



AGL 2022

51st GLOBAL CONGRESS ON MIGS

December 1–4, 2022 | Gaylord Rockies Resort and Convention Center | Aurora, Colorado

SYLLABUS

HSC-602: Hysteroscopy – Taking Your First Steps in Intrauterine Surgery

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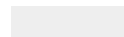
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HSC-602: Taking Your First Steps in Intrauterine Surgery

Co-Chairs: *Jude E. Okohue, MD, Christina A. Salazar, MD*

Faculty: *Alka Kumar, MBBS, MS, Bolarinde Ola, MBBS, MD, Erica F. Robinson, MD*

Course Description

This course provides a comprehensive beginner's tutorial on the basics of intrauterine surgery. You will learn how to identify the optimal candidates as well as how to preoperatively plan for success. We will review the principles for performing intrauterine surgery using vaginoscopy and use videos to demonstrate techniques for tips and tricks to overcome commonly encountered challenges, as well as review both normal and abnormal findings in the uterus. Through hands-on simulation, we will demonstrate the way to safely explore the intrauterine cavity to identify abnormalities and treat pathology using the basic hysteroscopic tools.

Learning Objectives

At the conclusion of this course, the participants will be able to: 1) Demonstrate an understanding of the indications for intrauterine surgery and how to plan for success; 2) Become comfortable performing vaginoscopy and exploring the uterine cavity; and 3) Acquire basic skills with hysteroscopic scissors and graspers.

Course Outline

7:00 am	Welcome, Introduction and Course Overview	C.A. Salazar/J.E. Okohue
7:05 am	When & Why: Preoperative Screening and Planning	C.A. Salazar
7:30 am	Ergonomics and Vaginoscopy, How to Overcome the Cervix	B. Ola
7:55 am	Staying Safe: Exploring the Uterine Cavity	J.E. Okohue
8:20 am	Using Your Tools	E.F. Robinson
8:45 am	Seeing the Endometrium: Normal & Abnormal	A. Kumar
9:10 am	Questions & Answers	All Faculty
9:30 am	Adjourn	

Taking First Steps in Intrauterine Surgery



When and Why: Preoperative Planning & Screening

Christina A Salazar, MD FACOG

Minimally Invasive Gynecologic Surgery Division
Assistant Professor, Department of Women's Health
UT Austin Dell Medical School



Disclosures

- None.



Aims

- 1 Identify optimal candidates for hysteroscopy
- 2 Review evidence-based pre-procedure planning
- 3 Increase awareness of complications



Aim 1

Identify optimal candidates
for hysteroscopy



Common Indications for Hysteroscopy

- Evaluation and treatment of submucous fibroids and polyps.
- Diagnosis and treatment of intrauterine adhesions.
- Correction of septate and dysmorphic uteri.
- Detection and diagnosis of malignancy.
- Management of rPOC or focal accreta.
- Foreign body removal (IUD with non-visualized strings or malpositioned IUD).
- Detection and treatment of isthmocele.
- Management of cesarean scar pregnancy.



Aim 2

Review evidence-based pre-procedure planning



Where to Operate

- RCTs have shown that patients prefer office-based hysteroscopy over same-day surgery center.
- ✓ Patient and physician convenience.
- ✓ Avoidance of general anesthesia.
- ✓ Less patient anxiety related to familiarity with the office setting.
- ✓ Cost effectiveness.
- ✓ System-wide efficiency that increases use of the OR for complex cases.

Kremer C, Duffy S, Moroney M. Patient satisfaction with outpatient hysteroscopy versus day case hysteroscopy: randomized controlled trial. *BMJ*. 2000 Jan 29;320(7230):779-82.

Marsh SA, Regerson LA, Duffy SR. A randomized controlled trial comparing outpatient versus daycase endometrial polypectomy. *BJOG*. 2006 Aug;113(8):996-901.



Original Article

Office versus Institutional Operative Hysteroscopy: An Economic Model

Malcolm G. Munro, MD, Jamie L. Kasiewicz, BS, and Vrunda B. Desai, MD

From the Department of Obstetrics and Gynecology, Kaiser Permanente, Los Angeles Medical Center and Department of Obstetrics and Gynecology, David Geffen School of Medicine at UCLA (Dr. Munro), Los Angeles, California, and CooperSurgical, Inc. (Ms. Kasiewicz and Dr. Desai), Trumbull, Connecticut

ABSTRACT **Study Objective:** Model and compare estimated health system costs and gynecologic practice revenues when hysteroscopic surgery is performed in the office or institutional setting, either an ambulatory surgical center (ASC) or a traditional operating room (OR).

Design: Economic modeling exercise.

Munro MG, Kasiewicz JL, Desai VB. Office versus Institutional Operative Hysteroscopy: An Economic Model. *J Minim Invasive Gynecol*. 2022 Apr;29(4):535-546.



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Endometrial polyps. An evidence-based diagnosis and management guide

Salvatore Giovanni Vitale^a, Sergio Haimovich^b, Antonio Simone Laganà^a, Luis Alonso^a, Attilio Di Spiezio Sardo^a, Jose Carugno^{a,c}, From the Global Community of Hysteroscopy Guidelines Committee

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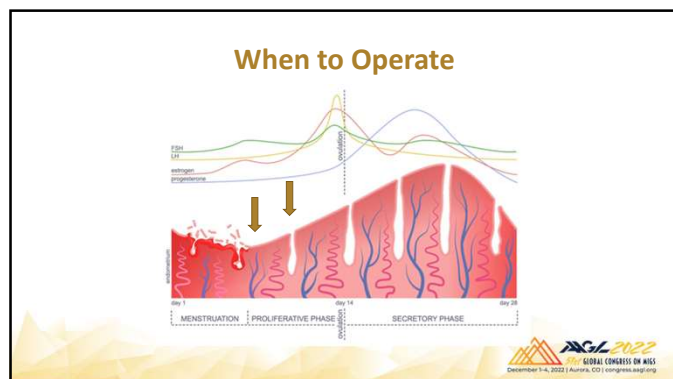
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Vitale SG, Haimovich S, Laganà AS, Alonso L, Di Spiezio Sardo A, Carugno J. From the Global Community of Hysteroscopy Guidelines Committee. Endometrial polyps. An evidence-based diagnosis and management guide. *Eur J Obstet Gynecol Reprod Biol*. 2021 May;260:70-77.





Which Meds to Consider Pre-Op

Cicciulli E, Pileo V, Quattromini P, Fucci MR, Lepora A, Mitola PC, et al. Endometrial preparation with estradiol plus dienogest (Qiera) for office hysteroscopic polypectomy: randomized pilot study. *J Minim Invasive Gynecol* 2012;19:356-9.

Lagina AS, Vitale SG, Mucila V, Rossetti P, Buscema M, Trillo O, et al. Endometrial preparation with Dienogest before hysteroscopic surgery: a systematic review. *Arch Gynecol Obstet* 2017;295:661-7.

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Which Meds to Consider Pre-Op

Konarthi MR, Kalampokas EE, Kalampokas TE. Use of GnRH analogues pre-operatively for hysteroscopic resection of submucous fibroids: a systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol* 2014;177:11-6.

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Which Meds to Consider Pre-Op

Al-Fozan H, et al. Preoperative ripening of the cervix before operative hysteroscopy. *Cochrane Database of Systematic Reviews* 2013, Issue 4.

Casadei L, et al. Role of vaginal estradiol pretreatment combined with vaginal misoprostol for cervical ripening before operative hysteroscopy in postmenopausal women. *Obstet Gynecol Sci* 2016;59:220-6.

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Which Meds to Consider Intra-Op

Phillips DR, Nathanson HG, Millin SJ, Haselkorn JL, Khopra A, Ross PL. The effect of dilute vasopressin solution on blood loss during operative hysteroscopy: a randomized controlled trial. *Obstet Gynecol* 1996;88:751-6.

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European Journal of Obstetrics & Gynecology and Reproductive Biology 252 (2020) 70-81

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European Journal of Obstetrics & Gynecology and Reproductive Biology

Journal homepage: www.elsevier.com/locate/ejogrb

Local anaesthesia for office hysteroscopy: A systematic review & meta-analysis

Prathiba M. De Silva^{a,*}, Alasdair Carnegie^b, Paul P. Smith^a, T. Justin Clark^c

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^cBirmingham Women's Hospital, Birmingham Women's and Children's NHS Foundation Trust, Mindbroke Way, Birmingham, B15 2TG, UK

De Silva, Prathiba M, et al. "Local Anaesthesia for Office Hysteroscopy: A Systematic Review & Meta-Analysis." *European Journal of Obstetrics & Gynecology and Reproductive Biology* 252 (2020): 70-81.

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Aim 3

Increase awareness of complications




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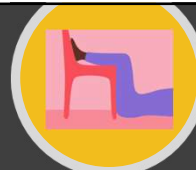
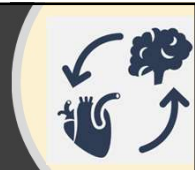
Table 2. Potential Complications, Incidence, and Risk Factors of Hysteroscopy

Potential Complication	Incidence	Risk Factors
Perforation	0.12% to 1.61% ^{a,11}	Blind insertion of instruments, cervical stenosis, anatomic distortion (eg, leiomyomas and congenital anomalies, intrauterine adhesions, myometrial thinning, and uterine malposition [extreme anteversion or retroversion])
Air and gas embolism (clinically significant)	0.03% to 0.09% ¹¹	Repetitive instrumentation through cervix, inadequate purging of air from tubing and instruments, excessive intrauterine pressure
Fluid overload	0.20% ¹	Excessive absorption of any distending fluid, resection of large or deep lesions and high intrauterine pressure; increased risk of hyponatremia with use of electrolyte-free distending media, and cerebral edema with hypotonic distending media.
Hemorrhage	0.03% to 0.61% ^{a,19}	Cervical laceration, uterine perforation, adhesiolysis, resection of cavity lesions
Vasovagal reaction	0.21% to 1.85% ⁶	Triggering of parasympathetic nervous system during manipulation of the cervix and instrumentation of the cervical canal or uterine cavity

The Use of Hysteroscopy for the Diagnosis and Treatment of Intrauterine Pathology: ACOG Committee Opinion Summary, Number 800. Obstet Gynecol. 2020 Mar;135(3):754-756.




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Vasovagal Syncope & Air Embolus

Ahmad G, Saluja S, O'Flynn H, Sorrentino A, Leach D, Watson A. Pain relief for outpatient hysteroscopy. Cochrane Database Syst Rev. 2017 Oct 5;(10)(10):CD007710.



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Taking First Steps in Intrauterine Surgery





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Ergonomics and Vaginoscopy; How to Overcome the Cervix

Mr Bolarinde Ola FRCOG
Consultant Gynaecologist
Subspecialist in Reproductive Medicine & Surgery



My Professional Affiliations

Ancient City of Sheffield, UK



Much Newer City of Abuja, Nigeria

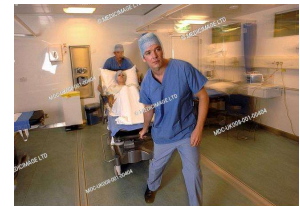
Aims

- Present theoretical knowledge as foundation to safe vaginoscopic hysteroscopy
- Emphasise principles of ergonomics as it relates to:
 - Team, task, equipment and set-up
 - Navigating the vagina and finding the cervix
 - Safely navigating through the cervical canal
 - Dealing with the difficult cervix

Ergonomics: Definition

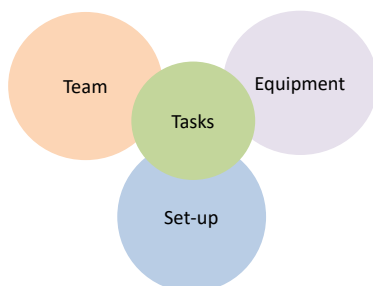
Ensuring that.....

