

# IAGE CONNECT

News Bulletin, Vol. 1 (2019-2020)

$E=mc^2$



Dr. Sunita Tandulwadkar  
President, IAGE



Dr. Bhaskar Pal  
Hon. Gen. Secretary, IAGE

## From The President's Desk

### *Dear Colleagues,*

Thank you so much for putting your faith in me and electing me for this esteemed duty. I feel honoured and humbled to take this position of Presidency of the Indian Association of Gynaecological Endoscopists for the year 2019-2020.

I am thankful to all my friends and colleagues across the country that have helped me reach this position: Dr. PC Mahapatra, Dr. Hrishikesh Pai, Dr. Nandita Palshetkar, Dr. Rishma Pai, Dr. Prakash Trivedi, Dr. Sanjay Patel, Dr. Mahesh Gupta, Dr. Vineet Mishra and many more.

From its conception till date, the past Presidents and their teams have taken the organization to great heights and I definitely believe that I will contribute my best to take this organization further ahead and keep the legacy going.

I am very happy that Dr. Bhaskar Pal is appointed to be my Hon. Gen. Secretary, Dr. Krishna Kumar as Vice-President, Dr. Pandit Palaskar as Joint Secretary, Dr. Atul Ganatra as Honorary Treasurer and my exceptional team of Managing Committee Members – Dr. Abhishek Chandavarkar, Dr. Kalyan Barmade, Dr. Kishore Pandit, Dr. Mahindra Borse, Dr. Niranjana Chavan, Dr. Nitin Shah, Dr. Sandesh Kade and Dr. Vivek Salunkhe. I am looking forward to welcoming the remaining 8 members and I am sure they will be an advantage to the 2019-20 team.

**My theme of the year is,**

**E = mc<sup>2</sup>  
Endoscopy = mastering challenges<sup>2</sup>**

During the entire year we have planned various projects.

**“Knowledge will bring you the opportunity to make a difference.” – ‘STAR EndoGyn Conclave 2019-2020’** brings Endoscopic surgeons from smaller cities together to organize a State Conference where Endoscopic surgeons will be invited to present lectures and share their surgical knowledge with the audience. We will be organizing 15 conferences in 11 states in the year 2019-2020.

**“Tomorrow belongs to those who prepare for it today.” – ‘Project Eagle’** focuses on spreading the knowledge of Endoscopy among post-graduate students. We will be reaching out to medical colleges across the country, to organize one-day operative training workshops for residents in the Obstetrics and Gynecology department to broaden horizons for our aspiring gynecologists.

**“Education is life itself” – ‘STAR Drive: Simplified Endoscopy Teaching with Audio/Video Recordings’** where Educational Videos will be shared via pen-drives on topics, such as, Hysteroscopy, Myoma, Hysterectomy, Pelvic Floor, Vaginal Hysterectomy, Ovarian Adnexal Masses, Endometriosis. These will include various subgroups of each procedure by expert surgeons from across the country, with audio and video, keeping teaching as a purpose in mind.

We will be organizing two **‘Focus Expert Group Meetings’** during our tenure. One meeting on **‘Myoma’** will take place in Hyderabad and the other on **‘Endometriosis’** will take place in Delhi.

I intend to review the **Journal of Gynaecological Endoscopy and Surgery.**

We will also have several **‘Membership Drives’**. The strength of any organization depends on the strength of the members they have. In India, we have 10,000+ Endoscopic Surgeons or Gynecologists who are performing Endoscopic surgeries, but unfortunately, they are not part of our organization. We will try to ensure that more start getting involved academically and become members of this prestigious organization.

We will be planning **‘Family Planning Camps’**, across the country. This will be in association with doctors from PHC. Together along with my team and fellow members of IAGE, I wish to see the organization growing and achieving greater heights.

“Consistency with the right strategic plan is the ultimate key to success.”

- Endmond Mbiaka

**Dr. Sunita Tandulwadkar**

“The idea is not to live forever, but to create something that will”

- Andy Warhol



## From The Hon. General Secretary's Desk



Dear Friends,

It is indeed an honour and a great privilege to assume the office of the Hon. General Secretary of the Indian Association of Gynaecological Endoscopists (IAGE) for the year 2019-20 and I will strive to meet your expectations. IAGE is the largest body of Gynaecological Endoscopists in the country, and the membership strength is increasing at a rapid pace. With the advent of state chapters, we expect to see more members joining the organization and a consequent rise in activities.

Team IAGE 2019-20, under the dynamic leadership of our President Dr Sunita Tandulwadkar, has planned an exciting year of conferences, training, providing platform to young endoscopists and reaching out to young postgraduates to ignite their interest in minimally invasive surgery. We urge all members to participate in the activities and we will be happy to see a broader involvement of members. We are an email away if you want to take an active part in any of the events and courses.

Constructive criticism is very important for progress. We would seek feedback from members about the organization, the conferences, the courses and the publications. We can only improve if we critically look at our performance as an organization and your feedback is an essential tool for achieving that goal. Suggestions for new activities are welcome as well.

We should finally be able to move into our new permanent office this year. We will let you know once it is ready and invite you to drop in at your convenience. We are grateful to our past Presidents for laying a strong foundation; it is now up to all of us to make the organization more active, more visible, more vibrant and more useful to all of us. Together we need to ensure that more and more women in India can access minimally invasive surgery in a safe and economical way.

I look forward to a busy year and hope to interact with most of you personally during the events. I thank you again for reposing your faith in me.

With warm personal regards

**Dr Bhaskar Pal**  
Hon. General Secretary, IAGE

## IAGE ACADEMIC ACTIVITIES

- 1. Post Graduate Students –**  
**EAGLE – Every Aspiring Gynaecologist Learns Endoscopy**
- 2. Young Gynaecologists -**  
**Knowledge Enclave**
- 3. Gynaecologists who wish to advance their skills –**  
**BALI – Balancing Advanced Laparoscopy in India**
- 4. Platform for State Endoscopists -**  
**STAR EndoGyn Conclave 2019-20**
- 5. Expert Gynaecologists –**  
**FEM – Focus Expert Group Meetings**
- 6. STAR Drives –**  
**Simplified Endoscopy Teaching with Audio/Video Recordings**

