeus, right
Coxygeus, left

Internal Anal Sphincter

Iliococcygeus, right
Iliococcygeus, left

Puborectalis, right
Puborectalis, left

Perirectal Fibres

Anatomy of the Female Pelvic Floor Muscles
Posterior View

Piriformis, left
Piriformis, right

Cocygeus, left

Iliococcygeus, left

Iliococcygeus, right

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Recurrence in endometriosis

Based on clinical studies, recurrence in endometriosis is due to the method of treatment used and/or incomplete excision\textsuperscript{183}. However, some doctors’ link recurrence to the way the disease occurs (reflux menstruation). Endometriosis is not the only cause of pelvic pain; therefore, it is important to know that persisting pain after excision surgery done by an experienced endometriosis specialist, does not necessarily mean recurrence of the disease.

There are very few studies done to observe the long term benefits of excision vs ablation. Ablation, ovarian cysts drainage or conservative surgery has a high rate of recurrence of up to 80%. Based on direct observation, patients’ reports and studies, excision surgery has the lowest recurrence rate, and at the same time can be the curative method in some cases. With excision, all affected tissues are removed until healthy ones are seen. To do this, the surgeon needs to know the pelvic anatomy very well and to be well trained in laparoscopy.

A 10 years excision recurrence study\textsuperscript{183} found a maximum cumulative rate of 19% achieved in the 5th postoperative year. When surgery is done by a multidisciplinary team with experience in endometriosis surgery, a team that can treat from simple to complex cases using excision, the recurrence is low, and in some cases is zero. There are some cases when recurrence is higher due to different factors, such as:

\textbf{Endometrioma cysts.} Recurrence for endometrioma cysts is slightly higher after excision surgery than other types of endometriosis. This is because often during surgery only the visible endometrioma cysts are removed.

\textbf{Note:} Hemorrhagic cysts after surgery are common, and both doctors and patients might interpret this as recurrence of endometriomas. These cysts do go away typically in a couple of months; therefore, is important to maintain post-surgery contact with the doctor.

\textbf{Rectal shaving.} For rectovaginal nodules, when surgical conservative approach is being used, shaving, there is the presumption that recurrence is higher according to some studies. A study done by Prof Wattiez, to demonstrate the difference on a medium-term between the three surgical methods used for rectovaginal nodules, concluded that rectal shaving has a higher recurrence of the symptoms\textsuperscript{184}. Another study done by Prof Roman and Dr Donnez\textsuperscript{185} showed that post-op complication rate is lower with rectal shaving and a higher recurrence rate has not been demonstrated.

Methods of preventing surgical adhesions

In gynaecologic surgeries, adhesions result from abdominal and pelvic surgical procedures, especially open abdominal surgeries, and are the result of trauma to the mesothelium (membrane) by surgical handling, instrument contact and foreign materials.

The process of adhesion formations starts immediately after surgery, and it lasts up to 7 days. Trauma to the tissues causes inflammation followed by different biological activities to repair the damage, starting with macrophage (large cell found especially at sites of infection, playing a role in the detection and destruction of bacteria), fibroblasts (wound healing cell) and fibrin (a protein involved in the clotting of blood).
A meticulous surgical technique is a primary way of preventing adhesions. When the fibrinolytic activity (a process that prevents blood clots from growing and becoming problematic) is suppressed, the fibrin adhesions are formed. The fibrinolytic activity suppression can be prevented by paying attention during surgery to haemostasis, tissue handling, constant irrigation, and prevention of infection.

Ovarian suspension is a procedure whereby the ovaries are suspended to the anterior abdominal wall for 36-48 hours after the surgery. The purpose of this method is to prevent contact between the ovaries, and the excised nearby peritoneum in order to heal.

A study done by Wee Liak Hoo et al., found that temporary ovarian suspension does not result in a significant reduction of postoperative ovarian adhesions. Another study done on 80 patients at a hospital in Bologna, Italy, concluded that ovarian suspension seems to be an additional effective surgical procedure to reduce adhesions.

Anti-adhesion gel-based agents, solid and liquid such as hyaluronic acid are also used to reduce prevention of adhesions. A Cochrane literature review on the use of different agents found insufficient evidence on the effectiveness of anti-agents in the prevention of adhesions.

Endometriosis surgery complications

Endometriosis surgery is one of the most difficult and complex surgeries in the human body. Endometriosis can cause inflammation, organ dysfunction and distortion of the normal anatomy.

Most surgical complications are minor and resolve quite quickly and, in the hands of experts, both minor and severe complications can be avoided and reduced as much as possible.

Intraoperative surgical complications include excessive bleeding, damage to organs and big vessels, thermal and direct traumas, etc. Postoperative complications include infections (urinary, incisions), constipation, urinary difficulties, prolonged vaginal bleeding, low anterior resection syndrome, etc.

The potential complications of deep infiltrating endometriosis surgery can be divided into:

- Intraoperative complications;
- Immediate postoperative complications;
- Delayed postoperative complications;

Intraoperative complications may be related to trocars insertion or complications caused by extensive pelvic dissections and resections.

The lesions caused by the creation of pneumoperitoneum are:
- vascular lesions such as vessels of the anterior abdominal wall, common iliac vessels, and vessels of the stomach
- abdominal visceral lesions (stomach, epiplon, transverse colon, small bowel)

Intraoperative lesions caused by extensive pelvic dissections can include:
- lesions of the structures of the digestive tract;
- liver injury - when there is endometriotic liver injury or due to the diaphragmatic extent of the disease - liver mobilization is required;
- urinary tract injuries;
- vascular lesions:
- uterine vessels (often one or both uterine arteries are “sacrificed” during excision of large uterosacral and parametrial nodules);
- automatic and somatic nerves;
Lesion can be produced during the 'detachment' of these organs from the endometriotic lesions, during the excision of the endometriotic nodules, or during the restoration of pelvic anatomy. It is important to recognize these types of lesions and to treat them immediately, reducing, therefore, the risk of postoperative complications. The patient should always be informed of all intraoperative incidents and the risks that may arise as a consequence.

The immediate postoperative complications are mainly represented by abdominal bleeding, which, depending on its severity (quantity, blood flow), must be resolved urgently or may be delayed.

Delayed postoperative complications can are those of extensive pelvic surgery and can include digestive and urinary fistulas, and intestinal occlusion. Intestinal occlusion can form after surgery, due to postoperative adhesions. It is quite rare in laparoscopic interventions and requires surgical intervention.

Uroperitoneum (the presence of urine in the peritoneal cavity) may occur when there is a lesion in the bladder or in one of the ureters. It appears (as in the case of uro-vaginal fistula) when accidental injury of the bladder or pelvic ureter occurs during surgery.

Surgical instruments based on thermal effect, and used for different surgical gestures can cause thermal injuries of the various tissues adjacent to the endometriotic lesions excised. During surgery, these injuries are 'invisible', causing postoperative complications (digestive, urinary fistulas).

Haemorrhagic cysts are a common postoperative complication following surgery for endometriomas, and they can appear within days/weeks after the surgery during ovulation. After surgery, as part of normal ovulation, many patients will develop a haemorrhagic cyst from ovulation, often formed in the empty space following endometrioma removal. In some cases, the haemorrhagic cyst can be bigger than the endometrioma removed, and the patient will complain of pain in the area.

Fistulas

A severe complication of deep endometriosis surgery is represented by the intestinal and urinary fistulas. A fistula is an abnormal communication between two organs or vessels that do not usually connect. The rectovaginal fistulas occurrence varies between 2.5% and 10%, according to published studies. The risk of this complication increases when the endometriotic nodule affecting the recto-vaginal space exceeds 4 cm.

Digestive fistulas, are manifested by signs of severe infection: diffused, severe abdominal pain, persistent fever (> 38-39 degrees Celsius), altered general condition, nausea, vomiting. This risk is much greater when excision of the endometriotic nodule imposes a resection of the vaginal posterior wall (most commonly affected by the disease).

Also, the risk of fistulas varies depending on the type of excision used: rectal shaving, disc excision, segmental intestinal resection. The more "radical" the surgery is, the higher the risk of recto-vaginal fistula.
Alarm signals for recto-vaginal fistulas include fever, acute postoperative pain (between day 1 and postoperative day 10), and altered general condition of the patient. An important role in strengthening the diagnosis of suspicion of this complication may be the paraclinical signs of inflammation.

A vesico-vaginal fistula may be caused by bladder peritoneum dissection, hysterectomy, or excision of bladder nodules. Vesico-vaginal fistula is manifested by the loss of urine in the vagina, which is extremely disturbing for the patient. The complication is also resolved surgically, but the surgery can be delayed. Conservative treatment can be done by inserting a bladder catheter for a few months.

Careful postoperative monitoring (in-hospital and after discharge) is important.

**Anaesthesia-Wellborn**

General anaesthesia is one type of anaesthesia necessary for surgical interventions. In endometriosis surgeries, due to the long duration of the surgery, general anaesthesia is the most used type of anaesthesia. The anaesthetic is based on:

- Hypnosis (patient's sleep)
- Anxiolysis (diminishing the patient's state of anxiety)
- Amnesia (the patient loses memory strictly during the surgery, without affecting the background memory)
- Analgesia (the patient does not feel the pain)
- Muscle relaxation for the benefit of surgery

Anaesthesia is carried out using inhaled and intravenous anaesthetic agents, depending on each individual patient.

After the patient falls asleep, an intubation probe is inserted into the patient's throat through the vocal cords; this probe is connecting the patient to an anaesthetic machine that breathes for the patient during the operation. At the end of the operation, this probe is removed from the patient's throat without the patient feeling pain nor remembering it afterwards.

General anaesthesia provides psychological comfort to the patient and has the advantage of being able to be used for patients allergic to local and general anaesthetics because of the multiple ways that a general anaesthetic can be made.

