ព្រះរាជាណាចក្រកម្ពុជា

ជាតិ សាសនា ព្រះមហាក្សត្រ

មគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិក

CLINICAL PRACTICE GUIDELINES

ផ្នែក

FOR

សម្ភព និងរោគស្ត្រី

OBSTETRICS AND GYNECOLOGY

នាយកដ្ឋានសេវាសុខភាព

ឆ្នាំ ២០២៥

Kingdom of Cambodia
Nation Religion King

CLINICAL PRACTICE GUIDELINES

FOR

OBSTETRICS AND GYNECOLOGY

Department of Health Services
December 2025

Ministry of Health

CLINICAL PRACTICEGUIDELINES FOR

OBSTETRICS AND GYNECOLOGY

December 2025

ព្រះរាជាណាចក្រកម្ពុជា
ជាតិ សាសនា ព្រះមហាក្សត្រ

ក្រសួងសុខាតិបាល
លេខ ០៣៦ ប្រ.ស/ន.ស.ប្រ.ក

ប្រកាស
ស្តីពី
ការជាក់ឱ្យអនុវត្តមគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិក ផ្នែកសម្ភពនិងរោគស្ត្រី

រដ្ឋមន្ត្រីក្រសួងសុខាតិបាល

- បានឃើញរដ្ឋធម្មនុញ្ញនៃព្រះរាជាណាចក្រកម្ពុជា
- បានឃើញព្រះរាជក្រឹត្យលេខ នស/រកត/០៨២៣/១៩៨១ ចុះថ្ងៃទី២២ ខែសីហា ឆ្នាំ២០២៣ ស្តីពីការតែងតាំងរាជរដ្ឋាភិបាលនៃព្រះរាជាណាចក្រកម្ពុជា
- បានឃើញព្រះរាជក្រឹត្យលេខ នស/រកត/០២២៤/២០៥ ចុះថ្ងៃទី២១ ខែកុម្ភៈ ឆ្នាំ២០២៤ ស្តីពីការបំពេញបន្ថែមសមាសភាពរាជរដ្ឋាភិបាលនៃព្រះរាជាណាចក្រកម្ពុជា
- បានឃើញព្រះរាជក្រឹត្យលេខ នស/រកត/០៩២៤/១១៦៩ ចុះថ្ងៃទី២០ ខែកញ្ញា ឆ្នាំ២០២៤ ស្តីពីការកែសម្រួល និងតែងតាំងសមាសភាពរាជរដ្ឋាភិបាលនៃព្រះរាជាណាចក្រកម្ពុជា
- បានឃើញព្រះរាជក្រឹត្យលេខ នស/រកត/១១២៤/១៤៧៧ ចុះថ្ងៃទី២០ ខែវិច្ឆិកា ឆ្នាំ២០២៤ ស្តីពីការកែសម្រួល និងតែងតាំងសមាសភាពរាជរដ្ឋាភិបាលនៃព្រះរាជាណាចក្រកម្ពុជា
- បានឃើញព្រះរាជក្រមលេខ នស/រកម/០៦១៨/០១២ ចុះថ្ងៃទី២៨ ខែមិថុនា ឆ្នាំ២០១៨ ដែលប្រកាសឱ្យប្រើច្បាប់ ស្តីពីការរៀបចំ និងការប្រព្រឹត្តទៅនៃគណៈរដ្ឋមន្ត្រី
- បានឃើញព្រះរាជក្រមលេខ នស/រកម/០១៩៦/០៦ ចុះថ្ងៃទី២៤ ខែមករា ឆ្នាំ១៩៩៦ ដែលប្រកាសឱ្យប្រើច្បាប់ស្តីពីការបង្កើតក្រសួងសុខាតិបាល
- បានឃើញព្រះរាជក្រមលេខ នស/រកម/១១១៦/០១៤ ចុះថ្ងៃទី១៦ ខែវិច្ឆិកា ឆ្នាំ២០១៦ ដែលប្រកាសឱ្យប្រើច្បាប់ ស្តីពីការគ្រប់គ្រងអ្នកប្រកបវិជ្ជាជីវៈសុខាតិបាល
- បានឃើញអនុក្រឹត្យលេខ២៣៩ អនក្រ.បក ចុះថ្ងៃទី០៣ ខែធ្នូ ឆ្នាំ២០២៥ ស្តីពីការរៀបចំ និងការប្រព្រឹត្តទៅរបស់ក្រសួងសុខាតិបាល
- យោងតាមការចាំបាច់របស់ក្រសួងសុខាតិបាល

អាសយដ្ឋាន៖ ដីឡូតិ៍លេខ៨០ វិថីសម្តេច ប៉ែន នុត (២៨៩) សង្កាត់បឹងកក់ទី២ ខណ្ឌទួលគោក រាជធានីភ្នំពេញ
ទូរស័ព្ទ៖(+៨៥៥) ២៣ ៨៨៥ ៩៧០
អ៊ីម៉ែល៖ info@moh.gov.kh
គេហទំព័រ៖ www.moh.gov.kh
តេឡេក្រាម៖ t.me/MOHCambodia

សម្រេច

ប្រការ១.-

ត្រូវបានដាក់ឱ្យអនុវត្តមគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិកផ្នែកសម្ភព និងរោគស្ត្រី (Clinical Practice Guidelines For Obstetrics and Gynecology) ដែលជាឧបសម្ព័ន្ធនៃប្រកាសនេះ។

ប្រការ២.-

ប្រកាសនេះមានវិសាលភាពអនុវត្តចំពោះគ្រប់មូលដ្ឋានសុខាភិបាលសាធារណៈ និងឯកជនក្នុងព្រះរាជាណាចក្រកម្ពុជា។

ប្រការ៣.-

បទប្បញ្ញត្តិទាំងឡាយណាដែលផ្ទុយនឹងប្រកាសនេះ ត្រូវទុកជានិរាករណ៍។

ប្រការ៤.-

អគ្គលេខាធិការ អគ្គនាយកបច្ចេកទេសសុខាភិបាល អគ្គាធិការក្រសួងសុខាភិបាល គ្រប់ប្រធានអង្គភាពក្រោមឱវាទក្រសួងសុខាភិបាល ទាំងមូលដ្ឋានសុខាភិបាលសាធារណៈ និងឯកជន ត្រូវទទួលបន្ទុកអនុវត្តតាមប្រកាសនេះឱ្យមានប្រសិទ្ធភាព ចាប់ពីថ្ងៃចុះហត្ថលេខាតទៅ។

ថ្ងៃ ពុធ ១២ កើត ខែ បុស្ស ឆ្នាំម្សាញ់ សប្តស័ក ព.ស.២៥៦៩
ធ្វើនៅរាជធានីភ្នំពេញ ថ្ងៃទី ៣១ ខែ ធ្នូ ឆ្នាំ២០២៥

រដ្ឋមន្ត្រីក្រសួងសុខាភិបាល

សាស្ត្រាចារ្យ ឈាង រ៉ា

កន្លែងទទួលៈ
- ទីស្តីការគណៈរដ្ឋមន្ត្រី
- ក្រសួងសេដ្ឋកិច្ចនិងហិរញ្ញវត្ថុ
- ឧទ្ធរណ៍យឯកឧត្តមសាស្ត្រាចារ្យរដ្ឋមន្ត្រីក្រសួងសុខាភិបាល
- ដូចប្រការ៤
- រាជកិច្ច
- ឯកសារ កាលប្បវត្តិ

អារម្ភកថា

ក្រោមកិច្ចដឹកនាំរបស់រាជរដ្ឋាភិបាលនីតិកាលទី៧ នៃរដ្ឋសភា នៃ **ព្រះរាជាណាចក្រកម្ពុជា** ក្រសួងសុខាភិបាល យកចិត្តទុកដាក់ខ្ពស់ដល់សុខភាព និងសុខុមាលភាពប្រជាជនគ្រប់រូប និងប្តេជ្ញាចិត្តយ៉ាងមុឺងម៉ាត់លើកកម្ពស់ការផ្តល់សេវាសុខាភិបាលប្រកបដោយ គុណភាព សុវត្ថិភាព និងសមធម៌ ដោយផ្តោតលើអ្នកជំងឺ ជូនដល់ប្រជាជនកម្ពុជាគ្រប់រូបស្របតាម ផែនការយុទ្ធសាស្ត្រសុខាភិបាល ២០២៥-២០៣៤ ក៏ដូចជា ផែនទីបង្ហាញផ្លូវឆ្ពោះទៅការគ្របដណ្តប់សុខភាពជាសកលនៅកម្ពុជា ឆ្នាំ ២០២៤-២០៣៥ របស់រាជរដ្ឋាភិបាល។

មគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិកផ្នែកសម្ភព និងរោគស្ត្រី នេះជាមាគ៌ាណែនាំថ្នាក់ជាតិពាក់ព័ន្ធនឹងពិធីសារ នៃការគ្រប់គ្រងបញ្ហាសុខភាពផ្នែកសម្ភព និងរោគស្ត្រីជាអាទិភាពនៅកម្ពុជា ដោយផ្តោតសំខាន់លើបែបបទ នៃការធ្វើរោគវិនិច្ឆ័យ និងការថែទាំ ការព្យាបាល និងការបង្ការជំងឺ រាប់ទាំងការតាមដានបញ្ហាសុខភាព ឬជំងឺ។

មគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិកផ្នែកសម្ភព និងរោគស្ត្រីនេះ ត្រូវបានរៀបចំចងក្រងជាលើកដំបូងដោយក្រុមការងារបច្ចេកទេសជំនាញ នៃក្រសួងសុខាភិបាល ដោយមានការចូលរួមពីដៃគូសំខាន់ៗ អ្នកជំនាញ ឯកទេសជំនាញពីផ្នែកពាក់ព័ន្ធទាំងឡាយ រួមទាំងគ្រូពេទ្យព្យាបាល គ្រូពេទ្យឯកទេសផ្នែកសម្ភព និងរោគស្ត្រីបម្រើការងារនៅតាមមន្ទីរពេទ្យគ្រប់លំដាប់ថ្នាក់ មន្ត្រីបំពេញការងារនៅការិយាល័យសុខាភិបាលស្រុកប្រតិបត្តិ និងមន្ទីរសុខាភិបាលនៃរដ្ឋបាលរាជធានី ខេត្ត កម្មវិធីជាតិ សមាគមវិជ្ជាជីវៈសុខាភិបាលផ្សេងៗ ក៏ដូចជាអង្គការដៃគូពាក់ព័ន្ធ ។

មគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិកនេះ ត្រូវបានរៀបចំឡើងសម្រាប់អ្នកវិជ្ជាជីវៈសុខាភិបាល និងអ្នកវិជ្ជាជីវៈពាក់ព័ន្ធ ជាពិសេសអ្នកផ្តល់សេវាសុខភាព រាប់បញ្ចូលទាំង វេជ្ជបណ្ឌិត និងអ្នកប្រកបវិជ្ជាជីវៈសុខាភិបាលផ្សេងទៀត នៅមូលដ្ឋានសុខាភិបាលសាធារណៈ និងឯកជន ក៏ដូចជាសិក្ខាកាម អ្នករៀបចំគោលនយោបាយ អ្នកពាក់ព័ន្ធនានា គណៈវិជ្ជាជីវៈ និងសមាគមវិជ្ជាជីវៈផ្សេងៗ។

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FOREWORD

Under the leadership of the Royal Government of the 7th Legislature of the National Assembly of the Kingdom of Cambodia, the Ministry of Health pays high attention to the health and well-being of the entire population. The Ministry of Health is strongly committed to ensuring the provision of equitable, safe and quality patient-centered health services for the Cambodian population in line with the Health Strategic Plan 2025-2034 and the Royal Government Roadmap Towards Universal Health Coverage in Cambodia 2024-2035.

This Clinical Practice Guidelines (CPG) for Obstetrics and Gynecology provides national guidance on the management protocols of priority health problems related to obstetrics and gynecology with a focus on diagnosis and care, including curative and preventive care, as well as follow-up of health problems.

The Guidelines, first ever published in Cambodia, was developed by the Technical Working Group of the Ministry of Health with participation from various stakeholders and individuals, including experts from relevant fields ranging from clinicians and doctors specialized in obstetrics and gynecology working in hospitals at all levels to district health officers, Provincial Health Department, national programs, health professional associations, as well as partner organizations.

The Guidelines is intended for use by health professionals and other relevant professionals, especially health care providers, including doctors and other health practitioners in both public and private health facilities as well as trainees, policymakers, relevant individuals, professional councils and professional associations.

The Ministry of Health guides all health professionals and relevant individuals to use this Guidelines in their professional practice with the aim of improving effectiveness, efficiency and quality in patient care and safety, as well as contributing to human resource capacity building.

Phnom Penh, 31 December, 2025

Minister of Health

Prof. CHHEANG RA

ACKNOWLEDGEMENT

The Ministry of Health wishes to extend its profound appreciation to Excellencies, Professors, Doctors, Experts, Officials of the Ministry at all levels as well as partner organization officials and all individuals who have shared their experiences and inputs contributing to the development of this important Clinical Practice Guidelines.

We particularly thank H.E. Prof. **Pech Sothy**, Secretary of State, Chair and all Vice-chairs and members of the Technical Working Group of Clinical Practice Guidelines for Obstetrics and Gynecology, under the overall leadership and guidance of the Steering Committee for National Medical Care and Therapy of the Ministry of Health.

We would also like to express our deep gratitude to all partners involved, including the World Health Organization and other partners, for their technical and financial contributions to the formulation of the guidelines.

This Clinical Practice Guidelines for Obstetrics and Gynecology represent another significant and commendable achievement of the Ministry of Health of the Kingdom of Cambodia.

Phnom Penh, 31 December, 2025

Chair of the Steering Committee for

National Medical and Therapy

H.E. Prof. Yit Sunnara

TABLE OF CONTENTS

ABBREVIATION

ABG - Arterial Blood Gases
AFP - Alpha-Fetoprotein
AVD - Abnormal Vaginal Discharge
BID - Bis In Die (Twice a day)
BMI - Body Mass Index
BSE - Breast Self-Examination
BRCA1/2 - Breast Cancer 1 and 2 (genes associated with a higher risk of breast and ovarian cancer)
CC - Choriocarcinoma
CCT - Controlled Cord Traction
CEA - Carcinoembryonic Antigen
CNS - Central Nervous System
CRP - C-Reactive Protein
CTG - Cardiotocography
CXR - Chest X-Ray
D&E - Dilatation and Evacuation
DIC - Disseminated Intravascular Coagulation
DM - Diabetes Mellitus
ECOG - Eastern Cooperative Oncology Group
EOC - Epithelial Ovarian Cancer
ET - Endocrine Therapy
FGR - Fetal Growth Restriction
FFP - Fresh Frozen Plasma
FNA - Fine-Needle Aspiration
GFR - Glomerular Filtration Rate
GTN - Gestational Trophoblastic Neoplasia
GTD - Gestational Trophoblastic Disease
HELLP - Hemolysis, Elevated Liver Enzymes, Low Platelets
HR - Hormonal Receptor
HCG - Human Chorionic Gonadotropin
HRT - Hormonal Replacement Therapy
ICU - Intensive Care Unit
INR - International Normalized Ratio
IVF - In Vitro Fertilization
IUFD - Intrauterine Fetal Death
IUP - Intrauterine Pregnancy
LDH - Lactate Dehydrogenase
LNG-IUS - Levonorgestrel-Releasing Intrauterine System
MRI - Magnetic Resonance Imaging
MVA - Manual Vacuum Aspiration
NASG - Non-Pneumatic Anti-Shock Garment
NATA - Nucleic Acid Amplification Test
NICU - Neonatal Intensive Care Unit
NSAIDs - Non-Steroidal Anti-Inflammatory Drugs
PE - Pre-eclampsia
PCR - Polymerase Chain Reaction
PID - Pelvic Inflammatory Disease
PPH - Postpartum Hemorrhage
PPROM - Preterm Prelabor Rupture of Membranes
RH - Resuscitative Hysterotomy
SLN - Sentinel Lymph Node
STI - Sexually Transmitted Infection
TIBC - Total Iron-Binding Capacity
TIA - Transient Ischemic Attack
UAE - Uterine Artery Embolization
UA - Umbilical Artery
VIA - Visual Inspection with Acetic Acid
VVC - Vulvovaginal Candidiasis

INTRODUCTION

I. BACKGROUND

The Ministry of Health of the Kingdom of Cambodia is committed to improve the health and well-being of all Cambodian population through the provision of quality, safe, acceptable, equitable and affordable healthcare services. Implementing evidence-based, appropriate, and cost-effective health interventions within care packages at various levels of the health system, guided by contextually relevant best practices in Clinical Practice Guidelines for Obstetrics and Gynecology, can significantly enhance women's health and reduce maternal mortality and morbidity.

The main causes of preventable maternal deaths in Cambodia are post-partum hemorrhage, pre-eclampsia/eclampsia, infections. This Clinical Practice Guidelines offers selected priority Obstetric interventions for saving mothers' and newborns' lives. Other obstetric interventions and Emergency Obstetric Care are available in the National Clinical Safe Motherhood Protocol for Referral Hospital. Then, common gynecological interventions are described in this Clinical Practice Guidelines.

II. DEVELOPMENT PROCESS

This Clinical Practice Guidelines (CPG) was formulated by "Technical Working Group of Clinical Practice Guidelines for Obstetrics and Gynecology" of the Ministry of Health through face-to-face and online meetings of the working group and small group meetings and discussions with guidance and endorsements from the Steering Committee for the National Medical Care and Therapy of the Ministry of Health mainly through its meetings. The development process of these guidelines was actively participated by various stake holders and individuals, including experts from related fields ranging from clinicians working in hospitals at all levels, district health officers, provincial health department, national institutes, national programs, health professional associations as well as experts and officials of partner organizations. Each section follows standard format except in few cases.

III. PURPOSE AND USERS

The aim of these guidelines is to assist health care providers and practitioners make informed decisions on clinical diagnosing and treatment based on recommended protocols based on system review of evidence and an assessment of the benefits and harms of alternative care options. The guidelines is used for health professionals and relevant stake holders in both public and private sectors, including doctors, related health professionals, trainees and medical students, policy makers, professional societies, in public and private health facilities and institutions, including provincial and district hospitals, private clinic, training and research institutions.

The main end users of the CPG are clinicians, managers and other health professionals practicing in patient care setting to support the delivery of consistently safe, quality and cost effective and equitable health care. They should be harmonized with the CPA guidelines, IPC guideline, AMR guideline, CHAS and Quality Enhancement Monitoring Tool (QEMT) and other MoH guidelines to motivate and facilitate their relevance and use. CPG can also be used by other relevant bodies and people such as in training and research institutions as well as by other organization or institutions as per the relevancy of their mandates.

POST-PARTUM HEMORRHAGE (PPH)

Prof. Tung Rathavy, Prof. Pech Sothy, Prof. Kruy Leang Sim, Prof. Koum Kanal, Prof. Sann Chansoeung, Prof. Keth Lysotha, Dr. Ros Saphath, Prof. Ass. Korn Aun, Dr. Chhun Samsorphea, Dr. Lay Sanine, Dr. Sea Sreyla, Dr. Uy Sopha, Dr. Heng Rithsopanha, Dr. Lim Sokong

I. DEFINITION

Postpartum Hemorrhage (PPH) is commonly defined as a blood loss of 500ml from the genital tract after vaginal delivery or a blood loss of 1000 ml after caesarian delivery.

It is now recommended to initiate first-response treatment when ≥300 mL of blood loss is accompanied by abnormal hemodynamic signs (pulse > 100 bpm, shock index ≥ 1, systolic blood pressure < 100 mmHg, or diastolic blood pressure < 60 mmHg) or when ≥500 mL of blood loss occurs within 24 hours, whichever occurs first within 24 hours after birth, and with particular vigilance during the first 2 hours.

The importance of a given of blood loss varies with the mother's hemoglobin level. A mother with a normal hemoglobin level will tolerate blood loss, but maybe fatal for anemic mother. Bleeding may occur at a slow rate over several hour and the condition may not be recognized until the mother suddenly enters a state of shock.

Although the woman is healthy with no anemia, she might be facing the risk of danger due to blood loss.

II. INCIDENCE

PPH affects approximately 2% of all women who give birth. It is associated not only with nearly one quarter of all maternal deaths globally, but it is also the leading cause of maternal mortality in Cambodia (36% of all investigated maternal deaths in 2017). PPH is a significant contributor to severe maternal morbidity and long-term disability.

III. ETIOLOGY/RISK FACTORS

The causes of PPH are called the four Ts (Tone, Trauma, Tissue and Thrombin).

Tone - Uterine atony refers to a soft and weak uterus when its muscles do not contract enough to clamp the placental blood vessels shut. This is the most common cause of PPH (70%) and caused by:

- Abnormalities of uterine contraction
- Overdistension of uterus polyhydramnios, multiple gestation, fetal macrosomia,
- Intra-amniotic infection, fever, prolonged rupture of membranes,
- Functional/anatomic distortion of uterus, rapid labor, prolonged labor, fibroids, placenta praevia, uterine anomalies,
- Some medication (uterine relaxants)
- Bladder distension may prevent uterine contraction.

Trauma - Uterine trauma, 19% of PPH caused by:

- Genital tract injury
- Lacerations of the cervix, vagina, or perineum (precipitous delivery, operative delivery)
- Uterine rupture (previous uterine surgery)
- Uterine inversion (high parity with excessive cord traction).

Tissue - Retained placenta, 10% of PPH is usually caused by conditions that affect uterus's ability to contract after delivery:

- Retained products of conception
- Retained cotyledon or succenturiate lobe
- Retained blood clots.

Thrombin - Coagulopathy, 1% of PPH caused by

- Abnormalities of coagulation: disseminated intravascular coagulation (DIC), hemophilia, idiopathic thrombocytopenic purpura Bruising, HELLP syndrome (hemolysis, elevated liver enzymes, lower platelets)
- Gestational hypertensive disorder of pregnancy with adverse conditions (coagulopathy in utero fetal demise)
- Severe infection (fever, neutrophilia/neutropenia)
- Abruption antepartum hemorrhage
- Amniotic fluid embolus (AFE) sudden collapse
- History of thromboembolic disease.

IV. CLASSIFICATION

Primary postpartum hemorrhage is bleeding that occurs in the first 24 hours after childbirth.

Secondary postpartum hemorrhage is bleeding that occurs 24 hours to 12 weeks after childbirth.

The light bleeding continuously or immediate heavy bleeding is an emergency that requires prompt and strong intervention.

V. DIAGNOSIS

i. Clinical diagnosis

Table 1: Blood Loss- Clinical Features (Safe motherhood 2020 and ICOE)

	Compensated	Mild	Moderate	Severe
Blood loss	500-1000 ml 10 – 15%	1000-1500ml 15-25%	1500-2000ml 25-35%	2000-3000ml 35-45%
Changes of blood pressure	no change (80-90 mmHg)	slightly reduce (70-80mmHg)	drop in BP (50-70 mmHg)	collapse
Clinical features	palpitations, dizziness, tachycardia	weakness, sweating, tachycardia	hustle, pale, oliguria	collapse, Kussmaul respiration, anuria

Table 2: Diagnosis of abnormal vaginal bleeding after vaginal delivery

Diagnosis	Common signs and symptoms	Other possible signs and symptoms
Uterine atony:	• Primary PPH • Uterus is soft, no contraction	• Shock
Uterine trauma: cervical, vaginal, perineal tears (hematoma).	• Primary PPH	• Completed delivery of placenta • Uterus well retracted
Retained placenta	• Placenta did not detach within 30 minutes after delivery	• Primary PPH • Non retracted uterus
Retained placental fragments	• A portion of maternal surface of the placenta remains in uterus	• Primary PPH • Uterus retracted
Uterine inversion	• Uterus fundus not felt on abdominal palpation • Slight or intense pain	• Uterus tissue is visible through vagina • Primary PPH
Uterine rupture	• Primary PPH internal (inside abdomen) with or without vaginal bleeding • Severe abdominal pain (pain may decrease after rupture of uterus)	• Shock • Increased in pulse • Abdominal pain

ii. Laboratory test: Blood group, full blood count, coagulation screen (prothrombin (PT), Activated partial thromboplastin time (APTT), D-dimer test), liver and renal functions (alanine transaminase (ALT), blood urea nitrogen (BUN), C-reactive protein (CRP), creatinine), electrolytes, procalcitonin, blood culture, urinalysis.
iii. Abdomen-pelvic ultrasound to get a detailed image of uterus and other organs.
iv. Electrocardiogram (EKG)
v. Anatomopathological diagnosis: in case of suspect of trophoblastic tumor.

VI. COMPLICATIONS

Short term (Immediate)

- Hypovolemic shock
- Disseminated intravascular coagulation
- Renal failure
- Respiratory distress syndrome
- Cerebral anoxia
- Maternal death

Long term (Late complication)

- Anemia
- Puerperal sepsis
- Sheehan's Syndrome
- Blood transfusion complication
- Infertility
- Depression

VII. THERAPEUTIC APPROACH

A standardized and timely approach to the management of postpartum hemorrhage, comprising an objective assessment of blood loss and use of a treatment bundle for PPH (E-MOTIVE) supported by an implementation strategy, is recommended for all women having a vaginal birth. The care bundle for first-line treatment of postpartum hemorrhage should include Early initiation of Massage of uterus, administration of an Oxytocic agents and Tranexamic acid, Intravenous fluids, Examination of the genital tract and escalation of care.

The treatment of patients with PPH has two major components: (1) Resuscitation and management of obstetric hemorrhage and, possibly, hypovolemic shock and (2) identification and management of the causes of the hemorrhage.

i. Resuscitation of patients and management of PPH:

a. Shout for help, urgently mobilize all available personnel (multi-disciplinary team approach: midwives, obstetrician, anesthetist, lab-technician)

b. Rapidly assess mother's condition:

- Monitor temperature every 15 minutes,
- Continuous pulse, blood pressure and respirator rate recording (using oximeter, electrocardiogram and automated blood pressure reading if possible).
- Insert urethral (Foley) catheter to monitor urine output.
- Consider transfer to intensive therapy unit once the bleeding is controlled or monitoring at high.
- Clinicians (multi-disciplinary team) should be prepared to use a combination of pharmacological, mechanical, and surgical methods to stop PPH.

c. Resuscitation:

- Measures for minor PPH (blood loss 500-1000ml) without clinical shock:
  - Intravenous access.
  - Immediate venipuncture (20ml) for: blood X-match (4 units minimum), blood group, full blood count, coagulation screen, including fibrinogen, renal and liver function for baseline.
  - Pulse, respiratory rate, and blood pressure recording every 15 minutes.
  - Commence warmed crystalloid infusion (sodium chloride 0.9% or Lactate Ringer's solution).
- Measures for major PPH (blood loss greater than 1000ml and continuing to bleed or clinical shock:
  - A and B – assess airway and breathing
  - C – evaluate circulation.
  - Position the patient on supine and head down (Trendelenburg) position.
  - Keep the patient warm using appropriate available measures.
  - Transfuse blood as soon as possible, if clinical required.
  - Until blood available, **infuse up** to 3.5L of warmed clear fluids, initially 2L of warm isotonic crystalloid.
  - Further **fluid resuscitation** can continue with additional isotonic crystalloid or colloid.

d. Fluid therapy and blood product transfusion:

- **Crystalloid Up** - to 2L isotonic crystalloid (normal saline or Lactate Ringer's solution) ratio (3:1).
- **Colloid Up -** to 1.5L colloid ratio (1:1) until blood arrives.
- Blood if immediate transfusion is indicated, give emergency group O, rhesus D (RHD)-negative, K-negative red cell units. Switch to group-specific red cells as soon as feasible.
- **Fresh frozen plasma (FFP) -** Administration of FFP should be guided by hemostatic testing and whether hemorrhage continuing:
  - If prothrombin time (PT) or activated partial thromboplastin time (APTT) are prolonged and hemorrhage is ongoing, administer 12-15 ml/kg of FFP.
  - If hemorrhage continues after 4 units of red blood cells (RBCs) and hemostatic tests are unavailable, administer 4 units of FFP.

- **Platelet concentrates** - Administer 1 pool of platelets if hemorrhage is ongoing and platelet count less than 75 x 10^9/L.
- **Cryoprecipitate** - Administer 2 pools of cryoprecipitate if hemorrhage is ongoing and fibrinogen less than 2g/L.

ii. Identification and management of causes of the bleeding:

a. When uterine atony is perceived to be the cause of bleeding, then a sequence of mechanical and pharmacological measures should be instituted in turn until the bleeding stop:

- Palpate the uterine fundus and perform uterine massage.
- Ensure that the bladder is empty (Foley catheter, leave in place)
- Give Oxytocin 10 UI IM or 20 UI infuse in sodium chloride 0,9% or Lactate Ringer's solution at 250ml/hour
- Give Ergometrine/methylergometrine 200 micrograms IM (in context where hypertensive disorders can be safely excluded prior to its use).
- Give Carboprost 0.25mg IM repeated at interval of not less than 15 minutes (for a maximum of eight doses = 2mg)
- Give Misoprostol 200 to 1000 micrograms (orally or vaginally or rectally use)
- Give Prostaglandin E2 (PGE2)
- Tranexamic acid (TXA) should be used in all cases of PPH, regardless of whether the bleeding is due to genital tract trauma or other causes within 3 hours of birth. TXA should be administered at a fix dose of 1g in 10ml (100mg/ml) IV at 1 ml per minute, with a second dose of 1g IV if bleeding continues after 30 minutes or if bleeding restarts within 24 hours of completing the first dose.
- Check the emptiness of the uterus (retained placenta)
- Check uterine tonus: bimanual examination. Rub up contraction. Expel blood clots.
- Check for perineal and cervical tears
- Check blood for eventual coagulopathy
- Perform Bimanual Uterine Compression
- Perform External Aortic compression.
- Perform Uterine balloon tamponade (UBT)
- Apply non-pneumatic anti-shock garment (NASG) (refer to operation theatre or to CEmONC facility for surgery and blood transfusion).

If mechanical and pharmacological measures fail to control the bleeding, surgical interventions should be initiated sooner rather than later:

- Examination under anesthesia
- Apply Brace sutures
- Bilateral ligation of uterine arteries
- Bilateral ligation of internal iliac arteries
- Perform Hysterectomy (sub-total or total hysterectomy).

b. For uterine trauma: Examine and determine the degree of tears. If it is a third degree of tear (until rectum or anus), **repair the tears**. For other tears: apply pressure over the tears with sterile pad or gauze and put legs together. Check after 5 minutes, if bleeding persists, repair the tears.

c. Retained placenta:
   - If the placenta did not detach (after 30 minutes) and there is no bleeding, must:
     - Empty the urine bladder
     - Gently perform **controlled cord traction** again
     - If the placenta is still not delivered and no bleeding, it is suspected a "placenta accreta".
   - If there is no bleeding and the placenta did not detach within another 30 minutes (1hour in total), it might be a sign of placenta accreta and must refer woman to operation theatre for attempting manual removal of placenta or surgical intervention.

Retained placental fragments (RPF):
   - If possible, explore for placental fragments inside the uterus. Manual exploration of the uterus is a technique similar to the one's use for the manual removal of placenta.
   - If it is not possible to remove placental fragment by hand, use ovum forceps or blunt wide curette.

d. Uterine inversion:
   - Reposition the uterus as soon as possible,
   - Perform Hysterectomy

e. Uterine rupture:
   - Perform Hysterectomy

iii. Therapeutic approach Secondary PPH

In women presenting with secondary PPH, an assessment of vaginal microbiology should be performed (high vaginal and endocervical swabs) and appropriate use of antimicrobial therapy should be initiated when endometritis is suspected.

A pelvic ultrasound may help to exclude the presence of retained products of conception, although the diagnosis of retained products is unreliable. Surgical evacuation of retained placental tissue should be undertaken or supervised by an experienced clinician.

iv. Monitoring/follow up

Major obstetric hemorrhage can be traumatic for the woman, her family and birth attendants; therefore, debriefing is recommended at the earliest opportunity by a senior member of the team who was involved at the time of events. Arrangement for proper follow up and investigations such as screening for anemia, coagulopathies and other long-term complications should be offered if appropriated.

VIII. PREVENTION OF POSTPARTUM HAEMORRHAGE

Minimizing the risk of PPH starts during the antenatal period, by the identification and treatment of anemia, identify any women with increased risk of PPH.

The use of **Oxytocin 10 IU IM/IV is recommended during the 3rd stage of labor for all births for the prevention of PPH for vaginal delivery and cesarean section**. **If oxytocin is unavailable or the quality cannot be guaranteed**, the other uterotonics (carbetocin, misoprostol, and ergometrine) can be used.

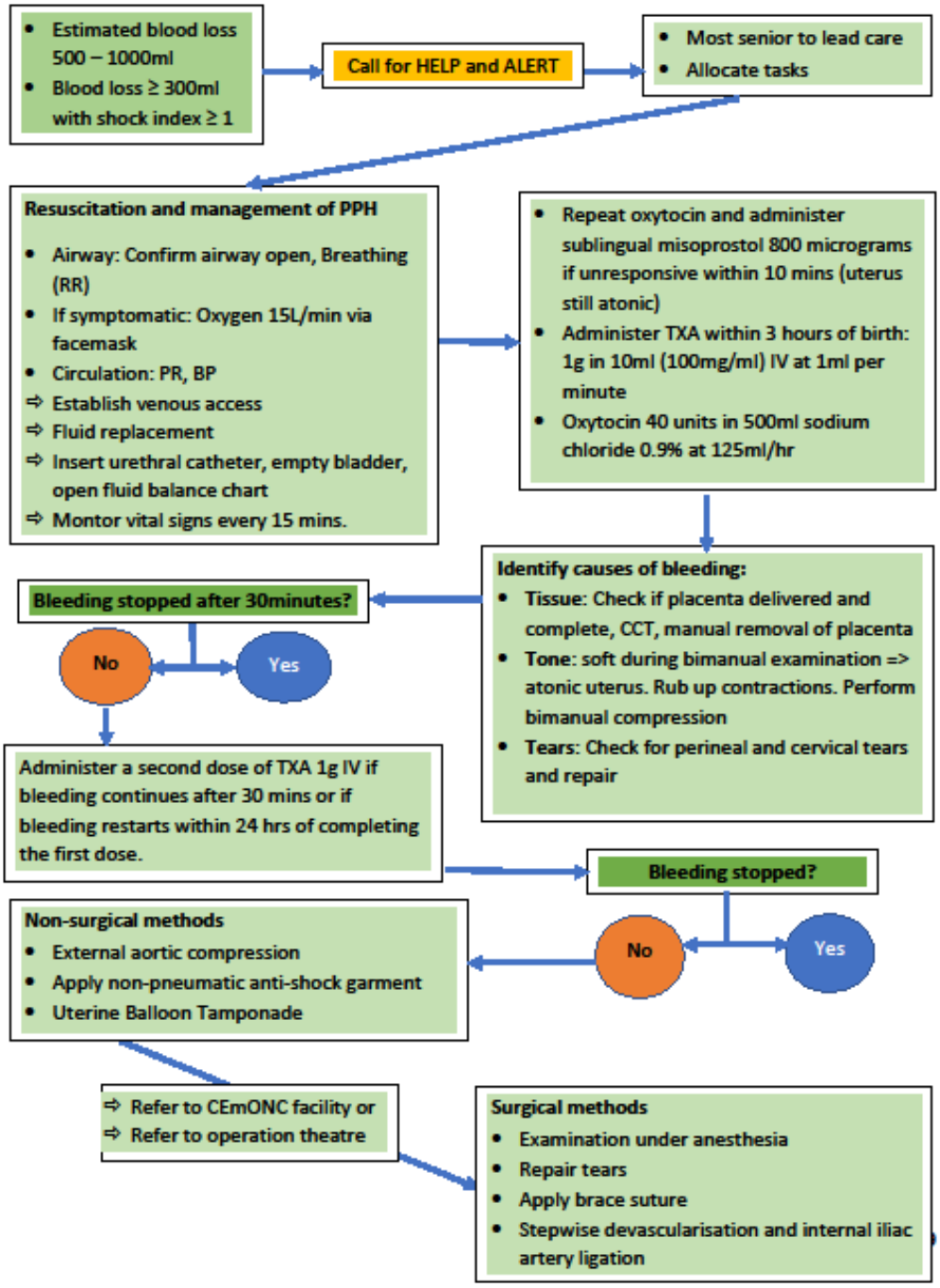
- The use of carbetocin 100 micrograms IM/IV is only recommended for the prevention of PPH for all births in contexts where its cost is comparable to other effective uterotonics.
- Ergometrine could be used in the absence of oxytocin in contexts where hypertensive disorders can be safely be excluded prior to its use.
- Oral misoprostol (400-600ug) can be used for the prevention of PPH in the absence of oxytocin.
- Late cord clamping (performed after 1 to 3 minutes after birth) is recommended for all births while initiating simultaneous essential newborn care.
- Sustained uterine massage is not recommended as an intervention to prevent PPH in women who have received prophylactic oxytocin
- Postpartum abdominal uterine tonus assessment for early identification of uterine atony is recommended for all women.
- Controlled cord traction (CCT) is the recommended method for removal of the placenta in cesarean section.

Characteristics of potential uterotonics

Characteristics	Brief description	Pharmaco-kinetics	Half-life:
Oxytocin	Synthetic cyclic peptide form of the naturally occurring posterior pituitary hormone.	IV: almost immediate action with peak concentration after 30 minutes. IM: slower onset of action, taking 3-7 minutes, but produces a longer-lasting clinical effect of up to 1 hour.	1-6 minutes
Carbetocin	Long-acting synthetic analogue of oxytocin with agonist properties.	IV: sustained uterine contractions within 2 minutes, lasting for about 6 minutes and followed by rhythmic contractions for 60 minutes IM: sustained uterine contractions lasting for about 11 minutes and rhythmic contractions for 120 minutes	40 minutes

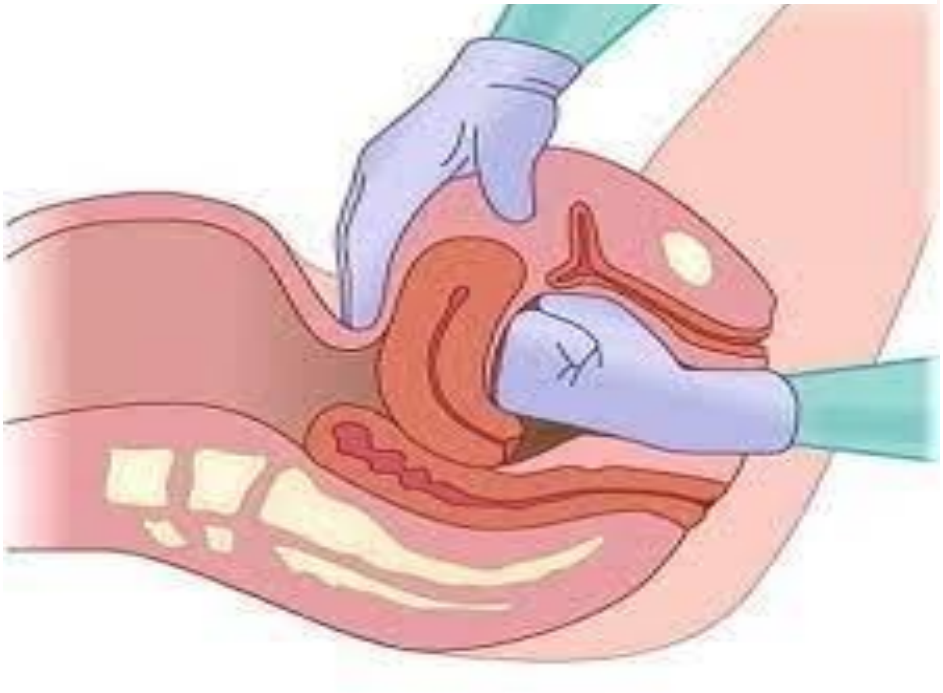
Misoprostol	Synthetic analogue of natural prostaglandin E1	Absorb 9-15 minutes after sublingual, oral, vaginal, or rectal use. Oral and sublingual routes have the advantage of rapid onset of action, while the vaginal and rectal routes result in prolonged activity and greater bioavailability	20-40 minutes
Injectable prostaglandins	Injectable prostaglandins (systemic) trialled for PPH prevention include prostaglandin F2 analogues (carboprost), prostaglandin E2 (dinoprostone) and prostaglandin E2 analogues (sulprostone)	IM: 15-60 minutes to peak plasma concentration	8 minutes
Ergometrine	Ergometrine and methyl ergometrine are ergotalkaloids that increase uterine muscle tone by causing sustained uterine contractions	IM: onset of action within 2-3 minutes, lasting for about 3 hours. IV: onset of action within 1 minute, lasting 45 minutes (although rhythmic contractions may persist for up to 3 hours.	30-120 minutes

IX. ALGORITHM

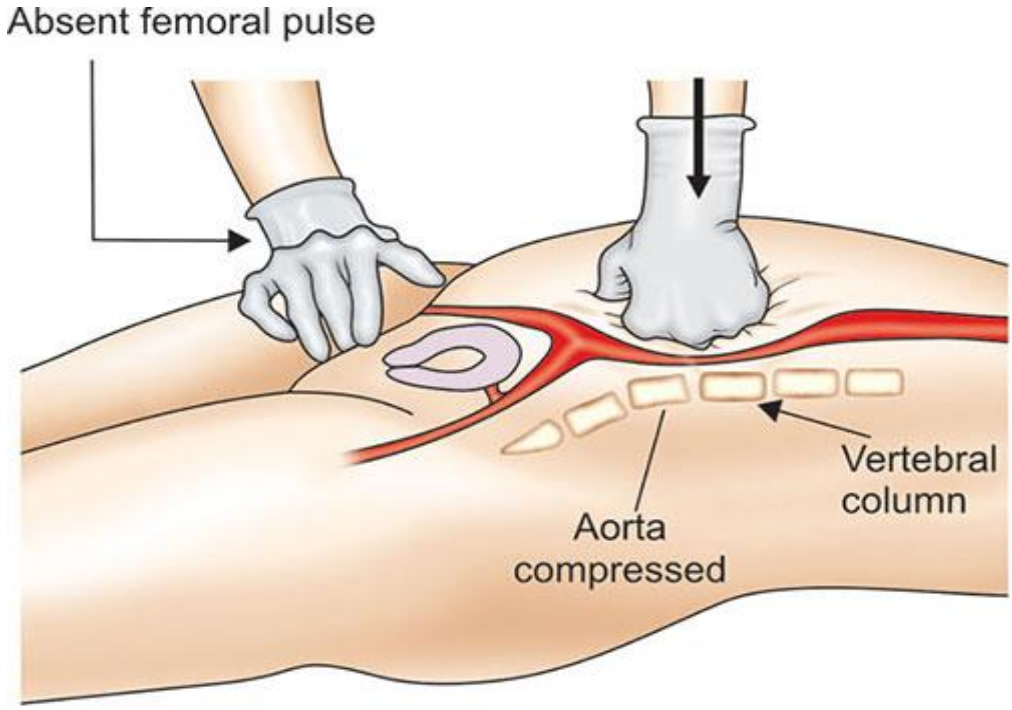


X. ANNEX

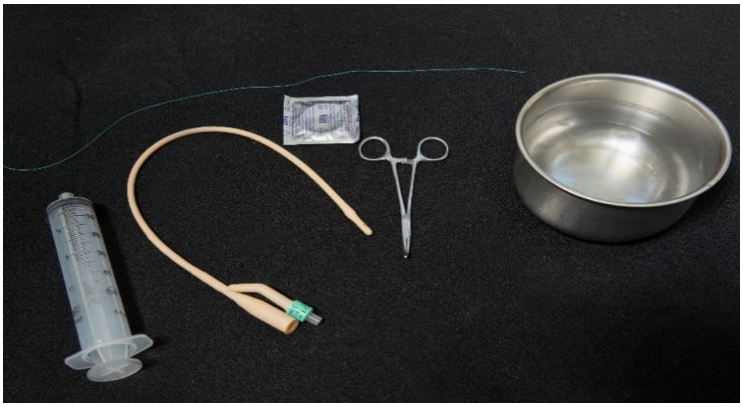
Annex 1: Bimanual compression

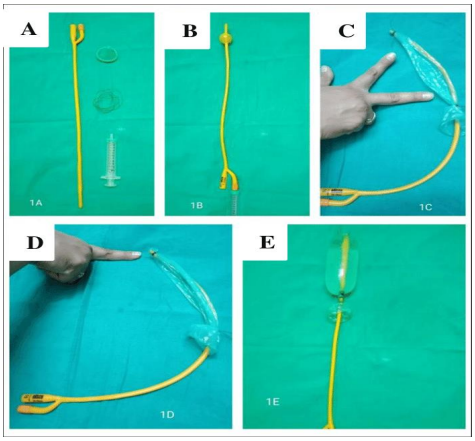


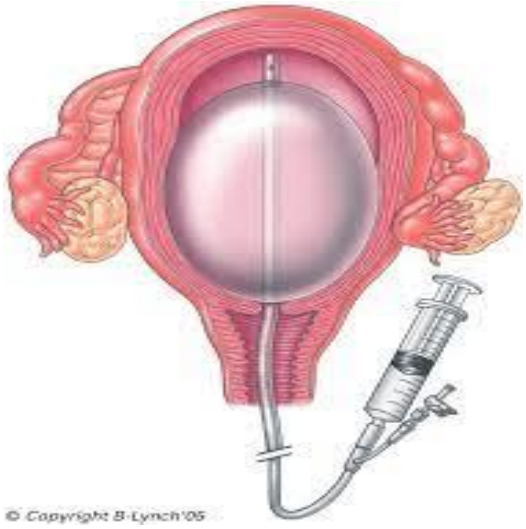
Annex 2: Aortic Compression



Annex 3: Uterine Balloon Tamponade (UBT)

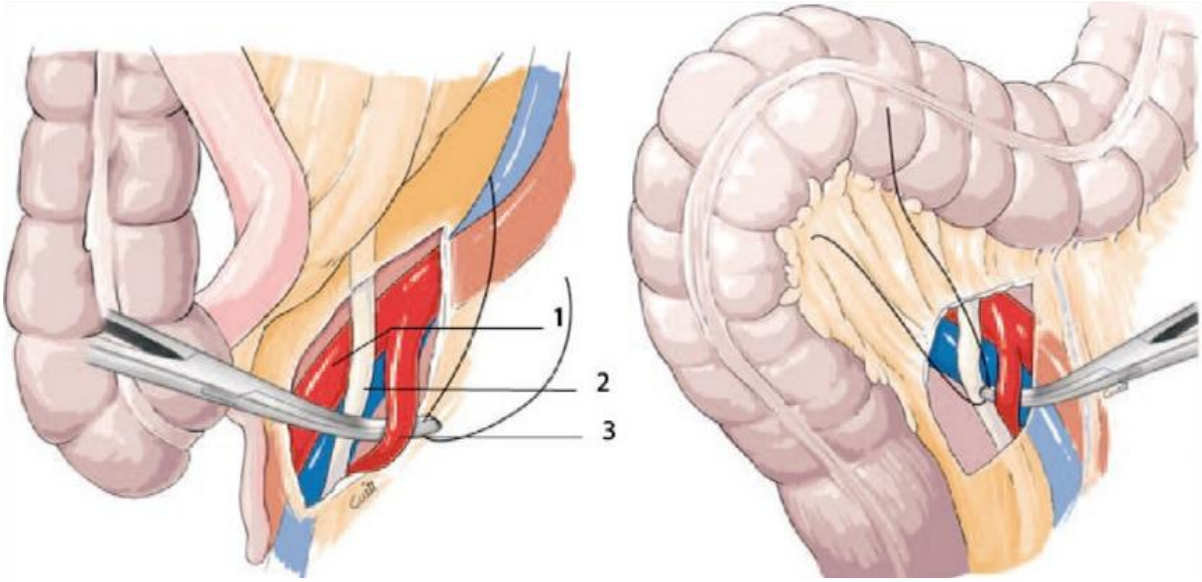


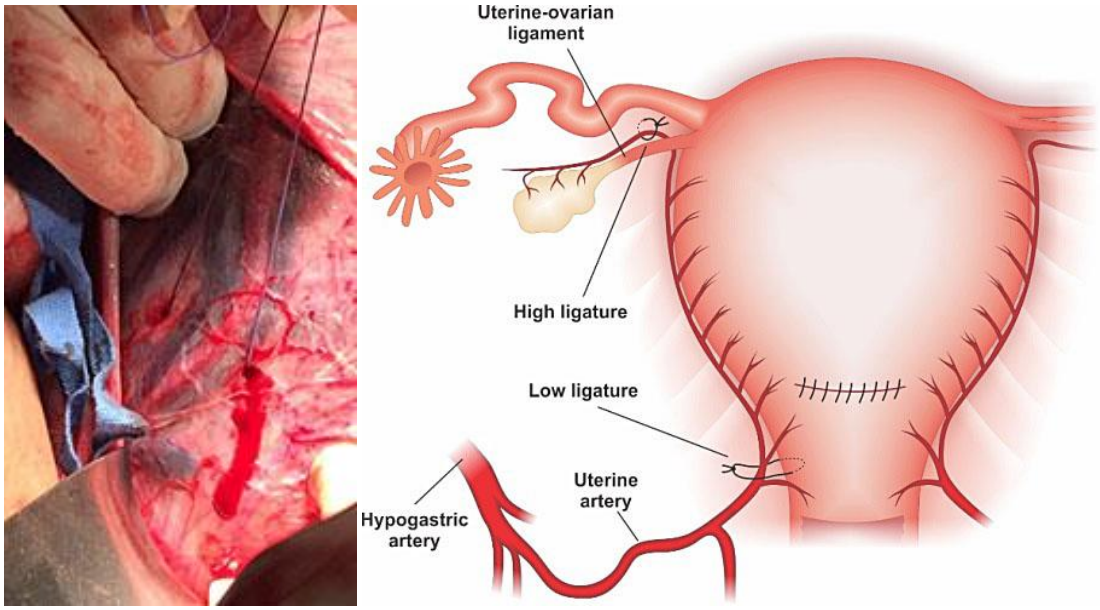




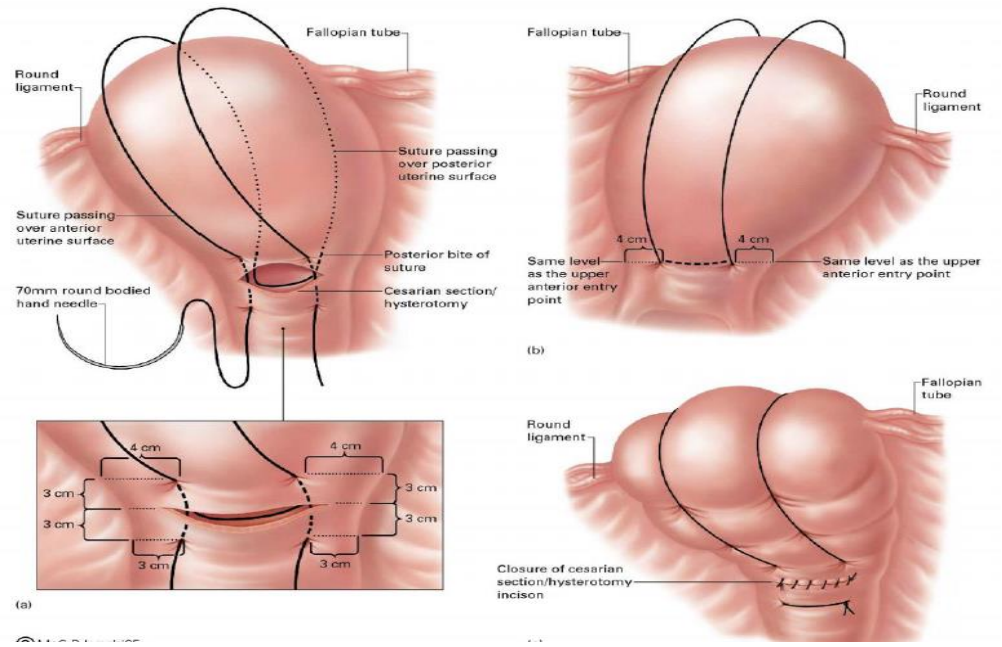
Annex 4: Non-pneumatic anti-shock garment (NASG)

Annex 5: Artery ligations

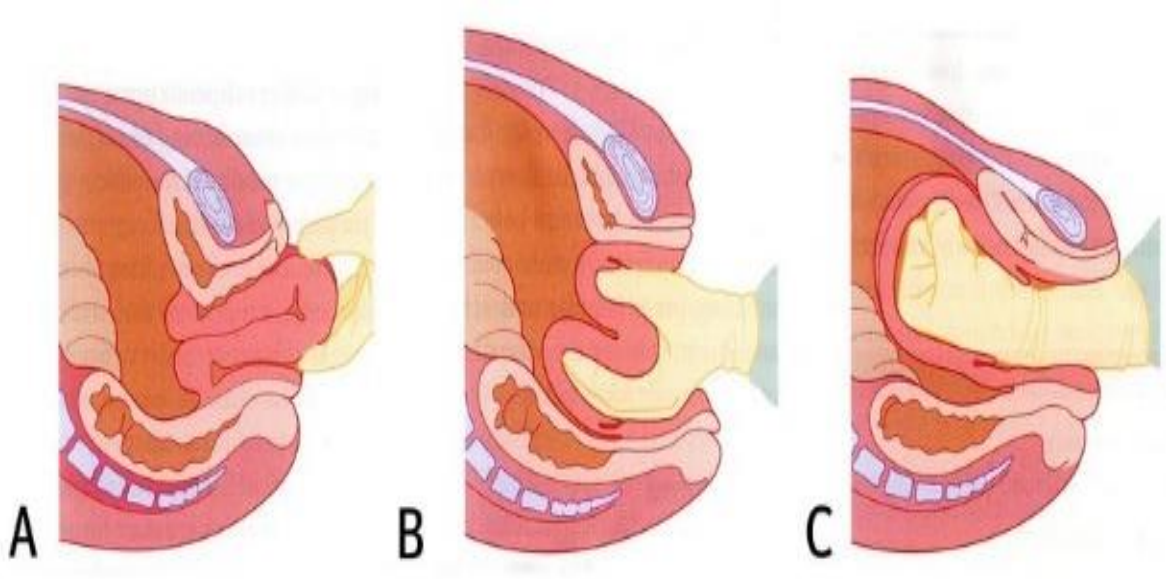




Annex 6: B-Lynch surgical technique for control of massive postpartum hemorrhage



Annex 7: Repositioning uterus



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PRE-ECLAMPSIA AND ECLAMPSIA

Prof. Koum Kanal, Dr. Ros Saphath, Dr. Hang Sovanara, Prof. Tung Rathavy,
Prof. Kim Rattana, Prof. Keth Lysotha

I. DEFINITION

PRE-ECLAMPSIA: is defined as a multisystem disorder that only occurs during pregnancy after 20 weeks gestation and up to 1month post-partum, characterized by hypertension and proteinuria.