## SOCIAL ACTIVITY

*IAGE will be organizing Family Planning camps all over India.*



## IAGE Managing Committee 2019 - 2020



**Dr. Sunita Tandulwadkar**  
President  
2019-2020



**Dr. Bhaskar Pal**  
Hon. General Secretary  
2019-2020



**Dr. Rishma Dhillon Pai**  
Immediate Past President  
2018-2019



**Dr. Krishnakumar Subramaniam**  
Vice President  
2019-2020



**Dr. Pandit Palaskar**  
Joint Secretary  
2019-2020



**Dr. Atul Ganatra**  
Honorary Treasurer  
2019-2020

### MANAGING COMMITTEE MEMBERS



**Dr. Abhishek Chandavarkar**



**Dr. Kalyan Barmade**



**Dr. Kishore Pandit**



**Dr. Mahindra Borse**



**Dr. Niranjan Chavan**



**Dr. Nitin Shah**



**Dr. Sandesh Kade**



**Dr. Vivek Salunkhe**

# STAR EndoGyn Conclave 2019-2020

**Nagpur**  
STAR ENDOGYN CONCLAVE 2019  
July 5<sup>th</sup> - 7<sup>th</sup>, Nagpur

**Indore**  
STAR ENDOGYN CONCLAVE 2019  
August 3<sup>rd</sup> - 4<sup>th</sup>, Indore

**Coimbatore**  
STAR ENDOGYN CONCLAVE 2020  
October 18<sup>th</sup> - 20<sup>th</sup>, Coimbatore

**Guwahati**  
NE STAR ENDOGYN CONCLAVE 2019  
November 15<sup>th</sup> - 17<sup>th</sup>, Guwahati

**Mumbai**  
FOGSI - IAGE CONCLAVE  
November 22<sup>nd</sup> - 24<sup>th</sup>

**Jaipur**  
STAR ENDOGYN CONCLAVE 2019  
November 29<sup>th</sup> - 1<sup>st</sup> December, Jaipur

**Surat**  
YIVA IAGE CONCLAVE 2019  
December 6<sup>th</sup> - 8<sup>th</sup>, Surat

**Thrissur**  
FOGSI IAGE CONCLAVE 2019  
December 20<sup>th</sup> - 22<sup>nd</sup>, Thrissur

**Latur**  
STAR ENDOGYN CONCLAVE 2019  
December 27<sup>th</sup> - 29<sup>th</sup>, Latur

# STAR EndoGyn Conclave 2019-2020

**Pune**  
STAR ENDOGYN CONCLAVE 2020  
January 10<sup>th</sup> - 12<sup>th</sup>, Pune

**Patna**  
STAR ENDOGYN CONCLAVE 2020  
February 22<sup>nd</sup> - 23<sup>rd</sup>, Patna

**Bengaluru**  
STAR ENDOGYN CONCLAVE 2020  
March 13<sup>th</sup> - 15<sup>th</sup>, Bengaluru

**Kanpur**  
STAR ENDOGYN CONCLAVE 2020  
March 20<sup>th</sup> - 22<sup>nd</sup>, Kanpur

**Noida**  
STAR ENDOGYN CONCLAVE 2019  
April 3<sup>rd</sup> - 5<sup>th</sup>, Noida

**Kolkata**  
IAGE ANNUAL CONFERENCE ENDOGYN 2020  
May 22<sup>nd</sup> - 24<sup>th</sup>, Kolkata

These are 15 Conferences in 11 States. The aim of these conferences is to reach out to many Gynaecologists from smaller cities and popularize Endoscopy among all. In today's era, everyone should know at least level I/level II Endoscopy so as to serve his or her patient in the best possible way. These conferences will also ensure that Endoscopists from the states are given a platform to showcase their talent in these conferences. Our vision is to show the 3D Laparoscopic Surgeries, from basic to advanced. We will be helping people to learn from the basics of laparoscopy and hysteroscopy until the advanced surgery with the lateral pelvic wall and pelvic floor surgeries. This will either be a 2 or 3 day conclave, where 1 day will be a live operation workshop and subsequently will be the didactic discussions where we will try and involve as many Endoscopic surgeons of that state to present their lectures.

# CATCH THEM YOUNG – EAGLE

## National Competition



The project carries the acronym EAGLE – Every Aspiring Gynaecologist Learns Endoscopy. This would be in the form of a two-day project at Medical colleges across the country. Johnson & Johnson have academically partnered for this project. It will be in 2 stages. First stage will consist of 1-day program organized at individual medical colleges across all states, where, open surgery suturing exercises for 3 hours and eye-hand coordination exercises and Endo suturing techniques will take place. First stage will be evaluated. The competition will take place between medical colleges at State Level. The state level winners will continue to compete at National Level. A total of 3 winners will be announced at the Kolkatta IAGE Conference in 2020. Second stage will consist of Live Surgery Observership at individual medical colleges.

The Indian Association of Gynaecological Endoscopists (IAGE) has initiated a project for postgraduate trainees in Obstetrics and Gynaecology across India. Our aim is to initiate the Gynaecologists of tomorrow to common endoscopic procedures like Laparoscopic Hysterectomy, Myomectomy, Ovarian Cystectomy as well as Hysteroscopic procedures.



Dr. Abhishek Chandavarkar



Dr. Abhishek Mangeshikar



Dr. Ajay



Dr. Amit Ashok Tajane



Dr. Anita Singh



Dr. Anurag Bhate



Dr. Anuja Kulkarni



Dr. Alok Deb



Dr. Ashwath Kumar  
Convenor



Dr. Asna Ashraf



Dr. Annasaheb Birajdar



Dr. Archana Baser



Dr. Arun Madhab Boruah



Dr. Aruna Tantia



Dr. Asha Baxi



Dr. Ashvin Vacchani



Dr. Bhaskar Pal



Dr. Bhaurao Yadav



Dr. Balaji Reddy Nalwad



Dr. Chaitanya Ganpule



Dr. Damodar Rao



Dr. Deepak Goenka



Dr. Deven Jugal



Dr. Diganta Chetia



Dr. Divyesh Shukla



Dr. Ganpat J Sawant



Dr. Harinath K S



Dr. Hareh Vaghasiya



Dr. James Elangbam



Dr. Jay Mehta



Dr. Jyoti Mishra



Dr. Jyotirmoy Das



Dr. Jayaprakash B Patil



Dr. Kiran Kurtakoti



Dr. Kalyan Barmade



Dr. Kishore Pandit



Dr. Krishna Mandade



Dr. Krishnakumar Subramaniam



Dr. Laxmi Shrikhande



Dr. Mala Raj



Dr. Manish Pandya



Dr. Manoj Parbat



Dr. Madhuri Dabhade



Dr. Mahindra Borse



Dr. Manish Machave



Dr. Manjula Anagani



Dr. Makarand Masrani



Dr. Manik Gurram



Dr. Meenakshi Sundaram



Dr. Neelam Ohri



Dr. Nitin Shah



Dr. Nagendra Sardeshpande



Dr. Nilakshi Phukan Kumar



Dr. Pragnesh Shah



Dr. Parul Kotdawala



Dr. Prashant Mangeshikar



Dr. Prabha Agrawal



Dr. Pandit Palaskar



Dr. Yashodhan Deka



Dr. Rajendra S Sankpal



Dr. Pragya Mishra Choudhary



Dr. Prakash Trivedi



Dr. Rajini M



Dr. Raju Dabade



Dr. Rajesh Darade



Dr. Gaurav Desai



Dr. Sandesh Kade



Dr. Sanket Pisat



Dr. Saraswathi Ramesh



Dr. Sadhana Patwardhan



Dr. Sam Abraham

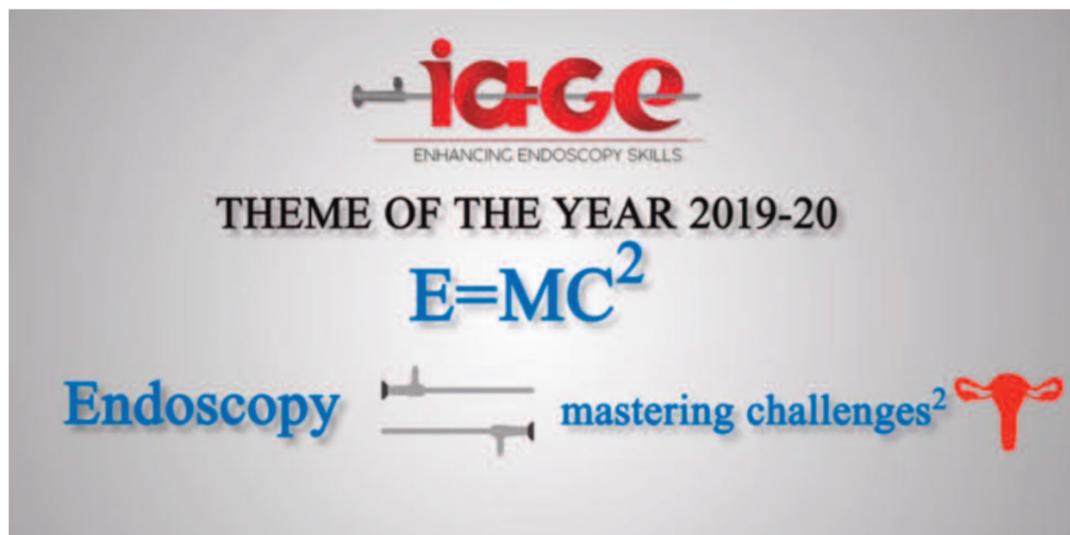


Dr. Sanjay Makwana



Academic support by Johnson & Johnson

# Theme of the Year



"The best way to predict your year, is to create it!"