- theatre set-up
- environment
- tasks
- equipment
- Information
- team functioning



..... all fit EACH key worker

Ergonomics



Tasks

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Patient Selection

Always take good gynae history – (standard questionnaire)

- Age
- Past medical and surgical histories
 - Concurrent medical conditions
 - Previous surgery (retrieve old records)
 - Previous surgical complications
 - Is prior cervical preparation required?
- Examine and review available images
 - acute anteversion
 - acute retroversion
 - Axial uterus
- Provide adequate analgesia/anaesthesia
- Prepare for the planned and unplanned

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Type of Hysteroscope

The smaller the better

Reproductive Failure: Inner sheath: 2.7 - 5mm, Outer: 3 - 6mm

General Gynaecology: Inner sheath: 2.7 - 5mm, Outer: 3 - 6mm

Paediatric: Inner sheath: 2-3mm, Outer: 3 - 4mm

Equipment

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Know Your Equipment

- Rigid Office Hysteroscope
- Flexible
- Resectoscope

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Know Your Equipment

Angle of Objective Lens

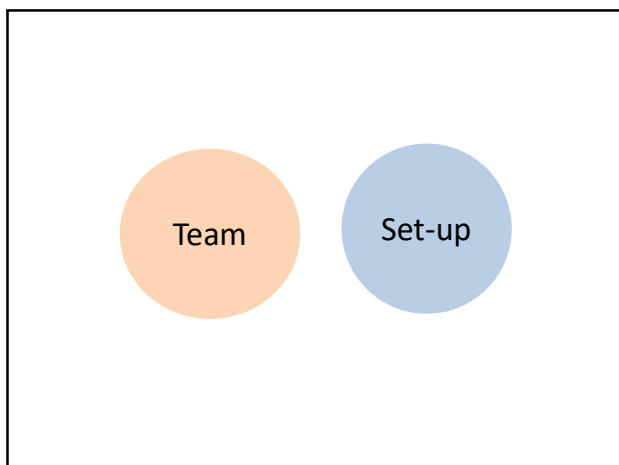
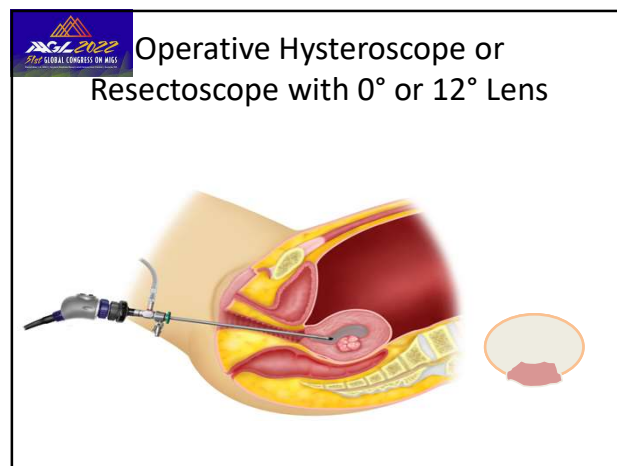
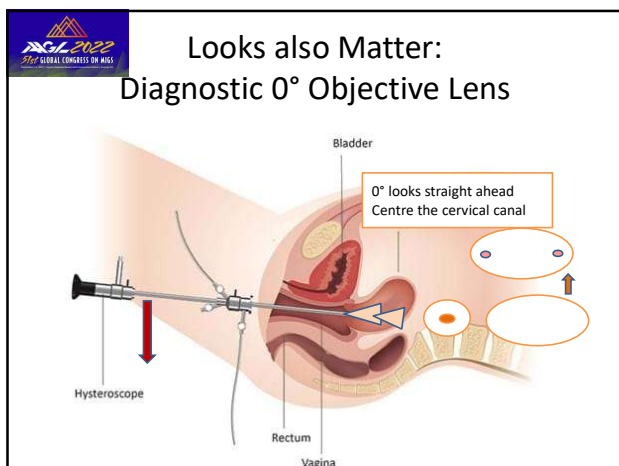
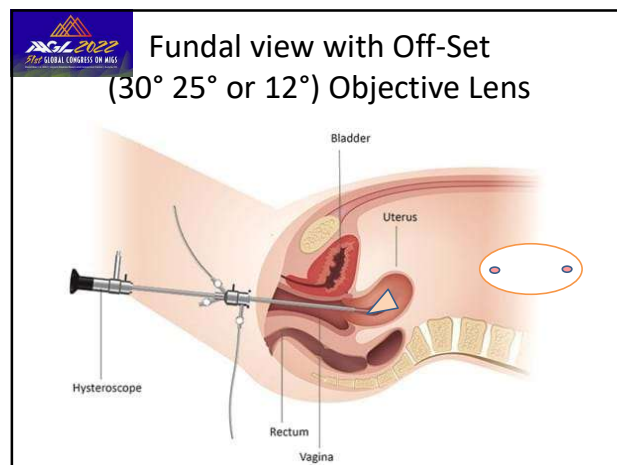
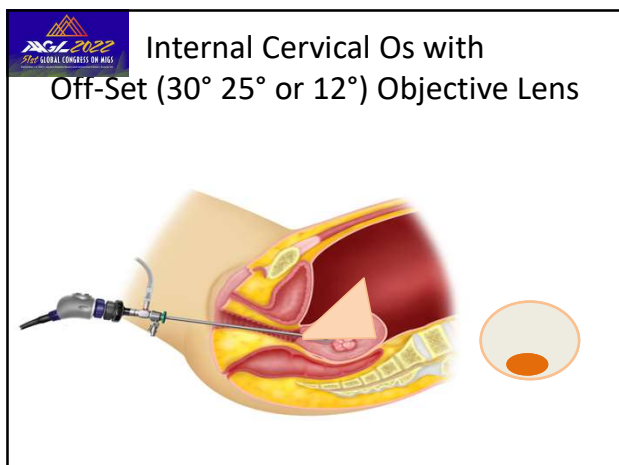
30°

12°

0°

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Internal Cervical Os with Off-Set (30° 25° or 12°) Objective Lens



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- ### Team and Set-Up
- Experienced Nurse
 - Trained Auxiliary Staff
 - Ask patient to empty bladder just before start
 - Adjustable theatre bed and monitor
 - Adjustable surgeon's stool / position assistant
 - Diagnostic hysteroscopic set up
 - Operative hysteroscopic set up
 - Analgesia / Local Anaesthesia
 - Entonox (50% Nitrous oxide & 50% Oxygen)

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Step-by-Step of Vaginoscopic Hysteroscopy


- Select patients carefully / look at available images
 - Adequate analgesia
- Room Set-up: Check your equipment
- Insert hysteroscope into lower vagina & start Saline
- Advance hysteroscope up posterior vaginal wall
- Identify cervix
- Insert tip of hysteroscope into cervical canal
- Keep cervical canal view at 6° Clock for off-set objectives
 - Minimises risk of posterior wall perforation
- Centre the canal view for 0° objectives

How I Do It

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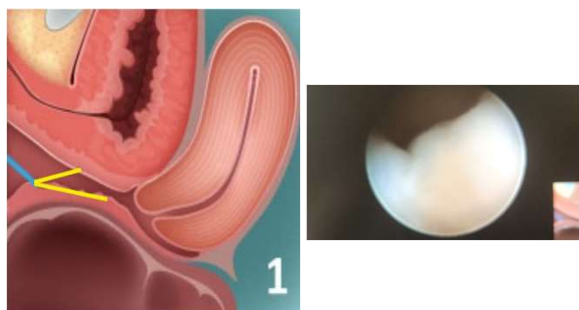
Preamble

- I review all available gynae images
- I don't usually rely on reports alone
 - Acute anteversion may be reported simply as anteverted
 - Same for acute retroversion



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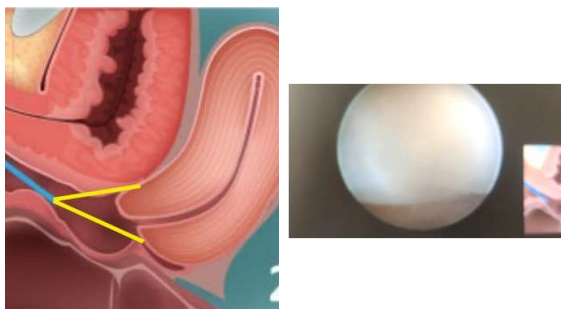
Navigating Lower Vagina: with 30° Objective Lens



Courtesy <https://elearning.rcog.org.uk/uterine-cavity-surgery/outpatient-hysteroscopy/no-touch-technique-diagnostic>,

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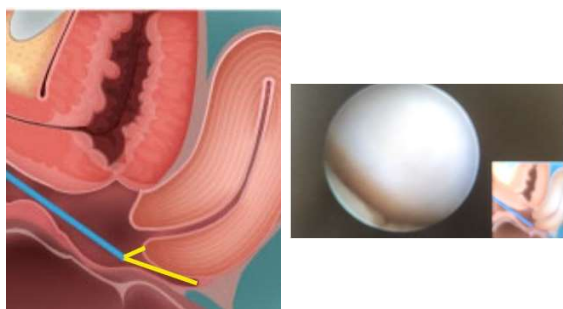
Navigating Mid-Vagina: with 30° Objective Lens



Courtesy <https://elearning.rcog.org.uk/uterine-cavity-surgery/outpatient-hysteroscopy/no-touch-technique-diagnostic>,

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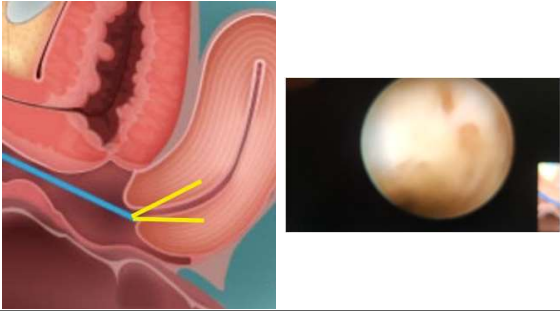
Navigating Upper Vagina: Finding the Cervix with 30° Lens



Courtesy <https://elearning.rcog.org.uk/uterine-cavity-surgery/outpatient-hysteroscopy/no-touch-technique-diagnostic>,

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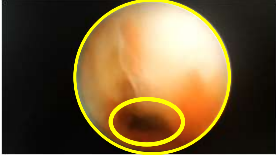
Navigating the Cervix: with 30° Objective Lens



Courtesy <https://elearning.rcog.org.uk//uterine-cavity-surgery/outpatient-hysteroscopy/no-touch-technique-diagnostic>

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Navigating the Cervix: with 30° Objective Lens



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The Difficult Cervix: Causes

- External Cervical stenosis
- Lower canal stenosis
- Internal os stenosis
- Complete stenosis
- Deficient cervix - surgery
- Absent cervix
- The gaping patulous cervix

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The Difficult Cervix: Management

- Review images
- Analgesia
- Avoid blind dilatation
- Use 0° miniaturised hysteroscope (2/3mm)
- Blunt dissection: gently rotating tip of scope
- Sharp dissection with hysteroscopic scissors
- Consider using tenaculum



Video courtesy of Dr Jude Okohue FWACS

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The Difficult Cervix – Rescheduled Further Attempt

- Review history
- Review images again
- Consider pre-treatment with misoprostol
- Analgesia
- Consider day case under RA or GA
- Consider ultrasound guided attempt
- Use miniaturised hysteroscope (2/3mm)

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Summary

- Select patients carefully
 - Look at available images
 - Adequate analgesia
- Room set-up: check your equipment
- Insert hysteroscope into lower vagina & start Saline
- Advance hysteroscope up posterior vaginal wall
- Identify cervix
- Insert tip of hysteroscope into cervical canal
 - Keep cervical canal view at 6° Clock for off-set objectives
 - Keep view at centre for 0° Objective Lens
- In difficult cases; review strategy or re-schedule



In Summary



References

- <https://elearning.rcog.org.uk/tutorials/core-knowledge/surgical-procedures-and-postoperative-care/uterine-cavity-surgery>
- <https://elearning.rcog.org.uk/uterine-cavity-surgery/outpatient-hysteroscopy/no-touch-technique-diagnostic>

Staying Safe: Exploring the Uterine Cavity

Prof. Jude Okohue

Gynescopie Specialist Hospital & Madonna University, Nigeria.
Vice President, Association of Gynaecological Endoscopy Surgeons, Nigeria.
Board member, AAGL Hysteroscopy SIG
West African Representative @Global Community of Hysteroscopists.
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Declaration

I have no financial interest to declare



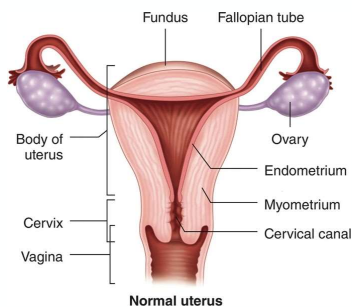
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Objectives

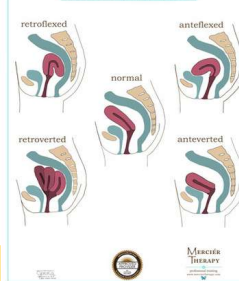
At the conclusion of this presentation, participants should be able to:

- Apply tricks learned on how to navigate a difficult cavity in cases of moderate/severe Asherman's syndrome
- Recognize uterine perforation and employ steps in preventing a perforation.