ECLAMPSIA: is one of complication of preeclampsia with convulsion or unconscious.

II. ETIOLOGY/RISK FACTORS

i. Etiology: etiology of preeclampsia remains uncertain. It is likely that maternal and placenta factors are involved and there is overlap in the pathogenesis.

ii. Risk Factors: factors that may put pregnant woman at risk for pre-eclampsia are:

- Being pregnant for the first time (primigravida)
- Preeclampsia in the past pregnancy
- Extremes of maternal age (< 18 years old, or > 40 years old)
- Renal disease
- Diabetes
- Obesity
- Multiple pregnancies (twin, triplets or more)

III. CLASSIFICATION

i. Pre-eclampsia (PE):

- New onset high BP at 2 readings at 15 minutes apart:
- Systolic BP (SBP) ≥140mmHg or Diastolic BP (DBP) ≥90mmHg **PLUS**
- Proteinuria 300mg of protein in a 24hrs urine collection or ++ on dipstick

ii. Severe Pre-eclampsia (SPE):

- New onset high SBP ≥ 160mmHg or DBP≥110mmHg with proteinuria +++ (All 2 majeure signs) **OR**
- PE plus any one of the following:

  Danger signs reported by the woman:
  - Severe headache unrelieved by analgesics
  - Visual changes (blurred vision)
  - Right upper quadrant pain (epigastric pain)
  - Difficulty breathing **OR**

  Dangers signs that can be measured
  - Acute Pulmonary oedema
  - Oliguria <400ml of urine output in a 24hours

iii. Eclampsia: PE with convulsion or unconscious

IV. DIAGNOSIS

i. Clinical Diagnosis:

A diagnosis of pre-eclampsia can be made when hypertension arises after 20 weeks gestation and is accompanied by one or more of the following signs of organ involvement:

- Proteinuria: spot urine protein/creatinine ratio (PCR) > 30 mg/mmol (0.3mg/mg) or > 300mg/day or at least 1g/L (2+) on dipstick testing.

OR in the absence of proteinuria:

- Other maternal organs dysfunction:
  - Renal insufficiency: serum or plasma creatinine > 90 µmol/L
  - Hematological involvement: Thrombocytopenia (<100,000/µL), hemolysis or disseminated intravascular coagulation (DIC)
  - Liver involvement: Raised serum transaminases, severe epigastric and/or right upper quadrant pain
  - Neurological involvement: eclampsia, hyperreflexia with sustained clonus, persistent new headache, persistent visual disturbances (photopsia, scotomata, cortical blindness, posterior reversible encephalopathy syndrome, retinal vasospasm), stroke
  - Pulmonary oedema.
- Uteroplacental dysfunction (fetal growth restriction).

ii. Obstetric Examination and Assessment of Cervix:

- Confirm gestational age
- Confirm cervix score.

iii. Imagery:

- Obstetric ultrasound:
  - Baby weigh, amniotic fluid, placenta (Grannum classification)
  - Uterine artery Doppler
  - Umbilical Artery Doppler (UA) (Pulsatility Index)
  - Middle Cerebral Arteries Doppler (MCA) (Resistance Index)
- Chest X-ray: in case of acute pulmonary oedema
- Head MRI scan: in case of eclampsia

	Signs/symptoms
Pre-eclampsia	Onset of a new episode of high blood pressure (BP) on 2 readings at 15 minutes apart: • Systolic Blood Pressure (SBP) ≥ 140mmHg or • Diastolic Blood pressure (DBP) ≥ 90mmHg Proteinuria: 0.3g/24 hours or 2+ on dipstick.
Severe pre-eclampsia	Onset of high blood pressure • SBP ≥ 160mmHg or • DBP ≥ 110mmHg Proteinuria 3+ on 2 random urine samples collected at least 4 hours apart or PCR ≥ 30 mg/mmol or 0.3

	Or Pre-eclampsia (PE) plus any one of the following: • Danger signs reported by the woman: — Severe headache unrelieved by analgesics — Visual changes (blurred vision) — Right upper quadrant pain (epigastric pain) — Difficulty breathing Or • Danger signs that can be measured: — Acute Pulmonary oedema — Signs of clonus — liver tenderness Platelet count falling to below 100 x 10^9/L Alanine amino transferase rising to above 50 IU/L Urea/uric acid (serum creatinine ≥ 1.1 mg/dl) Oliguria < 400ml of urine output in a 24hours
Eclampsia	Pre-eclampsia associated with convulsion or unconscious

V. EVOLUTION/COMPLICATIONS

i. Evolution

The hypertensive disorder of pregnancy, in particularly pre-eclampsia and eclampsia, are significant contributors to the global burden of maternal and perinatal mortality.

ii. Complications

Pre-eclampsia/eclampsia remains in one of the top four causes of maternal mortality (and morbidity) and its adverse perinatal outcomes include stillbirth, neonatal death, oligohydramnios, bronchopulmonary dysplasia, and fetal growth restriction (FGR).

The adverse conditions that define pre-eclampsia and severe pre-eclampsia:

Organ system affected	**Adverse conditionals (that increase the risk of severe complications**	**Severe complications (that warrant delivery)**
Central Nervous System	— Headache/Visual symptom	— Eclampsia — Posterior reversible leukoencephalopathy syndrome (PRESS) — Cortical blindness or retinal detachment — Glasgow coma scale < 13 — Stroke, transient ischemic attack (TIA), or reversible neurological deficit < 48hours
Cardio-respiratory	— Chest pain/dyspnea — Oxygen saturation < 97%	— Uncontrolled severe hypertension (over a period of 12hours despite use of three hypertensive agents)

		— Oxygen saturation < 90%, need for ≥ 50% oxygen for > 1hour, intubation (other than for Caesarean section), pulmonary oedema — Positive inotropic support — Myocardial ischemia or infarction
Haemato-logical	— Elevated WBC count, — Elevated international normalized ratio (INR) or activated partial thromboplastin time (aPTT) — Low platelet count	— Platelet count < 50 x 109/L — Transfusion of any product
Renal	— Elevated serum creatinine — Elevated serum uric acid	— Acute kidney injury (creatinine >150μM with no prior renal disease) — New indication for dialysis
Hepatic	— Nausea or vomiting — Right upper quadrant or epigastric pain — Elevated serum AST, ALT, LDH, or bilirubin — Low plasma albumin	— Hepatic dysfunction (INR >2 in absence of disseminated intravascular coagulation (DIC) or warfarin/coumarin) — Hepatic hematoma or rupture
Feto-placental	— Non-reassuring fetal heart rate (FHR) — Intrauterine growth restriction (IUGR) — Oligohydramnios — Absent or reversed end-diastolic flow by Doppler velocimetry	— Abruption with evidence of maternal or fetal compromise — Reverse ductus venosus A wave — Stillbirth
HELLP syndrome	— Hemolysis — Elevated liver enzymes — Low platelets	— Microangiopathic hemolytic anemia with fragment schistocytes on blood film — Elevated transaminases (greater than twice the normal range) — Platelet count of less than 100 x 10^9/L

VI. MANAGEMENT

i. General Management

Resuscitation and Stabilization:

If the woman is unconscious or convulsing:

- Shout for help and mobilize all available personnel, including anesthetist. The consultant obstetrician should be informed, so that they can be involved at an early stage in management. This should be document in the notes.
- Perform a rapid evaluation of the general condition of the woman including vital signs
  - If the woman is not breathing, assist ventilation using an Ambu bag and mask or give oxygen at 4-6L per minute by endotracheal tube.
  - If she is breathing, give oxygen at 4-6L per minute by mask or nasal cannula.

If the woman is unconscious:

- Check the airway
- Position her on the left side
- Check for stiff neck
- Protect her from collision injury.

If the woman is convulsing:

- Position her on her left side or reduce the risk of aspiration of secretion, vomit,
- Clean and insert tongue depressor to open the airway or prevent tongue biting
- Protect her from injury
- Provide constant supervision
- If eclampsia is diagnosed, give MgSO4 as indicated below.
- If the cause of convulsion has not been determined, manage as in case of eclampsia, and continue to investigate other causes.

ii. Management of Pre-Eclampsia

A large bore intravenous cannula for infusion drugs or fluid should be inserted, but not necessarily used until either an indication presents, or a decision is made to deliver. If intravenous fluid is given, it should ideally be administered by controlled volumetric pump.

Basic investigations

Blood should be sent for:

- urea. creatinine, urate, and serum electrolytes
- Liver function tests
- Full blood count
- Clotting screen
- Group and save serum

Monitoring

- Blood pressure and pulse should be measured every 15 minutes until stabilized and then half hourly.

- Urethral catheter should be inserted, and urine output measured hourly whenever intravenous fluids are given.
- Oxygen saturation should be measured continuously. If saturation falls below 95% then medical review is essential.
- Respiratory rate should be measured hourly.
- Temperature should be measured four-hourly.
- Fetal well-being should be assessed carefully.

Counselling

- Counsel the woman and her family about danger signs of severe pre-eclampsia and eclampsia
- Encourage woman to eat normal diet

Do not give anti-hypertensive, anticonvulsant, sedatives, tranquilizers, or diuretics.

iii. Management of Severe Pre-Eclampsia

Start intravenous infusion of Ringer's lactate. Careful fluid balance is aimed at avoiding fluid overload.

a. Administer Magnesium Sulphate (MgSO4)

Give magnesium sulphate (MgSO4) to prevent seizures. MgSO4 is given as a loading dose followed by a continuous infusion for 24 hours or until 24 hours after delivery.

- The loading dose:
  - MgSO4 50% 5g (10ml) dilute with 20ml of NSS - IV slowly over 15-20 minutes (either through volumetric pump or a scalp vein 25G needle into IV infusion line).
  - MgSO4 50% 5g – IM deeply inject to the right buttock of the woman, then another 5g – IM deeply inject to the left buttock.
  - If the woman has recurrent fit after a full loading dose has been given, give another 2g of MgSO4 (4ml and dilute with 6ml of NSS) – IV slowly.
- Continue treatment: give MgSO4 50% 5g – IM every 5 hours until 24 hours after delivery or after last convulsion.
- Important observations before administering next dose:
  - Continuous monitor vital signs,
  - Deep tendon (knee) reflexes (every 4 hours)
  - Urine output hourly.
- Cessation/reduction of the MgSO4 infusion should be considered if:
  - The biceps (knee) reflex is not present
  - the respiratory rate is < 12 per minute
  - Amount of urine is less than 100ml in 4 hours.
- When the respiratory rate is less than 10 per minute, MUST STOP MgSO4, give 1g of Calcium Gluconate 10% (antidote of MgSO4) slowly through IV (for 10 minutes) and assist ventilation with Ambu bag and mask.

b. Treat hypertension

If DBP remains above 100mmHg, give antihypertensive drug after giving MgSO4.

Hydralazine (IV):

Initial dose: 10mg (1ml) of hydralazine dilute with 9ml NSS – IV slowly (3-4 minutes). If after 30 minutes, DBP remains > 90mmHg, repeat the dose until DBP decrease to 90mmHg (to maximum of 20mg)
Maintenance dose: Hydralazine 20mg dilute in NSS 500ml infusion for 6 hours.
Hydralazine: 25mg (PO) (1tablet) 3 times per day.
Alpha methyldopa: 250mg (PO) every 6 to 9 hours.
Nicardipine:
Initial dose: if SBP > 160mmHg, give bolus injection of 0.5 – 1mg, then infusion of 4-7mg for 30 minutes (using pump).
Maintenance dose: 1-6mg per hour (using pump)
(Note: maintain SBP = 140mmHg and DBP = 90mmHg)
Labetalol:
Initial dose: 20mg IV bolus over 2 minutes.
Repeat dose: 40 - 80mg IV every 10 minutes to maximum of 300mg if required
(Note: Labetalol is contraindicated in mother with asthma and heart block).
Precisely monitor (hourly) fluid input-output.

c. Delivery

The delivery should be well planned as soon as feasible (within 24 hours of onset of symptom) using a multidisciplinary approach. If the mother is unstable then delivery is inappropriate and increase risk. Once mother is stabilized, and in the absence of convulsions, then a decision should be made. Continued close monitoring of mother and baby is needed. The mode of delivery based on maternal and fetal condition/wellbeing and should be discuss with the team (induction of labor, vaginal delivery or Caesarean section). For pregnancy less than 34 weeks, steroids should be given 24 hours prior to delivery.

Corticosteroids:

Give Dexamethasone: 12 mg - IM for 2 doses with 12 hours interval or
Betamethasone: 12mg - IM for 2 doses with 24 hours interval.

iv. Management of Eclampsia

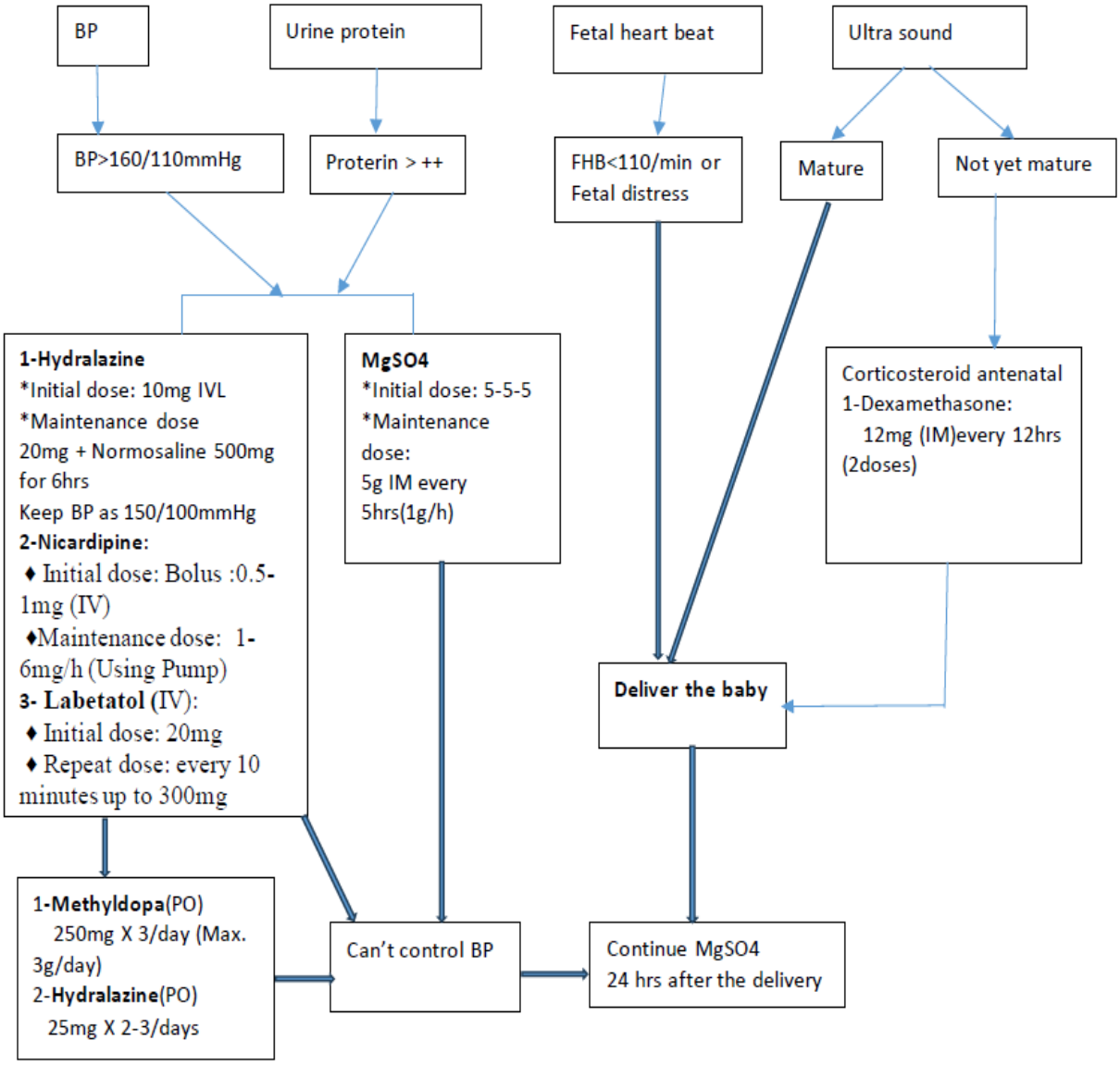
- All above,
- Shout for help, call appropriate personnel
- Resuscitation, remember ABC
- Give the loading dose of MgSO4
- Start an infusion of MgSO4
- Give antihypertensive drugs
- Once stabilized the woman should be delivered within 12 hours of onset of convulsion

VII. PREVENTION OF PRE-ECLAMPSIA FOR THE NEXT PREGNANCY

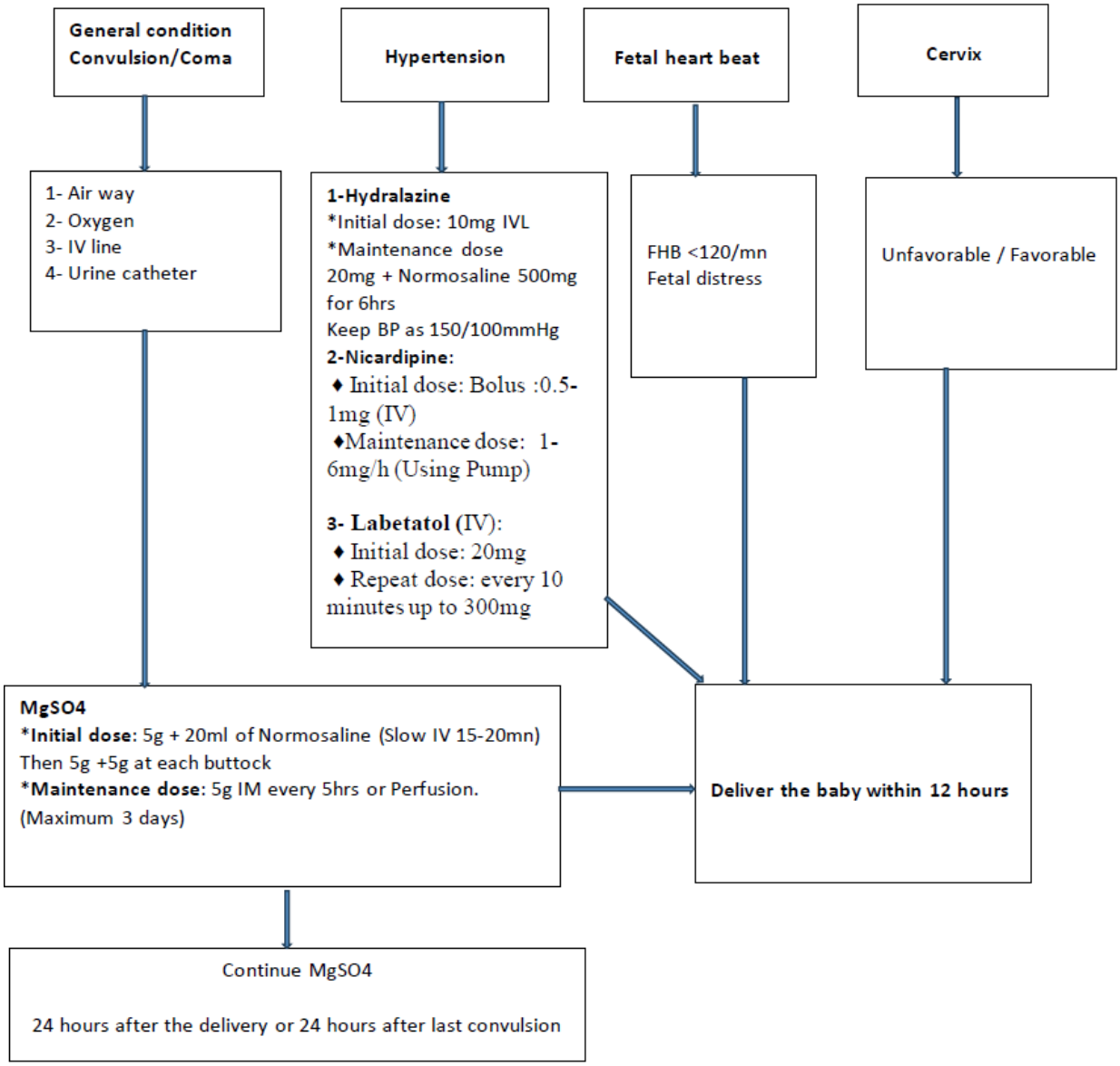
- Calcium supplement (of at least 1g/day orally) is recommended for women with low dietary intake of calcium.
- Calcium supplement of 1.5 – 2g/day is recommended for women with high risk of pre-eclampsia.
- Low dose Aspirin (81mg/day) should be administered at bedtime and initiated after diagnosis of pregnancy, but before 20 weeks (from 12 weeks if possible) of gestation and continued until delivery for women with high risk of pre-eclampsia.

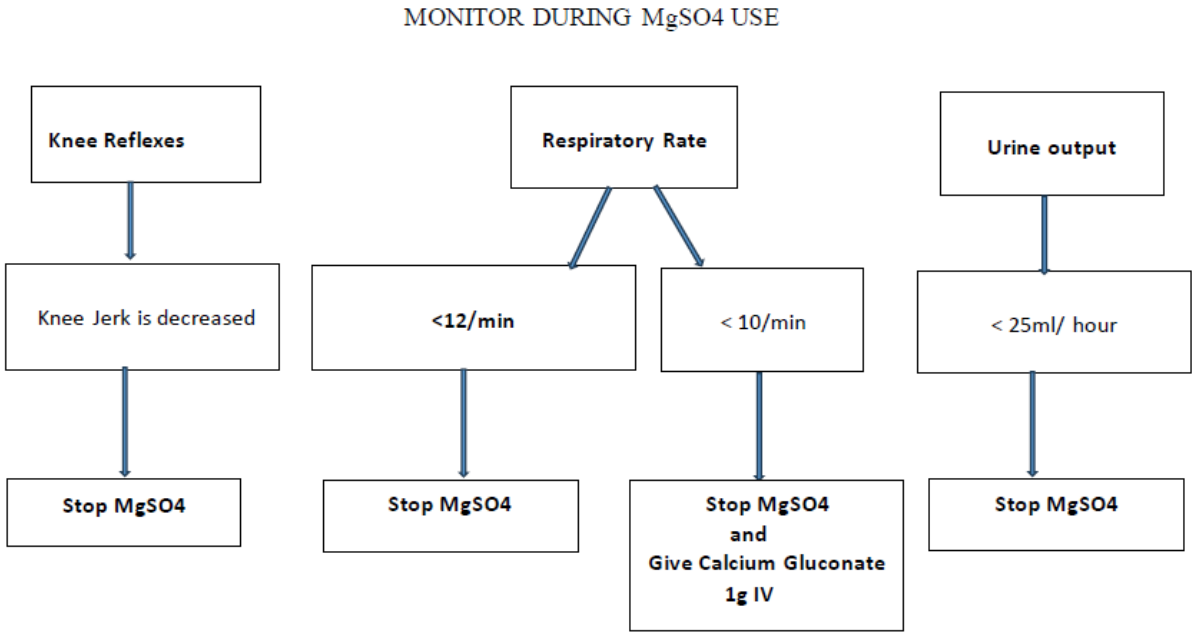
VIII. ALGORITHM

MANAGEMENT OF SEVERE PRE-ECLAMPSIA



MANAGEMENT OF ECLAMPSIA





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PRETERM LABOR AND BIRTH

Prof. Keth Lysotha, Dr. Hang Sovanara, Dr. Ros Saphath, Prof. Tung Rathavy,
Prof. Pech Sothy, Prof. Koum Kanal

I. DEFINITION

Preterm labor is defined as labor occurring between 26 0/7 weeks gestation and 36 6/7 weeks.

II. INCIDENCE

An estimated 13.4 million babies were born preterm in 2020 (before 37 completed weeks of gestation). Across countries, the rate of preterm birth ranges from 4–16% of babies born in 2020. Preterm birth complications are the leading cause of death among children under 5 years of age, responsible for approximately 900 000 deaths in 2019. Three-quarters of these deaths could be prevented with current, cost-effective interventions.

III. ETIOLOGY/RISK FACTORS

Preterm labor occurs for a variety of reasons. Most preterm labors happen spontaneously, but some are due to medical reasons. The causes include:

- Past history of preterm birth (could also be a genetic influence)
- Multiple birth (twins, triplets or higher order)
- Maternal age: younger than 20 years old or older than 40 years old
- Women who smoke during pregnancy (or substance use)
- High or low body mass index (BMI)
- Moderate to severe anemia
- Short interpregnancy interval less than 12 months
- Physical or psychological stress
- Infections: asymptomatic bacteriuria, periodontal disease, genital tract infection (bacterial vaginosis), malaria
- Polyhydramnios/oligohydramnios
- Preterm prelabor rupture of the membranes (PPROM)
- Cervical polyp, congenital uterine anomalies, uterine leiomyoma
- Abdominal surgery during pregnancy
- Cervical conization, LEEP, prior dilatation and curettage
- Vaginal bleeding
- Assisted reproduction
- Acute medical conditions (e.g preeclampsia, antepartum hemorrhage)

IV. CLASSIFICATION OF PRETERM BIRTH

There are sub-categories of preterm labor, based on gestational age:

- Extremely preterm (less than 28 0/7 week)
- Very preterm (28-31 6/7 weeks)
- Late preterm (32-36 6/7 weeks)

V. DIAGNOSTIC PROCEDURE

Clinical assessment of preterm labor

Identifying and treating women with symptoms of preterm labor, provides the opportunity to utilize interventions to minimize the impact of preterm birth. Appropriate clinical diagnosis of preterm labor may reduce unnecessary interventions and hospitalization.

Aspect	Consideration
Review history	- Medical - Surgical - Obstetric - Psychological and lifestyle - Risk factors associated with preterm birth
Signs and symptoms	- Cervical ripening (shortening of the cervix), followed by decidual membranes activation and then contractions, characterized by: o cervical effacement/dilatation o pelvic pressure o lower abdominal cramping o lower back pain o vaginal loss (mucous, blood or fluid) o regular uterine activity
Physical examination	- Vital signs - Abdominal palpation to assess uterine tone, contractions, fetal size and presentation - Sterile speculum examination to: o confirm or exclude rupture of the membranes o assess liquor (e.g clear, meconium stained, bloody) o visualize cervix and membranes - Trans-vaginal ultrasound: A short cervix < 25 mm before 34 weeks of gestation is predictive of an increased risk for preterm birth in all population (or if indicated, perform transvaginal cervical length measurement) - Collect vaginal swab for microscopy culture and sensitivity to test for bacterial vaginosis - Collect vaginal-perineal swab for group B streptococcus
Fetal surveillance	- Fetal heart rate - Continuous cardiotocography (CTG):

	o consider gestational age (interpret with caution if less than 28 weeks gestation) - Ultrasound examination for fetal growth and wellbeing: o fetal number, presentation, liquor volume and placenta localization
Laboratory investigations	- White blood count (WBC) and C-reactive protein (CPR) - Vaginal swab for bacterial vaginosis - Vaginal-perineal swab for group B streptococcus - STI testing (chlamydia, gonorrhea, syphilis) - Urine cyto-bacteriology testing

VI. DIFFERENTIAL DIAGNOSIS

False preterm birth (irregular contraction of uterus, cervix has not changed).

VII. EVOLUTIONS/COMPLICATIONS

- For mother:
  - At risk for recurrent preterm birth
  - Infection
  - Anxiety
  - Postpartum depression
  - Post traumatic stress disorder (PTSD)
  - Problems bonding with their babies
- For newborn:
  - Preterm birth
  - Low birth weight
  - Infection
  - Membrane hyaline disease
  - Intra-ventricular hemorrhage
  - Cerebral palsy
  - Newborn death

VIII. MANAGEMENT OF PRETERM LABOR

Tocolysis and steroids are the main strategies to manage preterm labor. Management option will depend on:

- Gestational age and individual clinical circumstance.
- Resource (equipment and human) to provide required care.
- If necessary, refer to a service with higher level capability for further advice when access to services is unavailable/limited.

i. Planning care

Admission and develop planning care, which include:

- Admit and observation/investigations
- Consider In-utero transfer (as relevant to service capability)
- Communicate with multidisciplinary team as relevant to the circumstance (neonatology consultation, anesthetic involvement)
- Discuss plan for on-going care with the woman in a manner that supports informed choice.
- Document plan of care in the health record

- Clinical reassessment as required

ii. In utero-transfer

The best way to ensure that preterm newborns benefit from neonatal expertise as soon as they are born is to transfer the mother and baby to an appropriate neonatal facility before birth ("In-utero").

iii. Management of preterm labor

- If labor continues, monitor progress of labor using partograph.
- Prepare for management of preterm birth and anticipate the need for resuscitation
- Administration of antenatal corticosteroids before preterm birth is an important intervention that improves outcomes for preterm babies and may provide:
  - Significant reduction in rates of neonatal death, respiratory distress syndrome and intra-ventricular hemorrhage.
  - Reduction in necrotizing enterocolitis, respiratory support, intensive care admission and systematic infections in the first 48 hours of life.

a. Antenatal corticosteroids

Antenatal corticosteroid therapy is recommended for women with a highly likelihood for a preterm birth from 26 to 34 weeks gestation:

- Either Dexamethasone 12 mg x 2 IM (12h interval) or
- Betamethasone 12 mg x 2 IM (24h interval)
- Maximum dose is 24 mg.

b. Tocolysis/Tocolytics

Give a tocolytic drug to provide a window for administration of antenatal cortico-steroids and/or in utero fetal transfer to an appropriate neonatal heath care facility.

1. Calcium channel blockers (Nifedipine LP)

- Inform the woman to be aware of side effect of nifedipine such as headache, flushing, dizziness, tiredness, palpitation and itching.
- Monitor maternal and fetal condition (pulse, blood pressure, sings of respiratory distress, uterine contraction, loss of amniotic fluid or blood, fetal heart rate).
- Do not give tocolytic drug for more than 48 hours.
- Do not give a combination of tocolytic agents as there is no additional benefit.
- Tocolytics should not be used in the following condition:
  - Preterm prelabor rupture of membranes (PPROM)
  - Chorioamnionitis
  - Placenta abruption
  - Cardiac disease.

- Dosage of nifedipine:
  - Give start dose nifedipine 20mg. The tablet should be chewed or crushed to aid the speed of absorption.
  - If uterine contractions persist, give the second dose of nifedipine 20mg, 30 minutes after the first dose.

  - The maximum dose of nifedipine in the first hour is 40mg. Do not give any further nifedipine until 3 hours after the second dose.
  - If contractions continue, give nifedipine 20mg every 3 to 6 hours, for 48 hours (unless contractions cease, or the woman establishes in labor).
  - The maximum dose of nifedipine is 160mg in 24 hours.
- Stop the nifedipine if:
  - There is marked hypotension: systolic < 90 mmHg
  - Significant dyspnea.

- Continue hourly monitor blood pressure and pulse.

2. Beta-agonist (Terbutaline)

- The beta-2 receptor agonists cause myometrial relaxation, therapy for tocolysis.
- Side effects: tachycardia, palpitations, lower blood pressure and hypokalemia.
- Monitoring:
  - Cumulative fluid intake, urine output and maternal symptoms, especially shortness of breath, chest pain or tachycardia (not exceed 120 beats/min)
  - Glucose and potassium concentrations should be monitored every four to six hours during parenteral drug administration.
- Dose:
  - Continuous intravenous infusion at 2.5 to 5mcg/min
  - Increasing by 2.5 to 5mcg/min every 20 to 30 minutes to a maximum of 25 mcg/min, or until the contractions have abated.
  - Reduced by decrements of 2.5 to 5mcg/min to the lowest dose that maintains uterine quiescence.
  - Not beyond 48 to 72 hours.
- Contraindications:
  - Patients with tachycardia-sensitive cardiac disease
  - Patients with poorly controlled hyperthyroidism or diabetes mellitus.

3. Beta-agonist (Salbutamol)

- Dose:
  - Dilute 5mg in 500 ml of 5% glucose or 0.9% sodium chloride to obtain a solution of 10 micrograms/ml.
  - Start infusion at the rate of 15 to 20 micrograms/minute (30 to 40 drops per minute).
  - If contractions persist, increase the rate by 10 to 20 drops/minute every 30 minutes until uterine contractions cease. Do not exceed 45 micrograms per minute (90 drops/minute).
  - Continue for one hour after contractions have ceased, then reduce the rate by half every 6 hours.

c. Magnesium sulfate

Magnesium sulfate administered shortly before birth may assist in reducing the risk of cerebral palsy and protect gross motor function in those babies born preterm. Administer Magnesium sulfate to women from 26 to 32 weeks gestation:

- Give magnesium sulfate as an intravenous infusion or intramuscular injection.
- Initial dose is 5g IM and maintenance doses are 5g every 5 hours, for 24 hours.
- Monitor urinary output and signs of magnesium overdose or toxicity (respiratory rate and patellar reflexes).
- restart only after signs of overdose or toxicity disappear.

d. Antibiotics

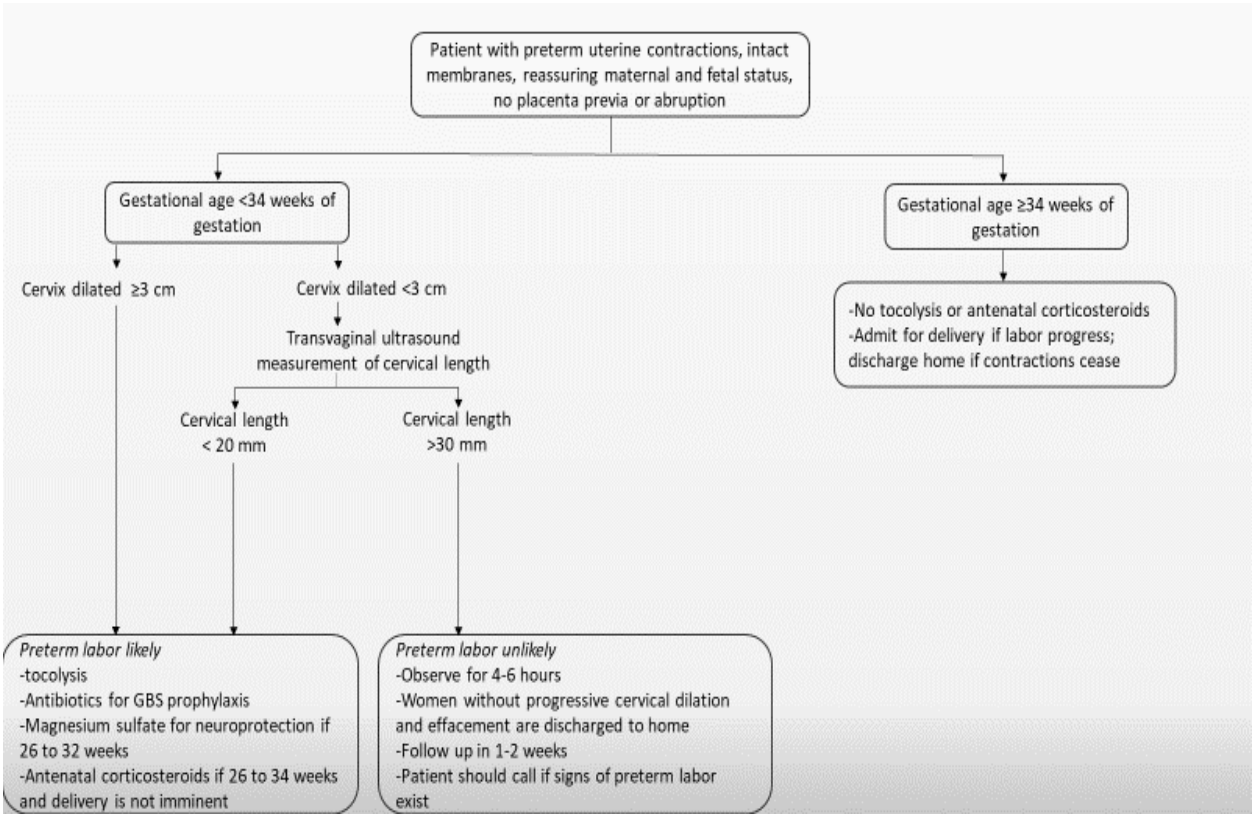
- Do not give prophylactic antibiotic, if amniotic membranes are intact and there are no clinical signs of infection.
- If the woman has confirmed group B streptococcal colonization, give Amoxicillin 500mg orally (PO) every 8 hours for seven days.
- If amniotic membranes are ruptured or there are clinical signs of infection, give an antibiotic to reduce the risk of chorioamnionitis in the mother and the risk of neonatal infection (pneumonia, cerebral abnormality):
  - Erythromycin 250mg orally (PO) every 6 hours for 10 days (or until birth) or
  - Ampicillin 2g IV every 6 hours until birth.
- Do not use amoxicillin plus clavulanic acid in case of PPROM, it increases the risk of necrotizing enterocolitis.

IX. PREVENTION

Assessment risk factors and risk reduction measures should be conduct:

- Assess risk factors preconception
- Perform a comprehensive review of all previous pregnancies because the most important historical factor is prior spontaneous preterm birth.
- Provide Progesterone therapy between 16 to 36 weeks gestation:
  - Utrogestan 200mg, intra-vaginal every evening.
- Daily low-dose aspirin beginning in the late first trimester for women with a history of early-onset preeclampsia and preterm delivery at less than 34 0/7 weeks of gestation:
  - Low-dose aspirin (81 mg/day) prophylaxis is recommended in women at high risk of preeclampsia and should be initiated between 12 weeks and 28 weeks of gestation (optimally before 16 weeks) and continued daily until delivery.
- Compare with no treatment, Cervical cerclage reduces the incidence of preterm birth in women at risk of recurrent preterm birth:
  - Cervical insufficiency => Cerclage of uterine cervix (between 14 and 24weeks gestation).

X. ALGORITHMS



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AMNIOTIC FLUID EMBOLISM

Prof. Kim Rattana, Dr. Ros Saphath, Dr. Hang Sovanara, Prof. Pech Sothy,
Prof. Tung Rathavy, Prof. Koum Kanal

I. DEFINITION

AMNIOTIC FLUID EMBOLISM (AFE): is defined as a rare but catastrophic emergency in which amniotic fluid, and other debris, enters the pregnant woman's blood stream via the placental bed of uterus and causes allergic reaction.

II. INCIDENCE

The incidence of AFE varies widely because of the obscurity of the problem and the wide range of signs and symptoms associated with it. AFE ranged from 1 in 8,000 to 1 in 80000 pregnancies. AFE occurred during labour, caesarean section, immediately after vaginal delivery and it also has been reported first-trimester surgical termination of pregnancy, and second trimester termination. AFE is a leading cause of maternal death and unpreventable obstetric emergency. Despite technological advance in critical care support, the maternal mortality rate for AFE is 80% (61% in the US national registry), a large percentage of survivors have permanent hypoxia-induced neurological damage. The fetal mortality rate is 21%, and 50% of the surviving neonates experience permanent neurological injury.

III. RISK FACTORS/PHYSIOPATHOLOGY

i. Risk Factors

No definite risk factors have been established in literature. Although the most frequently cites risk factors for AFE appear to be caesarean delivery, instrumental vaginal delivery, amniocentesis, placental abnormalities (previa, abruption, accreta), pre-eclampsia/eclampsia, maternal age > 35 years, induction of labor and abdominal/uterine trauma.

ii. Physiopathology

The physiopathology of AFE is poorly understood. The entrance of amniotic fluid into the maternal circulation, possibly under a pressure gradient, is the principal mechanism invoked in the pathogenesis of AFE. This resulting in in an abnormal activation of proinflammatory mediator systems. The typical presentation of amniotic fluid embolism includes a triad symptom: hypoxia and hypotension, following in many cases by coagulation.

IV. DIAGNOSIS

i. Signs and symptoms

Presumptive: based on clinical presentation after considering other causes of hemodynamic instability.

Premonitory symptoms have been described and include breathlessness, chest pain, feeling cold, light headedness, restlessness, distress, panic, nausea and vomiting, pins

and needles. The diagnosis is suspected in a woman experiencing several of the following features:

- A sudden onset of dyspnea and hypotension which is frequently followed by cardiovascular collapse and respiratory arrest,
- Acute hypoxia
- Coagulopathy or severe hemorrhage
- Tonic-clonus seizures
- Acute fetal distress prior to maternal collapse
- Uterine hypotonic and placenta abruption leading to massive hemorrhage. OR
- Women in whom the diagnosis was made at post-mortem examination with the finding of fetal squames or hair in the lungs.

The woman is often conscious at the onset of symptoms. Not all AFE is rapidly progressive and early diagnosis and supportive treatment may result in better outcomes. Acute shivering, sweating, anxiety and coughing, followed by respiratory distress, altered mental status, seizures-like activity and cardiovascular collapse (profound hypotension, tachycardia and possible arrhythmia). More than 80% of women with AFE experience cardio-respiratory arrest within the first few minutes. Disseminated intravascular coagulation (DIC) can occur quickly, causing massive maternal hemorrhage.

ii. Laboratory tests

Laboratory tests are nonspecific: Complete blood count, coagulation profile, arterial blood gases, cardiac enzymes, electrolyte.

- WBC may be elevated
- Hemoglobin and hematocrit will be low
- Prolong thrombin and partial thromboplastin time
- Decreased fibrinogen levels
- Thrombocytopenia (rare)
- Cardiac enzymes may be elevated
- Arterial blood gases may show hypoxemia.

iii. Paraclinical examination

ECG:

- Tachycardia with a right ventricular strain pattern in early stage,
- ST and T wave abnormalities
- Cardiac arrhythmia or asystole (Severe cardio-vascular collapse).

Pulse oximetry: drop in oxygen saturation

Chest X-ray: Opacity diffuses bilateral. **Trans esophageal echocardiography:**

- Severe pulmonary hypertension
- Acute right ventricular failure with a leftward deviation of the interatrial and intraventricular septum.

iv. Differential diagnosis

- Massive obstetric hemorrhage
- Placental abruption
- Uterine rupture
- Eclampsia
- Peripartum cardiomyopathy
- Anaphylaxis
- Aortic dissection
- Cholesterol embolism
- Acute myocardial infarction
- Pulmonary embolism (PE)
- Septic shock
- Transfusion reaction
- Local anesthetic toxicity

Clinical features of AFE compared to pulmonary embolism		
	AFE	PE
Timing of onset	Most likely occur during delivery	Any time
Early symptoms	Dyspnea, restlessness, panic, feeling cold, paresthesia, painless likely	Dyspnea, cough, hemoptysis
Collapse	Highly likely	May occur
DIC	Highly likely	Absent
ECG	Non-specific	Non-specific
CXR	Pulmonary oedema, ARDS, right atrial enlargement, prominent pulmonary arc	Segmental collapse, raised hemidiaphragm, unilateral pleural effusion
ABG	Non-specific	Non-specific
CTPA	Negative	Positive

V. PROGNOSIS/COMPLICATIONS

i. Prognosis

Maternal survival is uncommon, although the prognosis of AFE have improved significantly with early diagnosis and prompt resuscitation. The intact infant survival rate is 70%.

ii. Complications

For mother:

- Pulmonary oedema is a common occurrence in survivors.
- Left heart failure may occur.
- Disseminated intravascular coagulation (DIC).
- Massive maternal hemorrhage
- Persisting neuro-logical impairment. For infant:

- Persisting neurological impairment. Neurological status of the infant is directly related to the time elapsed between cardiac arrest and delivery.
- Ischemic encephalopathy
- Cerebral palsy.

VI. MANAGEMENT OF AMNIOTIC FLUID EMBOLISM

i. General Management: **Call for help early**:

- Multidisciplinary team including consultant obstetrician, anesthetist, midwives, theatre team, pediatrician, and liaise with hematology regarding the need for blood products as appropriate. The most senior person should take charge and assign roles and responsibilities to all other individuals with good communication and organization.
- Initiate Basic life support.
- Rapid transfer woman to the nearest hospital (with arrangement) or to operation theatre.
- Support and care for partner and family.
- Acute management (A, B, C approach)
- Airway/Breathing:
- Assess airway/breathing and maintain airway patency.
- Administered oxygen via mask to maintain normal saturation 100% O2 (via bag and mask may be required).
- Bag and mask ventilation should be undertaken until intubation can be achieved.
- Consider early intubation with a cuffed endotracheal tube using cricoid pressure to minimize the risk of aspiration.
- Circulation:
- Check for vital signs (pulse, blood pressure)
- If in doubt: chest compression at a rate of 30:2
- Apply lateral tilt (preferably left) to the woman or manually displace the uterus to reduce aorto-caval compression.
- Initiate cardiopulmonary resuscitation (CPR) if the woman has a cardiac arrest. If she has not responded to resuscitation after 4 minutes, perform a Resuscitative Hysterotomy caesarean section.
- IV access with 2 x 16gauge cannulae as soon as possible. If peripheral venous access is not possible, use central venous access, intraosseous access or venous cutdown.
- Take urgent bloods: for Group and X-match (for 6 units), complete blood picture (CBP) with platelets, coagulation profile, arterial blood gases (ABG).
- Treat hypotension with crystalloid and blood products. Avoid excess fluid administration.
- Insert urinary catheter.
- Maintain body temperature.

ii. Specific Management

Resuscitative hysterotomy (RH):

- Resuscitative hysterotomy should not be delayed
- Operator should use midline vertical incision or a suprapubic transverse incision.
- A scalpel and umbilical cord clamps should be available on the resuscitation trolley in all areas where maternal collapse may occur

Treatment of coagulopathy in AFE:

- Coagulation factors should be administered promptly after multidisciplinary decision
- If no clotting results are available and bleeding is continuing:
- 4 units of red blood cells, then FFP infuse at 12-15ml/kg until hemostatic test results are known.
- If prothrombin time/activated partial thromboplastin time >1.5 times normal and hemorrhage is ongoing: FFP 15ml/kg
- Recombinant factor VII should only be used if coagulopathy cannot be corrected by blood component replacement.

