11 - Safe Drugs Use In Pregnancy & Lactation

Gyan - Vahini

From

FOGSI, Food Drugs & Medicosurgical Equipment Committee November - 2025

Dr. Asha Jain

Editor & Chairperson, FOGSI FDMSE Committee

Message From Dr. Sunita Tandulwadkar

Dr. Sunita Tandulwadkar

President FOGSI-2025

Ensuring safety in the use of drugs and medical equipment is central to quality women's healthcare. As obstetricians and gynecologists, our daily decisions—what drug to prescribe, what device to use, how to procure and maintain equipment—directly impact patient outcomes.

This issue of the magazine, brought out by the Food, Drugs and Medicosurgical Equipment Committee, addresses these very concerns with clarity and clinical relevance. The focus on rational drug use, equipment safety, standard operating procedures, and regulatory awareness is timely and essential.

I appreciate the efforts of the Chairperson and her team for consistently highlighting practical issues faced by clinicians across the country. I also thank the contributors for sharing their experience and evidence-based perspectives.

I am confident this issue will help our members practice with greater confidence, safety, and accountability.

Warm regards,
Dr. Sunita Tandulwadkar
President, FOGSI

Message from Dr Abha Singh

Dr. Abha Singh
Vice President FOGSI-2025

ear Fogsians Seasons Greetings !

Safe and rational use of drugs and medical equipment forms the backbone of good clinical practice. In an era of rapidly advancing technology and expanding therapeutic options the health care professional should adopt the innovation and use it judiciously, ethically and in the best interest of patients.

Rational drug use is to prescribe the right medicine in the correct dose and duration based on sound scientific evidence. This will optimise therapeutic outcomes , minimise adverse effects, prevent antimicrobial resistance and reduce unneccassary health care costs.

It is equally important to use appropriate medical equipment, check its regular maintenance , calibration and adherence to standard operating procedures leading to enhanced patient safety and clinical effectiveness .

This issue of the magazine highlights key aspects of drug safety, equipment handling, procurement practices, and standard operating procedures. It reflects the committee's commitment to guiding clinicians through practical tips, often overlooked areas of practice.

I commend the Chairperson and members of the Food, Drugs and Medicosurgical Equipment Committee for choosing these relevant topics and presenting them in a clinician-friendly manner. The emphasis on safety, compliance, and informed decision-making is commendable.

I am sure this issue will be useful to the Fogsi members across all levels of practice.

Happy Reading !

"Merry X-mas and a Very Happy and Healthy New Year to you and your Family."

With Warm Regards ,
Dr Abha Singh VP Fogsi

Message from Dr Suvarna Khadilkar

Dr. Suvarna Khadilkar
Secretary General FOGSI-2025

In an era of rapidly evolving drugs, devices, and technologies, staying informed is no longer optional—it is a professional responsibility. The Food, Drugs and Medicosurgical Equipment Committee has taken up this responsibility with seriousness and consistency.

This issue of the magazine focuses on real-world challenges such as drug safety, equipment selection, storage, maintenance, and compliance with standards. The content is practical and directly applicable to everyday clinical practice, whether one is working in a clinic, nursing home, or tertiary hospital.

I congratulate the editorial team for presenting complex issues in a simple and structured manner. Such publications strengthen FOGSI's commitment to patient safety and ethical practice.

I encourage all members to read this issue carefully and use it as a ready reference.

With best wishes,
Dr. Suvarna Khadilkar
Secretary General, FOGSI

Dr. Asha Jain
Chairperson
FOGSI FDMSE Committee

FOREWORD

Safety Begins with Everyday Decisions

Clinical practice is shaped not only by major interventions but also by the many small decisions we make every day. The choice of a drug, its dose and duration, the timing of exposure, the equipment we procure, how it is stored, maintained, and used—each of these directly influences patient safety and outcomes. Yet, these decisions are often taken silently, without discussion, audit, or reflection.

I am deeply grateful to our FOGSI leadership for their guidance and encouragement. I sincerely thank **Dr. Sunita Tandulwadkar**, **President FOGSI**, for her unwavering focus on patient safety and quality of care. Her vision continues to guide meaningful academic and clinical initiatives. I also thank **Dr. Suvarna Khadilkar**, **Secretary General FOGSI**, for her structured leadership and continued support for academic rigor. My appreciation extends to **Dr. Abha Singh**, **Vice President In-Charge**, for her consistent emphasis on standardisation, ethics, and clinician support.

This issue of the magazine is dedicated to bringing these foundational aspects of practice into focus. The Food, Drugs and Medicosurgical Equipment Committee has consciously chosen to address areas that are common, practical, and sometimes uncomfortable to examine—rational drug use, prevention of drug-induced fetal harm, safe equipment practices, documentation, standard operating procedures, and regulatory awareness.

Across the country, obstetricians and gynecologists work in varied clinical environments. While infrastructure and resources differ, the principles of safe, ethical, and evidence-based practice remain universal. This issue has been curated keeping these diverse realities in mind, with the intention of offering guidance that is applicable in clinics, nursing homes, and hospitals alike.

This issue reflects the collective commitment of authors and reviewers who have contributed with sincerity and responsibility. I extend my heartfelt thanks to the authors who shared their clinical experience, insights, and evidence-based perspectives:

Dr. Ginny Gupta, Dr. Kiran Chhabra, Dr. Sujayasri Sangita, Dr. Ruche Bhargava, Dr. R. Jyoti Mahajan, Dr. Sarita Kumari, Dr. Sandhya Rani, Dr. Prerna Saigal, Dr. Sreedevi Vellanki, Dr. Priyanka Rai, Dr. Neetha George, Dr. Urvashi Barman, Dr. Rimpi Singla, Dr. Archana Singh, Dr. Prabhdeep Kaur, and Dr. Sonal Gupta.

Each contribution addresses real-world clinical dilemmas and reinforces the importance of rational, safe, and informed decision-making.

Equally important is the role of our peer reviewers, whose work often remains behind the scenes but is critical to the quality of any scientific publication. I place on record my sincere appreciation for **Dr. Sugandha Goel, Dr. Shikha Sachan, Dr. Dolly Mehra, Dr. Renu Jain, Dr. Jyothi G.S., Dr. V. Padmaja, Dr. Himleena Gautam,** and **Dr. Okram Sarda Devi. Their** careful review, constructive feedback, and commitment to accuracy have significantly strengthened this issue.

As clinicians, we are continually adapting to new drugs, devices, and technologies. In this rapidly changing landscape, revisiting fundamentals becomes even more important. Patient safety begins long before the labour room or operation theatre—it begins with informed choices made in everyday practice.

I hope this issue serves not just as reading material, but as a ready reference—prompting reflection, reinforcing best practices, and supporting safer care for the women we serve.

Warm regards,

Dr. Asha Jain
Chairperson
Food, Drugs & Medicosurgical Equipment Committee FOGSI

"Know Your Numbers" is an ambitious health initiative.

- This project seeks to gather vital health data- Weight, Blood pressure, Blood Sugar Level with HbA1C, and Hemoglobin level -from women across India.
- By focusing on these key health indicators, the project aims to foster a proactive health management culture among women.
- The data collected will be instrumental in identifying prevalent health issues early and promoting interventions that can significantly reduce the incidence of che diseases.
- This initiative not only emphasizes the importance of regular health monitoring but also strives to empower women with the knowledge and tools needed to take charge of their health, ensuring they lead longer, healthier lives.
- Collect key health data: weight, blood pressure, blood sugar, HbA1C, and hemoglobin from women across India.
- Encourage proactive health management for early identification of prevalent health issues.
- Promote timely interventions to reduce chronic disease incidence.
- Empower women with knowledge and tools for better health and longevity.
- Gather vital health data: weight, blood pressure, blood sugar (HbA1C), and haemoglobin levels from women across India.
- Foster proactive health management among women.
- Identify prevalent health issues early and promote timely interventions.
- Reduce the incidence of chronic diseases through regular monitoring.
- Empower women with knowledge and tools for healthier, longer lives.

SURVEY FOR KNOW YOUR NUMBER (KYN) PROJECT

KNOW YOUR NUMBER

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INDEX- MENOPAUSE

01

Decoding the Label: Understanding the Pregnancy and Lactation Labeling Rule (PLLR)

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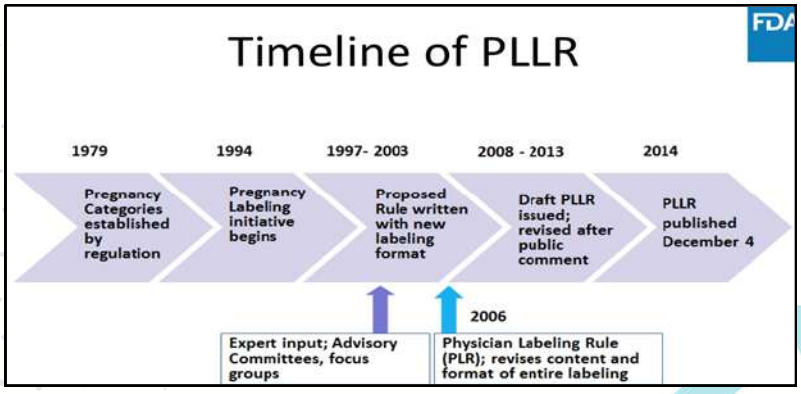
Abstract

The Pregnancy and Lactation Labeling Rule (PLLR), implemented by the U.S. Food and Drug Administration (FDA) in 2015 (1), replaced the outdated pregnancy risk category system (A, B, C, D, X)(5,6) with a more comprehensive and evidence-based framework. PLLR requires narrative labeling for drug safety in pregnancy, lactation, and reproductive potential, enabling clinicians to make informed decisions based on both human and animal data(1,4).It assists healthcare providers in assessing benefits vs risk & in subsequent counselling of pregnant & nursing mothers who take medication to make informed & educated decisions for themselves & their children.This article explores the structure and purpose of PLLR, highlights strategies to interpret drug labels, discusses the meaning of risk language, and provides case-based applications. Emphasis is placed on the importance of integrating PLLR with clinical judgment, patient counseling, and ethical considerations(5,7). Furthermore, the PLLR underscores the ethical responsibility of healthcare providers to communicate risk information effectively, ensuring informed and shared decision-making. This article explores the rationale, structure, and implementation of the PLLR, provides guidance for interpreting narrative drug labelling , and discusses the practical implications for clinical practice and policy. Ultimately, the PLLR represents a pivotal step toward evidence-informed, patient-centered pharmacotherapy during pregnancy and lactation(10).

Introduction

Medication use during pregnancy and lactation presents a major clinical dilemma. Physiological changes during pregnancy alter pharmacokinetics, while the potential for teratogenic or neonatal harm makes prescribing a careful balancing act. Similarly, during lactation, clinicians must weigh maternal therapeutic needs against infant safety from drug exposure via breast milk.(5,6)

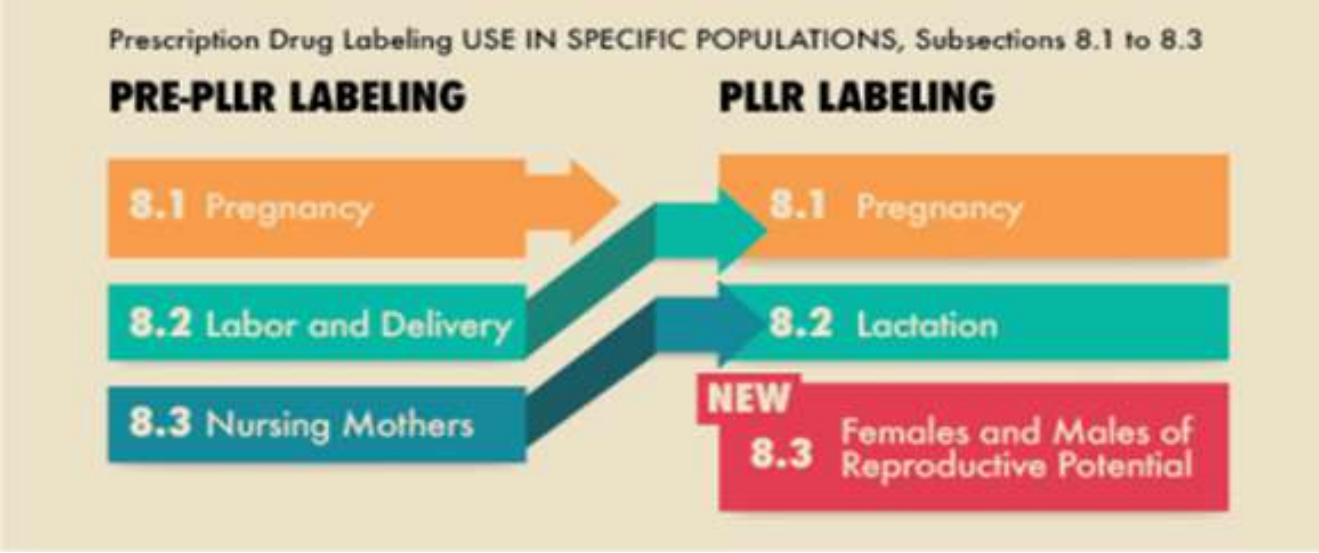
Historically, clinicians relied on the FDA Pregnancy Risk Categories (A, B, C, D, X) introduced in 1979



While simple, this system
was criticized for:

- Oversimplification of complex risk data.
- Failure to distinguish between human and animal evidence.
- Misleading hierarchy that suggested "A" was always safe and "X" always dangerous, without nuance...
- A drug with adverse information in animals could be labelled as same category as a drug with no animal information.

In response, the FDA introduced the Pregnancy and Lactation Labeling Rule (PLLR) in June 2015(1). PLLR eliminated categories and replaced them with narrative summaries that provide context, clinical considerations, and data sources. This shift marked a paradigm change from categorical to evidence-based, individualized risk interpretation.



PLLR provides more detailed & contextualised information to help physicians communicate risks & benefits more clearly to patients

Global and Clinical Relevance

Medication use during pregnancy is extremely common, with studies estimating that over 80% of women take at least one prescription or over-the-counter drug during pregnancy. This underscores the urgent need for accurate, evidence-based information regarding drug safety in this population(7).

Limitations of the Old Category System

The previous A–X system often led to misinterpretation. For example, Category B drugs were frequently perceived as "safe," even when supporting data came only from animal studies, while Category C drugs with limited human data were sometimes avoided unnecessarily. This resulted in both over-prescription of inadequately studied medications and under-treatment of necessary conditions in pregnant and lactating women.

Ethical and Communication Challenges

The lack of nuanced labeling posed ethical challenges for healthcare providers. Inadequate risk communication could lead to anxiety, misinformation, or non-adherence, highlighting the need for a system that supports shared decision-making and transparent patient counseling.

Rationale Behind PLLR Reform

Recognizing these shortcomings, the FDA sought to develop a labeling system that reflects current scientific understanding, emphasizes contextual risk–benefit evaluation, and integrates clinical judgment with individualized patient care(2,3,4). The Pregnancy and Lactation Labeling Rule (PLLR) therefore represents not just a labeling reform, but a shift toward evidence-informed maternal pharmacotherapy.

Bridging Knowledge and Practice

Despite being implemented in 2015, awareness and application of PLLR principles remain limited among prescribers worldwide(10). Bridging this knowledge gap through education, training, and regulatory alignment is critical to ensure that clinicians interpret drug information correctly and counsel patients effectively(8).

Discussion

1. Overview of PLLR

PLLR reorganizes drug labeling into three key subsections under section 8:

1. **Pregnancy**

- Risk summary-contains a summary of risks to pregnant woman and developing foetus, often including a pregnancy registry.
- Clinical considerations-multiple considerations when determining potential human risks from animal data
- Does the adverse developmental outcome occur in more than one animal species ? Is adverse developmental outcome consistent across animal species ? Does the adverse developmental outcome occur in the absence of maternal toxicity?
- Based on Pharmacology
- When a drug has well understood pharmacologic mechanism of action that may result in adverse developmental outcome,the risk summary must explain mechanism & potential risks.
- Reference of clinical pharmacology should be provided.
- Data supporting conclusions

2**. Lactation**

- Risk summary -When the drug is not contraindicated for usein breast feeding women, but breast feeding is not recommended during drug use because of potential risk to the breast fed child eg: cytotoxic drugs the labelling should include a statement describing the reasons to avoid breast feeding . And risk & benefit statement should be omitted as such a statement may be misleading .
- Clinical considerations -When human data are available animal data must not be included.
- Data supporting conclusions

1. Females and Males of Reproductive Potential

- Need for pregnancy testing – Timing & Frequency of pregnancy testing & type of test used should be individualised
- Contraceptive recommendations – Contraception is required or recommended before , during ,or after drug therapy for the appropriate use of a drug with potential risk of adverse developmental outcome .
- If there is an interaction between the drug and hormonal contraception ,summary statement concerning the interaction and recommendation to use a nonhormonal or additional method of contraception to be included (cross reference to Drug Interactions should be included for more detailed description of interaction)
- Fertility considerations – Describe the availability of human data that demonstrate adverse effects on male or female fertility. Also include description about the potential reversibility of adverse effects.
- Include data if from animal studies or mechanism of action raises concern about impairment of human fertility.

This structured approach ensures uniformity and transparency across drug labels.
The lettering system seems arbitrary. The PLLR will also reduce the innocent until proven guilty phenomenon where newer untested drugs with no harmful side effects were perceived to be safer category B than drugs with possible or known side effects category C.

PLLR provides detailed risk summaries and more comprehensive information derived from clinical experience (if available), animal data and concerns related to the pharmacological activiy of the drug. In addition, the label includes information on the risks associated with gametogenesis in men and women.
Possible challenges that may be faced by DGCI in our country in implementing the PLLR

Where Do You Find This Information?
Finding information on the reproductive safety of medication is not that straightforward. Not so long ago, you could find the information continued within the product label in the Physician's Desk Reference or PDR which was updated regularly and mailed to doctors' offices every year. Now we go to the internet and find all kinds of stuff, much of it outdated or misleading.

Many commonly used and reputable websites, such as WebMD and the Mayo Clinic do not include the new information provided in the PLLR. And there are many other websites of variable quality that continue to use the old lettering system.

Even when you try to make sure the information comes from a reputable source, the information can be misleading. For example, if you search for "lorazepam package insert", the first listing is from the FDA, the governmental organization responsible for approving the language contained in package inserts seemingly legitimate but, with some digging the document was outdated (from 2007).

Hence the internet cannot be trusted as a source of drug information.

Updated information on all drugs in market to be made available on a nationally certified forum.
For example,

DailyMed is a useful website which is hosted by NIH and posts updated drug listings (package insert information) as submitted by the Food and Drug Administration (FDA). It's relatively easy to use; the PRECAUTIONS section outlines data on pregnancy and lactation safety(9).

Re training of healthcare providers, prescribers about using PLLR at a national level would be a huge project spanning some considerable time(10).

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02
A

"Timing Is Everything" — Teratogenicity and Critical Windows of Development

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Teratogenicity refers to the capacity of a substance to cause congenital malformations or developmental abnormalities in a developing embryo or fetus. A teratogen is any agent—chemical, physical, or biological—that can disturb embryonic or fetal development, leading to structural or functional defects.

Understanding the timing (critical windows) of exposure and the mechanisms of teratogenicity is crucial for preventing birth defects and ensuring safe medication use during pregnancy.

The concept of "Timing Is Everything" in teratology highlights that an embryo or fetus is not equally vulnerable throughout gestation. Each organ system develops during a defined critical window of susceptibility, and exposure to a teratogenic agent within that window can lead to specific congenital malformations. Conversely, exposure to the same agent outside that period may have minimal or no effect on that particular structure.

Mechanisms of Teratogenesis:

James Wilson proposed the following six principles of teratology[1]

- Susceptibility to teratogenesis depends on the genotype of the conceptus and how it interacts with environmental factors.
- Susceptibility to teratogenic agents varies with the developmental stage at the time of exposure
- Teratogenic agents act in specific ways on developing cells and tissue to initiate abnormal embryogenesis
- The final manifestations of abnormal development are death, malformation, growth retardation, and functionaldisorder
- The access of adverse environmental influences to developing tissues depends on the nature of the agent
- Manifestations of deviant development increase in degree as dosage increases
- from no effect to totally lethal effect

Critical Windows of Development

The teratogenic outcome of an exposure depends predominantly on the gestational age at which it occurs, reflecting the specific stage of embryonic or fetal development [2].

Developmental Stage	Period	Potential Outcome of Teratogenic Exposure
"All-or-none" period	Pre-implantation (0–2 weeks)	Exposure typically results in embryo death or complete recovery without malformation; teratogenesis is uncommon in this phase .
Organogenesis	Embryonic period (3–8 weeks)	Represents the period of maximal susceptibility to teratogens, when major structural malformations of the heart, limbs, and neural tube can occur 2,3.
Growth and functional maturation	Fetal period (9 weeks–term)	Exposure during this period mainly leads to functional abnormalities, growth retardation, and effects on the CNS and reproductive system rather than structural anomalies 2.