# STAR DRIVES

## SIMPLIFIED ENDOSCOPY TEACHING WITH AUDIO/VIDEO RECORDINGS



We will be releasing pen-drives with Educational Videos to share the knowledge by expert surgeons

### Hysterectomy



Dr. Vivek Salunkhe  
 Convenor



Dr. Abhishek Mangeshikar  
 Co-Convenor

### Myomectomy



Dr. Nitin Shah  
 Convenor



Dr. Saumil Trivedi  
 Co-Convenor

### Endometriosis



Dr. Sandesh Kade  
 Convenor



Dr. Kishore Pandit  
 Co-Convenor

### Vaginal Hysterectomy



Dr. Ganpat Sawant  
 Convenor



Dr. Archana Baser  
 Co-Convenor

### Pelvic Floor



Dr. Abhishek Chandavarkar  
 Convenor



Dr. Kalyan Barmade  
 Co-Convenor

### Hysteroscopy



Dr. Damodar Rao  
 Convenor



Dr. Sejal Naik  
 Co-Convenor

### Ovarian Adnexal Masses



Dr. Ashwath Kumar  
 Convenor

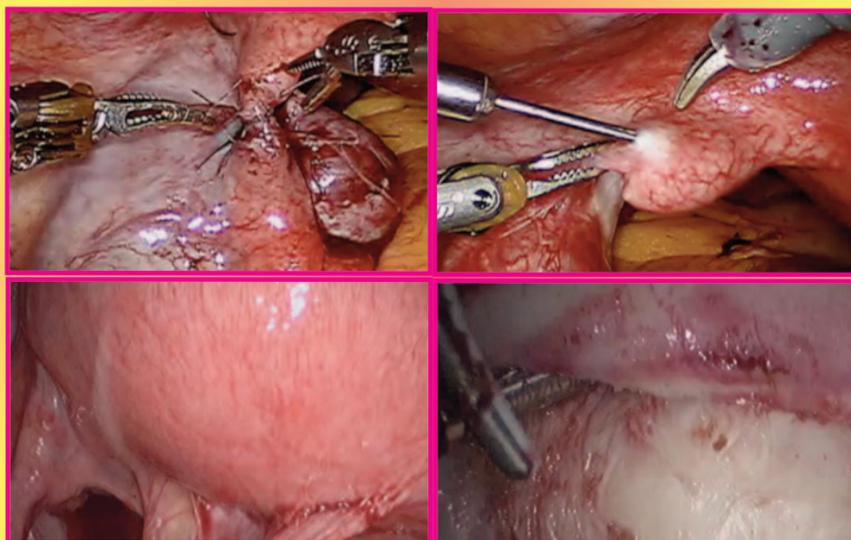


Dr. Kiran Kurtakoti  
 Co-Convenor



# HYSTEROSCOPY SIMPLIFIED

*By Masters*



**Dr. Sunita Tandulwadkar**  
Editor

Special Thanks to:  
Dr. Sujata Kar  
Dr. Sejal Naik



**Dr. Bhaskar Pal**  
Co-Editor

We will be releasing an International Book on Hysteroscopy titled '**Hysteroscopy Simplified by Masters**', where we have invited many National and International Faculty to contribute chapters and share their knowledge on various topics that consolidate the vast topic of Hysteroscopy. Through

this book, containing around 31 chapters where about 15 chapters have been contributed by International faculty, we wish to aggressively spread the knowledge of Hysteroscopy among aspiring Gynecologists and Post-Graduate students.

## FERTILITY ENHANCING ENDOSCOPY SURGERY WORKSHOP

A **FOGSI** Initiative along with **IAGE**



**Dr. Nandita Palshetkar**  
FOGSI President



**Dr. Sunita Tandulwadkar**  
National Convener

### Youth Council

**WEST ZONE:**

- Dr. Soumil Trivedi
- Dr. Rohan Krishnakumar
- Dr. Rohan Palshetkar
- Dr. Suyash Naval
- Dr. Gaurav Desai
- Dr. Kalyan Barmade

**NORTH ZONE:**

- Dr. Biswa Bhusan Dash
- Dr. Sonia Chawla
- Dr. Shubra Singh Goyal
- Dr. Arvind Vaid
- Dr. Ajay Aggarwal
- Dr. Jyoti Mishra

**SOUTH ZONE:**

- Dr. Ashok
- Dr. Subash Mallya
- Dr. Vimee Bindra
- Dr. Jayprakash Patil
- Dr. Bimal John

**EAST ZONE:**

- Dr. Arun Madhab
- Dr. Priyankur Roy
- Dr. Indranil Dutta
- Dr. Hafizur Rahman
- Dr. Shipra Singh

Join IAGE



## FEM - FOCUS EXPERT GROUP MEETING

Two 'Focus Expert Group Meetings' will be organized, during our tenure, so as to come with the standard practice guidelines and consensus. It will be on 'Myoma' on 25th September in Hyderabad and on 'Endometriosis' on 11th December in Mumbai.



Convenor of Myoma



Dr. Manjula Anagani  
Convenor

Convenor of Endometriosis



Dr. Atul Ganatra  
Convenor

## BALI - Balancing Advanced Laparoscopy in India

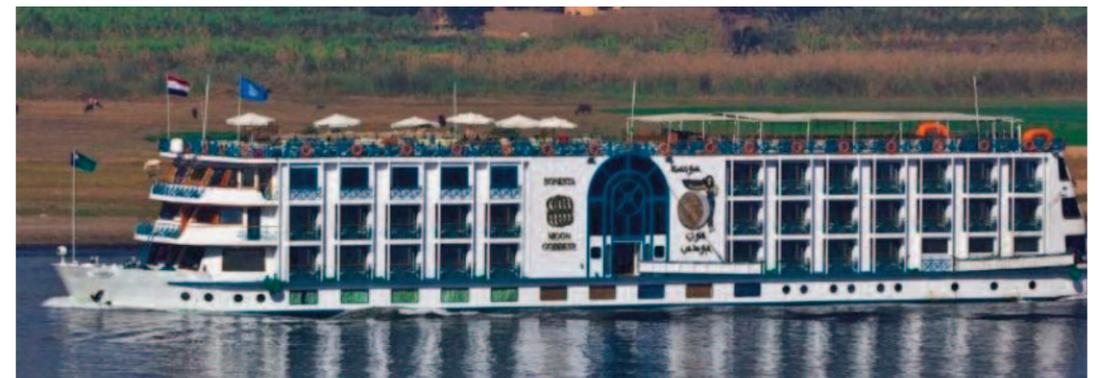
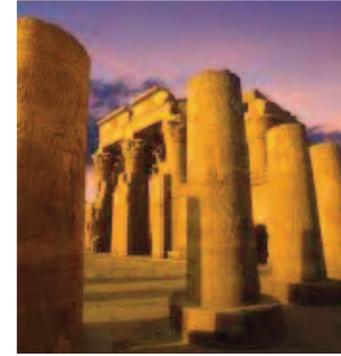
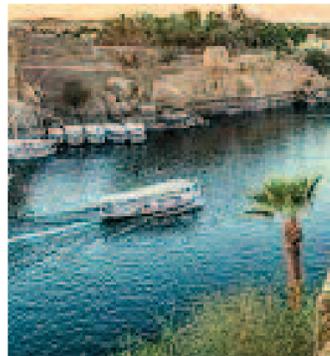
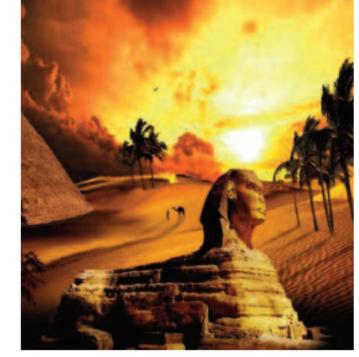
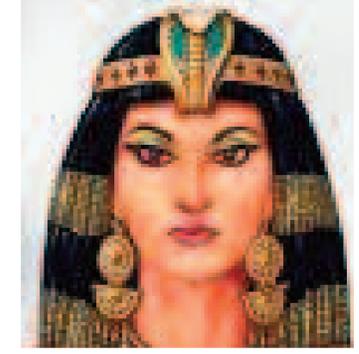
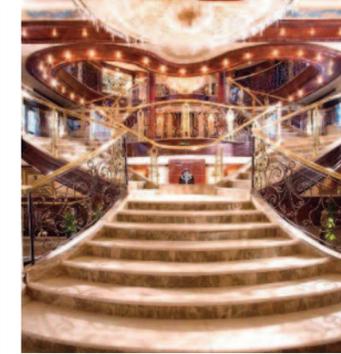
We will be providing one-day hands-on training on anaesthetized animals to 150 selected IAGE members, at the Johnson & Johnson animal lab in Mumbai and Chennai, where experts will teach them personally.