Introduction

Positions of the Uterus



Uterine Positions

- Anteverted
- Retroverted
- Anteverted
- Retroverted

Uterine Dimensions

- Uterus weighs an average 50 – 60g⁽¹⁾
- Length, 6 – 8.5cm and 8 – 10cm in nullipara and multipara, respectively.
- Endometrial cavity volume 5 – 10ml⁽²⁾
- Transfundal endometrial cavity width 22 – 34mm⁽³⁾

Landmarks

- External os
- Endocervical canal
- Internal os
- Endometrial cavity
- Tubal ostia

Most difficulties occur in cases of Asherman syndrome

- IUA with symptoms
- Mild/Moderate/Severe

Cold scissors versus electrosurgery for hysteroscopic adhesiolysis

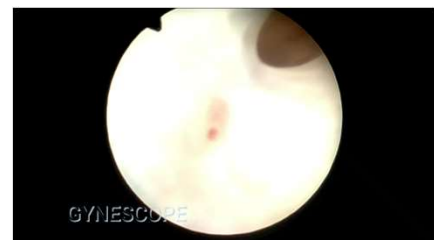
A meta-analysis

Luqiang Yang, MD, PhD¹, Ling Wang, BM², Yun Chen, MD, PhD³, Xiaohu Guo, MD, PhD⁴, Chenyun Miao, MD, PhD⁵, Ying Zhao, MD, PhD⁶, Lu Li, PhD⁷, Qin Zhang, BM⁸

Abstract
Background: Intrauterine adhesion seriously affects reproductive health in women. Hysteroscopic adhesiolysis using cold scissors or electrosurgery is the main treatment, although there is no consensus on the preferable method. This review aimed to compare the efficacy and safety of these methods for treating moderate to severe intrauterine adhesion.
Methods: PubMed, EMBASE, MEDLINE, Cochrane Database of Systematic Reviews, Web of Science, Chinese Biomedical Literature Database, and China National Knowledge Infrastructure were searched on April 30, 2020. Randomized controlled trials and observational studies that were published in all languages (must contain English abstracts) and compared hysteroscopic cold scissors with electrosurgery for the treatment of intrauterine adhesion were included. Mean differences, odds ratios, and 95% confidence intervals (CIs) were reported. Bias was evaluated using the Cochrane Risk of Bias assessment tool for randomized controlled trials and the Newcastle-Ottawa Scale for observational studies. Data were analyzed using RevMan software (Review Manager version 5.3; The Cochrane Collaboration, 2016). Two researchers independently extracted data and assessed the quality of the included studies. If a consensus was not reached, a third researcher was consulted.
Results: Nine studies (n=761) (4 randomized controlled trials and 5 retrospective studies) were included. The intrauterine adhesion recurrence rate with second look hysteroscopy was significantly lower (odds ratio=0.30, 95% CI=0.16-0.56, P=0.002) with hysteroscopic cold scissors than with electrosurgery. The total operation time was significantly shorter (mean difference=-7.26, 95% confidence interval=-9.80 to -4.80, P<0.0001), intraoperative blood loss was significantly lower (mean difference=-9.88, 95% CI=-11.26 to -8.51, P<0.0001), and the menstrual flow rate was significantly higher (odds ratio=3.46, 95% confidence interval=2.06-7.43, P<0.0001) with hysteroscopic cold scissors than with electrosurgery. There were no significant differences in the pregnancy rate. One complication (1 perforation case, hysteroscopic cold scissors group) was reported.
Conclusions: Hysteroscopic cold scissors is more efficient in preventing intrauterine adhesion recurrence, increasing the menstrual flow, reducing intraoperative blood loss, and shortening the operation time.
Abbreviations: CI = confidence interval, CS = cold scissors, ES = electrosurgery, HA = hysteroscopic adhesiolysis, IUA = intrauterine adhesions, MD = mean difference, NOS = Newcastle-Ottawa Scale, OR = odds ratio, RCTs = randomized controlled trials.
Keywords: Asherman syndrome, electrosurgery, gynaecology, hysteroscopy, recurrence



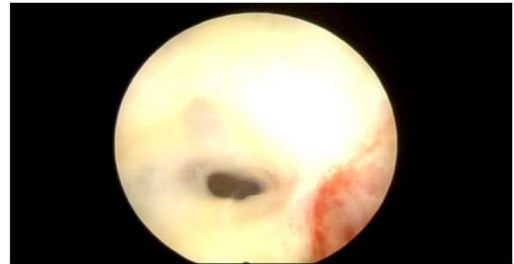
Central before Lateral Adhesions^(4,5)



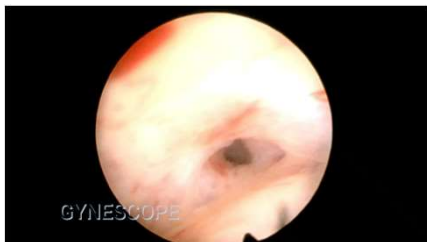
Exploring the hole



Exploring the hole 2



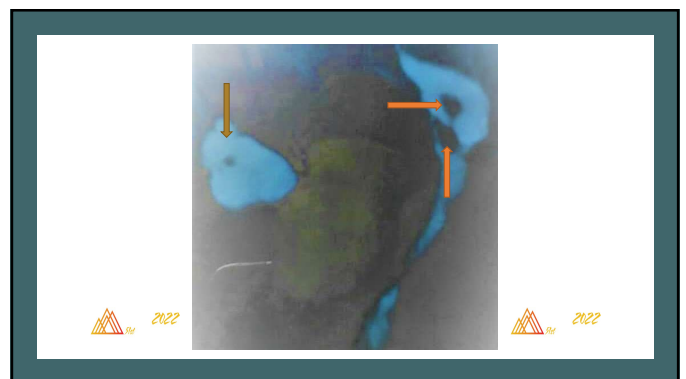
Exploring Dark Areas⁽⁶⁾

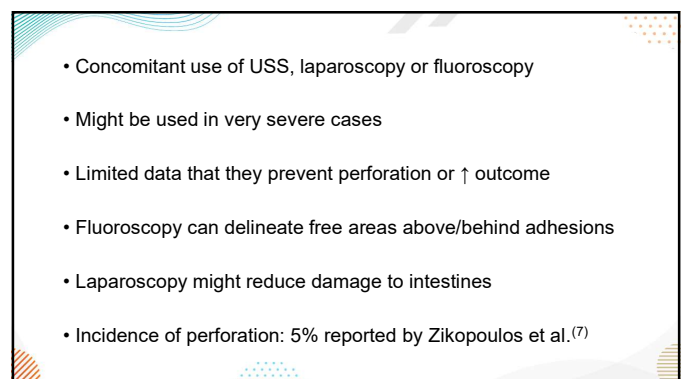
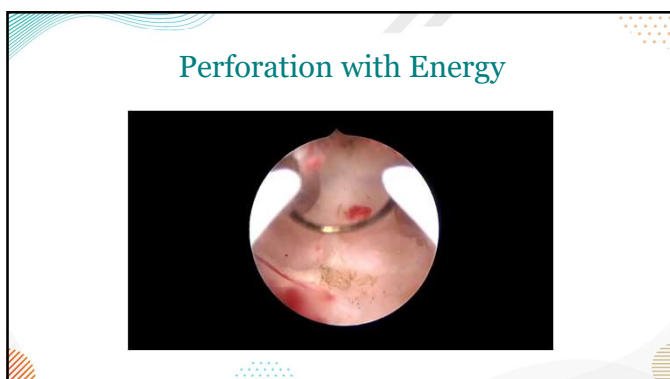


The Hole, Columnar Epithelium, and Dark areas



Deciding which Hole to explore





Conclusion

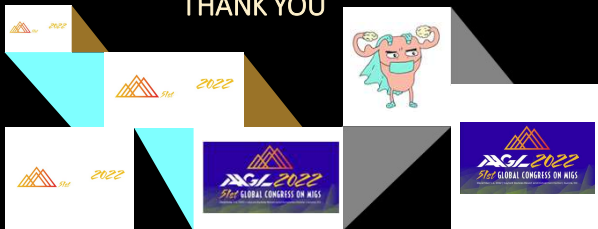
- The endometrial cavity is a small space
- Safer to explore moderate/severe adhesions with scissors
- Bowel and bladder can be injured following a perforation
- Extreme care and relevant expertise is key

References

- ¹Qingsong S, Ma N, Huang H, et al. Significance of preoperative calculation of weight as an indicator for preserving the uterus in pelvic reconstructive surgery. *Int J Clin Exp Pathol*. 2015; 8(1): 900-5
- ²Shild RL, Indefree D, Eschweiler S, et al. Three-dimensional endometrial volume calculation and pregnancy rate in an in-vitro fertilization programme. *Hum Reprod* 1999; 14(5): 1255-8
- ³Goldstuck ND. Dimensional analysis of the endometrial cavity: how many dimensions should the ideal intrauterine device or system have? *Int J Womens Health* 2018; 10: 165-8.
- ⁴Okohue JE. Role of Assisted operative hysteroscopy in Asherman's management. In: Manchanda R (ed). *Intra uterine adhesions*. Springer, Singapore. 2021; 123-35.
- ⁵Dearn A, Abbott J. Review of intrauterine adhesions. *J Minim Invasive Gynecol*. 2010; 17: 555-69.
- ⁶Emanuel HH, Hanstede M. Hysteroscopic treatment of Asherman syndrome. In: *Hysteroscopy*. Tinelli A, Alonso LP, Haimovich S (eds). Springer, Switzerland. 2018; 709-18.
- ⁷Zikopoulos KA. Live delivery rates in subfertile women with Asherman's syndrome after hysteroscopic adhesiolysis using the resectoscope or the versapoint system. *Reprod Biomed Online*. 2004; 8, 720-5



THANK YOU



Hysteroscopy: Knowing & Using Your Tools

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Vice Chair Clinical Operations and Affairs
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Disclosure

- Consultant: CooperSurgical™



Objectives



IDENTIFY THE CURRENT TOOLS
AVAILABLE FOR OPERATIVE
HYSTEROSCOPY



CLARIFY INDICATIONS FOR USE OF
EACH TOOL



APPRECIATE THEIR LIMITATIONS



Operative Scope

- Rigid scope with a Rod Lens (0°, 12°, 25°, 30°)
 - Light post opposite to direction of view
- Single sheath
- OD 5.5mm
- Instrument channel 5-7Fr
 - Rigid, semirigid, flexible instruments
 - Semirigid tend to give most stability for guidance and cutting
 - Biopsy forceps, scissors, alligator forceps
 - Can use bipolar electrodes for vaporization, desiccation, or cutting
 - Normal Saline for distension
- Continuous flow



Resectoscopes: Continuous flow

Monopolar

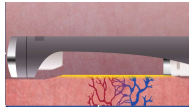
- Requires hypotonic, nonconductive and electrolyte free distension media
 - Glycine, sorbitol, mannitol
 - Max deficit <1000mL
- Pros: **GREAT** visualization
- Cons: Due to risk of hyponatremic hypervolemia, smaller deficits are tolerated and therefore increased risk of incomplete procedures.

Bipolar

- Isotonic, electrolyte containing distension media
 - Saline, lactate ringers
 - Max deficit <2500mL
- Pros: Safer than monopolar
- Cons: visualization can be murkier than the hypotonic solutions

RF Resection and Coagulation

- Closed loop saline fluid management with recirculation of filtered distension fluid
- Allows for resection and coagulation of leiomyomas and polyps
- Bladeless radiofrequency-based resection with simultaneous aspiration of debris. No blade dulling on tough tissue
 - Simultaneous sealing of microvascular bed while tissue is cut to decrease bleeding and fluid extravasation
- Bipolar cut current for resection
- 6.3mm OD scope, resection device disposable

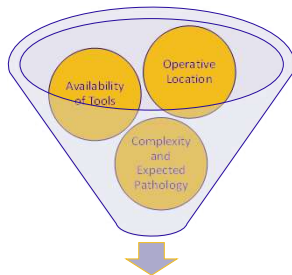



<https://minervasurgical.com/wp-content/uploads/2020/10/Symphion-device@1.5x.png>

Operative Hysteroscopy



What Tool Will You Choose?



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SEEING THE ENDOMETRIUM: NORMAL & ABNORMAL


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DISCLOSURE

CONSULTANT – ARTHREX, INC.

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LEARNING OBJECTIVE

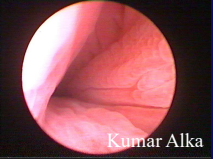

To be able to differentiate and recognize the normal
and the abnormal endometrium on hysteroscopy.