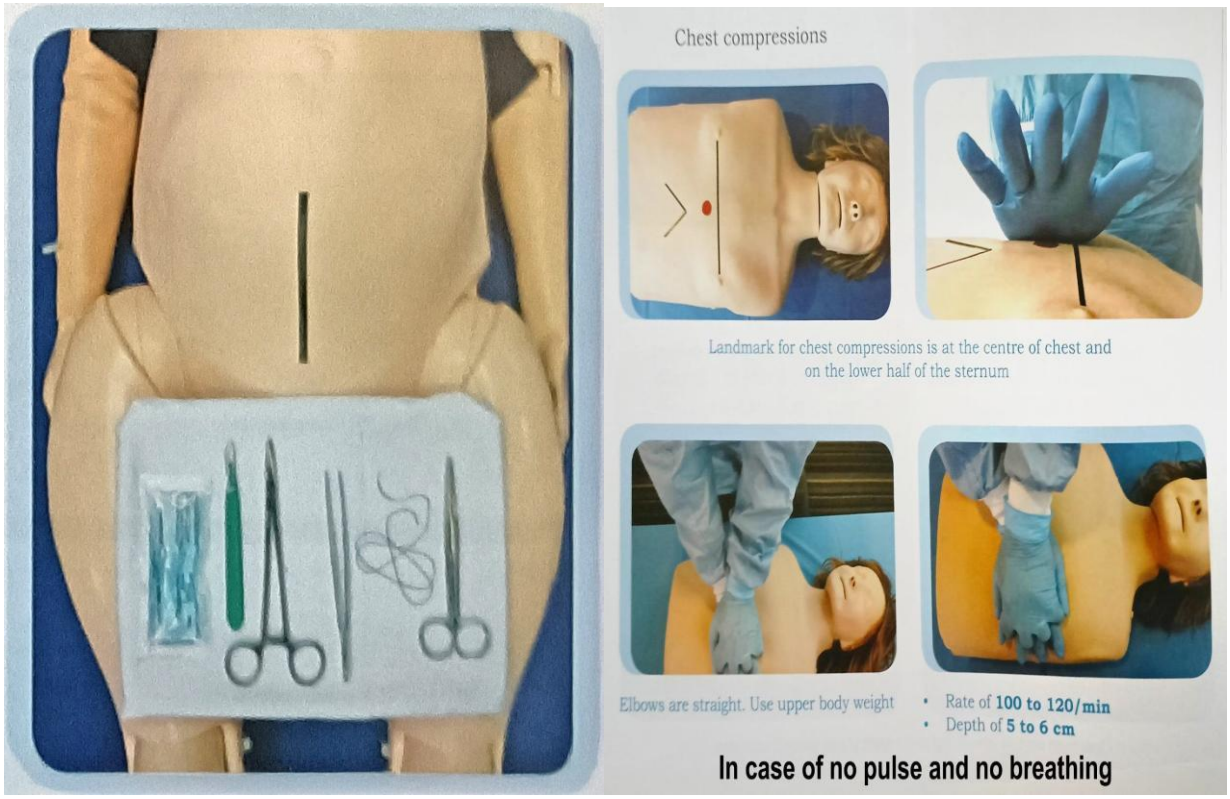
Management of massive hemorrhage:

Hemorrhage should be aggressively managed with uterotonic agents, uterine tamponade, and examination to exclude co-existent genital tract trauma that may exacerbate blood loss. Perform invasive techniques such as bracing suture (B-Lynch suture), uterine artery ligation, peripartum hysterectomy, if required.

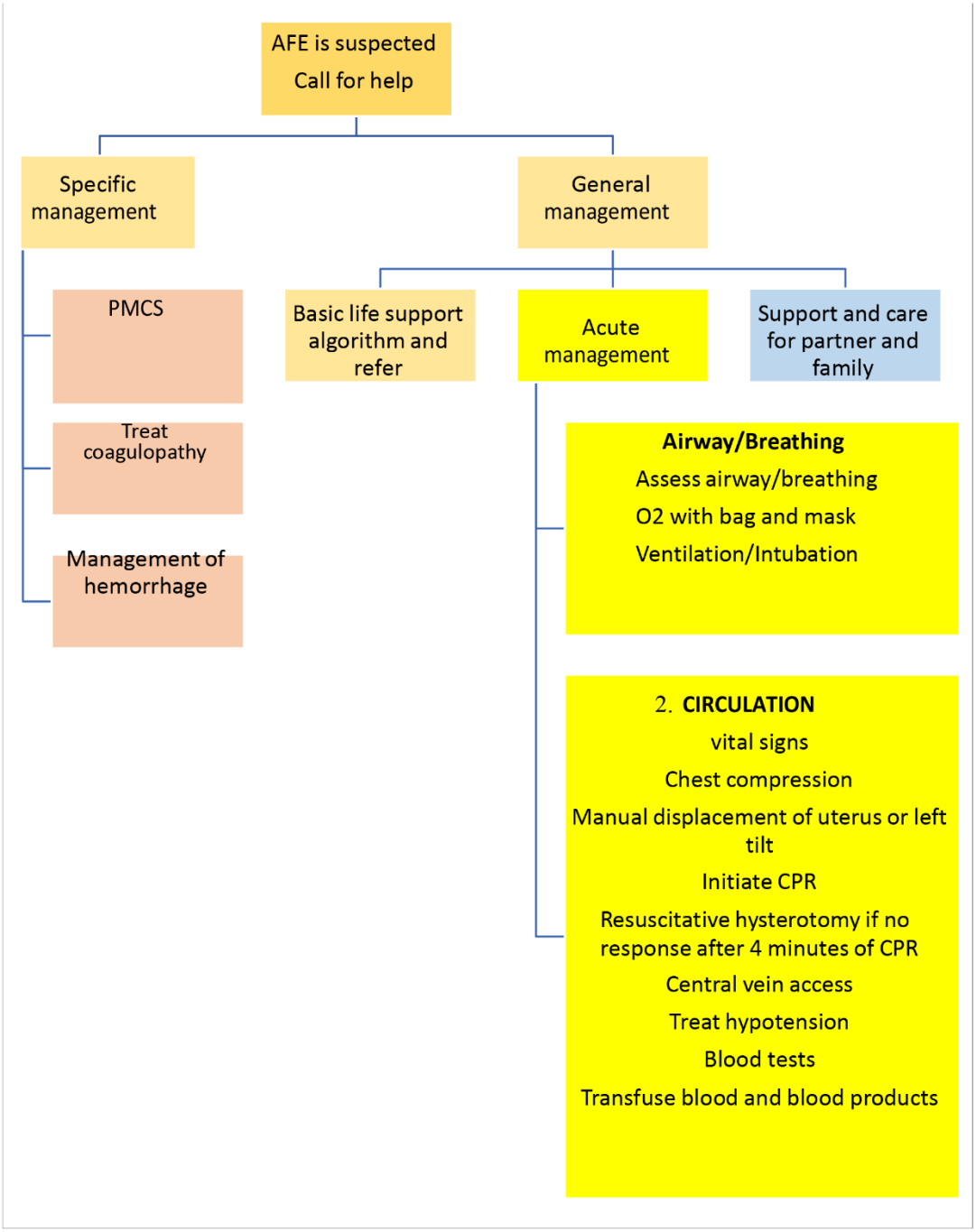
Resuscitation and **resuscitative hysterotomy** is successful:

- Care in a hospital with intensive care facilities.
- Provide adequate counselling to the woman/family as soon as possible and arrange further follow-up.
- Resuscitation and resuscitative hysterotomy unsuccessful:
- A post-mortem will be required (any medical devices, such as intravenous lines or tubes, should not be removed)
- Provide adequate counselling to the partner/family as soon as possible.

Resuscitative hysterotomy



VII. ALGORITHMS



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ECTOPIC PREGNANCY

Prof. Lieng Chanrith, Dr. Chhit Maryan, Dr. Uy Kyna, Dr. Chap Chanthida

I. INTRODUCTION

An ectopic pregnancy is a pregnancy that happens outside of uterus.

This occurs when a fertilized egg implants in a location that can't support its growth.

An ectopic pregnancy most happens:

- often in fallopian tube,
- more rarely can occur in ovary, abdominal cavity or cervix.

Ectopic pregnancy can become life-threatening, especially if fallopian tube ruptures.

A ruptured ectopic pregnancy can cause severe bleeding and sometimes death.

II. RISK OF AN ECTOPIC PREGNANCY

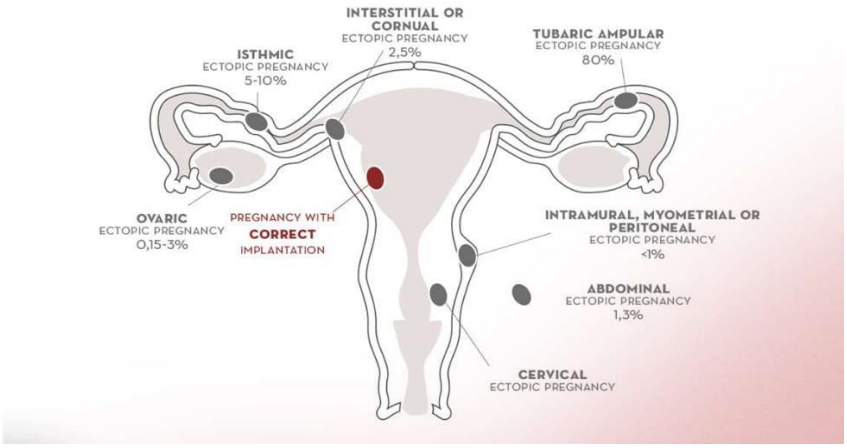
- A history of:
  - Pelvic inflammatory disease (PID)
  - Surgery on fallopian tubes (including tubal ligation)
  - Infertility.
- Risk can increase with age:
  - People over age 35 have a higher risk than people under 35.
  - Up to 50% of people who experience an ectopic pregnancy don't have any of the above risk factors.
- In vitro fertilization
- Prior ectopic pregnancy
- Tubal injury or surgery, including tubal ligation
- Pelvic inflammatory disease
- Salpingitis isthmic nodosa
- Endometrial injury
- Intrauterine contraceptive devices
- Endometriosis
- Previous placenta previa
- Congenital uterine anomalies
- Smoking
- Past history of spontaneous or induced abortions
- Maternal age (advanced maternal age increases the risk of ectopic pregnancy)
- History of subfertility

III. CAUSES OF ECTOPIC PREGNANCY

- In most cases, conditions that slow down or block the movement of the egg down the fallopian tube causes ectopic pregnancy.
- This could happen because:
  - Scar tissue, adhesions or inflammation from a prior pelvic surgery.
  - Fallopian tubes have damage, such as from a sexually transmitted infection (STI).
  - Congenital irregularly-shaped fallopian tube.
  - Treatment for infertility with in vitro fertilization (IVF).
  - Endometriosis.
  - Sexually transmitted infections (STIs).
  - An IUD in place at the time of conception.
  - A history of smoking tobacco.
- Ectopic pregnancy is more common in pregnant with:
  - an IUD (intrauterine device) in place,
  - a history of a tubal ligation.

IV. DIFFERENT TYPES OF ECTOPIC PREGNANCY

- 95% are in the Fallopian tube:
  - ampullary
  - isthmic
  - fimbrial
- 3% are interstitial
- < 1% are within a Caesarean section scar on the uterus
- < 1% are cervical
- < 1% are cornual
- < 1% are ovarian
- < 1% are intramural
- < 1% are abdominal
- < 1% are heterotopic pregnancies



V. SYMPTOMS OF AN ECTOPIC PREGNANCY

The early symptoms of an ectopic pregnancy can be very similar to typical pregnancy symptoms.

i. Unruptured ectopic pregnancy

The signs and symptoms of an unruptured ectopic pregnancy:

- Vaginal bleeding: bleeding or spotting that is different from the normal menstrual period, dark and watery, heavier or lighter than usual and prolonged.
- Pain in lower abdomen: mild cramping on one side of the pelvis; low back pain.
- Nausea and vomiting
- Dizziness or weakness

ii. Ruptured ectopic pregnancy

The symptoms of a ruptured ectopic pregnancy can include internal bleeding:

- Paleness of the skin
- hypotension
- Fainting
- Weakness
- Dizziness
- Sudden, severe pain in the abdomen or pelvis
- Shoulder pain
- Rectal pressure or bowel problems

VI. DIAGNOSIS AND TESTS

i. Signs and symptoms

ii. Clinical evaluation

Importance of history taking and physical examination.

iii. Laboratory investigations

- A urine test,
- A blood test:

a. Levels of the hormone human chorionic gonadotropin (HCG)

- An hCG level of:
  - less than 5 mIU/mL is considered negative for pregnancy,
  - above 25 mIU/mL is considered positive for pregnancy.
- An hCG level between 6 and 24 mIU/mL is considered a grey area, and likely to be retested.

Guideline to hCG levels in weeks during pregnancy

hCG levels during pregnancy (in weeks sincelast menstrual period)	
3 weeks LMP	5 - 50 mIU/ml
4 weeks LMP	5 - 426 mIU/ml
5 weeks LMP	18 - 7,340 mIU/ml
6 weeks LMP	1,080 - 56,500 mIU/ml
7 - 8 weeks LMP	7, 650 - 229,000 mIU/ml
9 - 12 weeks LMP	25,700 - 288,000 mIU/ml
13 - 16 weeks LMP	13,300 - 254,000 mIU/ml
17 - 24 weeks LMP	4,060 - 165,400 mIU/ml
25 - 40 weeks LMP	3,640 - 117,000 mIU/ml
non pregnant	55-200 ng/ml

- A low hCG level can mean any number of things and should be rechecked within 48-72 hours to see how the level is changing.
- A low level can indicate:
    - Miscalculation of pregnancy dating
    - Possible miscarriage or blighted ovum
    - Ectopic pregnancy.

b. Levels of serum Progesterone

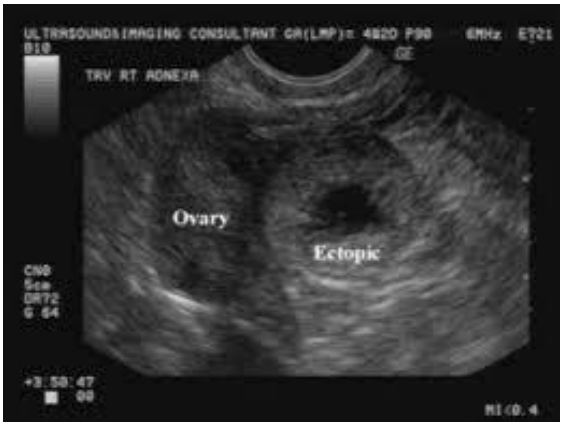
- In the past, some physicians have used serum progesterone levels as well.
- Particularly in the time window of 4–6 weeks of gestation: ultrasonography is inconclusive and serial β-hCG measurement at an interval of 48 hours poses a risk of complications; progesterone measurement could help in reaching the diagnosis at the earliest.
- In women with:
    - progesterone level below 10 ng per mL (31.8 nmol per L) and a human chorionic gonadotropin (hCG) level below 1,500 mIU per L (1,500 IU per mL), spontaneous resolution of ectopic pregnancy is more likely.
    - Serum progesterone levels:
        - have been designed to predict the success of expectant or medical management of ectopic pregnancy.
        - fell to normal (less than 1.5 ng per mL [4.8 nmol per L]) faster than hCG levels following treatment with methotrexate or laparoscopic salpingostomy and for this reason may be a better marker for predicting successful treatment.

Diagnostic Tests for Detecting Ectopic Pregnancy

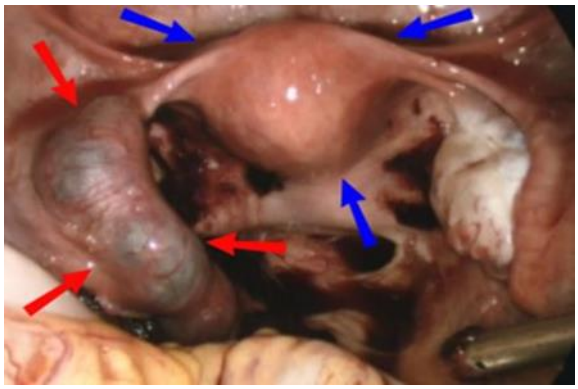
Diagnostic test	Sensitivity (%)	Specificity (%)
Transvaginal ultrasonography with beta-hCG level greater than 1,500 mIU per mL (1,500 IU per L)	67 to 100	100 (virtual certainty)
Beta-hCG levels do not increase appropriately	36	63 to 71
Single progesterone level to distinguish ectopic pregnancy from non-ectopic pregnancy	15	> 90
Single progesterone level to distinguish pregnancy failure from viable intrauterine pregnancy	95	40

iv. Imaging studies

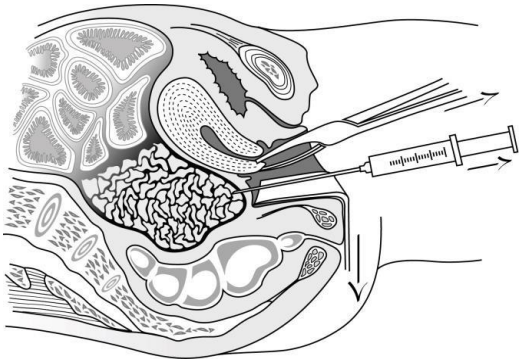
- Transvaginal Ultrasound (TVS)
- MRI (if TVS inconclusive)



v. Laparoscopy



vi. Culdocentesis: rarely used



VII. MANAGEMENT AND TREATMENT

i. Medical treatment (methotrexate)

- Single dose: 50 mg/m² at Day 0.
- hCG measurement: Days 0, 4, 7.
- Treatment success: hCG declines 15% between Day 4 and 7.
- In rare cases, a second injection of methotrexate is necessary if HCG levels don't decrease enough with one dose. Additional dose on Day 7 if hCG does not decline 15%.
- Close follow-up with hCG monitoring to ensure the medication is working effectively.
- Attention about the possible side effects and risks of methotrexate.

a. Criteria

- Stable hemodynamic condition
- Hematosalpinx < 4 cm (transvaginal ultrasound)
- Without symptoms or few symptoms
- hCG < 5 000 mui/ml

b. Contra-indication

- Refuse by patient
- Patient non-compliance
- Unstable hemodynamic condition
- Large amount of intra-abdominal free fluid
- Severe abdominal pain
- Anemia (hemoglobin < 9 g/dl)
- hcg > 10 000 mui/ml
- Thrombopenia ＜50 000 / mm3
- Leucopenia ＜2 000 / mm3
- Kidney GFR ＜ 30 ml/min
- Liver failure
- Coagulopathy
- Hematosalpinx ≥ 4 cm
- Visible fetal heartbeat activity

Day	Single-dose regimen	Two-dose regimen
1	Verify baseline stability of complete blood count and comprehensive metabolic panel; determine β - hCG level. Administer single dose of methotrexate 50 mg per m².	Verify baseline stability of complete blood count and comprehensive metabolic panel; determine β - hCG level. Administer single dose of methotrexate 50 mg per m².
4	Measure β - hCG level.	Measure β - hCG level Administer second dose of methotrexate, 50 mg per m².
7	Measure β - hCG level. If decrease from days 4 to 7 is ≤15%, offer choice of re-administration of single dose methotrexate, 50 mg per m² or refer for surgical management: - if β - hCG level does not decrease after two doses of methotrexate, refer to surgical management. If decrease from days 4 to 7 is > 15 %, measure β - hCG levels weekly until they are undetectable.	Measure β - hCG level. - If decrease from days 4 to 7 is ≤ 15 %, offer choice of further methotrexate doses or refer for surgical management, - Further methotrexate doses should be 50 mg per m² on day 7 with measurement of β - hCG level on day 11, then another dose of 50 mg per m² on day 11 if β - hCG level does not decrease ≤ 15 % from day 7 to 11; - if β - hCG level does not decrease ≤ 15 % from day 11 to 14, refer for surgical management, - if decrease from day 4 to 7 is > 15 %, measure β - hCG levels weekly until they are undetectable.

In the single-dose protocol, there is no action that should be taken based on the day 4 β – hCG level; it commonly increases from days 1 to 4.

Selection of appropriate patient for medical management of ectopic pregnancy

Contra-indicated	Good Patient	Poor Patient
- Hemodynamically unstable - Suspected ruptured EP - Sensitivity to MTX - Intrauterine pregnancy - Breastfeeding - Active pulmonary disease - Renal disease - Chronic liver disease - Preexisting blood dyscrasia - Immunodeficiency - Peptic ulcer disease - Unable to comply with visits and follow-up.	- Hemodynamically stable - Low hCG (< 5000 mIU/ml) - Small mass (<3.5 cm) - Unruptured mass - No embryonic cardiac activity - Certainly, that there is no IUP -Willingness for follow up - No known sensitivity to MTX	- High hCG (>5000 mIU/ml) - Large mass (>3.5 cm) - Embryonic cardiac activity present - Significant abdominal pain - IUP has not been ruled out - Questionable ability to return for all outpatient visits.

EP = ectopic pregnancy, IUP = intrauterine pregnancy, MTX = methotrexate

ii. Surgery for ectopic pregnancy

- The Ruptured ectopic pregnancy is not suitable for methotrexate treatment. It is an emergency surgery and a life-saving treatment.
- There are two main surgical techniques:
  - Laparoscopy
  - Laparotomy

1. Laparoscopic surgery

a. Salpingostomy

Small incision in the fallopian tube to remove the ectopic pregnancy while leaving the tube intact.

Indications:

- For patients who wish to preserve fertility.
- When the fallopian tube is not severely damaged or ruptured.

b. Salpingectomy

In this procedure, the entire fallopian tube containing the ectopic pregnancy is removed.

Indications:

- If the fallopian tube is severely damaged or ruptured.
- If the patient has no future desire for fertility or when preservation of the tube is not possible

c. Salpingo-oophorectomy

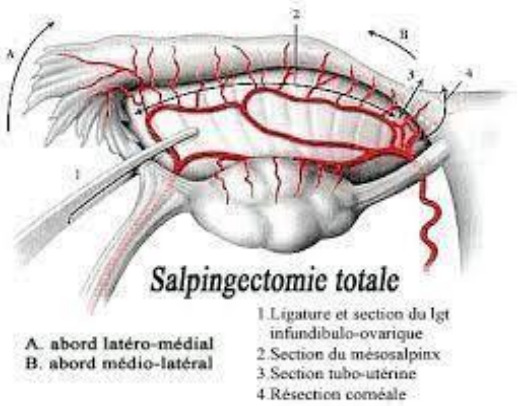
This procedure involves the removal of the fallopian tube and the ovary on the affected side.

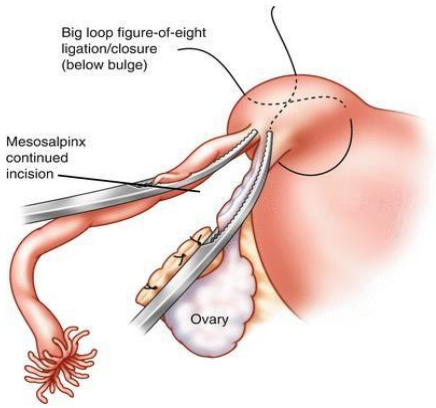
Rarely indicated but may be necessary if the ectopic pregnancy involves the ovary or there is significant damage to both the fallopian tube and ovary.

2. Laparotomy

Indications:

- Massive intra-abdominal bleeding.
- Unstable vital signs.
- Inability to perform laparoscopy due to prior abdominal surgeries, scarring, or other contraindications.





VIII. PREVENTION

- No smoking
- Preventing any sexually transmitted infections (STIs).
- Effective contraception to avoid pregnancy during the healing and monitoring period.

IX. PROGNOSIS

The prognosis of an ectopic pregnancy can vary depending on several factors, including early diagnosis and treatment.

i. Immediate Treatment
   - Ectopic pregnancies cannot proceed normally and require prompt medical intervention.
   - If left untreated, they can cause life-threatening complications such as severe internal bleeding.

ii. Future Fertility
   - Most women who experience an ectopic pregnancy can still have successful pregnancies in the future.
   - Even if one fallopian tube is removed, the other can often compensate.

iii. Recurrence Risk
   - There is about a 10% chance of having another ectopic pregnancy in the future.

iv. Alloimmunization Risk

- Rhesus D immunoglobulin is administered in ectopic pregnancy to prevent maternal sensitization in Rh-negative women.
- For ectopic pregnancy, the recommended protocol is:
  - Administer within 72 hours of the obstetric complication or procedure
  - Dose: 300 mcg (1500 IU) intramuscularly or intravenously
  - Route: Both intramuscular and intravenous routes are equally effective.

X. ABDOMINAL PREGNANCY

- Abdominal pregnancy (AG) is defined as the implantation and development of the fertilized egg in the peritoneal cavity.
- Abdominal pregnancies are divided into 2 groups:
  - Primary abdominal pregnancies due to the implantation of the egg in the peritoneal cavity due to delayed ovular uptake.
  - Secondary abdominal pregnancies, which are the most frequent, resulting from a tubo-abdominal abortion or a tubal pregnancy or the migration of an intrauterine pregnancy through a hysterectomy or uterine perforation breach, or a rudimentary horn.
- Abdominal pregnancy is a rare condition that poses the double problem of its diagnosis and management.

i. Clinical signs

- Digestive problems:
  - Nausea, vomiting, constipation, sub-occlusion, abdominal-pelvic pain concomitant with fetal movements
  - With or without metrorrhagia,
  - Anemia with alteration of the general condition
  - A very superficial fetus often in an upper transverse position.
- Vaginal examination:

  The cervix is often fixed under the pubic symphysis, hard and long.

ii. Diagnosis

a. Echography
- a fetus in a gestational sac outside the uterus,
- absence of a uterine wall between the fetus and the bladder,
- fetal heartbeat
- site of the aberrant insertion of the placenta.

b. CT examination and magnetic resonance imaging are only indicated:
- in case to know the limits of placental insertion in the peritoneal cavity or
- in case of diagnostic doubt.

c. Laboratory examinations (anemia)

iii. Treatment

The decision to operate is made taking into account the viability of the fetus and the risks to the mother.

a. In the case of a deceased fetus in utero

- To avoid exposing the mother to infectious risks and coagulation disorders, a scheduled intervention is indicated.
- Wait a few weeks before intervening so that placental involution reduces the risk of per - operative hemorrhage.

b. In the case of a living fetus in utero

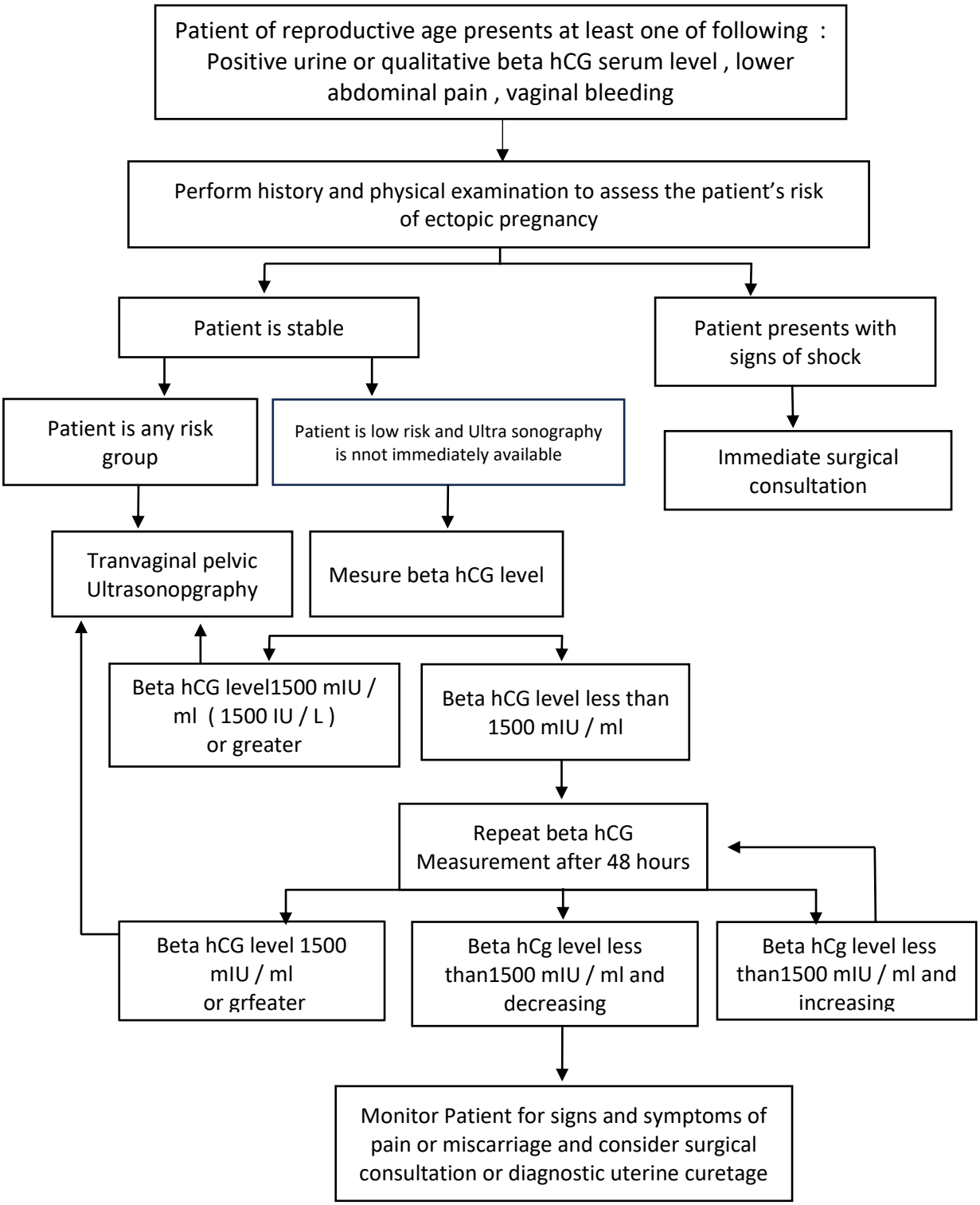
- **For a fetus younger than 28 weeks:**
  - Pulmonary maturation by administering glucocorticoids to the mother.
  - Avoid hypoxia, acidosis, and hypothermia of the fetus in utero, which depress surfactant synthesis.
- **After 28 weeks**:
  - if the fetus is viable, the intervention must be performed urgently.

c. Placental Gestion

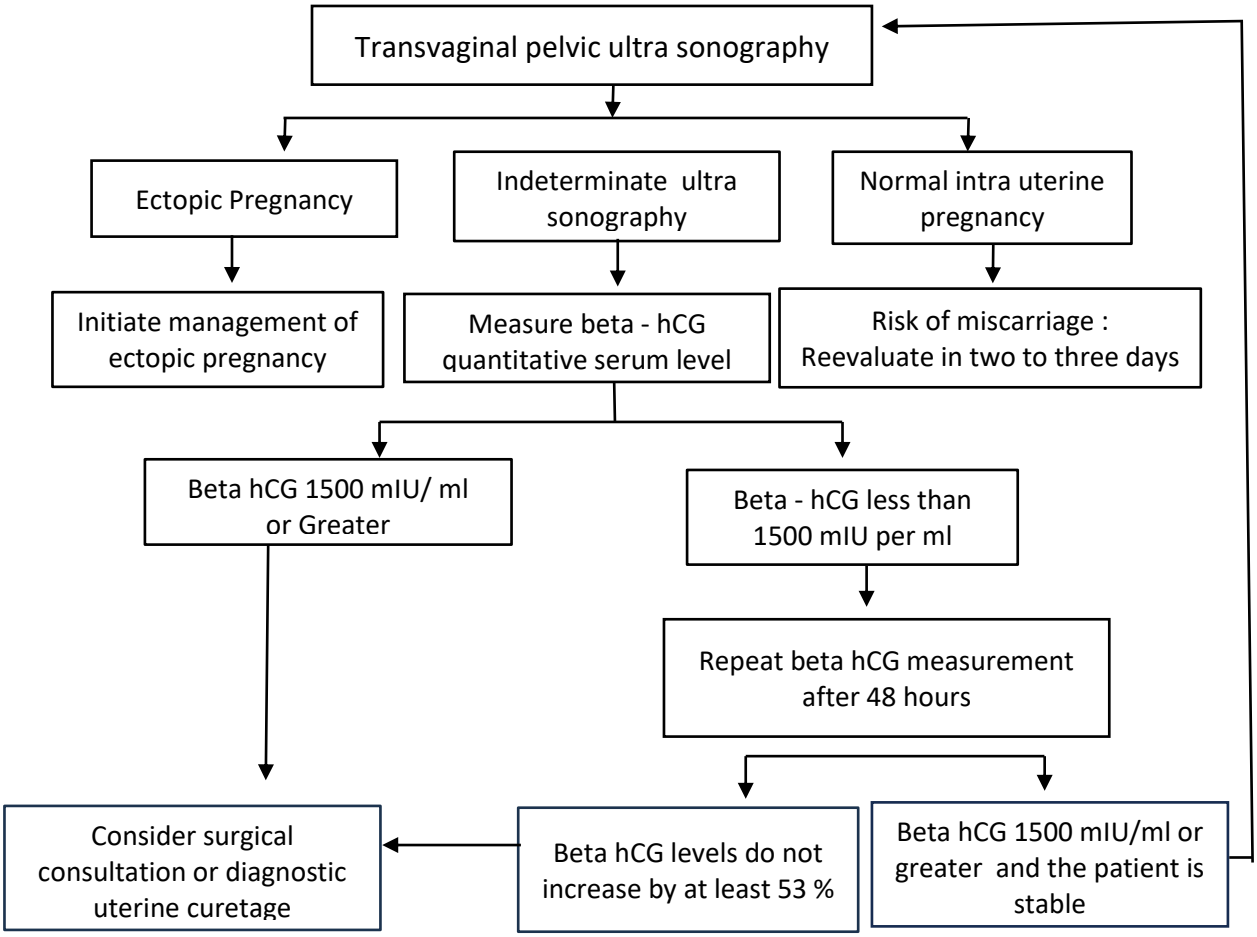
- Due to the risk of uncontrollable hemorrhage, all attempts at extraction are strictly prohibited.
- Leave the placenta in place by cutting the umbilical cord as close as possible.
- Strictly monitor the mother post-operatively to detect complications (fistula, peritonitis, abscess, secondary hemorrhage, intestinal obstruction).
- The spontaneous resorption of this placenta "in situ" should be monitored by ultrasound and measuring placental hormones.

XI. ALGORITHM

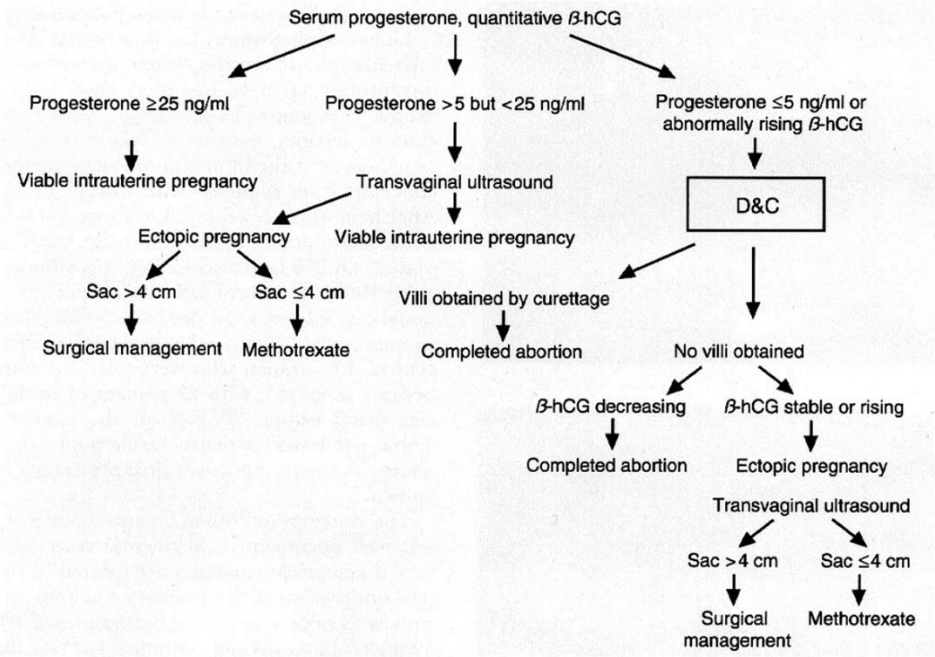
ALGORITHM NO 1 - DIAGNOSIS BY DOSAGE BETA HCG



ALGORITHM NO 2 - DIAGNOSIS BY ULTRASOUND



ALGORITHM NO 3 - DIAGNOSIS BETWEEN PROGESTERONE/ BETA HCG



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SPONTANEOUS ABORTION

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I. DEFINITION

Spontaneous abortion (SAB) or early pregnancy loss is a pregnancy that ends spontaneously before the fetus has reached a viable gestational age.

This is typically defined as a fetus less than 20 weeks of gestation (WHO)and less than 26 weeks for Cambodia.

II. CLASSIFICATION

Spontaneous abortion can be subdivided into complete abortion, incomplete abortion, inevitable abortion, missed abortion, septic abortion, recurrent abortion and threatened abortion.

Table 1: Spontaneous Abortion: Definitions of Subcategories

Complete abortion: all products of conception have been passed without the need for surgical or medical intervention.
Incomplete abortion: some, but not all, of the products of conception have been passed; retained products may be part of the fetus, placenta, or membranes.
Inevitable abortion: the cervix has dilated, but the products of conception have not been expelled. The bleeding persists; the membrane may be ruptured.
Missed abortion: a pregnancy in which there is a fetal demise (usually for a number of weeks) but no uterine activity to expel the products of conception.
Recurrent abortion: three or more consecutive pregnancy losses.
Septic abortion: a spontaneous abortion that is complicated by intrauterine infection.
Threatened abortion: a pregnancy complicated by bleeding, but the cervix has not dilated.

III. EPIDEMIOLOGY

- Spontaneous abortion is very common, occurring in up to 20% of all pregnancies.
- 80% of these losses occur in the first trimester.
- Once a fetal heart is documented, the risk of SAB drops to about 5%-10%, depending on maternal age.
- Approximately 1 in 4 women will experience a miscarriage in her lifetime.

IV. RISK FACTORS AND CAUSES

i. Risk factors

- Increasing maternal age ≥ 35 years old
- History of previous spontaneous abortion
- Intrauterine procedures such as chorionic villus sampling and amniocentesis
- Blunt abdominal trauma in the second trimester

ii. Causes

The causes of spontaneous abortion may include:

- Fetal causes
- Maternal causes

a. Fetal causes

50% of SAB in the 1st trimester are due to chromosomal anomalies: mostly trisomy's, also can be monosomy and triploids.

b. Maternal causes

- Infections T: Toxoplasma, R: Rubella, O: Others (syphilis, parvovirus B19), C: Cytomegalovirus, H: Herpes (TROCH).
- Environmental: Alcohol, smoking, stress, drug abuse, radiation.
- Immunological: Autoimmune diseases, Alloimmune response
- Endocrinal abnormalities: Hypo or hyperthyroidism, DM, luteal phase defect
- Uterine abnormality: Congenital, Fibroid, Cervical incompetence
- Others: unknown, trauma, intoxication.

V. DIANGOSIS

i. Clinical argument

General argument

- History of amenorrhea
- Vaginal bleeding
- Abdominal cramps or pain
- Endo-uterine bleeding on speculum

Physical exam is important to assess hemodynamic stability, abdominal tenderness or peritoneal signs, the degree of bleeding, uterine size and cervical dilatation.

Specific argument

- Threatening abortion: vaginal bleeding, the cervix is closed and fetal heart beat still present
- Inevitable abortion: the cervix is open and the products of conception are still in utero
- Incomplete abortion: the cervix is open and the products of conception are not completely evacuated
- Complete abortion: the cervix is open and the products of conception are not present

- Missed abortion: the heart beat is absent
- Blighted Ovum: gestational sac present but absence of the embryo.

ii. Investigation

- Pregnancy test positive
- Pelvic ultrasound
- Complete Blood Count (CBC), Blood Group, Coagulation profile and vaginal swab with culture
- For repeated miscarriage: the additional investigations: Genetical, Immunological profile, Infection Screening, Hysteroscopy, Endocrine.

VI. DIFFERENTIAL DIAGNOSIS

Differential diagnosis of first trimester vaginal bleeding:

- Cervical abnormalities (e.g., excessive friability, malignancy, polyps, trauma)
- Ectopic pregnancy
- Idiopathic bleeding in a viable pregnancy
- Infection of the vagina or cervix
- Molar pregnancy
- Subchorionic hemorrhage
- Vaginal trauma

VII. COMPLICATIONS

- Hemorrhage and subsequent complications secondary to hypovolemic shock
- Anemia
- Infection/Septic shock
- Traumatic complications of surgical management (eg, cervical laceration and uterine perforation)
- Disseminated Intravascular Coagulation (DIC)
- Retained products of conception (POC)
- Hematometra

VIII. MANAGEMENT

Threatened abortion

- Bed rest, avoid sexual intercourse and heavy physical exertion
- 50-70% of cases proceed to a normal pregnancy
- Progesterone oral 100mg tablet three times daily or Progesterone vaginal 200mg twice daily for one month. **Short cervix**: continue Progesterone vaginally 200 mg at night until 36 weeks and **Recurrent miscarriage** until 16 weeks.
- Antibiotics are used only if there are septic abortion, bacterial vaginosis, cervicitis
- Review every week until symptoms resolve or immediately if any complications

Inevitable abortion

- Assess the general status of the patient
- If unstable: correct the hypovolemic shock then proceed with surgical management (Manual Vacuum Aspiration (MVA), Electric Vacuum Aspiration (EVA), Dilatation& Evacuation (D&E)
- If stable: Discuss with the patient the following options:
  a. **Medical Management**: give Misoprostol 200 mcg (2 tablets) every 6h orally or vaginally. **Side effect**: Diarrhea, Pain due to uterine contraction, increase of temperature with shivering both are dose dependent and settle rapidly without treatment
  b. **Surgical treatment**: MVA, EVA or (D&E).

Incomplete abortion

- Assess the general status of the patient:
- If unstable: correct the hypovolemic shock then proceed with surgical management (MVA, EVA or D&E)
- If stable: Discuss with the patient the following options:
  a. **Medical Management**: Give Misoprostol 200 mcg (2 tablets) every 6h orally or vaginally
  b. **Surgical treatment**: MVA, EVA or D&E

Complete Abortion

- Assess the general status of the patient
- If unstable: correct the hypovolemic shock.
- If stable: Reassure the patient

Missed abortion and Blighted Ovum

Medical management:

- Cervical ripening prior to uterine instrumentation: give Misoprostol 200 mcg,
- 2 tablets orally or vaginally 3h before the procedure
- Missed abortion (<12 weeks gestation): give Misoprostol 200 mcg, 4 tablets vaginally or sublingually every 24h for 2 days
- Missed abortion (12–22 weeks gestation): give Misoprostol 200 mcg, 1 tablet every 12h or 2 tablets every 4h vaginally or sublingually until expulsion
  - **Surgical Management**: MVA, EVA or D&E

Septic abortion

- Hospitalization
- Antibiogram
- Assess the general status of the patient
- If unstable: correct the hypovolemic and septic shock (include antibiotics) then proceeds with surgical management MVA, EVA, or D&E

- If stable: Surgical Management
- Antibiotics for septic abortion

Treatment of first choice: give Ceftriaxone1g IV every 12 hours, Gentamycin 80 mg twice daily and Metronidazole PIV 500mg every 8 hours for 48 h, after change antibiotics according to antibiogram result if needed. The patient status is better, and the fever is no longer available, they can continue antibiotics orally for 7 days.

Contra-indication: if allergy to beta-lactam, Metronidazole 500mg orally twice daily and Clindamycin 300 mg orally twice daily for 7 days.

NOTE: - Surgical management needs to use antibiotherapy orally for 7 days, eg: Amoxicilline 500 mg every 8 h.
- Spontaneous abortions, If mother have a negative blood group Rhesus, Give Immunoglobulin Anti-D 300 µg IM single dose within 72 h.

Recommendations:

- Tell the patient to come back if bleeding, fever, foul smelling discharge or pelvic pain
- Screen and treat anemia, infection or retained tissue.
- Discuss family planning
- For repeated miscarriage need additional investigations.

IX. PROGNOSIS

- Because complication rates are similarly low for expectant, medical, and surgical management, the prognosis of early pregnancy loss is typically good.
- However, hemorrhage and infection due to miscarriage can contribute to maternal mortality, especially in low-income countries, where the social determinants of health decrease access to high-quality obstetrical care.
- Psychological counseling post-abortum for weeks to months after a miscarriage are often accompanied by feelings of grief, guilt, anxiety and depression for both the patient and her partner, especially in cases of recurrent loss, fertility challenges, loss of a highly desired pregnancy and in patients with pre-existing mental health concerns.

X. PREVENTION

- Random chromosomal abnormalities are unpreventable so preconception health should be optimized in order to reduce the chances of a future SAB. This may include avoiding stress, tobacco, moderate to heavy alcohol use, drug abuse when trying to conceive. Women should aim to achieve a healthy body weight prior to conception and should be consuming a daily multivitamin with folic acid (400 to 800 mcg) daily.
- If a woman is taking a teratogenic medication, she should be transitioned to an alternative prior to conception.

- Finally, women with medical problems such as diabetes mellitus, hypertension, lupus and thyroid disease should have their disease under control prior to conception.
- Attempting conception immediately after resolution of early pregnancy loss is safe, and couples who attempt conception within 3 months after miscarriage experience higher rates of successful pregnancy and live birth than those who postpone conception.

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SAFE ABORTION CARE

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I. DEFINITION

An induced abortion is when a pregnancy is intentionally ended through a medical procedure.

Unsafe abortion is defined by the World Health Organization (2014) as a procedure for terminating an unintended pregnancy carried out by either persons lacking the necessary skills or in an environment that does not conform to minimal medical standards, or both.

Globally around half of all unintended pregnancies end in induced abortion. Women under 25 years account for 34% of all unsafe abortions (11% among 15-19 years old and 23% among 20-24) (Shah & Ahman 2012). In Cambodia where abortion has been legal since 1997 induced abortion increases with age (National Institute of Statistics, Directorate General for Health, and ICF International, 2015). The percentage of women who have had at least one abortion increases sharply from less than 1 percent at age 15-19 to a peak of 21 percent at age 35-39 before declining to 20 percent at age 40-44 and 16 percent at age 45-49.

II. CLINICAL MANAGEMENT

i. Pre-abortion care

a. Medical history

The woman should be asked about the first day of her last menstrual period (LMP), i.e. the first day of bleeding and whether the menstruation was normal, as well as about her menstrual history, including the regularity of her cycles. Other symptoms in early pregnancy include breast tenderness and engorgement, nausea sometimes accompanied by vomiting, fatigue, changes in appetite, and increased frequency of urination.

History-taking should include:

- Personal and family history of relevant diseases
- Obstetric and gynecological history, including previous ectopic pregnancy
- Any bleeding tendencies or disorders
- History of or presence of sexually transmitted infections (STIs)
- Current use of medications,
- Known allergies,
- Risk assessment for violence or coercion. The health-care provider must be alert to the possibility of violence or coercion in the context of unintended pregnancy.

Determining the gestational age is a critical factor in selecting the most appropriate abortion method. Bimanual pelvic examination, abdominal examination and recognition of symptoms of pregnancy are usually adequate. Laboratory or ultrasound testing may also be used, if needed.

b. Physical examination

Basic routine observations (pulse, blood pressure and, in some cases, temperature) are useful baseline measurements. Health-care providers must confirm pregnancy and estimate its duration by a bimanual pelvic and an abdominal examination. Uterus that is larger than expected may indicate:

- A pregnancy that is more advanced than calculated from the date of the LMP,
- A multiple pregnancy,
- A full bladder,
- The presence of uterine fibroids or other pelvic tumors, or
- A molar pregnancy.

A physical examination is generally more accurate and reliable if the woman empties her bladder prior to the examination.

During the physical examination, the health-care provider should also assess whether the uterus is anteverted, retroverted or otherwise positioned in a way that might affect assessment of the gestational age or complicate a surgical abortion and recognize signs of STIs and other reproductive tract infections (RTIs), as well as health conditions, such as anaemia or malaria, that may require additional procedures or services, or referral.

c. Other investigations

Routine laboratory testing is not a prerequisite for abortion services. Where it is available, a scan can help identify an intrauterine pregnancy and exclude an ectopic one from 6 weeks of gestation. It may also help determine gestational age and diagnose pathologies or non-viability of a pregnancy.

d. Information and counselling

Every pregnant woman who is contemplating abortion should receive adequate relevant information and be offered counselling from a trained health-care professional with comprehensive knowledge and experience of different methods of abortion. Information must be provided to each woman, regardless of her age or circumstances, in a way that she can understand, to allow her to make her own decisions that is free from pressure about whether to have an abortion and, if so, what method to choose.

Provision of counselling to women who desire it should be voluntary, confidential, non-directive and by a trained person. If health-care workers suspect coercion, they should talk with the woman alone, or refer her for additional counselling. If staffs know or suspect that the woman has been subjected to sexual violence or other abuse, they should offer her referrals for other counselling and treatment services as appropriate.

Information regarding post-abortion contraception also needs to be provided.

ii. Methods of abortion

a. **Medical method of abortion** for pregnancies of gestational age up to 9 weeks – oral mifepristone followed by repeated doses of misoprostol. Success rate: 93-97%.

b. **Manual or electric vacuum aspiration** for pregnancies of gestational age up to 12 weeks. Success rate: 95-100%. Complication 2%. Cervical preparation before surgical abortion is recommended for all women.

c. For pregnancies of gestational age **more than 12 weeks**, mifepristone followed by repeated doses of misoprostol.

Medication for pain management for both medical and surgical abortions should always be offered and provided without delay. In most cases, analgesics, local anesthesia and/or conscious sedation supplemented by verbal reassurance are sufficient. The need for pain management increases with gestational age.

iii. After care and follow-up (contraceptive use)

- For surgical abortion, women can leave the health-care facility as soon as they feel able and their vital signs are normal.
- Following uncomplicated surgical and medical abortion using mifepristone with misoprostol, a follow-up visit may be scheduled at 7–14 days after the procedure.
- Before leaving the health-care facility following the surgical abortion procedure or administration of medical abortion pills, all women should receive contraceptive information and, if desired, the contraceptive method of their choice or referral for such services.
- Before leaving the facility, women should receive oral and written instructions about how to care for themselves after they leave. These instructions should include: how much bleeding to expect, how to recognize potential complications, and how and where to seek help if required. Where possible, a phone number that women could call to ask questions or express concerns may reduce the need to return to the clinic.

III. ALGORITHMS

The Abortion Law of Cambodia was passed in 1997[5], and the *Prakas*[6] was passed in 2002. The box below provides Article 8 of the Kram dated November 12th 1997 on abortion.