*\*Selection will be done by IAGE office bearers*



## ARTOSCOPIA & HYSTEROSCOPIA ON CRUISE

Sail into History & Learn Hysteroscopy



Dr. Osama Shawki  
Convenor



Dr. Jaideep Malhotra  
President ISAR



Dr. Sunita Tandulwadkar  
President IAGE



Dr. Nandita Palshetkar  
President FOGSI



Dr. Varsha Baste  
Internation Exchange  
Committee FOGSI

# KNOWLEDGE ENCLAVE

Academic Partner – Johnson & Johnson

One-day workshop with live surgeries till lunch and post lunch there will be a scientific discussion on the same topics. This will be organized mainly in tier II and tier III cities.



## Hysteroscopy in Chronic Endometritis



**DR SERGIO HAIMOVICH – MD, PHD**  
 Head of the Hysteroscopy Unit. Del Mar University Hospital. Barcelona, Spain.  
 Director of Gynecology Ambulatory Surgery at Hillel Yaffe Medical Center, Hadera, Israel. Technion – Israel Institute of Technology

**DR NILI RAZ- MD, M.SC.**  
 Department of Obstetrics and Gynecology, Hillel Yaffe Medical Center, Hadera, Israel.  
 The Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel.

### Abbreviations

UI=Unexplained Infertility, RIF=Repeated Implantation Failure, RPL=Recurrent Pregnancy Loss, PC=Plasma Cells, CE=Chronic Endometritis, IUA=Intrauterine Adhesions, TCRA=Transcervical Resection of Adhesions, OPR=Ongoing Pregnancy Rate, LBR=Live Birth Rate.

### DEFINITION, EPIDEMIOLOGY AND ETIOLOGY:

Chronic endometritis is a persistent inflammation of the endometrium, characterized by plasma cell infiltration of endometrial stroma.

Chronic endometritis is histologically detected in 8% of endometrial specimens of women with clinically suspected cervicitis, in 3%-10% of women who undergo endometrial biopsy to investigate abnormal uterine bleeding and in 12%-46% of hysteroscopy-guided endometrial biopsies in infertile patients.

A strong association between endometriosis and chronic endometritis was also described.

Research detected microorganisms in the endometrial cavity of healthy asymptomatic women, i.e., the uterine microbiome, thus challenging the previous paradigm about endometria being sterile. It is not yet clear whether CE follows acute endometritis or caused by other factors, yet the finding that antibiotic treatments might be an effective treatment for CE suggests it has an infectious origin. Bacteria found in uterine cavity of CE patients are *Streptococcus* spp., *Staphylococcus* spp., *Escherichia Coli*, *Enterococcus Faecalis*, *Klebsiella pneumoniae*, *Corynebacterium* and *Mycoplasma/Ureaplasma* spp. Theories about the origin of the uterine microbiota include vagina (via ascending pathway), peritoneum (via fallopian tubes) and oral gingivitis (via hematogenous spread). Predisposing conditions to CE were found to be intrauterine leiomyomas, a recent endometrial biopsy, or curettage and IUD use. Altered maternal immune tolerance towards the embryo, immunologic effects on the mechanisms of implantation, and a defective trophoblastic invasion, all effected by altered distribution of immune cells, such as natural killer cells in the endometrial mucosa of infertile CE patients, might be part of the pathophysiology of the effect of CE on reproduction. For example, chronic endometrial inflammation can alter endometrial cytokine and chemokines production (such as IL11, CCL4 etc), a decrease in CD56 lymphocytes, and an increase in CD16 lymphocytes and B cells infiltrating and aggregating in the stroma of the endometrial functional layer and epithelial cells, related to aberrant expression of adhesion molecules and cytokines in the endometrium. These mecha-

nisms can result in decreased endometrial receptivity of embryos and other symptoms mentioned in this chapter.

### SYMPTOMS

Unlike Acute Endometritis which presents with abdominal pain, fever, discharge and sometimes leukocytosis, CE is mostly asymptomatic, making CE rarely clinically suspected. CE was described as associated with abnormal uterine bleeding, pelvic pain, dyspareunia, leucorrhea, recurrent abortion, RIF and infertility.

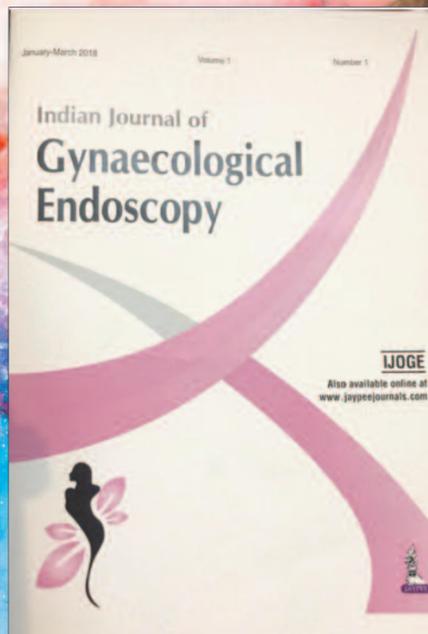
### DIAGNOSIS

CE is mostly asymptomatic and not identified by most diagnostic tests.

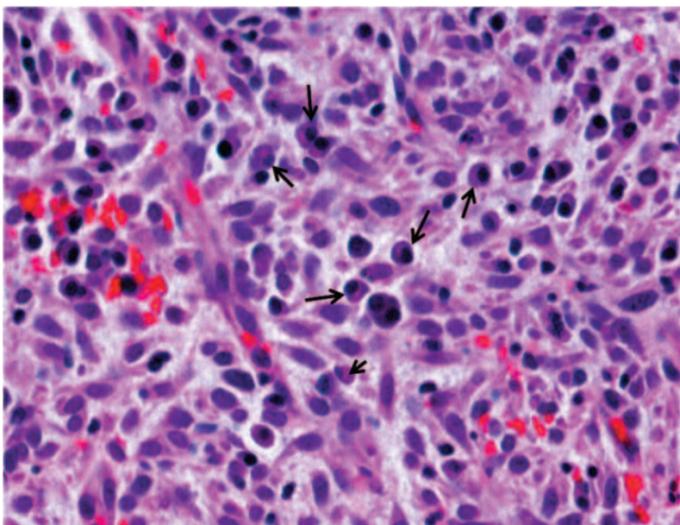
The gold standard for the diagnosis is histological testing of an endometrial biopsy, mainly identification of plasma cells in the endometrial stroma. In 1981, Greenwoods and Moran described the morphologic features found to be of value in diagnosing CE: superficial stromal edema, increased stromal density, and pleomorphic stromal inflammatory infiltrate dominated by lymphocytes, in the absence of premenstrual changes or any other significant pathological endometrial lesions. When these changes were present, a plasma cell infiltrate was invariably found. More histological features described as associated with chronic inflammation were abnormal percentages of lymphocytes, leukocytic infiltration of both glands and stroma, high stromal cell proliferation, dissociated maturation between the epithelium and stroma, a pronounced predecidual reaction and the presence of Eosinophils or macrophages. The search for plasma cells can be interfered with, or mimicked by, other conditions, such as mononuclear inflammatory cell infiltrates, stromal cell proliferation, plasmacytoid appearance of stromal cells, or a pronounced predecidual reaction in a late secretory endometrium. Identification of plasma cells by routine hematoxylin and eosin (H&E) stain is challenging, due to their sometimes-low numbers and their obstruction by other stromal cells.