Critical Windows for Specific Teratogens

The teratogenic impact of a substance is closely linked to the timing of exposure relative to organ development.

Developmental Event	Timing After Conception	Common Teratogens	Potential Congenital Defects
Central Nervous System (CNS) development	3–5 weeks	Alcohol, Valproic acid, Radiation	Neural tube defects (e.g., spina bifida), microcephaly
Craniofacial development	3–8 weeks	Valproic acid, Isotretinoin	Cleft lip/palate, facial dysmorphisms seen in fetal alcohol syndrome
Cardiac development	3–6 weeks	Valproic acid, Alcohol, Isotretinoin	Ventricular or atrial septal defects

Limb development	4–8 weeks	Thalidomide	Phocomelia (limb reduction or absence)
Brain and spinal cord maturation	Throughout pregnancy	Alcohol	Fetal Alcohol Syndrome, cognitive and behavioral impairment

- Organogenesis is the **critical window** for most teratogenic effects .
- Later exposures primarily affect **cell differentiation**, **organ growth**, and **functional maturation**[2].
- The severity of effect is influenced by **dose, duration, route of exposure, and placental pharmacokinetics**[3]**.**

Dose–Response Relationship in Teratogenicity:

The dose–response relationship describes how the likelihood or severity of fetal damage increases with the dose or duration of exposure to a teratogen.

Concept	Explanation
Threshold dose	Most teratogens have a minimum dose below which no adverse effect occurs
Above threshold	Once the threshold is crossed, risk and severity of defects rise sharply.
Dose–dependent effect	Mild exposure → minor anomaly; High exposure → major malformation or fetal death.
Cumulative effect	Repeated small exposures can add up to reach the harmful threshold.

Pharmacokinetic Considerations in Teratogenicity

Teratogenic risk is closely linked to the extent and timing of fetal drug exposure. Pregnancy induces significant pharmacokinetic alterations that modify maternal drug levels, placental transfer, and ultimately fetal dose. These changes must be understood to interpret the potential teratogenicity.

Maternal Pharmacokinetic Changes

Absorption

Pregnancy is associated with delayed gastric emptying, reduced gastrointestinal motility, and increased gastric pH. These alterations may influence oral drug bioavailability and the rate at which a teratogenic agent reaches systemic circulation.

Distribution

Plasma volume expands by nearly 40–50%, whereas maternal fat stores increase. Consequently, hydrophilic drugs exhibit dilutional lowering of peak concentrations, while lipophilic drugs have an increased volume of distribution. Reduced albumin concentrations increase the unbound fraction of highly protein-bound drugs, facilitating placental passage.

Metabolism

Pregnancy induces selective changes in hepatic enzyme activity. CYP3A4, CYP2D6, and CYP2C9 activities commonly increase, enhancing clearance of many agents. CYP1A2 and CYP2C19 activities decrease, resulting in higher maternal levels of their substrates. Teratogenic risk depends on whether the parent compound or its metabolites exert the harmful effect.

Excretion

Glomerular filtration rate and renal plasma flow increase by up to 50–60% during pregnancy. Drugs eliminated primarily through the kidneys may have reduced maternal concentrations unless dose adjustments are made, potentially altering fetal exposure.

Placental and Fetal Pharmacokinetics

Placental Transfer

Drug passage across the placenta depends on molecular weight, lipophilicity, ionization, protein binding, and transporter activity. Early gestation permits relatively easy diffusion due to a thin placental barrier, while later pregnancy involves more active transport mechanisms.

Fetal Metabolism

Fetal metabolic pathways, particularly CYP activity and conjugation systems, are immature. The fetus therefore has limited ability to detoxify , increasing susceptibility to even modest maternal exposures.

Fetal Excretion

Drugs excreted into amniotic fluid may undergo recirculation via fetal swallowing, prolonging exposure.

Placenta as a Barrier:

The placenta functions as a **selective barrier** between the maternal and fetal circulations. While it allows the transfer of oxygen, nutrients, and certain drugs, it simultaneously protects the fetus by **restricting** the passage of harmful substances. This dual role—**exchange + protection**—is essential for fetal survival and development.

Structural Features Contributing to Barrier Function

a. Syncytiotrophoblast Layer (Primary Barrier)

- The outer multinucleated syncytiotrophoblast is the main interface with maternal blood.
- It lacks intercellular gaps → prevents paracellular movement of large molecules.
- Contains metabolic enzymes that can degrade maternal xenobiotics before fetal exposure.

b. Cytotrophoblast + Fetal Capillary Endothelium

- Form deeper layers through which substances must pass.
- These layers become thinner with gestational age, increasing permeability in late pregnancy.

c. Tight Junctions

- Limit movement of hydrophilic molecules and ions

2. Functional (Physiological) Barriers

a. Molecular Weight Barrier

- Molecules **>1000 Da** generally cannot cross (e.g., heparin, insulin).

b. Protein Binding Barrier

- Highly protein-bound drugs have lower free concentrations → reduced transfer.

c. Ionization / pH Gradient

- Weak bases become trapped in the more acidic fetal circulation ("ion trapping").
- Provides **partial protection** but may also **lead to fetal accumulation** of basic drugs.

d. Lipophilicity

- Lipid-soluble molecules cross easily; hydrophilic molecules are restricted.

3. Active Transporter Barrier

The placenta expresses several **efflux transporters** designed to protect the fetus:

a. P-glycoprotein (P-gp / ABCB1)

- Pumps many xenobiotics back into maternal blood, reducing fetal exposure.
- Highly active in 1st trimester → critical protective role during organogenesis.

b. Breast Cancer Resistance Protein (BCRP / ABCG2)

- Limits transfer of drugs such as antivirals, antibiotics, chemotherapeutics.

c. Multidrug Resistance Proteins (MRP Family)

- Transport conjugated metabolites and organic anions.

4. Enzymatic Barrier

Placenta contains metabolic enzymes including:

- **CYP1A1, CYP19** (aromatase)
- **UGT, SULT**, and other Phase II enzymes

These enzymes can detoxify drugs before they reach the fetus.
Some xenobiotics may be activated into more toxic metabolites, though this is less common.

5. Immunological Barrier

- Syncytiotrophoblast expresses **HLA-G**, a non-classical MHC molecule that prevents maternal immune rejection. Prevents direct contact between maternal immune cells and fetal antigens.

Thus, it is better described as a **"selective filter"** rather than a true impermeable barrier.

Factors influencing placental drug transfer:

Parameter	Favours Transfer	Restricts Transfer
Molecular weight	< 500 Da (e.g., ethanol, phenytoin)	> 1000 Da (e.g., heparin, insulin)
Lipid solubility	High (lipophilic drugs cross easily)	Low (hydrophilic drugs cross poorly)
Ionization	Non-ionized (uncharged molecules diffuse faster)	Ionized (charged species poorly diffusible)
Protein binding	Low (free fraction available to cross)	High (protein-bound drugs less available)
Concentration gradient	High maternal-to-fetal gradient	Low gradient
Placental thickness	Thin (late gestation)	Thick (early gestation)
Blood flow	High utero-placental perfusion	Low perfusion reduces diffusion
Gestational age	Late (↑ permeability & surface area)	Early (↓ permeability)

INTERPRETATION OF EARLY EXPOSURE:

Interpretation of teratogenic exposure in the earliest stages of pregnancy—before implantation and organogenesis—requires a distinct framework. During this pre-organogenesis **period (first ~14 days post-fertilization)**, the embryo possesses biological characteristics that make structural malformations highly unlikely.

Developmental Characteristics

In this stage, the conceptus consists of a small number of **totipotent, highly regulative blastomeres** with the ability to replace or reorganize damaged cells. Because germ layers and organ primordia have not yet formed, pathways required for classical teratogenesis are not active.

Mechanism of Response to Early Exposure

The embryo's response centers on **cell survival and compensatory repair**, not organ-specific disruption. Limited injury is corrected through apoptosis, redistribution of healthy blastomeres, and robust DNA repair activity. When cellular injury exceeds the embryo's compensatory threshold, the result is **embryonic lethality** rather than malformation.

Expected Outcomes

1. Embryonic Demise

Significant cytotoxic damage results in implantation failure, biochemical pregnancy loss, or early miscarriage—usually unrecognized clinically.

2. Normal Development

If the embryo survives the early insult, subsequent development is generally normal because structural differentiation has not yet begun, and no increased risk of congenital anomalies is expected .

Shepard's Criteria and Evidence for Early Exposure Interpretation

Shepard's Catalog of Teratogenic Agents outlines criteria for identifying true teratogens, including the requirement that exposure occurs during a **critical period of structural development**. Since organogenesis has not begun in the pre-implantation and peri-implantation period, exposures during this phase **cannot fulfill the timing criterion for structural teratogenesis**[3] Shepard's evidence demonstrates that even potent teratogens produce:

- **Embryonic lethality** if exposure is severe, or
- **No effect** if the embryo compensates
- Thus, early exposure outcomes align strictly with embryotoxicity or recovery, and not malformation[3].

Role of Exposure Dose and Route

Before implantation, there is no established maternal–fetal circulation, and exposure occurs only through tubal and uterine secretions, greatly limiting embryonic dose .

- **Non-cytotoxic drugs or short exposures** rarely reach harmful concentrations.
- **Cytotoxic agents, high-dose radiation, or severe systemic disease** are more likely to result in embryonic demise rather than malformation.

Clinical Interpretation

In clinical practice, exposures occurring before the missed menstrual period are interpreted as **embryotoxic rather than teratogenic**. Surviving pregnancies do not require specialized malformation surveillance and can be followed with routine first-trimester and anomaly scans.

Accidental first trimester exposure algorithm:

The first trimester (0–13 weeks) is the critical window for organogenesis (3–8 weeks post-conception).

Drug exposure during this phase may cause structural malformations, but risk varies by drug type, dose, duration, and timing.

Most inadvertent exposures occur before pregnancy recognition (i.e., before 6 weeks gestation) [4]

Steps After Discovery

Step 1 — Confirm Timing & Dosage

Calculate gestational age precisely from LMP or early scan. Identify drug name, dose, duration, and timing relative to conception. Assess cumulative exposure (single vs chronic use)[5].

Step 2 — Risk Assessment

Classify the drug using reliable databases such as TERIS, Reprotox, LactMed, MotherToBaby, or FDA Pregnancy and Lactation Labeling Rule (PLLR).

Consider the teratogenic mechanism (e.g., folate antagonism, oxidative stress) and the background risk of ~3–5% malformation even without drugs[5,6].

Step 3 — Stop or Modify the Drug

Discontinue or switch to a safer alternative, unless the drug is essential (e.g., antiepileptics, antiretrovirals).

For essential drugs, use the minimum effective dose and provide folate supplementation where appropriate [4,6].

Counseling the Patient

Topic	Key Counseling Points
Reassurance	Most exposures before organogenesis or in subteratogenic doses do not cause harm 4.

All-or-None Phenomenon	Exposure during 0–2 weeks post-fertilization either causes no effect or pregnancy loss, not malformations 5.
Uncertain Risks	Some drugs lack human data — explain limitations and document the discussion 7.
Shared Decision-Making	Discuss risks vs benefits; allow patient autonomy with medical support 8.

Investigations & Monitoring:

a. Targeted Ultrasound

- 11–13 weeks: confirm viability and detect gross anomalies.
- 18–22 weeks: detailed structural scan for CNS, cardiac, renal, and limb malformations[5,6].

- **b. Additional Screening**
- Fetal echocardiography: if exposure to drugs like lithium or valproate[6].
- Amniocentesis / cfDNA testing: indicated if a structural defect is suspected.
- Maternal serum screening may aid in detecting neural tube defects (↑ AFP)[8].

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02
B

Drug-Induced Birth Defects: Red Flags and Safer Alternatives

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Introduction: Why This Topic Still Matters

In modern obstetric practice, very few pregnant women go through nine months without taking any medication. Some enter pregnancy already on long-term treatment for epilepsy, hypertension, diabetes, psychiatric illness, thyroid disorders, or autoimmune disease. Others start medicines during pregnancy for common problems such as acidity, nausea, infections, skin conditions, pain, or anxiety. Added to this is the growing use of over-the-counter drugs, nutraceuticals, herbal products, and "natural" supplements, often without informing the treating doctor.

Most medications used in pregnancy are safe. However, a **small but clinically significant group of drugs can interfere with normal fetal development**, leading to congenital anomalies, growth restriction, organ dysfunction, or long-term neurodevelopmental problems. These are known as **drug-induced birth defects**. Though they account for a minority of all congenital anomalies, they are particularly important because **many are preventable**.

Studies show that nearly **65–90% of women take at least one medication during pregnancy**, and almost **70% are exposed during the first trimester**, when organogenesis is underway. This makes early pregnancy the most vulnerable period. The role of the clinician is therefore not to avoid all drugs, but to **identify red-flag medicines, understand when they are harmful, and replace them with safer alternatives wherever possible**

This article discusses common clinical conditions encountered in daily practice, drugs known to cause fetal harm, the **trimester during which the risk is highest, how such anomalies are detected,** and practical guidance on safer options. The aim is to inform, not alarm, and to support rational, evidence-based prescribing as recommended by **FOGSI, ICMR, and international guidelines.**

Understanding Teratogenic Risk: Timing Is Everything

The effect of a drug on the fetus depends on three critical factors: **timing of exposure, dose, and duration.** The **first trimester**, especially between **3 and 8 weeks of gestation**, is the period of organ formation. Exposure during this time is most likely to result in major structural malformations, such as neural tube defects, congenital heart disease, craniofacial abnormalities, or limb defects.

During the **second trimester**, drugs are less likely to cause gross malformations but may affect **organ growth and differentiation**, leading to problems such as renal dysplasia, impaired brain development, or abnormal skeletal growth.

In the **third trimester**, drug exposure more commonly results in **functional effects**, such as fetal growth restriction, oligohydramnios, ductal constriction, neonatal withdrawal, metabolic disturbances, or long-term neurodevelopmental effects.

Understanding this timeline helps clinicians correlate drug exposure with ultrasound findings and counsel patients appropriately.

Epilepsy: Preventing Seizures Without Harming the Fetus

Epilepsy is a condition where treatment cannot be stopped abruptly without risking maternal and fetal life. However, not all antiepileptic drugs carry the same risk.

Valproic acid is one of the most clearly established teratogens in clinical practice. First-trimester exposure is strongly associated with **neural tube defects**, particularly spina bifida. In addition, valproate increases the risk of congenital heart disease, facial dysmorphism, limb anomalies, and urogenital defects. Beyond structural anomalies, valproate exposure has been linked to **long-term neurodevelopmental impairment**, including reduced IQ and increased risk of autism spectrum disorders. The risk increases with higher doses and when multiple antiepileptic drugs are used together.

Neural tube defects may be suspected early through elevated maternal serum alpha-fetoprotein levels and confirmed on targeted ultrasound. A detailed anomaly scan with careful assessment of the spine and heart is essential, and fetal echocardiography may be indicated.

Safer alternatives such as **lamotrigine and levetiracetam** have shown a much lower risk of major congenital anomalies and are now preferred. FOGSI and international bodies strongly recommend **pre-pregnancy counselling**, dose optimisation, avoidance of polytherapy, and **high-dose folic acid supplementation** for women with epilepsy.

Hypertension: The Silent Risk of ACE Inhibitors and ARBs

Chronic hypertension is increasingly common in young women, many of whom are treated with **ACE inhibitors or angiotensin receptor blockers (ARBs)** before pregnancy. These drugs are particularly dangerous once pregnancy is established.

First-trimester exposure may be associated with cardiac and central nervous system anomalies, but the most severe effects occur with **second- and third-trimester exposure. These include fetal renal dysplasia, anuria, oligohydramnios, pulmonary hypoplasia,**

skull ossification defects, intrauterine growth restriction, and neonatal renal failure. In severe cases, fetal or neonatal death may occur.

On ultrasound, **oligohydramnios is often the earliest sign**, followed by poorly visualised fetal kidneys and growth restriction. Once significant damage has occurred, stopping the drug may not reverse fetal injury.

FOGSI and ICMR recommend that women of reproductive age should ideally be managed with **labetalol, methyldopa**, or **nifedipine**, all of which have a long track record of safety in pregnancy. Any woman planning pregnancy should be switched off ACE inhibitors or ARBs well in advance.

Diabetes Mellitus: Disease Control Is More Important Than the Drug

Pre-existing diabetes is itself a strong risk factor for congenital anomalies. Poor glycaemic control during early pregnancy increases the risk of **neural tube defects, cardiac anomalies, skeletal defects, and caudal regression syndrome.**

Concerns are sometimes raised about antidiabetic drugs, but it is important to emphasise that **hyperglycaemia is more teratogenic than insulin**. Insulin does not cross the placenta and remains the safest and most effective treatment during pregnancy.

Women with diabetes require early dating scans, meticulous glucose control, and a **targeted mid-trimester anomaly scan**, with special attention to the fetal heart and spine. Fetal echocardiography is often advised.

Acne and Dermatological Treatments: A Preventable Disaster

Isotretinoin is one of the most potent teratogens known. Exposure at any time in pregnancy, especially during the first trimester, can result in severe anomalies involving the craniofacial structures, heart, central nervous system, thymus, and ears. The pattern of defects is often striking and devastating.

Most anomalies are detected at the anomaly scan, but by then, the damage is already done. There is no safe trimester for isotretinoin use, and even short exposure can be harmful.

Safer alternatives such as topical azelaic acid, topical clindamycin, and non-retinoid skin care should always be preferred. Strict contraception and pregnancy testing are mandatory for women of reproductive age on isotretinoin.

Infections and Antibiotics: Choosing Wisely

Antibiotics are among the most commonly prescribed drugs in pregnancy. While many are safe, some carry specific fetal risks.

Aminoglycosides, particularly streptomycin, are associated with irreversible fetal ototoxicity, leading to congenital deafness. Fluoroquinolones are best avoided due to concerns about cartilage and musculoskeletal development.

For common infections such as urinary tract infection, safer options include penicillins and cephalosporins. Nitrofurantoin is generally safe in early pregnancy but should be avoided close to term.

Fungal infections deserve special mention. A single low dose of fluconazole is usually safe, but high-dose or prolonged use during the first trimester has been associated with craniofacial, skeletal, and cardiac anomalies. For vaginal candidiasis, topical azoles remain the treatment of choice.

Psychiatric Medications: Treating the Mother, Protecting the Baby

Mental health disorders are common and often under-treated in pregnancy. Untreated depression and anxiety can lead to poor nutrition, substance use, inadequate antenatal care, and even suicide.

Certain antidepressants, particularly paroxetine, have been associated with an increased risk of congenital heart defects when used in early pregnancy. Other SSRIs, such as sertraline and fluoxetine, have a better safety profile and are preferred when medication is required.

Late-pregnancy exposure to SSRIs may lead to transient neonatal symptoms such as jitteriness or respiratory distress, which are usually self-limiting. Fetal echocardiography may be considered if first-trimester exposure has occurred.

Migraine and Pain Management: Avoiding Ergot Derivatives

Ergotamine causes intense vasoconstriction and uterine stimulation. Its use during pregnancy can result in reduced uteroplacental blood flow, fetal growth restriction, and preterm birth. It should never be prescribed to pregnant women.

Paracetamol, used judiciously, remains the safest analgesic in pregnancy. Lifestyle modification and trigger avoidance should be encouraged.

Lipid-Lowering Drugs: When Treatment Can Wait

Statins interfere with cholesterol synthesis, which is essential for fetal cell membranes and hormone production. Although recent studies suggest the risk of major malformations may be lower than previously believed, routine use of statins in pregnancy is still not recommended.

Women should discontinue statins once pregnancy is confirmed and focus on dietary and lifestyle measures. Treatment can usually be resumed after delivery.

Antacids, H2 Blockers, and Proton Pump Inhibitors: Are They Really Safe?

Acidity and reflux are extremely common in pregnancy, and many women self-medicate even before consulting a doctor. Fortunately, most commonly used antacids are safe when used appropriately.

Simple antacids containing calcium carbonate or magnesium hydroxide are generally safe throughout pregnancy. However, excessive use of sodium-containing antacids should be avoided due to the risk of fluid retention and hypertension.

H2 receptor blockers, such as ranitidine and famotidine, have a good safety record and can be used when antacids are insufficient.

Proton pump inhibitors (PPIs), including omeprazole and pantoprazole, have not been associated with a significant increase in congenital anomalies and are considered safe when clinically indicated. Current evidence suggests no increased risk even with first-trimester exposure.