Box showing Article 8 of the Kram on Abortion

The law states that: abortion may only be carried out for those foetuses that are under 12 weeks old. If the foetuses are over 12 weeks old, they may be authorised to be aborted only if, after a diagnosis, it is found out that:

- There is a probable cause that such a foetus does not develop itself as usual or which may cause danger to the mother's life.
- The baby who is going to be born may have a serious and incurable disease.
- In case, if after victimised of a rape a woman became pregnant, the abortion may be carried out despite the above stated conditions. However in all cases, there must be a request from the concerned person – if such a person is 18 years old or above, or from an insistent request from parents or guardian and from the concerned person for women under 18 years old.
- Decisions on this above matter requires an approval from a group of 2 to 3 doctors and also a consent form from the concerned person (or her parents or guardian).

Under the declaration in the guidelines for the execution of the abortion law of 2002, several conditions are stipulated under which an abortion can be performed legally. These are:

- For each abortion, there must be written consent with signatures or thumbprints of the woman.
- Abortions can be performed only in hospitals, health centres, and clinics authorised by the Ministry of Health (MoH).
- Only physicians, medical assistants or secondary midwives can perform abortions, and they must have CAC training and a certificate from the MoH.
- Anyone not qualified to perform abortions under this declaration may be imprisoned for between one month and ten years for performing illegal abortions.
- Public and private facilities must record information about each abortion and provide monthly reports including number of first- and second-trimester abortions, the methods used, ages of clients, and number and reason for referral.

Protocol for medical abortion for 2nd trimester

Assessment

- Medical history
- Physical examination and determine gestational age
- Counselling and Informed consent
- Pain management medications: Non-narcotic analgesics such as nonsteroidal anti-inflammatory agents, Ibuprofen, when given Misoprostol. Adding dose as needed at appropriate intervals. Supplemental use of other drugs as needed (narcotics and/or anxiolytics)

Regimen

Mifepristone + Misoprostol (preferred regimen)

Misoprostol alone

Points to consider

- **If the foetus does not expel within 24 hours**

-Do an abdominal examination and possibly ultrasound to rule out the rare event of uterine rupture:

  - Repeat the original regimen or
  - Rupture the membranes and continue the same dose and interval of misoprostol administration
  - D&E, as an alternative to a prolonged induction procedure

- **If the placenta does not expel within 2 hours**
  - Use the forceps to grasp the base of the cord and apply slight tension on the cord or
  - Use misoprostol 400-600 mcg or
  - Vacuum aspiration should be performed to evacuate the placenta (MVA)
- **Others:**
  - Using misoprostol will develop a fever during the induction process, give paracetamol.
  - Previous uterine surgery / women with a scarred uterus

Medical abortion from 12-24 weeks gestational age

- Day 1 oral mifepristone, 200 mg, for cervical preparation followed 24-48 hours later by:
- Misoprostol, 400 mcg, vaginal or sublingual or buccal route, every 3 hours.

NB: Clinical re-evaluation if the foetus does not expel after 5 doses.

Medical abortion from 12-24 weeks gestational age with previous uterine surgery

- Day 1 oral mifepristone, 200 mg, for cervical preparation followed 24-48 hours later by:
- **12-16 weeks gestational age**: Misoprostol, 200 mcg, vaginal or sublingual or buccal route, every 4 hours.
- **16-24 weeks gestational age**: Misoprostol, 200 mcg, vaginal or sublingual or buccal route, every 6 hours.

NB: Clinical re-evaluation if the foetus does not expel after 5 doses.

Medical abortion from 24-26 weeks gestational age

- Day 1 oral mifepristone, 200 mg, for cervical preparation followed 24-48 hours later by:
- Misoprostol, 200 mcg, vaginal or sublingual or buccal route, every 4 hours.

NB: Clinical re-evaluation if the foetus does not expel after 5 doses.

Equipment and drugs required for emergency resuscitation

Management of the airway and respiration	Self-inflating (Ambu) bag Oral airway Oxygen supply Suction apparatus
Control of bleeding / haemorrhage	Oxytocic drugs (ergometrine, oxytocin) IV fluids
Intravenous fluid replacement	IV set up
Control of pain	Anxiety: • Verbal support • Diazepam (Valium): -PO: 10mg 1 hour prior to procedure -IV: 2-5mg IV 20mn prior to procedure Cervical Dilatation : • Xylocaine (Lidocaine, Lignocaine) : -15-20ml of 1% solution in paracervical block -Not to exceed 4.5 mg/kg Uterine Manipulation: • Ibuprofen (Naproxen, Advil): -PO: 400-800mg 1 hour before procedure • Acetaminophen (Tylenol, Paracetamol): -PO: 500-1000mg 30-60mn before procedure

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GESTATIONAL TROPHOBLASTIC DISEASES (GTD)

Prof. Sann Chansoeung, Prof. Pech Sothy, Prof. Kruy Leangsim, Prof. Koum Kanal, Prof. Lieng Chanrith, Prof. Keth Lysotha, Prof. Ass. Korn Aun, Dr. Khor Hok Sunn. Dr. Uy Kyna, Dr. Ros Saphath. Dr. Krouch Rayounette, Dr. Sophean Sahakcheat, Dr. Leap Sovann, Dr. Chhit Maryan

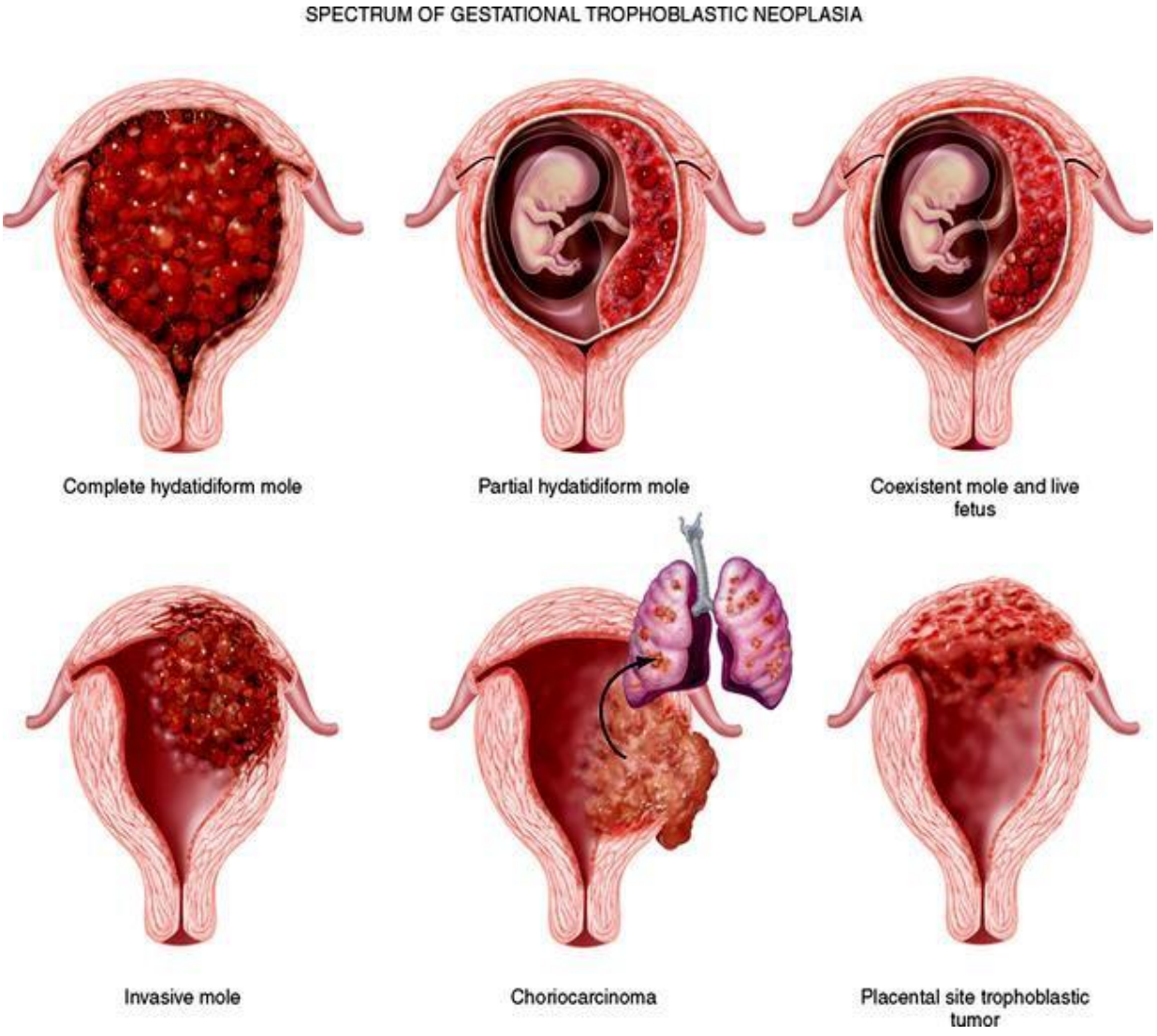
I. BACKGROUND

- Gestational trophoblastic diseases (GTD) is a term for a group of tumors with abnormal trophoblast proliferation produce human chorionic gonadotrophin (Beta hCG).
- Gestational trophoblastic neoplasia (GTN) is a type of GTD that is almost always malignant.
- GTN is a rare variation of pregnancy of unknown etiology and usually presents as a benign disease called hydatidiform mole (molar pregnancy).
- Persistent or malignant disease will develop in approximately 20% of patients with molar pregnancy and it is responsive to chemotherapy if earlier detection. It may
- occur with any pregnancy, although it most commonly follows molar pregnancy.
- Key clinical features of GTN include:
  1. Clinical presentation as pregnancy,
  2. Reliable means of diagnosis by pathognomonic ultrasound findings, and
  3. A specific tumor marker (quantitative serum Beta-hCG).

II. CLASSIFICATION OF GTD

GTD histologically divided into:

- Benign: Hydatidiform moles/ molar pregnancy (partial & complete represent premalignant condition)
- Malignant (GTN):
  - Invasive mole (IM)
  - Choriocarcinoma (CC)
  - Placental site trophoblastic tumor (PSTT)
  - Epithelioid trophoblastic tumor (ETT)



* Dr Tabitha Oosterhouse and Ms Charity Knight, Protocol for the Management of Molar Pregnancy 2023

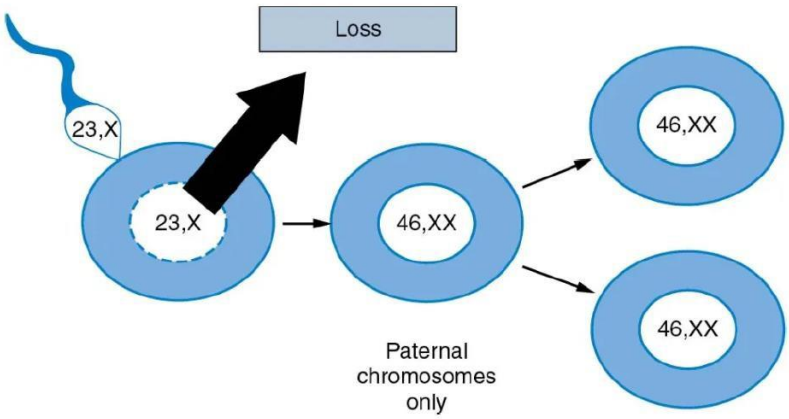
III. HYDATIDIFORM MOLES (HMS)

i. Overview

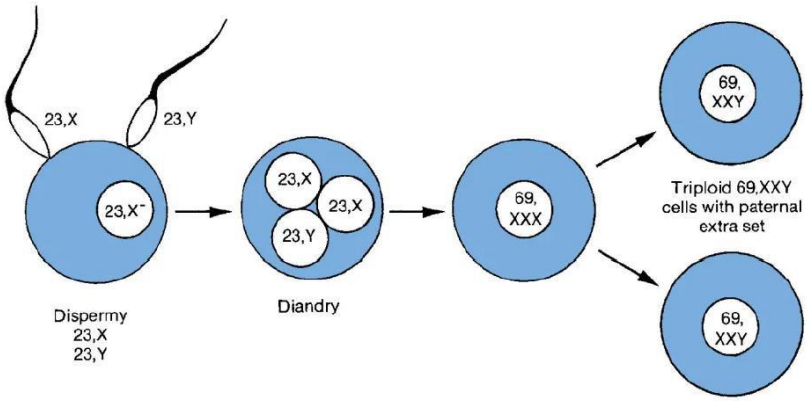
- Is the most common type of GTD, also called a molar pregnancy with unknown causes.
- A hydatidiform mole is not cancerous but malignant transformation is possible.
- Histologically characterized by: trophoblastic proliferation & edema of villous stroma (hydropic).
- Complete moles do not have identifiable embryonic or fetal structures.
- Partial moles are characterized by focal trophoblastic proliferation, degeneration of placenta, & identifiable fetal/embryonic structures.

ii. Pathogenesis

Complete moles have chromosomes entirely of paternal origin. The karyotype of a complete mole is usually 46, XX.



Partial mole is usually a triploid: one haploid set of maternal chromosomes and two haploid sets of paternal chromosomes.



(From Szulman AE, Surti UL. The syndromes of partial and complete molar gestation. Clin Obst et Gynecol 1984)

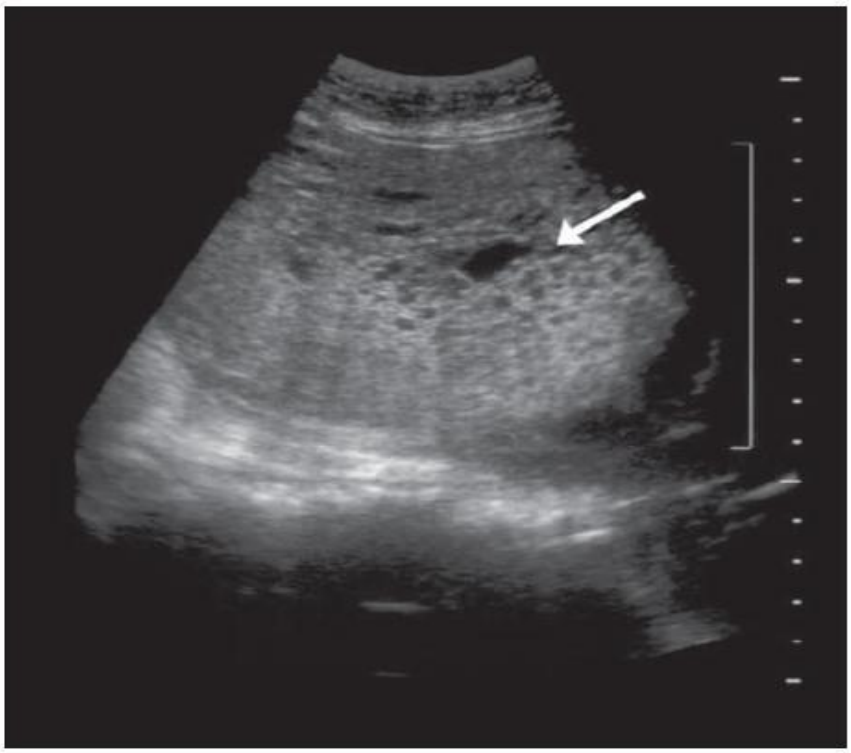
iii. Clinical presentation

a. Clinical presentation of complete mole: Inpatients with confirmed pregnancy:

- Vaginal bleeding occurring from 6-14 weeks of gestation from spotting to severe hemorrhage is very common in most of cases.
- Uterus enlarge greater than expected with soft consistency.
- Ultrasonography provides image of “Snowstorm” appearance, absence of fetal heart tones Elevation of hCG levels above expected for gestational age. Approximately half of patients with complete mole have pre-evacuation hCG levels >100,000 mIU/ml.
- Medical complications can be observed such as hyperemesis gravidarum, anemia, hyperthyroidism, pregnancy-induced hypertension and respiratory distress.

- The early use of ultrasonography in the first trimester and accurate measurement of hCG lead to early diagnosis of hydatiform mole, the medical complications become less frequent.
- and bilateral theca lutein cyst of the ovaries.

Ultrasound imaging of complete mole



"Snowstorm" appearance of complete mole on ultrasound examination, Soper JT. Gestational trophoblastic disease. Obst et Gynecol. 2006;108(1):178

b. Clinical presentation of partial mole
History:
- Vaginal bleeding
- Usually diagnosed as missed/incomplete abortion
- Physical examination:
- The uterus is often larger than expected for gestational age.

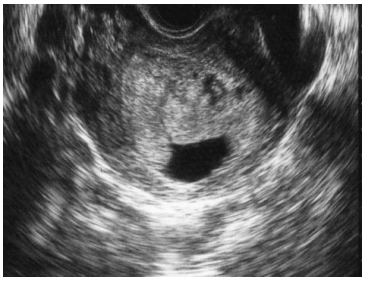
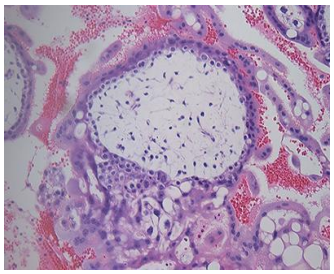
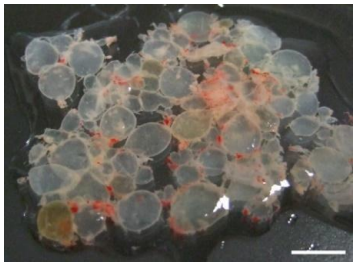
iv. Diagnosis of HMs

Diagnosis is based:
- Medical history
- Clinical examination
- Ultrasound examination
- Serum beta-hCG levels
- Histopathological examination

Preoperative evaluation of HMs
- Complete blood count (CBC)
- Blood typing with antibody screen

- Beta-hCG level
- Creatinine levels
- Coagulation profile
- Liver function testing
- Chest X-ray
- Other appropriate tests if clinical evidence
- Hyperthyroidism and or gestational hypertension

v. Management for hydatidiform moles (HMs)
   a. Treatment:
      - Vacuum aspiration of molar tissue is carefully observed under ultrasound with oxytocin infusion
      - Pathological examination is strongly recommended
      - Ultrasound check before discharge (if necessary)
      - The duration of hospital stays or discharge is depending on each hospital
      - Wait until 2 weeks after evacuation to check again: beta-hCG level, ultrasound or other investigations if having any clinical evidences

*Developing GTD guideline in Cambodia, Prof. Eiko Yamamoto, Nagoya University Graduate School of Medicine 2023

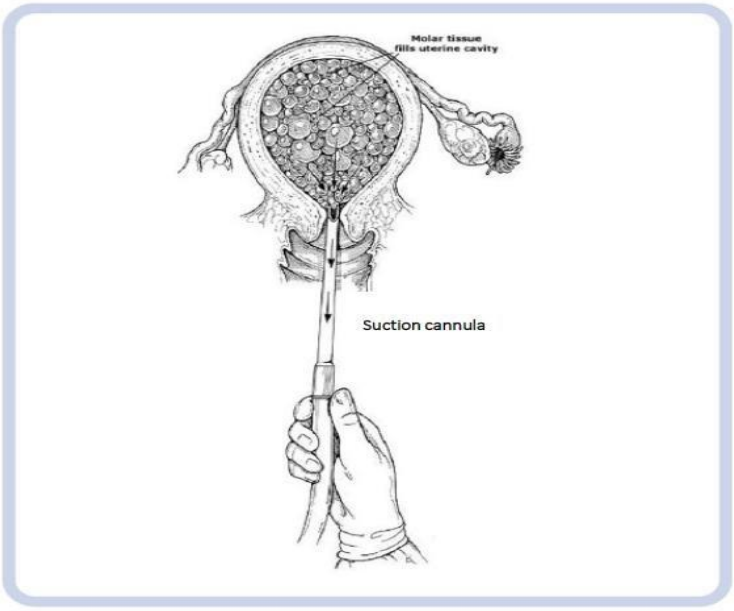


*Figure from Courtesy of William J Mann, Jr, M

b. Follow-up

The aims of follow-up are:

- To confirm successful treatment and to identify women with persistent or malignant GTD who may require adjuvant chemotherapy or surgery at an early stage
- Persistent vaginal bleeding and above all elevation of serum beta-hCG levels are the main indicators of residual disease.
- Beta-hCG follow up: every two weeks after evacuation, until 3 negatives (≤ 0.5mIU/mL); then monthly for 6 times.
- Pelvic examination
- Pelvic ultrasound after 14 days of evacuation (>17mm re-evacuation)
- Chest X-ray for metastasis if having clinical evidences or when beta-hCG rise.
- Contraceptive: Oral contraceptive start after discharge; Intrauterine device (IUD) is prohibited
- Duration of follow up:

  The duration of follow up should be dependent on type of GTD:

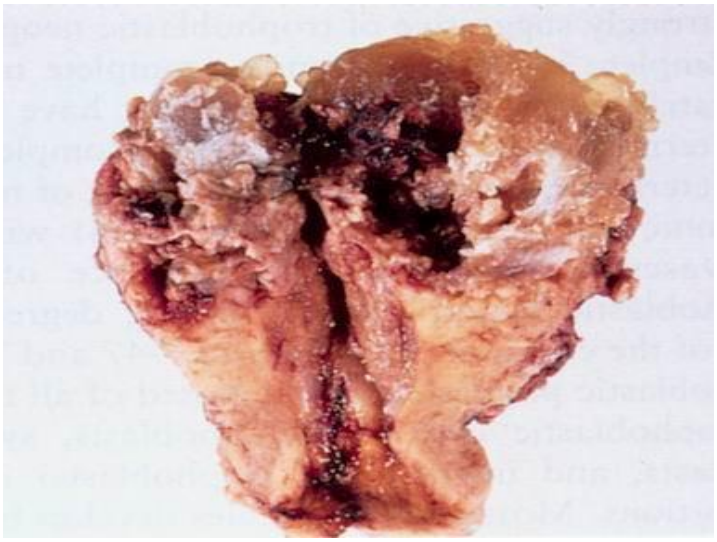
  - Partial mole: stop when beta-hCG normal on 2 samples taken 4 weeks apart
  - Complete mole: at least 6 months from the date of uterine evacuation (Next pregnancy will allow at least 1 year after evacuation)
  - Any mole with a multiple pregnancy: monthly for 12 months.

IV. GESTATIONAL TROPHOBLASTIC NEOPLASIA

i. Diagnosis:

- When beta-hCG plateaus +/- 10%, or rises >10% of three consecutive tests over four weeks (day1, day14, day28) before reaching normal level, the patient is diagnosed as gestational trophoblastic neoplasia (GTN). Most cases are low-risk GTN (invasive mole).
- Confirm histologic evidence of choriocarcinoma
- Evidence of metastasis
- Raised hCG level 6 months after evacuation.

Gestational trophoblastic neoplasia (GTN) is a term used to describe GTD requiring chemotherapy.

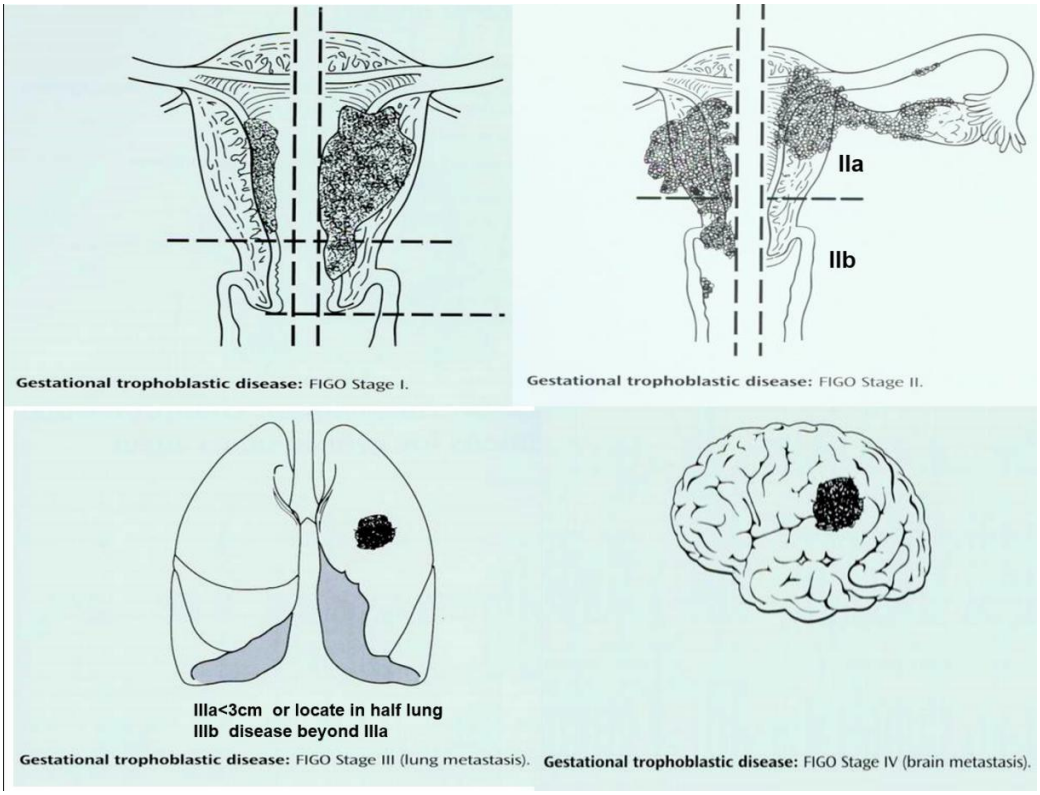


*Invasive hydatidiform mole infiltrating the myometrium
[Gestational trophoblastic disease, Fahmida Aqeel, Associate Professor,

FIGO staging system for GTN

Stage	
Stage I	Disease confined to the uterus
Stage II	Disease outside of uterus but is limited to the genital structures
Stage III	Disease extends to the lungs with or without known genital tract involvement
Stage IV	All other metastatic sites

(Lurain. Gestational trophoblastic disease II. Am J Obstet Gynecol 2001)



Gestational trophoblastic disease: FIGO Stage I.

Gestational trophoblastic disease: FIGO Stage II.

Gestational trophoblastic disease: FIGO Stage III (lung metastasis).

Gestational trophoblastic disease: FIGO Stage IV (brain metastasis).

*Dr Mohammed Ashraful Amin (ASIF) ID-927 Case presentation. dated 10.10.2024

Revised (2010) FIGO scoring system for Gestational trophoblastic neoplasia

	FIGO Score[a]			
Finding	0	1	2	4
Age (years)	<40	≥40		
Antecedent pregnancy	Hydatidiform mole	Abortion	Term pregnancy	
Interval from last pregnancy (months)	<4	4–6	7–12	>12
Pretreatment hCG level	1,000	1,000–10,000	>10,000–100,000	>100,000
Largest tumor size including uterus (cm)	3	3–4	≥5	
Site of metastases	Lung	Spleen, kidney	Gastrointestinal tract	Brain, liver
Number of metastases	0	1–4	5–8	>8
Previous failed chemotherapy			Single drug	Two or more drugs

a: The total score for a patient is obtained by adding the individual scores for each prognostic fact

ii. Treatment:

1. The chemotherapy: is the following:
   (1) When pathological diagnosis is made: Invasive mole → single-agent chemotherapy
   Choriocarcinoma → multi-agent chemotherapy (do at oncology service)
   (2) When diagnosis is made clinically (without surgery)
   Total score ≤ 6 = low-risk GTN → single-agent chemotherapy
   Total score ≥ 7 = high-risk GTN → multi-agent chemotherapy (do at oncology service)
2. Surgery:
   - When patients do not hope a baby and GTN lesion found in the uterus, hysterectomy can be performed but either of ovaries should be left.
   - When patients hope to keep fertility, GTN should diagnosed clinically.
   - After surgery, chemotherapy is needed until beta-hCG is down to the normal range.
3. Radiation:
   Radiation is not effective in GTN treatment.
4. Chemotherapy:
   GTN is greatly sensitive to chemotherapy with curable rates surpassing 90%.

For low-risk GTN patients, single-agent chemotherapy recommended.is Methotrexate (MTX), most commonly prescribed as a first-line treatment due to low toxicity.

Women with an initial pretreatment hCG of 1000 IU/l may stay as inpatients for longer as they have a higher risk of bleeding; the larger tumors shrink rapidly with the initiation of chemotherapy:

- During chemotherapy, beta-hCG should be checked at least once a course (before starting each course).
- If hCG values have not fallen by at least 10% over two cycles of therapy or have risen more than 10% over two cycles, or if significant toxicity has developed, alternative

therapy should be used.

- Chemotherapy should be given until beta-hCG is <5IU/L and then 3 additional courses of chemotherapy is necessary.
- After chemotherapy is finished, beta-hCG should checked every month for 12 months.
- Next pregnant is allowed 12 months after chemotherapy. Patients should take contraception pills correctly.

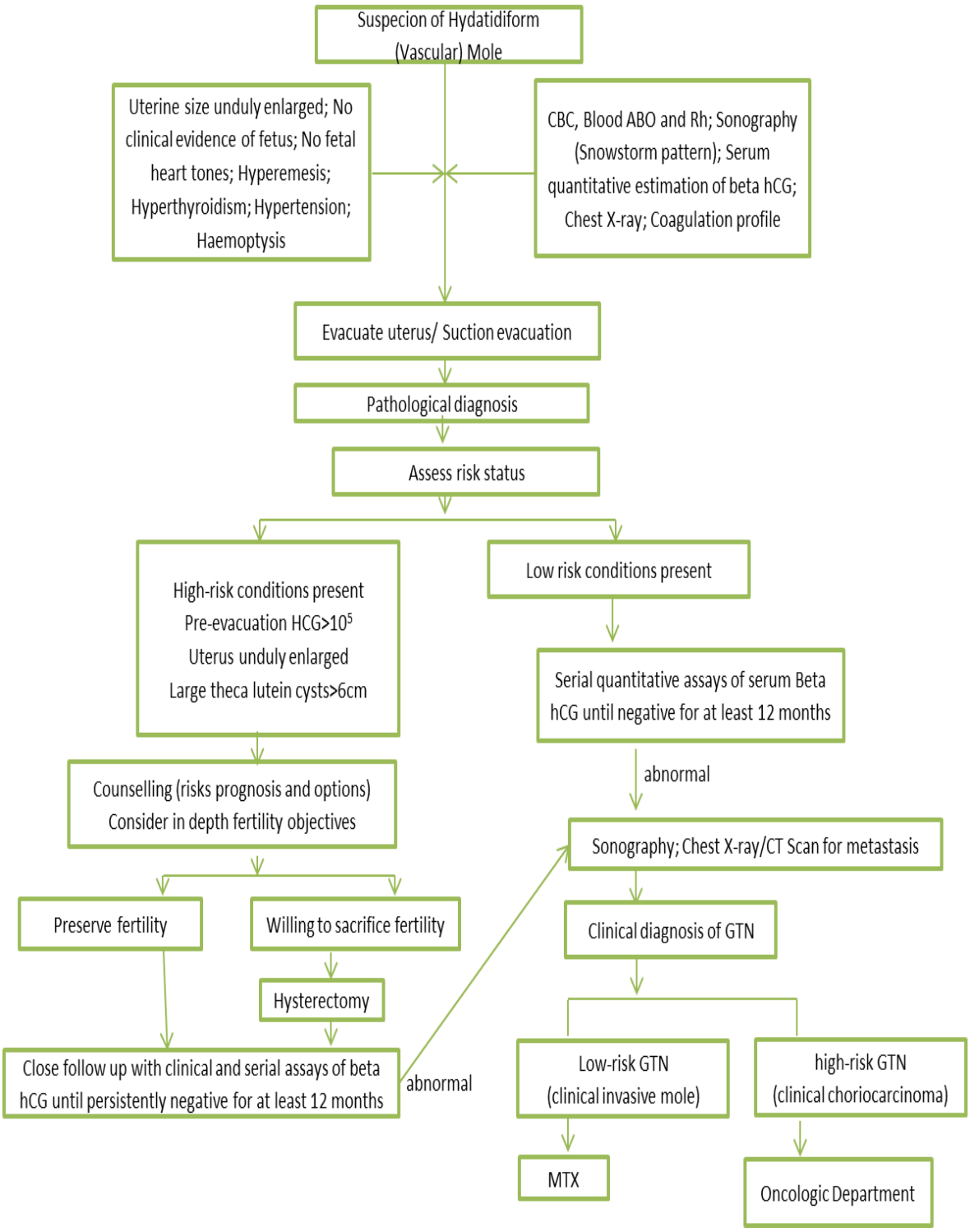
Single-agent chemotherapy (low risk GTN, invasive mole, clinical invasive mole
Methotrexate regimen:

1. First line: 5-day MTX (methotrexate)				
Day 1-5	MTX	0.4 mg/kg daily for 5 days (or 20mg/body)	IM	Every 2 weeks (interval: 9 days (day6-14)

- Possible side effects of Methotrexate are increased risk of infection, nausea and vomiting, abdominal pain or cramps, sensitive skin, mouth ulcers, and dry eyes.
- When side effect is severe (stomatitis, elevation of liver enzyme) the 5-day regimen can be shortened to 4-day.
- Calcium leucovorin (Folinic acid) rescue 0.1mg/kg in severe Methotrexate toxicity.
- When toxicity occurs or hCG dose not decrease refer to oncology service.

* When beta-hCG > 100,000 IU/L, and/or age ≥40 years, hysterectomy after MVA is an option to reduce the incidence of invasive mole. However, the incidence of invasive mole cannot be zero after hysterectomy, and the patients should be followed using pregnancy test or beta-hCG.

V. ALGORITHMS



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VAGINAL DISCHARGE

Dr. Chhun Samsorphea, Dr. Lay Sanine, Prof. Ass. Korn Aun, Dr. Uy Sopha, Dr. Sea Sreyla, Dr. Lim Sokong

I. DEFINITION

Vaginal discharge is a mixture of cervical mucus, vaginal epithelial cells, vaginal transudate, and secretions from Bartholin's and Skene's glands. It is a normal physiological secretion that plays a crucial role in maintaining vaginal homeostasis, lubrication, and protection against pathogenic organisms.

Normal changes in vaginal discharge:

- Volume: 1 to 4 ml per 24 hours
- Color: White or transparent
- Consistency: Thick or thin
- Odor: Mostly odorless
- Role: Maintains vaginal hygiene, lubrication, prevents dryness, irritation and pH balance which prevents pathogenic bacterial growth.
- Composition: Cervical mucus, epithelial cells, and bacteria (Lactobacillus spp.)

Vaginitis is the general term for the disorders of the vagina caused by infection, inflammation, or changes in the normal vaginal flora.

Abnormal vaginal discharge (AVD) is defined as anyone of the three presentations:

1. Excessive vaginal discharge not associate with menstruation, pre, mid, and post period
2. Offensive or malodorous discharge
3. Yellowish or mucopurulent discharge
4. Vaginal irritation
5. Urinary symptoms

II. ETIOLOGIES

Pathological vaginal discharge occurs due to infections, hormonal imbalances, or inflammatory conditions, genital tract neoplasm.

Around 90% of vaginitis is caused by infection, mainly bacterial vaginosis, vulvovaginal candidiasis, and trichomonas. These three diagnoses should be excluding in all patients before considering other less common causes.

Less common cause include: vaginal atrophy/atrophic vaginitis, cervicitis, foreign body, irritants and allergens, and several rare entities, including some systemic medical disorder.

III. DIAGNOSTIC PROCEDURE

Clinical Assessment of Vaginal Discharge

Assessment Component	Details
1. History of Presenting Complaint	• Color of discharge • Odor • Presence of blood • Relationship to menstrual cycle • Associated symptoms
2. Factors Affecting the Vagina	• Past medical history • Sexual history • Obstetric history • Gynecological history • Contraception history • Menstrual history • Drug history • Family history • Social history
3. Physical Examination	• Patient examined in lithotomy position • Visual inspection of external genitalia and vaginal walls • Speculum exam to assess cervical and vaginal discharge (infectious vs. non-infectious) • Bimanual exam to assess tenderness, masses, or inflammation
4. Laboratory Investigations	• Vaginal pH test • Vaginal swab for microscopy and culture • NAAT (Nucleic Acid Amplification Test) for STIs

Infectious vaginal discharge characteristics

Cause	Pathogen	Mechanism	Symptoms	Discharge characteristics
Bacterial Vaginosis (BV)	*Gardnerella vaginalis and anaerobes*	Disruption of normal Lactobacillus → Overgrowth of anaerobic bacteria	Malodor, increased discharge	Thin, gray-white, fishy odor discharge
Candidiasis	*Candida albicans*	Yeast overgrowth due to antibiotic use, diabetes, immunosuppression	Itching, dysuria, vulvar erythema	Thick, white, curd- like discharge, intense itching
Trichomoniasis	*Trichomonas vaginalis*	STI with flagellated protozoa causing inflammation	Itching, dysuria, dyspareunia	Yellow-green, frothy, foul- smelling discharge
Gonorrhea & Chlamydia	*Neisseria gonorrhoeae, Chlamydia trachomatis*	STI affecting cervix and causing mucopurulent cervicitis	Mucopurulent discharge, postcoital bleeding	Yellow-green, mucopurulent discharge
cervical Cancer			Watery, blood-streaked, or foul-smelling	Persistent discharge, postcoital bleeding, pelvic pain, late weight loss
Endometrial Cancer			Watery or bloody discharge, often in postmenopausal	Postmenopausal bleeding, pelvic discomfort
Advanced Gynecological Cancers			Malodorous, necrotic discharge	Severe pelvic pain, bleeding, weight loss, fatigue

Non-infectious vaginal discharge diagnosis

	Pathophysiology	Symptoms
Atrophic Vaginitis	Estrogen deficiency in postmenopausal women	Dryness, irritation, dyspareunia
Foreign Body (e.g., tampon, contraceptive devices)	Retained objects cause bacterial overgrowth	Foul-smelling discharge, pelvic pain
Irritants/Allergens	Douching, perfumed soaps, latex	Burning, irritation
Endocrine Disorders (Diabetes, PCOS)	Altered vaginal flora	Recurrent infections

Diagnostic tests

Test	Purpose
pH Testing	BV (>4.5), Trichomoniasis (>5.0), Candida (<4.5)
Vaginal swab	Clue cells (BV), hyphae (Candida), motile trichomonas (Trichomoniasis)
PCR Test (NAAT)	Gold standard for STIs, BV, Candida
Gram Stain	Nugent Score for BV
Culture	For recurrent infections

Infectious vaginal discharge diagnosis

Causes	Pathogen	Diagnosis
Bacterial Vaginosis (BV)	*Gardnerella vaginalis and anaerobes*	Amsel criteria: pH >4.5, Clue cells, positive whiff test
Vulvovaginal Candidiasis (VVC)	*Candida albicans*	KOH test, culture
Trichomoniasis	*Trichomonas vaginalis*	Vaginal swab, NAAT
Gonorrhea & Chlamydia Cervicitis	*Neisseria gonorrhoeae, Chlamydia trachomatis*	NAAT

Non-infectious vaginal discharge diagnosis

Causes	Symptoms	Diagnosis-investigations
Atrophic Vaginitis	Dryness, irritation, dyspareunia	Vaginal pH >5, epithelial thinning
Foreign Body (e.g., tampon, contraceptive devices)	Foul-smelling discharge, pelvic pain	Pelvic exam
Irritants/Allergens	Burning, irritation	History of exposure
Endocrine Disorders (Diabetes, PCOS)	Recurrent infections	Blood glucose, hormonal assays

IV. COMPLICATIONS

Abnormal vaginal discharge can indicate infections or underlying medical conditions. Left untreated, these conditions can lead to serious health complications.

1. Bacterial Vaginosis (BV)
   - Increased susceptibility to STIs (e.g., HIV, chlamydia, gonorrhea, HPV): BV alters vaginal pH, making it easier for pathogens to invade.
   - Pelvic Inflammatory Disease (PID): BV can ascend to the upper reproductive tract, causing PID, which increases infertility risk.
   - Pregnancy Complications: Preterm labor, premature rupture of membranes, low birth weight.
2. Sexually Transmitted Infections (STIs): Chlamydia, Gonorrhea, Trichomoniasis
   - Pelvic Inflammatory Disease (PID): Chronic inflammation damages fallopian tubes, leading to infertility and ectopic pregnancy. The symptoms: Purulent vaginal discharge, pelvic pain, fever.
   - Increased HIV Transmission Risk: STIs increase susceptibility to HIV infection by disrupting vaginal mucosa.
   - Adverse Pregnancy Outcomes: Untreated STIs may cause miscarriage, stillbirth, neonatal pneumonia, or conjunctivitis.
3. Vulvovaginal Candidiasis
   - Recurrent candidiasis (≥4 episodes/year), often linked to diabetes or immune suppression.
   - Severe inflammation, ulceration, and secondary bacterial infections.

V. MANAGEMENT

Non-infectious vaginal discharge

Causes	Management
Atrophic Vaginitis	Vaginal estrogen
Foreign Body (e.g., tampon, contraceptive devices)	Foreign body removal
Irritants/Allergens	Avoid triggers, antihistamines
Endocrine Disorders (Diabetes, PCOS)	Manage underlying condition

Infectious vaginal discharge characteristics

Condition	First-Line Treatment	Alternative
Bacterial Vaginosis	Metronidazole 500mg BID × 7 days	Clindamycin cream
Candidiasis	Fluconazole 150mg PO single dose	Topical clotrimazole
Trichomoniasis	Metronidazole 2g PO single dose	Tinidazole 2g PO
Gonorrhea	Ceftriaxone 500mg IM + Azithromycin 1g	Doxycycline 100mg BID × 7 days

Management of Vaginal Discharge in Gynecological Cancers

Aspect	Details
1. Identify Underlying Cause	Vaginal discharge in cancer is **secondary** to tissue necrosis, ulceration, or infection due to the tumor. A **confirmed cancer diagnosis** (e.g., cervical or endometrial cancer) must guide treatment.
2. Cancer-Specific Treatment	Management depends on **cancer type and stage**: - **Surgery (hysterectomy, radical trachelectomy)** - **Radiotherapy** - **Chemotherapy** - **Concurrent chemoradiation** for advanced cervical cancer
3. Symptomatic Relief of Discharge	- **Vaginal irrigation** with saline (in selected cases) - **Antibiotics** if secondary infection is suspected - **Metronidazole** may reduce anaerobic odor-producing bacteria
4. Palliative Care (Advanced stages)	- Local wound care for ulcerated tumors - **Antibiotics** for secondary infection - **Deodorizing agents** (e.g., metronidazole gel, activated charcoal dressings) to control odor
5. Hygiene & Comfort	- Daily perineal hygiene - Use of **absorbent pads** - Psychological support for distress due to odor or bleeding

VI. PREVENTION

Education and preventive measures reduce recurrence and improve women's health. Preventive strategies:

- Safe Sex Practices: Use of condoms reduces STIs.
- Avoid Douching & Irritants: Alters vaginal flora.
- Regular STI Screening: Early detection in high-risk populations.
- Treatment Compliance: Complete full course of prescribed medication.
- Probiotics: Some studies suggest Lactobacillus can restore normal flora.

Normal changes in vaginal discharges

Condition	First-Line Treatment	Alternative
Bacterial Vaginosis	Metronidazole 500mg BID × 7 days	Clindamycin cream
Candidiasis	Fluconazole 150mg PO single dose	Topical clotrimazole
Trichomoniasis	Metronidazole 2g PO single dose	Tinidazole 2g PO
Gonorrhea	Ceftriaxone 500mg IM + Azithromycin 1g	Doxycycline 100mg BID × 7 days

Life Stage	Characteristics
Neonatal Period	Estrogen-induced, whitish discharge
Childhood	Minimal discharge, neutral pH(~7)
Puberty & Reproductive Age	Increased estrogen → Increased discharge, pH ~4.0-4.5
Menstrual Cycle Variation	Ovulatory phase: Clear, Stretchy mucus (Spinnbarkeit Phenomenon)
Pregnancy	Increased secretions due to high estrogen and progesterone

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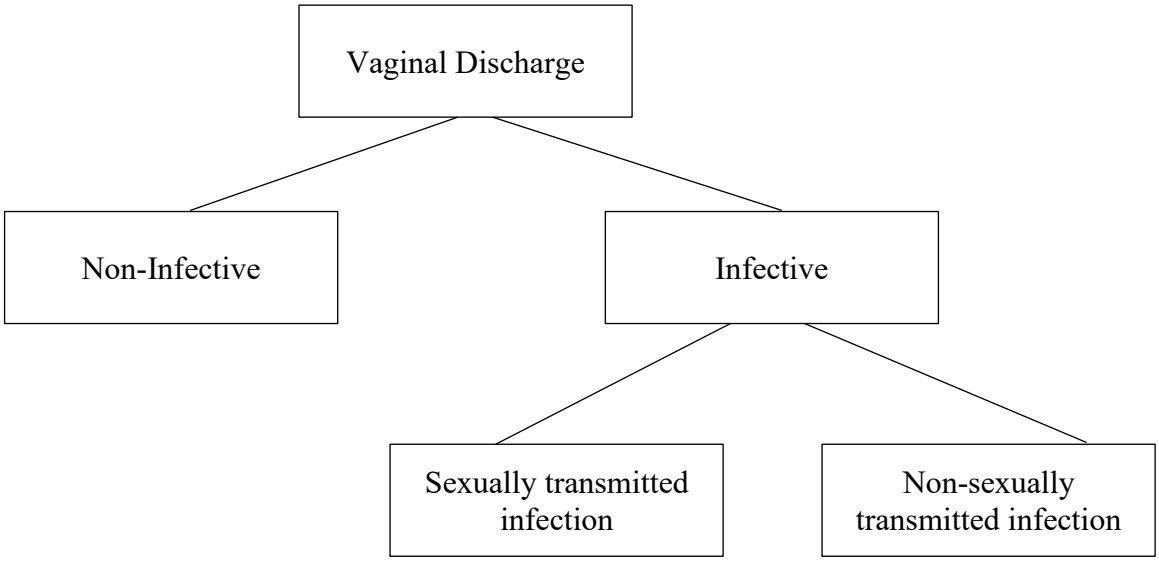
VII. ALGORITHMS



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MANAGEMENT OF ADNEXAL MASS

Prof. Ass. Korn Aun, Prof. Lieng Chanrith, Prof. Pech Sothy, Prof. Koum Kanal, Dr. Sophean Sahakcheat

I. EPIDEMIOLOGY

Prevalence is estimated at:

- 15-20% in post-menopausal women
- 7% in asymptomatic women of childbearing age
- Incidence during pregnancy: 0.5 to 5%.

II. CLASSIFICATION

Classification is carried out in 2 stages:

1. Is it a functional cyst or an organic cyst?
2. If the cyst is organic, is it benign or malignant?

III. DIAGNOSIS

These depend on age, menopausal status, circumstances of discovery and the existence of clinical signs. Clinical signs are not very specific, but certain characteristics can be identified, depending on age, menopause and pregnancy.

IV. INVESTIGATION

The diagnostic approach, based primarily on trans-vaginal ultrasonography.

i. Ultrasound and Doppler

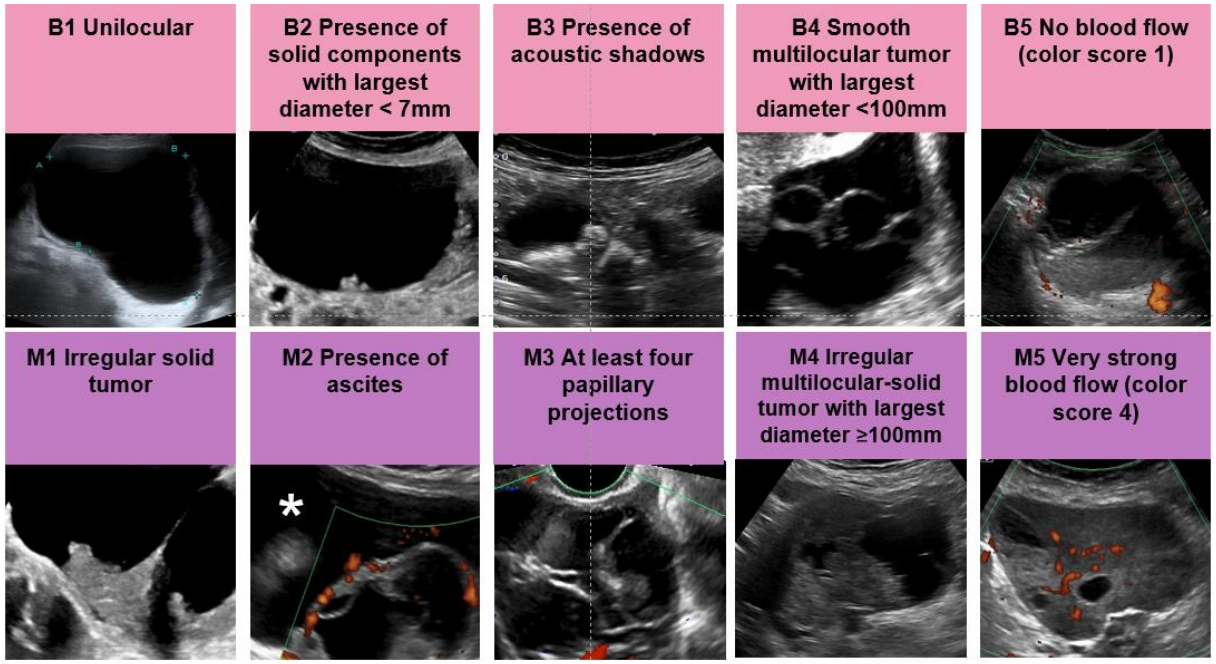
Pelvic ultrasound, performed vaginally, is the first-line examination. The various ultrasound signs will be described and grouped according to whether they indicate benign or malignant potential.

The classification of IOTA (International Ovarian Tumor Analysis) presents 5 signs in favor of benign B and 5 in favor of a malignant M process.

Rules for predicting a malignant tumor (M rules)	
M1	Irregular solid tumor
M2	Presence of ascites
M3	At least 4 papillary projections
M4	Irregular multilocular solid tumor ≥10 cm
M5	Very strong blood flow (CS 4)

Rules for predicting a benign tumor (B rules)	
B1	Unilocular cyst
B2	Presence of solid components, largest solid component < 7 mm
B3	Presence of acoustic shadows
B4	Smooth multilocular tumor < 10 cm
B5	No blood flow (CS 1)

1 or more M rules	**No B rules**	**Malignant**
1 or more B rules	**No M rules**	**Benign**
Both M and B rules apply		**Cannot be classified**
None of the rules apply		**Cannot be classified**



ii. MRI and CT scan

In patients with an undetermined ovarian mass on ultrasound, MRI increases diagnostic specificity and sensitivity. MRI provides better tissue characterization than CT.

iii. Tumor markers: **Ca125**

Ca125 is the most important tumor marker in ovarian cancer; it is a marker for epithelial tumors and may be missed in non-epithelial ovarian tumors. It may be moderately elevated for non-cancerous conditions such as endometriosis.