H&E alone is not enough for CE diagnosis, due to high interobserver variability, as shown by Kasius et al., who

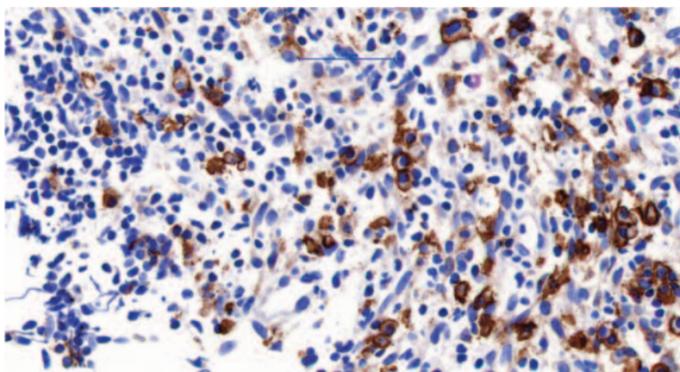
## Revival of the Journal



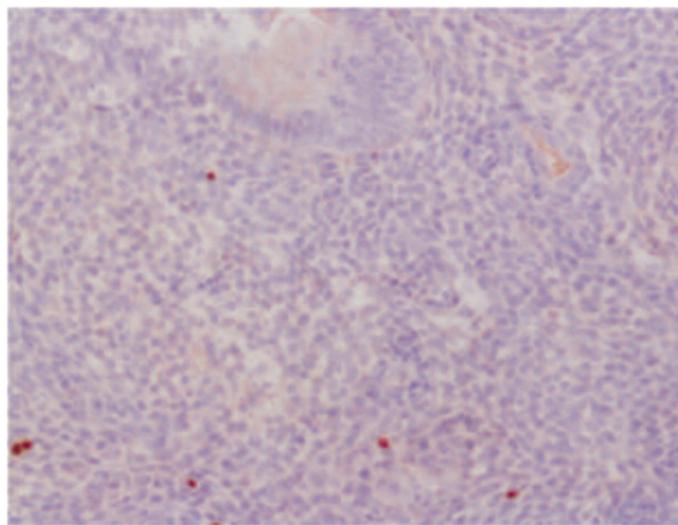
showed interobserver similar diagnostic categories (no CE, Possible CE, and Evident CE) in 88% of 100 infertile patient biopsies. The kappa-value for interobserver agreement was 0.546 (95% CI: 0.351–0.741), which represents a moderate agreement only. Adding another immunohistochemical stain to the H&E (by CD138 alone, or combined with other plasma cell stains such as CD20 and CD79a) improved the kappa-value for interobserver agreement to 0.659 (95% CI: 0.463–0.855), which represented a substantial agreement. CD138, a marker for plasma cells which outlines the cell membranes, can thus readily be used. The disadvantages of CD138 as a marker are stromal-glandular background staining and difficulty in visualizing nuclear details of the plasma cells. Lately, MUM1 immunostain demonstrated superiority over CD138 in diagnosing CE. In addition to having a clean background, MUM1 was found to be a more sensitive stain than CD138 for the detection of Plasma cells in endometrium. MUM1 is a transcription factor, thus stains the cell nucleus. Cicinelli et al. suggests using a triad of hysteroscopy, standard microbiology culture, and endometrial biopsy to best assess for the presence of CE.



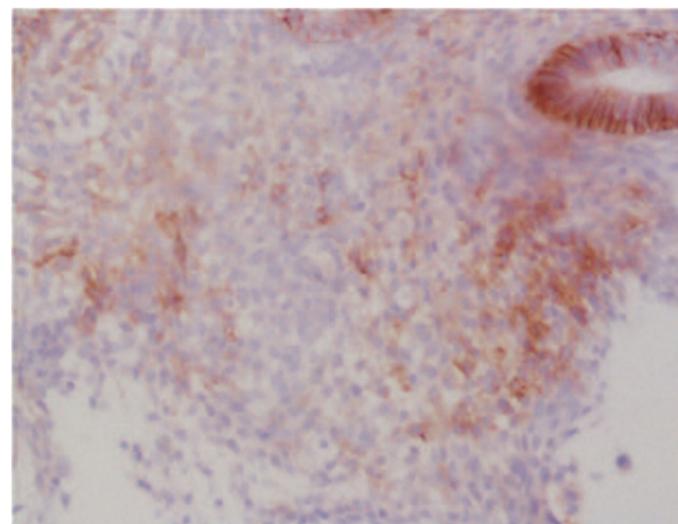
**Fig. 1: Chronic endometritis; High-power view reveals plasma cells in the stroma (black arrows). H&E, 400x (with permission from Dr. Lea Shekhtman, Pathology department, Hillel Yaffe Medical Center).**



**Fig. 2: A CD138 immunostain highlights the plasma cells, 400x (with permission from Dr. Lea Shekhtman, Pathology department, Hillel Yaffe Medical Center).**



**Fig. 3A: Comparison between MUM1(A) and CD138(B) immunostain highlighting the plasma cells, X200 (Same patient). With permission from Dr. Lea Shekhtman, Pathology department, Hillel Yaffe medical center.**



**Fig. 3B: Comparison between MUM1(A) and CD138(B) immunostain highlighting the plasma cells, X200 (Same patient). With permission from Dr. Lea Shekhtman, Pathology department, Hillel Yaffe medical center.**

#### CHRONIC ENDOMETRITIS AND INFERTILITY

CE is highly prevalent in patients with infertility: CE was present in 12%–46% of the hysteroscopy-guided endometrial biopsies in infertile patients. CE was diagnosed in 14%–67.5% of women with RIF and 9%–56% of women with recurrent miscarriage.

In RIF patients undergoing IVF treatments, the implantation rate of patients diagnosed with CE was lower than those without CE. Chronic endometritis is highly prevalent in patients with unexplained infertility. Cicinelli et al. investigated 97 women with unexplained infertility using hysteroscopy and biopsy. They found that 57% had CE by hysteroscopy and 56% by histology. These data suggest a correlation between CE and impaired implantation and early embryonal development. Cicinelli et al. also demonstrated, in

several studies, that antibiotic treatment in RIF patients and recurrent aborters improved reproductive outcomes. Chen Y. et al. described that among the 82 women with moderate to severe IUAs (i.e., Asherman's syndrome), undergoing hysteroscopic adhesiolysis (TCRA), the prevalence of CE was 35% and more. When comparing those patients with CE to the patients without CE, a higher adhesion recurrence rate in second look hysteroscopy was found in patients with CE (45%) in comparison with the patients without CE (21%), thus CE may be a contributing factor in higher adhesion recurrence.

#### Hysteroscopy in CE

CE diagnosis is challenging: anamnesis, symptoms, physical exam, blood work and US are not specific. Although histology is the gold standard for diagnosis, it is challenging, due to mimicking conditions discussed earlier in this chapter, especially in a late secretory endometrium. This emphasizes the importance of hysteroscopy in CE diagnosis. Hysteroscopy is a useful and reliable technique for detecting chronic endometritis. Hysteroscopy is highly accurate in diagnosing CE and highly correlates with histologic results. A study suggesting a lower sensitivity included only 6 patients with CE.

CE diagnosis using hysteroscopy is based on direct observation of the uterine cavity and demonstration of micropolyps, stromal edema, and focal or diffuse hyperemia, preferably at the mid-follicular phase of the menstrual cycle when the endometrial lining is the thinnest.