The key message is that symptom-driven, supervised use is safe, but prolonged unsupervised self-medication should be discouraged.

Self-Administered Nutraceuticals and "Natural" Supplements: The Hidden Risk

A growing concern in antenatal care is the unregulated use of nutraceuticals, herbal preparations, and "natural" remedies. Many women assume these are safe simply because they are not labelled as medicines. High doses of vitamin A are clearly teratogenic and can cause severe craniofacial and central nervous system anomalies. Certain herbal products may contain heavy metals or undisclosed

pharmacological agents. The lack of standardisation and safety data makes these products unpredictable. FOGSI and ICMR strongly advise that only prescribed prenatal supplements should be used in pregnancy. Anything beyond routine iron, calcium, iodine, vitamin D, and folic acid should be taken only after medical advice.

Detection of Drug-Induced Fetal Anomalies

Early dating scans help establish the timing of exposure. The 18–20 week anomaly scan remains the cornerstone of detection, with targeted assessment based on the suspected drug. Fetal echocardiography, neurosonography, and serial growth scans may be required.

Equally important is counselling. Not every exposure leads to harm, and many pregnancies continue normally despite early drug exposure. Clear communication reduces anxiety and supports informed decision-making.

Conclusion

Drug-induced birth defects are uncommon but often preventable. For almost every high-risk drug, a safer alternative exists. The responsibility of the clinician is to prescribe thoughtfully, counsel clearly, and remain updated with guidelines. A careful prescription today can prevent lifelong disability tomorrow.

Summary Chart: Common Conditions, Risky Drugs, and Safer Alternatives

Condition	Common Drug	Main Fetal Risk	High-Risk Trimester	Safer Alternative
Epilepsy	Valproate	Neural tube defects, low IQ	First	Lamotrigine, Levetiracetam
Hypertension	ACE inhibitors / ARBs	Renal dysplasia, oligohydramnios	Second–Third	Labetalol, Methyldopa
Diabetes	Poor control / older OHA	Cardiac, NTDs	First	Insulin
Acne	Isotretinoin	Severe multisystem defects	All	Topical azelaic acid
UTI	Aminoglycosides	Deafness	All	Cephalosporins
Fungal infection	High-dose Fluconazole	Craniofacial defects	First	Topical azoles
Depression	Paroxetine	Cardiac defects	First	Sertraline
Migraine	Ergotamine	IUGR, preterm birth	All	Paracetamol
Hyperlipidemia	Statins	Possible neural defects	All	Diet control
Acidity	Unregulated OTC use	Minimal but misuse risk	Any	Antacids, H2 blockers

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03
A

Treatment Of Some Common Infections In Pregnancy

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Syphilis in Pregnancy

Syphilis is a chronic systemic infection caused by a spirochaete, Treponema pallidum. It is a sexually transmitted disease (STD) and is an important cause of genital ulcer. The clinical features are grouped into primary, secondary, latent, and tertiary according to duration from first infection and infectivity rate.

Vertical transmission causes perinatal morbidity and mortality. Congenital infection can lead to abortion, stillbirth, prematurity, low birth weight, or neonatal death.

Primary and secondary syphilis have very high transmission rates (100% and 50–60% respectively). Late syphilis transmits rarely.

Treatment of Syphilis in Pregnancy

A) Early Syphilis (Primary, Secondary, Early Latent <2 years)

- Benzathine Penicillin G 2.4 million units IM – Single dose
- Erythromycin 500 mg QID for 14 days
- Ceftriaxone 1 g IM daily for 10–14 days
- Azithromycin 2 g orally – Single dose

B) Late Syphilis or Unknown Duration

- Benzathine Penicillin G 2.4 million units IM weekly × 3 weeks
- Erythromycin 500 mg QID for 30 days (alternative when penicillin cannot be used)

If penicillin allergy exists and desensitization is not possible:

- Erythromycin 2 g/day × 20 days, OR
- Azithromycin (with caution) — full fetal treatment is NOT guaranteed; neonatal evaluation is mandatory.

C) Partner Management and Follow-Up

- Identify and treat all sexual partners from the preceding 3 months (early) or 1 year (late).
- Start treatment immediately after positive screening.
- If non-penicillin regimens are used, treat the newborn after delivery.

NOTE

- Penicillin is preferred and is the only drug that reliably treats congenital infection.
- Erythromycin and Azithromycin DO NOT cross the placenta completely — fetal treatment is incomplete.
- Doxycycline is contraindicated in pregnancy.

Jarisch–Herxheimer Reaction (JHR)

- Acute febrile reaction within 24 hours of treatment
- Seen in **40% of pregnant women treated for syphilis**
- May cause uterine contractions, preterm labor or non-reassuring FHR
- Manage supportively (antipyretics, fluids) and monitor fetal wellbeing

Antenatal Surveillance

- Universal serologic screening
- If non-treponemal test is >1:16, confirm with treponemal test
- Repeat testing at 28–32 weeks and at delivery if high-risk
- Screen partners
- Women with syphilis should also be tested for HIV

Dengue in Pregnancy

A common arboviral disease associated with miscarriage, premature delivery, and low birth weight. Pregnant women have higher risk of severe dengue.

Laboratory Evaluation

Parameter	When	Interpretation
CBC (baseline)	At presentation	Normal or low WBC → consider dengue
CBC (24 hours later)	Repeat	• Falling WBC or platelets• PCV rise >10% = clinically significant

Management Overview

A) Dengue without Warning Signs

Measure	Details
Fever control	Paracetamol 500–650 mg q4–6h
Avoid	NSAIDs, aspirin
Monitoring	Vitals q4h, daily CBC
Hydration	If severe vomiting → IV fluids @100 ml/hr
Observation	Look for lethargy, pulse pressure <20, delayed cap refill (>2 min), especially when fever subsides

B) Dengue with Warning Signs

Measure	Details
Monitoring	Hourly vitals, pulse pressure, urine output
Fluids	Normal saline resuscitation
Labs	CBC and LFT monitoring
Obstetric caution	Avoid induction or planned surgery

C) Dengue with Shock on Admission

Measure	Details
Care	ICU management
Stabilization	Resuscitation followed by assessment of fetal wellbeing and supportive therapy

NOTE

- Avoid prophylactic platelet transfusion unless delivery is inevitable
- Safe platelet levels: >50,000 for normal delivery; >75,000 for operative delivery
- Dengue is not an indication for termination
- Avoid planned induction/cesarean during the critical thrombocytopenic phase
- If delivery unavoidable: ensure blood and blood products available

Typhoid in Pregnancy

Typhoid causes fever, malaise, abdominal pain and may result in miscarriage, fetal death, or premature birth.

Treatment

- Azithromycin – first line for uncomplicated cases (safe in pregnancy)
- Ceftriaxone – preferred for severe disease (safe)
- Ampicillin/Amoxicillin – possible if locally susceptible

Avoid

- Fluoroquinolones (e.g., Ciprofloxacin) unless no alternative
- Chloramphenicol (risk of Gray Baby Syndrome)

Urinary Tract Infections in Pregnancy

Urinary Tract Infections in Pregnancy

Asymptomatic bacteriuria (ASB), urinary tract infection (UTI) and pyelonephritis are common complications in pregnancy with significant maternal and foetal risks. Here's a concise, trimester-wise and guideline

OVERVIEW

Condition	Definition	Clinical Relevance in Pregnancy
Asymptomatic bacteriuria (ASB)	$\geq 10^5$ CFU/mL bacteria in urine without symptoms	Risk of progressing to symptomatic UTI or pyelonephritis (~30%)
Cystitis (lower UTI)	Bacteriuria with dysuria, frequency, urgency, suprapubic pain	May cause preterm labour, low birth weight
Pyelonephritis	Bacteriuria with fever, flank pain, CVA tenderness, systemic signs	Risk of sepsis, ARDS, preterm labour, foetal compromise

WHO TO SCREEN & WHEN

Category	Screening Recommendations
Pregnant women (routine)	✅ Screen once early in pregnancy (ideally at 12–16 weeks or first prenatal visit) with urine culture
High-risk groups (recurrent UTI, diabetes, renal disease, catheter use)	May repeat screening in 3rd trimester
Nonpregnant women, men, diabetics, elderly, catheterized, institutionalized	❌ Do NOT screen or treat ASB (per IDSA)

WHO TO TREAT

Condition	Treat?	Duration
ASB in pregnancy	✅ Yes	5–7 days
Cystitis in pregnancy	✅ Yes	5–7 days
Pyelonephritis	✅ Yes (hospitalize, IV therapy initially)	10–14 days total
ASB in nonpregnant adults	❌ No	–

FIRST-LINE ANTIBIOTIC REGIMENS
For ASB or Cystitis in Pregnancy

Drug	Dose	Duration	Notes / Safety
Nitrofurantoin (NF)	100 mg PO BID	5 days	Avoid in 1st trimester (possible rare birth defect) and near term (risk of haemolysis in G6PD deficiency / neonate)
Cephalexin (1st gen cephalosporin)	500 mg PO QID	5–7 days	Safe throughout pregnancy
Amoxicillin-clavulanate	500/125 mg PO TID	5–7 days	Safe; increasing resistance among E. coli
Fosfomycin trometamol	3 g single dose	1 dose	Safe, convenient, but may be less effective for recurrent UTI

For Pyelonephritis in Pregnancy
Initial (IV) therapy:

- **Ceftriaxone 1 g IV daily**
  or Cefotaxime 1 g IV q8h
- **Ampicillin + Gentamicin** (if enterococcus suspected)
- **Aztreonam** (if penicillin allergy)

Switch to oral once afebrile 24–48 h, to complete **10–14 days total** with oral cephalosporin or amoxicillin-clavulanate.
Avoid nitrofurantoin or fosfomycin in pyelonephritis → they don't achieve adequate renal tissue levels.

WHAT TO AVOID & WHEN

Drug	Dose	Duration	Notes / Safety
Nitrofurantoin (NF)	100 mg PO BID	5 days	Avoid in 1st trimester (possible rare birth defect) and near term (risk of haemolysis in G6PD deficiency / neonate)
Cephalexin (1st gen cephalosporin)	500 mg PO QID	5–7 days	Safe throughout pregnancy
Amoxicillin-clavulanate	500/125 mg PO TID	5–7 days	Safe; increasing resistance among E. coli
Fosfomycin trometamol	3 g single dose	1 dose	Safe, convenient, but may be less effective for recurrent UTI

SPECIAL CONSIDERATIONS

- **Follow-up:** Always repeat urine culture 1–2 weeks after therapy to confirm clearance.
- **Recurrent UTI (>2 in pregnancy):** Prophylaxis with **nitrofurantoin 100 mg daily at bedtime** or **cephalexin 250–500 mg daily** may be considered until delivery.
- **Beta-lactamase–producing organisms:** Use **amoxicillin–clavulanate** or **3rd-gen cephalosporins (e.g. cefixime, ceftriaxone).**
- **Pyelonephritis complications:** Sepsis, ARDS, preterm labour, anaemia — hence early hospitalization and IV antibiotics..

TRIMESTER-WISE SAFETY SUMMARY

Drug	1st Trimester	2nd Trimester	3rd Trimester / Near Term
Nitrofurantoin	⚠️ Use if no alternative	✅ Safe	⚠️ Avoid near term (G6PD risk)
TMP-SMX	❌ Avoid (folate antagonism)	✅ If needed	❌ Avoid (kernicterus risk)

Cephalosporins	✅	✅	✅
Amox-Clav	✅	✅	✅
Fosfomycin	✅	✅	✅
Fluoroquinolones / Tetracyclines	❌	❌	❌

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MALARIA IN PREGNANCY

INTRODUCTION

- **Malaria in pregnancy (MiP)** increases risk of:
  - Maternal anaemia, hypoglycaemia, severe illness, death
  - Miscarriage, IUGR, stillbirth, preterm delivery, low birth weight
  - Congenital malaria (especially P. vivax, P. falciparum)
- **India:** Both P. vivax (~50%) and P. falciparum (~50%) are prevalent.
  - High endemic states: Odisha, Chhattisgarh, Jharkhand, NE states, MP.
  - P. falciparum causes severe disease.

SCREENING & PREVENTION

	Recommendation
Screening	All pregnant women in endemic areas — screen at each ANC visit for
Vector control	Promote insecticide-treated nets (LLINs) and indoor residual spraying
Chemoprophylaxis / IPTp	See below — varies by region.

INTERMITTENT PREVENTIVE TREATMENT IN PREGNANCY (IPTp)

🌍 **WHO Guidelines (for sub-Saharan Africa, not routinely used in India)**

- **Drug:** Sulfadoxine–pyrimethamine (SP)
- **Dose:** 3 tablets (each 500 mg sulfadoxine + 25 mg pyrimethamine) once per dose
- **Schedule:** Starting from **second trimester,** at least **3 doses** spaced ≥1 month apart until delivery
- **Not for India:** Because of widespread SP resistance and low stable transmission in most areas.

🇮🇳 India (NVBDCP / NMEP 2023):

- IPTp with SP **not recommended.**
- Focus is on **early detection and prompt treatment (EDPT)** and **LLIN use.**

TREATMENT BY TRIMESTER

✅ **1st Trimester**

Infection	Drug of Choice	Notes
P. falciparum	Quinine + Clindamycin for 7 days	Safe in 1st trimester; quinine may cause hypoglycaemia—monitor.
P. vivax	Chloroquine (25 mg base/kg over 3 days)	Safe in all trimesters. No primaquine (contraindicated).

✅ **2nd and 3rd Trimester**

Infection	Drug of Choice	Alternative / Notes
P. falciparum (uncomplicated)	ACT = Artemether–Lumefantrine (AL) for 3 days	Safe and effective after 1st trimester.
P. falciparum (chloroquine-sensitive area) *	Chloroquine	If known sensitivity confirmed.
P. vivax	Chloroquine 3 days	No primaquine until after delivery.
Mixed infection	ACT (as for falciparum)	—

⚠️ ACTs (especially AL, DHA–PPQ, AS–AQ) are **contraindicated in 1st trimester,** safe in 2nd and 3rd**.**

Primaquine Use

Stage	Use	Reason
During pregnancy	❌ Contraindicated	Risk of foetal haemolysis (G6PD not tested in foetus)
After delivery (postpartum)	✅Single dose 0.75 mg/kg (falciparum) or 14-day course (vivax)	To prevent relapse / gametocyte clearance

SEVERE MALARIA IN PREGNANCY

Definition (same as non-pregnant)

- Impaired consciousness, convulsions
- Severe anaemia (Hb <7 g/dL)
- Hypoglycaemia (<40 mg/dL)
- Pulmonary edema, renal failure, acidosis, shock, high parasitaemia

Treatment of Severe Malaria (All Trimesters)

Stage	Drug of Choice	Regimen	Notes
Any trimester	IV Artesunate	2.4 mg/kg IV at 0, 12, 24 h, then daily until	Safe in all trimesters, preferred per WHO and
Alternative (if artesunate unavailable)	IV Quinine dihydrochloride	Loading 20 mg/kg over 4 h, then 10 mg/kg q8h	Risk of hypoglycaemia; avoid bolus
After recovery (once oral tolerated)	Complete 3-day ACT course (AL or DHA-	Ensure full eradication	

Supportive care: IV fluids, transfusion for anemia, antipyretics, glucose monitoring, fetal surveillance.

SAFETY SUMMARY BY TRIMESTER

Drug	1st Trimester	2nd Trimester	3rd Trimester
Chloroquine	✅	✅	✅

Quinine + Clindamycin	✅	✅	✅ (monitor hypoglycaemia)
ACT (AL, DHA–PPQ, AS–AQ)	❌ Avoid	✅	✅
Primaquine	❌ Avoid	❌ Avoid	❌ Avoid
IV Artesunate (severe malaria)	✅ Safe	✅	✅

COUNSELLING POINTS (India-relevant)

Topic	Key Counselling Message
Prevention	Use LLINs every night; avoid mosquito exposure; clear breeding sites.
Early reporting	Report fever immediately; do not self-medicate.
Adherence	Complete full treatment course even if symptoms subside.
Follow-up	Return for review on day 3, day 7, and post-treatment blood smear.
Family protection	LLIN use for all family members, especially children.
Postpartum prophylaxis	Primaquine (after G6PD test) to prevent relapse for P. vivax.
Foetal monitoring	More intensive & frequentfoetal monitoring with Ultrasound for growth parameters, viability, NST as indicated after severe disease.

DOCUMENTATION (For Medico-Legal & Public Health Purposes)

Documentation Item	Purpose
ANC record entry	Note malaria test (RDT/microscopy) result and treatment given.
Drug details	Name, dose, duration, start/stop date, trimester noted.
Counselling note	Record that LLIN use, relapse prevention, and follow-up were advised.
Notification	Report all falciparum and mixed malaria to NVBDCP (mandatory in India).
Discharge summary	Include diagnosis, species, drug used, trimester, complications, foetal outcome.
Maternal death review	If malaria-related, notify per MDSR protocol.

REFERENCES

1. **WHO Guidelines for Malaria, 2023.**
2. **National Vector Borne Disease Control Programme (NVBDCP / NMEP India) Guidelines 2023.**
3. **FOGSI Good Clinical Practice Recommendations, 2021.**
4. **ICMR Malaria Research Updates, 2022.**
5. **MoHFW India Maternal Health Division, 2023.**

ToRCH infections

ToRCH infections (Toxoplasmosis, "Other" [syphilis, varicella, parvovirus B19, etc.], Rubella, Cytomegalovirus, Herpes simplex) are crucial to understand for both **preventive obstetric care** and **perinatal infection management.**

Below is a **clinically oriented summary** covering:
✅ Who to screen and when
✅ Treatment and prevention by infection
✅ Drugs to avoid and trimester-specific precautions
✅ Safety and counselling aspects — all per **FOGSI 2021, RCOG 2022, CDC 2023, and ICMR/NCDC India 2024 guidelines**

ToRCH INFECTIONS IN PREGNANCY
(Screening, Treatment, and Drug Safety Summary — India 2024 Update)
OVERVIEW

Infection	Major Foetal Risk	Transmission Timing
Toxoplasmosis	Hydrocephalus, intracranial calcifications, chorioretinitis	Transmission increases with gestational age
Syphilis (O of ToRCH)	Stillbirth, neonatal death, congenital syphilis	Any time
Rubella	Congenital rubella syndrome (CRS): deafness, cardiac, cataract	Highest <12 weeks
CMV	Microcephaly, sensorineural hearing loss	Any trimester
HSV	Neonatal herpes, encephalitis, death	Peripartum
Others (Parvovirus B19, Varicella)	Hydrops fetalis, varicella pneumonia	Trimester dependent

SCREENING — WHO & WHEN

Infection	Who to Screen	When
Syphilis	✅ All pregnant women	At 1st ANC, repeat in 3rd trimester & at delivery (per NACP & FOGSI)
HIV, HBV (part of "O")	✅ Universal screening	Early pregnancy
Toxoplasmosis, Rubella, CMV (TORCH panel)	❌ Not for routine screening in India (FOGSI, ICMR)	Only if bad obstetric history (BOH), fetal anomalies, IUGR, or IUFD
HSV	Test if genital ulcers or preterm labour; otherwise not routine	As indicated
Varicella immunity	History or serology if uncertain	Preconception/early pregnancy
Parvovirus B19	Only during outbreak or hydrops fetalis	As indicated

TOXOPLASMOSIS

Transmission

- Usually via undercooked meat or cat feces.
- Transmission ↑ with gestational age, but fetal damage ↓ later in pregnancy.

Diagnosis

- Maternal IgM & IgG (avidity testing to date infection)
- PCR on amniotic fluid (if foetal infection suspected)

Treatment

Situation	Regimen	Notes
Maternal acute infection (before 18 wks)	Spiramycin 1 g PO q8h	Reduces transplacental transmission. Safe in all trimesters.
Confirmed foetal infection (amniotic PCR +)	Pyrimethamine 50 mg/day + Sulfadiazine 1 g q6h + Folinic acid 10–20 mg/day	Start after 18 wks (pyrimethamine is teratogenic early).
Follow-up	Serial USG q2–4 wks	Foetal brain, liver, ascites, hydrocephalus

Avoid / Caution

Drug	Avoid When	Reason
Pyrimethamine	1st trimester	Folate antagonist, teratogenic
Sulfonamides	Near term	Risk of neonatal kernicterus
Spiramycin	Safe throughout	—

SYPHILIS (O of ToRCH)

Screening

Universal screening via **VDRL/RPR** (quantitative) → Confirm with **TPHA/FTA-ABS.**

Treatment (per NACP / WHO 2023)

Stage	Regimen	Notes
Early syphilis (<1 year)	**Benzathine penicillin G 2.4 million units IM single dose**	Single dose effective
Late latent / Unknown duration	**2.4 million units IM weekly × 3 weeks**	—
Neurosyphilis	**Aqueous crystalline penicillin G 18–24 million units/day IV × 10–14 days**	—
Penicillin allergy	**Desensitize and treat with penicillin**	Other antibiotics less effective for fetus

Avoid

- Doxycycline, tetracycline – contraindicated (tooth discoloration, hepatotoxic).
- Erythromycin – doesn't cross placenta, not adequate for foetal cure.