Disadvantage of general anaesthetic is that it requires a preoperative patient preparation, has high costs and can generate adverse reactions such as nausea, vomiting, irritation of the vocal cords for several hours, drowsiness. Although mentioned in the literature, there are no cases of an intraoperative awakening of the patient in Wellborn hospital. At the end of the surgical procedure, the anaesthetist decides at the appropriate time to cease the administration of any anaesthetic substances and starts monitoring the resumption of spontaneous respiration of the patient, and the return to the state of consciousness.

In 99.9% of cases, at Wellborn we do not use antagonist substances of anaesthetics to wake patients; we prefer to do this naturally. The quality of general anaesthesia is based on the anaesthetist's experience. Postoperatively, the anaesthetist prescribes intravenous, antiemetic analgesics, so that the patient does not feel any pain and can be mobilized early.
Endometriosis and associated diseases

In some cases, endometriosis is the only condition that a person suffers from, and in other cases, endometriosis co-exists with other gynaecological conditions such as adenomyosis and fibroids\textsuperscript{186}. Endometriosis is also associated with auto-immune diseases and overlapping conditions such as IBS, chronic fatigue and Interstitial Cystitis. It is important to know that there is no research to show if endometriosis is a cause for some of the mentioned medical problems.

In cases of co-existing conditions with overlapping symptoms, it is very hard to determine which one of them is responsible for some of the symptoms or the pain. Infertility, various pain symptoms and fatigue are caused by endometriosis, fibroids and/or adenomyosis.

Endometriosis and cancer

Endometriosis is a benign disease, the malignant transformation in endometriosis is extremely rare, and it occurs in 1\% of the cases, and the most common site is the ovaries\textsuperscript{173}. From the 205 reported cases of malignant neoplasm transformation\textsuperscript{174} in 1990, 44 were extragonadal endometriosis foci malignant transformation. In 2004, Kondi et al., have presented 14 cases of malignant neoplasms arising in endometriosis\textsuperscript{175} in women 37-70 years of age over 15 years of activity, with ovaries being the most common site.

A rare case of endometriosis and cervical cancer was reported by Wellborn Centre, in a 38 year old woman with a well-differentiated squamous carcinoma of the cervix. The patient was known with a right ovarian endometriotic cyst of about 8 centimetres diameter. The pelvic examination revealed a right vaginal fornix retraction caused by fibrosis from endometriosis as per the surgery findings.

Endometriosis and auto-immune diseases

Autoimmune disease refers to illness or disorder that occurs when the body attacks and damages its own tissues. A study done in 2002 by the National Institute of Child Health and Human Development, the George Washington University and the Endometriosis Association\textsuperscript{176} found that patients with endometriosis are more likely to have autoimmune disorders such as Lupus, Sjögren’s Syndrome, rheumatoid arthritis as well as chronic fatigue, fibromyalgia\textsuperscript{177} and endocrine disease.

A study done in Denmark\textsuperscript{178} regarding the occurrence of autoimmune diseases in patients with endometriosis concluded that the associated risk must await clarification in future large-scale prospective studies. A study done in Barcelona\textsuperscript{179} to estimate the prevalence of fibromyalgia among patients with endometriosis concluded that the estimated prevalence of fibromyalgia was higher among patients with deep infiltrating endometriosis.

Endometriosis and thyroid diseases

Endometriosis and thyroid disorders have been associated, without the theory to explain in exact terms as to why the two pathologies are linked. A study\textsuperscript{180} done on two groups of patients, 148 with surgically confirmed endometriosis, and 158 in control group, the results showed no significant increase in thyroid disease in patients with endometriosis, 20.9\% in the endometriosis group vs 26.5\% in the control group. A 3-year population-based study done in South Korea\textsuperscript{181} found a high relevance of grave diseases in patients with endometriosis.
Endometriosis and depression

Depression is either a symptom of endometriosis or is caused by having endometriosis, and it does not get much attention. As a chronic disease, endometriosis can cause different types of symptoms. Living in pain, and trying to get the medical help you need can affect your emotional health. Likewise being diagnosed with endometriosis after years of being in pain, the lack of support or understanding from family and friends, dealing with infertility, anxiety, not being able to work or go out with your friends, and changes to body image can all have an impact on one’s life.

Living with endometriosis is for quite a lot of people a constant battle, and for some, it is a long battle. Due to a late diagnosis, one can suffer a long time without having a name for the symptoms. When a diagnosis is made, one can have a sense of empowerment and relief or can be shocked, frustrated, depressed, sad. Symptoms like fatigue, pain, exhaustion, painful intercourse, and problems at work or in relationships, anxiety can all lead to depression and for some in suicide.

A review done by Pope et al \(^{187}\) found that that patients presenting with endometriosis are at risk of psychosocial disturbances, especially depression, anxiety and a poor quality of life. Several studies have found that patients with endometriosis have a high risk of developing depression and anxiety disorders.

Lagana et al., 2015, noted a vicious circle of chronic pelvic pain and psychological disease; chronic pain leads to physiological disease, which leads to increased chronic pelvic pain resulting in worsening of psychological diseases.

Symptoms can range from mild to severe and can be: anxiety, feeling tired all the time, feeling sad, low mood, poor sleep, lack of appetite, guilt, hopelessness, irritable, worthless, pessimistic, thinking about suicide, spending a lot of time in bed/indoors, not wanting to see/speak with people, trouble concentrating, aches and pains.

**Depression can be treated**, speak with your doctor if you think you have depression. The treatment for depression usually involves a combination of talking therapies, self-help and medicines.

Endometriosis and Fatigue

Fatigue is a common endometriosis symptom that, according to a cohort study done by Annika Ramin-Wright et al., should be addressed as a routine part, by the healthcare practitioners \(^{259}\). The medical plan should include ways to reduce stress, insomnia, pain and depression to manage the fatigue better. There is little information on how endometriosis causes fatigue, but one reason for fatigue is due to the body fighting to eliminate the diseased tissues.

Endometriosis is an inflammatory illness, and fatigue is linked to inflammation. A study done \(^{260}\) by Andrei Malutan et al., at the University of Medicine in Romania, found that patients with endometriosis have elevated levels of key proinflammatory cytokines. Cytokines are a large group of proteins that are secreted by specific cells of the immune system and act as a messenger between the cells. Another study done on patients with Chronic Fatigue Syndrome found that, when the activation of basal ganglia at the base of the brain, which controls motion and motivation, is low, the fatigue level is higher. The basal ganglia is also vulnerable to cytokines.
Another explanation is the chronic exposure to high stress that can lead to adrenal fatigue. Estrogen can be found on the adrenal glands, and when stress is higher, the glands will produce more estrogen. Anaemia, as a result of heavy bleeding, is also a cause of fatigue. Chronic fatigue in endometriosis patients is constant exhaustion that can reduce a person’s activity, and is often accompanied by headaches, difficulty in sleeping, brain fog (difficulty in concentrating or remembering things). Some patients have learned to listen to their body and recognise the signs of exhaustion that, in some cases, might be an alert for a flare-up.

Endo belly-bloating

Probably, one of the most upsetting symptoms that affects self-confidence is bloating, known among the endometriosis patients as endo belly. Before and during menstruation, some bloating is expected as part of premenstrual symptoms. Research has shown that bloating before and during period might be due to changes in hormones which make the body to retain more salt and water.

For endometriosis though, the cause of bloating, that can happen any time during the cycle, and can last anything between a few hours to a whole day or even more, is not known. There are a few theories, and one of them is that bloating is caused by ailments that cause inflammation. Another theory is that endometriosis tissues can flare at any time, creating an immune response as a result, which includes swelling.

Apart from being painful and uncomfortable, endometriosis patients have to deal with comments from friends and family as well as random people, and the two things that are often assumed are a) the person is pregnant or b) the person is fat. Painful abdominal bloating in endometriosis patients can occur regardless of the affected areas. Some studies have shown bloating as being a symptom of gastrointestinal endometriosis.

Brain fog- clouding of consciousness

Mental fog, known as confusion, lack of mental clarity or lack of concentration, is a cognitive dysfunction commonly encountered in patients with endometriosis. Fibromyalgia is also associated with mental fog.

Although not mentioned as a symptom of endometriosis, a large number of endometriosis patients experience brain fog, also known as mental fatigue. Mental fatigue is not a medical condition itself but a symptom of medical conditions associated with inflammation or fatigue, such as chronic fatigue syndrome.

Brain fog is a symptom of endometriosis that interferes with both professional and social or personal life. Brain fog affects several mental processes, such as memory and concentration. Brain fog causes problems of concentration, confusion, difficulties in thinking and communication, memory disorders, irritability, anxiety, fatigue, mood swings.
Other types of pain

Endometriosis is not the only cause of pelvic pain; adenomyosis, fibroids, the uterus, different types of ovarian cysts, adhesions, are also causes of pelvic pain; therefore excision of endometriosis will only treat endometriosis symptoms. Excision is step one as per Nancy’s Nook Endometriosis group; saying that when excision is done by an experienced endometriosis specialist, the pain due to endometriosis will improve.

In some cases, the patients find relief in a short time after excision surgery, while in other cases it might take a while until the results are seen, providing that endometriosis was the cause of the pelvic pain. However, surgery alone might not be enough to improve the quality of life of endometriosis patients; thus, other medical treatments or therapies to address social or emotional problems or other types of pain might also be needed.

Identifying the cause of pain in the first place is very hard, therefore after excision in order to identify other pelvic pain generators and find a treatment plan(s), it is important to work with your doctor, where possible. Pelvic floor dysfunctions, adenomyosis, interstitial cystitis, irritable bowel syndrome, emotional support are just some of the things that need to be addressed as well in cases of persisting pain.