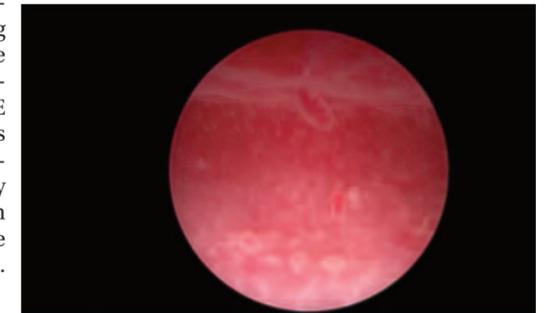
**Table 1: Hysteroscopic Characteristics of Chronic Endometritis [6,34,35,36,37], See Fig. 4-9:**

1. Mucosal edema
2. Focal or diffuse endometrial hyperemia
3. Presence of micropolyps (<1mm)

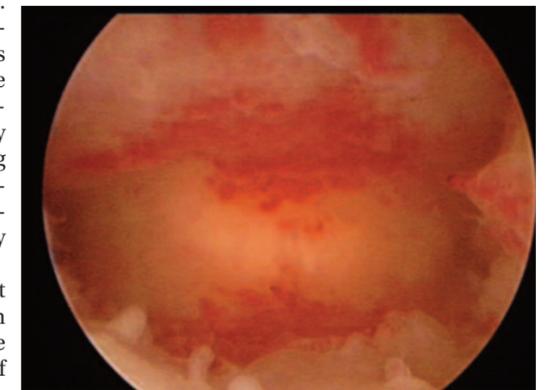
In their 2008 publication Cicinelli et al. showed that the diagnostic accuracy of CE by hysteroscopy was 93.4% when using hyperemia, mucosal edema and micro polyps as diagnostic parameters for CE in hysteroscopy. Zargar et al. reported an 86% sensitivity and 87% specificity for hysteroscopic diagnosis of CE in IVF patients suffering from RIF or RPL, and a 70% and 95% PPV and NPV, respectively. Song D. et al. studied the correlation between hysteroscopy findings and chronic endometritis. They examined 322 biopsies with CD138 cells present, and found the prevalence of endometrial hyperemia, endometrial interstitial edema, micropolyps were 52.5%, 8.4% and 3.4%, respectively. The  $\kappa$  value of intra-observer and inter-observer agreement on the presence or absence of the hysteroscopic feature of CE was 0.86 and 0.73, respectively. The sensitivity, specificity, positive and negative predictive value, and diagnostic accuracy of the presence of one or more of these hysteroscopy features were 59.3%, 69.7%, 42.1%, 82.8%, and 66.9%, respectively. Cravello Let al. identified "strawberry aspect" pattern in correlation with CE, "strawberry spots" were also described by Song Det al. as hyperemic endometrium, which appears flushed with a white central point.

In summary, the high prevalence of CE in infertile patients, and especially the effectiveness of treatment in UI patients, suggests that hysteroscopy should be an important part of the pre-ART diagnostic work-up, especially in patients with UI, RIF and recurrent abortions.

**Fig. 4- "Strawberry Aspect"**



**Fig. 5 A, B – Focal Hyperemia**



**Fig. 6: Hemorrhagic Spots**



**Fig. 7: Sparse Micro Polyps**

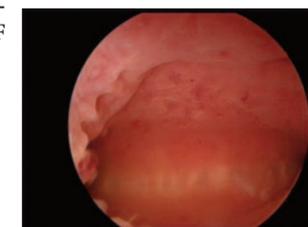




Fig. 8 : Diffuse Micro Polyps

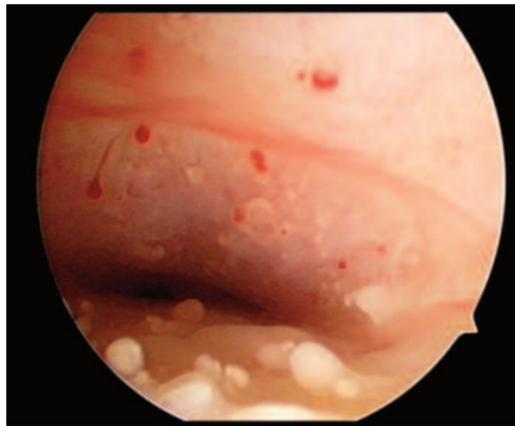


Fig. 9: Thick and Pale Endometrium in the Follicular Phase Due to Stromal Edema

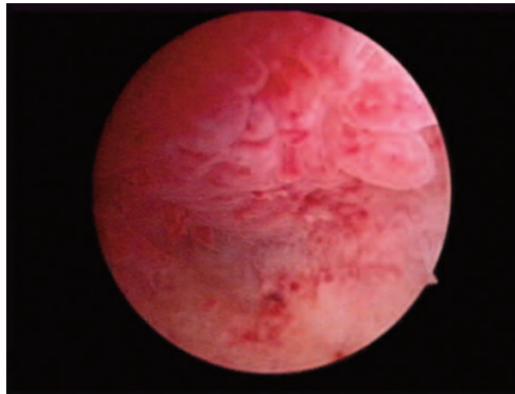


Fig. 10: Hyperemic and Polypoid Endometrium

#### TREATMENT

As increasing amount of evidences suggest the negative impact of CE on fertility. Questions arise: Is ABX an effective therapeutic option? Would ABX treatment for CE patients restore normal endometrial histology and improve reproductive outcomes? In an effort to solve these dilemmas, several studies demonstrated a very high cure rate, up to 92%, after a single antibiotic cycle, and 99% after second line ABX TX in RIF patients (TX protocols were different in those studies: option No 1: first-line: doxycycline 100mg, Twice a day for 14 days. Second-line was combination of oral metronidazole 250 mg, twice per day, 14 days and ciprofloxacin hydrochloride 200 mg, twice per day, 14 days. Option 2 was detailed in the following Cicinelli studies. Cicinelli et al. treated 53 UI patients, hysteroscopically and histologically diagnosed with CE, with ABX and repeated hys-

teroscopy and biopsy following AXB TX. Antibiotic therapy resulted in chronic endometritis histologic resolution in 82% of patients, while in 17.6% positive cultures was persistent. UI patients with cured chronic endometritis showed higher pregnancy rate and live birth rate in comparison with both women with persistent disease following ABX TX and women without chronic endometritis diagnosis (Spontaneous pregnancy rates were 76.3% vs. 20% vs. 9.5%; live birth rates were 65.8% vs. 6.6% vs. 4.8% respectively). The ABX protocols used in this study were: Ciprofloxacin 500 mg twice a day for 10 days for Gram-negative infections, Amoxicillin + Clavulanate 1 g twice a day for 8 days for Gram-positive bacteria, Josamycin 1g or Minocycline or 100 mg or Doxycycline 100 mg twice a day for 12 days for Mycoplasma and Ureaplasma, Ceftriaxone 250 mg IM in a single dose plus oral Doxycycline 100 mg twice a day for 14 days plus oral Metronidazole 500 mg twice a day for 14 days for women with negative cultures. In patients with RIF and CE who had been treated with ABX and had been cured, improved IVF outcomes were achieved including OPR, LBR, CPR and IR, in comparison with patients with persistent CE. IVF outcomes (OPR/LBR, CPR, and IR) of women with cured CE were comparable to women without CE. Miscarriage rate was not significantly different between groups. ABX ability to restore normal endometrial histology suggests a causal relationship between CE and defective endometrial receptivity. Regarding recurrent miscarriage, Cicinelli et al. found a significantly higher number of spontaneous pregnancies in RM patients antihistologically cured from CE (78%) in comparison to 15%-17% in patients for whom CE was still present at hysteroscopy.

In summary, CE negatively affects implantation and fertility. Antibiotic administration treats CE effectively. Treatment can be easily administered in an outpatient setup. When CE is cured by antibiotic in infertile patients mentioned in this chapter (RIF, IU), the pregnancy rates, and in some patients also the live birth rates, significantly improve.

#### KEY LEARNING POINTS

- CE is a common underdiagnosed condition
- CE is mostly asymptomatic, yet it relates to AUB, pelvic pain and mainly infertility
- CE is most frequently diagnosed by hysteroscopy and Endometrial biopsy. The gold standard for diagnosis is presence of Plasma cells in Histology
- The hysteroscopic diagnostic criteria for CE are: mucosal edema, focal or diffuse endometrial hyperemia and presence of micro-polyps
- ABX treatment frequently cures CE
- CE is closely related to infertility, mostly RIF, RPL and UI, and curing CE by ABX TX is related to major improvement in fertility (both spontaneous and ART).

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## HYSTEROSCOPIC MYOMECTOMY BIOLOGICAL AND CLINICAL IMPACT OF MYOMECTOMY BY PSEUDOCAPSULE SPARING.