RUBELLA

Screening

- Not for routine antenatal screening.
- Test if clinical rubella or suspected congenital infection.

Treatment

- No antiviral treatment available.

Management

Finding	Recommendation
Infection before 12 weeks	Offer termination (high CRS risk 80–90%)
Infection 12–20 weeks	Counselling, targeted USG, consider amniocentesis
Infection >20 weeks	Foetal risk low (<1%)

Prevention

Stage	Vaccine	Note
Preconception	MMR vaccine (2 doses 4 weeks apart)	Avoid pregnancy for 1 month after
During pregnancy	❌ Live vaccine contraindicated	Vaccinate postpartum

CYTOMEGALOVIRUS (CMV)

Transmission

- Sexual, salivary, transplacental, breast milk, blood transfusion.
- Primary infection highest risk.

Diagnosis

- IgG avidity, IgM, PCR from amniotic fluid (fetal infection).

Treatment

Condition	Regimen	Notes
Primary maternal CMV infection	No approved safe antiviral	Supportive only
Severe fetal disease (experimental)	Valganciclovir / Ganciclovir under specialist use	Risk of bone marrow suppression, teratogenic in animals
Immunoglobulin (CMV hyperimmune globulin)	Investigational	Limited efficacy

Avoid

- **Valganciclovir, Ganciclovir** — potential teratogenicity.
- **No proven prophylaxis** during pregnancy.

Prevention

- Hygiene (handwashing, avoid saliva exchange with toddlers, safe sex).

HERPES SIMPLEX VIRUS (HSV)

Types

- HSV-2 > HSV-1 for genital infection.
- Risk highest if primary infection near delivery.

Treatment

Condition	Regimen	Notes
Primary genital herpes	**Acyclovir 400 mg PO TID × 7–10 days**	Safe in all trimesters
Recurrent HSV	**Acyclovir 400 mg PO BID or Valacyclovir 500 mg PO BID suppressive from 36 weeks**	Reduces recurrence and need for C-section
Neonatal exposure / active lesion at labor	**Cesarean section**	Prevents neonatal HSV

Avoid

- Topical antivirals unnecessary.
- No live vaccine available.

VARICELLA (O of ToRCH)

Situation	Management	Notes
Non-immune exposed pregnant woman	Varicella-zoster immune globulin (VZIG) within 96 hours	Prevents/severity reduction
Maternal infection <20 weeks	Fetal varicella syndrome risk (1–2%)	Serial USG
Active infection	Acyclovir 800 mg PO 5×/day × 7 days (if <24 hrs onset)	Safe; reduces severity
Varicella pneumonia	IV Acyclovir 10 mg/kg q8h	ICU support
Delivery within 5 days before or 2 days after rash onset	Give neonate VZIG	Prevent neonatal varicella

PARVOVIRUS B19

Situation	Management	Notes
Maternal infection (IgM+)	Monitor fetus for anemia/hydrops	USG, MCA-PSV Doppler
Fetal hydrops	Intrauterine transfusion	Treats fetal anemia

No antiviral or vaccine available.

Drug	1st Trimester	2nd Trimester	3rd Trimester / Near Term	Comments
Spiramycin	✅	✅	✅	Preferred for toxoplasmosis
Pyrimethamine	❌	✅	⚠️ Avoid near term (folate antagonism)	Use with folinic acid
Sulfadiazine	⚠️	✅	❌ Avoid near term (kernicterus)	—
Benzathine Penicillin	✅	✅	✅	Syphilis treatment of choice
Acyclovir / Valacyclovir	✅	✅	✅	For HSV / varicella
Chloroquine / Spiramycin	✅	✅	✅	Safe
MMR / Varicella vaccine	❌	❌	❌	Postpartum only
Valganciclovir / Ganciclovir	❌	⚠️	⚠️	Only under specialist guidance

COUNSELLING POINTS (India-Relevant)

Topic	Message
Food hygiene	Avoid raw meat, wash vegetables (toxoplasma).
Pet hygiene	Avoid cat litter cleaning (toxoplasma).
Vaccination	MMR & Varicella before conception; not during pregnancy.
Sexual health	Safe sex, avoid new partners (CMV, HSV).
Antenatal testing	Targeted testing for BOH, IUGR, anomalies.
Documentation	Record infection status, drugs, gestational age, counselling given, consent for termination if applicable.
Neonatal evaluation	For exposed or infected pregnancies — TORCH testing, ophthalmic and audiology screening.

REFERENCES

1. FOGSI Good Clinical Practice Recommendations 2021 – TORCH Infections
2. RCOG Green-top Guideline No. 36 (2022): Viral Infections in Pregnancy
3. CDC STD Treatment Guidelines 2023
4. WHO Congenital Infections Guidance 2023
5. NCDC & ICMR Maternal Infections Update 2024

04 No more Guess work" Nausea, vomiting & Hyper emesis stepwise Antiemetic

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Nausea and vomiting of pregnancy is a spectrum of disorder which ranges from mild nausea to the Severest form Hyper emesis. The HELP Score is a validated scoring System to assess the severity of the condition.

Key areas assessed are

- Nausea level
- Vomiting and Retching episodes
- Hydration status
- Oral intake
- Weight loss
- Functional status
- Psychological Functioning
- Treatment Effectiveness

Classification of severity

- None or mild ≤ 19 points
- Moderate 20 - 32 points
- Severe 33 - 60 points

Mild to moderate NVP is typically managed in the ambulatory setting white Hyper emesis requires admission The management usually followsstepwise or ladder approach.

Step 1- Lifestyle modification dietary adjustments

- Eat small frequent meal, avoid skipping meals, avoid fried fatty, spicy or food with strong smell.
- Try dry bland food like crackers or roasted chana before stepping out of bed.
- Avoid drinking water imm after a meal.
- Ginger is recommended as a candy or in tea.
- Rest.

Step 2 - 1st Line pharmacological Agents

- Pyridoxine (Vit B6) either alone or in combination with H2

- receptor antagonist (Antihistamine), like Doxylamine.
- Other pharmacological agents like cyclizine or promethazine may be used.

Step 3 - Second Line pharmacological Agents

One can switch to or add the following .

- Dopamine Antagonist/ Pro kinetics like metoclopramide or phenothiazines.
- Serotonin Antagonists such as Ondansetron (Though there may be safety conceans like cleft palate, it is widely used and considered safe by many guidelines).
- Fluid management - For moderate to severe cases esp Hyperemesis fluid replacement with electrolytes and supplementation with Thiamine to prevent wernicke'sencephalopathy esp before giving dextrose is imp preferably in a hospital setting

Step 4 - 3rd Line (Hospitalisation)

- In case of persistent vomiting not responding to steps (1-3) inpatient management is mandatory.
- Combination Antiemetic
- Use of multiple antiemeties from different classes.
- Corticosteroids: such as methyl prednisolone or Prednisone are to be given to resistant cases .To be avoided in 1st 10 weeks of pregnancy.
- Additional medications - other drugs like H2 receptor antagonist or PPI's may be added to treat the esophageal reflux and gastritis
- Nutrition - In care the patent doesn't tolerate anything orally leading to weight loss or nutritional deficiencies Tube Feeding or TPN (Total parenteral Nutrition)has to be thought of. A case of severe NVP or HG is ready for Discharge when
- She is able to tolerate oral intake.
- Her NVP are improved and controlled with oral drugs.
- Dehydration is corrected.
- Electrolyte imbalance and ketonurea if present, are resolved.
- Weight stabilisation.

Follow up with Advice on

- Regular use of medications.
- She should be advised to follow the dietery and lifestyle modifications.
- Freq weight checks.

She should be advised to report immediately if

- There is inability to tolerate oral fluids or drugs.
- There are Signs of dehydration (Extreme thirst, dizziness very dark urine).
- Weight loss (significant).
- It new symptoms like. blood in vomiting or pain abdomen develop.

Conclusion -

It is the recommended standard of care, stressing upon early initiation,aggressive treatment and individualization. There is a small often theoretical risk to the foetus which is outweighed by the benefits of effective antiemetic treatment. Untreated severe NVP Can Cause severe maternal morbidity andlead to adverse fetal outcomes. The overall treatment plan must be individualised based on how severe the symptoms are,as assessed by scoring systems like PUQE or H.E.L.P Score. Pt preference and response to prev Tt should also be taken into consideration.

References

- ACOG Practice Bulletin NVP obst & Gynae 2018, 131: e15-30.
- RCOG Green top Guideline No.69 (2024) Nausea & vomiting in pregnancy and Hyperemesis gravidarum.
- Boelig RC, et al ondansetron in pregnancy evidence Review AMJ obs & gynae 2017; 216:451-7.
- Niebyl JR NVP Review N Engl J med 2010; 363: 1544-50.
- Fejzoms, etal Hyper emesis - Clinical guidance BMJ 2019; 366:14897.

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05
A

Venous Thromboembolism in Pregnancy

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Introduction

Pregnancy is an independent risk factor for venous thromboembolism (VTE) and remains one of the leading non-obstetric causes of maternal morbidity and mortality. The risk of VTE increases four- to five-fold during pregnancy and the puerperium compared with the non-pregnant state. This heightened risk is multifactorial, with all three components of Virchow's triad—hypercoagulability, venous stasis, and endothelial injury—being present.

Hormonal changes during pregnancy lead to increased venous capacitance in the lower limbs and pelvis, resulting in venous stasis. This is further aggravated by the mechanical compression of the pelvic veins and inferior vena cava by the enlarging uterus, as well as the vasodilatory effects of estrogen.

Pregnancy is also characterized by a pronounced procoagulant state. Localized intravascular coagulation occurs particularly within the placental vessels, contributing to a physiological reduction in platelet count. Several coagulation factors—V, VII, VIII, IX, X, XI, XII, and von Willebrand factor—increase significantly, while natural anticoagulant mechanisms are impaired. The protein C–dependent pathway becomes less effective due to alterations in thrombomodulin and protein C receptor levels, leading to acquired activated protein C resistance, similar to that seen in individuals with Factor V Leiden mutation. In addition, protein S levels decrease, further enhancing the prothrombotic tendency.

Conversely, fibrinolysis—the mechanism opposing coagulation—is suppressed because of elevated levels of plasminogen activator inhibitors 1 and 2 (PAI-1 and PAI-2). These combined changes create a physiological hypercoagulable state that serves to minimize bleeding during delivery but substantially increases the risk of thromboembolic events.

The postpartum period, particularly the first six weeks after delivery, carries the highest risk for VTE as the hemostatic system gradually returns to the non-pregnant state by approximately the 12th postpartum week.

Table 1. Risk Factors for Venous Thromboembolism (VTE) in Pregnancy and the Postpartum Period
Adapted from references 12–15)

Category	Risk Factor	Relative Risk (RR)
Medical Conditions	Obesity (BMI >30 kg/m²)	53
	Strict bed rest ≥1 week	>6 (range 7–62)
	Comorbidities (e.g., heart disease, connective tissue	7–10
	Anemia	2
	Blood transfusion	7
	Previous VTE	25
	Smoking	2
	Diabetes mellitus	2
	Drug abuse	11
	Hypertension	18
	Antiphospholipid antibodies	16
	Family history of VTE	2–4
Pregnancy-Related	Age >35 years	2
	Cesarean delivery – elective	2
	Cesarean delivery – urgent	46
	Multiparity	16
	Infection after vaginal delivery	20

	Infection after cesarean delivery	6
	Assisted reproduction	44
	Preeclampsia	38
	Eclampsia	44
	Placenta previa	36
Thrombophilias	Factor V Leiden (FVL) – heterozygous	83
	FVL – homozygous	34 (range 10–40)
	Prothrombin gene mutation – heterozygous	68
	Prothrombin gene mutation – homozygous	26
	Combined FVL and prothrombin mutations	9–107
	Protein S deficiency	8
	Protein C deficiency	48
	Antithrombin deficiency	4.7–10

[a] Relative risk >6 corresponds to an estimated ~3% absolute risk of VTE.
[b] Due to the rarity of these inherited disorders, risk estimates may be conservative.

Prophylaxis

The HIGHLOW study compared intermediate-dose vs low-dose LMWH for thromboprophylaxis in pregnant and postpartum women at risk of VTE.

Inclusion criteria:

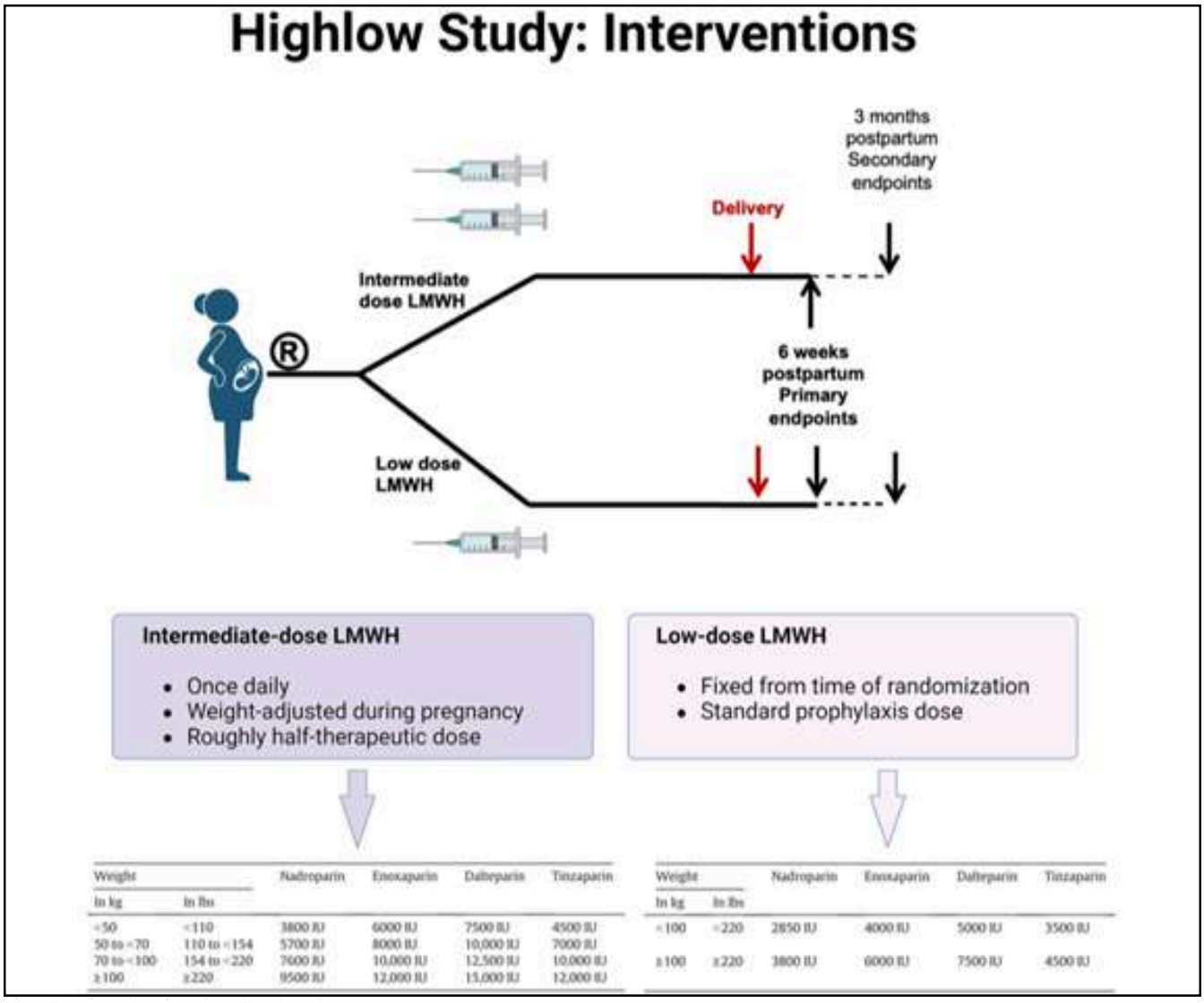
- Pregnant woman >18 years of age
- Previous history of VTE
- Presence of high-risk factors
- POG ≤14 weeks

Key management points:

• LMWH should be stopped before onset of labour or 24 hours before delivery.

• For neuraxial block: discontinue LMWH 24 hours before intermediate-dose and 10–12 hours before low-dose LMWH.

Conclusion:Low-dose LMWH is appropriate to prevent pregnancy-related recurrence of VTE. High-dose LMWH complicates peripartum management due to longer neuraxial anesthesia delay, higher cost, and increased side effects (e.g., bruising, bleeding).



Weight		Nadroparin	Enoxaparin	Dalteparin	Tinzaparin
In kg	In lbs				
<50	<110	3800 IU	6000 IU	7500 IU	4500 IU
50 to <70	110 to <154	5700 IU	8000 IU	10,000 IU	7000 IU
70 to <100	154 to <220	7600 IU	10,000 IU	12,500 IU	10,000 IU
≥100	≥220	9500 IU	12,000 IU	15,000 IU	12,000 IU

Weight		Nadroparin	Enoxaparin	Dalteparin	Tinzaparin
In kg	In lbs				
<100	<220	2850 IU	4000 IU	5000 IU	3500 IU
≥100	≥220	3800 IU	6000 IU	7500 IU	4500 IU

Figure 1. Highlow Study: Interventions – comparison of intermediate- versus low-dose LMWH during pregnancy and postpartum.

Monitoring of anti Xa level

Monitoring of LMWH via anti-Xa levels is generally not required during pregnancy, as current data do not support dose adjustments based on these levels.However, in selected high-risk scenaio„ anti-Xa monitoring may be warranted,

for 1) the twice-daily LMWH regimen, The target anti-Xa level (measured 4 h postdose) Is 0.5–1 IU/m

2) the once-daily dosing, a target Range of 1–2 IU/ml (4–6 h postdose) is considered acceptable.

Diagnosis

A diagnostic strategy based on **clinical probability, D-dimer, compression ultrasonography (CUS)**, and **CT pulmonary angiography (CTPA)** can safely exclude PE in pregnancy.

Wells' criteria

The risks of PTE are then assessed according to the scores into low (0-2 points), moderate (3-6 points), and high (> 6 points) risks.