A retroverted uterus is a uterus tilted backwards towards the rectum and is associated with endometriosis due to scar tissues that can hold it back, fibroids and pelvic inflammatory disease. Some women have no symptoms while others will experience some symptoms: pain in the vagina or lower back during intercourse, pain during menstruation, urinary tract infection.

Primary dysmenorrhea is common menstrual cramps that are recurrent and are not caused by other conditions. The pain is accompanied by nausea, vomiting, fatigue, or diarrhoea. Symptoms typically last less than three days, and the pain is usually in the pelvis or lower abdomen. Primary dysmenorrhea affects more than 50% of women and in about 10% is quite severe.

The role of surgery

The only way to correctly diagnose endometriosis is through exploratory laparoscopy followed by biopsy. At the same time, laparoscopy is the main treatment method. Surgery plays an important role in reducing the pain, improving the quality of life, restoring organ functions and normal anatomy, as well as increasing/improving fertility rate.

The indication for surgery is given by symptoms, infertility or both. If the term ‘treatment’ of endometriosis means its eradication, as in the case of infection disappearance after antibiotic treatment, then the only curative treatment of endometriosis is excision surgery.

During exploratory laparoscopy, endometriosis lesions can be seen in different locations and in different phases of evolution. One of the pelvic forms of the disease is ovarian cyst, endometrioma. A simple inspection of the abdominal cavity can miss profound lesions such as endometriotic nodules. Frequently they are located at the level of uterosacral ligaments. During the dissection of the endometriotic nodules which looked quite small (both at the surgical inspection and the MRI), there is often a profound infiltration of the neighbouring tissues.
Endometriosis surgery aims to remove as much of the endometriosis tissues as possible, preserve the reproductive organs (where possible), repair the damage done by the disease and prevent/delay disease relapse. While excision remains the main method of removing the tissues in practice, each endometriosis case is treated individually; therefore, the surgical gestures/approaches might be different.

Endometriosis surgery is an extensive surgery and as with every surgery, carries risks. Factors such as patient safety, personal circumstances, health, body weight, age, intraoperative and postoperative risks, all play an important role in deciding whether to use a radical or a conservative approach. Equally, a patient can have an extensive disease in one part of the pelvis and just a couple of lesions in the other part. In this case, both radical and conservative approaches might be used.

Jason Abbott noted that surgical treatment is an excellent option for patients with endometriosis and infertility. According to him, surgery has a number of advantages for the often symptomatic patients, and patients should be referred to a specialist centre, in cases where the surgeon cannot remove the disease.

The curative treatment of endometriosis is represented by excisional surgery. Endometriosis surgery is a complex surgery, and its approach might be multidisciplinary. Thus, the needs for specialized centres to diagnose and treat this disease. What is very important to know is that the treatment should be tailored to each individual patient, depending on the symptoms and the needs of each patient.

Besides the diagnosis and therapeutic role, laparoscopy is also useful in evaluating the status of the uterus, ovaries, in the evaluation of other genital or extragenital pathologies.

Conservative - medical treatment

There are many types of drugs currently used in the "treatment" of endometriosis: anti-inflammatory medications, anti-allergic medication and many hormonal drugs. All of these therapeutic options only combat the symptoms of the disease - pelvic pain, dysmenorrhea, etc.

A conservative treatment of endometriosis is the induction of amenorrhea. This can be done through multiple methods. One of them is pregnancy. Hence the false idea that pregnancy treats endometriosis.

Wellborn team often sees patients who have previously consulted other specialists, and they have been advised to become pregnant. Indeed, during pregnancy, the symptoms of the disease can be alleviated (unfortunately, temporarily). But most often, the disease causes infertility, as it is known that 50% of infertile patients have endometriosis.

As a conclusion, we can say that the treatment of endometriosis is a surgical one. Pelvic surgery/endometriosis surgery aims to restore pelvic anatomy and combat pain, which is the main symptom of the disease.
Endo pain-free- managing expectations

When does one become pain-free after endometriosis surgery? Providing that endometriosis was the sole cause of the pain, surgery aims to reduce the pain. In some cases, the patient is symptom-free soon after the surgery, in other cases, the patients have seen improvements in their symptoms, including in the pain levels but are not completely pain-free.

In the majority of studies done to observe the efficacy of endometriosis surgery measured by pain relief, the conclusions show mainly pain reduction, which happens in time. A study done by Angioni et al., to observe the pain relief in patients treated with GnRH and excision, noted that at 1 year follow up, the excision group showed the lowest pain scores and the highest quality of life.

An admin in the Nancy’s Nook Endometriosis group has written an interesting article about managing expectations. The admin mentions that although excision is very important, it is only the beginning of the pain-free journey. Endometriosis patients have anatomic distortion and have been in pain for years, therefore repairing this damage will take time, from months to years and can be fully or partially repaired.

Surgery is done to alleviate the pain and to improve quality of life. After years of being in pain caused by endometriosis, it is normal to want a life free of pain. The expectations after surgery are based on personal circumstances, and while some want to have no pain at all, others will be happy with any improvements. To be able to see the benefits of the surgery, you have to look back at your journey and compare before and after. In some cases, the benefits are immediate, and in other cases, they appear gradually.

“ENDOMETRIOSIS ISN’T JUST HAVE EXCISION SURGERY AND BOOM YOU’RE BETTER. HEALING IS A JOURNEY”
-DR. SALLIE SARREL PT ATC DPT
Pelvic floor therapy

Surgery alone often isn’t enough to relieve symptoms of endometriosis. That’s where pelvic floor therapy comes into play. Baker Pk, 1993, noted that musculoskeletal dysfunctions often contribute to the signs and symptoms of chronic pelvic pain, causing lower abdominal and pelvic floor pain. TU FF et al., noted that piriformis and levator ani pain is present in a significant proportion of female chronic pelvic pain patients. The study was done on 987 patients, and 212 had tenderness of the levator ani muscles, while 128 had tenderness of the piriformis muscle during examination.

The piriformis is a small stabilizing muscle located deep in the back of the hip. Due to close proximity, the piriformis muscle can cause irritation or compress the sciatic nerve. Levator ani is a small muscle comprised of 3 muscles and has a crucial role in supporting the pelvic organs. The symptoms of levator ani syndrome consist of pain and/or pressure in the rectum that can be felt when sitting.

Pelvic Floor Therapy (PFT) is part of physical therapy and involves working with everything that affects the pelvic area, including muscles, bones, ligaments, and fasciae. PFT for endometriosis is different from pelvic floor therapy and consists of:

- Working on the core, hips, and feet;
- Internal physical therapy to work on the affected muscles that line the inside of the pelvis;
- Manual therapy to help break up scar tissue;
- Exercise, yoga, or Pilates;
- Breathing exercises, as breathing affects the pelvis through the diaphragm;

Sallie Sarrel, a pelvic floor endometriosis therapist, explains how PFT helps with endometriosis symptoms. Endometriosis can cause reactive pelvic floor spasms, as well as pain and spasms throughout the pelvis. It can also turn up the volume on the nerves in the pelvis and abdomen, and that can create pain.

Excision surgery is the best way to treat endometriosis, but some of the pain, as well as the adaptations the body may have made to cope with endometriosis pain for many years, is not solved with surgery alone. We need to attend to the nerve hypersensitivity, the muscle spasms, any postural alignment problems, the weakened core, and all the other things that have happened to the body as a result of endometriosis.

Endometriosis specialist vs a regular obstetrician-gynaecologist (ES vs OG)

In 1941, Meigs believed that Sampson had a higher incidence of endometriosis due to the high number of patients suspected of having the disease that were sent to him as a result of his work with endometriosis. At the same meeting, Dr James C. Masson noted that “those who are endometriosis-minded find this condition frequently, whereas the general surgeons, and those who are not especially interested in this subject, see it rather rarely”. Regarding Sampson’s high incidence, he noted that many surgeons do not remove or record tiny areas of discoloured peritoneum when operating for other pathologic conditions.
A specialist in endometriosis surgery is a gynaecologist that deals with endometriosis as one of his/her main activities. Becoming a specialist in endometriosis surgery, requires time, dedication and intensive training. Some of the ES have been in fellowship programmes, have been trained by well-known gynaecologists who have dedicated their time to treat endometriosis or have self-taught themselves how to treat endometriosis.

The speciality OG involves dealing with pregnancy and treating gynaecology problems. It is known that endometriosis is studied very little in med schools; therefore, all the knowledge about endometriosis is acquired over time by showing interest to treat this pathology. An OG that deals with pregnancies does not have the time to deal with endometriosis. Equally, an ES does not have the time to deal with pregnancies, and natural births as both of them require time and can interfere with one another.

Endometriosis comes in different colours and shapes, can hide in different spaces (peritoneal pockets), and it affects a whole range of area/organs in the pelvic cavity and other parts of the body. While laparoscopic training is the first step, to be able to handle endometriosis in all its forms, it takes time and years of practice. A proper diagnosis and treatment can only be done by an endometriosis specialist, who can search all areas, recognise and remove endometriosis tissues from the affected areas/organs. An endometriosis specialist that works with a multidisciplinary team is able to remove all the disease in one surgery.

An ES is able to search for and identify endometriosis lesions in the absence of an endometrioma. An ES knows that ovaries are not the most commonplace for endometriosis and that endometriomas are a sign of infiltrative disease, therefore will search the pelvis and abdominal cavities as well. The ESHRE 44 surgical management of endometriosis, notes that a surgeon sees only what he/she recognises and the disease can be left behind, especially in cases where endometriosis is hidden beneath the peritoneal surface.

Disease treated partially can lead to more severe disease, which will result in other surgeries, and organ loss and resection.

In Jan 19, a patient was treated at Wellborn Centre for deep endometriosis. The patient had had another surgery for endometrioma removal in 2016. The disease had affected her intestines, and the medical team had to resect 35cm from the intestine due to multiple nodules. Another patient was operated on for extensive deep pelvic and diaphragmatic endometriosis and a diaphragm hernia after three previous incomplete surgeries done by general OG.