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CERVICAL CANAL

HYSTEROSCOPY ASPECTS


- Papillary structures are most noticeable in the first 2 cm above the external os
- Glandular crypts are situated between the papillae
- Arbor vitae form the lateral columns
- Cervical polyps, adhesions, cervical atresia, cervical cysts are pathologies clearly diagnosed with hysteroscopy



Kumar Alka

Kumar Alka

Hamou et al, Hysteroscopy and Microcolposcopy text and atlas, 1991, 5:55-79


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ENDO CERVICAL MUCOUS STRANDS

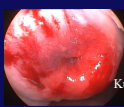

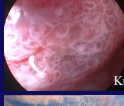

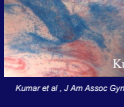




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Kumar Alka

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MICROCOLPOHYSTEROSCOPY – Hamou Microhysteroscope II

Kumar Alka

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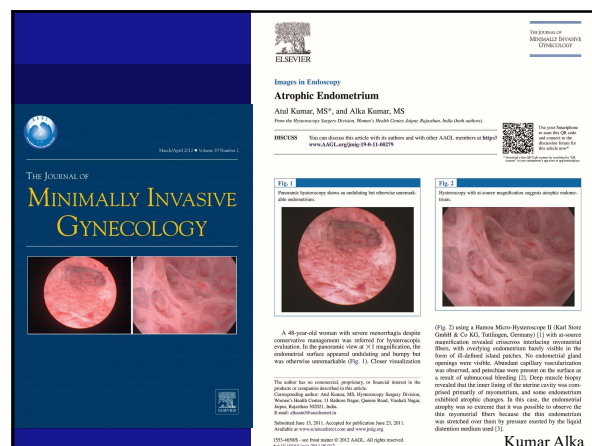
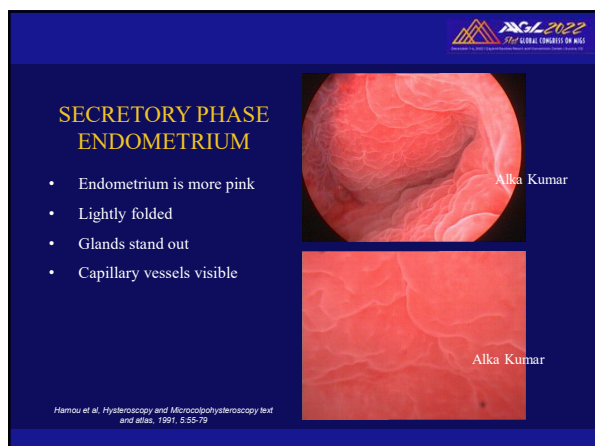
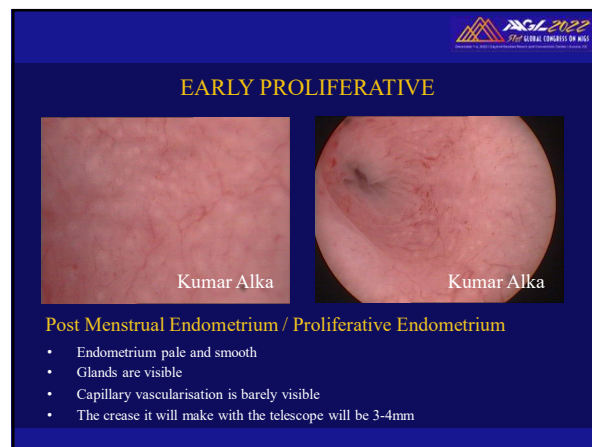
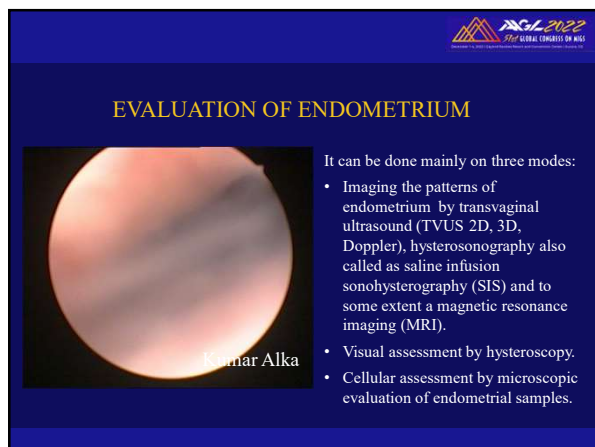
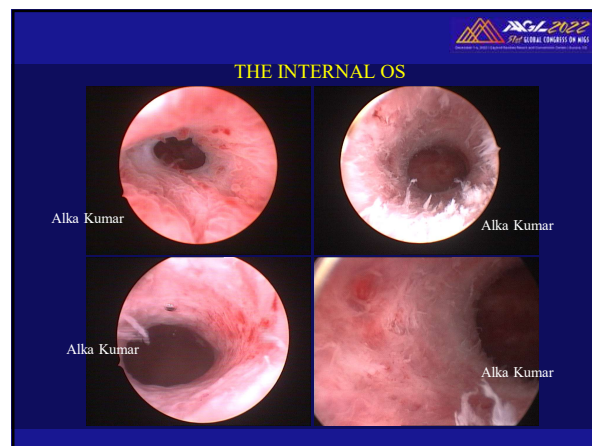
Kumar Alka




Movie

Kumar Alka

Kumar et al., J Am Assoc Gynecol Laparosc 2004, 11(2): 131-2







ASG 2022

ASG 2022

ATROPHIC ENDOMETRIUM


Alka Kumar

Alka Kumar

- Crisscross interlacing myometrial fibers, with overlying endometrium barely visible in the form of ill-defined island patches
- No endometrial gland openings visible
- Abundant capillary vascularization observed

Alka Kumar

Kumar A, Kumar A. J Minim Invasive Gynecol. 2012 Mar-Apr;19(2):148-9




ASG 2022

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DECREASED ENDOMETRIAL RECEPTIVITY

1. Leiomyomata – Submucous
2. Septum
3. Polyps
4. Endometritis
5. Thin Endometrium
6. Hyperplasia
7. Adhesions / Synechiae




ASG 2022

ASG 2022

DECREASED ENDOMETRIAL RECEPTIVITY


FIBROID



- Obstacles to sperm migration
- Impairment of embryo implantation
- Obstacles to oocyte transport
- Altered contour of the uterine cavity
- Anomalies of uterine contractility
- Alterations in focal endometrial perfusion
- Endometrial inflammation, secretion of vasoactive substances or androgen local increase

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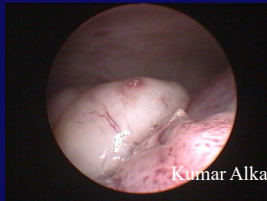
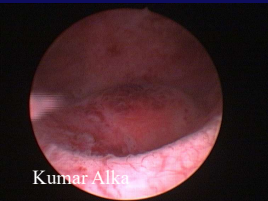
Somigliana E et al. Reprod Update, 2007; Betocchi S et al. Hum Reprod 2002; Butra VC et al. Fertil Steril 1981; Ciccinelli Et al. Obstet Gynecol 1998; Butra VC et al. Fertil Steril 1981



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SUBMUCOUS FIBROID

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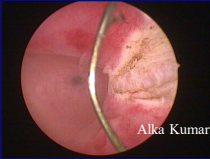


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SEPTOPLASTY







Alka Kumar

Alka Kumar

Alka Kumar

Alka Kumar



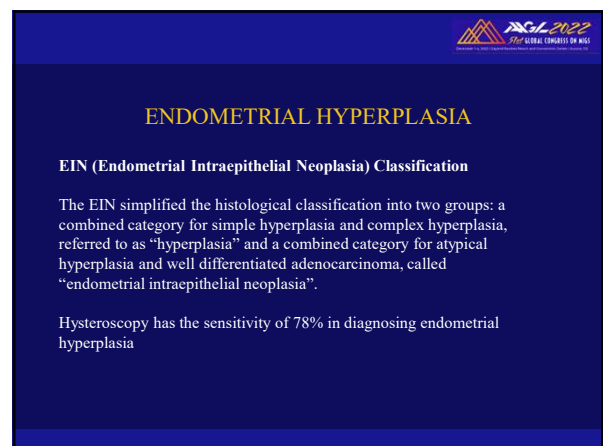
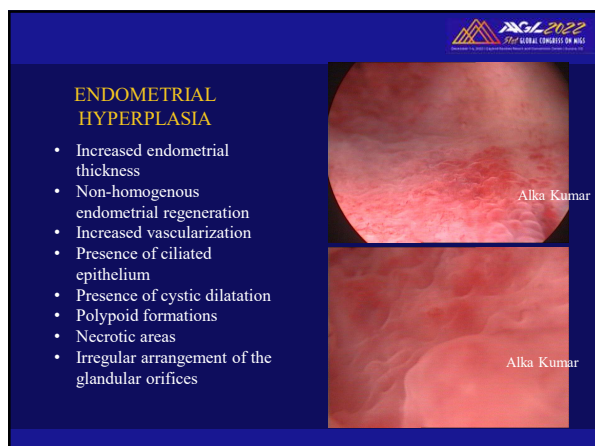
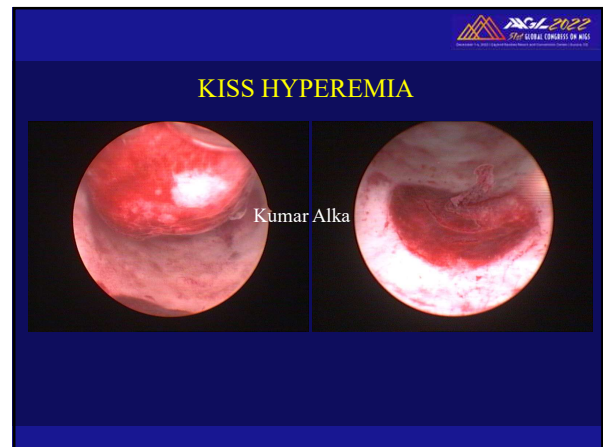
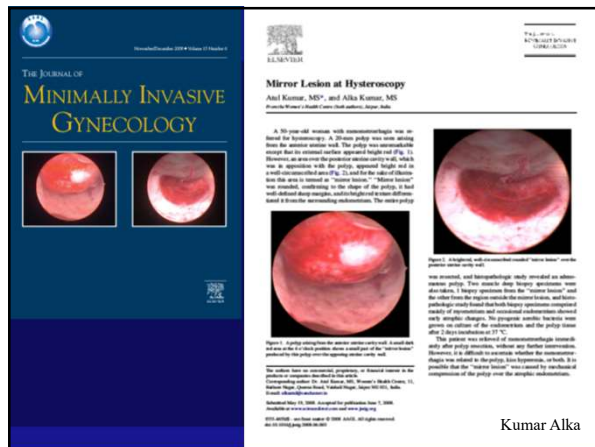
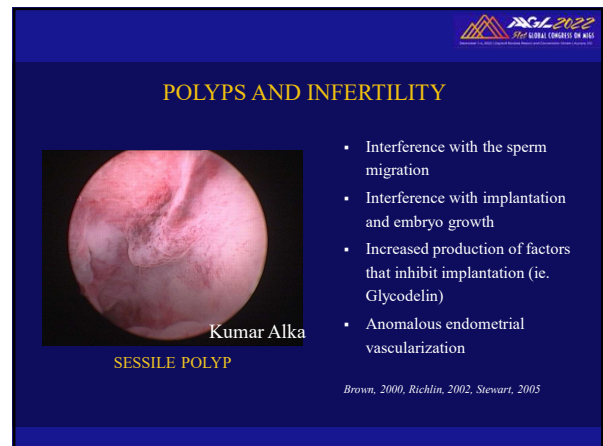
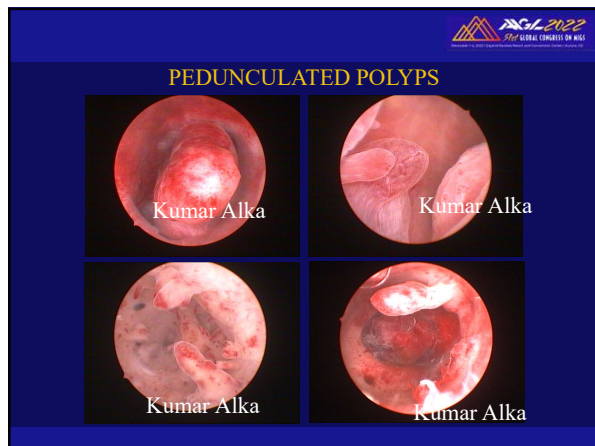
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POLYPS

- Endometrial polyps are exophytic mucous lesions that differ greatly in shape, size, number and appearance.
- The surface epithelium of the single or multiple sessile forms is similar to that of the surrounding endometrium and soft in consistency upon contact with the tip of the hysteroscope
- Polyps can be associated with glandular hyperplasia and can remain latent for rather long periods
- Once diagnosed, endometrial polyps should be treated by hysteroscopy because curettage has been shown to be ineffective.

Luca Mencaglia, Luiz Cavalcanti de Albuquerque Neto and R. Alfonso Arias Alvarez, Manual of hysteroscopy- Diagnostic, Operative and Office Hysteroscopy 2015: 29-30



ENDOMETRIAL HYPERPLASIA

Diagnosis

More than 90% of patients present with abnormal uterine and bleeding

Transvaginal Ultrasonography

In post menopausal women Endometrial thickness >4mm
Endometrial Stripe abnormalities – Heterogeneity or cystic changes
Junction between endometrium and myometrium
Endometrial volume
Endometrial vascularization index and flow index – increased in CA

Hysteroscopy

ENDOMETRIAL HYPERPLASIA

Hysteroscopy

The morphological criteria derived on hysteroscopic inspection are subjective, operator related, and poorly reproducible. In the diagnosis of endometrial hyperplasia, hysteroscopy sensitivity is no more than 78%

Clark TJ, Yoti D, Gupta JK, Hyde C, Song F, Khan KS. Accuracy of hysteroscopy in the diagnosis of endometrial cancer and hyperplasia: a systematic quantitative review. JAMA 2002;288:1610

ENDOMETRIAL HYPERPLASIA

Endometrial hyperplasia always results from chronic oestrogen stimulation unopposed by the counterbalancing effects of progesterone leading to a wide range of manifestation creating various clinical conditions.

- Women at extremes of age groups, i.e. puberty and perimenopause due to anovulatory cycles.
- Women of the reproductive age group due to anovulatory cycles, e.g. polycystic ovary syndrome (PCOS).
- Postmenopausal women on oestrogen therapy.
- Obese women with a high rate of peripheral conversion of androgens to oestrogens.
- Women on tamoxifen, a nonsteroidal antiestrogenic compound used for treatment of breast cancer.