Clinical Feature		Score
1. Active cancer (treatment ongoing, within previous 6 months, or palliative)		1
2. Paralysis, paresis, or recent plaster immobilization of the lower extremities		1
3. Recently bedridden for >3 days or major surgery within the last 4 weeks		1
4. Localized tenderness along the distribution of the deep venous system		1

5. Entire leg swollen		1
6. Calf swelling ≥2 cm larger than asymptomatic leg		1
7. Pitting edema confined to the symptomatic leg		1
8. Collateral superficial (non-varicose) veins		1
9.Previously documented DVT		1

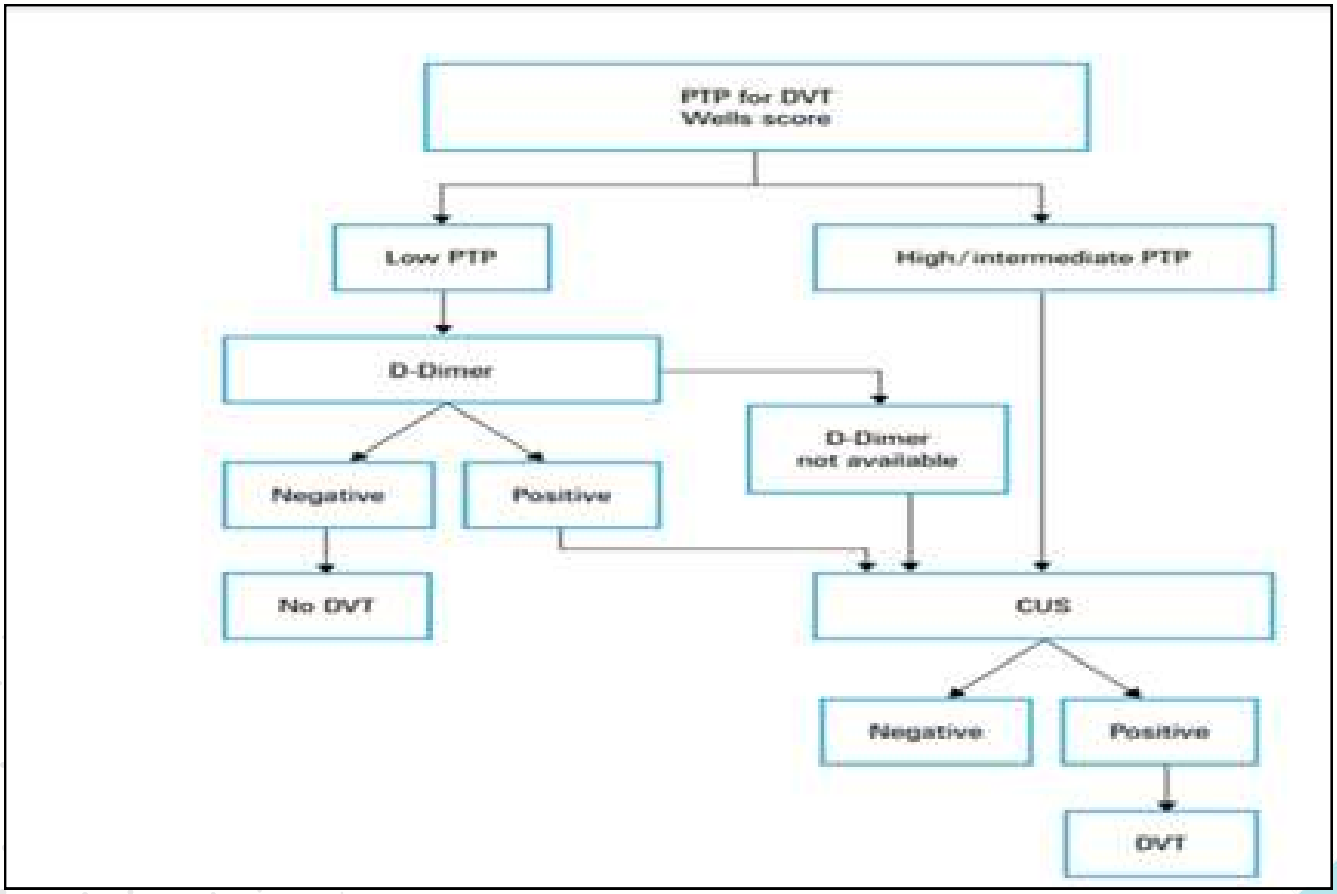


Figure 2

Pregnancy modified Geneva risk score

The score interpretation 0-1 low risk, 2-6 intermediate risk >_7 high risk

Variable	Points
Age 40 years or old	1
Surgery /lower limb fracture in past month	2
Previous DVT or PE	3
Unilateral lower limb pain	3
Hemoptysis	2
Pain on lower limb palpation and unilateral edema	4
Heart rate more than 110bpm	5

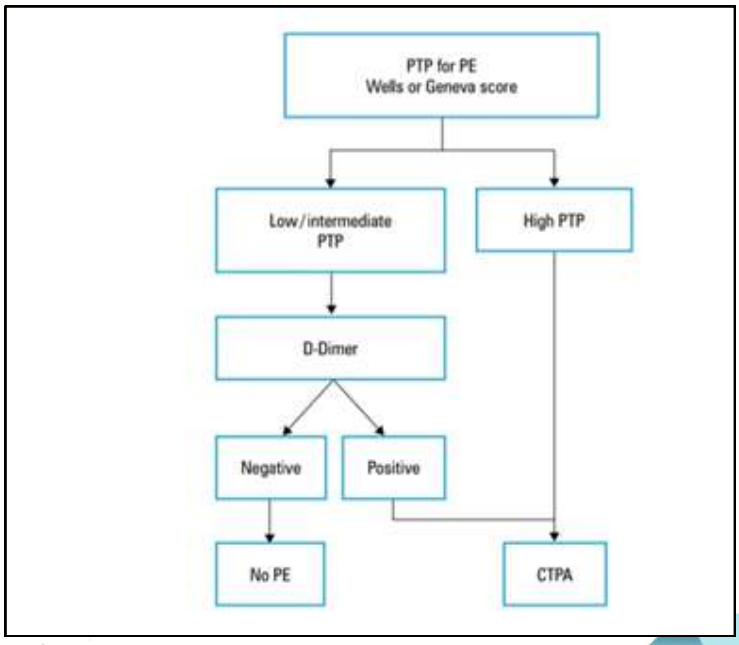


Figure 3
YEARS CRITERIA

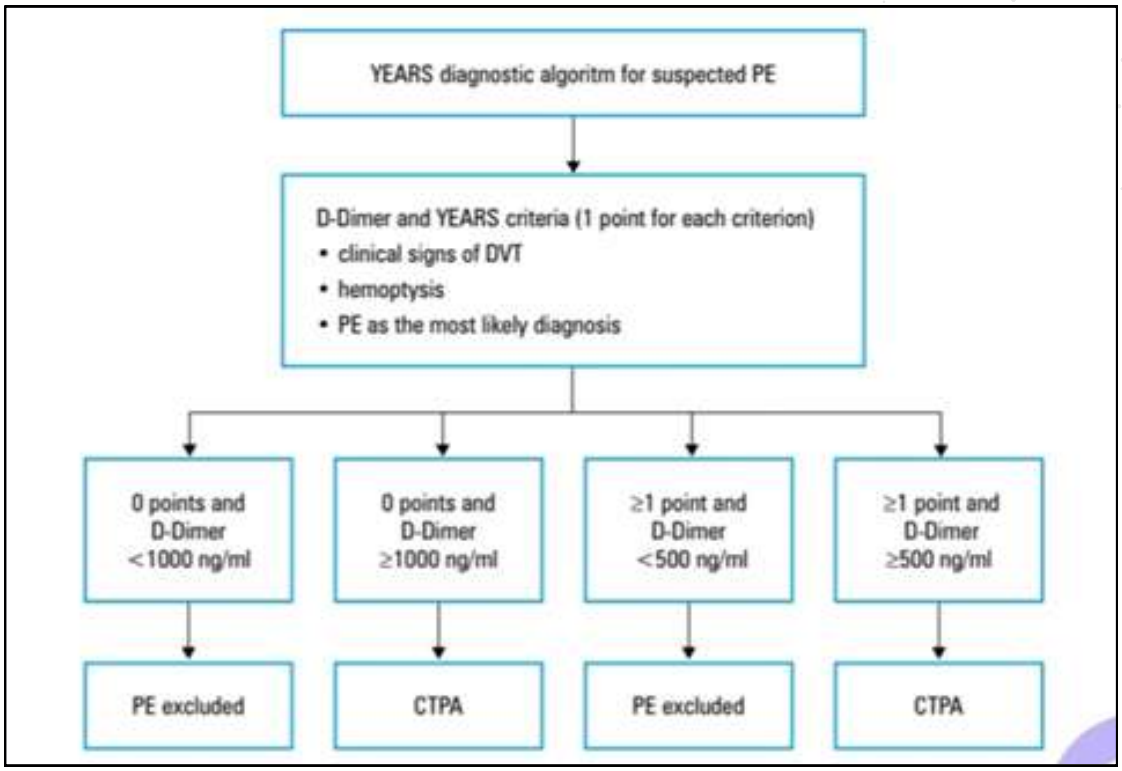
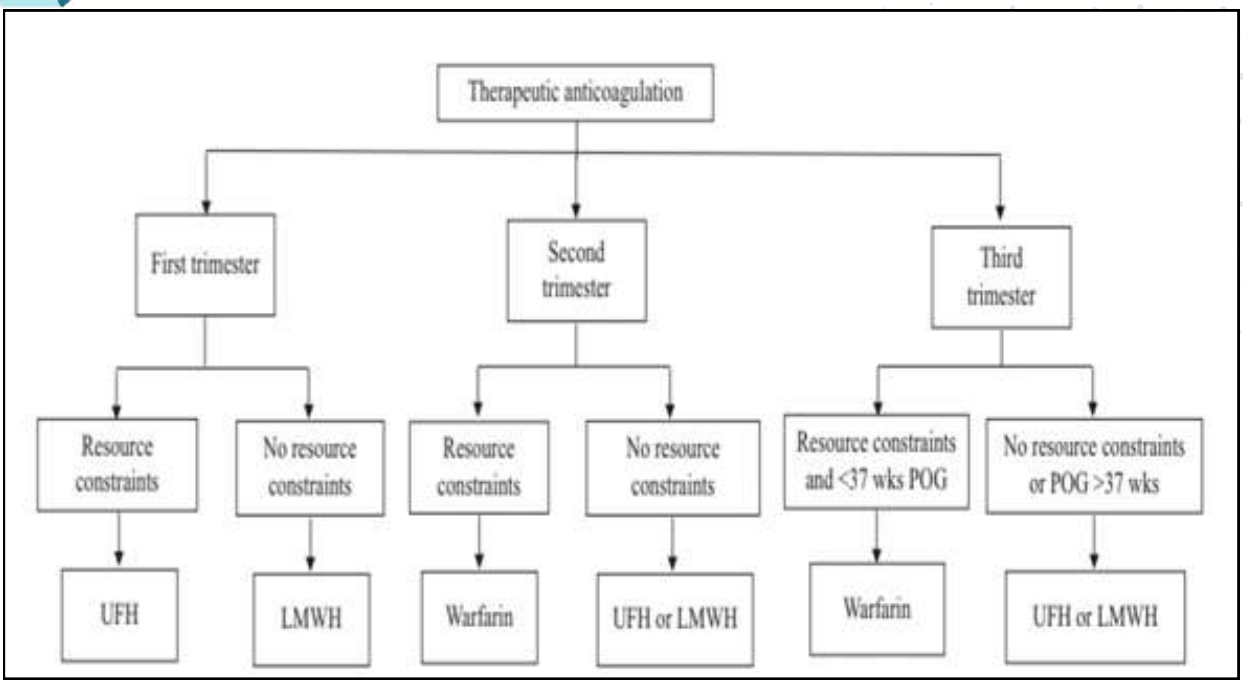


Figure 4
Treatment

LMWH is the treatment of choice for PE during pregnancy.

- Labour and delivery require close planning to prevent spontaneous labour while anticoagulated.
- Key peripartum recommendations:
- Delay regional anaesthesia until ≥24 hours after last LMWH dose (if renal function normal).
- In high-risk patients (e.g., recent PE), convert LMWH to UFH ≥36 hours before delivery.
- Stop UFH infusion 4–6 hours before delivery and ensure aPTT is normal before regional anaesthesia.

Postpartum anticoagulation:



• Continue anticoagulant therapy for ≥6 weeks postpartum
• Minimum total treatment duration: ≥3 months

Figure 5

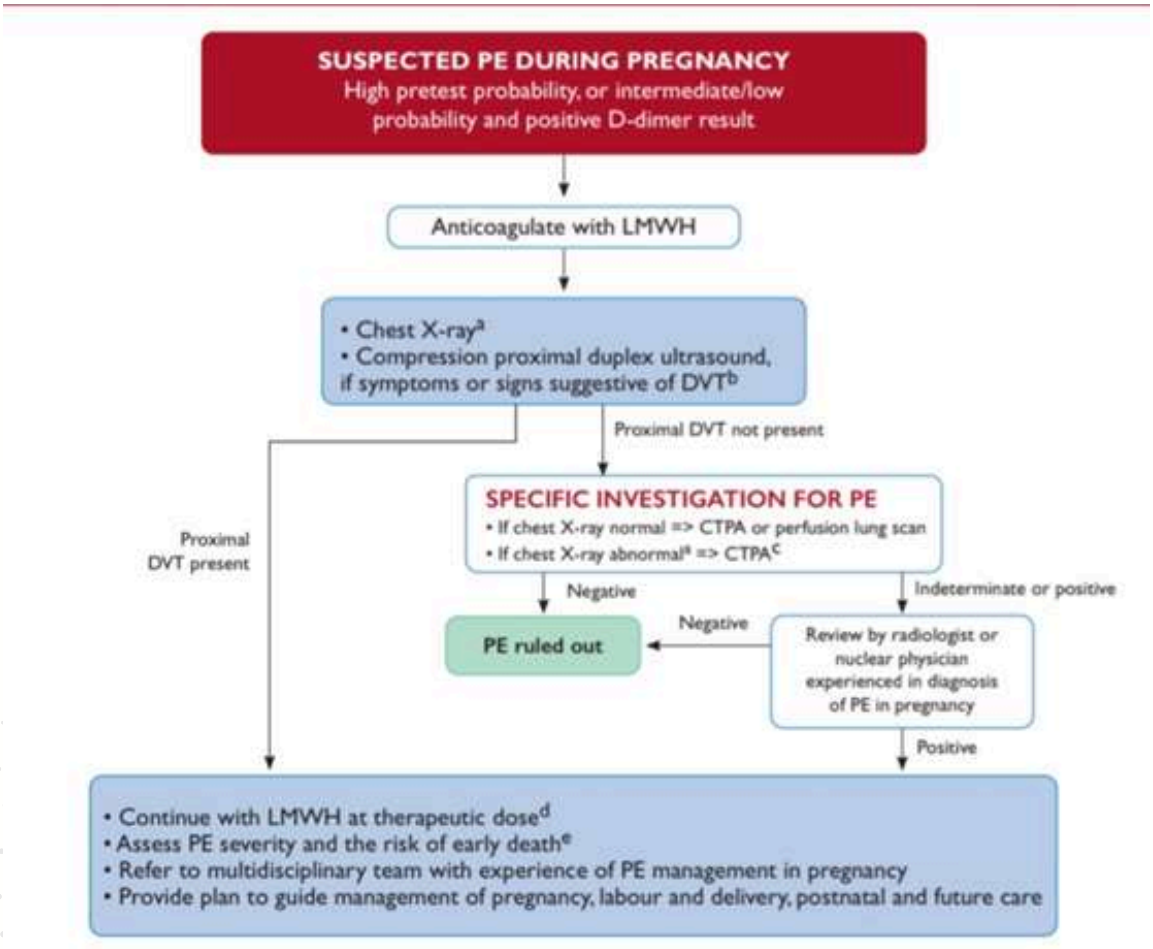


Figure 6

05 B

Expanded Neuraxial MHV Thrombophilia Lactation Discharge

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1. Neuraxial Anaesthesia: Timing and Reversal in Obstetrics

Neuraxial anaesthesia (spinal, epidural, combined spinal–epidural) is widely used in obstetrics. The major concern in anticoagulated patients is spinal/epidural haematoma, a rare but potentially catastrophic complication.

1.1 General principles

- Always balance maternal thromboembolic risk against the risk of neuraxial bleeding.
- Consider drug type, dose (prophylactic vs therapeutic), timing of last dose, renal function, and presence of epidural catheter.
- Follow institutional protocol and ASRA/ESRA guidance wherever available.

1.2 Timing of neuraxial block with common anticoagulants

Drug	Dose	Minimum interval before neuraxial block	Restart after neuraxial / catheter removal
UFH (SC)	Prophylactic	4–6 hours	4–6 hours
UFH (IV)	Therapeutic	4–6 hours + normal aPTT	4–6 hours
LMWH (enoxaparin)	Prophylactic	12 hours	12 hours
LMWH (enoxaparin)	Therapeutic	24 hours	24–48 hours
Fondaparinux	Any dose	36–48 hours (avoid if possible)	36–48 hours
Warfarin	Therapeutic	INR ≤1.4	Same day / next day
DOACs	Any dose	48–72 hours	48–72 hours

1.3 Epidural catheter removal

Timing of epidural catheter removal follows the same principles as insertion. Catheter should be removed when anticoagulant effect is minimal, and the next dose delayed accordingly.

1.4 Recognition and management of spinal/epidural haematoma

Red flag symptoms:

- Severe or increasing back pain
- Motor weakness or sensory loss
- Bowel or bladder dysfunction

Urgent MRI and neurosurgical consultation are mandatory. Decompression within 8–12 hours offers best neurological outcome.

1.5 Reversal of anticoagulation (summary)

- UFH: Protamine sulfate (complete reversal)
- LMWH: Protamine (partial reversal only)
- Warfarin: Vitamin K ± PCC/FFP
- Dabigatran: Idarucizumab
- Factor Xa inhibitors: Andexanet alfa (where available)

2. Mechanical Heart Valves in Pregnancy

Pregnancy in women with mechanical heart valves (MHV) carries significant maternal and fetal risk. Valve thrombosis is life-threatening, and optimal anticoagulation is essential.

2.1 Anticoagulation strategies

Options include:

- Warfarin throughout pregnancy (except near delivery)
- LMWH (dose-adjusted, anti-Xa monitored)
- Sequential regimens (LMWH in first trimester, warfarin in second trimester)

Warfarin provides superior maternal protection but is associated with embryopathy when used between 6–12 weeks. LMWH is safer for the fetus but associated with higher valve thrombosis risk if under-dosed.

2.2 Peripartum management

- Planned delivery with conversion to UFH or LMWH near term
- Clear plan for timing of last anticoagulant dose and neuraxial eligibility
- Early postpartum resumption of therapeutic anticoagulation

3. Thrombophilias in Pregnancy

3.1 Inherited thrombophilias

Includes Factor V Leiden, prothrombin G20210A mutation, antithrombin deficiency, protein C deficiency, and protein S deficiency.

Management depends on personal history of VTE, family history, and thrombophilia type.

3.2 Antiphospholipid syndrome (APS)

- Clinical criteria: thrombosis or pregnancy morbidity
- Laboratory criteria: lupus anticoagulant, anticardiolipin, anti-β2 glycoprotein I

Obstetric APS is treated with low-dose aspirin plus prophylactic LMWH; thrombotic APS requires therapeutic anticoagulation.

4. Lactation Compatibility of Common Drugs

Most drugs used in obstetrics and cardiology are compatible with breastfeeding. Decisions should consider infant maturity and maternal dose.

Drug	Compatibility	Comments
LMWH	Compatible	Minimal transfer into breast milk
Warfarin	Compatible	Safe during lactation
DOACs	Avoid / insufficient data	Prefer warfarin or LMWH
Aspirin (low dose)	Generally safe	Avoid high doses
Beta-blockers (labetalol)	Compatible	Monitor infant for bradycardia

5. Postpartum Discharge Checklist

Maternal assessment:

- Vitals stable, bleeding controlled, pain managed
- Anticoagulation plan clearly documented

Neonatal assessment:

- Feeding established, screening completed

Counselling and follow-up:

- Danger signs explained
- Contraception and follow-up appointments discussed

6. Key exam and viva points

- Neuraxial anaesthesia is contraindicated within 24 hours of therapeutic LMWH.
- Warfarin is safe in breastfeeding but contraindicated in early pregnancy.
- Mechanical valves require uninterrupted, therapeutic anticoagulation.

7. References

- UpToDate: Anticoagulation and neuraxial anaesthesia; Mechanical heart valves in pregnancy
- Williams Obstetrics, latest edition
- ASRA / ESRA guidelines on regional anaesthesia

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06

Evolving Role of Tocolysis in Preterm Labour: Evidence, History, and Clinical Integration

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Abstract

Preterm birth remains the leading cause of neonatal morbidity and mortality worldwide. Pharmacological tocolysis aims to transiently inhibit uterine activity, providing time for essential interventions such as antenatal corticosteroid administration and maternal transfer. While evidence shows that tocolytics can delay delivery for 48 hours to 7 days, they do not consistently improve neonatal survival or reduce morbidity. Among available agents calcium-channel blockers demonstrate the best efficacy–safety balance, whereas β-mimetics and magnesium sulphate are associated with higher maternal risks. Historical exploration reveals cyclical enthusiasm and declines with each generation of agents. Current WHO, ACOG, RCOG, and NICE guidelines emphasise selective, short-term use of tocolysis rather than routine or maintenance therapy.

Introduction

Preterm birth, defined as delivery before 37 completed weeks of gestation, accounts for nearly one million neonatal deaths annually and remains a major global health challenge [1]. The worldwide prevalence is about 11%, with the burden disproportionately higher in low- and middle-income countries [2]. Survivors face heightened risks of respiratory distress syndrome (RDS), intraventricular haemorrhage (IVH), necrotising enterocolitis, sepsis, and long-term neurodevelopmental impairment [3].

Pharmacologic inhibition of uterine contractions—tocolysis—was developed not to prevent preterm birth entirely, but to gain a short temporal window for evidence-based interventions such as corticosteroid administration, maternal transfer to tertiary centres, or magnesium sulphate for fetal neuroprotection.

Historical Perspective on Tocolysis

Efforts to control premature uterine activity began almost a century ago.

Vitamin E (1930s). Early hypotheses by Evans and Bishop suggested a biochemical imbalance in pregnancy that vitamin E supplementation could correct [5]. Human trials failed to reproduce benefits.

Relaxin (1950s). In 1955, Abramson and Reid administered relaxin to five women with preterm contractions, achieving transient success [6]. A 2013 Cochrane review concluded insufficient evidence [7].

Ethanol (1960s). Ethanol was proposed to inhibit oxytocin and vasopressin release, reducing uterine activity [8]. However, maternal toxicity and poor neonatal outcomes led to abandonment [9].