Endometriosis centres

A cohort study done at the Tuebingen University Women's hospital during 2005 to 2015 concluded that the treatment of endometriosis should be done in specialized centres with interdisciplanry teams to reduce the number of surgical interventions in individuals diagnosed with endometriosis in the digestive system and/or urologic. Surgical treatment of deep endometriosis is one of the most difficult surgeries in the human body. Therefore, deep endometriosis surgery should be performed in experienced teams (gynaecologist, urologist, general surgeon, etc.)

Any patient presenting to the gynaecologist with pelvic pain, and for the appearance of an endometrioma ovarian cyst should be thoroughly investigated to confirm (or not) the infiltration of the adjacent organs. While endometriosis is known as a condition of the reproductive organs, the disease affects different organs/area outside the gynaecology area, and the extent of the disease and the necessary surgical gestures becomes clear during surgery.
Endometriosis from A to Z

Endometriosis Centres due to their teams experienced in resolving all cases of endometriosis and lead by highly trained, and experienced endometriosis specialists, with multiple specialists that can be called when needed, can perform complex cases in a single surgery and greatly reduce the risk of complications. Practically, endometriosis surgery is more than gynaecological surgery. It involves urological surgical gestures (bladder dissections and sutures), gestures of digestive surgery (dissections and sutures of digestive tract structures), things that need to be handled by a general surgeon/urologist and a gynaecologist needs to be aware of these requirements.

How to prepare for surgery?

Endometriosis surgery can be divided into first-time surgery and second/third/... surgery. Regardless of the category, the majority of patients are more or less worried about the surgery. The reasons can vary from, “will they find any endometriosis” to “will it be just another failed surgery and I will be in pain again”? Surgery is an important act, and the results of it are of paramount importance to any person undergoing surgery.

For a faster recovery as well as being able to put up with the emotions/worries of having surgery it is important to prepare yourself, both mind and body as well as pre-arranging things that you usually do.

Prepare yourself mentally. Whether is the first surgery or not, the results have the same importance so it is advisable to prepare mentally for the possibility of organ removal, especially if they are reproductive, and one of the reasons you are doing the surgery is to have children, as well as for the possible answer of “no endometriosis was found”.

This is no doubt one of the most difficult things to accept, especially when you think that you have to live in pain for the rest of your life. Even though this might be seen as a dead-end at the time, it can be a starting point as well. Other issues are causing pelvic pain which will need to be investigated, to find the cause of the symptoms. It might also mean that you might need greater expertise or a second opinion.

Prepare your body. It is well known that a healthy and fit person, generally, will recover faster and surgery risks will be very low. Before surgery, 1-2 months (providing that you know the date), eat healthily, give up/reduce smoking/drinking, start being active, do things that make you happy. After surgery, do not be harsh with yourself for not recovering faster and do not compare yourself with other people.

Prepare things in advance- inform people/get help. Each person’s necessities vary based on their personal and professional circumstances. Whether you live alone, or you have a family to look after, make a few prior arrangements, like cleaning, cooking, grocery shopping, hiring a person to walk/look after your pets, asking friends, family, schools parents to help you with the children’s activities in case your partner can’t take time off from work.

Bowel preparation

Due to the high possibility of endometriosis affecting the intestines, bowel preparation might be recommended. Although this sounds daunting, bowel preparation means emptying the intestines using a laxative or an enema. This needs to be done in the day/evening prior to the surgery. Some doctors also recommend a light diet a few days prior to the surgery.
Endometriosis surgery recovery

“Surgery is an act, recovery is a process”- Endopaedia. It is very important to remember that, recovery can take time and equally important is that each person recovers differently. It is well known that in most cases, the more healthy and fit you are, the faster you will recover. Also, the recovery process has ups and downs, and the process, in some cases, can be very fast or very slow. During this time, some issues might arise that can make the recovery even longer. Try and stay positive and keep in contact with your doctor. Should any complications arise, he/she will be able to advise you accordingly.

The ablation vs excision recovery process can be different, and this is due to the differences between the two procedures. Endometriosis excision surgery is a very complex one, and it can take from just a couple of hours to 5-6 hours (even longer) depending on how much the illness has affected the patient.

Even though laparoscopy (in cases when is used) is a minimally invasive technique, excision surgery can be very extensive. Surgery is an injury, and as with every injury, will need some time to heal. During excision surgery, organs are cut, pushed, poked, moved out of the way, repositioned; their functionality is restored, and so on.

Surgery risks, as well as complications during surgery, can make the recovery process longer and slower. Post-op complications such as fistulas, infection, haemorrhage, can slow down the recovery process as well. In those cases, different types of medication and surgeries to address the post-op complications are mandatory, followed by specific medical recommendations.

Mental health also plays a role, so do not beat yourself up for not recovering as fast as you thought you would or you were told in advance of your procedure.

Due to the disturbance to the hormonal cycle, periods timings following surgery might be affected. In some cases, it might start earlier than expected and in other cases might be late. The duration and the flow might be affected as well. The first couple of periods after the surgery are likely to be painful. After surgery, some doctors might recommend birth control to suppress ovulation in order to give the ovaries time to heal. Cysts forming after surgery can be quite painful.

Persisting pain after surgery

Postoperative pain is almost the rule after pelvic surgery. The advantages of minimally invasive surgery (laparoscopic surgery) are fast recovery and minimal postoperative pain. However, in extensive surgery, such as deep endometriosis surgery, postoperative pain is present for a variable period of time. Sometimes, immediate postoperative pain is greater than preoperative surgery, which makes many patients feel no benefit from the operation.

Postoperative pain can be caused by pelvic nerve injury during surgery. This is due to the infiltration of nerve fibres by endometriotic fibrous nodules. Thus, during surgeries, the surgeon must sometimes choose between radicality and functionality/side effects.

In severe cases where all pelvic organs are affected - ‘frozen pelvis’ - a thorough dissection is required to restore normal anatomy. Thus, after surgery, postoperative pain can be of increased intensity. In the long run, pain can persist due to the processes of reshaping and scarring of areas where the peritoneum was removed.
For endometriosis infiltrating the sciatic nerves, Prof Possover noted that the normal gait recovery might take at least 3 years and intensive physiotherapy, after the surgery. Sometimes, the process of healing after such major surgeries may take up to one year.

Therefore, patients that undergo such interventions should be carefully monitored for a long time. This is necessary not only to monitor the postoperative evolution (pain relief, the occurrence of pregnancies, etc.) but also to discover the early occurrence of relapses or late complications of surgical interventions (late ureteral obstruction, digestive anastomosis obstruction).

Managing endometriosis symptoms

While surgery so far remains the only method of managing the disease itself, symptoms might be managed with different therapies/approaches and lifestyle changes. Depending on the severity of the symptoms/pain, one might find relief by altering the diet, regular physical activity, reducing stress, trying Chinese medicine and holistic therapies. A healthy lifestyle has been reported by patients as one of the efficient methods of reducing endometriosis pain. A healthy lifestyle includes a balanced and healthy diet, stress management and relaxation, sleep and physical activities.

Diet

Endometriosis is an inflammatory disease, and as such will react to certain types of food. Although there is not enough information regarding the impact of the diet on the progression and development of endometriosis, eliminating certain foods might help to manage the symptoms, such as nausea, abdominal pain, bloating and cramps. It is important to remember that each person is different, and what works for one might not work for another. Consuming a healthy balanced diet for general health and well-being is advisable. Each category of foods plays an important role in the overall health and attention should be paid when eliminating certain types of food from the daily intake.

A balanced healthy diet should consist of macronutrients and micronutrients, combining meat or poultry, fish, fruits, vegetables, healthy fats and dairy, with some of the aliments consumed in moderation. It is important to know that endometriosis cannot be prevented as long as the cause is unknown. Also, the dietary and lifestyle changes will not cure endometriosis but might help in alleviating some of the symptoms. Avoiding food and chemicals that increase estrogen levels might reduce the risks of developing endometriosis symptoms.

Note: Check Fabien Piasco, Dietician and Nutritionist
### Endometriosis patients- What do we all need to know?

Endometriosis is as common as diabetes, asthma and other diseases; and yet the world has not heard of this disease. Despite a large number of patients suffering from endometriosis, and the extreme impact this disease has on patients, their families and friends, endometriosis patients are being let down by the medical system. As per Nancy Petersen an endometriosis advocate saying, endometriosis patients have failed everything gynaecology has to offer, except excision surgery.

One of the most important things that all specialist doctors should know is that the first diagnosis of suspicion in a patient with chronic pelvic pain is endometriosis, not the last as most often happens.

Endometriosis patients are often misdiagnosed, and people can’t understand why they are sick when they do not look sick. Endometriosis patients are seen/considered by friends and family, as being lazy or overreacting. For endometriosis patients it is very difficult to explain why the general gynaecologist can’t do the surgery, why despite having surgery they are still in pain, why they refuse to have a hysterectomy or a baby to “cure” them, why they keep cancelling plans, why they can’t keep up with them, why they need to rest all the time and so on.

For the non-endometriosis people, you can’t tell what an endometriosis patient goes through unless you are willing to learn a few things about endometriosis. By doing so, you have a better understanding of the effects of this illness on a person and what you can do to help that person. So before judging that person, before assuming anything, try and put yourself in that person’s shoes and then you might have a better understanding about what that person is going through.

Endometriosis patients are not lazy, moody, overreacting or attention seekers, are more tired and fed up than you are; they want to go out as much as you want. For partners, understand that she/he isn’t turning you down because s/he doesn’t love you, but because sexual intercourse hurts. For the ones suggesting to have a kid or a hysterectomy may be helpful (the cure), none of those methods is a cure for endometriosis. Only excision surgery can provide relief for many years, hence why endometriosis patients cannot be seen by a general gynaecologist.