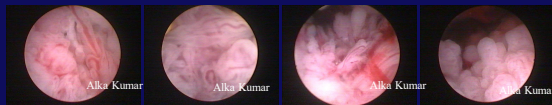
All These conditions giving to conditions like:

- Endometrial hyperplasia.
- Endometrial polyp.
- Endometrial carcinoma.

HYSTEROSCOPIC MORPHOLOGICAL CRITERIA FOR ENDOMETRIAL HYPERPLASIA

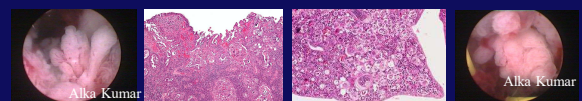
1. Nonhomogeneous endometrial thickness
 - Less than 4mm in post menopausal women
 - No compression on the endometrium (high intra uterine pressure to avoided)
 - Micro polypoid mucosal thickening
 - Focal Endometrial thickness
 - Sessile polyp
2. Surface
 - Notice glandular openings, vascular projections, cystic or necrotic areas, etc.
3. Vascular abnormalities
 - Increased Capillary density
 - Venulocapillary dilatation
4. Glandular cystic dilatation
 - Multi focal or group pseudopolypoid areas
5. Architectural distortion of glandular outlets
 - Revealed only with close range hysteroscopic view
 - Abnormal spacing of glands
 - Dilatation of glands yellowish white color of gland openings

ENDOMETRIAL CARCINOMA

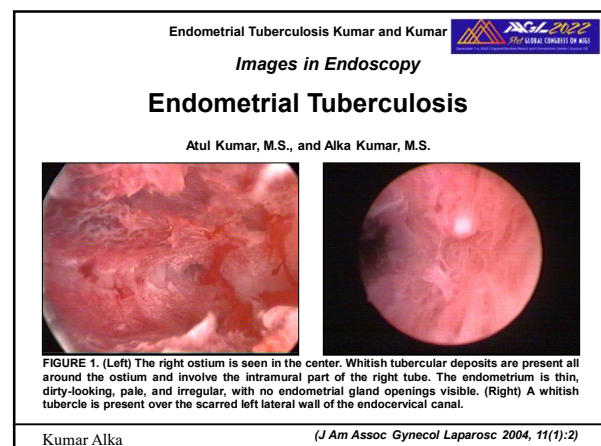
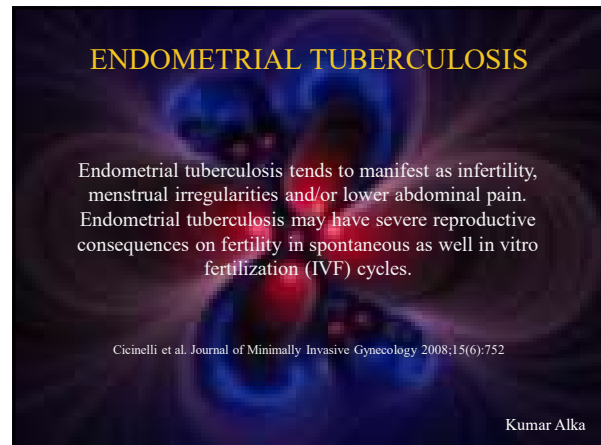
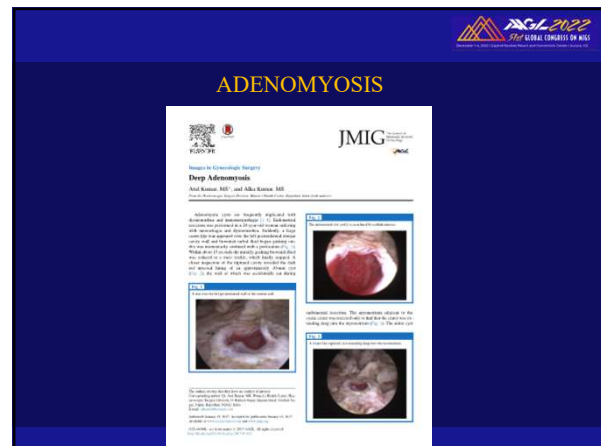
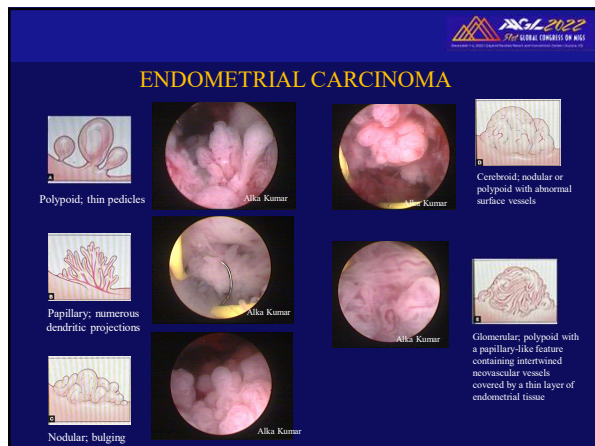


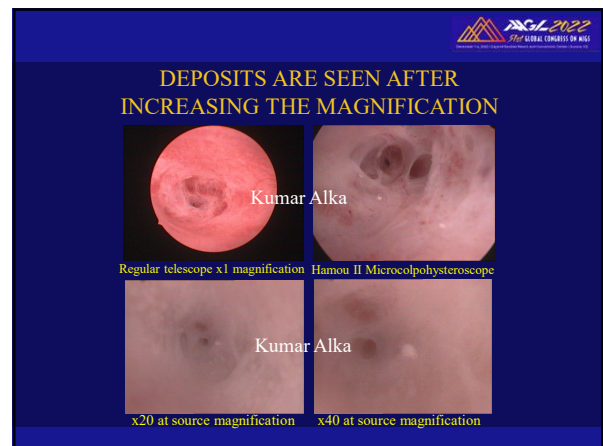
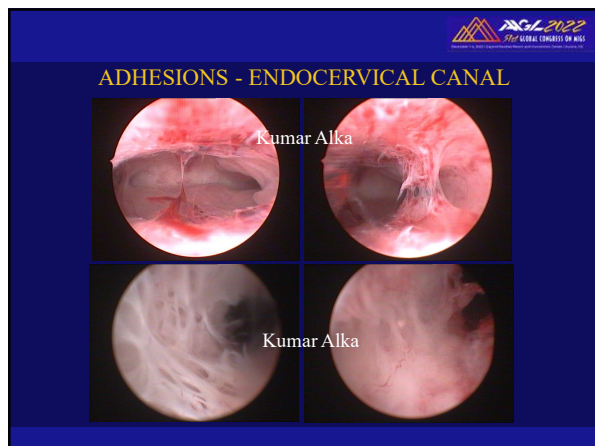
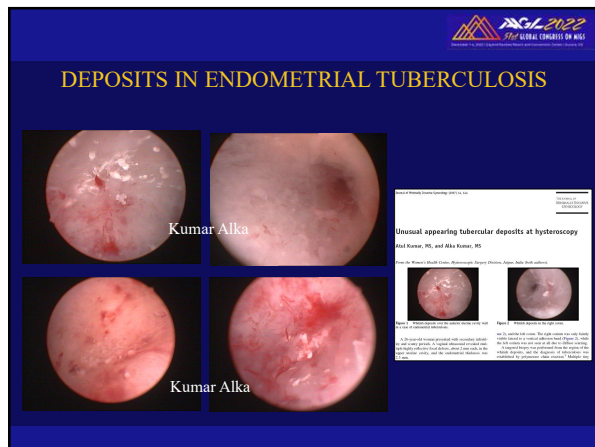
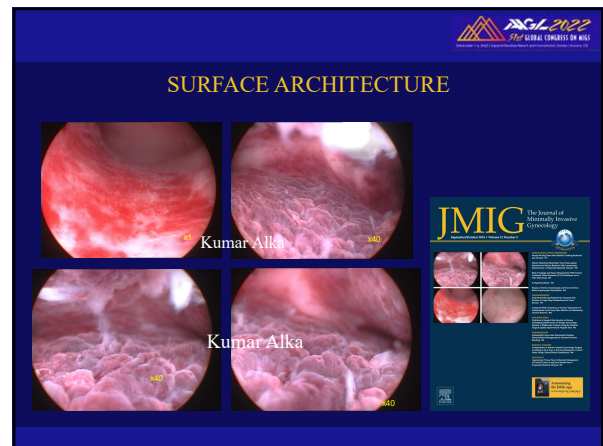
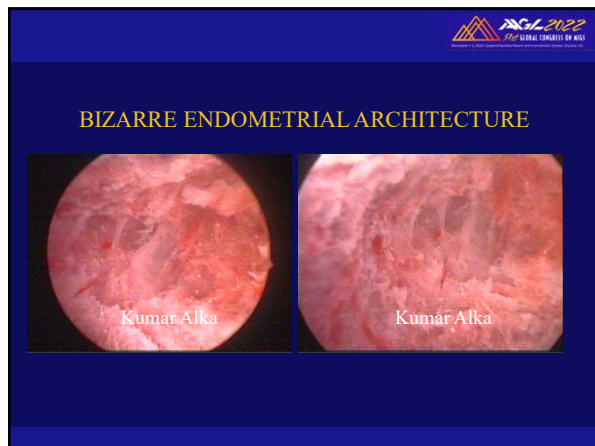
- Endometrial carcinoma: Fourth most common malignancy in females.
- Most common malignancy of the female reproductive tract
- The prevalence of endometrial cancer is increasing with rising levels of obesity.
- App. 75% cases occur in postmenopausal women, median age at diagnosis is 70 years.
 - Postmenopausal bleeding—most common symptom.
 - Adenocarcinomas account for 90% of endometrial neoplasms,
 - Uterine sarcomas-- only 2%–6%;
 - remaining include adenocarcinoma with squamous cell differentiation and adenosquamous carcinoma.

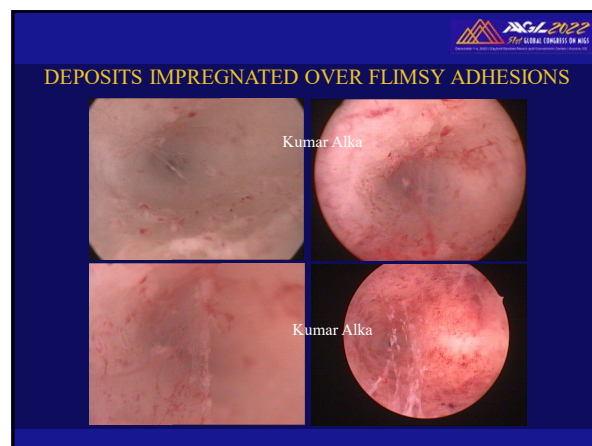
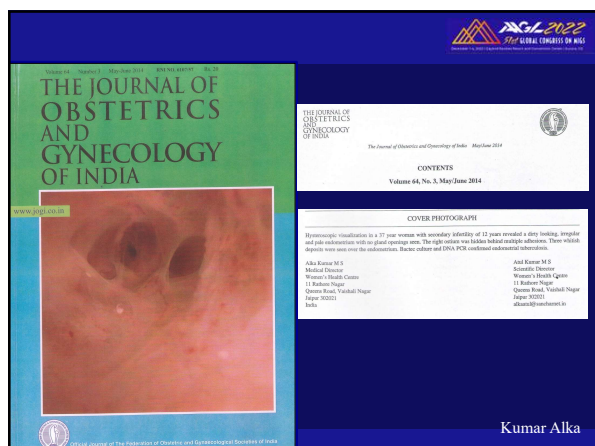
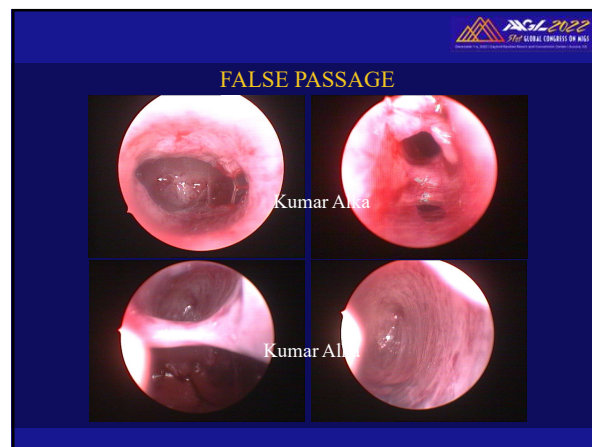
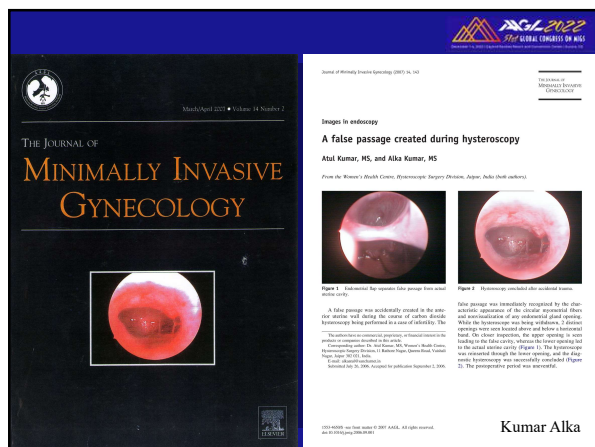
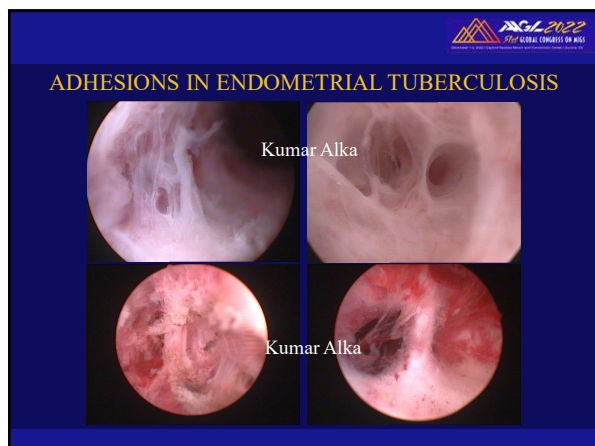
ENDOMETRIAL CARCINOMA