Magnesium sulphate (1920s–1980s). Initially used for eclampsia, magnesium sulphate was evaluated for labour inhibition [10]. Subsequent meta-analyses found it ineffective as a tocolytic [11], though its neuroprotective value for fetuses <32 weeks remains well established [12].

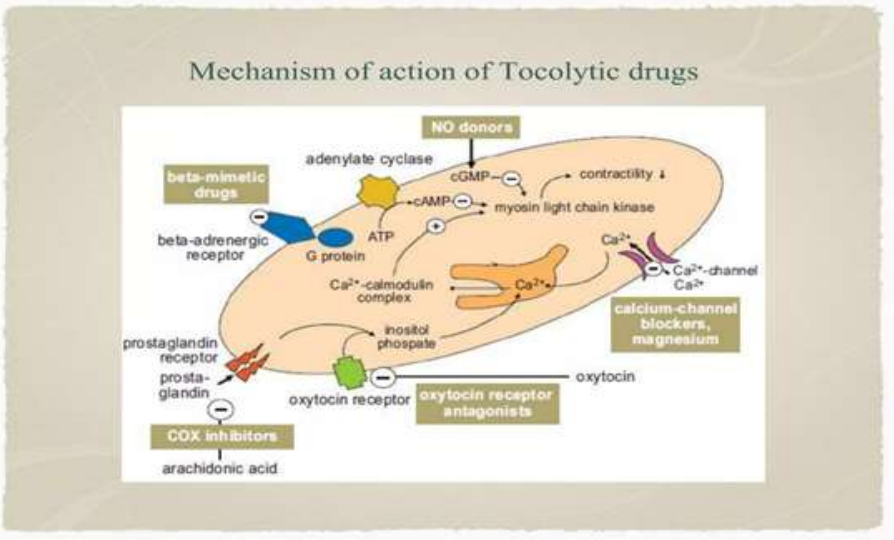
β-Adrenergic agonists (1960s–1980s). Isoxsuprine and ritodrine represented the first formally approved tocolytics [13,14]. While capable of delaying birth 48 hours, they caused significant maternal adverse effects —tachycardia, pulmonary oedema, and hyperglycaemia [15].

Prostaglandin-synthesis inhibitors (1970s). Indomethacin and related NSAIDs inhibit cyclo-oxygenase and reduce prostaglandin-mediated myometrial contractions [16]. They remain effective but pose fetal risks such as ductus arteriosus constriction and oligohydramnios if used beyond 32 weeks [17].

Calcium-channel blockers (1980s). Nifedipine became a mainstay after Ulf Ulmsten a Swedish obstetrician demonstrated potent uterine relaxation in non-gravid as well as gravid uterus [18]. It is now the preferred first-line oral agent worldwide [20].

Oxytocin-receptor antagonists (1990s–present). Atosiban competes with oxytocin at the myometrial receptor to prevent calcium release. Trials show similar efficacy to other agents but superior tolerability [21]. High cost and limited availability restrict widespread adoption.

Mechanisms of Preterm Labour and Pharmacologic Targets



Comparative Efficacy and Safety of Major Drug Classes

Drug class	Example	Mechanism	Delay ≥ 48 h	Key maternal/fetal effects
β-mimetics	Ritodrine, Isoxsuprine	↑ cAMP → ↓ Ca^{2+}	Effective but poor safety	Tachycardia, pulmonary oedema
Calcium-channel blockers	Nifedipine	Blocks voltage-gated Ca^{2+} channels	OR ≈ 2.7	Headache, hypotension
Prostaglandin inhibitors	Indomethacin	COX inhibition → ↓ PG synthesis	OR ≈ 5.4	Oligohydramnios, ductus closure > 32 wk
Oxytocin antagonists	Atosiban	Receptor blockade	OR ≈ 2.0	Minimal maternal effects
Magnesium sulphate	—	Competes with Ca^{2+} entry	OR ≈ 2.8	Flushing, hypotension
Nitrates	Nitroglycerin	↑ NO → smooth-muscle relaxation	Weak	Headache, hypotension

Global Guideline Perspectives

- **WHO (2015):** Short-term (≤48 h) tocolysis may be used to complete antenatal corticosteroid therapy or transfer; routine or maintenance use discouraged [24].
- **ACOG (2018):** Supports individualized, short-term therapy; maintenance tocolysis lacks evidence of benefit [25].
- **RCOG (UK):** Recommends nifedipine as first-line agents; therapy beyond 48–72 hours is unwarranted [26].
- **NICE (2015):** Advises nifedipine as preferred agent when tocolysis is indicated [27].

Clinical Integration of Tocolysis

Indications

1. To allow completion of antenatal corticosteroids.
2. To enable maternal transfer to tertiary care.
3. In selected cases, to achieve brief pregnancy prolongation when neonatal care access is limited.

Contraindications

Tocolytics should not be used when continuation of pregnancy poses risk, including:

- Chorioamnionitis
- Placental abruption
- Severe pre-eclampsia
- Fetal compromise or demise
- Significant maternal cardiac disease
- Preterm pre-labour rupture of membranes (PPROM) with infection risk [28].

When Patients Arrive on Progesterone + Tocolytics

1. Assess Context

- Determine indication: short cervix, threatened miscarriage, or active preterm contractions.
- Evaluate maternal vitals and fetal wellbeing.

2. Progesterone

"This medicine supports uterine stability and is safe up to 34–36 weeks."

3. Tocolytics

(a) Calcium-channel blocker — first-line)

Nifedipine 10–20 mg orally every 6–8 hours for 24–48 hours.

Monitor for hypotension and headache.

(b) Oxytocin antagonist — where available)

Atosiban: IV loading 6.75 mg over 1 min → 300 µg/min × 3 h → 100 µg/min × 45 h.

(c) NSAID (before 32 weeks)

Indomethacin 50 mg PO/PR then 25–50 mg 4–6 hourly × 48 h.

Avoid > 32 weeks to prevent ductus arteriosus constriction and PPHN.

(d) β-mimetics (Isoxsuprine, Ritodrine)

1.Isosuxprine: 10 mg IM/IV 8–12 hourly or 10–20 mg PO 8 hourly.

Use cautiously; limited evidence and frequent side effects.

2.Ritodrine: intravenous- initial infusion 0.05 mg/min gradually increasing until contractions are controlled (max 0.35mg/min) followed by oral 10 mg every 6-8 hours once labor is stabilized with iv therapy.

(e) Magnesium sulphate

Loading 4 g IV over 20 min → 2 g/h × 24 h (also provides benefit of neuroprotection at <32 weeks).

Avoid prolonged infusions beyond 5–7 days as risk of fractures in fetal bones increases due to hypocalcemia[29].

4. Patient Communication

- Explain that tocolytics are **temporary measures:**

"These medicines relax the uterus briefly to let your baby's lungs mature or allow safe transfer."

- Discuss side-effects and expected duration (usually ≤48 hours).
- Reassure regarding progesterone safety.

Evidence from Systematic Reviews and Meta-analyses

The **BMJ 2012 network meta-analysis** found prostaglandin inhibitors most effective in delaying birth ≥48 hours, followed by calcium-channel blockers and magnesium sulphate

[23].

A **Cochrane review (2018)** on progestogens concluded minimal impact on reducing preterm birth risk [30].

Cochrane 2014 confirmed magnesium sulphate's lack of tocolytic benefit but validated neuroprotection [11,12].

No pharmacologic agent has consistently improved long-term neonatal outcomes, reinforcing tocolysis as an adjunctive, not curative, therapy.

Discussion

Across decades of innovation, tocolysis demonstrates a paradox: reliable delay of delivery without proportional neonatal survival benefit. The determinants of neonatal outcome—gestational age, infection control, antenatal corticosteroid use, and neonatal intensive care quality—outweigh the modest temporal extension provided by tocolysis [31].

Among available options, **nifedipine** and **indomethacin** offer optimal efficacy with acceptable safety. **Atosiban** provides an alternative where resources permit. **Magnesium sulphate** should be reserved for neuroprotection, not labour inhibition, and **β-mimetics** are largely obsolete except in limited settings.

Conclusion

Tocolysis remains a **time-gaining measure** in preterm labour management. Its role is limited to transient prolongation of pregnancy, allowing administration of corticosteroids and safe maternal transfer. Prostaglandin inhibitors and calcium-channel blockers provide the most favourable efficacy–safety profile, while β-mimetics and prolonged magnesium sulphate use carry substantial risk. Current WHO, ACOG, and RCOG guidelines concur that routine or maintenance tocolysis offers no benefit.

Effective preterm labour management demands **judicious, evidence-based use of tocolytics integrated with comprehensive maternal–fetal care**, prevention strategies, and continuous evaluation of neonatal outcomes.

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07 Chronic & Autoimmune Disease -Medication that actually help -HTN, Diabetes, Epilepsy, Mental Health & auto immune disease & STEROIDS

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Introduction

Pregnancy places unique physiological stress on virtually every organ system, unmasking or aggravating many chronic medical conditions. The interplay between physiological changes of pregnancy, maternal disease activity, medication safety, and fetal development concerns necessitates evidence-based, multidisciplinary care. The framework follows four chronological pillars of reproductive care: Preconception, Antenatal, Intrapartum, and Postpartum.

I. Preconception Care

The preconception phase is the optimal window to achieve disease remission, optimise organ functions, adjust medications, prevent teratogenic exposure, and educate women about potential maternal–fetal risks. The objectives of pre-conceptional care are to:

1. **Achieve disease stability or remission** for at least 3–6 months prior to conception.
2. **Discontinue teratogenic drugs** and substitute pregnancy-compatible alternatives.
3. **Initiate preventive supplements**, especially folic acid.
4. **Identify comorbidities** that amplify risk (diabetes, hypertension, renal dysfunction, obesity).
5. **Provide multidisciplinary counselling** and ensure continuity between specialists and obstetric teams.

General Measures

1. **Preconception counselling clinic:**

All women with chronic disease should be reviewed jointly by obstetrician, fetal medicine specialist and the relevant specialty (internal medicine, endocrinology, cardiology, nephrology, neurology). Medication review, baseline investigations, and vaccination review are done at this visit. Switching to medications that are safe during conception are prescribed after proper counselling and co-ordination with the physician.

2. Lifestyle and nutrition:

Optimize body-mass index, achieve smoking and alcohol cessation, encourage regular exercise, and ensure balanced nutrition rich in calcium, iron, and vitamin D.

3. Folic acid supplementation:

A high-dose regimen (5 mg/day) is indicated for women with diabetes, obesity, epilepsy on antiepileptic drugs, or autoimmune conditions on antifolate therapy.

4. Vaccination:

All vaccines missed in childhood and adolescence can be given in the pre-conceptional care, like Tdap, Hepatitis B, HPV etc. Live vaccines (MMR, varicella) should be completed at least 1 month before conception. Influenza and COVID-19 vaccines are safe and recommended.

Disease-Specific Preconception Considerations

1. Chronic Hypertension -

Hypertensive disorders complicate 5–10 % of pregnancies and remain a leading cause of maternal morbidity. Preconception counselling focuses on optimization of BP control and medication safety.

- **Medication transition:**

Discontinue ACE inhibitors, ARBs, and thiazide diuretics prior to conception. These are associated with congenital renal and cardiovascular anomalies. If they become pregnant while taking ACE inhibitors or ARBs, stop these medications and offer alternatives, preferably within 2 working days of notification of pregnancy. Substitute with labetalol, methyldopa, nifedipine.

- **Blood-pressure target:**

Aim for ≤135/85 mmHg before conception.

- **Systemic assessment:**

Baseline creatinine, urea, electrolytes, and urine protein are done to assess renal function. ECG or Echocardiography may be advised in some cases to assess cardiac function.

2. Diabetes Mellitus -

Hyperglycaemia during organogenesis causes diabetic embryopathy, markedly increasing congenital malformations of the central nervous system (neural tube defects like spina bifida, anencephaly), cardiovascular system (congenital heart defects), and skeletal system (caudal regression syndrome). Therefore, strict preconception control is essential.

- **Glycaemic goals:**

HbA1c < 6.5 % (48 mmol/mol) is the goal, without causing hypoglycaemia. Nutritional interventions are a key component of care along with the necessary medicines.

- **Medication changes:**

Discontinue SGLT2 inhibitors, GLP-1 receptor agonists, DPP-4 inhibitors and sulfonylureas. Insulin (preferred) should be started after consultation with endocrinologist or continue metformin if already effective and well tolerated.

- **Adjunctive care:**

Stop statins and ACE inhibitors. Start 5 mg folic acid daily. Screen for retinopathy and nephropathy. These need to be treated and optimised before conception.

3. Epilepsy -

The aim is to optimize health, medication, and seizure control before pregnancy with minimal teratogenic risk; with care offered by multidisciplinary team of obstetrician, neurologist and maternal-fetal medicine specialist

- **Drug review:**

Evaluation is needed regarding seizures control and to determine if any treatment changes are needed. Switching to the lowest effective dose of a single anti-epileptic drug(AED) i.e. monotherapy is preferred, if polytherapy is currently used. Pre-pregnancy blood tests can help establish baseline levels for certain drugs, such as lamotrigine and carbamazepine, to guide future dose adjustments during pregnancy. Valproate should be stopped. Consider substituting phenytoin, carbamazepine, or topiramate with **lamotrigine** or **levetiracetam** where feasible; although carbamazepine is also a safer drug. If patient gets pregnant without planning, AEDs should not be abruptly stopped or changed without appropriate discussion.

- **Seizure-free interval:**

Ideally ≥6 months before conception.

- **Supplementation:**

High-dose folate (4-5 mg/day) from preconception through 12 weeks.

- **Counselling**:

Discuss the importance of adherence to medications, identifying and avoiding seizure triggers, need of close maternal - fetal surveillance and necessary dose adjustments.

4. Perinatal Mental Health -

Depression and anxiety are common, with incidence gradually increasing. But such issues are under-reported and under-treated in reproductive-age women.

- **Assessment**:

Use validated tools (PHQ-9, EPDS) for assessing the current mental state and explore remission and relapse history.

- **Medication planning:**

For women stable on SSRIs, continuation through pregnancy is often safer than abrupt discontinuation. SSRIs are often the 1st choice. Sertraline and citalopram are preferred; Escitalopram and fluoxetine are also used. Paroxetine should be avoided due to first-trimester cardiac risk. Some SNRIs can be used like Duloxetine and venlafaxine; but close monitoring of blood pressure is necessary. Benzodiazepines should not be given due to risk of birth defects

- **Non-pharmacologic strategies:**

Encourage cognitive-behavioural therapy or interpersonal therapy prior to conception. This helps in reducing the dose requiremnts.

5. Autoimmune and Rheumatic Disorders -

Autoimmune diseases, especially systemic lupus erythematosus (SLE), antiphospholipid syndrome(APS), ankylosing spondylitis(AS), psoriasis, vasculitis, connective tissue disorders and rheumatoid arthritis(RA) affect women of reproductive age group. They require meticulous preconception care with multidisciplinary team of obstetrician, fetal medicine specialist, rheumatologist, internal medicine specialist, hematologist etc.

- **Disease quiescence:**

Conception should be delayed until remission has been sustained for at least 6 months. Blood and clinical parameters help in determining that.

Medication adjustment:

- Continue hydroxychloroquine, azathioprine, sulfasalazine, and low-dose prednisone. Cyclosporine and tacrolimus which are mainly transplant medications can also be continued
- Discontinue methotrexate, mycophenolate, cyclophosphamide and leflunomide at least 3 months before conception. Newer oral treatments like JAK inhibitors (tofacitinib, upadacitinib) and apremilast are to be avoided. Rituximab should be stopped 1year before conception.
- TNF inhibitors (like certolizumab) can be continued to conception. Adalimumab and etanercept can be continued but stopped in 3rd trimester.
- Avoid NSAIDs for pain relief, especially after 28weeks.

Dosage- minimum effective dose of the recommended drugs are to be given, enough to continue remission and prevent relapse

- **Preventive therapy:**

Begin low-dose aspirin(75-150mg) ± prophylactic heparin in patients with antiphospholipid antibodies. High dose folic acid supplementation is also needed.

6. Inflammatory Bowel Disease / Crohn's -

Fertility is normal when disease is quiescent but reduced during active inflammation. Achieving disease remission at least for 3months is very important along with optimising nutrition and making appropriate lifestyle changes like quitting smoking, alcohol. Gastroenterologist care must continue actively.

- **Medication review:**
  - Continue **5-aminosalicylates, azathioprine/6-mercaptopurine, and anti-TNF biologics like vedolizumab, ustekinumab.**
  - Discontinue **methotrexate** ≥3 months pre-conception.
- **Nutritional optimization:**

Address iron, vitamin B_{12}, folate, and vitamin D deficiency and avoid malnutrition. Thus, preconceptional vitamins are necessary. The levels of these vitamins may be checked before planning pregnancy. Dietician advise is needed if taking any specific diet.

- **Vaccination**:

Taking the live vaccines pre-pregnancy are important because biologic therapy may preclude them postpartum.

II. Antenatal Care

Objectives

Once pregnancy is established, the clinical emphasis shifts to maintaining maternal disease stability while protecting fetal growth and development. Antenatal management requires close collaboration among obstetricians, specialists, and allied health professionals. Key goals include:

1. **Preventing disease flare or decompensation.**
2. **Ensuring safe pharmacologic therapy throughout gestation without affecting fetus.**
3. **Monitoring fetal growth and well-being.**
4. **Detecting complications early**
5. **Supporting maternal mental health and adherence.**

General measures-

All pregnancies with chronic-disease benefit from a structured protocol encompassing routine obstetric care plus disease-specific surveillance.

1. **Early booking (before 10 weeks):**

Ideally all of these patients should be followed up routinely from preconception. However, they should have their 1st antenatal check-up as early as possible in the 1st trimester. All baseline laboratory values (CBC, renal, liver, and metabolic panels) should be checked. Review all medications and doses. Dosage and medications might need to be changed in consultation with the concerned speciality.

2 .Ensuring proper lifestyle- maintaining calorie, salt intake and exercise of minimum 30mis/day is advisable specially in hypertension, diabetes and obesity

3. High dose folate(4-5mg/day) : this is a must in all the chronic and autoimmune disorders.

4.Low-dose aspirin:

75-150mg aspirin should be started at 10-12 weeks in women with hypertension, diabetes, renal disorders, autoimmune disorders or prior pre-eclampsia. Some practitioners and studies have started it as early as 6weeks; but proper data is lacking

5. Frequent monitoring:

- BP, weight measurement at each visit.
- Urinalysis, especially for protein, at least once in each trimester.
- Anomaly scan at 11-13weeks and 18-22weeks. Growth ultrasound every 4 weeks from 28 weeks.

6. Laboratory surveillance:

- Renal and liver function each trimester for hypertensive and autoimmune patients.
- HbA1c or glucose profile every 4–6 weeks in diabetes.
- AED drug levels (especially lamotrigine) every trimester in epilepsy.

7. Fetal monitoring: all the fetuses should undergo detailed anomaly scan at 11-13weeks and 18-22weeks, followed by growth scans every 4weeks from 28weeks. Antepartum fetal surveillance using umbilical artery, cerebral artery, ductus venosus dopplers and CTG are advised as per indication and complications on a case-to-case basis.

8. Mental-health screening:

Repeat EPDS or PHQ-9 every trimester; escalate care if score ≥13 (EPDS) or ≥10 (PHQ-9).

9. Multidisciplinary case reviews:

In each trimester, review with the specific speciality for any laboratory evaluation, medication review and dose adjustments should be done. At 20, 28, and 34 weeks, convene obstetric, medical, and neonatal teams to plan timing and mode of delivery.

10. Antenatal corticosteroids-

ACS may be prescribed in cases suspected of delivering preterm.

Disease-Specific Antenatal Management

1. Hypertension

Chronic hypertension in pregnancy requires individualized therapy and close monitoring to detect superimposed preeclampsia.

- **Blood-pressure targets:**

Maintain ≤135/85 mmHg.

- **Preferred antihypertensives:**

Labetalol(drug of choice), nifedipine and methyldopa are preferred agents as shown in table. However, methyl dopa is not available. IV labetalol, IV hydralazine and Nifedipine are given in severe uncontrolled hypertension.

- **Monitoring**:

Renal function and urine protein is usually done monthly. 24-hour urinary protein or urine protein: creatinine ratio gives better idea of proteinuria. Liver function, serum uric acid are done in case of increasing or uncontrolled BP or suspected and diagnosed preeclampsia.

- **Fetal monitoring:** as mentioned
- **Complications**:

Watch for superimposed pre-eclampsia; manage in secondary/tertiary care.

- **Delivery**:

If stable, plan birth between 37–39 weeks. If preeclampsia detected, deliver after 34weeks.