V. THE DECISION TREE

The proposed decision tree is based on IOTA criteria; these criteria are relevant.

In the case of a purely unilocular cystic mass (and all IOTA benignity criteria) of ≤ 5cm, therapeutic abstention and surveillance are the rule. 60% of these cysts disappear after 3 months for functional cyst and persistent for organic cyst.

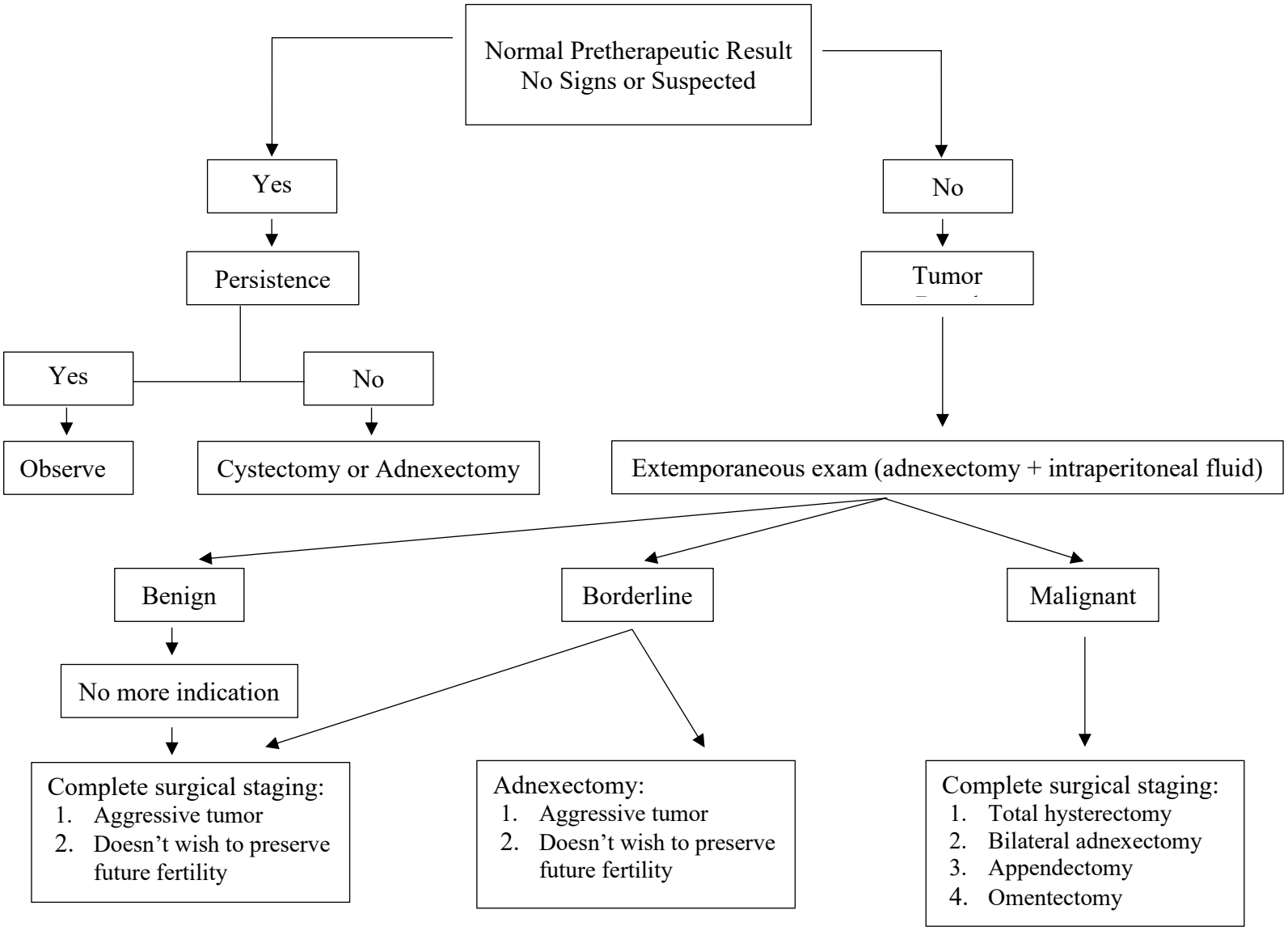
The indication for surgery is based on:

- ultrasonographic signs suggesting malignancy
- tumors of undetermined nature (see IOTA)
- cysts of benign appearance but ≥ 7cm
- painful symptoms suggesting torsion
- persistence of cyst

If surgery is indicated, the aim of surgical treatment is to:

- ensure complete removal of the cyst
- limit the risk of recurrence

- prevent any risk of tumor dissemination in the case of malignancy,
- and to preserve as much healthy ovarian tissue as possible, so as not to compromise future fertility in premenopausal women.



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SALPINGITIS (UPPER PID)

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I. DEFINITION

Acute or chronic infection of the tubes, ascending from the vagina or cervix.

II. RISK FACTORS AND CAUSES

i. Risk factors

Salpingitis mainly affects young women in the reproductive age with multiple sexual partners or their partners have multiple sexual partners, an intrauterine device (IUD, etc.), and/or a history of sexually transmitted diseases (STDs).

ii. Causes

Salpingitis is mainly due to bacterial infections

The main pathogens: agents responsible for sexually transmitted infections (STIs)

- Chlamydia trachomatis
- Neisseria gonorrhoeae
- Mycoplasma genitalium
- Opportunistic pathogenic germs from the vaginal flora
- Streptococci, staphylococci, enterobacteria, (E. coli +++, Klebsiella, anaerobes, Bacteroides fragilis)

III. DIAGNOSIS

i. Clinical argument

- Asymptomatic, fever - pelvic pain - dirty leukorrhea – metrorrhagia - dyspareunia
- Speculum exam: to check for vaginal wall, aspect of cervix and discharge
- Bimanual examination: to check for tenderness and discharge

ii. Investigations

a. Laboratory test

- CBC, CRP or ESR (often normal in the absence of complications): leucocytosis with neutrophilia and raised CRP or ESR

- Beta-hCG to eliminate ectopic pregnancy
- Urinalysis (eliminate pyelonephritis)
- PCR on vaginal swab to detect an STI
- Endocervical sampling with suitable transport medium (search for other pathogens)
- Removal of a possible IUD and culture with sensitivity test
- Serology (according to STI risk): syphilis, HIV-1 and 2 (patient's agreement), Hepatitis B and C; TB screening test

b. Imaging/ Radiology

- Transvaginal and/or abdominal ultrasound: to image the pelvic organs specially the fallopian tubes: Evidence of inflammatory collection or abscess and demonstrating thickened, fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex;
- Doppler studies indicating pelvic infection (e.g., tubal hyperemia)
- Laparoscopy: is visualizing the inflammatory tubes, often associated with abscesses and pelvic adhesions. It also allows samples to be taken for bacteriological purposes, and it can have a therapeutic role (adhesiolysis and drainage of possible abscesses).
- Abdomino-pelvic region CT-Scan or MRI: can do differential diagnosis with acute appendicitis and others; demonstrating thickened, fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex

IV. DIFFERENTIAL DIAGNOSIS

- Acute appendicitis
- Urinary infection
- Other pelvic pain
  - Adnexal torsion
  - Endometriosis
  - Ovarian pathology (oophoritis etc.)
  - Peri-ovulatory and peri-menstrual pain
  - Diverticular sigmoiditis

V. COMPLICATIONS

- Acute complications: Pelvic abscess: pyosalpinx, ovarian abscess, abscess of the recto-uterine Douglas pouch; Tubo-ovarian abscess, Pelvi-peritonitis, Death
- Chronic complications: Infertility, Ectopic pregnancy and Chronic pelvic pain, Perihepatitis (Fitz-Hugh-Curtis syndrome)

VI. MANAGEMENT

The goals of management are:

- **Etiological treatment:** intravenous or intra muscular or per os antibiotic therapy based on AB sensitivity test or empiric and broad-spectrum coverage of likely pathogens
- **Symptomatic treatment:** analgesics, non-steroidal anti-inflammatory drugs (NSAIDs) with gastroprotective agents
- **Management of the sexual partner(s):** assessment of sexually transmitted infections (STIs), and antibiotic therapy.

i. Acute salpingitis

- Admit the patient
- **First line treatment: Ceftriaxone** 1 g IV every 24 hours plus **Doxycycline** 100 mg orally every 12 hours plus **Metronidazole** 500 mg orally or IV every 12 hours at least 3 days;
- After clinical improvement with parenteral therapy, transition to oral therapy with doxycycline 100 mg 2 times/day and metronidazole 500 mg 2 times/day is recommended to complete 14 days of antimicrobial therapy.
- **Alternative treatment: Clindamycin** 900 mg IV every 8 hours plus **Gentamicin** loading dose IM (2 mg/kg body weight), followed by a maintenance dose (1.5 mg/kg body weight) every 8 hours; single daily dosing (3–5 mg/kg body weight) can be substituted.
- When using the clindamycin and gentamicin alternative parenteral regimen, women with clinical improvement after 24–48 hours can be transitioned to clindamycin (450 mg orally 4 times/day) or doxycycline (100 mg orally 2 times/day) to complete the 14-day therapy.

ii. Chronic salpingitis

For uncomplicated genital chlamydia, the recommended treatment are:

	First choice	Alternatives
Uncomplicated genital, chlamydia infection	**Azithromycin** 1g orally as a single dose OR **Doxyxycline** 100 mg orally twice a day for 7 days	**Tetracycline** 500 mg orally four times a day for 7 days **OR** **Erythromycin** 500 mg orally four times a day for 7 days
Anorectal chlamydia infection	**Doxyxycline** 100 mg orally twice a day for 7 days	**Azithromycin** 1g orally as a single dose
Chlamydia infection in pregnant women*	**Azithromycin** 1g orally as a single dose	**Amoxicillin** 500 mg orally three times a day for 7 days **OR** **Erythromycin** 500 mg orally four times a day for 7 days
Chlamydia infection in PID	**Doxyxycline** 100 mg orally twice a day for 14 days	
Chlamydia infection in Scrotal Swelling	**Doxyxycline** 100 mg orally twice a day for 14 days	**Erythromycin** 500 mg orally four times a day for 14 days
Neonates with chlamydial conjunctivitis	**Azithromycin** 20 mg/kg/day orally, one dose daily for 3 days	**Erythromycin** syrup, 50 mg/kg per day orally, in 4 divided doses for 14 days

*3) * Doxycycline and Tetracycline are contra-indicated in pregnant women*

- **First line treatment: Ceftriaxone** 500 mg IM in a single dose plus **Doxycycline** 100 mg orally 2 times/day for 14 days with **Metronidazole** 500 mg orally 2 times/day for 14 days
- **Alternative treatment:** same as acute salpingitis
- **Other alternative therapy** can be considered with one of the following alternative regimens: 1) levofloxacin 500 mg orally once daily in combination with metronidazole 500 mg orally 2 times/day for 14 days, 2) moxifloxacin 400 mg orally once daily for 14 days, or 3) azithromycin 500 mg IV daily for 1–2 doses, followed by 250 mg orally daily for a total azithromycin duration of 7 days or in combination with metronidazole 500 mg 3 times/day for 12–14 days

**** Treatment guidelines CDC of US, Last Reviewed: September 21, 2022***

VII. PROGNOSIS

- Upper genital infections progress silently towards complications.
- The risk of recurrence is increased after a first episode

VIII. PREVENTION

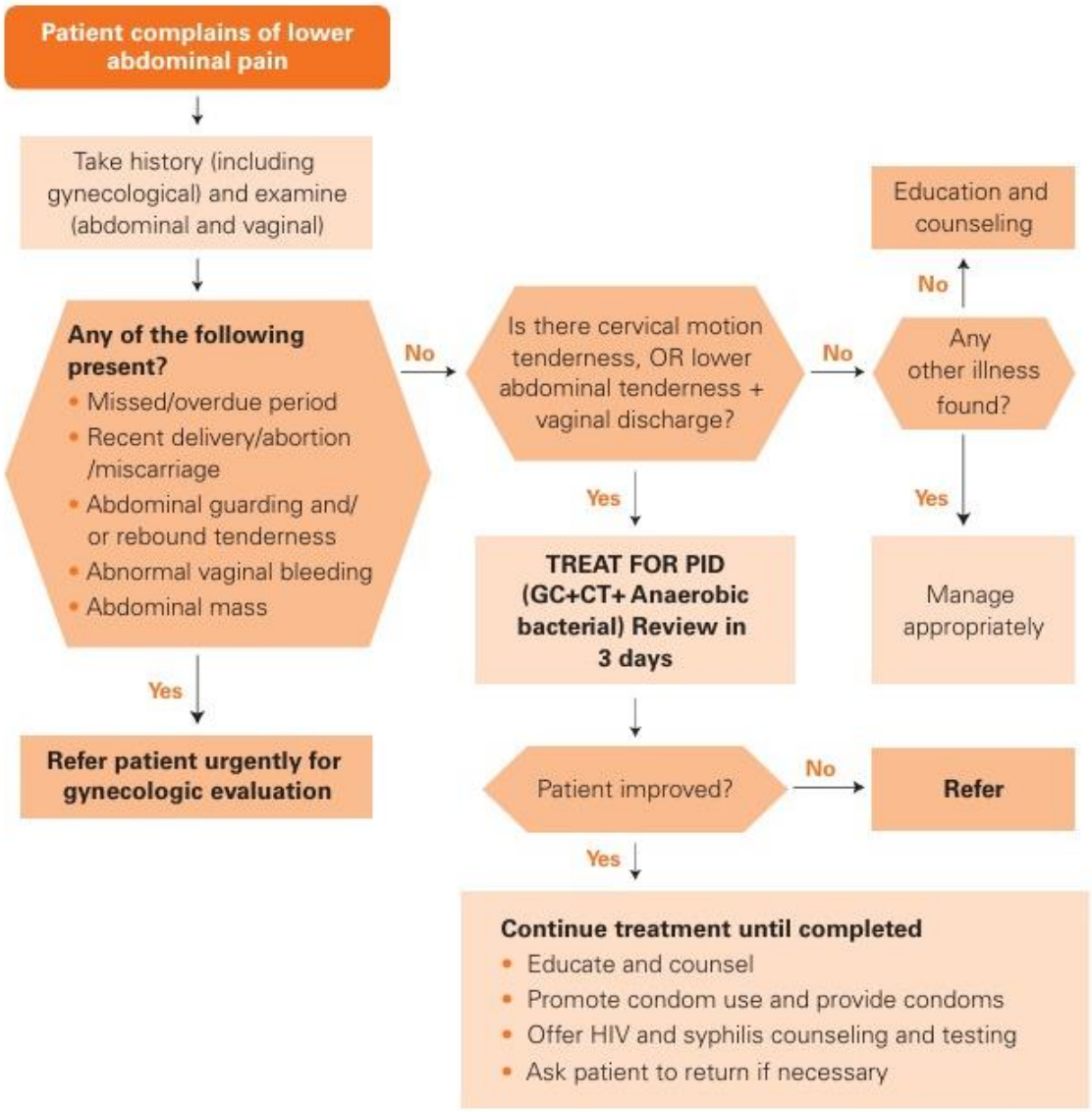
- Information on STIs and the benefits of condoms
- Detection and early treatment of lower genital infections
- Screening and treatment of partners

IX. FOLLOW UP

- Women should demonstrate clinical improvement (e.g., defervescence; reduction in direct or rebound abdominal tenderness; and reduction in uterine, adnexal, and cervical motion tenderness) <3 days after therapy initiation.
- If no clinical improvement has occurred <72 hours after outpatient IM or oral therapy, then hospitalization, assessment of the antimicrobial regimen, and additional diagnostics, including consideration of diagnostic laparoscopy for alternative diagnoses, are recommended.
- All women who have received a diagnosis of chlamydial or gonococcal PID should be retested 3 months after treatment, regardless of whether their sex partners have been treated.
- If retesting at 3 months is not possible, these women should be retested whenever they next seek medical care <12 months after treatment.

X. ALGORITHMS

Lower Abdominal Pain Syndromic Management Flowchart



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ENDOMETRIOSIS

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I. DEFINITION

- Endometriosis is a common benign disorder defined as presence of functional endometrial glands and stroma in any extrauterine site, and may be suspected based on history, symptoms, physical examination, laboratory & imaging info.
- Implants of endometriosis are most often found on the pelvic peritoneum, but other frequent sites include the ovaries and uterosacral ligaments. Endometrial tissue located within the myometrium is termed adenomyosis.

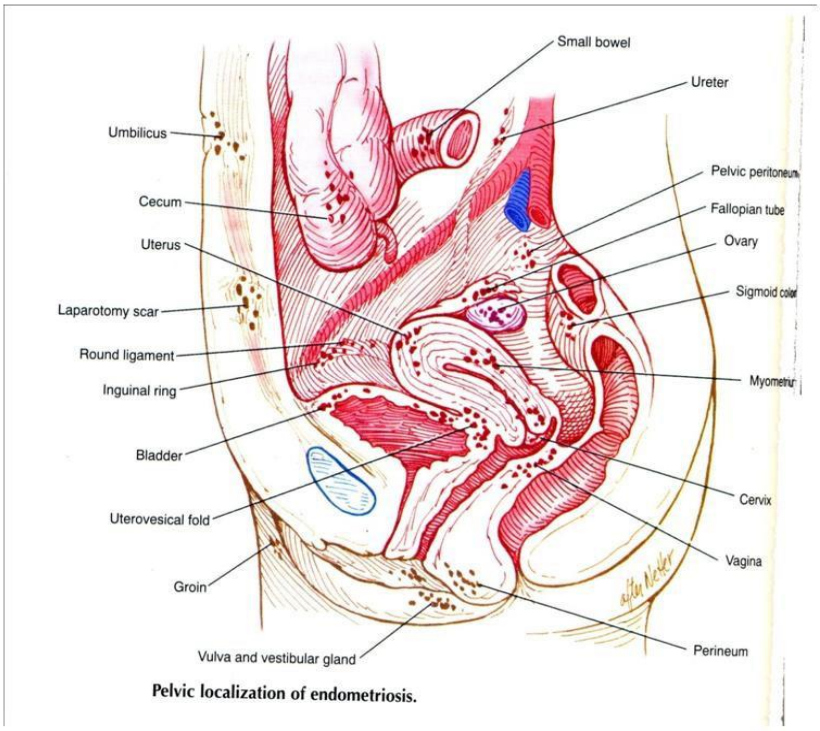
II. RISK FACTORS

- Family history of endometriosis
- Early age of menarche
- Short menstrual cycles (<27 d)
- Long duration of menstrual flow (>7 d)
- Heavy bleeding during menses
- Defects in the uterus or fallopian tubes

III. ANATOMICAL SITES

Endometriosis may develop anywhere within the pelvis and on other extra pelvic peritoneal surfaces.

Most common locations:	Less common locations:	Rarely locations:
- Pelvis - Ovaries - Anterior and posterior cul-de-sac - Uterosacral ligaments - Uterus (Adenomyosis) - Fallopian tubes - Sigmoid colon - Round ligament - Pelvic peritoneum	- Vagina - Cervix - Rectovaginal septum	- Inguinal canal - Abdominal or perineal scar - Lung and pleura - Ureters - Urinary bladder - Kidneys - Nasal mucosa



Pelvic localization of endometriosis.

5

IV. DIAGNOSTIC PROCEDURE

- Complaints: dysmenorrhea, abnormal menstruation, chronic pelvic pain, dyspareunia, diarrhea during period, pain at defecation, infertility etc. Worsen by her age (progressive)
- Pelvic exam: to assess location, tenderness, and mobility of uterus and adnexa
- Imaging: detection of endometriotic (chocolate) cyst. Echogenic (solid) part in cyst may indicate existence of cancer
- Histological diagnostic and blood test: CA125 (cancer antigen 125)
- Final diagnosis is based on gross/pathological view by biopsy under laparoscopy.

V. DIFFERENTIAL DIAGNOSIS

- In patients with chronic abdominal pain, chronic pelvic inflammatory disease, pelvic adhesions gastrointestinal dysfunction, and other etiologies of chronic pelvic pain should be considered.
- In patients with dysmenorrhea, both primary & secondary dysmenorrhea should be considered.
- In patients with dyspareunia, chronic pelvic inflammatory disease, ovarian cysts and symptomatic uterine retroversion.
- Sudden abdominal pain may be caused by a ruptured endometrioma as well as by ectopic pregnancy, acute pelvic inflammatory disease, adnexal torsion, and rupture of a corpus luteum cyst or ovarian neoplasm.

VI. COMPLICATIONS

- Fertility problems
- Adhesions and ovarian cysts
- Rupture of chocolate cyst
- Infection of chocolate cyst
- Surgery complications
- Bladder and bowel problems
- Rare malignancy: adenocarcinoma

VII. MANAGEMENT

There is no curative treatment.

Available therapies include:

- expectant,
- medical,
- surgical,
- and combination medical and surgical treatment.

A. Expectant Management:

- For patients with limited disease whose symptoms minimal or nonexistent
- and patients who are attempting to conceive
- and older patients.

B. Medical Therapy for pain and disease:

- Patients who are currently symptomatic,
- have documented endometriosis beyond minimal disease,
- and who desire pregnancy in the future.
- Drug therapy:
    - Nonsteroidal anti-inflammatory drugs (NSAID) for pain: start before pain = start at opening of period

      Recommended mefenamic acid: initiate at 500 mg, followed by 250 mg 6 hourly as necessary, usually not more than 1 week.
    - Continuous progestin for 6 months: Dinogest 2 mg or Depo-Provera® or Intrauterine devices (IUD) system
    - Gonadotropin hormone-releasing hormone (GnRH) agonist (Leuprone for 6 months, main side effect: climacteric symptom/osteoporosis)

      The standard dosage of Lupron for endometriosis is an intramuscular injection every month. Each shot contains 3.75 mg of the drug.
    - Danazol for 6 months

      200-400 mg/day per os (PO) divided 2 times a day (BID). Moderate-to-severe: 800 mg/day PO divided BID. Titrate downward to dose sufficient to maintain amenorrhea. Main side effect: virilization

C. Surgical Therapy:

- Conservative surgery: excision, cauterization, or ablation of visible endometriotic lesions and preservation of reproductive organs.
- Extirpative surgery is reserved only for cases in which disease is so extensive that conservative medical or surgical therapy is not feasible, or when patient has completed her family & wishes definitive therapy for adenomyosis of uterus is total abdominal hysterectomy with bilateral salpingo-oophorectomy, lysis of adhesions and removal of endometriotic implants and follow up after extirpative surgery
- Pathological study for all surgical specimens

VIII. PREVENTION

- At present, there is no known way to prevent endometriosis.
- Enhanced awareness, followed by early diagnosis and management may slow or halt the natural progression of the disease and reduce the long-term burden of its symptoms, including possibly the risk of central nervous system pain sensitization.
- Currently, there is no cure.

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OVARIAN CANCER

Prof. Ass. Korn Aun, Dr. Ly Chhiv Ieng, Dr. Chhun Samsorphea, Dr. Chuong Sokneth, Dr. Uy Sopha, Dr. Khor Hok Sunn

I. DEFINITION

Ovarian cancer is a cancerous tumor of an ovary. It may originate from the ovary itself or more commonly from communicating nearby strictures such as fallopian tubes or the inner lining of the abdomen.

The ovary is made up of different cell types including epithelial cells, germ cells, and stromal cells and others.

II. EPIDEMIOLOGY

In 2022, 470 new cancer cases and 335 cancer deaths are projected to occur in Cambodia, based on the report of the Global Cancer Observatory.

Epithelial ovarian cancer (EOC) represents a heterogenous spectrum of disease entities at a clinical, pathological and molecular level.

III. DIAGNOSTIC PROCEDURE

i. Clinical argument

In advanced disease, ascites and abdominal masses lead to bloating, nausea, anorexia, dyspepsia, and early satiety.

ii. Investigation

The standard work-up for patients suspected of having EOC should include detailed history and clinical examination with relevant laboratory and imaging tests.

Measurement of serum cancer antigen 125 (CA-125) aids diagnosis and is elevated in about 85% of patients with advanced disease.

iii. Pathology and molecular biology

EOC represents the majority (about 90%) of ovarian malignancies.

WHO classification and recommendations:

WHO's classification, based on histopathology, immunohistochemistry (IHC), and molecular analysis, recognizes at least five distinct subtypes of malignant EOC:

1. High-grade serous carcinoma (HGSC: 70% of cases)
2. Endometrioid carcinoma (EC:10%)
3. Clear-cell carcinoma (CCC: 5%)
4. Low grade serous carcinoma (LGSC: 5%) and
5. Mucinous carcinoma (MC:3-4%)

Table 2. Pathology and molecular biology of EOC subtypes

		HGSC	EC	CCC	LGSC	MC
IHC staining	p53	Abnormal	Abnormal/normal	Normal	Normal	Normal
	p16	+	−	−		
	WT-1	+	−	−	+	−
	ER	+/−	+	−	+	−
	PAX8	+	+		+	−
	Vimentin		+			
	HNF1β			+		
	CDX2					+
Molecular alterations (decreasing prevalence from top to bottom)		*TP53* *BRCA1/2* HRD	*CTNNB1* *ARID1A* *PTEN* *KRAS* *TP53* (high-grade EC) MSI/dMMR	*ARID1A* *PI3KCA* *PTEN* MSI/dMMR	*KRAS* *BRAF* *RAF*	*CDKN2A* *KRAS* *HER2*

CCC, clear-cell carcinoma; CDX2, homeobox protein CDX-2; dMMR, mismatch repair deficiency; EC, endometrioid carcinoma; EOC, epithelial ovarian cancer; ER, estrogen receptor; HGSC, high-grade serous carcinoma; HNF1β, hepatocyte nuclear factor-1β; HRD, homologous recombination deficiency; IHC, immunohistochemistry; LGSC, low-grade serous carcinoma; MC, mucinous carcinoma; MSI, microsatellite instability; PAX8, paired box gene 8; WT-1, Wilms tumour 1.

WHO's Recommendations

- If EOC is suspected, diagnostic work-up should include serum CA 125 measurement, pelvic US by ab expert examiner and CT scan of the thorax, abdomen and pelvis (III,A)
- Pathological diagnosis should be made according to the 2020 WHO classification by an expert gynecological pathologist (IV,A).
- All patients with high-grade ovarian cancer should be tested for germline and/or somatic BRCA1/2-muts at diagnosis (I,A)
- Testing for HRD is recommended in advanced high-grade cancers (I,A)

Staging and Risk assessment

Recommendation, the revised 2014 FIGO staging system for EOC should be used.

IV. DIFFERENTIAL DIAGNOSIS

- Other cancers: colon cancer, gastric adeno-carcinoma, metastatic GI carcinoma, uterine cancer, cervical cancer, bladder cancer and rectum cancer.
- Uterine fibroids,
- Other conditions: ovarian cysts, endometriosis (endometrioma, adenomyosis), GI tract and urological diseases.

V. MANAGEMENT

i. Management of early EOC **(FIGO STAGE I-II)**

a. Surgery

The aim of surgery for early EOC is complete resection of the tumor and to undertake adequate staging. Including:

- Midline laparotomy
- Inspection and palpation of the whole abdominal cavity
- Peritoneal washing with cytological examination

- Biopsies from all visible lesions and all abdominal fields
- Bilateral salpingo-oophorectomy
- Hysterectomy
- Omentectomy
- Appendicectomy
- Systematic pelvic and para-aortic lymphadenectomy

The availability of an intra-operative frozen section to identify a malignant epithelial cancer may allow the appropriate surgical staging to be done without the need for a second operative procedure.
Fertility-sparing surgery can be considered in young patients, but always after a full discussion with the patient about potential risks.

Figure1, provides a treatment algorithm for the management of FIGO stage I-II EOC.

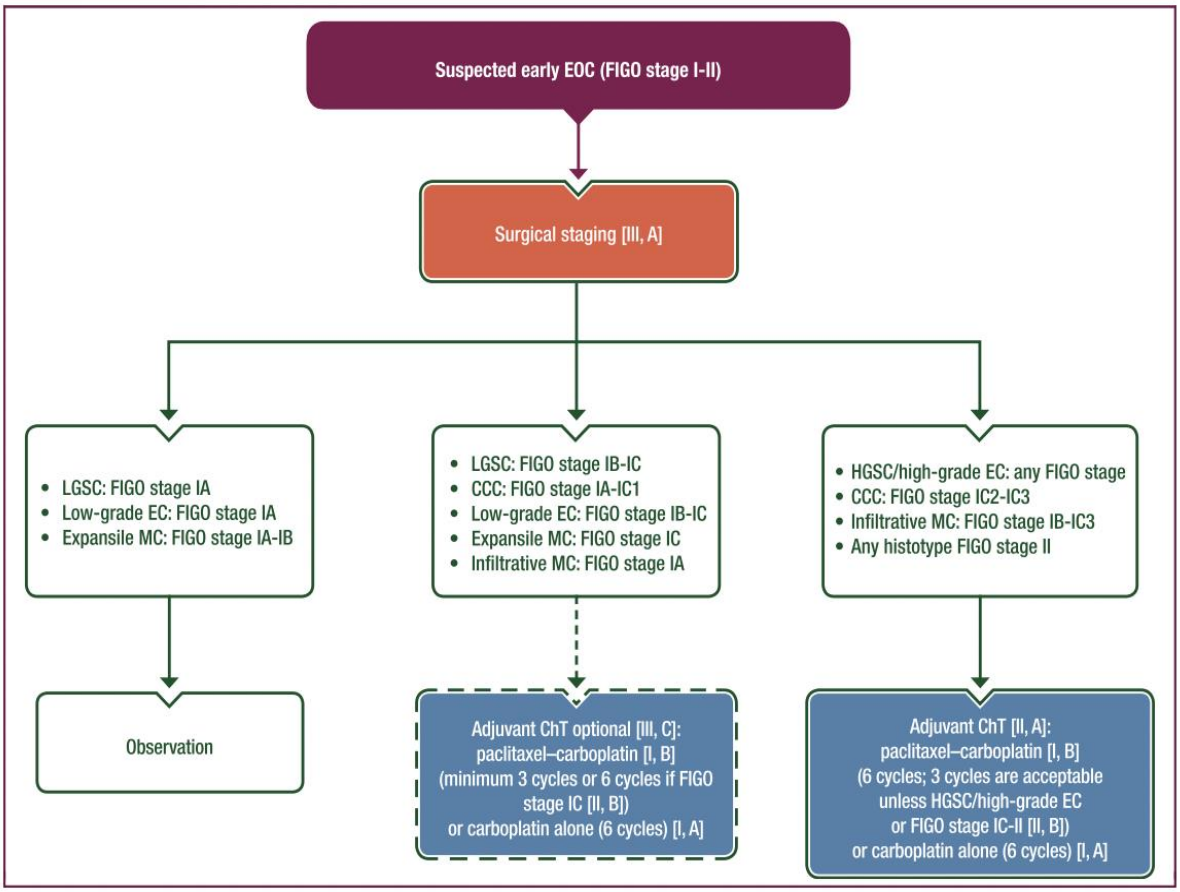

Figure 1. Management of early EOC (FIGO stage I-II).
See Supplementary Table S1, available at https://doi.org/10.1016/j.annonc.2023.07.011, for a summary of the benefit of adjuvant systemic therapy for early EOC (FIGO I-II stage).
Purple: general categories or stratification; red: surgery; blue: systemic anticancer therapy; white: other aspects of management; dashed lines: optional therapy.
CCC, clear-cell carcinoma; ChT, chemotherapy; EC, endometrioid carcinoma; EOC, epithelial ovarian cancer; FIGO, International Federation of Gynecology and Obstetrics; HGSC, high-grade serous carcinoma; LGSC, low-grade serous carcinoma; MC, mucinous carcinoma.

b. Systemic therapy

Adjuvant platinum-based Chemotherapy significantly prolongs overall survival rate and progression-free survival rate (PFS) in patients with early-stage EOC. (Discussion in multi-disciplinary team (MDT) group: Gynecologic Oncology Group: GOG)

Recommendations

- Surgical staging is recommended for presumed early-stage ovarian cancer for classification and recommendation of optimal systemic therapy [II,A].
- Adjuvant chemotherapy in early-stage ovarian cancer is generally recommended for FIGO stage I-IIB [II,A], either paclitaxel-carboplatin. A minimum of three cycles is recommended, except for HGSC/high-grade EC or any stage IC-II regardless of histotype, for which six cycles are suggested [II,B].
- For patients receiving paclitaxel-carboplatin or carboplatin (six cycles) alone.
- The benefit of adjuvant chemotherapy is uncertain and can be considered as optional [III,C] for:
    - LGSC stage IB-IC
    - CCC stage IA-IC1
    - Low-grade EC stage IB-IC
    - Expansile MC stage IC
    - Infiltrative MC stage IA
- Adjuvant ChT is not recommended in completely stage patients with LGSC STAGE IA, low-grade EC stage IA or expansile MC stage IA-IB [II,E].

ii. Management of advanced EOC **(FIGO stage III-IV)**

a. Surgery

In advanced EOC, surgery aims to achieve a complete or optimal cytoreduction, defined as total macroscopic tumor clearance with no residual visible disease, since this has been shown to significantly increase OS (Overall Survival) and PFS (Progression-Free Survival)

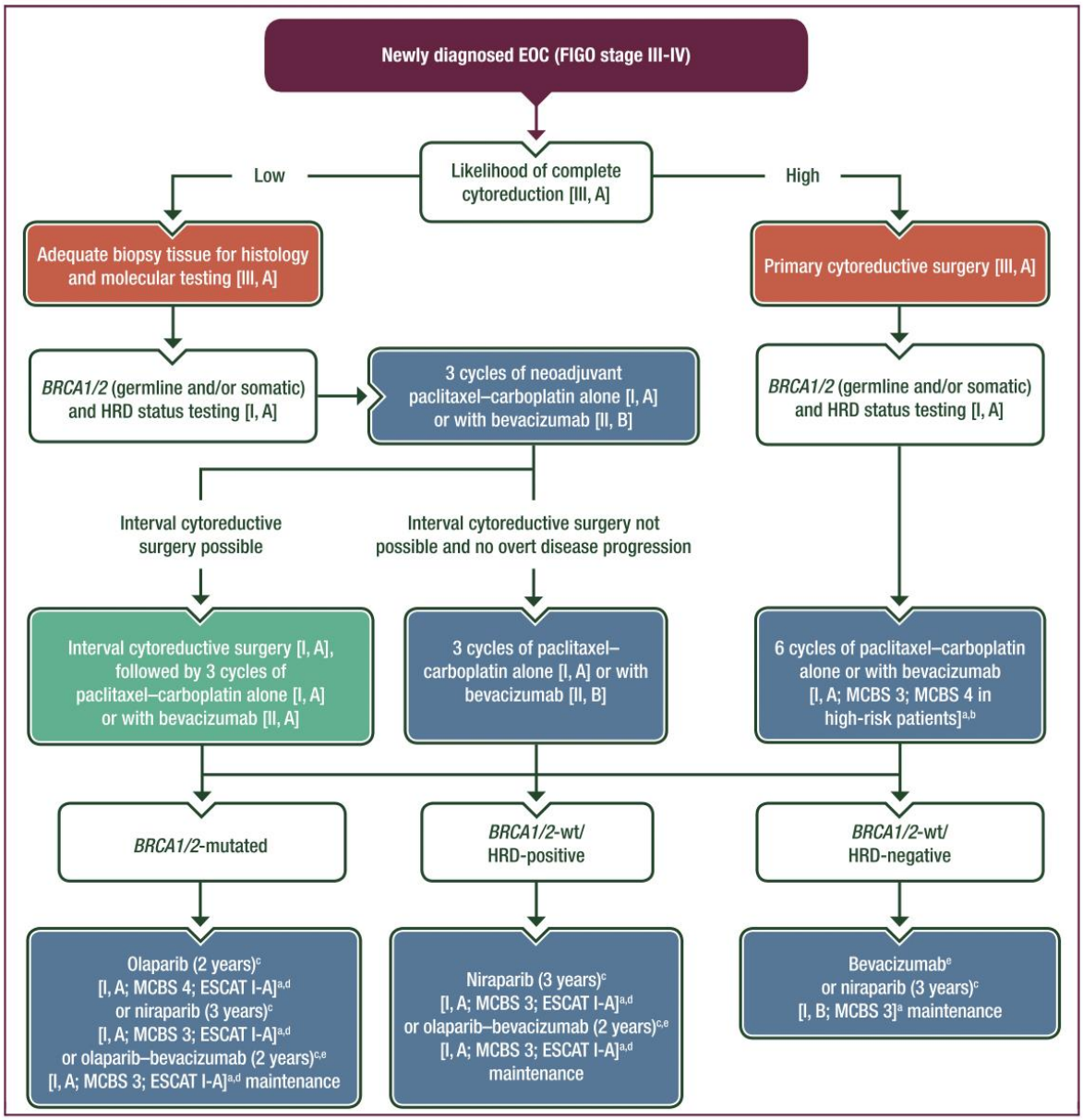

Figure 2. Management of advanced EOC (FIGO stage III-IV).
Purple: general categories or stratification; red: surgery; blue: systemic anticancer therapy; turquoise: combination of treatments or other systemic treatments; white: other aspects of management.
AUC, area under the curve; ChT, chemotherapy; EMA, European Medicines Agency; EOC, epithelial ovarian cancer; ESCAT, ESMO Scale for Clinical Actionability of molecular Targets; FDA, Food and Drug Administration; FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous recombination deficiency; MCBS, ESMO-Magnitude of Clinical Benefit Scale; PARPi, poly (ADP-ribose) polymerase inhibitor; wt, wild type.
[a]ESMO-MCBS v1.1[104] was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-evaluation-forms).
[b]Weekly ChT with paclitaxel (60 mg/m^2)—carboplatin (AUC 2) can be an alternative in frail patients [I, B].
[c]Only when patients have complete or partial response to platinum or no evidence of disease. For patients without response to platinum, a PARPi is not indicated; these patients can be managed with bevacizumab maintenance if appropriate (mainly stable disease), or with second-line therapy if they have progressive disease (see Figure 3).
[d]ESCAT scores apply to alterations from genomic-driven analyses only. These scores have been defined by the guideline authors, assisted if needed by the ESMO Translational Research and Precision Medicine Working Group.[103] See Supplementary Table S3, available at https://doi.org/10.1016/j.annonc.2023.07.011, for more information on ESCAT scores.
[e]Option for patients for whom bevacizumab was added to paclitaxel—carboplatin.

iii. Management of recurrent EOC

Up to 70% of patient with stage III-IV high-grade ovarian cancer will relapse within 3 years. Relapse rates for early-stage ovarian cancer are much lower.

Several factors need to be assessed when selecting treatment for patients with recurrent disease (see algorithms).

VI. PREVENTION

To prevent new cancers from starting, scientists look at risk factors and protective factors. Anything that increases your chance of developing cancer is called a cancer risk factor; anything that decreases your chance of developing cancer is called a cancer protective factor.

- The following are risk factors for ovarian, fallopian tube, and primary peritoneal cancers:
  - Family history of ovarian, fallopian tube, and primary peritoneal cancers
  - Inherited risk
  - Hormone replacement therapy
  - Weight and height
  - Endometriosis
- The following are protective factors for ovarian, fallopian tube, and primary peritoneal cancers:
  - Oral contraceptives
  - Tubal ligation
  - Giving birth
  - Salpingectomy
  - Breastfeeding
  - Risk-reducing salpingo-oophorectomy

VII. FOLLOW-UP, LONG-TERM IMPLICATIONS AND SURVIVORSHIP

Although a cure is unlikely after relapse, effective therapies exist for the treatment of patients with recurrent ovarian cancer. Therefore, surveillance in these patients is indicated with a combination of thorough symptom review and physical examination.

CA-125 has been evaluated in the surveillance of ovarian cancer and has been noted to be elevated 2-5 months before radiographic detection of cancer.

Radiological detection methods, such as PET-CT, and complete secondary cytoreduction and targeted therapy, have been shown to improve outcomes.

BRCA1/2-mut carriers and survival

Although surveillance is generally undertaken for 5 years after the most recent remission, longer follow-up may be considered in BRCA1/2-mut carriers, given their improved long-term survival and need for breast cancer surveillance.

Recommendation:

- Surveillance of ovarian cancer patients can include CA-125 determination, physical examination, and CT-scan evaluation.
- BRCA1/2-mut carriers can be considered for follow-up beyond 5 years.
- Long-term BRCA1/2-mut survivors should be referred to high-risk breast cancer clinics for follow-up.
- Suspicion of ovarian cancer -> Refer to oncology service of national hospital

VIII. ALGORITHM

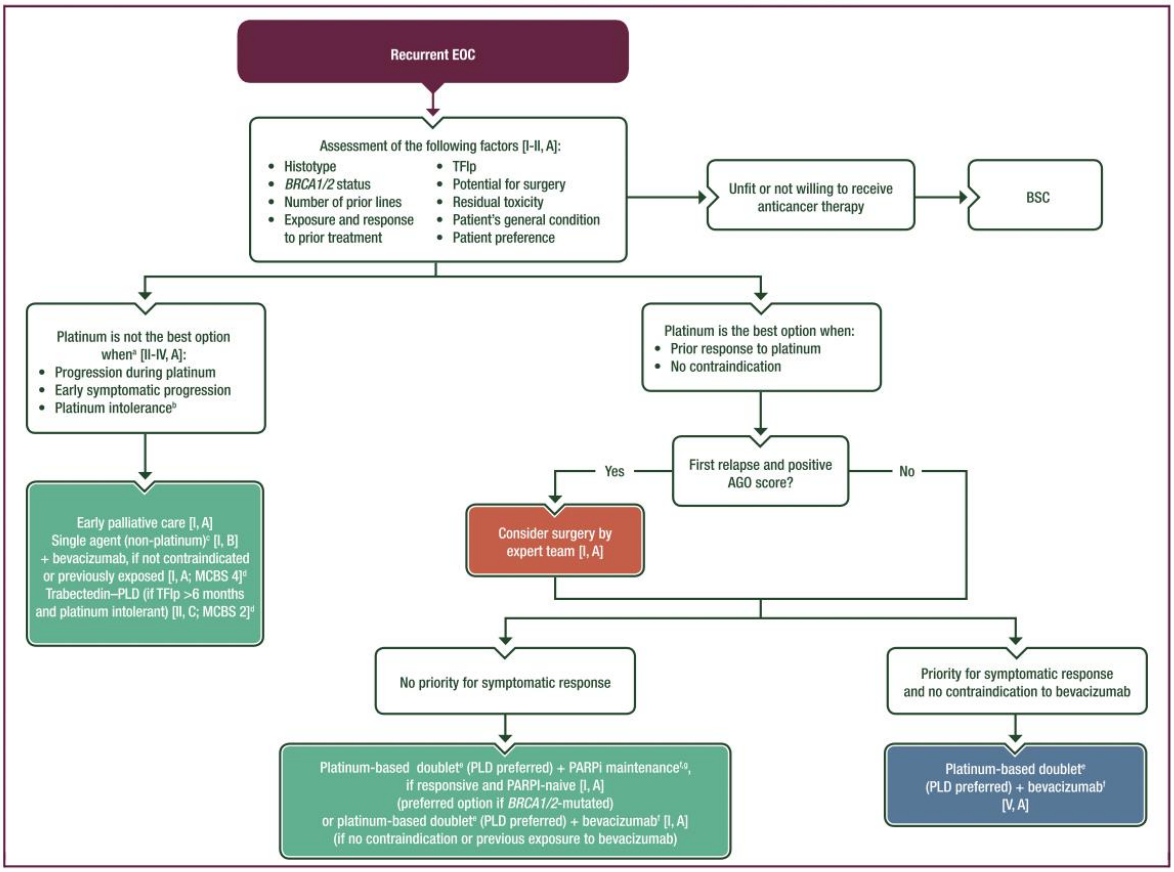

Figure 3. Management of recurrent EOC.

Purple: general categories or stratification; red: surgery; blue: systemic anticancer therapy; turquoise: combination of treatments or other systemic treatments; white: other aspects of management.

AGO, Arbeitsgemeinschaft Gynaekologische Onkologie; BSC, best supportive care; EMA, European Medicines Agency; EOC, epithelial ovarian cancer; FDA, Food and Drug Administration; MCBS, ESMO-Magnitude of Clinical Benefit Scale; mut, muation; PARPi, poly (ADP-ribose) polymerase inhibitor; PLD, pegylated liposomal doxorubicin; TFIp, treatment-free interval from last platinum.

[a]Patient choice and quality-of-life issues may also suggest that platinum is not the best option.

[b]In patients with platinum intolerance who have relapsed >6 months from previous platinum, the combination of trabectedin and PLD may be recommended [II, C; ESMO-MCBS v1.1 score: 2 for patients with platinum-sensitive disease; EMA approved, not FDA approved].

[c]Weekly paclitaxel, PLD, topotecan or gemcitabine.

[d]ESMO-MCBS v1.1[104] was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-evaluation-forms).

[e]Paclitaxel, PLD or gemcitabine (carboplatin—gemcitabine—bevacizumab: ESMO-MCBS v1.1 score: 3).[d]

[f]Until disease progression or next line of treatment is started [I, A].

[g]Olaparib for *BRCA1/2*-mutated: ESMO-MCBS v1.1 score: 2;[d] niraparib regardless of *BRCA1/2*-mut status: ESMO-MCBS v1.1 score: 3;[d] rucaparib regardless of *BRCA1/2*-mut status: ESMO-MCBS v1.1 score: 3.[d]

IX. ANNEXES

Table 1. Diagnosis of EOC
Work-up if EOC is suspected
• Detailed history and clinical examination • Serum CA-125 • Serum CEA and CA 19-9, in the case of MC, and endoscopy, if either or both are elevated • Transabdominal and transvaginal US by expert examiner • CT of thorax, abdomen and pelvis • Pathological examination of adequate tumour sample from diagnostic biopsy or surgical specimen • Cytological assessment of pleural effusion if present

CA 19-9, carbohydrate antigen 19-9; CA-125, cancer antigen 125; CEA, carcinoembryonic antigen; CT, computed tomography; EOC, epithelial ovarian cancer; MC, mucinous carcinoma; US, ultrasound.

Table 3. FIGO staging system for EOC[11]	
Stage I: Tumour confined to ovaries or fallopian tube(s)	
IA	Tumour limited to one ovary (capsule intact) or fallopian tube, without tumour on ovarian or fallopian tube surface and without malignant cells in the ascites or peritoneal washings
IB	Tumour limited to both ovaries (capsules intact) or fallopian tubes, without tumour on ovarian or fallopian tube surface and without malignant cells in the ascites or peritoneal washings
IC	Tumour limited to one or both ovaries or fallopian tubes, with any of the following:
IC1	Surgical spill
IC2	Capsule ruptured before surgery or tumour on ovarian or fallopian tube surface
IC3	Malignant cells in the ascites or peritoneal washings
Stage II: Tumour involves one or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or primary peritoneal cancer	
IIA	Extension and/or implants on uterus and/or fallopian tubes and/or ovaries
IIB	Extension to other pelvic intraperitoneal tissues
Stage III: Tumour involves one or both ovaries or fallopian tubes or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes	
IIIA1	Positive retroperitoneal lymph nodes only (cytologically or histologically proven):
IIIA1(i)	Metastasis ≤10 mm in greatest dimension
IIIA1(ii)	Metastasis >10 mm in greatest dimension
IIIA2	Microscopic extra-pelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes
IIIB	Macroscopic peritoneal metastasis beyond the pelvis ≤2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes
IIIC	Macroscopic peritoneal metastasis beyond the pelvis >2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumour to capsule of liver and spleen without parenchymal involvement of either organ)
Stage IV: Distant metastasis excluding peritoneal metastases	
IVA	Pleural effusion with positive cytology
IVB	Parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

EOC, epithelial ovarian cancer; FIGO, International Federation of Gynecology and Obstetrics.
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BREAST CANCER

Prof. Lieng Chanrith, Dr. Huy Vinnika, Dr. Chhit Maryan, Dr. Rith Rophearin, Dr. Heng Viroth, Dr. Chin Roza, Dr. UY Kyna

I. DEFINITION

Breast cancer is a disease in which abnormal breast cells grow out of control and form tumors. If left unchecked, the tumors can spread throughout the body and become fatal.

Breast cancer is always caused by a mistake in genetic material (called a genetic abnormality).

Still, only 5% to 10% of cancers are linked to genetic abnormalities inherited from a parent. About 85% of breast cancers are caused by genetic abnormalities that are a result of getting older and the wear and tear of life in general.

II. EPIDEMIOLOGY

In 2022, there were 2.3 million women diagnosed with breast cancer and 670 000 deaths globally. The new incidence of breast cancer in Cambodia is estimated 2116 cases, around 19.9% among cancer in women (Globocan 2022)

Global estimates reveal striking inequities in the breast cancer burden according to human development. For instance, in countries with a very high Human Development Index (HDI), 1 in 12 women will be diagnosed with breast cancer in their lifetime and 1 in 71 women die of it.

In contrast, in countries with a low HDI; while only 1 in 27 women is diagnosed with breast cancer in their lifetime, 1 in 48 women will die from it.

III. RISK FACTORS

Unchangeable Risk factors:

- Mutations in the genes BRCA1, BRCA2 and PALB2,
- Age,
- Family history of cancer,
- Reproductive history (menarche age and age at first pregnancy, age of menopausal).

Changeable Risk factors:

- smoking,
- abuse of alcohol,
- living style,
- history of radiation exposure,
- oral contraception pill.

IV. DIAGNOSIS

i. Clinical argument:

Most people will not experience any signs and symptoms when the cancer is still early hence the importance of early detection.

Breast cancer can have combinations of signs and symptoms, especially when it is more advanced.

Signs and symptoms of breast cancer can include:

- a breast lump or thickening, often without pain
- change in size, shape or appearance of the breast
- dimpling, redness, pitting or other changes in the skin
- change in nipple appearance, nipple turning inward or the skin surrounding the nipple (areola)
- nipple/ skin ulcer
- axillary mass
- pathological nipple discharge (serous, bloody, pus, other than breastmilk)

These changes also can be signs of less serious conditions, such as an infection or a cyst.

ii. Investigations:

a. Imaging/ Radiology

Mammogram: is used for screening to:

- Look for signs of breast cancer in women who don't have any breast symptoms.
- Diagnose if there are symptoms or problems.