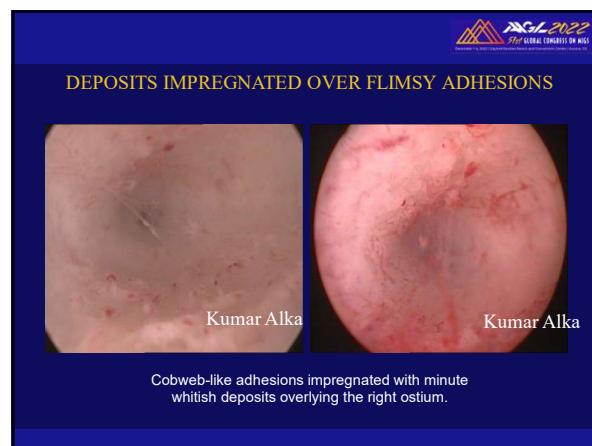
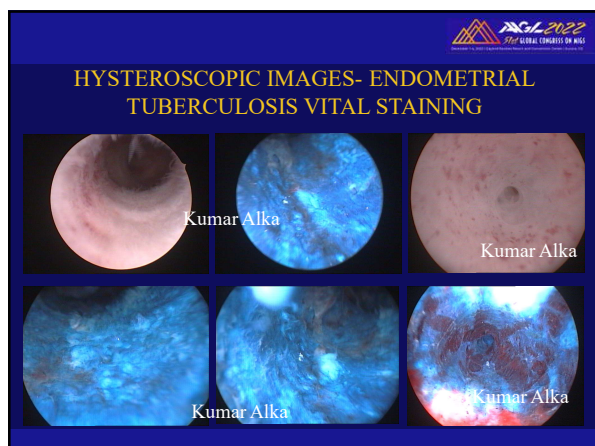
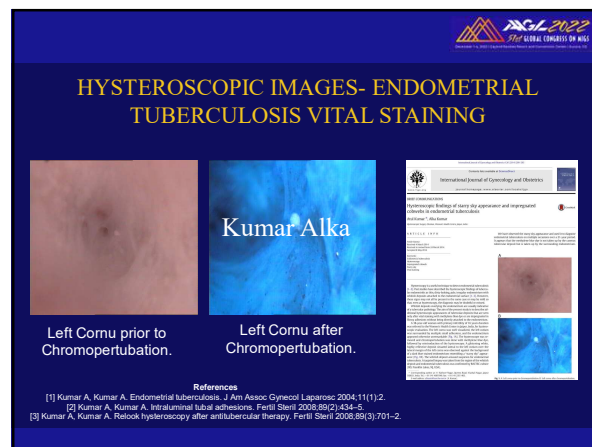
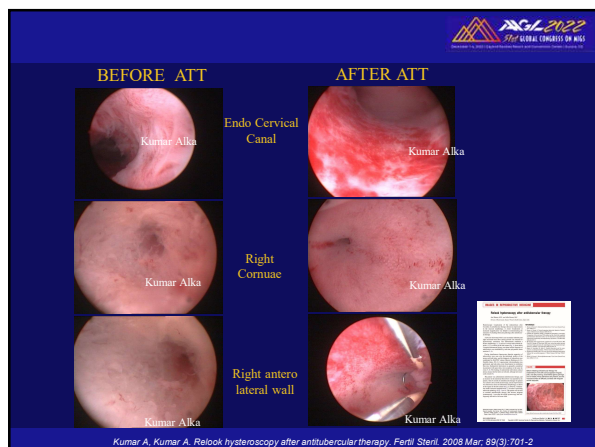
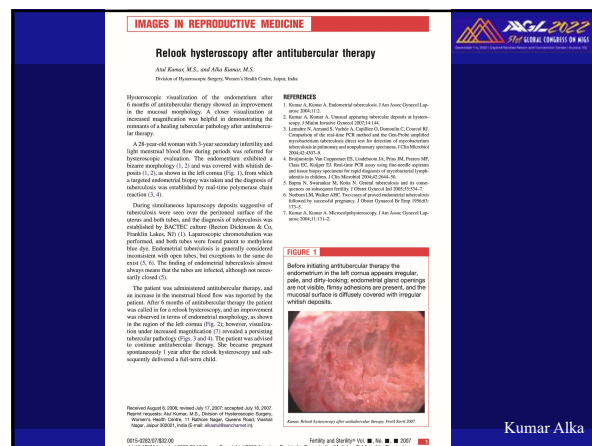
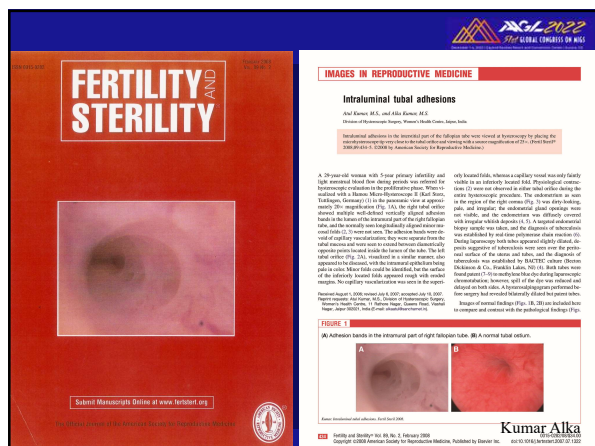


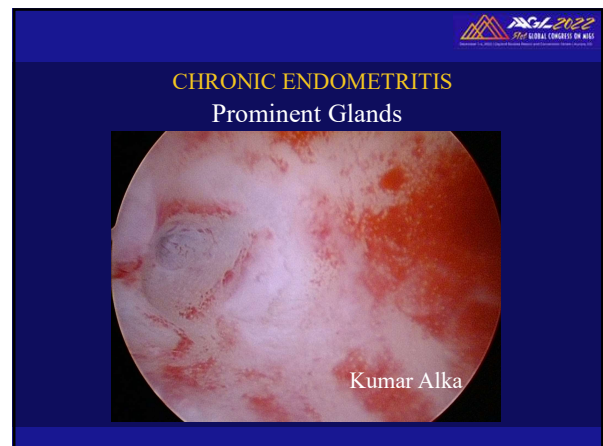
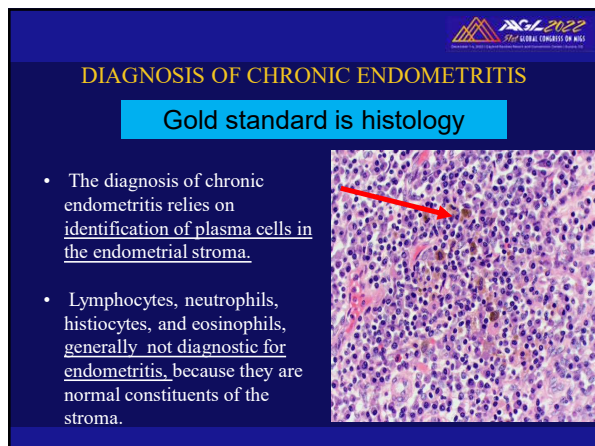
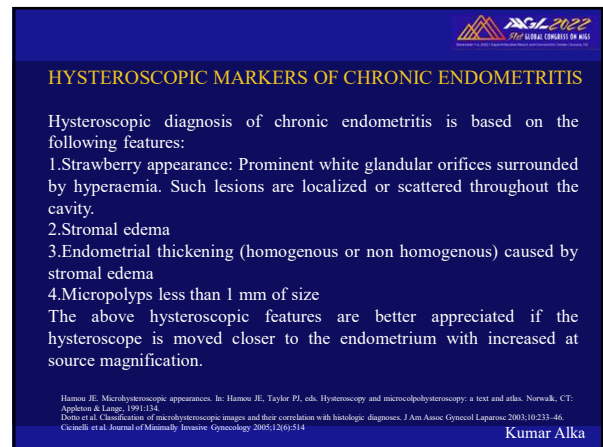
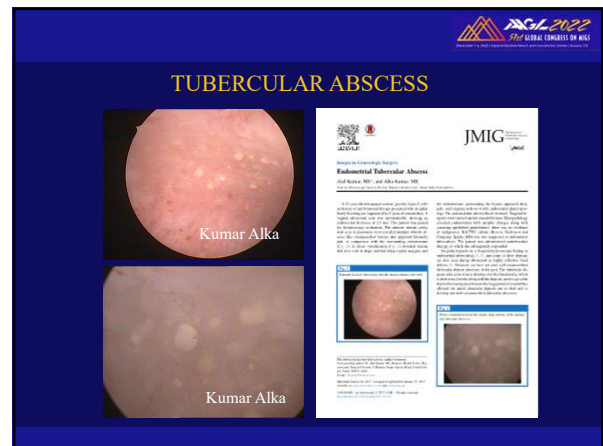
- Depth of myometrial invasion is the most important morphologic prognostic factor, correlating with tumor grade, presence of lymph node metastases, and overall patient survival.

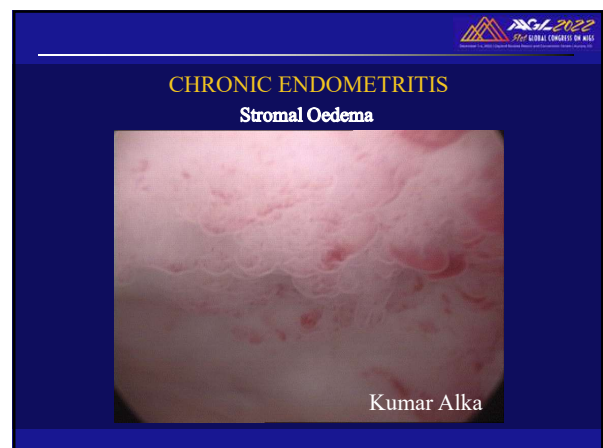
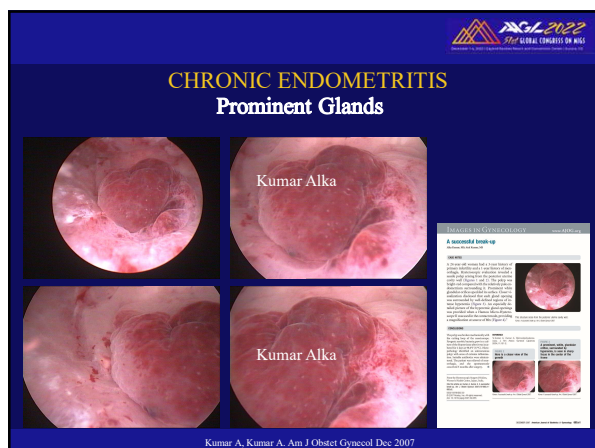
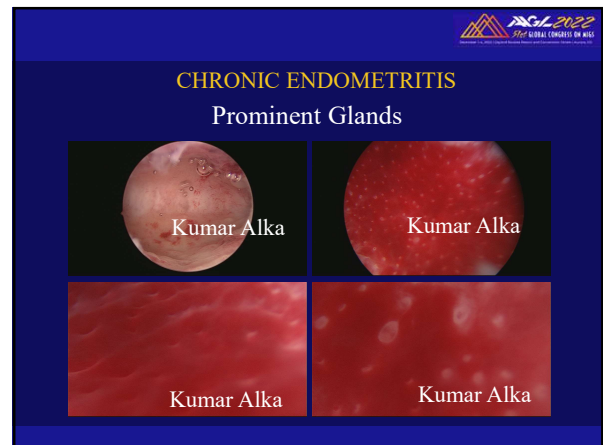
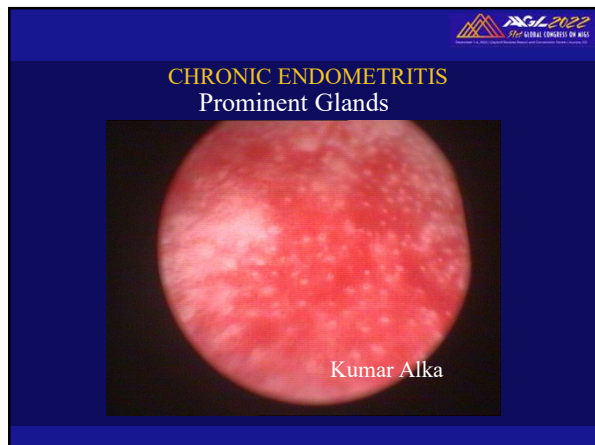
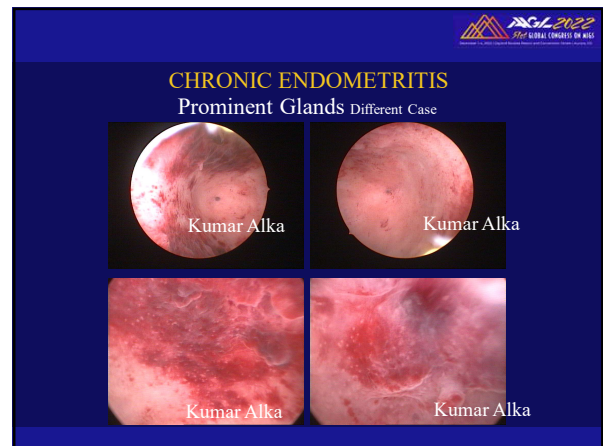
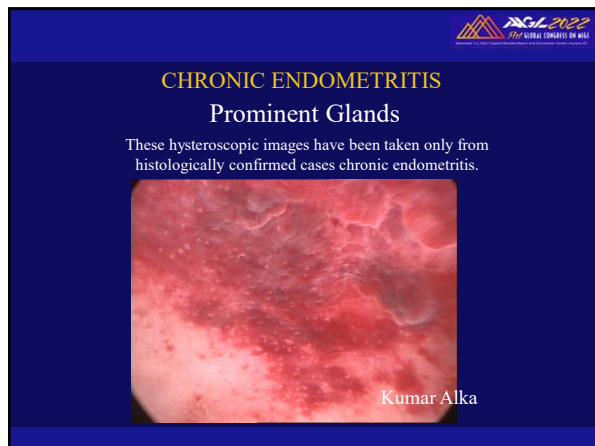