#### INTRODUCTION

Uterine fibroids, myomas or leiomyomas, are the most common benign genital tumors, with high rate in general populations. In women aged 19-82 years, almost 25% had fibroids and the 20 - 30% of reproductive age woman shows fibroids, with a continuous incidence increasing in pregnancy and a first trimester of pregnancy prevalence in about 10.7% of pregnancies.

Anatomically, myometrium has smooth muscle cells with a delicate network of arteries, veins and lymphatic vessels. Fibroids are composed of disordered fascicles of smooth muscle cells with varying amount of fibrous tissue; fibroids are structurally rigid, characterized by excessive deposition of disordered components of extracellular matrix (ECM), especially collagen I, III, and IV, proteoglycans, and fibronectin. During its growth, myoma induces the progressive formation of a sort of pseudocapsule, due to compression on the surrounding structures and which separates myomas from the healthy myometrium.

#### ANATOMY AND BIOLOGY OF MYOMA PSEUDOCAPSULE

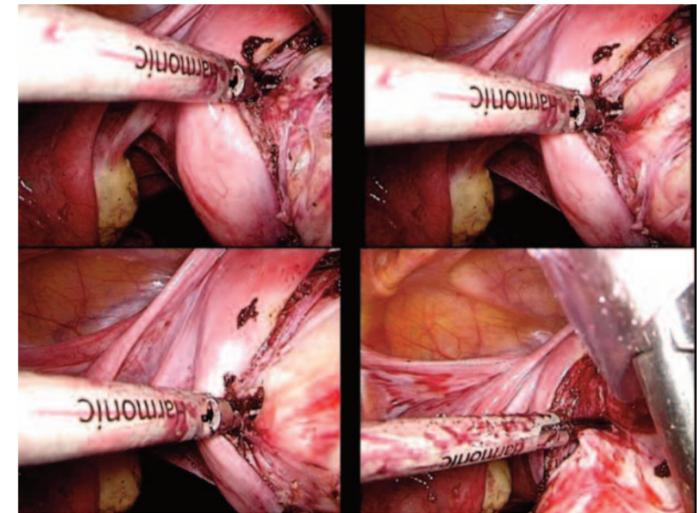
At the ultrastructural level, visualized by transmission electron microscopy, the pseudocapsule cells have the features of smooth muscle cells similar to the myometrium, indicating that the pseudocapsule is part of the myometrium compressed by the myoma.

This pseudocapsule causes a dislocation action on the myometrium, which is not destructive since the integrity and contractility of uterine structure is maintained.

Pseudocapsule is plentiful of collagen fibers, neurofibers and blood vessels. Occasionally bridges of collagen fibers and vessels that anchor myoma to myometrium interrupt the continuous surface of the pseudocapsule. Those phenomena result in the formation of a clear cleavage plane both between myoma and the pseudocapsule and between the pseudocapsule and the surrounding myometrium as well.

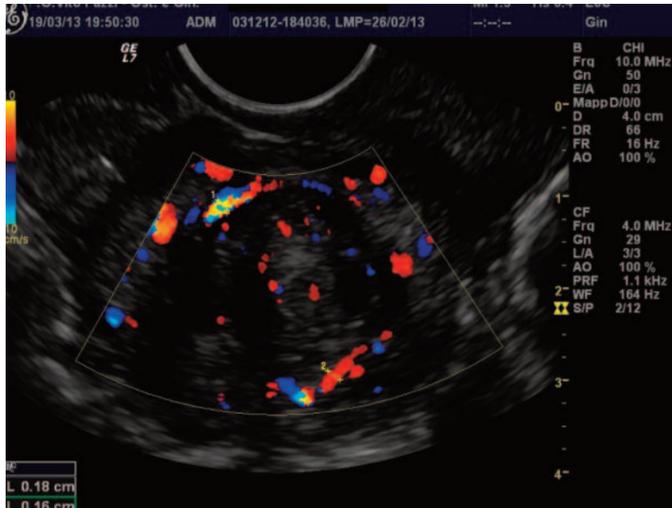
Microstructural studies of the architecture of the myometrium and the ECM, in presence of fibroids, authors found that the myoma is anchored to the pseudocapsule by connective bridges, but lacks its own true vascular pedicle, with a vascular network surrounding the myoma into the pseudocapsule. The biochemical growth factors evaluation in pseudocapsule vessels showed intense angiogenesis in pseudocapsule, probably promoted by the myoma presence itself.

As a sort of neurovascular bundle, the myoma pseudocapsule is rich in neuropeptides and neurotransmitters. Investigation showed myoma' pseudo-



capsules rich of active neuropeptides and neurotransmitters. These substances are thought to have a vital role in wound healing and innervation repair, and may be important for both reproductive and sexual function. Literature data indicate that in regenerative processes associated to pseudocapsule sparing, neuropeptides and neurotransmitters are involved in wound healing. Scientific evidence indicates that the nervous system and its neurotransmitters, namely Substance P (SP), Vasoactive Intestinal Peptide (VIP), neuropeptide Y (NPY), Oxytocin (OXT), Vasopressin (VP), PGP 9.5, calcitonin gene-related peptide (CGRP), growth hormone-releasing hormone (GHRH), play a role in mediating inflammation and wound healing. Regarding uterine musculature scar physiology, sparing these substances promotes a proper healing of

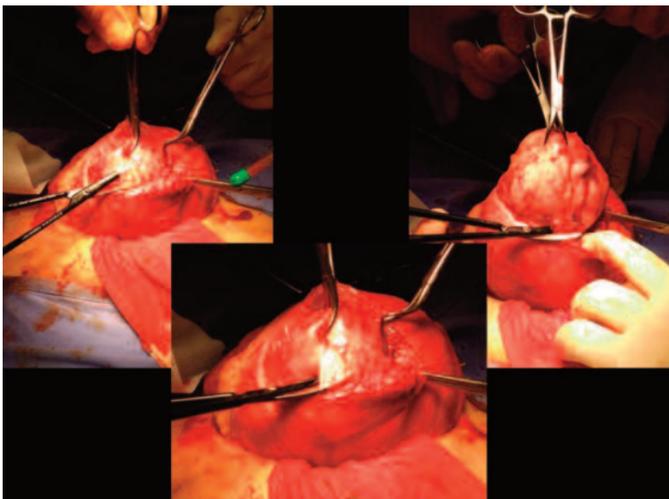
a hysterotomy, as documented by Mettler et al. Most of abovementioned substances have been highlighted in the myoma pseudocapsule and positively impact on myometrial wound healing, an interactive, dynamic process involving neuromodulators, angiogenic factors, neuropeptides, blood cells, extracellular matrix, and parenchymal cells that follows three complex and overlapping phases: inflammation, tissue formation, and tissue remodeling.



Growth factors present in the myoma pseudocapsule induce angiogenesis peripherally to myometrium, which is probably enhanced by myoma, considering that researches on gene expression in myoma pseudocapsule presented an angiogenic profile in pseudocapsule.

#### TRANSLATION OF MYOMA PSEUDOCAPSULE SCIENTIFIC RESEARCHES IN SURGERY

Myomectomy remains the most efficient and mainstay fertility-sparing treatment of fibroids. A correct myomectomy, in addition to improve clinical symptoms and influence quality of life, can improve the fertility rate and reproductive outcome in



woman affected by myoma. To the best of our knowledge, literature lacks the data regarding the rationale of the surgical technique, explaining in details all the steps of the surgical techniques, as we tried to do so. In this manner, we explained the rationale for the reproductive surgery procedures, aiming enucleation of myoma with the preservation of its pseudocapsule.

Extensive research performed by gynecologists and urologists, on analogies of myoma pseudocapsule with the prostate capsule lead to an idea of a neurovascular bundle surrounding myoma, inside pseudocapsule.

Prostate cancer surgery requires preservation of the neurovascular bundles surrounding prostate with the purpose to reduce probability of postoperative impotence and incontinence.