Breast Ultrasound:

- Ultrasound is not typically used as a routine screening test for breast cancer.
- It can show whether a breast lump is :
- A fluid-filled breast cyst (usually not cancerous)
- A solid mass (which could be cancer and may need further testing)
- Ultrasound can be especially helpful in women with dense breast tissue, which can make it hard to see abnormal areas on mammograms.

MRI:

- Can find some small breast tumors that a mammogram might miss.
- It can also produce false-positive and false-negative results.
- mostly indicated in BRCA mutation or in younger and dense breast patients.

Breast Imaging Report and Data System (BIRADS)

BIRADS 0	Not defined, need additional evaluation
BIRADS 1	Negative
BIRADS 2	Benign
BIRADS 3	Probably benign
BIRADS 4	Suspicious Abnormality
BIRADS 5	Highly suggestive of malignancy
BIRADS 6	Known biopsy (proven malignancy)

- BIRADS 1 : annual check up
- BIRADS 2 : follow up 6-12 months
- BIRADS 3 : follow up 4-6 months

Biopsy can be done on BIRADS 3 in case of discordance between clinical exam and imaging.

- BIRADS 4 & 5: indicates tissue biopsy.

b. Laboratory test

- **Breast cancer biomarker test**
  - Suggested in metastasis breast cancer:
  - CA 15-3
    - Higher levels of CA 15-3 may mean certain cancers, including breast cancer are present
  - CEA
    - Carcinoembryonic antigen (CEA) is a protein that can indicate colon cancer.
    - It can be used to determine if breast cancer has spread to other parts of the body.
- **Genetic tests:**
  - to identify mutations that cause breast cancer, BRCA1 and BRCA2, PALB2, CDH1, PTEN, by using the sample of blood or hair.
  - Genetic testing gives information if breast cancer or family history of breast cancer is due to an inherited gene mutation and to help guide treatment for breast cancer patient.
  - Patients should refer to genetic consultation.
  - A person could be considered at high risk for BRCA mutations if they have a family history of:
    - Breast cancer diagnosed before age 50.
    - Male breast cancer at any age.
    - Multiple relatives on the same side of the family with breast cancer, particularly if they are first-degree relatives (mother, sister, daughter).
    - Multiple breast cancers in the same woman, meaning breast cancer developing in both breasts over time or at the same time.

- Both breast and ovarian cancer in the same woman.
- A history of ovarian cancer in the woman's family, especially if a first degree relative.
- A significant history on the same family side (mother or father's side) of men diagnosed young with prostate cancer, ovarian cancer, melanoma, or pancreatic cancer. (These can be signs of a BRCA2 gene mutation presents in the family.)

- Genetic test at the moment of treatment
  - To discuss TM vs BCS in case of (TP53 mutation)
  - For metastasis breast cancer
  - PARP inhibitor.

c. Pathology

- **Biopsy is the only way to confirm diagnosis**.
  - Breast biopsy is done when mammograms, other imaging tests, or a physical exam
  - shows a breast change that may be cancer.
- **Immunohistochemistry (IHC):**
  - uses antibodies to detect antigens in a tissue sample on a biopsy sample.
  - is commonly used to predict treatment response,
  - determine the choice of treatment and likely outcomes (prognosis) of the disease.
  - The most common immunohistochemical breast cancer prognostic and therapeutic markers used include: ER, PR, HER2, Ki-67.

V. TYPE OF BREAST CANCER

i. Common types of breast cancer:

- Invasive ductal carcinoma (IDC):
  - This cancer starts in milk ducts and spreads to nearby breast tissue.
  - It's the most common type of breast cancer globally.
- Ductal carcinoma in situ (DCIS):
  - Like IDC, this breast cancer starts with milk ducts.
  - The difference is DCIS doesn't spread beyond your milk ducts.
- Lobular breast cancer:
  - This breast cancer starts in the milk-producing glands (lobules) in your breast and often spreads to nearby breast tissue.
  - It's the second most common breast cancer in the United States.

ii. Less common types of breast cancer include:

- Papillary carcinoma
- Mucinous ductal carcinoma
- Metaplastic carcinoma

- Tubular carcinoma
- Paget's disease of breast
- Angiosarcoma
- Inflammatory breast cancer (IBC).

iii. Breast cancer subtype:

- **Luminal A:**
  - ER (+), PR (+), HER2 (-), Ki67< 20%.
- **Luminal B:**
  - HER2 (+), ER (+), PR (+), Ki67> 20%.
  - HER2(-), ER (+), PR (+), Ki67> 20%
- **HER2 positive:**
  - ER/PR (-), HER2 (+), any ki67
- **Triple negative:**
  - ER/PR (-), HER (-), any ki67

VI. EXTENSION ASSESSMENT

The search for metastasis and staging should be done when cancer is confirmed.
Routine follow up metastasis:

- Standard Tests:
  - Chest Xray
  - Whole abdominal Ultrasound
  - Breast ultrasound
- When standard tests show suspicious finding, further investigation need to be performed:
  - Ca15-3, ACE
  - Thoraco-Abdomino- scan or TAP scan (chest, abdominal, pelvic)
  - Bone scan
  - PET scan
  - Positron Emission Tomography scans use a radioactive tracer to show how an organ is functioning in real time.
  - PET scan images can detect cellular changes in organs and tissues.
- It helps:
  - Determine whether the cancer has spread in the body
  - Assess the effectiveness of treatment
  - Determine if the cancer has returned after treatment (recurred)
  - Evaluate the prognosis (outlook) of the cancer.

VII. STAGE OF BREAST CANCER

TNM Classification for Breast Cancer

T: Tumor		
Tis:	Tumor in situ	
T1	Tumor ≤2cm	
	T1mic	micro invasion ≤0.1cm
	T1a	>0.1cm but <0.5cm
	T1b	>0.5cm but <1cm
	T1c	>1cm- 2cm
T2	Tumor ≥2cm≤5cm	
T3	Tumor >5cm	
T4	Tumor of any size with extension to chest wall or skin, inflammation tumor	
	T4a	invade chest wall
	T4b	invade skin
	T4c	T4a+ T4b
	T4d	inflamed breast cancer
N: Lymph node		
N0	No cancer in regional node	
N1	Regional movable metastasis	
N2	Non movable regional metastasis	
N3	Cancer in the internal mammary lymph node or sub-clavicular lymph node	
M: Metastasis		
M0	No distance metastasis	
M1	distance metastasis	
MX	undetermined metastasis	

VIII. TREATMENT

i. Multi-Disciplinary Team (MDT)

Every treatment of breast cancer depends on decision of Multi-Disciplinary Team (MDT).

ii. Surgery

a. In situ Carcinoma (DCIS)

- Breast conserving surgery (BCS) and WBRT:
  - If excision possible with good cosmetic result,
  - Unifocal
- Mastectomy ± reconstruction:
  - good cosmetic result not possible with BCS.

- multifocal
- Margin ≥ 2mm, if < 2mm, re-excision or mastectomy
- Sentinel Node: micro-invasive, mastectomy, solid component (clinic, imaging)

b. Invasive cancer
   - Breast conserving surgery (BCS)+ WBRT:
     - IF excision possible with good cosmetic result,
     - Unifocal, (use 4 clips during surgery for margin limit)
   - Mastectomy± reconstruction:
     - good cosmetic result not possible with BCS,
     - Multicentric
   - Margin (in case of BCS):
     - no Ink on tumor (cancer is not touching the edge of the tissue excised)
   - Sentinel Node:
     - always, unless US-guided needle aspiration is positive. (ALND)
   - Axillary lymph Node Dissection (ALND):
   - Positive lymph node proven by pathology or cytology, T4 even pCR after NAC, GS positive.

c. Paget disease
   - If present only on areola-nipple complex (imagine normal), indication of excision of areola-nipple complex. No ALND, no RT
   - If Paget disease + MMC, or tumor, indication of TM or BCS, axillary staging depends on associated cancer.
   - Indication Absolute (mastectomy is recommended)
     - Inflammatory breast cancer or invasive breast cancer with extensive skin or dermal lymphatic involvement
     - Diffuse suspicious or malignant-appearing microcalcifications
     - Inability to clear multiple positive pathologic margins after one or more re-excision attempts
     - Multicentric disease with any of the following criteria:
       - Receipt of neoadjuvant chemotherapy or endocrine therapy
       - Age ≤ 40
       - Triple negative breast cancer (ER-, PR-, and HER2-negative)
       - More than 2 lesions involving more than 2 quadrants by MRI evaluation
       - Any individual lesion ≥5 cm

- BRCA mutation carrier
- Multicentric pure DCIS
- Inability to achieve negative margins (defined as no ink on tumor for invasive cancers ± DCIS)
- cN2–N3
- Any reason for precluding the delivery of adjuvant WBRT+ boost

- Patients diagnosed with gestational breast cancer who cannot receive RT within 12–16 weeks.

d. Surgical complications

All surgeries have potential complications, and breast cancer surgery is no exception.

Potential complications, which may include:

- Infection at the surgical side
- hematoma
- Blood clot that can happen after surgery.
- Nerve damage
- Lymphedema
- frozen shoulder
- wound dehiscence

iii. Chemotherapy

a. Neoadjuvant chemotherapy (NAC) or preoperative systemic therapy:

- Treatment response provides important prognostic for TNBC or HER2- positive.
- Allows time for delayed decision-making for definitive surgery.
- cN (+) disease likely to become cN0 with preoperative systemic therapy.

Indication:

- inoperable mass, T4, multifocal
- IBC
- N2 or N3
- Patient need BCS
- cT1c, cN0 HER2 positive
- cT1c, cN0 HER2 TNBC

b. Adjuvant systemic chemotherapy

- should be done 3-5 weeks after surgery
- All N+
- HER2 positive, TNBC
- N0 if age <35, HR-, grade 2 or 3, T>20mm, with lymphovascular invasion, emboli vascular.

iv. Radiation therapy
   a. BCS: WBRT systematic
   b. Mastectomy: RT on chest wall if:
      - pT3-pT4
      - pT2, with one of these factors: age <40, emboli, grade 3, multifocal
      - margin positive.

v. Immunotherapy
   a. is the use of medicines to boost a person's own immune system to recognize and destroy cancer cells more effectively.
   b. Some immunotherapy drugs, work in more than one way to control cancer cells and may also be considered targeted therapy. Example: Trastuzumab, Pertuzumab.

vi. Hormonal Therapy
   a. is used for HR (+) cancer.
   b. can be used for adjuvant treatment,
   c. Neoadjuvant treatment.
      - Tamoxifen (TAM) should start at the end of radiotherapy for risk of potential skin and lung toxicity.
      - In contrast, Aromatase inhibitors (AI) can start with radiotherapy simultaneously.

IX. FOLLOW UP

- Physical exam 1– 4 times with standard tests per year as clinically appropriate for 5 y, then annually.
- Mammography every 12 month, beginning 6 months or more after completion of BCT.
- Routine imaging of reconstructed breasts is not indicated.
- If recurrence or metastasis detected, MDT should be conducted.

X. FERTILITY AND PREGNANCY

i. Fertility and birth control
   a. Patients who may desire future pregnancies should be referred to fertility specialists before chemotherapy and/or endocrine therapy to discuss the options of treatment.
   b. Patients should be advised not to become pregnant while on any systemic therapy
   c. Hormone-based birth control is discouraged regardless of the HR status of the patient's cancer
   d. Alternative methods of birth control include intrauterine devices (IUDs), barrier methods, or, for patients with no intent of future pregnancies, tubal ligation or vasectomy for the partner.

ii. Pregnancy and breastfeeding

a. Management of breast cancer during pregnancy should be close together and after the decision of Multi-Disciplinary Team (MDT)
b. Surgery: TM or BCS with GS (methylene blue dye is not recommended)
c. Chemotherapy: The indications for systemic chemotherapy should be discussed with MDT
d. Endocrine therapy and RT:
e. are contraindicated during pregnancy.
f. if indicated, should thus not be initiated until the postpartum period.
g. Pregnancy after breast cancer is possible at least 2 to 3 years after finishing treatment (depends on age, HR status, lymph node status)
h. Pregnancy is not a risk factor of recurrence but in case of ET, if a patient desires to stop tamoxifen, the patient needs to be informed about the decreasing risk reduction.
i. Breastfeeding following breast-conservation cancer treatment is not contraindicated.
j. Breastfeeding is not recommended during active treatment with chemotherapy and endocrine therapy or within 6 months of completing trastuzumab or pertuzumab.

iii. Management of breast cancer during pregnancy
Multi-Disciplinary Team (MDT)

a. 1st trimester:
- If a patient wishes to terminate the pregnancy or if locally advanced cancer that needs termination.
- Surgery for TM or BCS, with GS or ALND
- NAC or Adjuvant systemic therapy according to the decision of MDT
- Delivery from 37th week if possible
- Continued with treatment: chemo, RT, ET

b. 2nd and 3rd trimester
- Non-locally advanced cancer
- Surgery
- Adjuvant systemic therapy according to the decision of MDT
- Locally advanced cancer
- NAC +/- surgery according to the decision of MDT
- Delivery between 35-38 weeks, at least 3 weeks after the last cycle of chemotherapy
- Continued with treatment: chemo, RT, ET.

XI. MALE BREAST CANCER

- Male breast cancer represents lesser than 1% of the breast cancer. Frequently, it is related to genetic mutation (BRCA2). Treatment based on mastectomy and axillary lymph node staging.
- RT and Chemotherapy indication is the same as in woman's
- Preference ET is tamoxifen.

XII. SCREENING AND EARLY DETECTION

i. Screening for normal population

a. Mammography:

- Screening Mammogram:
  - Used for women without symptoms to detect early breast cancer.
  - Diagnostic Mammogram: Follow-up imaging if abnormalities are detected or if a woman has symptoms.
- Mammography:
  - Is the most widely used screening tool and can detect tumors that cannot be felt.
  - Is recommended because it reduces mortality from breast cancer, especially in women aged 40-74, Bi-annually.

b. Breast Ultrasound:

- Often used as a follow-up to mammography if an abnormal area is detected, or as a screening tool for women with dense breast tissue.
- Helps differentiate between solid tumors and fluid-filled cysts.

c. Magnetic Resonance Imaging (MRI):

Recommended for high-risk women (e.g., those with a strong family history or genetic mutations like BRCA1 or BRCA2).

- Advantages:
  - More sensitive than mammography and can detect cancers that mammogram may miss, especially in dense breasts.
- Disadvantages:
  - More expensive and can lead to more false positives.

c. Clinical Breast Exam (CBE):

- A physical examination of the breasts by a healthcare provider.
- Often done in conjunction with a regular health check-up, but its role in routine screening is debated due to inconsistent evidence on reducing mortality.
- CBE is not generally recommended as a primary screening tool but may be performed as part of routine care, especially in younger women.

d. Breast Self-Examination (BSE):
   - BSE may help detect some abnormality before the age of screening.
   - For confirming diagnosis, further investigations are still needed.
   - A woman checks her own breasts for lumps or changes.
   - BSE has not been shown to significantly reduce mortality, but it helps women become familiar with their breasts, making it easier to notice changes.
   - BSE is no longer recommended as a routine screening tool, but women should be aware of any breast changes.

ii. Breast Cancer Screening for women at higher risk

a. Women are considered at higher risk for breast cancer if they meet one or more of the following criteria:
   - Genetic Mutations:
     - Carry mutations in BRCA1 or BRCA2 genes, which greatly increase the risk of breast and ovarian cancers.
     - Other genetic mutations, such as TP53 (Li-Fraumeni syndrome) or PTEN (Cowden syndrome), also increase risk.
     - [Cowden syndrome = Cowden disease or multiple hamartoma syndrome, is a rare inherited condition with benign (non-cancerous) growths in different parts of the body, as well as an increased risk for some types of cancer.
     - CS belongs to a family of syndromes called the PTEN hamartoma tumor syndromes.
     - Li-Fraumeni syndrome (lee-FRAH-meh-nee) is a rare hereditary disorder that increases the risk you and your family members will develop cancer.
     - Li-Fraumeni syndrome can't be prevented. But early and consistent cancer screenings and treatment can limit the syndrome's impact on your life and your family's lives.].
   - Strong Family History:
     - Two or more first-degree relatives (e.g., mother, sister) with breast cancer, particularly if they were diagnosed at a young age (before 50).
     - Family history of ovarian cancer may also increase breast cancer risk.
   - Personal History of Breast Cancer or High-Risk Lesions:
     - Previous breast cancer diagnosis, particularly if it occurred before
     - menopause.
     - History of certain precancerous breast conditions like atypical hyperplasia or lobular carcinoma in situ (LCIS).

- Radiation Therapy to the Chest:
    - Women who received radiation therapy to the chest (e.g., for lymphoma) between the ages of 10 and 30.
- Other Factors:
    - Dense breast tissue may increase the risk and make cancers harder to detect on mammograms.
    - Reproductive factors: late menopause, early menstruation, or not having children.

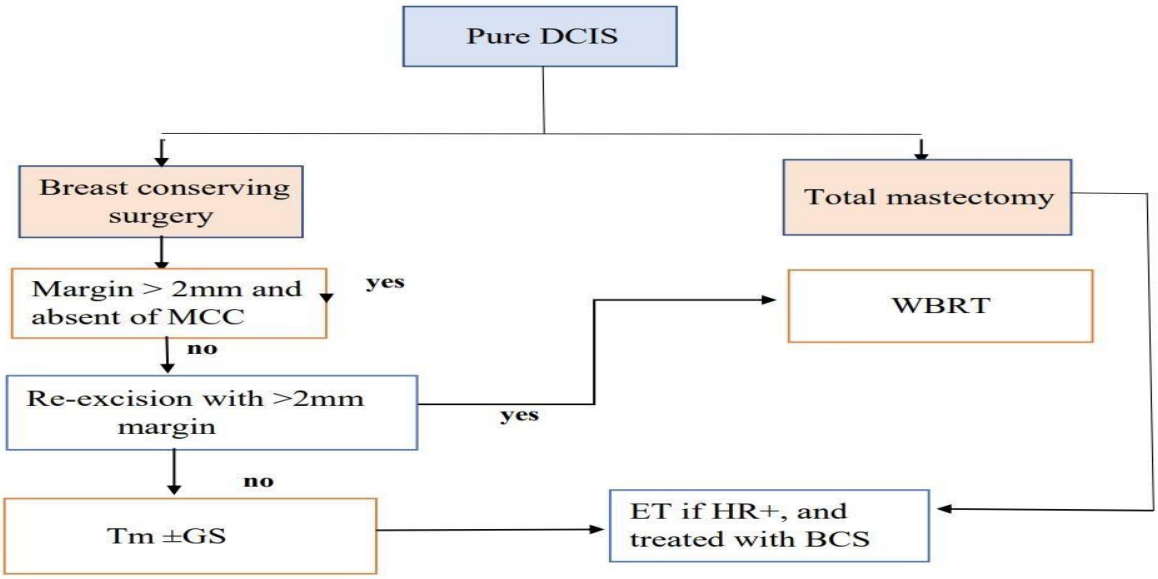
b. Screening Recommendations for High-Risk Women

For women with an elevated risk of breast cancer, more intensive screening protocols are recommended compared to average-risk women.

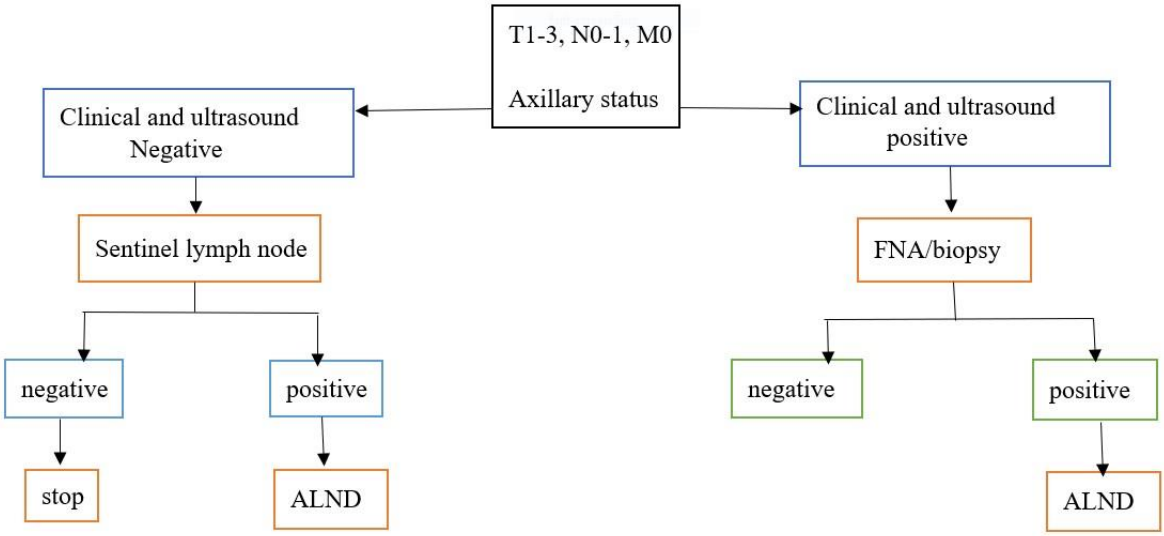
- Mammography
    - High-risk women should begin screening earlier, typically starting at age 30 (or even younger, depending on the specific risk).
    - Frequency: Annual mammograms are recommended.
    - Digital Mammography: This is preferred for high-risk women, especially for those with dense breast tissue, as it improves the ability to detect abnormalities in dense tissue.
    - Magnetic Resonance Imaging (MRI)
    - Breast MRI is recommended in addition to mammography for high-risk women.
    - MRI is recommended to complement mammography particularly in women with dense breasts or BRCA mutations.
- Ultrasound
    - Breast ultrasound may be used as an adjunct to mammography and MRI, particularly in women with dense breasts or when mammography detects a suspicious area.
    - Ultrasound is not typically used as a primary screening tool for high-risk women but is often reserved for targeted evaluation of abnormalities.
- Clinical Breast Exam (CBE)
    - High-risk women should have a clinical breast exam every 6 to 12 months.
    - Although not a primary screening tool, it can help detect physical changes in the breasts.
- Genetic Counseling and Testing
    - For women with a strong family history of breast cancer or known genetic mutations, genetic counseling is recommended.
    - Genetic testing for BRCA1, BRCA2, and other related mutations can provide more information about risk and guide screening and prevention strategies.

XIII. ALGORITHM

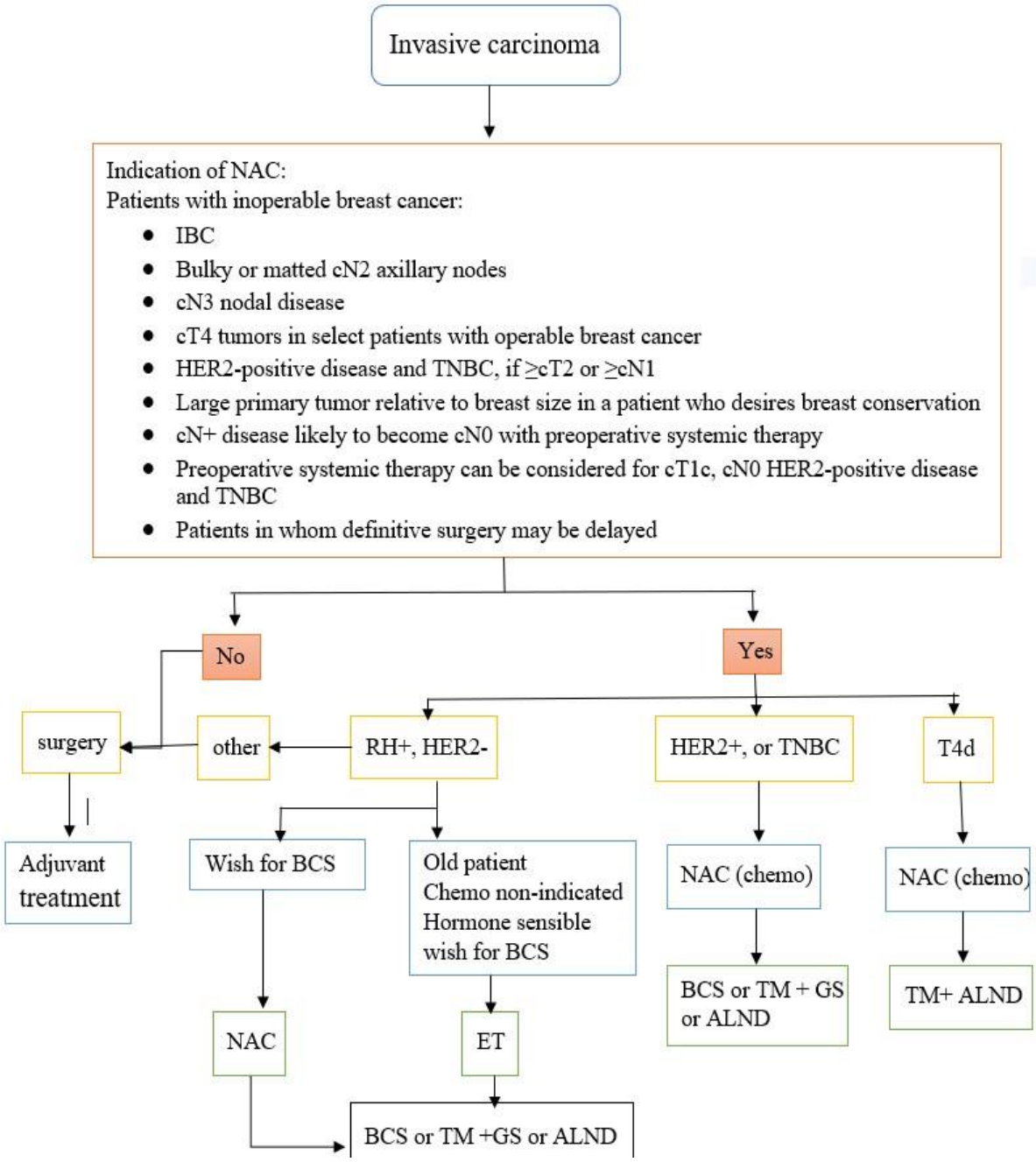
MANAGEMENT OF DCI



SURGERY AND LYMPH NODE SURGERY DECISION OF INVASIVE CANCER



NEO ADJUVANT DECISION



XIV. ANNEXES

SELF BREAST EXAMINATION

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PRECANCEROUS LESIONS OF CERVIX SCREENING, MANAGEMENT AND PREVENTION

Prof. Kruy Leangsim, Prof. Pech Sothy, Prof. Koum Kanal, Prof. Lieng Chanrith, Prof. Sann Chansoeung, Prof. Keth Lysotha, Dr. Krouch Rayounette, Dr. Sophean Sahakcheat, Dr. Leap Sovann, Dr. Uy Kyna, Dr. Chhit Maryan, Dr. Khor Hok Sunn, Dr. Hang Sovanara

I. OVERVIEW

- Globally, cervical cancer is the fourth most common cancer in women, with 604 000 new cases in 2020.
- About 90% of the 342 000 deaths caused by cervical cancer occurred in low- and middle-income countries.
- Cambodia has a reported annual cervical cancer incidence of 14 per 100,000 and an annual cervical cancer mortality of 8.3 per 100,000 in 2020 (WHO).
- About 1,135 new cervical cancer cases are diagnosed annually in Cambodia and annual number of deaths are 643 per year (estimations for 2020).

II. RISK FACTORS AND CAUSES

i. Risk factors:

- Early onset of sexual activity
- Multiple sex partners
- Partner with multiple sex partners
- History of STIs: Chlamydia, Genital herpes
- Multiparity
- Smoking
- Diethylstilbestrol (DES) exposure
- Family history of cervical cancer
- Lower socioeconomic predictors
- Minimal or neglected medical care (Pap test screening)
- Immunosuppression : HIV infection, immunosuppressive agents

ii. Causes

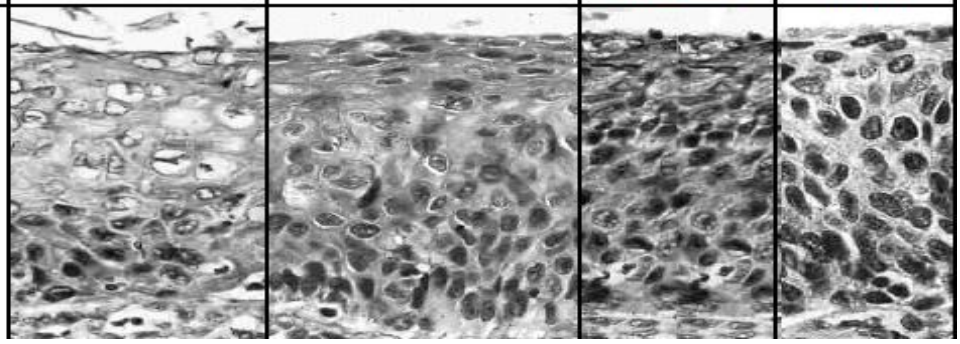
- Persistent high risk or oncogenic HPV infection of the cervix if left untreated, causes 95% of cervical cancers.
- Not all types of HPV can cause cervical cancer.
- There are about 15 types of HPV that are considered high risk and are responsible for the majority of cancers that are caused by HPV.
- Long-lasting (persistent) infection with high-risk types of human papillomavirus (HPV) causes virtually all cervical cancers. Two high-risk types, HPV 16 and HPV 18, cause 70% of cervical cancers worldwide.

III. CLASSIFICATION OF PRECANCEROUS LESIONS

- Precancerous lesions of the cervix are described based on how abnormal the cells look under a microscope and how severe the cell changes are.

- They are grouped based on the type of cell that is abnormal. Precancerous changes in the cervix are quite common.

Terminology regarding cytologic and histologic precancerous changes of the uterine cervix

<table>
<tr><td rowspan="2">LAST System[1]</td><td>Cytology</td><td>LSIL</td><td colspan="3">HSIL</td></tr>
<tr><td>Histology</td><td>LSIL</td><td colspan="2">p16 staining should be performed*</td><td>HSIL</td></tr>
<tr><td rowspan="2">Bethesda Classification System[2]</td><td>Cytology</td><td>LSIL</td><td colspan="3">HSIL</td></tr>
<tr><td>Histology</td><td>CIN 1</td><td colspan="2">CIN 2</td><td>CIN 3</td></tr>
<tr><td colspan="2">Previous terminology</td><td>Mild dysplasia</td><td colspan="2">Moderate dysplasia</td><td>Severe dysplasia</td><td>Carcinoma in-situ</td></tr>
<tr><td colspan="2">Histologic images</td><td colspan="5">  </td></tr>
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LAST: lower anogenital squamous terminology; LSIL: low-grade squamous intraepithelial lesions; HSIL: high-grade squamous intraepithelial lesions; CIN: cervical intraepithelial neoplasia.

* CIN 2 that is p16-positive is classified as HSIL. CIN 2 that is p16-negative is classified as LSIL.

IV. DIAGNOSTIC AND SCREENING METHODS

i. Symptoms

Precancerous changes in the cervix usually don't cause any signs or symptoms.

An abnormal Pap test result is often the first sign that some cells in the cervix are abnormal.

ii. Screening and Triage tests

There are three methods of cervical cancer screening:

- Visual inspection with acetic acid (VIA) test: uses dilute acetic acid (vinegar) on the cervix without magnification to identify aceto-white lesions that need treatment (e.g. ablation or excision) or further evaluation.
- Cytology: including the Papanicolaou smear test and liquid-based cytology (LBC) identify atypical cells on the cervix.
- High-risk HPV DNA test: Self-sampling or provider sampling can be used for HPV DNA testing.
- Colposcopy: facilitates and optimizes biopsy and excisional treatment after a primary positive screening test.

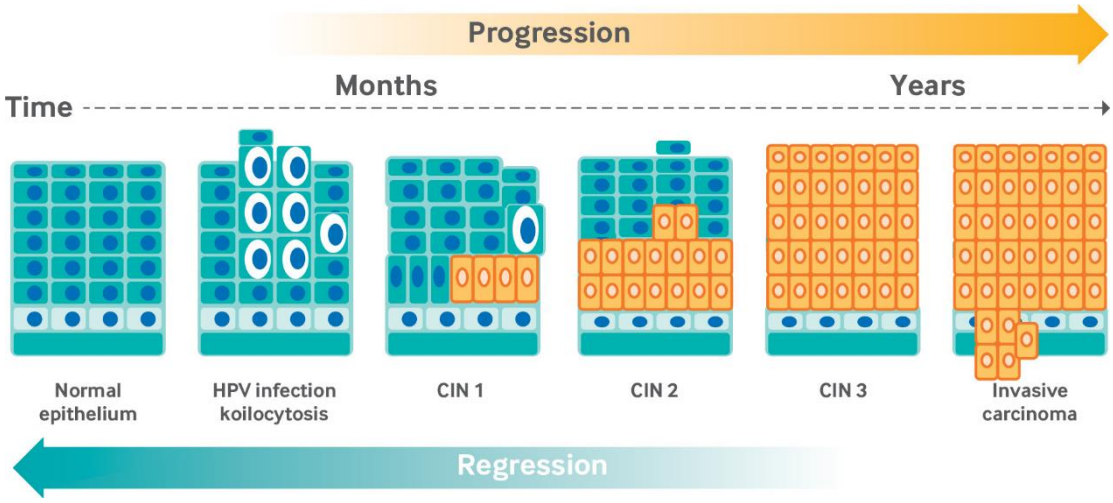
The triage tests include high-risk HPV DNA partial genotyping, cytology, VIA and colposcopy that may or may not include a biopsy for histological diagnosis.

The diagnosis of CIN is established by a histopathological examination of tissue such as obtained through cervical punch biopsy or endocervical curettage or excision. The accuracy of the histological diagnosis of CIN is dependent on the quality of the sample, the site of the biopsy, its preparation in the laboratory and its interpretation.

V. EVOLUTION

- HPV infections are usually asymptomatic and cannot be detected without a specific screening examination.
- About 90% of infected people naturally clear the virus.
- It is usually in the case of persistent infection, when the virus is still present after 2 years, that precancerous lesions appear.
- The reference statistics on the evolution of precancerous lesions of the cervix establish general data that can guide their management on a case-by-case basis.
  - CIN 1:
    regress spontaneously in 57% of cases,
    persist at the same stage in 32% of cases,
    progress to the next stage in 11% of cases, and
    develop into cancer in 1% of cases.
  - CIN 2:
    43% of them regress spontaneously,
    35% persistent,
    22% move on to the next stage and
    5% cause cervical cancer.
  - CIN 3:

32% of CIN3 regress spontaneously,
56% persist without causing cancer and
12% develop cervical cancer.

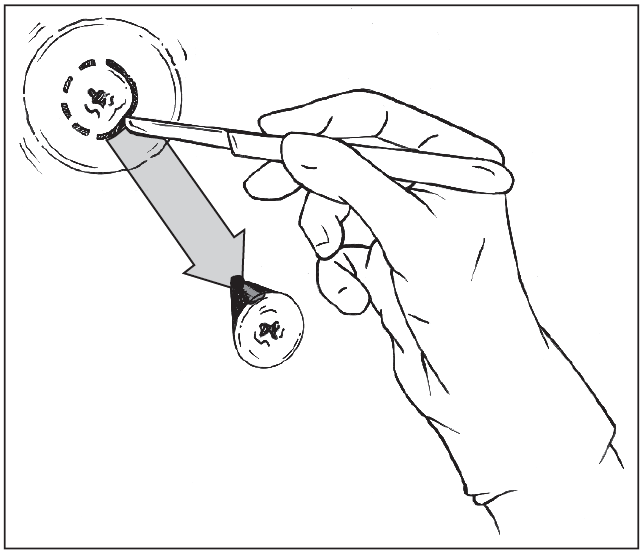


VI. TREATMENT

- Treatment for precancerous conditions of the cervix have an excellent outcome and their condition won't develop into cervical cancer.
  - Mild changes to the cervix often return to normal on their own without any treatment. Follow-up of women with a positive primary screening test but a negative triage test.
  - More severe abnormalities are more likely to develop into cervical cancer, especially if they aren't treated for a long time.
- According of high-grade CIN treatment, lesion and all of transformation zone should be destroyed either by ablation or excision.
- Because high grade CIN might extend along crypts of glands, treatment of high grade CIN should extend beyond depth of 5 mm to include crypts.
- Different types and modalities in treating preinvasive cervical lesions are as following:

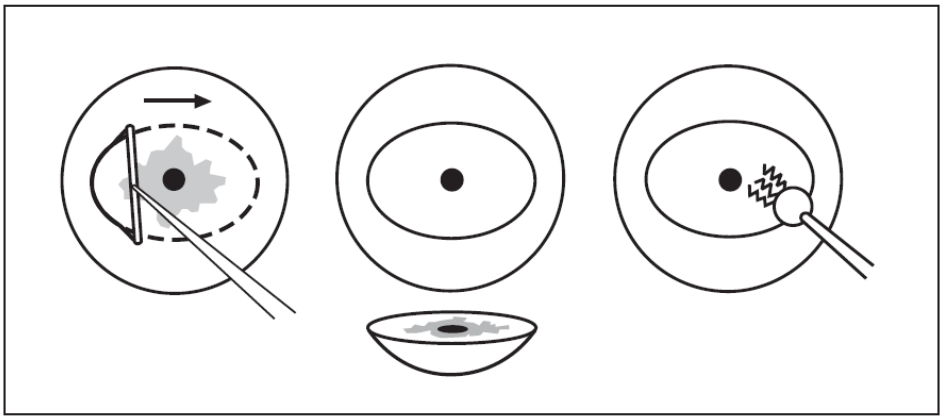
i. Treatments that remove the abnormal cells

- Cold knife conization:
  - Cervical conization with a scalpel is an excisional method generally reserved for treating AIS and microinvasive carcinoma.
  - After these treatments, the removed area of tissue is sent to a laboratory. It is checked to confirm the type of abnormal cell changes.



Removal of a cone-shaped area of the cervix

- LLETZ (large loop excision of the transformation zone)
  - removes abnormal cells from the cervix using a thin loop-shaped tool.
  - used to refer to excision of the transformation zone.
  - LLETZ uses local anesthesia, is done in an outpatient setting and yields a tissue specimen for pathology. In some countries, this terminology was changed to LEEP (loop electrosurgical excision procedure), and the two terms are often used interchangeably.



LEEP: excision of the lesion with wire electrode and coagulation with ball electrode

- Hysterectomy:
  This is not a common treatment for abnormal cells. In general, hysterectomy is not a primary treatment of CIN. However, it may be suitable in cases of AIS, where the patient does not need further fertility.

ii. Treatments that destroy the abnormal cells

Ablative treatments do not result in a tissue specimen for histological evaluation.

- Laser therapy

- This treatment uses a laser beam to burn away the abnormal cells.
- It is also called laser ablation.
- It is usually done under a general anesthetic and you may need to stay overnight in hospital.

- Cryotherapy
  - The temperature of the cervical epithelium underlying the probe is reduced to −20°C.
  - The treated epithelium will turn to cryo-necrosis and the new mature squamous epithelium will replace that area.
- Thermal ablation
  - The equipment uses a probe that is heated to 100° C and applied to the cervix for 20–45 s to destroy the epithelium.

VII. FOLLOW UP

Follow-up of women after treatment. Women who have been treated for histologically confirmed CIN2/3 or adenocarcinoma in situ (AIS), or treated as a result of a positive screening test are retested at 12 months with HPV DNA testing when available, rather than with cytology or VIA or co-testing and, if negative, move to the recommended regular screening interval (WHO).

VIII. PREVENTION

- Boosting public awareness, access to information and services are key to prevention and control across the life course.
- The most effective way to prevent cervical cancer is through:
  i. Primary prevention
     a. HPV Vaccination

        Prophylactic vaccination against HPV and screening and treatment of pre-cancer lesions are effective strategies to prevent cervical cancer and are very cost-effective.

        Cervical cancer can be cured if diagnosed at an early stage and treated promptly

        Being vaccinated at age 9–14 years is a highly effective way to prevent HPV infection, cervical cancer and other HPV-related cancer

     b. Health education
     - Counseling to change high-risk behavior
     - Delay age of first sexual intercourse
     - Use condoms
     - Avoid tobacco use
     - Voluntary male circumcision

  ii. Secondary prevention
     a. Screening:

Identify and treat precancerous lesions before they progress to cervical cancer

Screening from the age of 30 (25 years in women living with HIV) can detect cervical disease, which when treated, also prevents cervical cancer

b. Early diagnosis:

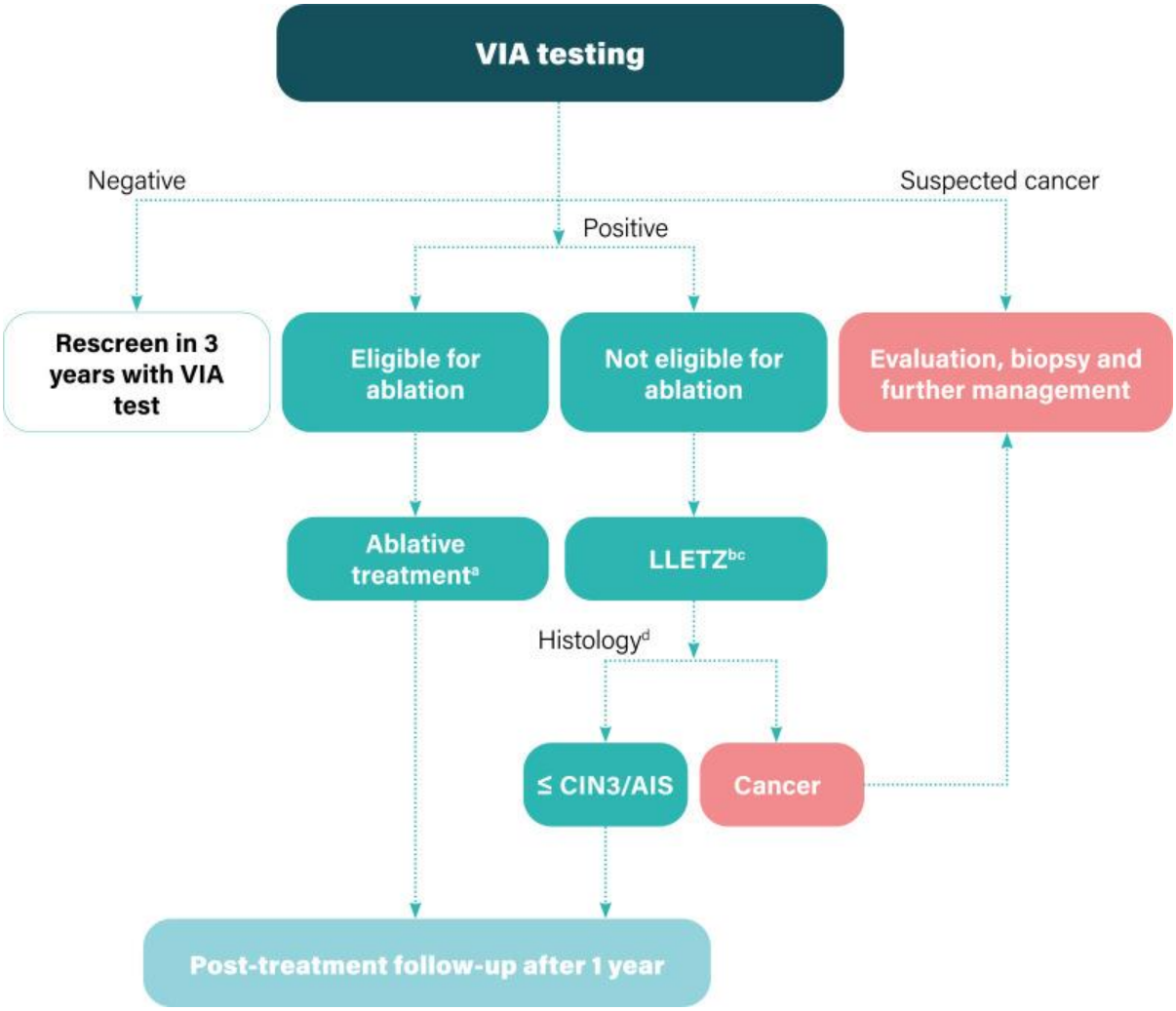
Identify and treat early cancer while chance of cure is still good (reduces cervical cancer mortality)

iii. Tertiary prevention

- Tertiary prevention of cervical cancer comprises treatment of cervical cancer and palliative care
- Surgical treatment, chemotherapy, radiotherapy and palliative are included in tertiary cervical cancer prevention
- The public health goal of tertiary prevention of cervical cancer is to reduce the number of mortality due to cervical cancer.

Primary prevention	Secondary prevention	Tertiary prevention
Girls 9-14 years • HPV vaccination	**Women 30 years old or older**	**All women as needed**
Girls and boys, as appropriate • Health information and warnings about tobacco use • Sex education tailored to age and culture • Condom promotion and provision for those engaged in sexual activity • Male circumcision	"Screen and treat" - single visit approach • Point-of-care rapid HPV testing for high-risk HPV types • Followed by immediate treatment • On-site treatment	• Surgery • Radiotherapy • Chemotherapy • Palliative care

IX. ALGORITHM



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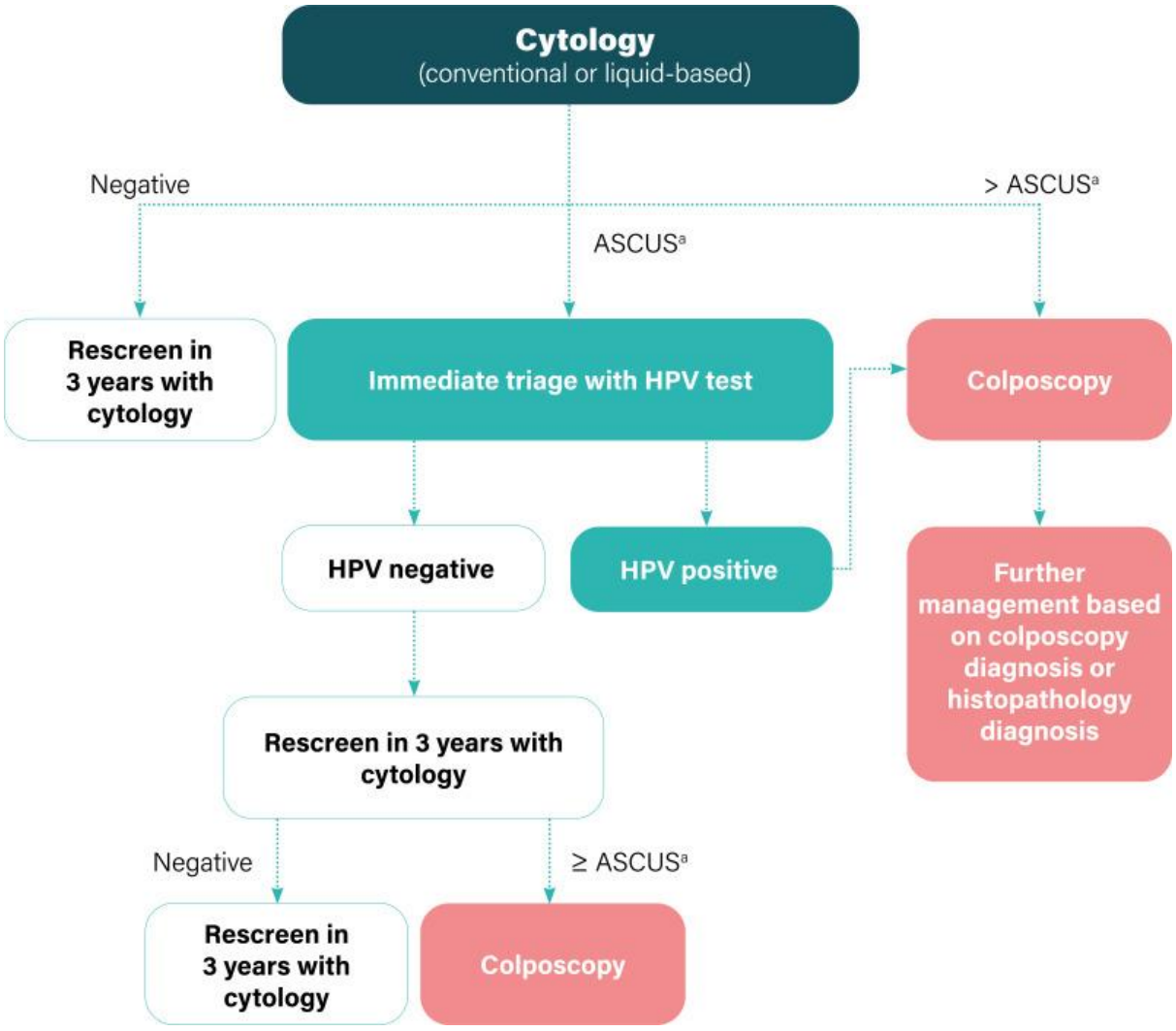

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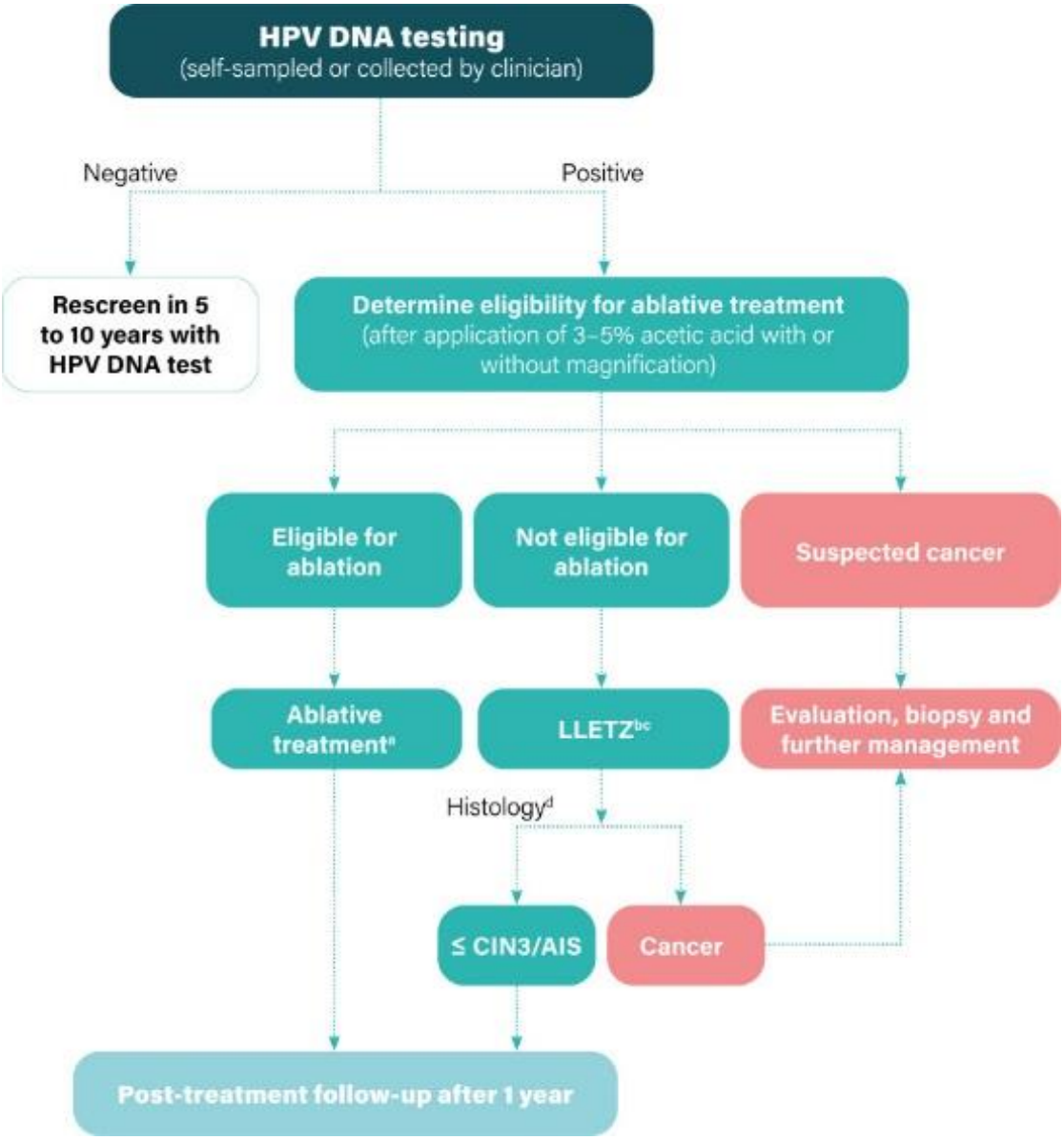

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BENIGN BREAST TUMORS

Dr. Uy Kyna, Prof. Lieng Chanrith, Dr. Chhit Maryan

I. OVERVIEW

Breasts are complex structures, filled with glands, tissue and fat. It's relatively common to develop a breast lump, cyst or tumor in the breast.