- **Adjunctive strategies:**

Advise 75 mg to 150 mg of aspirin daily from 12 weeks until delivery to women having any high risk or more than 1 moderate risk factor for pre-eclampsia. Advise weight control and salt moderation.

Drugs	Dosage	Side Effects	Comments
Nifedipine (Calcium ch	20–120 mg/day in 2–3 divided doses. In severe hypertension: 10–30 mg stat, can be repeated after 30–45 minutes; maximum dose 120 mg	Tachycardia, palpitations, headaches, and facial flushing	Not to be given sublingually
Labetalol (Beta blocker)	200–1200 mg/day in 2–3 divided doses. In severe hypertension: 200 mg, repeated hourly if needed, up to 3 doses.	Fatigue, dizziness, nausea, headache, diarrhea, edema	Contraindicated in asthma, CCF, and diabetes

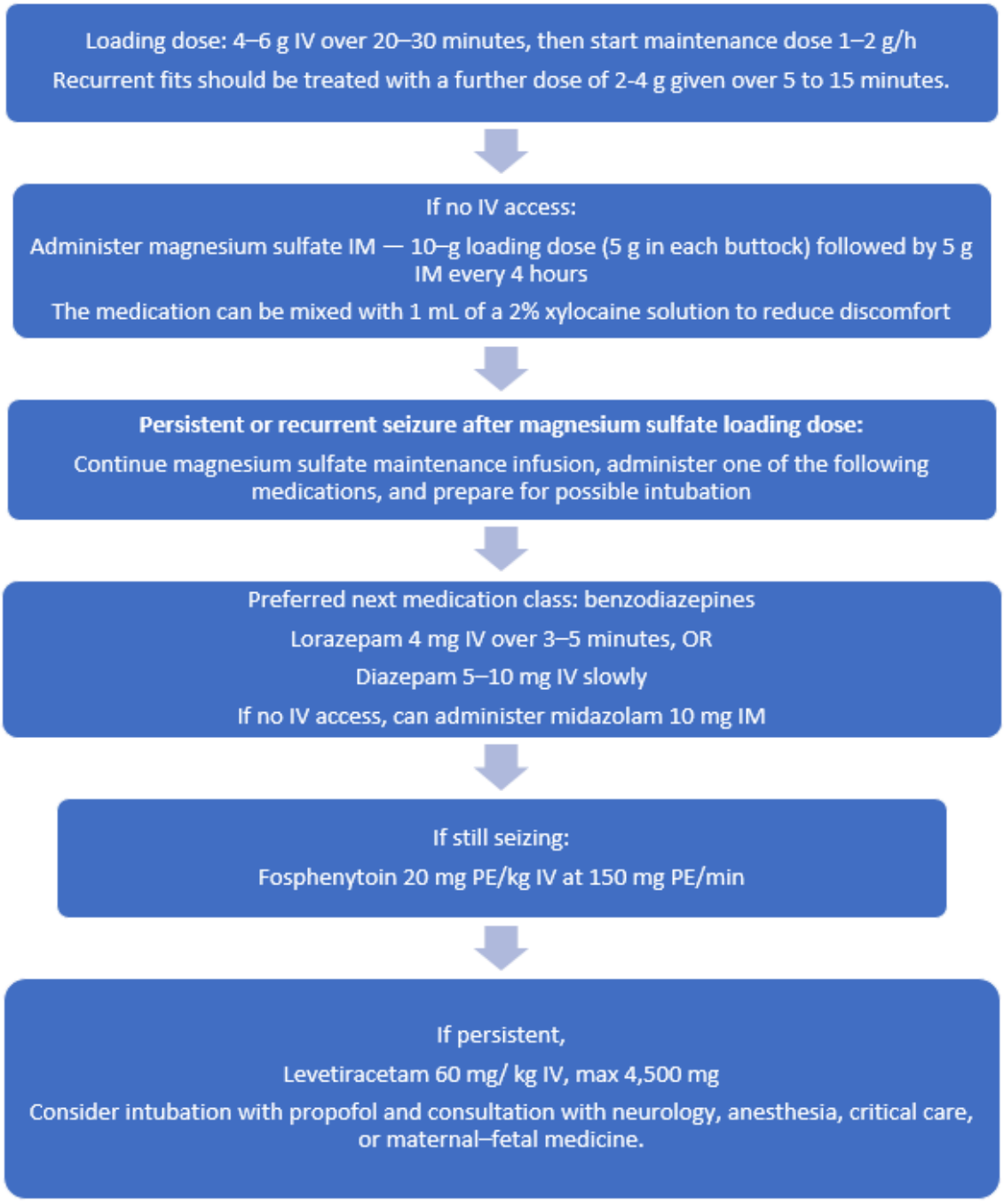
Methyldopa (Centrally acting alpha two adrenergic agonist)	500–2000 mg/day in 2–3 divided doses. 1000 mg single dose in severe BP	Bradycardia, orthostatic hypotension, depression, dizziness, lethargy, sedation, dry mouth, nausea, vomiting	Most of the time, it is tested and safe. To be discontinued in the postpartum period to avoid postpartum depression
IV Labetalol	Slow IV injections: 10–20 mg IV, then 20–80 mg every 20–30 minutes. Max total dose of 300 mg. Alternate regimen: 10–20 mg IV, then infusion at 1–2 mg/min and titrated until desired effect		
IV hydralazine (Vasodilator)	5 mg IV or IM, then 5–10 mg every 20–40 minutes; once BP controlled, repeat every 3 hours; for infusion: 0.5-10 mg/hour; if no success with 20 mg IV or 30 mg IM, consider another drug.	Maternal hypotension, placental abruptions, oliguria	

Table : various antihypertensives used in pregnancy(FOGSI- GESTOSIS- ICOG- Good Clinical Practice Recommendations 2019 and ISSHP 2021)

Table : Antihypertensive regimens for Severe hypertension

Labetalol:	Nifedipine:	Hydralazine
Labetalol 20mg IV over 20 minutes Check BP in 10 minutes ↓ SBP ≥ 160 or DBP ≥ 110 Give 40 mg labetalol IV over 2 minutes Check BP in 10 minutes ↓ SBP ≥ 160 or DBP ≥ 110 Give 80 mg labetalol IV over 2 minutes Check BP in 10 minutes ↓ SBP ≥ 160 or DBP ≥ 110 Convert to hydralazine Give hydralazine 10 mg IV over 2 minutes ↓ Check BP in 10 minutes SBP ≥ 160 or DBP ≥ 110 *Obtain emergent consultation from maternal–fetal medicine, if available, or critical care* ↓ Give additional antihypertensive medication per specific order as recommended by specialist ↓ Once BP thresholds are achieved, repeat BP Every 10 minutes for 1 hour- Then every 15 minutes for 1 hour- Then every 30 minutes for 1 hour- Then every hour for 4 hours	Immediate-Release Oral nifedipine 10mg Check BP in 20 minutes ↓ SBP ≥ 160 or DBP ≥ 110 Oral nifedipine 20mg Check BP in 20 minutes ↓ SBP ≥ 160 or DBP ≥ 110 Oral nifedipine 20mg Check BP in 20 minutes ↓ SBP ≥ 160 or DBP ≥ 110 administer IV labetalol 20mg over 2 min ↓ SBP ≥ 160 or DBP ≥ 110 administer IV labetalol 20mg over 20 min *Obtain emergent consultation from maternal–fetal medicine, if available, or critical care* ↓ Give additional antihypertensive medication per specific order as recommended by specialist ↓ Once BP thresholds are achieved, repeat BP Every 10 minutes for 1 hour- Then every 15 minutes for 1 hour- Then every 30 minutes for 1 hour- Then every hour for 4 hours	Administer hydralazine 5 mg or 10 mg IV over 2 minutes Check BP in 20 minutes ↓ SBP ≥ 160 or DBP ≥ 110 Administer hydralazine 10 mg IV over 2 minutes Check BP in 20 minutes ↓ SBP ≥ 160 or DBP ≥ 110 administer IV labetalol 20mg over 2 min Check BP in 10 minutes ↓ SBP ≥ 160 or DBP ≥ 110 IV labetalol 20mg over 2 min *Obtain emergent consultation from maternal–fetal medicine, if available, or critical care* ↓ Give additional antihypertensive medication per specific order as recommended by specialist ↓ Once BP thresholds are achieved, repeat BP Every 10 minutes for 1 hour- Then every 15 minutes for 1 hour- Then every 30 minutes for 1 hour- Then every hour for 4 hours
Avoid parenteral labetalol with active asthma, heart disease, or congestive heart failure Hold IV labetalol for maternal pulse under 60	Choose nifedipine, if IV access not available Capsules should be administered orally and not punctured or administered sublingually	Hydralazine may increase risk of maternal hypotension. Consider using up to 500 ml crystalloid fluid before first dose of hydralazine

Regimens for Magnesium Sulphate for Eclampsia:



Diabetes Mellitus

All guidelines emphasize tight glycaemic control throughout gestation. Consultation with endocrinologist and dietician should be taken

- **Glycaemic targets:**

Fasting < 95 mg/dL(<5.3 mmol/L), 1hour postprandial < 140 mg/dL(<7.8 mmol/L), 2hour < 120 mg/dL(<6.7 mmol/L). Ideally, the HbA1C goal in pregnancy is <6% (<42 mmol/mol) if there is no hypoglycemia, but the goal may be increased to <7% (<53 mmol/mol) if necessary, to prevent hypoglycemia.

- **Therapy:**
- Around 16 weeks onwards, insulin resistance begins to increase, and total daily insulin doses increase linearly 5% per week upto 36th week. This usually necessitates doubling of daily insulin dose compared to pre-pregnancy requirement.
- As pregnancy progresses, both basal and bolus insulin requirements increase, with bolus insulin requirements taking up a larger proportion of overall total daily insulin needs in individuals with preexisting diabetes. The need plateaus toward the end of the third trimester. However no particular fixed dose can be advocated and varies from case-to-case.
- A rapid reduction in insulin requirements can indicate the development of placental insufficiency.
- Both multiple daily insulin subcutaneous injections and continuous subcutaneous insulin infusion are acceptable delivery strategies.
- Most insulins are safe during pregnancy, including short acting and NPH insulins. Many insulin analogues are safe during pregnancy, such as aspart, FIASP, lispro(rapid acting), detemir, and degludec(Long acting). However, glargine and glulisine, are category C drugs.
- Metformin may continue in type 2 diabetes or gestational diabetes if insulin is refused or not tolerated. Metformin and glyburide, individually or in combination, should not be used as first-line agents. However, if patient conceived with metformin, it can be continued and later on switched to insulin or combination therapy.

- **Nutritional therapy:**

Balance of various nutrients is necessary including nutrient-dense fruits, vegetables, legumes, whole grains, and healthy fats with omega-3 fatty acids that include nuts, seeds and fish. Dietician input to maintain carbohydrate and protein distribution i.e. 175g of carbohydrates(35-45% of calories) and 71g of protein per day.

- **Monitoring**:

Self-monitoring of blood glucose(SMBG), both pre and postprandial is done 4–6 times daily; HbA1c every 4–6 weeks. However continuous glucose monitoring (CGM) has shown to improve better sugar control and reduce risk of macrosomia and neonatal complications.

- **Complications:**

Renal function needs to be monitored. Retinopathy may worsen; thus, repeat retinal exams each trimester.

- **Fetal surveillance**: done as per guidelines.
- **Timing of delivery**:

38–40 weeks for well-controlled diabetes; earlier if vascular disease or poor control.

3. Epilepsy

Guidelines stress on prevention of seizures, as maternal seizures carry greater risk than medication exposure. They should be counselled that some obstetric outcomes may be affected and thus needs frequent check-ups with obstetrician and neurologist.

- **Medication:**
- Existing AEDs should be continued; never stop abruptly.
- Lamotrigine doses may be increased as the levels tend to fall by 70% during pregnancy. Actually, due to changing pharmacokinetics all AEDs doses may need some increase. However, the appropriate dose is adjusted by the neurologist.
- Strict adherence to medicines is must.
- The preferred medicines are those already mentioned in preconceptional care
- **Monitoring:**
- Current practice in AED monitoring is either regular therapeutic drug monitoring or monitoring based on clinical features to adjust the AED dose. There is no clear evidence to show that therapeutic drug monitoring reduces the risk of seizure deterioration compared with monitoring based on clinical features. AED levels may be checked every trimester.
- **Obstetric care:**
- Routine obstetric care is needed with detailed anomaly scan and cardiac scan for fetus. Regular antepartum fetal surveillance is not recommended.
- **Counselling:**
- Avoid sleep deprivation, stress and missed doses, as these can trigger seizure.

DRUGS	USAGE	COMMENTS
Lamotrigine	Used in focal and generalised seizures	Safe and recommended
Levetiracetam	Used in focal and generalised seizures	Safe and recommended
Carbamazepine	If seizures not controlled with safer drugs	Mild risk of neural tube defects
Valproate	Avoid	Highly teratogenic
Phenytoin	Avoid. Use only in uncontrolled seizures	Teratogenic

Table: AEDs in pregnancy

4. Perinatal Mental Health

Perinatal mental health is a leading preventable cause of maternal mortality.

- **Screening schedule:**

At booking, mid-pregnancy, and postpartum visits.

- **Management:**

Mild cases → psychotherapy (CBT, IPT).
Moderate/severe → SSRI, preferably sertraline(Drugs mentioned in preconceptional care).
Monitor for neonatal adaptation syndrome; symptoms are transient.

- **Collaboration:**

Coordinate with psychiatry for bipolar or psychotic disorders. Avoid valproate and lithium unless absolutely necessary and under specialist supervision.

DRUG	INDICATION	COMMENTS
SSRIs (e.g., sertraline, fluoxetine)	Preferred. Used in anxiety, depression	Sertraline preferred; small risk of neonatal adaptation syndrome
SNRIs (e.g., venlafaxine)	Used if necessary – in anxiety, depression	Less data than SSRIs but generally considered safe
Tricyclic antidepressants (e.g., nortriptyline)	Used in specific cases if benefit outweigh risk	congenital malformations, preterm birth, low birth weight, and neonatal withdrawal symptoms. Nortriptyline can be used in late gestation
Bupropion	in specific cases if benefit outweigh risk. Used in smoking cessation	May have risk of cardiac defects, neonatal withdrawal. Avoid in seizure disorders
Benzodiazepines	Short-term use only in acute anxiety	Risk of cleft palate, neonatal withdrawal

Table: various medications used in mental health disorders

5. Autoimmune / Rheumatic Disorders

continuing maintenance therapy to prevent flares is very important during pregnancy.

- **Medications safe in pregnancy:**

Hydroxychloroquine, azathioprine (≤2 mg/kg/day), sulfasalazine and low-dose prednisone. Folate supplementation should be continued.

DRUGS	DOSES	SIDE EFFECTS	COMMENTS
Hydroxychloroquine (HCQ)	Used in SLE, RA Standard doses (e.g., ≤400 mg/day) can be continued throughout pregnancy and breastfeeding.	Nausea, vomiting, diarrhoea, abdominal pain, Headache, Loss of appetite and weight loss, Skin rash, itching, increased sensitivity to sunlight. Can be minimised if taken with food	HCQ helps prevent disease flares and improve outcomes in lupus patients.

Steroids- Prednisone, Prednisolone	Used in almost all autoimmune disorders. Use the lowest effective dose. Doses of ≤20 mg/day are generally considered safe	Higher risk of preterm birth, GDM, HDP, PROM, mood changes	Higher doses may be used for severe flares, but require monitoring for blood pressure and sugar
Immunosuppressants- Azathioprine (AZA), Cyclosporine, Tacrolimus, Sulfasalazine, Colchicine, 6 mercaptopurine	Used in SLE, RA, severe autoimmune disorders. Can be continued or initiated from before. AZA doses up to 2 mg/kg/day is considered safe.	Nausea, fatigue, diarrhoea, vomiting, abdominal pain, bone marrow suppression, liver function derangement, hypertension, increased risk of infection, risk of nephrotoxicity, muscle weakness.	Tacrolimus and Cyclosporine require monitoring of drug levels and blood pressure. Tacrolimus needs blood sugar monitoring.
Biologics- Certolizumab pegol, TNF inhibitors	used in RA, AS, psoriasis, IBD Certolizumab- initial loading dose phase of 400 mg at weeks 0, 2, and 4; followed by - 200 mg every two weeks or 400 mg every four weeks.	increased risk of infection, preeclampsia, and gestational diabetes, preterm birth, low birth weight.	Certolizumab has minimal placental transfer and can be used throughout pregnancy. Other TNF inhibitors (e.g., Infliximab, Adalimumab, Etanercept) may be continued, but some guidelines recommend stopping them in the third trimester. If given in 3rd tyrimester, no live vaccines to be given to the infant for 6months.

Low-dose Aspirin, Heparin	Low-dose aspirin (75-150 mg daily) low-molecular-weight heparin like Enoxaparin is used for APS. 40mg subcutaneously once daily is enough; however, in some therapeutic dose is recommended(60-80mg) depending on clinical scenario.	GI intolerance, easy bruising, gum bleeding Injection site pain, bruising in heparin	Aspirin is widely recommended for prophylaxis against pre-eclampsia and is safe in pregnancy.

Table: Drugs in autoimmune disorders in pregnancy

- **Flare management:**

Short courses of higher-dose steroids or pulse therapy; consider biologics such as certolizumab (minimal placental transfer). IV immunoglobulin may be needed in life threatening situations

- **Monitoring:**

blood pressure in each visit and CBC, renal function test, blood sugar and complement levels should be checked in each trimester; guided by clinical parameters. Fetal Doppler, anomaly scan and growth scans are necessary.

- **Patient education:**

Emphasize medication adherence. Discontinuation leads to flares which is far riskier than drug exposure.

6. Inflammatory Bowel Disease / Crohn's

Guidelines advocate that remission, not medication withdrawal, determines pregnancy outcome.

- **Medication continuation:**

5-ASA, thiopurines, and biologics are safe. Anti-TNFs can continue until 28–32 weeks; subsequent doses resume postpartum.

- **Monitoring**:

Disease activity by clinical scores, CRP, and fecal calprotectin every trimester.

- **Nutrition:**

Correct iron, folate, and vitamin D deficiencies.

- **Counselling:**

Breastfeeding is encouraged; most IBD medications are compatible.

III. Intrapartum Management

The intrapartum period is critical in chronic disease pregnancies due to the risk of maternal decompensation, disease flares, seizures, or obstetric complications. Successful outcomes rely on anticipatory planning, multidisciplinary coordination, and vigilant monitoring.

General Principles

1. **Delivery Planning**
   - Mode and timing of delivery should be discussed during antenatal visits along with the multidisciplinary team.
   - Aim for term delivery whenever maternal and fetal status are stable, unless maternal disease or fetal distress dictates early intervention.
2. **Monitoring**
   - Continuous maternal vital signs and fetal heart-rate monitoring for high-risk pregnancies. Cardiotocography is advisable.
   - Partograph use is preferred
   - Input/output monitoring for renal, cardiac, and autoimmune diseases.
3. **Medication Continuation**
   - Avoid abrupt discontinuation of chronic medications.
   - Adjust doses of steroids, antihypertensives, insulin, or AEDs according to intrapartum stress and oral intake limitations.
4. **Analgesia and Anesthesia Considerations**
   - Epidural analgesia is generally safe in autoimmune disease, epilepsy, or IBD.
   - Avoid drugs that may exacerbate maternal comorbidities (e.g., methyldopa in hypotensive episodes, high-dose opioids in respiratory compromise).
   - Anesthesiologist consultation is recommended in neuromuscular or autoimmune disease due to potential airway or cardiovascular involvement.

5.Neonatal care

All neonates born in these mothers need careful examination for any distress, hypoxia, hypoglycemia(diabetes), congenital anomalies(autoimmune disorders, epilepsy, use of multiple drugs), sedation(use of antipsychotics), adrenal suppression(chronic steroid use)

Disease-Specific Intrapartum Management

1. Chronic Hypertension

- **Target BP:** 140–150/90 mmHg to avoid hypotension-induced fetal compromise.
- **Preferred agents**: IV labetalol, IV hydralazine or Nifedipine for acute control. MgSO4 prophylaxis may be needed in imminent eclampsia or severe preeclampsia. IV fluids should be restricted to 80ml/hour.
- **Monitoring:** Continuous maternal BP and urine output monitoring; electronic fetal monitoring. BP is checked every 15–30 min.
- **Mode of delivery:** Vaginal birth is preferred unless obstetric indication exists; caesarean section for severe preeclampsia or maternal complications. Induction of labour is done at 37-39 weeks; earlier if severe preeclampsia is diagnosed. Exercise caution during epidural analgesia: Do not preload women who have severe pre-eclampsia with intravenous fluids.