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<tr>
<th>Recommended</th>
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<td>- Vegetables</td>
<td>- Alcohol</td>
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<td>- Legumes</td>
<td>- Deep-Fried food</td>
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<td>- Fruits</td>
<td>- Processed meat</td>
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<td>- Fish and seafood</td>
<td>- Hydrogenated cooking oils</td>
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<tr>
<td>- Nuts and seeds</td>
<td>- Sugary sweets and drinks</td>
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<td>- White meat and fish</td>
<td>- Coffee</td>
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<td>- Whole grains</td>
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<tr>
<td>- Olive oil</td>
<td>- Fast-food</td>
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<tr>
<td>- Organic food and hygiene products</td>
<td>- Cakes and doughnuts</td>
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<tr>
<td>- Reduce plastic usage</td>
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<td>- Physical activity daily</td>
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<td>- Drink plenty of water</td>
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For an endometriosis patient, endometriosis means not being able to make plans, to wake up at night because of the pain, to give up the things you like, to go to bed/wake up in pain, to lose your friends, to pretend you are okay when in fact you can’t breathe because of the pain, to go to many specialists, to be told that you are pretending, to be told that you do not look sick, to pass by mothers with children and to wonder if you will ever be a mother.

To be told that the pain is in your head, to separate from your partner, to be asked how many months of pregnancy you have when in fact you cannot have children, to faint because of the pain, to stop saying that you are not well, to be guinea pigs in medicine, to be told you exaggerate, to want to have at least one day without pain, to look for answers on the internet, to diagnose yourself, to find understanding/compassion from strangers.

To not be able to work, to lose your job, to give up studies, to have miscarriages, to live with the fear that your daughter will inherit your illness, to get to the emergency room, to be known in the local hospital, to not be able to eat something that you like, to want to end your days and so on.

Endometriosis is a complex condition and hard to understand fully by both patients and healthcare practitioners. I have operated on and seen enough patients to be able to say the following. First and foremost, excision is the only treatment that has been proven to be effective. It can eradicate the disease, reduce symptoms and improve fertility and has a low recurrence rate.

So anyone who has this disease should look into finding a specialist that offers excision.

Endometriosis surgery is quite difficult, and it requires knowledge and experience. Thus why the requirement of having surgery done by an endometriosis specialist. A specialist that works with/ in a multidisciplinary team and can treat the disease from all parts involved.

Ablation is an ineffective way of treating endometriosis. It has a high recurrence rate, disease on vital organs is left behind, and there will be little or no improvement in symptoms.

Endometriosis comes under different colours and shapes, and the stage does not correlate with the level of pain. Minimal disease can hurt more than severe disease. Some people have all the symptoms, others have some of them and others have no symptoms at all. Symptoms can occur during period/ovulation and/or throughout the whole month.

Hormonal therapy is not a cure for endometriosis; it only reduces some of the symptoms. GnRH has serious side effects when administered for a long time, especially in young patients. Studies have shown that first-line therapy (birth control) has the same effect in improving symptoms as GnRH.

Pregnancy is not a cure for endometriosis. Due to a physiologic process that happens during pregnancy, symptoms are quietened down. There are cases, though when there is no improvement in pain during pregnancy. Getting pregnant with endometriosis it can be a bit difficult due to a) endometriosis affecting fertility and b) painful intercourse. After postpartum and during breastfeeding, symptoms might continue to remain silent or will come back and can be even worse than before pregnancy.
Hysterectomy is not a cure. Endometriosis is outside of the uterus so as long as the disease is not removed entirely from all the affected parts, taking out the uterus will have little or no impact on symptoms. Having said that, there are patients who reported improvements in their symptoms after hysterectomy. However, this is a small percentage. Hysterectomy is a cure for uterine issues like fibroids or adenomyosis.

Removal of ovaries helps with recurrent ovarian cysts. For endometriosis though, this has little effect since endometriosis produces its own oestrogen. After the removal of the ovaries, endometriosis lesions in that area have one less source of oestrogen to react to, so patients might notice an improvement in their pain.

Recovery might be an easy or a long process. Be prepared! Excision is the first step of the recovery process, and it can only treat endometriosis symptoms. In some cases, other issues need to be attended to as well.
A wish noted! I wish that one day my daughter will not have to face the same pain I do. I wish she will not have to know the struggle that is life with endometriosis. I wish she wouldn't have to be poked with needles on countless visits to the emergency room. Most of all I wish for a CURE for me and my 179 million endo sisters battling this illness. Barrie, Ontario (The endometriosis network Canada)
Patients’ stories

Sara, UK

Sara was diagnosed about 10 years ago, and she is now on the waiting list for her 3rd endometriosis surgery. She was given 5% chance of getting pregnant and the doctor who was seeing her at that time told her that she shouldn't complain about the pain every time he had to do an internal scan as she was making his life difficult! After the doctor told her that she has very small chances of getting pregnant, she went to Portugal to seek help with her fertility; unfortunately, it did not work.

Sara works as an accountant, and the GP told her that the pains and spasms in her left shoulder that she was complaining about were due to her role. The pain got so bad that she ended up in A&E a few times. On one occasion, the pain got so bad that her husband took her to the hospital where she stayed in for a month. Despite having severe fever, heavy bleeding and unbearable pain, nothing was getting done to find the cause of her symptoms. After she decided not to communicate with the medical staff, she had a scan that showed a massive cyst on her left ovary.

The staff told her that she can go home, but she will need a laparoscopy. She ended up having the surgery, and the medical team were not able to remove her cyst. She was in a lot of pain afterwards, confused, tired and depressed. She didn’t understand endometriosis, nor did anyone explain it to her. She ignored yet again and tried to get on with her life.

After 2 weeks, Sara got pregnant but miscarried after 2 weeks; she carried on and didn't even tell her husband. The symptoms have returned, and she went to the doctor who explained things a bit better. Sara was referred to an endo specialist in Norwich, who was able to explain to her properly the ins and outs of the options and what was happening to her body.

She had another laparoscopy done, and the cyst was still untouched; however, some of the endo was removed. She ended up with an infection and after wards she was back at work and carried on as normal. Once again, the pain has returned, this time with a vengeance, she could not walk some days and cried herself to sleep or would wake up screaming in pain. She passed out from the pain a few times.

In January she found out she was possibly 2 months pregnant! Unfortunately, she had another miscarriage a month later, just before her scan. After this, she got in touch with the hospital to sort out her health problems, and she is now on the waiting list just for a laparoscopy, but this time, the doctor will probably take her ovaries, and part of her bowel as the disease is now quite profound.

She has been diagnosed with depression and anxiety, and she has also lost her job of 8 years due to being sick. At the moment, Sara is rebuilding her life, and she still wants children. She has a full-time job, still studying, and after the surgery, she is planning on losing some weight as the anxiety meds made her gain weight.
Lavinia, 37 years old, Romania

My period started when I was 12 years old, and with it, horrible, excruciating pain. Some say that endo pain starts later in life, but I know I had it from the very beginning. I remember it clearly, because my grandmother was battling cancer and living with us in that period, and my mother would sometimes give me some of her cancer pain medication because my pain was so unbearable and she didn't know what to do with me. Somehow, she didn't think to take me to a doctor, as she herself suffered from severe menstrual pain and gynaecologic problems all her life and thought this was normal.

I took myself to the doctor, but only years later, when I was 19, had a boyfriend whom I was very much in love with, and wanted to start my sex life. Only I just couldn't. It was too painful for me; it brought tears to my eyes and I couldn't stand to do it. So I went to the doctor. They did their tests and found nothing wrong with me. So I went to another. And another. Maybe two dozen of them. "There's nothing wrong with you", "All women have pain", "Try to think of your partner's pleasure", "You're too sensitive" "Maybe it's psychological".

So, what do I do? In the end, I tried psychotherapy to fix my "sex inhibitions". And positive affirmations, visualisations, etc. It didn't help. None of it did. My pain was still there, persistent, mocking me, bad as it always had been. My boyfriend was long gone at this point, and things were getting worse.

I started to get digestive problems, frequent diarrhoea, cramps, bloating. Doing everyday things started to become painful and uncomfortable. More doctors, more visits, more tests. "We can't find anything", "All tests are fine", "Maybe it's IBS", I've been told. So, I started going on all of these diets, hoping something would help ease the symptoms. A sugar-free diet, LOW FODMAP diet, LOW GI diet, Low Histamine diet, Vegetarian diet, Gluten-free diet, No Dairy. It didn't help. No matter what I ate, I was still feeling as sick as ever. Then more: probiotics, vitamins, yoga, acupuncture, naturopaths, everything.

I tried everything, and still, nothing. I was sick of being sick, and so was everyone around me. "Are you sure you are not imagining your pain?", "But, you don't even look sick!", "If there was something wrong with you, don't you think doctors would have found it?" "My friend's lives were blossoming around me, and they were starting families, advancing in their careers, buying houses. Meanwhile, my life was getting smaller and smaller. I couldn't seem to make any progress, I was always tired, my energy low. And things were getting worse.

I started to get all kinds of allergies and muscle pain in my back and in my hands. More doctors, other doctors, more tests. As usual, they couldn't find anything wrong with me. Their test showed I'm healthy when I was feeling anything but. "Maybe it's fibromyalgia", they said. The pain was claiming more and more of my body. Slowly but surely, I lost my ability to work, had to return home to live with my parents. My friends were long gone by this point. I was feeling very much alone and abandoned by the medical community.