A non-cancerous (benign) tumor of the breast:

- is a growth that does not spread (metastasize) to other parts of the body
- are not usually life-threatening.

They are typically removed with surgery and do not usually recur.

II. RISK FACTORS FOR BENIGN BREAST DISEASE

- Benign breast disease can affect anyone.
- Risk for benign breast disease increases:
  - Have a family history of breast cancer or benign breast disease.
  - Use hormone replacement therapy.
  - Have a hormonal imbalance.

III. CAUSES OF BENIGN BREAST DISEASE

Common causes of noncancerous breast lumps include:

- Fibrocystic breast changes.
- Mastitis.
- Scar tissue from a breast injury.
- Hormone fluctuations, especially during menstruation, pregnancy or menopause.
- Medication use, such as hormonal contraceptives and hormone replacement therapy.
- Consuming too much caffeine.

IV. SYMPTOMS OF BENIGN BREAST DISEASE

Detects the breast changes or a lump during:

- A breast self-exam,
- Clinical breast exam,
- A mammography.

Besides a breast lump, other signs of benign breast disease include:

- Breast pain (mastalgia).
- Nipple discharge.
- Change in breast size, shape or contour.
- Inverted, creased or scaly nipple.
- Dimpled, puckered or scaly breasts.

V. DIFFERENT NON-CANCEROUS TUMORS OF THE BREAST

i. Fibroadenoma

- are made up of connective and gland tissues.
- are common in young women between 15 and 35 years of age.
- can develop in one or both breasts.
- are mostly 1–2 cm in size, but they can grow as large as 5 cm.
- Simple fibroadenomas don't increase the risk for breast cancer.
- Complex fibroadenomas are made up of different tissues, including:
  - Cysts.
  - Calcification.
  - enlarged lobules.
- Complex fibroadenoma slightly increases the risk for developing breast cancer.
  - A fibroadenoma is usually found as a lump in the breast.
  - The lump feels rubbery or smooth, it is easy to move in the breast tissue and it has well-defined edges.

ii. Intraductal papilloma

- An intraductal papilloma is a wart-like tumor that develops in a breast duct.
- They are usually found close to the nipple.
- Most intraductal papillomas:
  - do not increase the risk of developing breast cancer.
  - may be slightly higher of developing breast cancer if there is a atypical hyperplasia.
- Most common symptom of an intraductal papilloma is:
  - nipple discharge clear or bloody.
  - lump near or under the nipple.
  - pain.

iii. Phyllodes tumors

- Terminology:
  - Due to its cystic components and fleshy appearance, this tumor was originally referred to as 'cystosarcoma'.
  - These tumors display benign behavior in the majority of the cases.
  - The World Health Organization recommended the use of the neutral expression 'phyllodes tumor'.
- The prevalence is predominantly in middle-aged females (incidence peak between age 40 and 50 years).
- The mean size is 4–5 cm.
- Phyllodes tumors:
  - are almost non-cancerous.
  - may be cancerous in rare cases.
- Other phyllodes tumors are classified as borderline.

- A phyllodes tumor can:
  - cause a firm round lump and pain.
  - grow very quickly.

iv. Breast cysts

- Up to 25% of breast lumps are fluid-filled cysts.
- Breast cysts:
  - can be tender and lumpy.
  - don't make more prone to cancer.
  - often go away without treatment.

v. Hyperplasia

- This condition occurs from an overgrowth of cells that line the mammary ducts or glands.
- Typical hyperplasia slightly increases breast cancer risk.
- Atypical hyperplasia may make more prone to breast and require surgery to remove the affected breast tissue.

vi. Mammary duct ectasia

- People who have reached menopause are more prone to mammary duct ectasia.
- It causes the milk ducts to swell, thicken and sometimes become blocked.
- The nipple may turn inward or leak discharge.
- Periductal mastitis doesn't increase cancer risk.
- Antibiotics if a bacterial infection causes the inflammation and blockage.
- Otherwise, no treatment.

vii. Traumatic fat necrosis

- These breast lumps form when scar tissue replaces breast tissue that's been damaged by an injury, surgery or radiation therapy.
- Fat necrosis doesn't raise the cancer risk and doesn't need treatment.

viii. Adenosis

- This is when the lobules in breast grow larger and contain more glands than usual.

ix. Rare non-cancerous tumors of the breast

- lipoma
- hemangioma
- hamartoma
- adenoma
- neurofibroma
- granular cell tumor.

VI. DIAGNOSIS AND TESTS

i. Imaging scans

- mammogram,
- ultrasound
- magnetic resonance imaging (MRI).

a. Mammography

- Mammograms can help detect and assess breast lumps, especially in women over 40.
- Diagnostic mammography to look for masses and calcifications
- Characteristics of benign lesions on mammography:
  - Well-defined, smooth, and round/oval shapes.
  - Benign breast tumors like fibroadenomas often have smooth edges, while
  - cysts appear as dark, well-circumscribed areas.
- Mammograms are reported in a format following the guidelines of breast.

Imaging Reporting and Data System (BI-RADS)

BI-RADS (Breast Imaging-Reporting and Data System) is a risk assessment and quality assurance tool. It applies to mammography, ultrasound, and MRI.

BI-RADS 0	Incomplete - need additional imaging evaluation (additional mammographic views or ultrasound) and/or - for mammography, obtaining previous images not available at the time of reading.
BI-RADS 1	Negative - symmetrical and no masses, architectural distortion, or suspicious Calcification
BI-RADS 2	Benign finding - 0% probability of malignancy
BI-RADS 3	Probably benign finding - < 2% probability of malignancy - short interval follow-up suggested
BI-RADS 4	Suspicious for malignancy - biopsy should be considered
BI-RADS 5	Highly suggestive of malignancy - >95% probability of malignancy - appropriate action should be taken.
BI-RADS 6	known biopsy-proven malignancy

b. Ultrasound
    - Often used for women under 40, as dense breast tissue in younger women can make mammogram interpretation challenging.
    - Ultrasound can differentiate between solid masses (like fibroadenomas) and fluid-filled cysts.
    - Cysts typically appear as round or oval, anechoic (black) structures with smooth borders on ultrasound.

c. Magnetic resonance imaging (MRI)
    - Breast magnetic resonance imaging (MRI) is increasingly being used for screening high-risk young women.
    - MRI is used if additional detail is needed or if other imaging methods are inconclusive.
    - MRI is especially helpful for patients with a family history of breast cancer, dense breast tissue, or for evaluating complex cases.

ii. Biopsy Techniques

Biopsy may be performed to obtain tissue samples for further examination.

a. Fine-Needle Aspiration (FNA):
    - A thin needle is used to remove cells or fluid from the lump.
    - FNA can confirm the presence of a cyst if fluid is withdrawn, which is indicative of a benign cyst rather than a solid mass.

b. Core Needle Biopsy:
    - A larger needle is used to extract a small cylinder of tissue from the lump.
    - Core biopsies provide more tissue for analysis than FNA, allowing pathologists to better distinguish benign from malignant features.

c. Surgical (Excisional) Biopsy:
    - In cases where the diagnosis remains uncertain, a surgical biopsy may be performed to remove the entire lump.
    - This is less common but is sometimes used when there is suspicion of a phyllodes tumor or if the lump has unusual features.

iii. Pathological Analysis

- Tissue from a biopsy is examined under a microscope to determine if it is benign or malignant.
- Common benign findings:
    - **Fibroadenoma**: Composed of fibrous and glandular tissue, usually well-defined with uniform cells.
    - **Cysts**: Fluid-filled sacs lined with benign epithelial cells.

- **Intraductal papilloma**: Benign wart-like growth inside the ducts, often associated with nipple discharge.
- **Phyllodes tumor**: Typically, benign but with a potential to grow rapidly; some phyllodes tumors can be borderline or malignant.

iv. Laboratory and Blood Tests

- Blood tests are not usually part of the diagnosis of benign breast tumors,
- CA 15-3 or CA 125 tumor markers may be evaluated in cases with a family history of breast cancer.
- However, these markers are more commonly used in monitoring diagnosed breast cancer rather than benign tumors.

v. Follow-Up and Monitoring

- For certain benign tumors, especially small and asymptomatic fibroadenomas, **regular monitoring** with periodic imaging (every 6-12 months) may be recommended to check for any changes in size or characteristics.

VII. MANAGEMENT AND TREATMENT

- The treatment of benign breast tumors depends on the type of tumor and the symptoms it causes.
- Some common approaches:

i. Monitoring and Observation

ii. Regular Check-Ups

- Regular monitoring through physical exams and imaging tests can help ensure they remain stable.
- Many benign breast tumors, like fibroadenomas and cysts, may not require immediate treatment.
- A fibroadenoma:
- usually doesn't need to be treated.
- needs s to surgical remove if it grows over time or changes the shape of the breast.

iii. Medications

- Pain Management:
  - Over-the-counter pain relievers can help manage discomfort if the tumor is causing pain.
- Hormonal Treatments:
  - In some cases, hormonal treatments may be used to manage symptoms or shrink the tumor.

iv. Surgical Options

a. Fine-Needle Aspiration:

- For cysts, a thin needle can be used to drain the fluid and relieve discomfort.

- During a fine-needle aspiration with a thin needle into the breast lump and attempts to aspirate fluid.
- Often, fine-needle aspiration is done using ultrasound to guide accurate placement of the needle.
- If fluid comes out and the breast lump goes away:
    - the diagnosis of a breast cyst can be done.
- If the fluid is not bloody and has a straw-colored appearance and the breast lump disappears:
    - no further testing or treatment.
- If the fluid appears bloody or the breast lump doesn't disappear:
    - a sample of the fluid for lab testing.
- If no fluid is withdrawn:
    - the lack of fluid or a breast lump that doesn't disappear after aspiration suggests that the breast lump or at least a portion of it is solid.
    - A sample of the tissue may be collected to check for cancer.

b. Lumpectomy:

- This surgical procedure removes the tumor while preserving as much breast tissue as possible.

c. Mastectomy for:

- Large cancerous phyllodes tumors or phyllodes tumors.
- Atypical hyperplasia may make more prone to breast and require surgery to remove the affected breast tissue.
- If the tumor is causing symptoms or growing, surgical removal may be recommended.

VIII. BREAST DISORDERS DURING PREGNANCY AND LACTATION

- In preparation for lactation, pregnancy is a time of unique change to breast tissue.
- Due to higher circulating levels of hormones, there is more ductal and lobular growth, increased vascularity and a reduction in stroma.
- Changes in hormone levels during pregnancy can cause breast lumps, tenderness and nipple discharge.
- Breast changes during pregnancy or breastfeeding are rarely cancerous.
- This usually results in significantly increased breast density, which can cause difficulty in the clinical and radiological diagnosis of pregnancy and lactation-associated breast masses.
- A pregnancy-related breast disorder is defined as a diagnosis made during pregnancy, within one-year post-partum or during lactation.
- The main differential diagnoses for palpable breast masses in pregnant or lactating women include: fibroadenoma, lactational adenoma, mastitis with or without abscess formation, galactocele and normal breast tissue with lactational change.

a. Galactocele:

- Galactocele:

    - is the most common benign mass lesion diagnosed during lactation.
    - can be associated with inflammation and necrosis.
    - appears clinically as a well circumscribed smooth mass that is often mobile.
- Ultrasound findings are those of a simple or complicated cyst, with a well circumscribed, ovoid, anechoic or hypoechoic mass showing posterior acoustic enhancement.
- Aspiration of a galactocele is both diagnostic and therapeutic.

b. Fibroadenoma
- Fibroadenoma:
    - are hormone sensitive.
    - are expected to grow during pregnancy and breastfeeding due to increased hormone levels.
    - may have complex features such as cystic spaces and increased vascularity due to rapid growth.
- These lesions may also undergo spontaneous infarction.
- This can result in imaging findings that are more suspicious such as heterogeneous echotexture and shadowing on ultrasound.
- A tissue diagnosis is required for presumed fibroadenoma that are solitary and palpable, or that display atypical features on clinical examination or imaging.

c. Puerperal Mastitis/Abscess Disease
- Puerperal mastitis is inflammation of the breast that occurs during pregnancy, lactation or weaning.
- A breast abscess forms as a complication of mastitis.
- Ultrasound is used to investigate whether abscess formation has occurred, and for image-guided abscess drainage.
- Malignancy must be ruled out with tissue sampling if a patient's condition does not improve with antibiotic therapy.

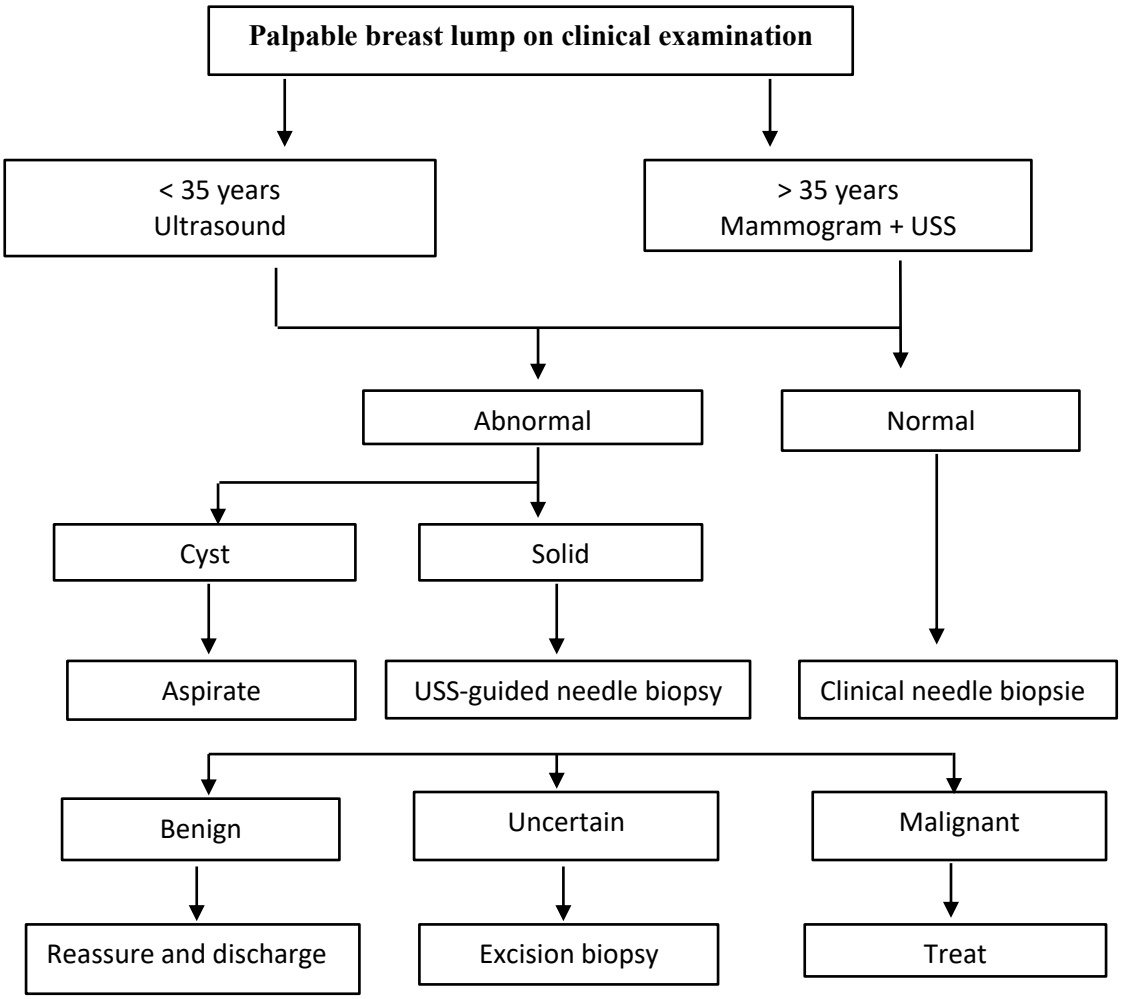
d. Lactating Adenoma
- A lactating adenoma is a benign stromal tumor which often presents as a palpable mobile mass with rapid growth during pregnancy.
- Ultrasound appearance of a lactating adenoma can be almost identical to a fibroadenoma.
- If imaging features suggestive of malignancy may be present, a tissue sample must also be sought to make a definitive diagnosis.

IX. PREVENTION

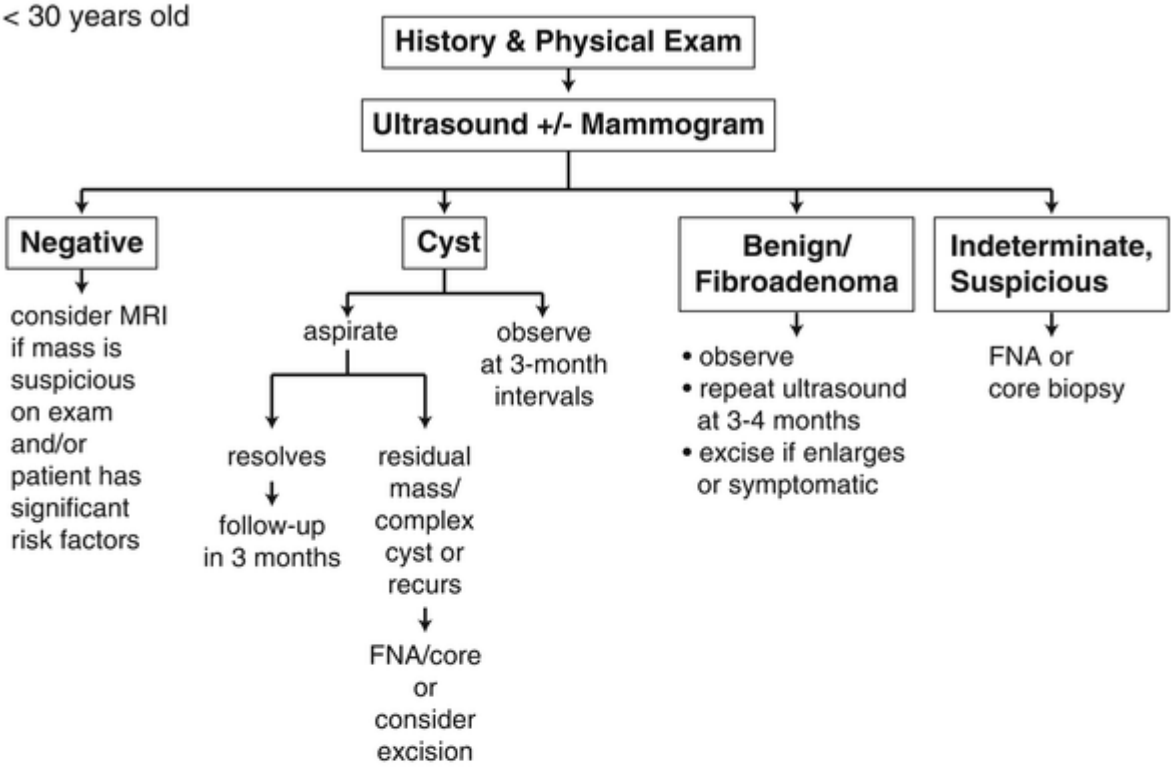
- Not be able to prevent benign breast disease, but can take steps to reduce the risk.
- Decreasing caffeine intake (coffee, tea, soda or chocolate, for example).
- Wearing well-fitted bras and avoiding underwire bras.
- Not smoking or quitting smoking.
- Avoiding drinking beverages containing alcohol.
- Get regular mammogram screenings.
- Perform self-breast exams to be familiar with how breasts look and feel.
- Maintain a healthy weight.
- Exercise regularly.
- Eat a nutritious diet.
- Reconsider the use of hormone replacement therapy.
- Switch to a non-hormonal birth control option.

X. ALGORITHM

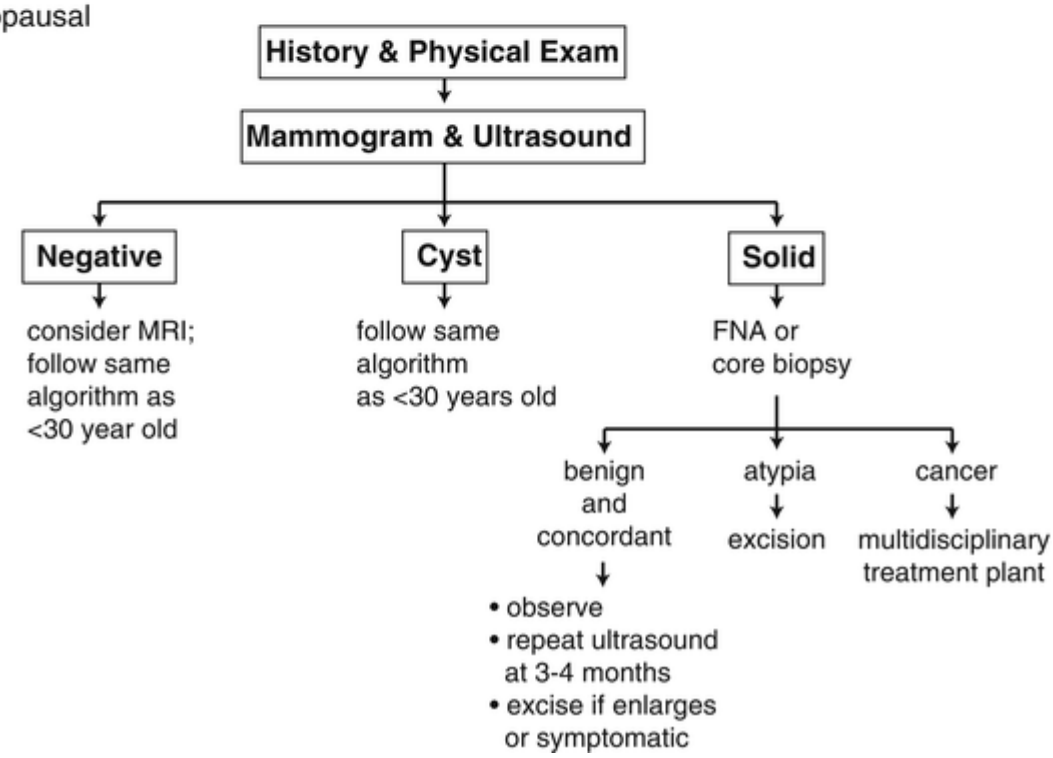
INVESTIGATION OF A BREAST LUMP



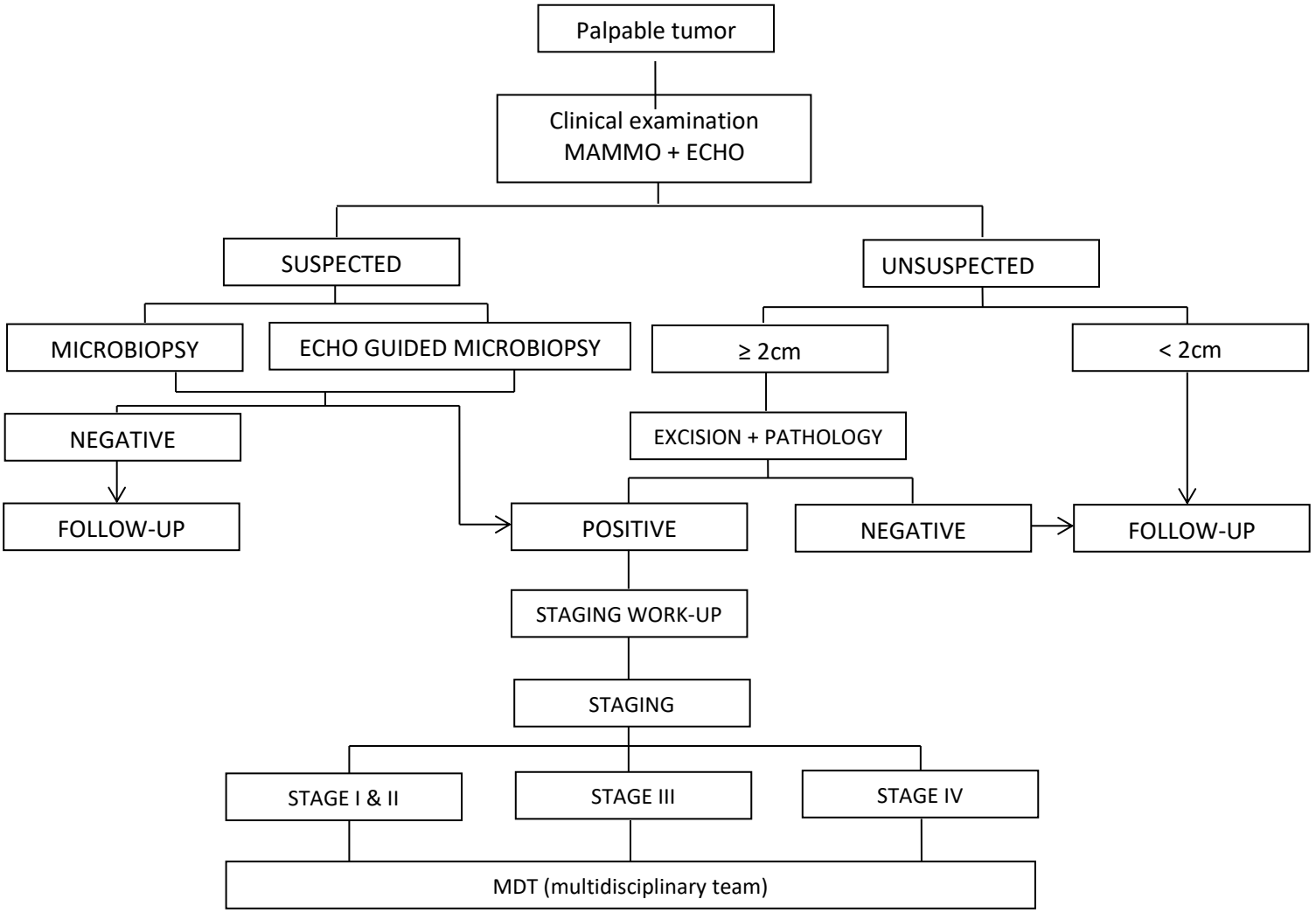
a PALPABLE BREAST MASS
< 30 years old



b PALPABLE BREAST MASS
≥ 30 years old
premenopausal



c PALPABLE BREAST TUMOR



SUSPECTED

- Age, Family, Breast feeding, Lymph node, size, Adhesion, Bloody nipple discharge, Early menarche, Contraceptive
- Imaging:
    - Mammography:
        - Micro-calcification,
        - ACR >3,
        - BIRAD >3.
    - Echography:
        - Hypoechoic,
        - irregular border,
        - architectural distortion

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LEIOMYOMA OF UTERUS

Dr. Khor Hok Sunn, Dr. Leap Sovann, Dr. Sophean Sahakcheat., Prof. Pech Sothy, Dr. Krouch Rayounette

I. DEFINITION

Uterine fibroids, or leiomyomas are benign tumors that originate from the uterine smooth muscle tissue, the most common benign tumors in women of reproductive age.

II. EPIDEMIOLOGY

Their prevalence is age dependent and most common in women aged 30-40 years, but they can occur at any age.

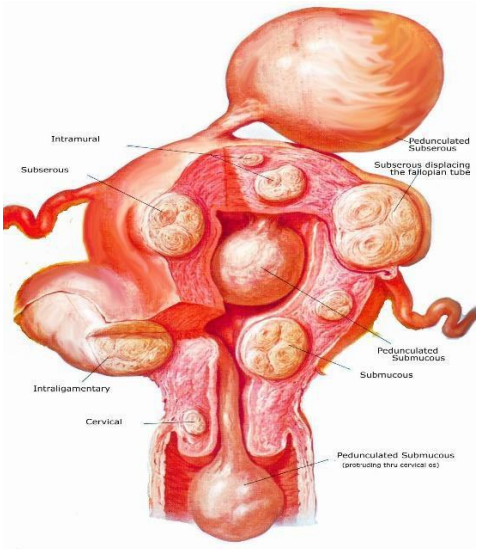
Uterine fibroids are the leading indication for hysterectomy (30%).

Although many are detected incidentally on imaging in asymptomatic women, 20% to 50% of women are symptomatic and may wish to pursue treatment.

III. TYPES OF LEIOMYOMAS OF UTERUS

Three most common types are:

- Submucosal (under endometrium).
- Intramural/interstitial (centered in muscle),
- Subserosal/subperitoneal (under uterine serosa)
- Other sites: cervix, broad ligament, peritoneal cavity stalk-like (pedunculated) or broad-based (*sessile*)



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IV. ETIOLOGY

Fibroids are benign tumors that originate from the uterine smooth muscle tissue whose growth is dependent on estrogen and progesterone.
Fibroids are rare before puberty, increase in prevalence during the reproductive years, and decrease in size after menopause.

Aromatase in fibroid tissue allows for endogenous production of estradiol, and fibroid stem cells express estrogen and progesterone receptors that facilitate tumor growth in the presence of these hormones
Factors that affect the risk of uterine fibroids:

- Decreased risk: increased parity, late menarche (older than 16 years), smoking, use of oral contraceptives
- Increased risk: African descent, age greater than 40 years, early menarche (younger than 10 years), family history of uterine fibroids, nulliparity, obesity

V. DIAGNOSIS

i. Clinical argument

Fibroids can cause abnormal uterine bleeding, pelvic pressure, bowel dysfunction, urinary frequency and urgency, urinary retention, low back pain, constipation, and dyspareunia.

The evaluation of fibroids is based mainly on the patient's presenting symptoms:

- Abnormal menstrual bleeding,
- Bulk symptoms,
- Pelvic pain,
- or findings suggestive of anemia.

Fibroids are sometimes found in asymptomatic women during routine pelvic examination or incidentally during imaging.
On abdominopelvic examination, uterine fibroids usually present as a large, midline, irregular-contoured mobile pelvic mass with a characteristic “hard feel” or solid quality.

ii. Investigations

a. Imaging/ Radiology

- Ultrasonography is the preferred initial imaging modality.
- Transvaginal ultrasonography is about 90% to 99% sensitive for detecting uterine fibroids, but it may miss subserosal or small fibroids.
- Sonohysterography or hysteroscopy improves sensitivity for detecting submucosal myomas.

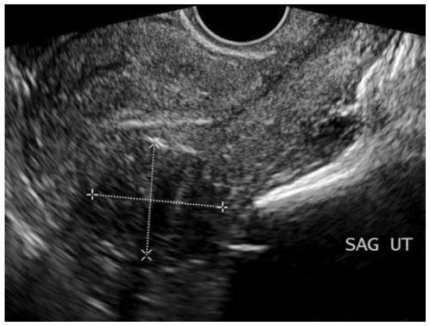


Figure: Transvaginal sonogram of an intramural leiomyoma (Dr. Elysia Moschos)

- Hysteroscopy, hysterosalpingography, and saline infusion ultrasonography are the best techniques for identifying intrauterine lesions such as submucosal myoma and polyps.
- Endometrial biopsy should not be relied on to provide additional diagnostic information.
- CT-Scan and MRI may be useful in evaluating extremely large myomas when ultrasonography may not image a large myoma well and MRI for cervical fibroids.

b. Laboratory test
- CBC, Blood groups, clotting profile
- Glycemia, liver function test, kidney function test
- Other tests if necessary

c. Histopathology

There are no reliable means to differentiate benign from malignant tumors without pathologic evaluation.

VI. DIFFERENTIAL DIAGNOSIS

Differential diagnosis of uterine masses:

- Adenomyosis
- Ectopic pregnancy
- Endometrial carcinoma
- Endometrial polyp
- Endometriosis
- Metastatic disease
- Pregnancy
- Uterine carcinosarcoma
- Uterine sarcoma (leiomyosarcoma, endometrial stromal sarcoma, mixed mesodermal tumor)

VII. TREATMENT

Treatment of uterine fibroids should be tailored to the size and location of the uterine fibroids; the patient's age, symptoms, desire to maintain fertility, and access to treatment; and the physician's experience.

- Uterine fibroids that do not cause symptoms, are small, or occur in a woman who is nearing menopause often do not require treatment.
- Medical therapy to reduce heavy menstrual bleeding includes hormonal contraceptives, tranexamic acid, and nonsteroidal anti-inflammatory drugs. Gonadotropin-releasing hormone agonists or selective progesterone receptor modulators are an option for patients who need symptom relief preoperatively or who are approaching menopause.
- Surgical treatment (conservative or radical) includes Myomectomy by laparotomy, laparoscopy; Hysterectomy (abdominal, vaginal, laparoscopic); Therapeutic or operative hysteroscopy; Endometrial ablation
- Interventional therapy: Myolysis, Uterine artery embolization (UAE), and magnetic resonance–guided focused ultrasound surgery (MRg-FUS),

Table: Recommended treatment options

Patient characteristics	Treatment options
Asymptomatic women	Clinical surveillance
Infertile women with distorted uterine cavity (i.e., submucosal fibroids) who desire future fertility	Myomectomy
Symptomatic women who desire future fertility	Medical treatment or myomectomy
Symptomatic women who do not desire future fertility but wish to preserve the uterus	Medical treatment, myomectomy, uterine artery embolization, magnetic resonance-guided focused ultrasound surgery
Symptomatic women who want definitive treatment and do not desire future fertility	Hysterectomy by least invasive approach possible

i. Medical therapies:

a. Gonadotropin-releasing hormone agonists (leuprorelin, triptorelin, goserelin)

Description	Advantages	Disadvantages	Fertility preserved?
Preoperative treatment to decrease size of tumors before surgery or in women approaching menopause	Decrease blood loss, operative time, and recovery time	Long-term treatment associated with higher cost, menopausal symptoms, and bone loss; increased recurrence risk with myomectomy	Depends on subsequent procedure

- The maximum recommended treatment duration is 3 months.
- E.g, Triptorelin (Decapeptyl LP) 1 inj. IM/4 weeks. Prolonged treatment (more than 3 months) with these products is not recommended given the lack of benefit: hot flashes, vaginal dryness and especially the risks of osteoporosis.
- There is no indication for preventive estrogen therapy for osteoporosis (AFSSAPS, 2004).

b. Levonorgestrel-releasing intrauterine system (LNG-IUS)

- LNG-IUS is not only a reasonable option for patients desiring long-term contraception but may also be beneficial in the management of symptomatic uterine fibroids.
- It is an effective and safe treatment option for symptomatic uterine fibroids in premenopausal women.

Description	Advantages	Disadvantages	Fertility preserved?
Treats abnormal uterine bleeding, likely by stabilization of endometrium	Most effective medical treatment for reducing blood loss, decreases fibroid volume	Irregular uterine bleeding, increased risk of device expulsion	Yes, if discontinued after resolution of symptoms

c. Nonsteroidal anti-inflammatory drugs

- Non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and mefenamic acid, can be taken 3 times a day from the first day of your period until bleeding stops or reduces to manageable levels.
- NSAIDs work by reducing your body's production of a hormone-like substance called prostaglandin, which is linked to heavy periods.
- Anti-inflammatory medicines are also painkillers, but they are not a form of contraception. Indigestion and diarrhoea are common side effects of NSAIDs.

Description	Advantages	Disadvantages	Fertility preserved?
Anti-inflammatories and prostaglandin inhibitors	Reduce pain and blood loss from fibroids	Do not decrease fibroid volume, gastrointestinal adverse effects	Yes

d. Oral contraceptives

- Lo Loestrin Fe offers the lowest daily dose of estrogen at 10 mcg. Loestrin is great for women with fibroids because it can decrease heavy periods and reduce pain from menstrual cramps, but the low dose of estrogen won't cause fibroids to grow.
- Progestin-only pill (POP): Norethindrone can effectively control side effects of fibroids such as heavy and painful menstrual periods. It's usually taken as a daily tablet from days 5 to 26 of your menstrual cycle, counting the first day of your period as day 1. The side effects
- of oral progestogen can be unpleasant and include weight gain, breast tenderness and short-term acne.

Description	Advantages	Disadvantages	Fertility preserved?
Treat abnormal uterine bleeding, likely by stabilization of endometrium	Reduce blood loss from fibroids, ease of conversion to alternate therapy if not	Do not decrease fibroid volume	Yes, if discontinued after resolution of symptoms

e. Selective progesterone receptor modulators (SPRMs)

- Both biochemical and clinical evidence suggests that SPRMs may reduce fibroid growth and ameliorate symptoms. Short-term use of SPRMs resulted in improved quality of life, reduced menstrual bleeding and higher rates of amenorrhea.
- These agents are commonly used in the treatment of endometriosis and uterine leiomyomas. Currently used forms include ulipristal acetate, Asoprisnil, and mifepristone.
- The spectrum of morphologic findings is wide and is referred in the literature as Progesterone receptor modulator (PRM)-associated endometrial changes (PAEC) (progesterone receptor modulators).

Description	Advantages	Disadvantages	Fertility preserved?
Preoperative treatment to decrease size of tumors before surgery or in women approaching menopause	Decrease blood loss, operative time, and recovery time, not associated with	Headache and breast tenderness, progesterone receptor modulator-associated endometrial changes,	Depends on subsequent procedure

f. Tranexamic acid

- They work by helping your blood to clot, reducing blood loss.
- Tranexamic acid tablets are taken 3 or 4 times a day during your period for up to 4 days.
- Feeling sick, being sick or diarrhea are possible side effects of tranexamic acid tablets.

Description	Advantages	Disadvantages	Fertility preserved?
Antifibrinolytic therapy	Reduce blood loss from fibroids, ease of conversion to alternate	Do not decrease fibroid volume, medical contraindications	Yes

ii. Surgical therapies:

a. Myomectomy

- It allows the uterus and reproductive function to be preserved.
- Its indication is guided by the woman's desire to preserve her fertility.
- It carries a risk of intraoperative hemorrhage as well as the possibility of late recurrence of the myoma. It is performed by abdominal, laparoscopic or even vaginal route.
- If the myoma is intracavitary, pedunculated or small (less than 4 cm), it can be hoped to be removed by hysteroscopy.

Description	Advantages	Disadvantages	Fertility preserved?
Surgical or endoscopic excision of tumors	Resolution of symptoms with preservation of fertility	Recurrence rate of 15% to 30% at five years, depending on size and extent of tumors	Yes

b. Hysterectomy

- Hysterectomy will raise three problems:
  - The choice between total hysterectomy and subtotal hysterectomy depends on the state of the cervix, the topography of the fibroid and the state of the perineum. Total hysterectomy should be preferred to subtotal hysterectomy.
  - The choice of route: Vaginal hysterectomy is indicated whenever possible and especially if there is an associated prolapse, or a superinfected intracavitary fibroid. It is contraindicated if the vagina is narrow and the fibroid is large.
  - The problem of ovarian conservation: The ovaries must be preserved if the adnexa are healthy and if the patient is under 50 years old.

Description	Advantages	Disadvantages	Fertility preserved?
Surgical removal of the uterus (transabdominally, trans-vaginally or laparoscopically)	Definitive treatment for women who do not wish to preserve fertility; transvaginal and laparoscopic approach associated with decreased pain, blood loss, and recovery time compared with	Surgical risks higher with transabdominal surgery (e.g., infection, pain, fever, increased blood loss and recovery time); morcellation with laparoscopic approach increases risk of iatrogenic dissemination of tissue	No

- Indications of hysterectomy: Uterine fibroids to be operated on are
  - Complicated fibroids, i.e. bleeding, which cause pain, late miscarriages, premature deliveries, we can add fibroids which compress and dilate the

urinary tract on ultrasound or intravenous urography, those which cause hypochromic anemia

- Fibroids associated with a patent genital lesion: Prolapse, ovarian cyst, sequelae of salpingitis, cervical dysplasia and even more so, cervical cancer or an ovarian tumor, with oncological treatment taking precedence over treatment of the fibroid.
- Large or increasing fibroids (>10 cm in diameter)

iii. Interventional therapies:

a. Uterine artery embolization (UAE)

Description	Advantages	Disadvantages	Fertility preserved?
Interventional radiologic procedure to occlude uterine arteries	Minimally invasive, avoids surgery, short hospitalization	Recurrence rate > 17% at 30 months, postembolization syndrome	Unknown

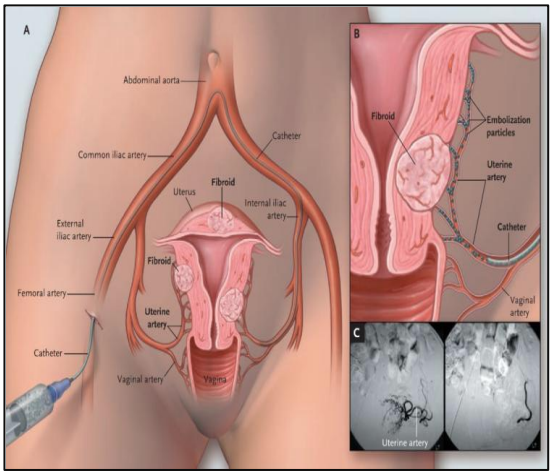


Figure : Embolization of uterine artery by Tulandi T. Treatment of uterine fibroids

b. Magnetic resonance-guided focused ultrasound surgery

Description	Advantages	Disadvantages	Fertility preserved?
In situ destruction by high-intensity ultrasound waves	Noninvasive approach, shorter recovery time with modest symptom improvement	Heavy menses, pain from sciatic nerve irritation, higher reintervention rate	Unknown

VIII. COMPLICATIONS

- Hemorrhagic & pelvic pressure => anemia and urinary and digestive symptoms
- Torsion or Red degeneration (aseptic necrobiosis)
- Sarcomatous changes: fibrosarcoma
- Calcification and Cystic degeneration
- Fibroid and pregnancy: recurrent miscarriage, infertility, premature labor & labor complications
- Infection/ulceration of pedunculated fibroid
- Association with endometrial cancer

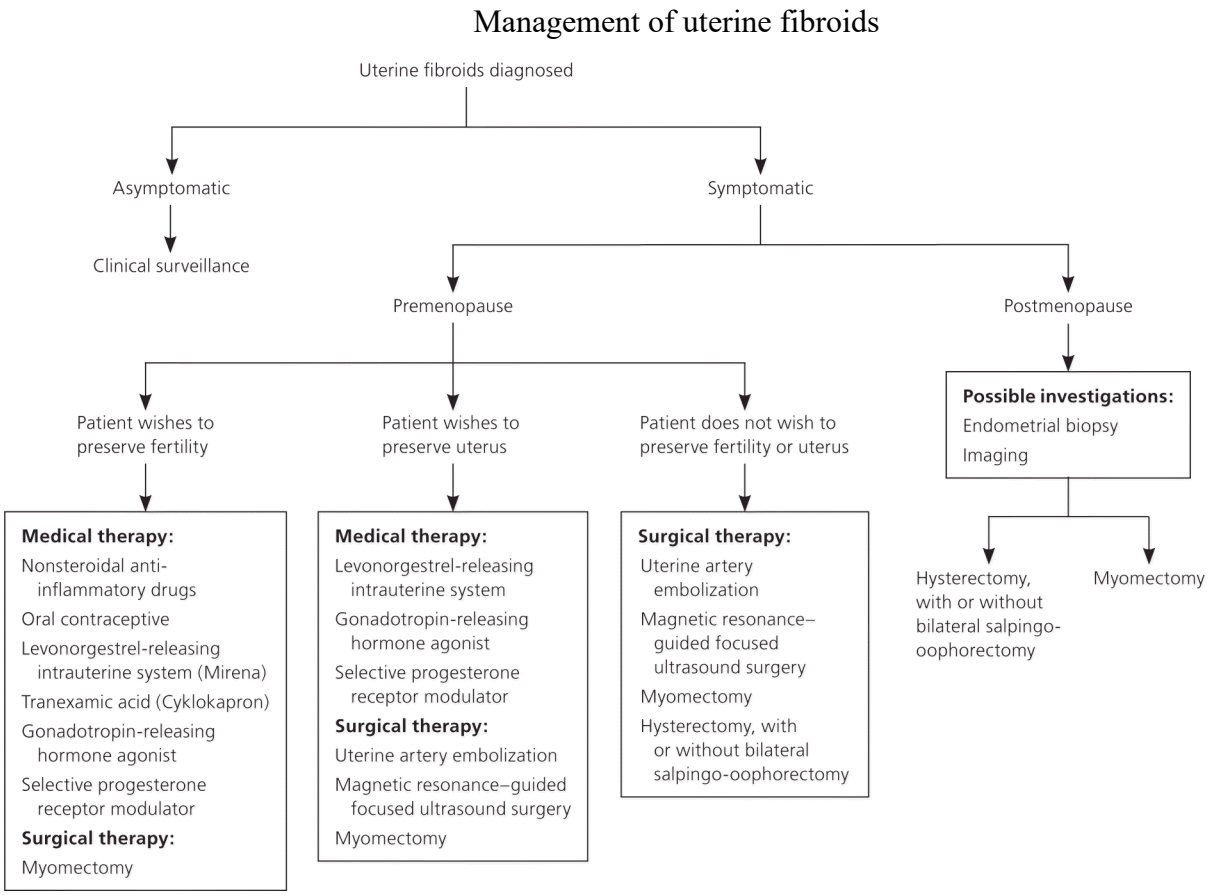
IX. PREVENTION

- It might not be possible to prevent uterine fibroids
- There are some tips to prevent: healthy lifestyle changes; try to stay at a healthy weight; get regular exercise, and eat a balanced diet with plenty of fruits and vegetables.
- Some research suggests that birth control pills or long-acting progestin-only contraceptives may lower the risk of fibroids. But using birth control pills before the age of 16 may be linked with a higher risk.

X. PROGNOSIS

- Many patients have an excellent prognosis and remain asymptomatic for many years or indefinitely.
- Whereas, others will fail medical management and depending on their desire for future fertility, may experience recurrent fibroids requiring multiple surgeries.

XI. ALGORITHM



Adapted from Vilos GA, Allaire C, Laberge PY, et al. The management of uterine leiomyomas. J Obstet Gynaecol Can. 2015;37(2):163.

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RECTOVAGINAL AND ANOVAGINAL FISTULAS

Dr. Uy Sopha, Dr. Chhun Samsorphea, Dr. Lay Sanine,
Dr. Lim Sokong, Prof. Ass. Korn Aun

I. DEFINITION

Anovaginal fistulas (AVFs) and rectovaginal fistulas (RVFs) are abnormal tracts that connect the lower gastrointestinal tract with the vagina.