These neurovascular bundles are situated on the peripheral to the prostate. With this purpose, both laparoscopic and robotic assisted prostatectomies are useful, as the resultant magnification ensures a less traumatic dissection, especially in cases of robotic assisted surgery.

Having in mind these findings regarding the importance of the prostatic capsule and clinical significance of nerve-sparing surgery, data on myoma pseudocapsule and its neurovascular bundle were reevaluated and implemented into reproductive surgery.

As a result, a distinct surgical technique evolved, called "intracapsular myomectomy", meaning myoma removal from its pseudocapsule.

It is performed, firstly, by coagulating, cutting and breaking up the fibrous bridges of pseudocapsule, then by stretching and extracting myoma directly from the cut surrounding fibromuscular skeleton. The general myomectomy dogma is that "each surgical fibroid enucleating needs to be gently performed to enhance a correct healing process of the uterine musculature and to facilitate successively the correct uterine musculature anatomical-functional restoring".

Intracapsular myomectomy meets the essential postulate of myomectomy: performing all manipulations as delicately and bloodlessly as it is possible. Thus, if the myoma is dissected entirely through the pseudocapsule opening, using traction on the surrounding myometrium and a gentle selective low energy hemostasis on pseudocapsule vessels, the myometrial bed collapses with poor bleeding once the myoma is removed.

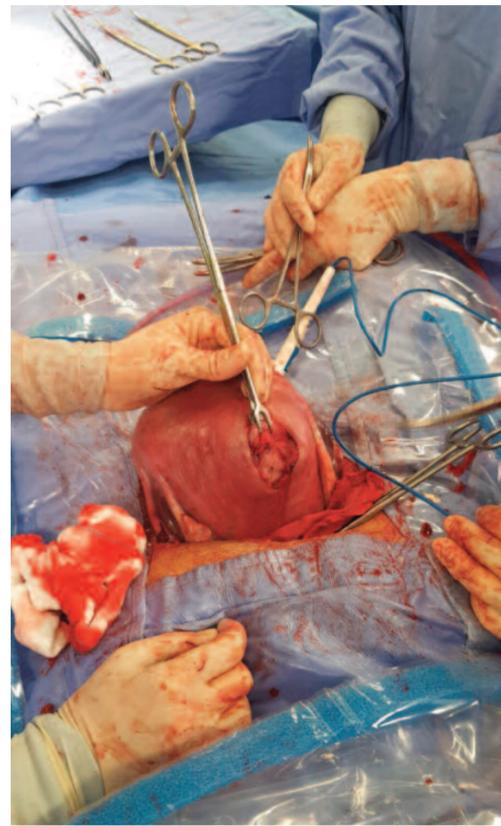
The surgical principle for intracapsular myomectomy can be applied to all myomectomies, resulting in its implementation for both hysteroscopic, vaginal, laparoscopic and laparotomic myomectomy, as well as for cesarean myomectomy.

#### HYSTEROSCOPIC MYOMECTOMY BY PSEUDOCAPSULE SPARING

Currently, the hysteroscopic myomectomy represents the gold standard in treatment of submucous myomas. Nevertheless, the treatment of submucous myomas is probably the hysteroscopic procedure more at risk for surgical complications, which varies from cervix laceration to those potentially fatal as uterine perforation with electrical loop or clinical intravasation syndrome.

It is almost difficult to assess the right frequency of surgical complications during hysteroscopic myomectomy, for its high variability according to pathology characteristics, surgeon skills and technique utilized to carry out the procedure.

The treatment of intracavitary myomas with an intramural extension of 50% or more has always been represented as a challenge for the hysteroscopic surgeons, for the increasing risk for intraoperative complications and necessity of multiple-step procedures, with a higher risk in multiple myomas. Resectoscopic slicing still represents the most widely used technique for treating submucous fi-



broids and, probably for this reason, myomectomy represents the hysteroscopic procedure with a higher complication rate. In addition, the classical slicing technique, even in expert hands, is limited in respecting the pseudocapsule and myometrium sparing after surgery. During the resection of the fibroid intramural part, the "pseudocapsular tissue" can be visualized over the entire resected area but in the context of the uterine wall.

To distinguish the myoma tissue from the pseudocapsule and form the healthy myometrium could become really arduous for non-skilled surgeons and in case of heavy bleeding. In addition, during the myoma slicing, the anatomic surgical dissection, by electrical loop, is generally altered and it is almost impossible to avoid the injury of the myometrial fibers, causing a direct (cutting) and indirect (thermal damage) damage of the pseudocapsule and surrounding healthy myometrium.

This step is responsible for all intraoperative complications during hysteroscopic myomectomy, such as uterine perforation with electrical loop, bleeding and clinical intravasation syndrome, all often closely interconnected.

Moreover, the role of surgical trauma to the healthy tissue of the uterine wall during hysteroscopic surgery in developing of synechiae is well known and already described.

The ideal hysteroscopic myomectomy should be a simple, well-tolerated, safe and effective procedure, ideally in one surgical step. In the last decades, several techniques have been developed in order to overcome the limits represented by the classical slicing for the treatment of the myometrial portion of submucous myomas.

The goal of these techniques was the detachment of deep portion of myoma, in order to facilitate the myoma sliding and delivery from the myometrium into the uterine cavity. Authors previously reported advantages from uterine contractions induced by manual massage, drug or changing intrauterine pressure. Combinations of multiple techniques and the ultrasound monitoring were also described. Others instead described the detachment of intra-

mural component of myomas by electrical incision of the fibro-connective bridges, anchoring myoma to its pseudocapsule.

Among the techniques conceived with the aim to go beyond the limits represented by the classical slicing, the first described was the cold loop hysteroscopic myomectomy in 1995. This method shifted the traditional approach by electric slicing to a different approach: the mechanical enucleation of the myoma from its pseudocapsule, taking advantage from the physiological contraction of myometrium. Dr. Mazzon, the father of this method named the technique "cold loop myomectomy" and it represented a revolution in the hysteroscopic treatment of submucous fibroids. The cold loop hysteroscopic myomectomy, allows to correctly distinguish the anatomical planes, respecting the anatomical and functional integrity of the myometrium and the pseudocapsule, while at the same time ensuring a safe and effective procedure. Generally, the fibro-connective bridges that anchor the fibroid to its pseudocapsule are mechanically disconnected by the cold loops, allowing to enucleate the intramural component of the myoma, without any consequence to the surrounding healthy myometrium. The cold loops between myoma and pseudocapsule allow to avoid uterine perforation by electrical loop and dramatic injury to abdominal organs or vessels. In addition, in case of perforation by cold loops, the damage induced can be considered as the same with a Hegar dilator. The respect of the myometrium also increases the free myometrial margin thickness. Moreover, the uterine contraction and the respect of the myometrial muscular fibers decreases the risk of bleeding and the absorption of the distension medium, enhancing the possibility to accomplish the treatment in a single procedure. The pseudocapsule respect enhances the myometrial physiologic healing, reducing drastically the scar and adhesions, with a favorable impact on successive fertility and decreased uterine rupture risk. Although it is not possible to consider as the treatment of choice, the pseudocapsule sparing during hysteroscopic myomectomy seems to be an excellent option for the treatment of submucous myomas, as it is a safe and effective procedure, respecting the fibroid pseudocapsule, allowing to accomplish the treatment in only one surgical step in a high number of cases.

#### CONCLUSIONS

The pseudocapsule sparing during myomectomy is a technique based on muscular physiology and respect for anatomy. It allows us to enucleate a fibroid respecting the surrounding structures through different approach techniques: laparotomic, laparoscopic, vaginal and hysteroscopic. The benefit is visible during the enucleation of the fibroids, as bleeding is reduced and the anatomical planes are largely detected. In addition, it provides significant benefits in terms of uterine muscular healing. Both clinical and ultrasound investigations on scar site after myomectomy by pseudocapsule sparing, suggested better functional results regarding myometrial integrity when compared to myomectomy scars following myomectomy in non-pregnant patients. Researches also suggested that favorable healing environment caused by pregnancy induced activation of the immune system enables safe vaginal delivery in subsequent pregnancies even following cesarean myomectomy, always by intracapsular method.

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