Finally, this year, some hope. After 25 years of doctor's visits, disappointment and frustration, I got my diagnosis by MRI with endo protocol: endometriosis and adenomyosis. Now, I'm on Visanne, which helps, as I no longer have the menstrual pain, but I'm still having severe abdominal pain, cramps, bloating, rectal pain, bladder pain, and pain down my right leg that keeps me up at night. I've started saving up money for surgery. For a better tomorrow, maybe?
Ruth, Kenya

“I would say to my younger self that period pain is not normal...my younger me would have had kids when she was young cos right now my only option is IVF. Any person who has been diagnosed with endo should seek excision surgery; this is the golden treatment”.

Ruth travelled 5,248 km = 3,261 miles from Kenya to Wellborn Endometriosis Centre to have her 5th endometriosis surgery and the 1st laparoscopy surgery. She had her first symptoms in 2012, at the age of 24 after she suffered her first miscarriage. She did not explain to anyone as she thought it was just normal pain. Prior to this, she only had one day of pain during periods when she had to take painkillers.

Ruth diagnosed herself since no doctor took her seriously. She kept having recurring chocolate cysts and started researching on her own about the type of cyst and the level of pain she was having, and this is how she found out about endometriosis. Ruth was told to get pregnant by one of her doctors as a method to get rid of her pain. Even though after her first surgery to remove an ovarian cyst, the results showed it was an endometrioma cyst, her doctor still said it can't be endometriosis.

Ruth’s symptoms were so severe that she used to miss work during periods. During her periods, she stayed indoors till the period ended, and she had personally withdrawn from people. She only spoke with her mom about her symptoms, who tried to help her by finding natural remedies which did not work for Ruth.

Ruth found out about excision in a Kenyan Facebook group, from a former patient of Dr Mitroi, who travelled to see him, and she was happy with her surgery results.

After having 4 laparotomies with no results and wanting to be normal, she started the process of travelling abroad for surgery. The surgery done by the team at Wellborn Centre, was laparoscopic excision, first excision and laparoscopic surgery for Ruth.

For her, excision surgery was like a dream, and she cried after the surgery when she realized that she finally had her dream surgery. A month after the surgery, she is experiencing recovery pain, but she remains optimistic, and she knows that the healing process is gradual. For the first time in years, since her symptoms first started, Ruth had her first non-painful period after the excision surgery.

Kristina, Croatia

“I finally have my life back. So dear endo girls never give up. Never give up not only from endo but also from yourself. Don’t trust doctors who are telling you that pain is a normal thing because it’s not. It is never normal that you are in pain, besides sometimes you know your body better than any doctor. Fight for yourself, do the education about what endometriosis really is and search for an endo specialist. Only with a real endo specialist who knows how to do excision, can you help yourself....it is a long way I know, but it is worth it”.

At the age of 23, after 5 years of experiencing symptoms, Kristina had been told that she has endometriosis. Endometriosis was something new for her family, and when she told them her diagnosis, their first question was, What is that? Even though she explained to her friends and family about endometriosis, their takeaway was that she has a normal cyst and she needs surgery.
Soon after she had her first surgery, she was told that there is no chance for relapse, she was declared “endo free” and was told to get pregnant. A year after the operation, the pain had returned, again endo and again, operation. After her 2nd operation she had a relapse within 3 months, but worse than ever. She had pain in her right shoulder every time during periods, she could not breathe normally, and her periods were too painful to do anything. She was sent for therapy for her shoulder, but nothing helped. The pain got worse and worse, she was tired, unable to go to work, and her whole day was spent sleeping.

Kristina spent lots of nights in the emergency room, and the staff did not believe that endometriosis can be so painful. She was accused of faking her symptoms, so she can skip work. Her gynaecologist was a nice person but had little knowledge about endometriosis. He sent her for scans (CT/MRI), and the CT showed endometriosis on her diaphragm, but the MRI came back clear.

In February 2018 she had thoracic surgery to remove the endometriosis from her diaphragm. A month after the surgery, her shoulder pain returned, and it was quite strong. The pain made her cry; she felt hopeless. She was told to “accept it as the way of your life and keep going on”.

For Kristina, this was not the answer she was after, and it was in a facebook group, that she was told about Dr Mitroi. The information came as a shock for her, due to the Dr Mitroi being in a different country. She made contact with him, and he advised her regarding the process and the necessary tests that she had to do.

Travelling abroad for surgery was not easy, but in Kristina’s case, it was the only option she had. The medical team in Croatia were amazed by her decision of seeking care abroad, especially since they thought that endometriosis can be dealt with at home. She travelled to Wellborn where she was admitted for 4 days. The surgery revealed endometriosis on the diaphragm, bladder, pelvis, rectum, ovaries and a hernia on her diaphragm.

This time the recovery was very fast, within 7 days, she walked normally, and within a month she was back to work. She started exercising a month and a half after the surgery. Four months after the surgery, Kristina is doing well, she goes to the gym, and she goes out with her friends, no more painful periods for her. Sometimes she is still in tears of happiness because she thought this was never going to happen, but it did happen.

Diana, USA

“Get help and lots of second opinions. Find a physician that you feel s/he really understands your pain even though they have no tests to prove it. Advocate for yourself. Don’t settle for just anything. Do lots of research. Take the disease/illness seriously. The sooner you get help, the better it’s for your life. Trust your gut feeling. If you don’t feel comfortable about a treatment, step back and research”.

Diana was about 11/12 years old when she started having symptoms. Her symptoms kept getting worse as she became older. Her mom was doing her best to make Diana comfortable at home during her periods, and she believed her when Diana was saying that she was in pain.

Diana went to emergency rooms many times due to painful periods, where she was always told to take more pain medicine since all the tests done came back all clear. Her periods were so painful that she missed a lot of days from school. As a teenager, she felt that she was not being taken seriously, and this made her think that she was just a complaining teenager. At 15, she saw a gynaecologist who told her that she might have endometriosis based on her symptoms.
She was put on birth control, her symptoms were reduced, and she took them for 9 years. At that time, she had no idea what it really was, and she believed she was fine since the pill helped her. She was officially diagnosed at the age of 27, by laparoscopic surgery with stage four endometriosis.

Because of the pill reducing her symptoms, endometriosis didn’t affect her life very much. After getting off birth control, she had no more painful periods, and she conceived within nine months. Symptoms wise, Diana, mostly “just” had to deal with infertility. Later on, she started having aching or sharp pain, and she took it more seriously. Her symptoms were constipation and sharp pain on her left side.

After seeing many doctors for surgical treatments and all they were talking about was Lupron and ablation, Diana found out about excision surgery via a Facebook group.

In August 2019, Diana travelled from her home country to Wellborn Centre, where she had excision surgery and bowel resection. After surgery, she felt sore and dizzy, and her pain was not as bad as she thought, so she did not take any pain medication. It took her 6 weeks to feel back to normal, and now six weeks later, she feels good. She feels sore at times from scar tissue, but no more aching or sharp pain.

**Ashley, Oregon**

“Don’t fall for the birth control, hysterectomy cure. Join groups with other women with endometriosis read up & never allow a doctor to fully dictate your care & try to tell you what is going on with your body & what is right or wrong”.

Ashley had her first endometriosis symptoms when she was almost 15. Although her friends were too young to understand her, her parents have been supportive and believed her. In Ashley’s case, endometriosis is hereditary, and her mother knew what was wrong, as soon as she heard about Ashley’s symptoms. She was still not diagnosed until the age of 23 when she found a doctor who took her seriously.

Ashley is one of the patients who have seen a large number of doctors, and all of them have told her that the pain is in her head, or gave her birth control that made her symptoms worse, and was told to continue taking them as it can take the body 6 months to react to it. Having a hysterectomy to get it over with, was also another advice that she had received from doctors and different people, without them even taking into consideration that maybe she would like to hopefully become a mother someday. Ashley’s own mother is an example that a hysterectomy is not a cure.

The doctors also told Ashley to have a baby as that will cure it. Because of endometriosis and the way it affected her, Ashley had been fired from every single job she had. She can’t afford to stay home as in the case of many other endometriosis patients, so she is forcing herself to get up out of bed every single day to go to work. She also lost her car as a result of losing jobs. She currently may have found a job that works for her after years of searching.
On a personal level, endometriosis has affected her both intimate and friendship relationships. The symptoms have increased in intensity, and it got harder for her to have sexual relationships. As for friendships, she lost a lot of friends because they think she is a flake because she always cancels plans last minute due to feeling unwell within minutes. Friends find it hard to believe her as much as she has tried to explain to them.

Her symptoms and pain have increased in intensity as the years have gone by; the lower back pain is so bad that it makes her faint and vomit. Legs go numb, and the abdominal pain feels like someone is stabbing her with a knife. She also has issues with her bladder, it hurts when it is full and she empties it, and the cramps & back pain wakes her up every two hours at night. Because of her mom’s personal experience with endometriosis, Ashley knew she was likely to have it around 15 yrs old when she told her mom about the symptoms she was having around her period.

The symptoms are now lasting for 3 weeks and are so bad that she no longer knows what it means to be normal. In 2010 after joining Nancy’s Nook Endometriosis Education, she found out about excision surgery, and in 2015 she had surgery with a nearby specialist. In her case, excision surgery did not help, and she has also tried pelvic floor therapy. The old her would say to younger Ashley to read up more on endometriosis, join a group of other women sooner, do not let the doctors try to tell you what is going on with your body & don’t back down.

**Alexandra, Hungary**

“Don’t ever let anyone invalidate the pain you are in. Don’t let time get away...time is precious, and so is your life, and so is your mental health. Girl, you are so not alone. Us with endometriosis are here to talk about cramps, emotional swings, number 2/bathroom problems, and so on. We have been there, and we have also been to Dr Mitroi - go for it. It’s scary, it’s difficult, but you will be in good hands!... and Dr Mitroi will play a song from Blue October if you like them while he removes your drain” 😊

**Wellborn**: How old were you when you had your first symptoms, and what were the reactions of your friends and family when you mentioned the symptoms/pain?