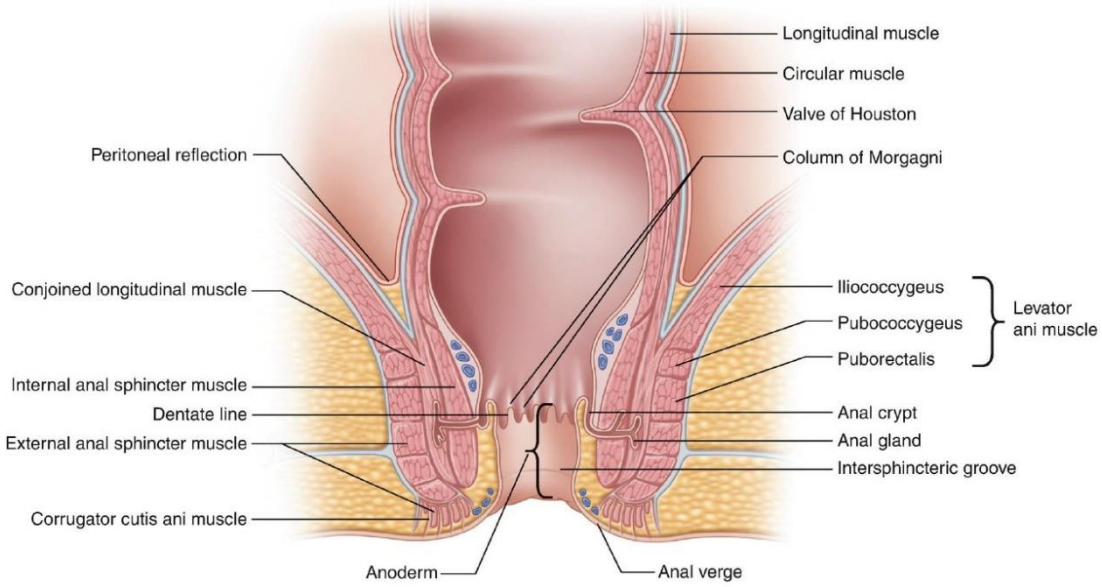
II. ETIOLOGY

- Obstetric trauma: prolonged obstructed labor can lead to pressure necrosis of the rectovaginal septum
- Third- or fourth degree laceration of the perineum
- Episiotomy infection
- Difficult hysterectomies
- Severe endometriosis
- Radiation damage
- Crohn's disease
- Extension or rupture of perirectal, perianal, Bartholin's abscesses
- Surgical procedures involving the posterior vaginal wall, perineum, anus, or rectum

III. CLASSIFICATION OF FISTULAS

According to anatomic landmarks

Type	Name	Anatomical Location
Type I	Anovaginal fistula	Distal to pectinate line
Type II	Rectovaginal fistula	Proximal to pectinate line
Type IIa	Deep-lying rectovaginal fistula	Between pectinate line and middle of rectovaginal space
Type IIb	High-lying rectovaginal fistula	Above the middle of the rectovaginal space



(Anorectal anatomy: Function, Anatomy, Conditions & Diagram)

IV. CLINICAL MANIFESTATIONS

- AVFs or RVFs present with uncontrollable passage of gas or feces from the vaginal
- Malodorous vaginal discharge
- Fecal soiling of the undergarments
- Fecal incontinence

V. EVALUATION AND DIAGNOSIS

- Patient complaint: passing flatus or stool per vagina
- Digital rectal and vaginal examination
- Speculum examination: can see the rectal mucosa distinguished from the paler pink vaginal skin
- Coming the bubbles through the blood/ urine in the posterior vagina when operating for a VVF
- Dye test: inject 200ml of dye through a naso-gastric tube or a Foley catheter passed 10cm into the rectum. use a swab to compress the anus so that the dye does not leak out, or inflate the foley balloon to keep the dye in.
- Pass a probe vaginally into the fistula and palpated rectally, or pass the probe rectally and palpate vaginally
- Endoanal ultrasound: defect in both the internal and external anal sphincter complexes

VI. DIFFERENTIAL DIAGNOSIS

- Fistula-in-ano: abnormal connection between the anal canal and the perianal or perineal skin
- Perianal abscess
- Anal incontinence
- Vaginal infection

VII. SURGICAL PRINCIPLES

Basic principles: The basic principles essential to all successful fistula repairs include:

- Wide mobilization of the adjacent tissue planes
- Complete excision of the fistula tract
- Multilayered closure, which reapproximates broad tissue surfaces without tension and avoids "dead space"
- Proper timing of the repair

Timing of repair:

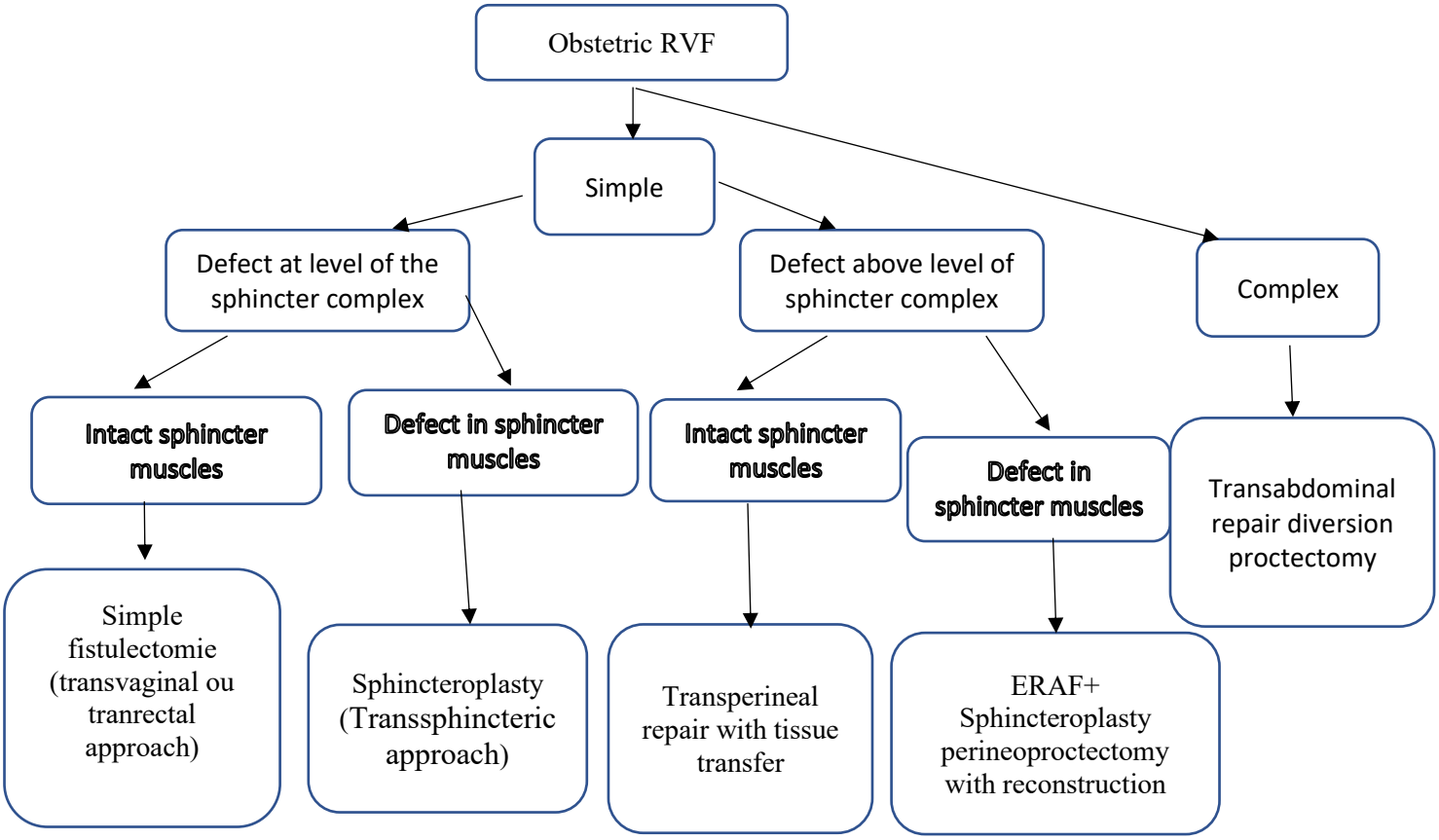
- Early repair provided when there is no infection, induration, or inflammation present in the tissues involved.
- Active wound infection or tissue induration: Patients should be provided with aggressive wound care (eg, sitz baths, debridement) and a 10 to 14-day course of broad-spectrum oral antibiotics. In addition, a low residue diet helps to decrease the frequency of bowel movements, prevent continuous seeding of the wound with liquid stool, and restore some degree of fecal continence.
- Surgery is deferred until all signs of infection, induration, and inflammation have subsided.

Choice of sutures: Use delayed absorbable sutures: Vicryl 2-0, such as polyglactin or polyglycolic acid, instead of chromic catgut in the repair of these fistulas.

VIII. SURGICAL APPROACH

Surgical approaches to anovaginal or rectovaginal fistula repair are dictated by fistula etiologies.

- Fistulas due to obstetric injury
- Fistulas with injured sphincter
- Fistulas above the sphincter
- Fistulas due to radiation
- Low fistulas
- High fistulas
- Fistulas due to inflammatory bowel disease
- Other complex fistulas

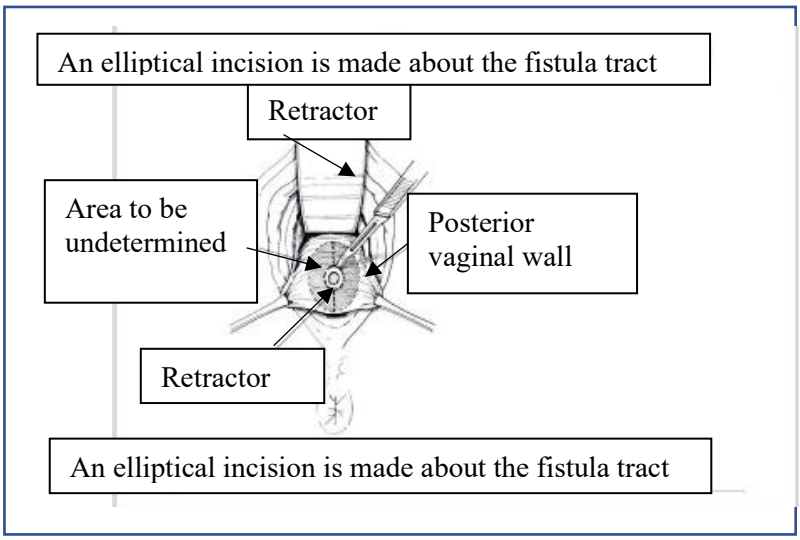


Fistulas due to obstetric injury: For women with anovaginal or rectovaginal fistulas from childbirth, we suggest a simple local repair with or without sphincteroplasty.

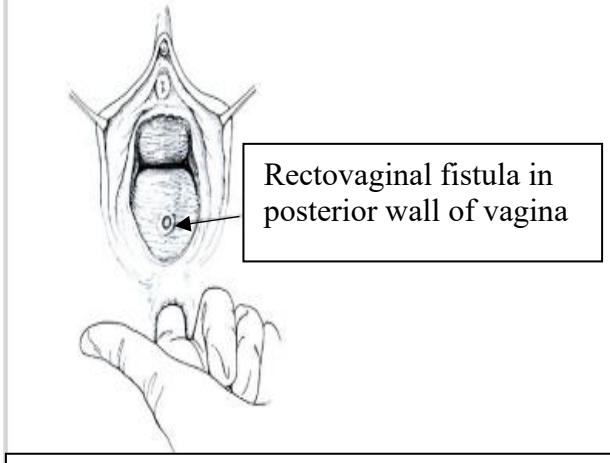
- Fistulas with intact sphincter (Simple fistulectomy): Small rectovaginal fistulas that do not involve the anal sphincter complex can often be repaired by simple fistulectomy via a transvaginal or transrectal approach.
    - An incision is first made around the fistula opening.
    - The surgeon's nondominant index finger can be inserted into the rectum during the procedure to assist the repair
    - Sharp mobilization of the vagina and rectum in a circumferential fashion should be accomplished next by providing traction and counter traction on the fistula
    - After the tissue planes are widely mobilized, the entire fistulous tract and any adjacent scar tissue are excised.
    - The edges of the surgical wound should only contain fresh, viable tissue.
    - The edges of the anterior rectal wall are then inverted, either by placing interrupted submucosal stitches of 3-0 or 4-0 delayed absorbable sutures or by placing a purse string suture.
    - The most cephalad and most caudal sutures should be placed at least 5 mm above and below the fistula.
    - A second layer of sutures of 2-0 delayed absorbable type is then placed in the muscularis of the anterior rectal wall to invert and take tension off of the first suture

line. This layer should begin and end approximately 5 mm above and below the first suture line.

- An additional layer of adjacent rectovaginal tissue is then approximated to provide a third layer of closure and take tension off of the underlying layers of repair
- If necessary, a modified Martius graft (a bulbocavernosus muscle or labial fat pad graft used in closing large or difficult rectovaginal or vesicovaginal fistulas, it provides neovascularity, fills in dead space, and enhances granulation tissue formation at the site of repair) can be interposed between the rectum and vagina before this step.
- Finally, the vaginal mucosa is approximated with a continuous 3-0 suture
- Complete hemostasis and closure of all potential dead space must be ascertained.
- Place a small vaginal pack soaked in a very dilute Betadine solution or use a petroleum-impregnated gauze to promote hemostasis and provide gentle pressure against the incision line.
- Removed the vaginal pack within the first 12 to 24 hours postoperatively.

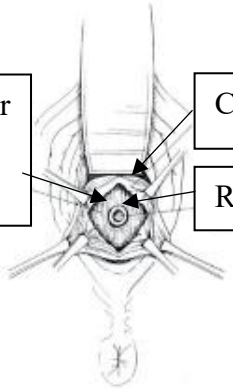


Repair of a small rectovaginal fistula through a transvaginal approach



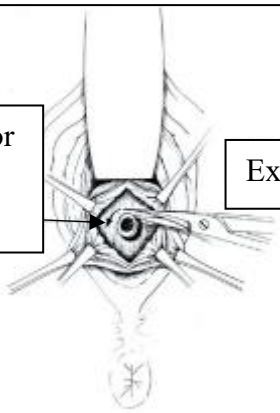
The surgeon places the nondominant index finger into the rectum to demonstrate the fistula

Repair of a small rectovaginal fistula through a transvaginal approach



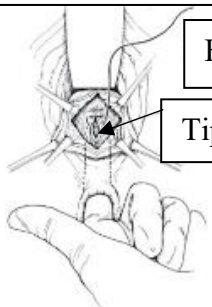
The posterior vaginal wall is sharply mobilized off of the anterior rectal wall

Repair of a small rectovaginal fistula through a transvaginal approach



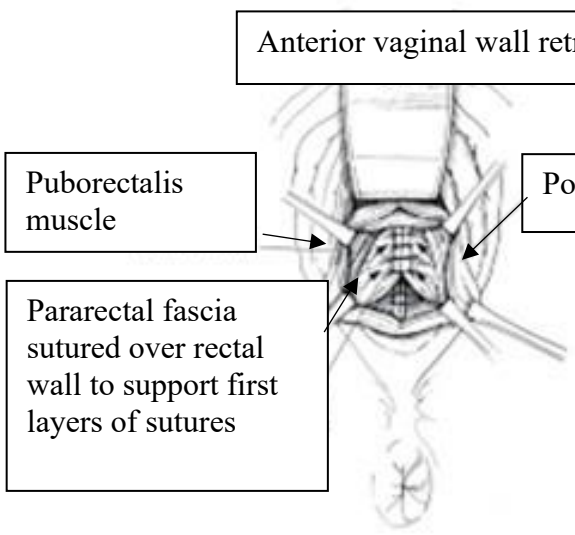
The fistula tract is excised, including the adjacent vaginal and rectal mucosa

Repair of a small rectovaginal fistula through a transvaginal approach



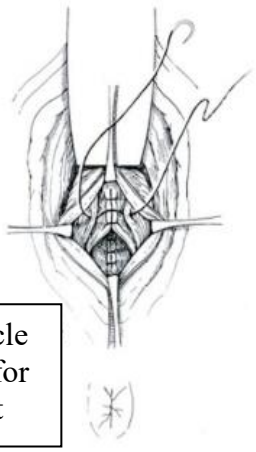
The rectal mucosa is closed using a delayed absorbable suture. Note that the suture line is begun at least 5 mm above the apex of the fistula.

Repair of a small rectovaginal fistula through a transvaginal approach

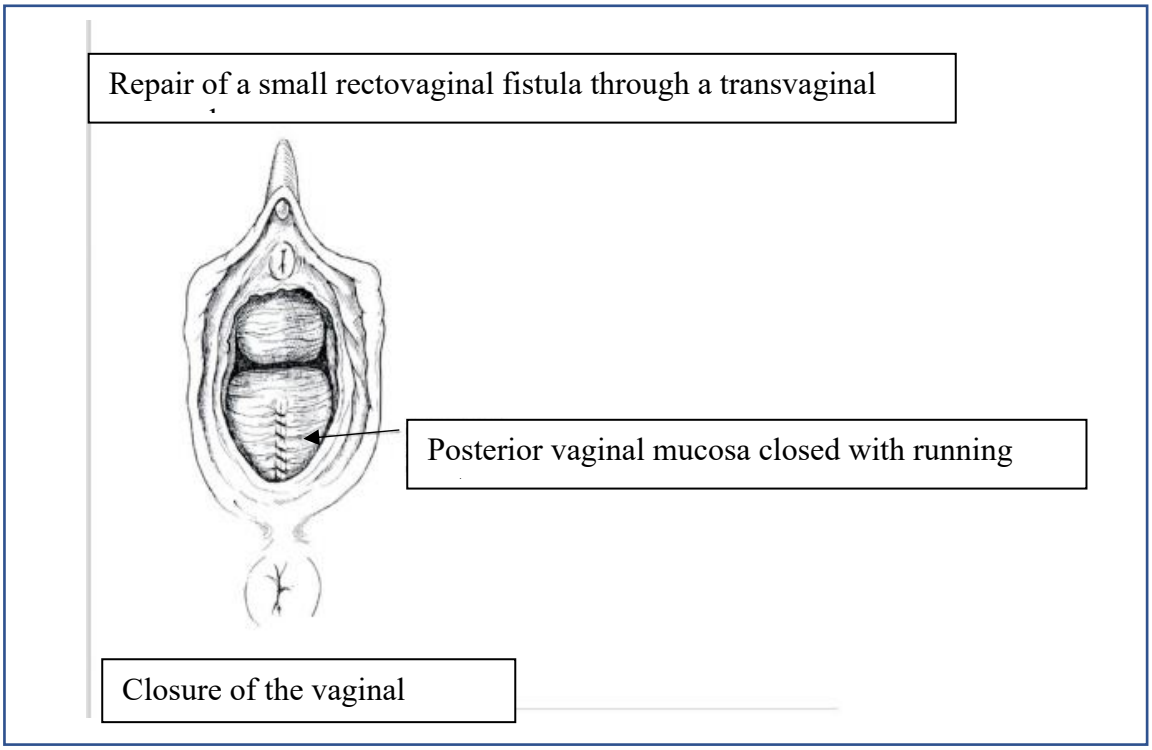


Repair of a small rectovaginal fistula through a transvaginal approach

Repair of a small rectovaginal fistula through a transvaginal approach



The puborectalis fibers are reapproximated in the midline to give a third layer of closure

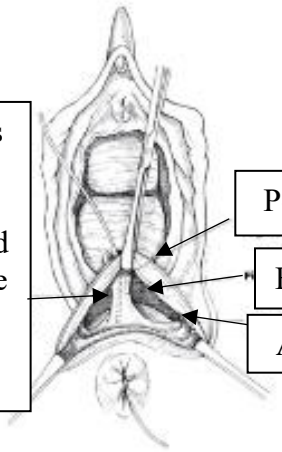


- Fistulas with injured sphincter: Transsphincteric approach in patients with concomitant sphincter injury and absent perineal body or a small bridge of perineal skin,
  - fistula repair may be performed in conjunction with repair of the external and internal sphincters
    - Reconstruction of the perineal body and rectovaginal septum.
    - The preferred approach in these patients is a midline perineal incision (transsphincteric or perineoproctomy) with wide mobilization of the posterior vaginal wall, followed by a multilayered closure as described for a chronic third- or fourth-degree laceration (see "Delayed surgical management of the disrupted anal sphincter"). In all cases, it is important that the fistula tract be excised in its entirety, as discussed above
- Fistulas above the sphincter: Transverse transperineal approach
    - A transverse incision is made across the perineal body above the sphincter complex.
    - Dissection is then carried out in the true rectovaginal space between the anterior rectal wall and the posterior vaginal wall to mobilize the tissues widely laterally and cephalad to the fistula tract.
    - The fistula tract and any adjacent scar tissue are then excised with Metzenbaum or Cooley scissors.
    - The rectal wall defect can be closed either longitudinally or transversely with interrupted 3-0 or 4-0 delayed absorbable sutures to invert the rectal mucosa

without tension. close the other layers longitudinally in all but the smallest fistulas.

- Close the rectal mucosal and perirectal fascial layers longitudinally, the anal canal is lengthened, which may help to reestablish the high-pressure zone of the anal canal.
- Closing the vaginal mucosa and perineal body longitudinally helps to avoid narrowing the vaginal introitus and also lengthens the perineal body.
- To avoid overlapping suture lines, the rectal defect should be closed transversely and the vaginal mucosa closed longitudinally to minimize narrowing of the vaginal introitus and avoid creation of a transverse ridge across the posterior vaginal wall, which can cause dyspareunia.
- The second layer of closure is placed into the muscularis of the rectum in the same direction as the first layer, thus imbricating the first layer and reinforcing the closure.
- The puborectalis muscles are approximated in the midline, providing an additional reinforcing layer between the anterior rectal and posterior vaginal walls.
- The subcutaneous tissues and skin of the perineal body can be approximated with a running nonlocking suture. The skin is closed with interrupted mattress sutures or a running closure of 4-0 delayed absorbable suture.
- Following this procedure, patients are generally hospitalized overnight for pelvic rest (no vaginal insertions), pain control, observation for bleeding, and vaginal pack removal.

Transverse transperineal approach to a rectovaginal fistula located at the sphincter complex



Fistulous tract easily identified with wire probe in place

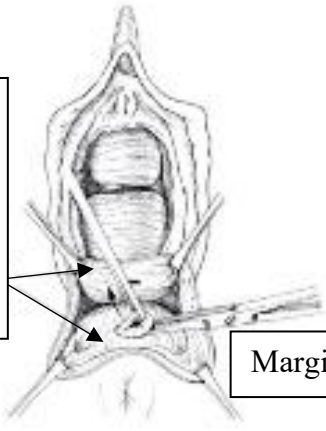
Posterior vaginal wall

Fistulous tract

Anterior rectal wall

Dissection above and lateral to the fistula tract is carried out using sharp dissection.

Transverse transperineal approach to a rectovaginal fistula located above the sphincter complex

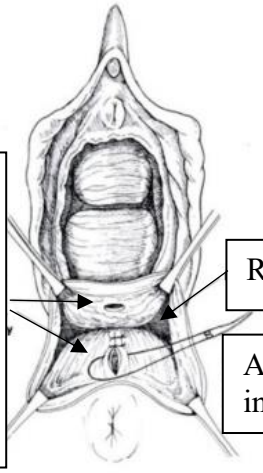


Posterior vaginal wall and anterior rectal wall completely mobilized

Margin of fistula being removed

The fistula tract is excised

Transverse transperineal approach to a rectovaginal fistula located above the sphincter complex



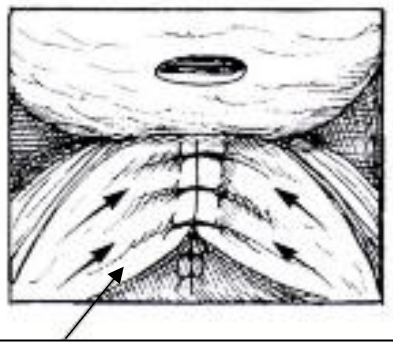
Posterior vaginal wall and anterior rectal wall widely mobilized laterally and superiorly

Rectovaginal space

Anterior rectal wall defect closed longitudinally with interrupted suture

The anterior rectal wall defect is closed longitudinally with interrupted 4-0 delayed absorbable sutures.

Transverse transperineal approach to a rectovaginal fistula located above the sphincter complex

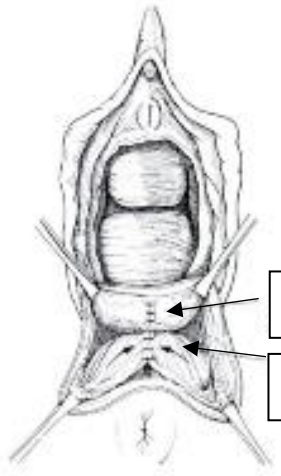


The anterior rectal wall defect is closed longitudinally with interrupted 4-0 delayed absorbable sutures

Pararectal fascia sutured over rectal wall to support first layer of sutures

The second layer of closure is placed into the muscularis of the rectum in the same direction as the first layer, thus imbricating the first layer and reinforcing the closure

Transverse transperineal approach to a rectovaginal fistula located above the sphincter complex

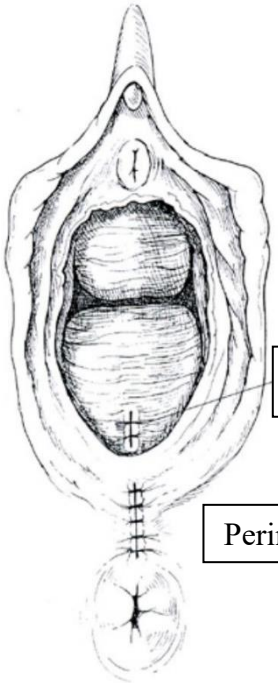


Defect in submucosal tissue of vaginal wall closed

Puborectalis muscles approximated in midline

The puberectalis fibers are reapproximated in the midline, providing an additional reinforcing layer between the anterior rectal and posterior vaginal walls.

Transverse transperineal approach to a rectovaginal fistula located about the sphincter complex

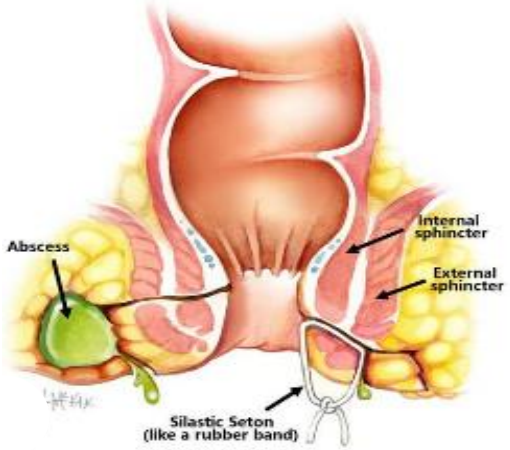


Vaginal wall/mucosa closed longitudinally

Perineal skin closed longitudinally

The perineal body is reapproximated longitudinally with interrupted sutures to lengthen it

For Silastic Seton (like rubber band) we use only in case of anal fistula by surgeon or protologue.



IX. POST OPERATIVE CARE

In hospital care: one night, check the wound one week later

- Check the bowel movement
- Remove vaginal pack

At home: instructions on diet, bowel regiment and general care

- Diet:
  - The first 24 to 72 postoperative hours: Clear liquid diet
  - 3-4 weeks or continue if constipation develops: The low residue diet
- Bowel regimen:
  - give the stool softener to lubricate the stool for one month.
  - If constipation, give milk of magnesia or other laxatives
- General care
  - Instruction in wound care
  - teach how to perform sit baths 2- 3 days following the procedure
  - keep area dry: use a heat lamp or a blow dryer on a cool setting

X. MORBIDITY AND MORTALITY

- Per-operative deaths are rare
- Major morbidities:
  - Wound infection
  - Urinary tract infection
  - Bowel obstruction or perforation
  - vaginal, anal or rectal stenosis
  - fecal incontinence

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UTERINE PROLAPSE

Dr. Ros Saphath, Dr. Hang Sovanara, Prof. Koum Kanal

I. DEFINITION

When the uterus and cervix drop down toward the vaginal entrance and may protrude outside the vagina.

II. RISK FACTORS/PATHOPHYSIOLOGY

i. Risk factors

- Multiple pregnancy and multiple vaginal birth
- Being older
- Chronic cough
- Constipation
- Obesity
- Lifting heavy objects and doing exercises that put pressure in the pelvic floor.

ii. Pathophysiology

Normally the uterus, bladder and rectum are supports by the tissues and muscles in the pelvis (Pelvic floor) keeping them in the appropriate position. If these tissues and muscles weaken, the organs in the pelvis will move down or prolapse

III. INCIDENCE

The incidence of pelvic organ prolapse is varies from 1.5 to 1.8 per 1000 women years and picks women aged 60-69.

IV. DIAGNOSIS PROCEDURE

The diagnosis is based on medical history and symptoms, physical examination and vaginal exam.

i. Clinical argument

- Women's perception of a vaginal bulge which can increase on stress and which is detectable intermittently during the day or during serious activities
- Pelvic heaviness
- Urinary symptoms: urinary incontinence, voiding dysfunction, recurrent urinary tract infections
- Anorectal disorders: anal incontinence, obstructed defecation, fecal urgency
- Discomfort during sexual intercourse

ii. Investigation

a. Urine cytobacteriology
b. Ultrasound
c. Hysterography
d. Urography intravenous
e. Colpocystogramme
f. Cancer screening (Cervix and endometrioid)

V. PELVIC ORGAN PROLAPSE STAGING

Stage I: Uterus, bladder and rectum descend halfway into the vagina

Stage II: Uterus, bladder and rectum descend lower than halfway into the vagina but not outside of the vagina

Stage III: Uterus, bladder and rectum descend partially out of the vagina.

Stage IV: Uterus, bladder and rectum descend completely out of the vagina.

VI. PROGNOSIS/COMPLICATIONS

1- **Prognosis**

It's generally not dangerous. It can expose a risk of complication if these organs permanently come out of the vagina.

2- **Complications**

- Difficulty urinating or unable to empty bladder
- Leaking of urine when sneezing or coughing
- The tissue or mass that extends out of the vagina causes friction and leads to injury.

VII. THERAPEUTIC APPRAOCH

1- **Exercise**: If the prolapse is mild, pelvic floor exercise is a simple way to strengthening the pelvic floor: contract the pelvic floor like trying to stop the flow of urine.

2- **Vaginal pessary**: this is a method to remove the pelvic organs prolapse back to their original position using donut rubber and shaped. It's a temporary solution.

3- **Surgery**

Surgery may be needed to repair uterine prolapse.

Minimally invasive surgery, called laparoscopic surgery, or vaginal surgery might be an option.

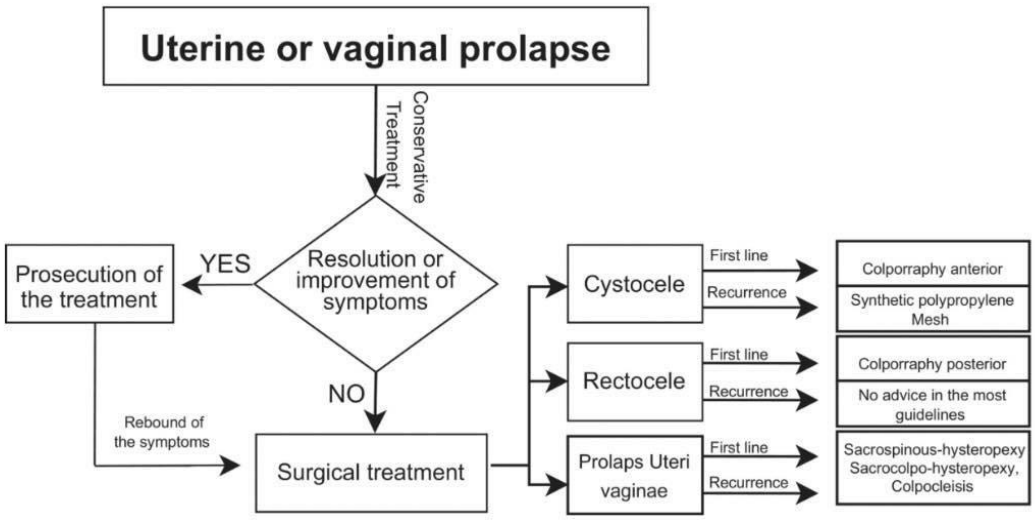
a. Taking out the uterus=hysterectomy
b. A procedure that keeps uterus in place: This is called a uterus-sparing procedure. These surgeries are for people need others pregnancy.
c. Use stitches to fix weak pelvic floor structures: This can be done in a way that keeps the deep and width of the vaginal tract for sexual function.
d. Close the opening of the vagina= Colpocleisis
e. Place a piece of mesh to support vaginal tissues: Vaginal tissues are suspended from the tail bone using a synthetic mesh material.

VIII. PREVENTION

- Do pelvic floor exercise regularly especially before and after child birth
- Avoid becoming constipation
- Maintain healthy weight by using your food and exercise
- Avoid smoking

- Avoid carrying heavy objects
- Hormone replacement therapy if menopausal: this can prevent muscles weakness and prolapse of the uterus. But HRT has certain risks.
- Avoid too many pregnancies and births

IX. ALGORITHMS



X. REFERENCES

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VESICOVAGINAL FISTULA (VVF)

Dr. Lim Sokong, Dr. Uy Sopha, Prof. Ass. Korn Aun, Dr. Chhun Samsorphea, Dr. Lay Sanine, Prof. Keth Lysotha

I. DEFINITION

Vesicovaginal fistula (VVF) is a communication between the bladder and vagina wall, resulting in continuous urine leakage through the vagina, most commonly after obstetrical and gynecological injury.

II. ETIOLOGY

- Obstetrical (trauma during labor and delivery such as instrumental assisted vaginal deliveries) and gynecological injury
- Prolonged or obstructed labor
- Malignant
- Radiation
- Congenital
- Infections and inflammatory diseases
- Foreign objects
- Sexual trauma and violence
- Vaginal laser procedures

III. DIAGNOSTIC PROCEDURE

a. Clinical Arguments

- History: Complaint of permanent urine leakage through the vagina
- Pelvic exam:
  - Speculum exam to identify:
    - Inflammation or other abnormalities
    - Urine leakage through vagina
    - After injecting methylene blue into the bladder, see it flows into vagina

b. Investigations

- Double Dye test: In this test, bladder is filled with a solution that's dyed blue and then a tampon is inserted into vagina. If the tampon turns blue, a VVF is present.
- Cystoscopy:
  - clarify exactly where the VVF is
  - classify the numbers and size
    - intermediate in size if measured at 0.5 to 2.5 cm.
    - complex vesicovaginal fistulas are large in size (>2.5 cm), and associated with chronic disease, post-radiation, or failed previous fistula repair.

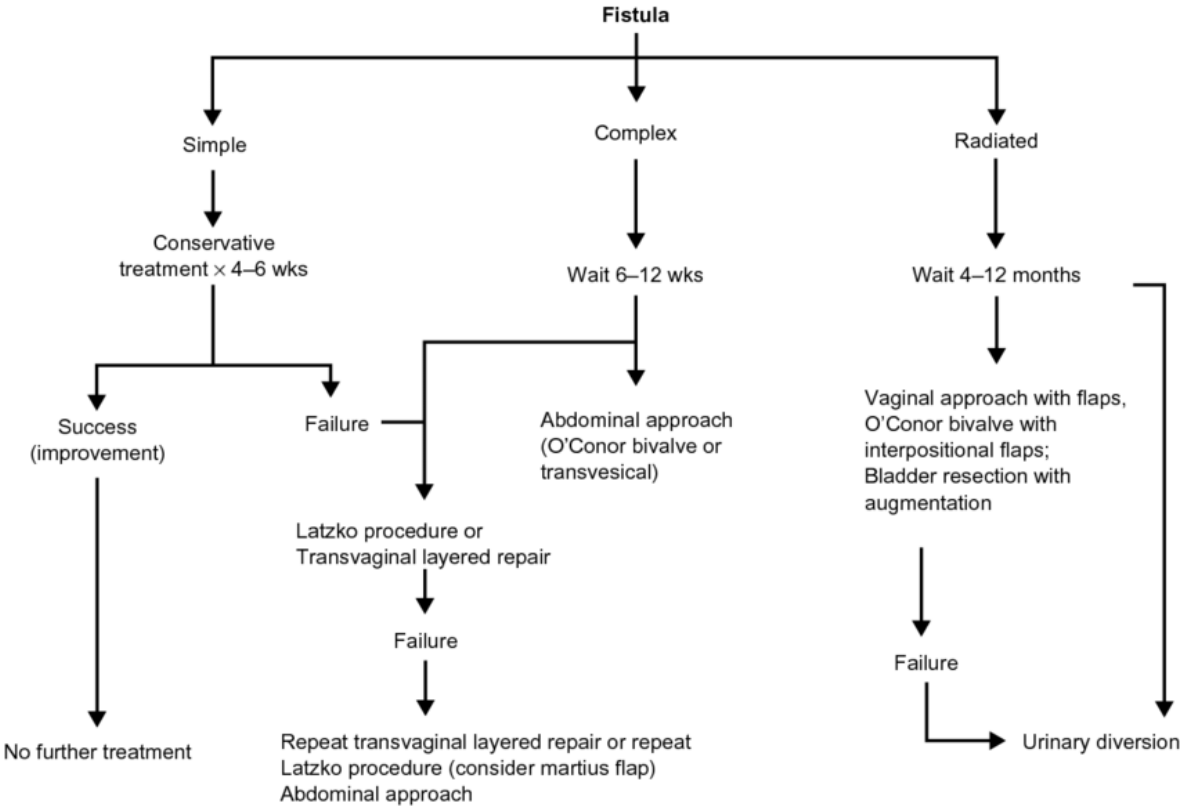
This can help with further aid in treatment planning.

IV. MANAGEMENT

a. Conservative treatment:

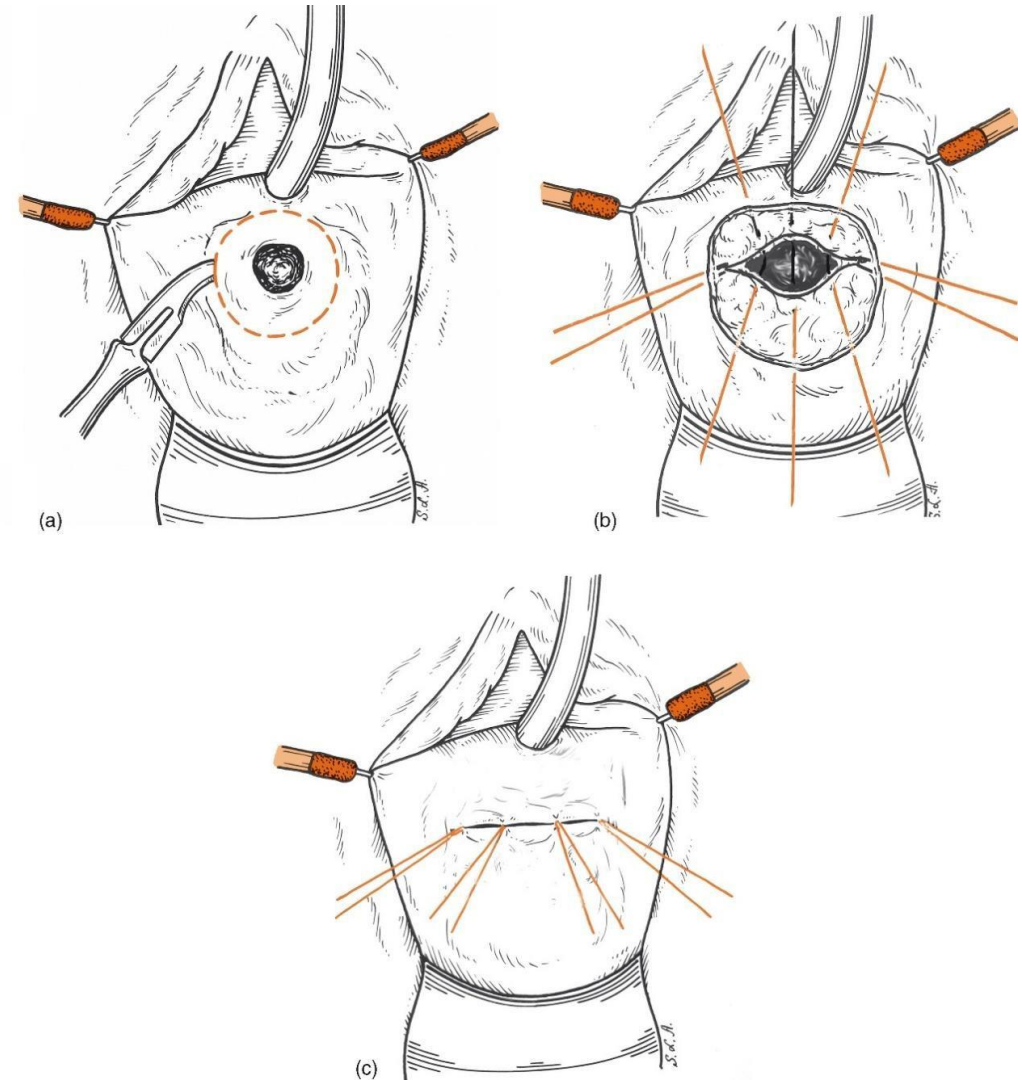
- For VVFs that have been found early, that are small (<0.5cm), and that are noncancerous.
- These can also help with the spontaneous closure of the fistula. To help with symptoms, a catheter may be placed for 4 to 6 weeks along with medications called anticholinergics that help stop some involuntary muscle movement. Antibiotic prophylactic therapy (one dose of cephazolin). Cystoscopy is often performed before catheter removal.
- All patients received anticholinergic treatment and topical estrogen treatment for six months.
- The topical estrogen treatment was started in the postoperative period and 1×1 daily in the first week and then twice a week for a total of six months was recommended. Our preferred agent for topical estrogen treatment was intravaginal 10 mcg estradiol.

Management of Vesicovaginal Fistula



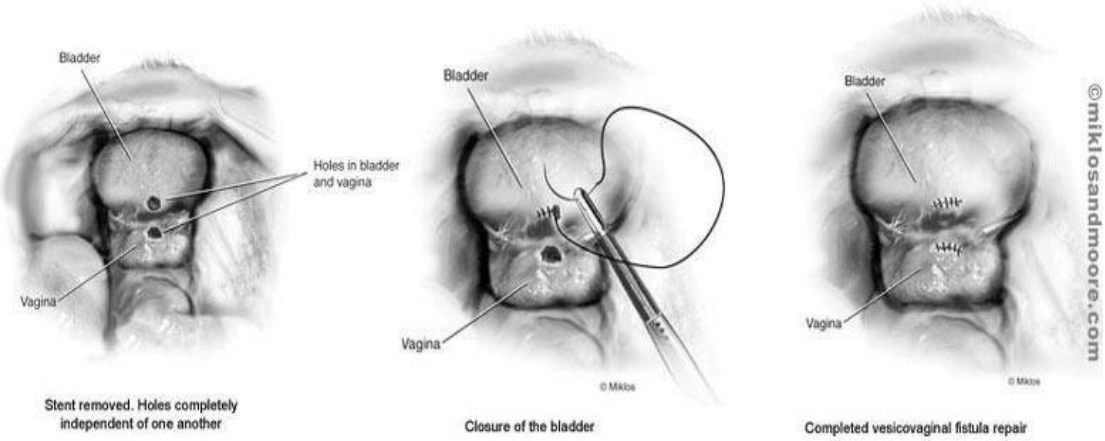
b. Transvaginal Technique: **Latzko procedure:**

- The location and size of the fistula were evaluated through an endoscope in the lithotomy position under anesthesia.
- Transvaginal inspection was performed with a speculum.
- A small right-angle clamp was inserted through the fistula tract and it was confirmed by endoscopy that the tip of the clamp was in the bladder. A 12 Fr Foley catheter was inserted through the transvaginal fistula tract with a right-angle clamp and the balloon was inflated with 5 mL saline.
- Vaginal exposure was made after the bladder was emptied with the Foley catheter.
- The fistula tract was cut annular completely with the traction of Foley catheter.
- The bladder and vaginal mucosa were separated from each other by sharp dissections without excision of the fistula tract.
- The bladder mucosa and the vaginal mucosa were sutured in a water-tight manner with 3/0 polyglactin sutures separately.
- An 18 Fr Foley catheter was inserted to the bladder at the end of the procedure.
- The catheter was removed after 21 days of bladder drainage.



c. Abdominal Technique (discuss with urologist)

- The bivalve technique was used.
- The bladder was exposed with a median incision in the supine position, then opened through the dome.
- Bladder was incised from the dome to the fistula tract.
- The fistula tract was excised after annular incision.
- The bladder around the excised fistula tract was also closed perpendicular to the vagina after the closure of the vagina.
- An omental tissue flap was inserted between the vagina and the bladder.
- The bladder was completely closed and the procedure was terminated with an 18 Fr Foley catheter insertion.
- The catheter was removed after 21 days of bladder drainage.



V. PROGNOSIS

- If conservative measures for vesicovaginal fistula fails, the surgery is pursued.
- A transvaginal approach to repair is typically less invasive and amenable to earlier repair.
- The interposition of flaps, such as those utilizing the labial fat pad or omentum, can provide a protective factor for recurrent cases.

VI. COMPLICATIONS

- Failure and recurrent fistula formation (occurred in 30% of vesicovaginal repair cases)
- In recurrent cases, consider a delay of 2 to 3 months from the previous attempted repair. Utilizing the interposition of flaps as a surgical technique should be considered to increase the chances of a successful repair.

VII. PREVENTION

- Access to Skilled Healthcare
- Timely intervention
- Cesarean Section
- Partograph
- Immediate Catheterization
- Avoidance of Prolonged Labor
- Avoidance of Unnecessary Vaginal Obstetric Procedure

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ANNEX

1. សមាសភាពក្រុមការងារបច្ចេកទេសមគ្គុទេសក៍ព្យាបាលគ្លីនិក សម្ភព និងរោគស្ត្រី

១	ឯកឧត្តមសាស្ត្រ.	**ប៉ិច**	**សុធី**	រដ្ឋលេខាធិការក្រសួងសុខាភិបាល	ប្រធាន
២	លោកជំទាវសាស្ត្រ.	**គ្រុយ**	**ណាឆស៊ីម**	អនុរដ្ឋលេខាធិការក្រសួងសុខាភិបាល	អនុប្រធាន
៣	ឯកឧត្តមសាស្ត្រ.	**កុំ**	**ការណាល់**	សមាគមសម្ភព និងរោគស្ត្រីវិទ្យាកម្ពុជា	អនុប្រធាន
៤	ឯកឧត្តមសាស្ត្រ.	**សាន់**	**ច័ន្ទសឿន**	ទីប្រឹក្សាក្រសួងសុខាភិបាល	សមាជិក
៥	លោកជំទាវសាស្ត្រ.	**ឆុង**	**រដ្ឋាវី**	ទីប្រឹក្សាក្រសួងសុខាភិបាល	សមាជិក
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១៨	លោកវេជ្ជ.ឯកទេស	**រស់**	**សុផាត**	មជ្ឈ.ជាតិគាំពាមាតា និងទារក	សមាជិក
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២២	លោកស្រីវេជ្ជ.ឯកទេស	**ណាត**	**សុចឥណ្ណ**	មន្ទីរពេទ្យមិត្តភាពកម្ពុជា-ចិន ព្រះកុសុម:	សមាជិក
២៣	លោកស្រីវេជ្ជ.ឯកទេស	**ខ**	**ហុកស៊ុន**	មន្ទីរពេទ្យមិត្តភាពកម្ពុជា-ចិន ព្រះកុសុម:	សមាជិក
២៤	លោកវេជ្ជ.	**ង៉ែត**	**ឥតូ**	ប្រធានផ្នែកសម្ភព និងរោគស្ត្រីមន្ទីរពេទ្យបង្អែកខេត្តបាត់ដំបង	សមាជិក
២៥	លោកវេជ្ជ.	**ឆ្ងាំ**	**ច័ន្ទណា**	មន្ទីរពេទ្យបង្អែកខេត្តបាត់ដំបង	សមាជិក
២៦	លោកស្រីវេជ្ជ.ឯកទេស	**ហេង**	**រិទ្ធសុបញ្ញា**	មន្ទីរពេទ្យព្រះអង្គឌួង	សមាជិក

២៧	លោកវេជ្ជ.	**ឈឹម**	**សុគន្ធ**	មន្ទីរពេទ្យបង្អែកខេត្តសៀមរាប	សមាជិក
២៨	លោកវេជ្ជ.	**សុខ**	**សុវណ្ណារិទ្ធ**	មន្ទីរពេទ្យបង្អែកខេត្តសៀមរាប	សមាជិក
២៩	លោកស្រីវេជ្ជ.	**ចាប់**	**ច័ន្ទធីតា**	អនុប្រធានមន្ទីរសុខាភិបាលនៃរដ្ឋបាលខេត្តកំពង់ចាម	សមាជិក
៣០	លោកវេជ្ជ.ឯកទេស	**ណែម**	**ប៊ុនឆឿន**	គ្រូពេទ្យព្យាបាលមន្ទីរពេទ្យបង្អែកខេត្តកំពង់ចាម	សមាជិក
៣១	លោកសាស្ត្រ.	**ឈៀង**	**ចន្ទរិទ្ធ**	ទីប្រឹក្សាបច្ចេកទេសមន្ទីរពេទ្យមិត្តភាព-សូវៀត	សមាជិក
៣២	អង្គការដៃគូអភិវឌ្ឍ			WHO, WB, USAID, UNFPA, CHAI, RHAC, ect…	សមាជិក

2. List of Members of the TWG of CPG for Obstetrics and Gynecology

	Name	Title
1	H.E Prof. Pech Sothy	Secretary of State, MoH
2	H.E Prof. Kruy Leangsim	Under Secretary of State, MoH
3	H.E Prof. Koum Kanal	President of Cambodia Society of Gynecology and Obstetrics (CSGO)
4	H.E Prof. Sann Chansoeung	Advisor to MoH
5	H.E Prof. Tung Rathavy	Advisor to MoH
6	H.E Dr. Krouch Rayounette	Advisor to MoH
7	Assist. Prof. Kim Rattana	Director of National Maternal and Child Health Center (NMCHC)
8	Dr. Sophean Sahakcheat	Deputy Director of Cambodia-China Friendship Preah Kossamak Hospital (CCFKH)
9	Dr. Ros Saphath	Deputy Director of NMCHC
10	Dr. Hang Sovanara	Deputy Director of NMCHC
11	Dr. Chap Chanthida	Deputy Director of Kampong Cham Provincial Health Department
12	Prof. Keth Lysotha	CSGO
13	Prof. Lieng Chanrith	Technical Advisor, Khmer Soviet Friendship Hospital
14	Prof. Som Vanrithy	Head of Technical Bureau, NMCHC
15	Dr. Seap Bel	Head of Technical Bureau, Luang Mè Hospital
16	Prof. Korn Aun	Head of Gynecology Department, Calmette Hospital
17	Dr. Chhun Samsorphea	Head of Maternity Department, Calmette Hospital
18	Dr. Uy Kyna	Head of Obstetrics and Gynecology Department, Khmer Soviet Friendship Hospital
19	Dr. Ngeth Viphou	Head of Obstetrics and Gynecology Department, Battambang Provincial Hospital
20	Dr. Lim Sokong	Head of Obstetrics and Gynecology Department, Siem Reap Provincial Hospital

21	Dr. Chhit Maryan	Deputy Head of Obstetrics and Gynecology Department, Khmer Soviet Friendship hospital
22	Dr. Khor Hok Sunn	Deputy Head of Obstetrics and Gynecology Service, Cambodia China Friendship Preah Kossamak Hospital
23	Dr. Lay Sanine	Calmette Hospital
24	Dr. Uy Sopha	Calmette Hospital
25	Dr. Leap Sovann	Cambodia China Friendship Preah Kossamak Hospital
26	Dr. Heng Rithsopanha	Preah Ang Duong Hospital
27	Dr. Nem Bunthoeun	Kampong Cham Provincial Health Department
28	Dr. Chea Longdy	Calmette Hospital
29	Dr. Sea Sreyla	Calmette Hospital
30	Prof. Keo Muoysroy	National Maternal and Child Health Center
31	Dr. Lam Channa	Deputy Head of Obstetrics and Gynecology Department, Battambang Provincial Hospital
32	Dr. Sok Sovannarith	Siem Reap Provincial Hospital
33		World Health Organization (WHO)
34		The World Bank (WB)
35		USAID
36		UNFPA
37		CHAI
38		RHAC