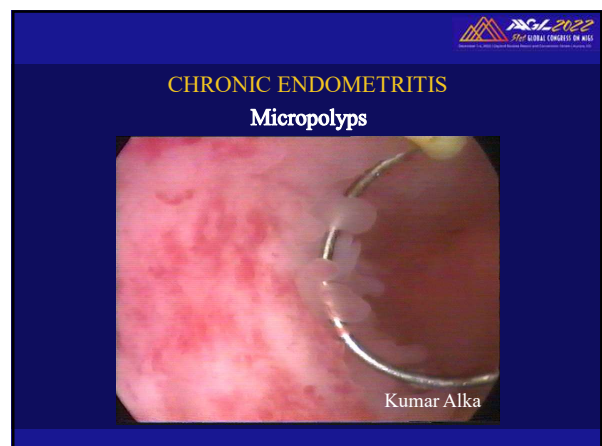
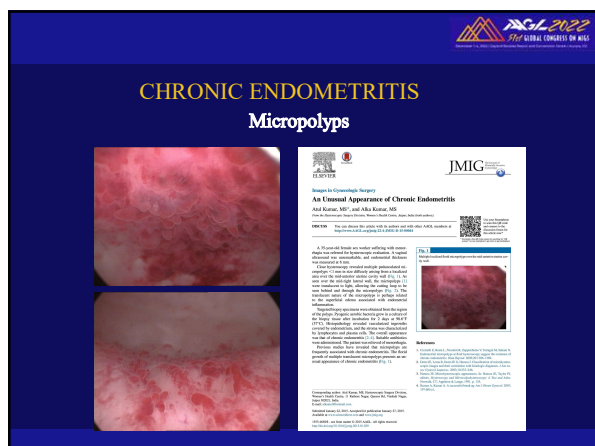
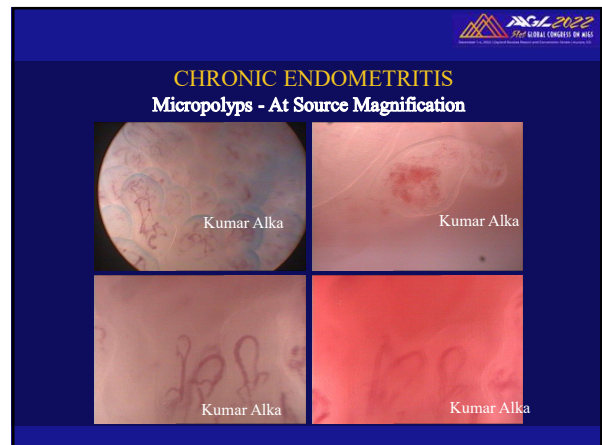
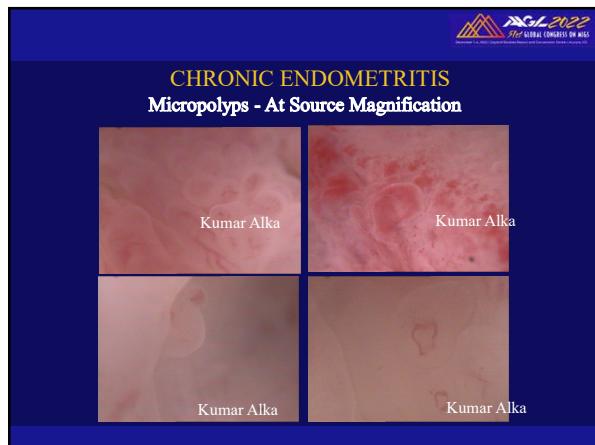
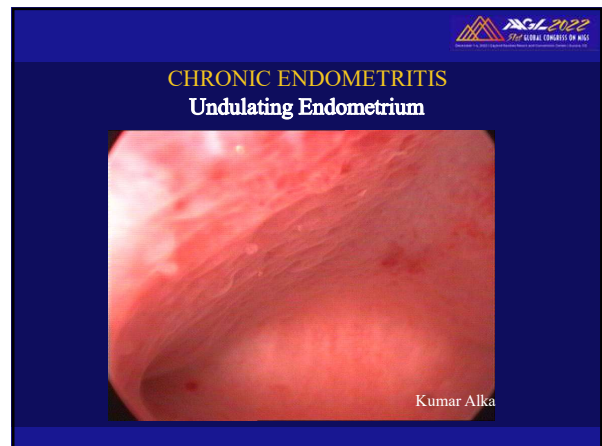
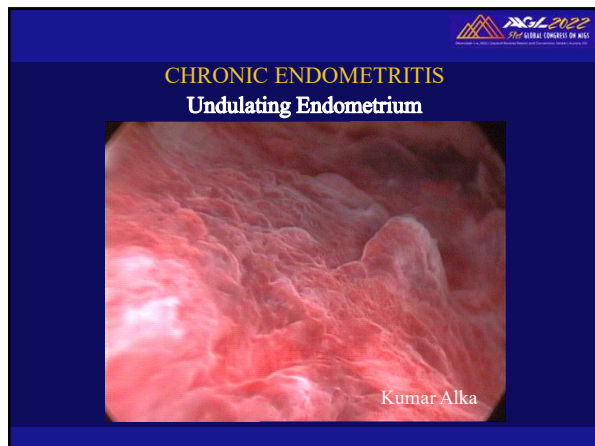


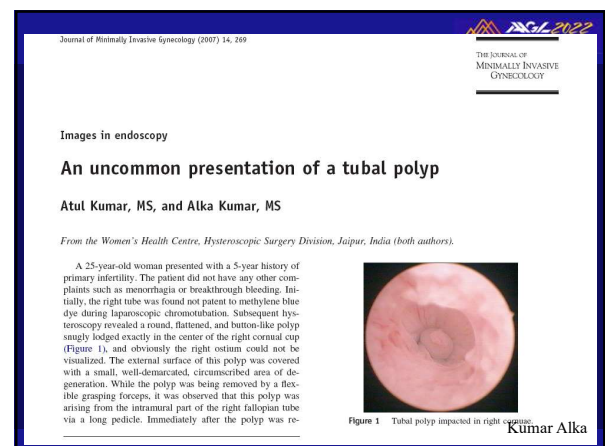
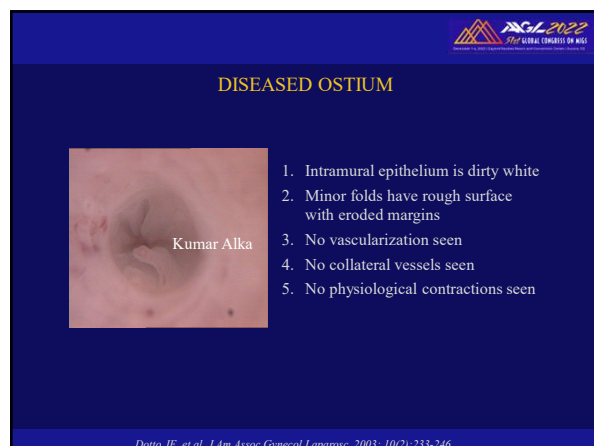
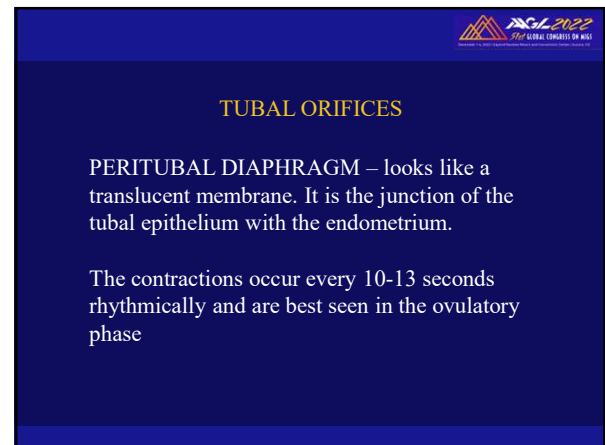
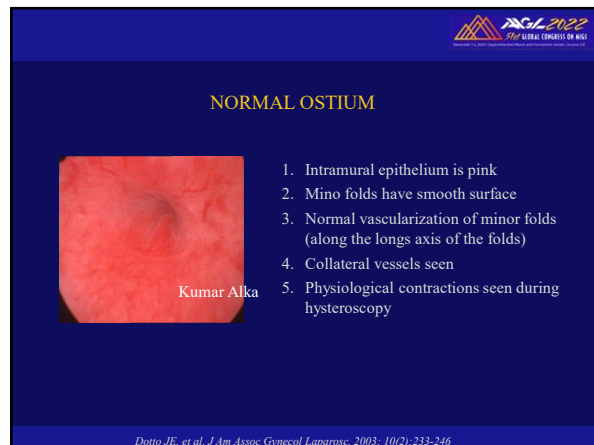
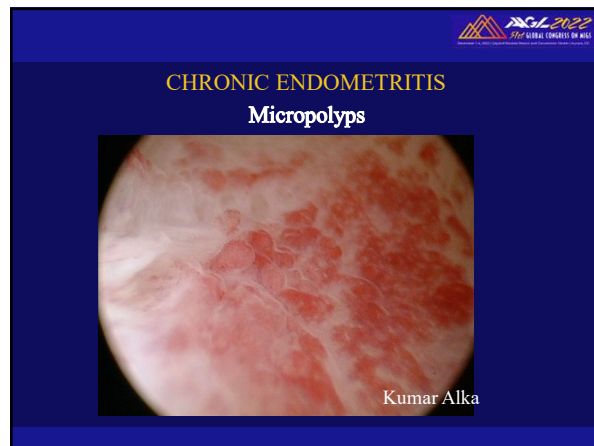