**Alexandra**: I was 14 years old when I got my first period. My GP said to my dad that it is totally normal to have such bad cramps and to have such strong bleeding. Later on, when I was 15, I was diagnosed with different pelvic inflammation, for which I was given antibiotics for months. One doctor told me that probably things would get better if my appendix was removed. It was removed when I was 16, but I kept getting diagnosed with pelvic inflammation then I was put on birth control which actually made my symptoms worse. People around me told me that probably I was just trying to get attention and that’s why I am saying that I am in pain. I was told many things. I was told that I am just being cranky, or I am weak and cannot take pain.

**W**: How difficult was it to make the doctors take your pain as real, and what were the treatment options offered?

**A**: Dr Mitroi was the 20th doctor that I saw. I went under laparoscopic surgery once, and they said they couldn’t find anything. Doctors told me that it is probably all in my head. Few doctors brought up the idea of endometriosis but never really took it seriously. I was given antibiotics for pelvic inflammation for months and months. Other times, they tried to put me on different birth control pills.
W: How did endometriosis affect your life, both personal and professional?

A: I had to cancel many meetings, I had very low energy, I was depressed and emotional many times. I felt confused and alone and looked down on most of the time. I felt so scared that there is no answer to my struggles. Often times, I couldn’t communicate what I was feeling. I was hurt by words from those around me. The most humiliating was when I started having digestive issues. I cried a lot, not only because of the emotional part but because of the horrible pain I felt.

As I am writing this, I am full of emotions and tears because I can’t believe how 15 years of my life was spent in this state both physically and emotionally. From such a young age, the most difficult part of this is the people that feel the right to tell you that you are making up this whole pain in your head. Professionally, I had to take at least 1 or 2 days off per month. I felt lucky when my period started on a weekend.

W: What were/are your symptoms and how/when did you realise you might have endometriosis?

A: Really strong cramps, shooting pain in my ankles/knees, nausea, sometimes throwing up, not being able to hold my stool, sweating from the cramps, switching between diarrhoea and constipation depending on where I was in my cycle. My period was never regular, and I normally spent 17-21 days in constant pain. The pain normally started with pressure, then it turned into such a feeling like a rubber band was put around my waist. I, of course, had a difficult time with sex. Many times the way I explained the pain that I felt was like I just sat on a sword. Closer to the end of my cycle, I had a difficult time sneezing and stretching because I felt like I was going to rip something on the inside.

It could have also been because of the adhesions.

W: How did you find out about excision being the gold standard treatment method for endometriosis?

A: I decided to go to Dr Mitroi because I kept reading up on doctors in my area and their patients. The patients have gone through numerous laparoscopic surgeries due to endometriosis because it kept coming back or because the drs missed parts of the endometriosis. I found Nancy’s group. I felt like a huge door was opened up in front of me to finally see the “light”. I was finally able to educate myself regarding this disease.

I feel that everything that is being posted in that group is really carefully reviewed, it is quality information, and it is provided by the best of the bests. I enjoy that this group is monitored and does not give the opportunity to the members to take away the focus from what is the most important: learning and making the right, educated decision. Don’t expect or trust your doctor to share 100% of the information with you. They are humans as well. Make sure that you do your part in this journey and educate yourself.

W: Have you had any surgery so far? How was/is the recovery for you?

A: I have had my second laparoscopic surgery on the 19th of February. It was my birthday gift for myself 😊 I had excision with Dr Mitroi. I am sure that I am not the only one that by the time I got to see him, I truly started to believe that the pain was not real... "funny story". Dr Mitroi said I was wrong to believe that. He spotted the endo in no time. He found DIE Endo on my bladder as well, which resulted in me having to have a catheter for 7-10 days. Man! I was sooo mad about that. 😛 really mad but also happy that after all.. I was not crazy.
After surgery, I instantly felt better. That pressure and rubber band feeling was gone. Recovery is still happening, but they say it takes longer to recover after excision. Bloating and that annoying little pain around/in the belly button was on and off for a good 3-4 months. Anytime, I have a lifestyle change - like I just switched jobs and I am having to stand more and run around more - my body has to adjust, and I definitely react differently to it.

My first period after the surgery was tough, but heck, after I watched the video of my surgery, I knew it won’t be easy. My body takes about 2 weeks to heal a scar on the outside. So just imagine what it has to do on the inside. The second period was much better. Six months after the surgery, my period was nothing. NOTHING!

The seventh month was painful again, but I had a major lifestyle change in between. Eight period is back to nothing compared to before the surgery BUT! I still had to manage it a little bit. I used to be on a pain level 10, and I would say its between1-3. I used to take 800mg ibuprofen 3 times a day, and it wouldn’t make my pain go away. Now if I have to, I take 400 mg in the morning and in the afternoon on the first day, but nothing later. I become a “mermaid” during those days (I stole this expression from a fellow patient of Mitroi 😊) means that I sit in the bathtub a lot more than usual because the hot water helps with the pain.

I believe the most important part is to be patient with yourself and with your body.

The Demon Within by Aimee Brown

We don’t know why you grow
Or even how you were born,
But your presence is certainly felt,
Leaving inside us, shredded and torn.

You tear apart relationships
You make us feel so low,
You operate invisibly,
So nobody can really know.

You’re sneaky in your tantrums
And cause a flare at any time
No treatment seems to stop you,
Its a constant uphill climb.

You take away our babies
Before they’re even born,
The toll you take on our lives
Leaves us feeling so empty and worn.

People question if you’re real,
Make judgements and mindless remarks,
You’re the cause of self-destruction,
A continuous road of darkness.

You ruin our pre-arranged plans
And bloat when the mood takes,
You strike and we have to cancel
Causing our jobs to be at stake.

I won’t stop raising awareness about you
And will scream for everyone to know,
I am 1 in 10 amazing women,
Battling daily with chronic endo!

Endometriosis groups and information sources

Lots of endometriosis patients are searching for information about their symptoms online, either through social media communities or different sites that are writing about endometriosis. Some endometriosis groups/pages are mainly for information and others are for support and information as well. By searching endometriosis and/or adenomyosis on facebook, a whole range of groups will appear.
Nancy's Nook Endometriosis Education, is one of the largest educational groups on Facebook and different medical specialists are part of the group. In addition to accurate information about endometriosis, the group has an international list of endometriosis specialists based on patients and well-known endometriosis specialists recommendations.

EndoMetropolis is another endometriosis Facebook group where members can receive support and information. The group is moderated by some of the endometriosis specialists, including Dr David Redwine.

ExtrapelvicNotRare Endo Support and Education Group is a group that focuses on thoracic endometriosis and other extra-pelvic locations.

Endometriosis, fibroids, cysts and infertility treatment support group UK, is a group that shares information about different gynaecology issues.

Endopeadia is a comprehensive, online resource on the origin, diagnosis, and optimal management of endometriosis, and represents the life's work of world-renowned endometriosis excision surgeon and gynaecologist, Dr. David B. Redwine.
Lupron Victims a support facebook group for victims of Lupron.

Wellborn Endometriosis Center is a facebook page posting information about endometriosis and the services provided by the medical team.

Dr Gabriel Mitroi facebook page where he posts information about endometriosis and other gynaecology conditions, surgical videos and case reports.

Endo girls blog, a facebook page sharing factual and educative information about endometriosis.

Facebook: Endometriosis and me (page), Endometriosis Association of Ireland, Endometriosis Foundation of Kenya, Endometriosis Wall, Endotherapylive, CentreForEndometriosisCare, Endometriosis Research Centre, Dr Andrea Vidali, Dr Iris Orbuch, National Endometriosis Sufferers Support (group), Endometriosis Australia, The endometriosis network (Canada), The Endometriosis Association of Iceland, Endo InVisible, Vital Health Endometriosis Centre- Dr Andrew Cook and many more.

Surgery photos
Endometriosis from A to Z

Figure 1 Diaphragm endometriosis
endometrioza diafragmatica

Figure 2 diaphragm endometriosis
endometrioza diafragmatica

Figure 3 endometriosis lesion
tesut endometriozic

Figure 4 bladder endometriosis lesion
endometrioza vezicala

Figure 5 endometriosis lesion
eziune endometriozica

Figure 6 endometriosis lesion on the ovary
focare endometriozice
Figure 7 endometriosis nodule
nodul endometriozic

Figure 8 endometriosis lesion on the ovary
foacar endometriozice

Figure 9 bladder endometriosis
endometrioza vezicala

Figure 10 sigmoid nodule/nodul sigmoidian

Figure 11 ileo-cecal nodule/nodul ileo cecal

Figure 12 frozen pelvis/pelvis inghetat
Figure 13 frozen pelvis/pelvis inghetat

Figure 14 dissection/disectie

Figure 15 adhesions/aderente

Figure 16 frozen pelvis/pelvis inghetat

Figure 17 frozen pelvis/pelvis inghetat

Figure 18 frozen pelvis/pelvis inghetat
Figure 19 adhesions/aderente

Figure 20 frozen pelvis/pelvis inghetat

Figure 21 c-section adhesions/cezariana aderente

Figure 22 endometrioma/chist endometriozic

Figure 23 endometrioma/chist endometriozic

Figure 24 endometrioma/chist endometriozic
Figure 25 endometrioma

Figure 26 endometrioma

Figure 27 excision endometrioma/excizie chist endometriozic

Figure 28 endometrioma excision/excizie chist

Figure 29 endometrioma excision/excizie chist

Figure 30 endometrioma excision/excizie chist
Surgery photos end
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About Wellborn Endometriosis Centre

Wellborn Endometriosis Center is an integrated medical center that offers surgical treatment for endometriosis, one of the most complex and frequent gynecological conditions. The medical team led by Dr Gabriel Mitroi treats all types of endometriosis using excision surgery.