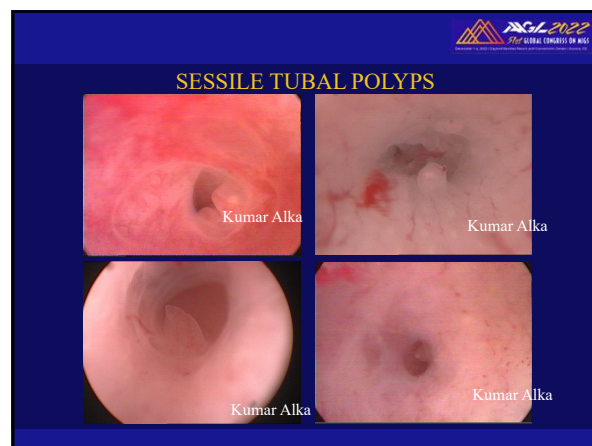
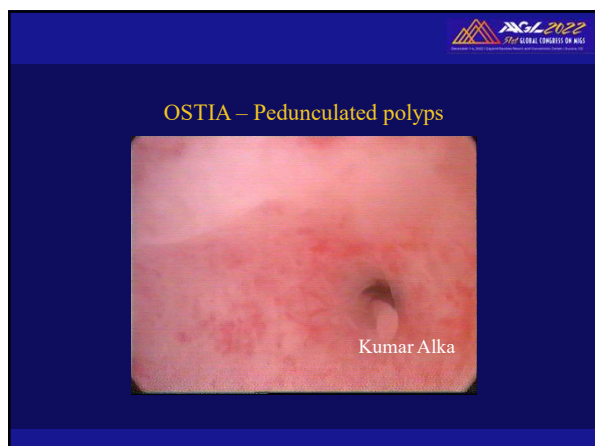
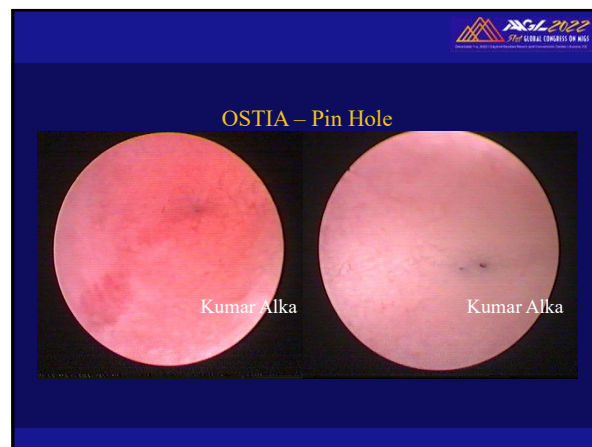
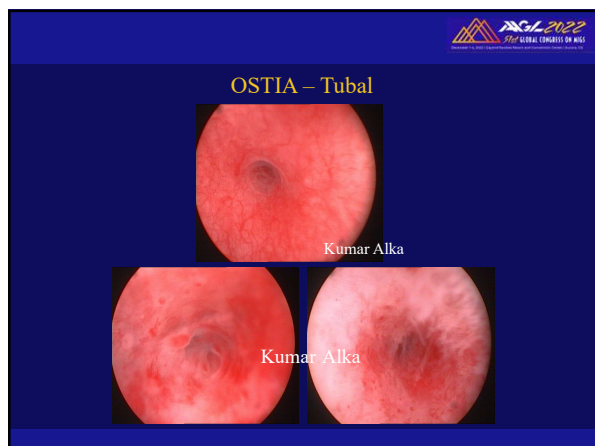


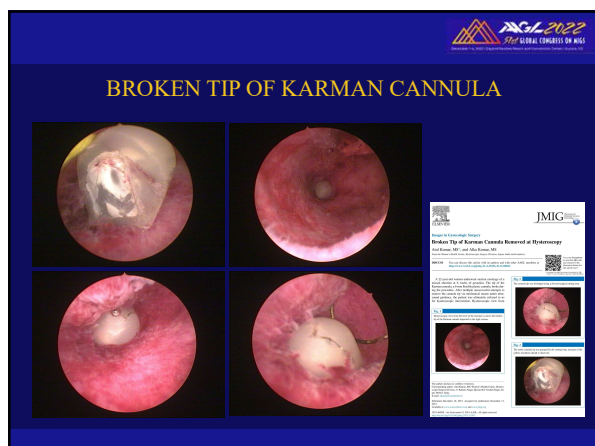
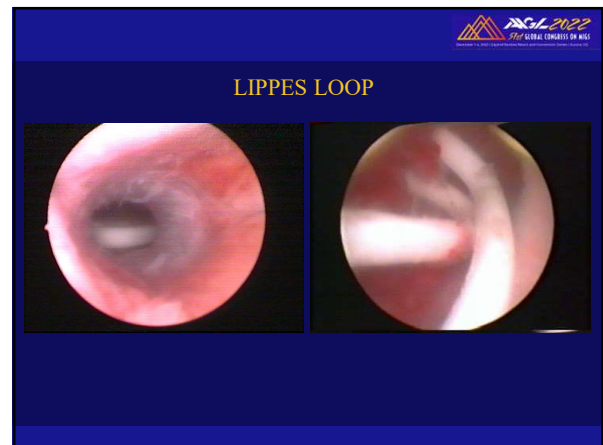
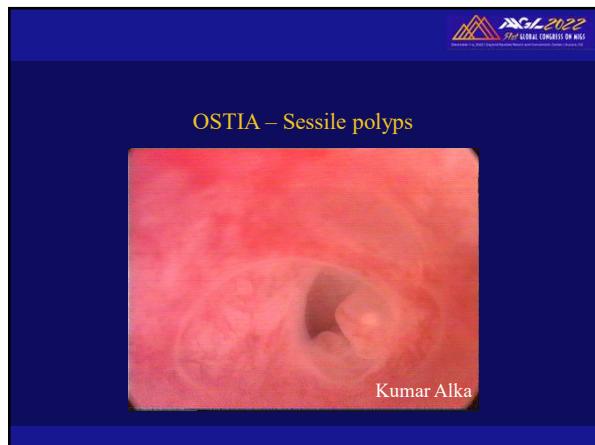
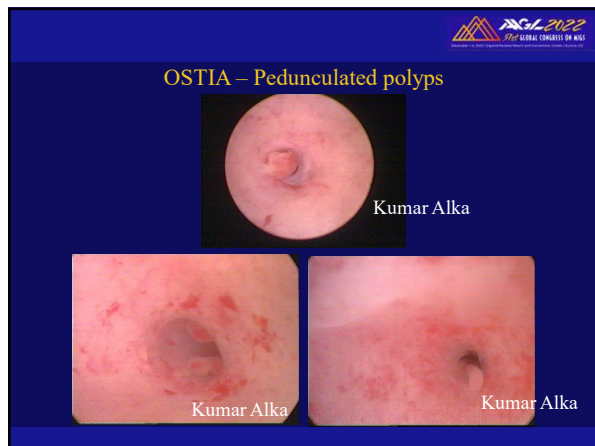












REFERENCES

13. Kumar A, Kumar A. Endometrial tuberculosis. *J Am Assoc Gynecol Laparosc* 2004;11(1):2.
14. Kumar A, Kumar A. Intraluminal tubal adhesions. *Fertil Steril* 2008;89(2):434-5.
15. Kumar A, Kumar A. Hysteroscopic finding of starry sky appearance and impregnated cobwebs in endometrial tunigerculosis. *Int. J Gynaecol Obstet* 2014 Sep; 126(3):280-1
16. Kumar A, Kumar A. Endometrial Tubercular Abscess, *J Minim Invasive Gynecol.* 2017 Feb 3; 24(7):1067-1068
17. Cicinelli E et al. *Fertil Steril*. Chronic endometritis: correlation among hysteroscopic, histologic, and bacteriologic findings in a prospective trial with 2190 consecutive office hysteroscopies. 2008 Mar;89(3):677-84.
18. Cicinelli E et al. *J Minim Invasive Gynecol.* Detection of chronic endometritis at fluid hysteroscopy. 2005 Nov-Dec;12(6):514-8.
19. Cicinelli E, et al. *Hum Reprod.* Endometrial micropolyps at fluid hysteroscopy suggest the existence of chronic endometritis. 2005 May;20(5):1386-9.
20. Cravello et al. Identification and treatment of endometritis. *Contracept Fertil Sex.* 1997;25:585-586
21. Greenwood et al. Chronic endometritis: morphological and clinical observations. *Obstet Gynecol.* 1981;58:176-184
22. Cicinelli et al. *Journal of Minimally Invasive Gynecology* 2005;12(6):514
23. Hamou JE. Microhysteroscopic appearances. In: Hamou JE, Taylor PJ, eds. *Hysteroscopy and microcolpohysteroscopy: a text and atlas.* Norwalk, CT: Appleton & Lange, 1991:134.

REFERENCES

24. Dotto et al. Classification of microhysteroscopic images and their correlation with histologic diagnoses. *J Am Assoc Gynecol Laparosc* 2003;10:233-46.
25. Hamou JE. Microhysteroscopic appearances. In: Hamou JE, Taylor PJ, eds. *Hysteroscopy and microcolpohysteroscopy: a text and atlas.* Norwalk, CT: Appleton & Lange, 1991:134.
26. Kumar A, Kumar A. Hysteroscopic Markers in Chronic Endometritis, *J Minim Invasive Gynecol.* 2017 Feb 16; 25(1):4-5
27. Kumar A, Kumar A. A successful break-up. *Am J Obstet Gynecol.* 2007 Dec; 197(6):685
28. Kumar A, Kumar A. An Unusual Appearance of Chronic Endometritis, *J Minim Invasive Gynecol.* 2015 Sep-Oct; 22(6):927-8
29. Kumar A, Kumar A. Mirror lesion at hysteroscopy. *J Minim Invasive Gynecol.* 2008 Nov-Dec; 15(6):662
30. Kumar A, Kumar A. A false passage created during hysteroscopy. *J Minim Invasive Gynecol.* 2007 Mar-Apr; 14(2):143
31. Kumar A, Kumar A. Intraluminal tubal adhesions. *Fertil Steril.* 2008 Feb; 89(2):434-5
32. Kumar A, Kumar A. An uncommon presentation of a tubal polyp. *J Minim Invasive Gynecol.* 2007 May-Jun; 14(3):269
33. Kumar A, Kumar A. Broken tip of Karman cannula removed at hysteroscopy *J Minim Invasive Gynecol.* 2015 May-Jun; 22(4):700-1

REFERENCES

34. Kumar A, Kumar A. Deep Adenomyosis, *J Minim Invasive Gynecol.* 2017 Nov - Dec; 24(7):1060-1061
35. *J Am Assoc Gynecol Laparosc* 2004, 11(1):2
36. Kumar A, Kumar A. Localized subendometrial leiomyomatosis at hysteroscopy. *J Minim Invasive Gynecol.* 2012 May-Jun; 19(3):284-5
37. Kumar A, Kumar A. Endometrial tuberculosis in a unicornuate uterus with a rudimentary horn. *J Minim Invasive Gynecol.* 2014 Feb 1; 21(6):974-5.
38. Somigliana E et al. *Reprod Update.* 2007
39. Bettochi S et al. *Hum Reprod* 2002;
40. Buttra VC et al. *Fertil Steril* 1981;
41. Cicinelli Et al. *Obstet Gynecol* 1998;
42. Utra VC et al. *Fertil Steril* 1981

CULTURAL AND LINGUISTIC COMPETENCY & IMPLICIT BIAS

The California Medical Association (CMA) announced new standards for Cultural Linguistic Competency and Implicit Bias in CME. The goal of the standards is to support the role of accredited CME in advancing diversity, health equity, and inclusion in healthcare. These standards are relevant to ACCME-accredited, CMA-accredited, and jointly accredited providers located in California. AAGL is ACCME-accredited and headquartered in California.

CMA developed the standards in response to California legislation ([Business and Professions \(B&P\) Code Section 2190.1](#)), which directs CMA to draft a set of standards for the inclusion of cultural and linguistic competency (CLC) and implicit bias (IB) in accredited CME.

The standards are intended to support CME providers in meeting the expectations of the legislation. CME provider organizations physically located in California and accredited by CMA CME or ACCME, as well as jointly accredited providers whose target audience includes physicians, are expected to meet these expectations beginning January 1, 2022. AAGL has been proactively adopting processes that meet and often exceed the required expectations of the legislation.

CMA CME offers a variety of resources and tools to help providers meet the standards and successfully incorporate CLC & IB into their CME activities, including FAQ, definitions, a planning worksheet, and best practices. These resources are available on the [CLC and IB standards page](#) on the CMA website.

Important Definitions:

Cultural and Linguistic Competency (CLC) – The ability and readiness of health care providers and organizations to humbly and respectfully demonstrate, effectively communicate, and tailor delivery of care to patients with diverse values, beliefs, identities and behaviors, in order to meet social, cultural and linguistic needs as they relate to patient health.

Implicit Bias (IB) – The attitudes, stereotypes and feelings, either positive or negative, that affect our understanding, actions and decisions without conscious knowledge or control. Implicit bias is a universal phenomenon. When negative, implicit bias often contributes to unequal treatment and disparities in diagnosis, treatment decisions, levels of care and health care outcomes of people based on race, ethnicity, gender identity, sexual orientation, age, disability and other characteristics.

Diversity – Having many different forms, types or ideas; showing variety. Demographic diversity can mean a group composed of people of different genders, races/ethnicities, cultures, religions, physical abilities, sexual orientations or preferences, ages, etc.

Direct links to AB1195 (CLC), AB241 (IB), and the B&P Code 2190.1:

[Bill Text – AB-1195 Continuing education: cultural and linguistic competency.](#)

[Bill Text – AB-241 Implicit bias: continuing education: requirements.](#)

[Business and Professions \(B&P\) Code Section 2190.1](#)

CLC & IB Online Resources:

[Diversity-Wheel-as-used-at-Johns-Hopkins-University-12.png \(850×839\) \(researchgate.net\)](#)

[Cultural Competence In Health and Human Services | NPIN \(cdc.gov\)](#)

[Cultural Competency – The Office of Minority Health \(hhs.gov\)](#)

[Implicit Bias, Microaggressions, and Stereotypes Resources | NEA](#)

[Unconscious Bias Resources | diversity.ucsf.edu](#)

[Act, Communicating, Implicit Bias \(racialequitytools.org\)](#)

<https://kirwaninstitute.osu.edu/implicit-bias-training>

<https://www.uptodate.com/contents/racial-and-ethnic-disparities-in-obstetric-and-gynecologic-care-and-role-of-implicitbiases>

<https://www.contemporaryobgyn.net/view/overcoming-racism-and-unconscious-bias-in-ob-gyn>

<https://pubmed.ncbi.nlm.nih.gov/34016820/>