Wellborn Endometriosis Centre has a team of specialists in endometriosis, general surgery, urology and fertility. Whether you are seeking a diagnosis and/or treatment, beginning your journey at Wellborn Centre means that you will have everything that you might need under one roof. Dr Mitroi offers free records review and continuous monitoring.

Wellborn Endometriosis Centre
Brodina Street, Nr 3
Bucharest, Romania
Email: dr.gabrielmitroi@gmail.com
Wellborn Centre-Case Reports

Case 1. A 29 year old patient with a history of endometriosis and infertility, with chronic pelvic pain, dysmenorrhea and moderate dyspareunia; without disturbances of the intestinal transit. The surgery reveals pelvic adhesion block involving the uterus, both adnexa, sigmoid colon, and the upper rectum. The team had performed, adhesiolysis, followed by the excision of the utero-sacral ligaments (both infiltrated), excision of the endometrioma and the recto-vaginal nodule and recto-sigmoid resection.

Case 2. A 33 yr old patient with deep endometriosis, the MRI revealed an endometriosis nodule at the level of the superior rectum and the recto-sigmoid junction without causing stenosis at this level. The surgery highlighted a frozen pelvis involving the uterus, ovaries, right fallopian tube, rectum, sigmoid and right ureter. After dissection of adhesions, the team performed rectal shaving for a 4cm nodule at the recto-sigmoid junction, excision of the utero-sacral ligaments nodules, ureterolysis, and ovarian cystectomy.

Case 3: A 43 yr old patient with chronic pelvic pain, dysmenorrhea and severe dyspareunia; severe disorders of the intestinal transit - constipation, (dyschezia). The MRI shows a pseudonodule infiltrating the cervix and the posterior vaginal recess, a pseudonodular nodule infiltrating the rectum and the recto-sigmoid junction with moderate stenosis of the intestinal lumen. The surgery reveals obliteration of the cul-de-sac with excision of the utero-sacral ligaments, the vaginal nodule flowed by sutures with Vycril O, excision of the recto-vaginal nodule and intestinal resection followed by anastomosis.

Case 4: A 38 yr old patient with previous surgery for ovarian endometrioma (open). The MRI reveals an endometriosis nodule at the level of the superior rectum and the recto-sigmoid junction, which affects all layers of the rectal wall, up to the mucosa and causes stenosis of about 80% of the lumen. The surgery highlights a frozen pelvis, and after the dissection of adhesions, the team performs recto-sigmoid resection followed by anastomosis for a 4cm nodule that infiltrates the intestinal muscular wall, excision of the ureteral and utero-sacral ligaments nodules, right anexectomy and ovarian cystectomy.

Case 5: A 26 yr old patient with a history of pelvic and diaphragmatic endometriosis and two prior surgeries for endometriosis, the MRI shows a 5mm endometriosis lesion lateral to the spleen, right side diaphragm a few 5mm lesions. The surgery reveals extensive adhesions involving the ovaries, left fallopian tube with hydrosalpinx, sigmoid, uterus and the bladder. After a careful dissection of adhesions, the surgery highlights, thick utero-sacral ligaments (nodules), excision, a rectal nodule, rectal shaving, multiple endometriosis lesions affecting the bladder peritoneum, en-bloc resection, multiple nodules on the diaphragm and a diaphragmatic hernia, excision of the nodules and hernia repair, left endometrioma, cystectomy.

Case 6: A 37 yr old patient with a previous surgery for endometriosis. The CT revealed recto-sigmoid junction and sigma traction at the posterior wall of the cervical canal and cervix, a rectal-sigmoid and sigmoid infiltrative lesion causing minimal stenosis of the intestinal lumen, sigma adherent to the left appendix (tumor transformed - endometrioma), with eccentric infiltration of the intestinal wall. The surgery highlights a frozen pelvis, after dissection is visible an endometriosis nodule at the recto-sigmoid junction, 4cm, a sigmoid nodule, an en-bloc intestinal resection is done followed by a T-T anastomosis, an endometriosis nodule at the level of the uterine wall that infiltrates two ileal loops - viscerolysis followed by ileal segmental resection, nodules in both uterine-sacral ligaments that infiltrate bilateral periureteral tissue - without ureteral compression - ureteral shaving, left endometrioma, cystectomy.
**Case 7:** A 37 yr old patient with a **previous anexectomy** (8cm endometrioma open surgery), the MRI reveals, adherent fibrotic changes latero-pelvic right, traction of the uterus, cervix and upper pole of the vagina, to the right, ovarian cysts, infiltrative nodular lesion with endometriotic aspect located deep retroperitoneal, involving the posterior uterine wall and cervix, the medial left ovarian slope, the distal sigmoid, thick utero-sacral ligaments. The surgery highlights a severe perivisceritis (inflammation of the tissue surrounding a viscus or the viscera) due to the previous surgery, after the viscerolysis, a frozen pelvis is revealed, also it was discovered the lack of continuity of the right ureter at the pelvic level probably due to the previous surgery (**uretero hydrenephrosis**). An intestinal resection is done for a 3cm nodule at the recto-sigmoidian junction followed by anastomosis, endometrioma excision.

**Case 8:** A 31 yr old patient with severe dyspareunia and chronic pelvic pain. The preoperative MRI examination revealed an enlarged uterus, which has multiple intramural fibromatous nodules of 1-2 cm in size; appearance of **diffuse adenomyosis**; both ovaries of normal appearance and size; no deep endometriosis lesions. The medical team performed a resection of about 4 cm from the **presacral nerve**, after dissection of the presacral space; left lateral - inferior mesenteric artery, right lateral - right ureter, superior - aortic bifurcation, posterior - longitudinal vertebral ligament and left common iliac vein. Postoperatively, the symptomatology of the patient recovered considerably, now having a normal sex life and a lower menstrual pain.

**Case 9: Multiple conditions.** A 38 yr old patient with deep endometriosis and fibroids diagnosis suffering from severe pelvic pain, intestinal transit disorders (constipation), severe dyspareunia and dysmenorrhea. The MRI showed ovarian endometrioma, multiple fibroids, focal adenomyosis, utero-sacral ligaments nodules. The surgery highlights, pelvic adhesions involving the sigmoid, ovaries, both fallopian tubes and the rectum. After dissection of adhesions, the team practices excision of the adenomyosis nodule, the endometrioma and the utero-sacral ligament nodule and fibroids removal.

**Case 10.** A 30 yr old patient with a **previous endometrioma surgery**. The MRI reveals deep-infiltrative lesions in both utero-sacral ligaments, with infiltration of the recto-sigmoid junction, a pseudonodular lesion infiltrating the posterior wall of the cervix and uterine isthmus, a pseudonodular lesion at cervix and posterior vaginal recess, adhesions between both ovaries, uterus, sigmoid colon, bilateral hydrosalpinx, small endometriotic cysts in both ovaries. The surgery highlights a frozen pelvis, and after the dissection, two nodules are highlighted one at the level of the sigmoid loop, and one at the recto-sigmoid junction. At the externalization of the sigmoid colon, multiple endometriotic nodules are revealed, which required an **extended intestinal resection - approx. 35 cm**, followed by anastomosis using the circular stapler.
Glossary

**Ablation**- 1) the surgical removal of body tissue. 2) the removal of snow and ice from a glacier or iceberg by melting or evaporation. In endometriosis surgery ablation means nr 2.

**Amenorrhea**- no menstruation

**Anovulation**- no ovulation

**Angiogenesis**- the development of new blood vessels

**Anlage** -the rudimentary basis of a particular organ

**Aponeurosis**- a type of connective tissue found throughout the body

**Apoptosis**- a type of cell death in which a series of molecular steps in a cell lead to its death

**BSGE** - The British Society for Gynaecological Endoscopy

**Capillaries**- the smallest of the body’s blood vessels

**Catamenial**- monthly

**CNGOF**- Collège National des Gynécologues et Obstétriciens Français

**Coelomic epithelium**- lines the surface of the body wall and abdominal organs

**Dysmenorrhea**- painful periods

**Dyspareunia**- painful intercourse

**Dyschezia**- painful, bleeding or difficult bowel movement

**Dysuria**- painful or difficult urination

**ESHRE**- European Society of Human Reproduction and Embryology

**Excision**- the act or procedure of removing by or as if by cutting out

**FDA** - Food and Drug Administration

**HAS**- Haute Autorité de Santé

**Hemipancreatectomy**- surgical resection of half of the pancreas

**Hemithorax**– one side of the chest

**Hemostasis**- the stopping of the flow of blood

**Hydatid**- cyst containing watery fluid and the larvae of certain tapeworms

**Hydronephrosis**- kidney swells due to urine failing to properly drain from the kidney to the bladder

**Hydrourereter**- swelling of the ureter

**Hyperalgesia**- abnormally heightened sensitivity to pain

**Hyperplasia**- an increase in the number of normal cells in a tissue or an organ

**Hypoestrogenic**- a lower than normal level of estrogen

**Iatrogenic**- due to the activity of a physician or therapy

**IBS**- Irritable Bowel Syndrome

**ICSI**- Intracytoplasmic Sperm Injection

**Innervation**- to supply with nerves

**Metaplasia**- the transformation of one cell type to another cell type

**Neovascularity**- new blood vessel formation in abnormal tissue or in abnormal position

**Nociceptive**- relating to the perception or sensation of pain

**Orthopnea** and dyspnea is shortness of breath (dyspnea) that occurs when lying flat, causing the person to have to sleep propped up in bed or sitting in a chair

**Parenchyma** - the functional tissue of an organ

**Pleurodesis**- is a procedure that is designed to get the two layers of the lung lining (the pleura) to stick together

**Salpingo** (tubes)-**oophorectomy**(ovaries) to remove the ovaries and fallopian tubes

**Stenosis**- the abnormal narrowing of a passage in the body
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