Diabetes Mellitus

- **Glycemic control:**
   - Check capillary blood glucose hourly during labor to maintain target 0f 70-126mg/dl
   - IV insulin with glucose infusion may be necessary if oral intake is limited. Oral hypoglycemic agents are usually stopped on the day of delivery.

- **Fluid management:**
  - Avoid dextrose-containing fluids if glucose > 180 mg/dL. Avoiding hyperglycemia is equally important to prevent acidotic complications. Fluid and electrolyte maintenance is extremely important if ketoacidosis develops.
- **Fetal considerations:**
  - Continuous fetal monitoring; anticipate and treat neonatal hypoglycemia post-delivery.
- **Cesarean considerations:**
  - Reserved for obstetric indications.

3. Epilepsy

- **Seizure precautions:**
  - Maintain therapeutic AED levels with proper medicine dosage; IV medications are given if orally not tolerated. IV medicines including benzodiazepines are given for breakthrough seizures.
  - Avoid hyperventilation, sleep deprivation, stress, dehydration
  - Continuous maternal and fetal monitoring; be alert for hypoxia, trauma, or aspiration.
  - Prophylactic clobazam can be given who are at risk of having seizures during labour
- **Labor analgesia:**
  - Pain relief is important; thus epidural, comibined spinal epidural analgesia, TENS can be administered safely.
- **In seizures during labour or status epilepticus-**
  - Lorazepam given as an intravenous dose of 0.1 mg/kg (or 4 mg bolus, with a further dose after 10−20 minutes)
  - Diazepam 5–10 mg administered slow IV is an alternative.
  - If there is no IV access, diazepam 10−20 mg rectally repeated once 15 minutes later if there is a continued risk of status epilepticus, or midazolam 10 mg as a buccal preparation are suitable.
  - consider phenytoin or fosphenytoin use if uncontrolled seizure. Loading dose of phenytoin given as 10–15 mg/kg by IV infusion, with the usual dosage of about 1000 mg.
- **Neonatal consideration-** expedite delivery or do LSCS if fetal distress detected. Monitor and treat neonatal withdrawal symptoms
- If general anaesthesia becomes necessary, it is prudent to avoid anaesthetic agents such as pethidine, ketamine and sevoflurane, as they increase risk of seizures

4. Perinatal Mental Health

- **Stress and anxiety management:**
  - Provide psychological support and reassurance; avoid sudden medication discontinuation. Use calming breathing exercise
- **Acute psychiatric events:**
  - Severe depression, psychosis, or suicidal ideation may require urgent psychiatric input; short-acting benzodiazepines may be given
- **Team coordination:**
  - Psychiatric liaison with obstetric team; ensure support for mother and family.

5. Autoimmune and Rheumatic Disorders

- **Steroid supplementation:**

Women on chronic corticosteroids may require stress-dose IV steroids during labor to prevent adrenal insufficiency.

- **Flare management:**

Monitor for joint pain, fatigue, or cutaneous signs; low-dose steroids can be continued.

- **Vascular risk:** heparin should be stopped 24hours before delivery
- **Mode of delivery:**

Vaginal birth preferred unless joint deformities, severe organ involvement, or obstetric indications exist.

6. Inflammatory Bowel Disease / Crohn's

- **Flare management:**
  - Maintain ongoing therapy; IV steroids may be needed if disease exacerbates.
- **Caesraen section:**
  - In active perianal disease or history of ileal pouch surgery.
- **Nutritional support:**
  - Ensure hydration, electrolyte balance, and caloric intake during labor.

IV. Postpartum Management

Postpartum care addresses **maternal stabilization, disease monitoring, medication adjustment, lactation, and contraception**. This period is high risk for disease flare, hypertensive crises, glycemic variability, and psychiatric decompensation.

- **General Principles**

1. **Monitoring**
   - Vital signs, fluid balance, and disease-specific laboratory tests within 24–48 hours.
2. **Medication review**
   - Resume pre-pregnancy or lactation-compatible medications.
   - Adjust doses for breastfeeding.
   - Provide clear instructions for tapering steroids or AEDs if indicated.
3. **Contraception**
   - Non-estrogen options preferred in autoimmune or thrombotic risk patients (e.g., progesterone-only pills, Cu-T, LNG-IUDs, subdermal implants).
   - Long-term planning essential to avoid unplanned pregnancy during active disease or while on teratogenic drugs.
4. **Multidisciplinary follow-up**
   - Obstetric review at 6 weeks postpartum.
   - Specialist review depending on disease: endocrinology, neurology, rheumatology, psychiatry, gastroenterology.

Disease-Specific Postpartum Management

1. Chronic Hypertension

- BP may rise in first 6days; monitor daily for the first 2 days after birth and at least once between day 3 and day 5 after birth. Continue antihypertensives.
- Monitor for postpartum preeclampsia, especially in women with history of superimposed preeclampsia.
- Can take Nifedipine, Labetalol, Amlodipine. Avoid ACE-I, ARBs. Review the medications after 2weeks
- Long-term lifestyle counseling and cardiovascular risk modification.

2. Diabetes

- Insulin requirements drop postpartum in type 1 and type 2 diabetes. Insulin and metformin are compatible with breastfeeding. Other drugs are not widely studies
- Breastfeeding is encouraged; provides modest glycemic benefit.
- Reinforce diet and lifestyle counseling. Monitor glucose periodically.

3. Epilepsy

- AED doses may need postpartum readjustment. Antenatal drugs can be continued. Valproate, carbamazepine, phenytoin can be started if indicated.
- Counselling and informed choice is important as limited data on infant safety though most recommendations advocate continuing breastfeeding
- Monitor for sleep deprivation and avoid stress.
- Continue high-dose folate if breastfeeding while on AEDs.

4. Perinatal Mental Health

- Screen for postpartum depression and anxiety (EPDS at 6 weeks).
- Psychosocial support for sleep, family assistance, and infant care.
- SSRIs(Sertraline,Paroxetine) are first line therapy. Fluoxetine can be used; but has higher breast milk concentration. Haloperidol, Quetiapine & Olanzapine are the drugs used as antipsychotics. However, the baby should be fed immediately after taking all these medicine and breastfeeding should be avoided between 5-8hours, for optimum effects; though this is not absolutely indicated. TCAs like nortriptyline, imipramine, amitryptiline are also drugs that can be used. Stopping or changing medicines without advise is not recommended at all
- Infant should bed monitored for any adverse effects
- Informed choice is must as many may opt for top-feeding to avoid drug transfer to baby

5. Autoimmune / Rheumatic Disorders

- Disease flares often peak in 3–6 months postpartum.
- All medicines given in antenatal period should be continued.
- Monitor renal, hematologic, and hepatic function.
- Reinforce thromboembolic prophylaxis where indicated (e.g., antiphospholipid syndrome).

6. Inflammatory Bowel Disease / Crohn's

- Monitor for flare within 3–6 months postpartum.
- Continue maintenance therapy; breastfeeding encouraged as most medications are compatible.

Steroid use in pregnancy-

Antenatal corticosteroids(ACS)- ACS are used in preterm births to achieve lung maturity.

- **Timing-**
- 24-34weeks of pregnancy, preferably if delivery is anticipated within next 7days.
- As per ACOG, a single course of betamethasone is recommended for pregnant women between 34weeks and 37 weeks of gestation who are at risk of preterm birth within 7 days, and who have not received a previous course of antenatal corticosteroids.
- **Drugs**- betamethasone & dexamethasone are used. Both cross the placenta in their active form and have nearly identical biologic activity. Both lack mineralocorticoid activity and have relatively weak immunosuppressive activity with short-term use. However, betamethasone has a longer half-life.
- **Dosage**- Betamethasone 12mg IM 12-24 hours apart or Dexamethasone 6mg IM every 12hourly. A first dose of antenatal corticosteroids should be administered even if the ability to give the second dose is unlikely, based on the clinical scenario.
- **Repeat dosing**- A single repeat course of antenatal corticosteroids can be considered in women who are less than 34weeks of gestation but at risk of preterm delivery within 7 days, if the prior course of steroids was administered more than 14 days back. Rescue course corticosteroids can be provided as early as 7 days also from the prior dose, if indicated. However regular and serial courses should not be given.
- **Use in PPROM**- ACS is recommended in PPROM cases also, except in presence of infection. However repeat dosing is not recommended.
- **Benefits**- ACS has shown to reduce incidence of transient tachypnea of the newborn(TTNB), bronchopulmonary dysplasia, respiratory distress syndrome(RDS), infant death, neurodevelopmental impairment, intraventricular hemorrhage, periventricular leukomalacia, and necrotizing enterocolitis in infants

Use of steroids in pregnancy for other indications-

Indications- Corticosteroids are used in pregnancies starting from preconceptionally throughout all trimesters in various autoimmune and chronic diseases like asthma, SLE, RA, ·IBD, ITP, post-transplant patients etc., for anti-inflammatory and immunosuppressive activity. Compared to many immunosuppressants and biologicals, steroids are considered safe to be used in pregnancy to prevent disease flares and maintain remission and optimise feto-maternal outcome. Inflammation from uncontrolled autoimmune activity is potentially more harmful to feto-maternal health than steroids. Now-a-days, steroids are also prescribed in some cases of RPL and IVF pregnancies.

- **Preferred drugs**- Prednisone and prednisolone are preferred as they are seen to have minimal placental transfer. They are largely converted into inactive forms by the placenta, minimizing fetal exposure. Studies have shown 8 to 10 times lower concentrations of fetal prednisolone compared to maternal prednisolone following maternal IV administration.

Dosage-

- minimum dosing is advisable ≤5mg. However, upto 20mg can be given if needed as per the clinical scenario.
- Beyond that the risk of adverse effects increases, though studies have shown usage upto 60mg/ day. Dosage is determined by the state of disease activity.
- High dose IV pulse therapy(250-1000mg/day for 1-5days) is needed in severe flares of the disease, specially SLE. However, the fetal risks increase many folds, with increased risk of fetal loss and preterm birth.
- Steroid sparing safer alternatives like hydroxychloroquine, azathioprine etc can be used during pregnancy in order to maintain steroids at lower doses.

Adverse effects on fetus- increased risk of preterm birth, preeclampsia, GDM and IUGR are seen in pregnancies receiving steroids. Also, there is increased chances of having cleft lip with or without cleft palate as shown by some studies, though not found to be highly significant. Preterm birth can be both iatrogenic due to underlying disease activity and complications or can be spontaneous.

Additional dose in labour-

- In the case of women with adrenal insufficiency, or taking 5 mg or more of daily oral prednisolone for more than 3 weeks or the equivalent amount of other forms of steroids, regular oral steroids should be continued.

- In addition, 6-hourly IV or IM hydrocortisone 50 mg or more should be added in the established first stage of labour and this dosage should be continued until 6 hours after the baby is born. IV or IM route is given because of lower absorption by oral route and vomiting during labour. However additional doses are not needed in those using inhalational steroids

- If evidence of adrenal insufficiency is there, then a crucial part of management is emergency steroid cover i.e. to administer 100 mg of hydrocortisone IM or IV at the onset of active labour (e.g., when the cervix is dilated >4 cm or with regular contractions). Such higher dose is also recommended in caesarean sections, especially those done during labour. This is typically followed by 200 mg every 24 hours, either via continuous IV infusion or 50 mg every 6 hours, until delivery.

After Delivery: For the first two to four days after birth, a double oral dose of the woman's usual maintenance steroid is often recommended (provided there are no complications) before gradually returning to the pre-pregnancy dose.

Neonatal care- If the mother is on long-term systemic steroids(specially ≥40mg), the infant may need monitoring for signs of adrenal suppression after birth, though clinical symptoms are rare.

Breastfeeding- prednisolone can be used safely during lactation as minimal drug is excreted in breastmilk.

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OTC, Supplements, Herbal & Cannabis — Myths vs Facts

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Introduction

Every clinician has faced it — a patient confidently saying, "Don't worry, doctor, it's all natural!" or "My friend took this supplement and her baby was fine."

In today's world of wellness trends and online recommendations, pregnant and breastfeeding women often reach for over-the-counter (OTC) medicines, supplements, herbal blends, or even cannabis, believing they are harmless or safer than prescriptions.

But "natural" doesn't always mean "safe."

This article aims to separate common myths from evidence-based facts and provide practical counselling tools — including rational supplementation guidance, points to discuss around herbal and cannabis use, lactation safety notes, and even a ready-to-use EMR dot-phrase and one-slide counselling checklist.

1. The Real-World Challenge

Surveys consistently show that up to half of pregnant women use some form of non-prescribed or herbal product. Many do so without telling their obstetrician, often out of fear of judgment or simply because they assume it's safe.

However, OTC and herbal markets are largely unregulated, and cannabis use in reproductive-age women has been steadily rising. As clinicians, our task is not only to identify risks but to counsel in a way that encourages honesty and trust.

2. Myths and Facts — Practical Pearls

A. OTC Medicines

Myth: "Ibuprofen is safe during pregnancy if it's sold over the counter."

Fact: NSAIDs like ibuprofen or naproxen should not be used at or after 20 weeks' gestation due to the risk of fetal renal impairment and oligohydramnios. Acetaminophen (paracetamol) remains the preferred analgesic for fever and mild pain when used appropriately.

(FDA, 2020)

Myth: "Breastfeeding mothers can't take any pain or cold medicine."

Fact: Most single-ingredient OTC pain or fever medicines (such as acetaminophen and ibuprofen) are compatible with breastfeeding. The concern usually arises with combination products that include decongestants or antihistamines — always check LactMed or MotherToBaby for product-specific advice.

B. Rational Supplementation — Iron, Calcium, and Vitamin D
Myth: "More vitamins mean a healthier pregnancy."
Fact: Excessive supplementation can be just as harmful as deficiency.

- **Iron**: About 27 mg of elemental iron daily is ideal for most pregnant women. Higher doses should be guided by lab results confirming anemia.
- **Calcium**: Roughly 1000 mg daily (preferably from food sources) helps reduce pre-eclampsia risk and supports fetal bone development.
- **Vitamin D**: 600 IU daily meets the basic requirement; higher doses may be used under supervision for confirmed deficiency.

C. Herbal Products and "Natural" Supplements
Myth: "If it's herbal, it can't do any harm."
Fact: Herbal products are not standardized like prescription drugs. Their strength, purity, and even ingredient list can vary dramatically between brands.

Some "herbal tonics" have been found to contain undeclared pharmaceuticals, heavy metals, or unsafe levels of active compounds. Even herbs promoted for pregnancy — such as raspberry leaf or ginseng — lack strong safety data.

Patients often appreciate a non-judgmental statement like:
"Many herbal remedies aren't tested for pregnancy, and some can cause contractions or interact with other medicines. Let's look up yours together on a trusted database like MotherToBaby."
(Kennedy DA et al., Reprod Toxicol 2016)

D. Cannabis — Compassionate Counselling, Firm Facts
Myth: "Cannabis helps with nausea and anxiety — it's safer than pills."
Fact: Cannabis is not safe in pregnancy or while breastfeeding.
THC crosses the placenta, affects fetal brain development, and is detectable in breast milk for days after use. Studies link prenatal cannabis exposure to lower birth weight, preterm delivery, and potential neurodevelopmental issues.

ACOG's 2025 Clinical Consensus recommends universal screening, non-punitive counselling, and support for cessation.

A helpful conversation starter might be:
"Many women use cannabis to cope with nausea or stress. I understand that — but studies show it can affect the baby's growth and brain. Let's find safer ways to manage those symptoms."

3. Lactation: The Quick Reference

- **Safe options:** Acetaminophen and ibuprofen remain the go-to analgesics while breastfeeding.
- **Use with caution:** Long-acting NSAIDs (like naproxen) or multi-ingredient cold medicines.
- **Avoid or review:** Cannabis and poorly characterized herbal supplements.
- **Best resource:** LactMed — a free, evidence-based database updated regularly.

4. The Quality Question — Choosing Safe Supplements

Patients frequently purchase supplements online or from social media vendors. Encourage them to:

- Look for GMP-certified and third-party tested products (USP, NSF, or equivalent marks).
- Prefer food-based nutrition wherever possible.
- Bring all bottles or photos of products to appointments for review.

This empowers patients while reinforcing partnership in care.

5. Counselling in One Slide

Title: OTC, Supplements, Herbal & Cannabis — Quick Counselling Checklist

1. **Ask**: "What medicines, supplements, herbs, or cannabis are you using?"
2. **Clarify** pregnancy stage or lactation status.
3. **Advise**:
    - Avoid NSAIDs at ≥ 20 weeks.
    - Use acetaminophen for pain/fever if necessary.
    - Continue rational supplementation (iron ~ 27 mg, calcium ~ 1000 mg, vitamin D ~ 600 IU).
4. **Review** herbals for purity and safety; discourage unverified blends.
5. **Screen** for cannabis use at each visit; counsel cessation supportively.
6. **Document** counselling in EMR.

(Adapted from ACOG, FDA, MotherToBaby, and LactMed guidelines.)

6.Key Takeaways for Clinicians

- Always ask — patients often won't volunteer supplement or cannabis use unless prompted gently.
- Reinforce that "natural" doesn't automatically mean "safe."
- Provide alternatives instead of only restrictions — offer evidence-based symptom management.
- Use trusted references (MotherToBaby, LactMed, ACOG) to individualize advice.
- Document counselling clearly in EMR and follow up regularly.

7. References

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Conclusion

OTC medicines, supplements, herbal products, and cannabis are part of modern prenatal and postpartum reality — whether or not clinicians ask about them. Our role is to provide clarity amidst the noise, to replace fear with informed choice, and to use empathy as much as evidence.

With structured screening, rational supplementation, and honest communication, we can ensure that "natural" health truly aligns with maternal and fetal safety.

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Navigating Over-the-Counter (OTC) Supplements and Medications During Pregnancy Clinical Guidance from the FDA and ACOG

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Introduction

Pregnancy is a time of profound physiological change, marked by increased nutritional demands and heightened sensitivity to medications and environmental exposures. While over-the-counter (OTC) supplements and medications are widely accessible, their safety profiles during pregnancy vary significantly. Misuse or overuse even of seemingly benign products can pose risks to both maternal and fetal health.

This article provides a comprehensive overview of FDA and ACOG guidance on OTC supplements and medications during pregnancy. It covers essential nutrients, common remedies, contraindicated drugs, and general safety principles to support informed decision-making for expectant mothers and healthcare professionals.

Essential OTC Supplements: ACOG Recommendations

ACOG recommends that all pregnant individuals take a daily prenatal vitamin and, when needed, additional supplements to meet increased nutritional demands.

Folic Acid

Royal College of Obstetrics and Gynecologists Recommendation.

All pregnant women	400 µg/day preconception until 12th week of pregnancy
High-risk pregnant women†	5 mg/day

†High-risk women:

– History of neural tube defect in previous pregnancy
– History of neural tube defect in pregnant woman or in her partner
– Using certain epilepsy medications
– Diabetes or celiac disease
– BMI 30 or more
– Sickle cell anemia or thalassemia

International Guidelines for Preventive Folic Acid Dosage in Pregnancy American Congress of Obstetrics and Gynecology Recommendation.

Level of evidence	Low-risk women	400 µg/day
Level A[†]	High-risk women/women who have had NTD in previous pregnancy	4 mg/day
	MSAF evaluation is an effective screening test for NTDs and should be offered to all pregnant women	
Level B[‡]	Women with elevated serum AFP	Should have a specialized ultrasound examination to further assess the risk of NTDs
	Fetus with an NTD	Should be delivered at a facility that has personnel capable of handling all aspects of neonatal complications
Level C[§]	Women capable of becoming pregnant	400 µg/day
	The ideal dose of folic acid has not been appropriately evaluated in prospective clinical trials	
	Route of delivery for the fetus with an NTD	Should be individualized due to the lack of data indicating that any one dosage provides a superior outcome

[†]Level A: The following recommendations are based on good, consistent scientific evidence.
[‡]Level B: The following recommendations are based on limited or inconsistent scientific evidence.
[§]Level C: The following recommendations are based primarily on consensus and expert opinion.
AFP: Alfa fetoprotein; MSAF: Maternal serum alfa fetoprotein; NTD: Neural tube defect

- Function: Prevents neural tube defects (NTDs); supports DNA synthesis and cell division.
- Side Effects: Rare; high doses may mask B12 deficiency.

Iron

- Function: Supports increased maternal blood volume and fetal oxygen delivery.
- Recommended Intake: 27 mg/day of elemental iron.

Pregnant women and lactating mothers	Daily, 1 Iron and Folic Acid tablet starting from the fourth month of pregnancy (that is from the second trimester), continued throughout pregnancy (minimum 180 days during pregnancy) and to be continued for 180 days, post-partum Each tablet containing 60 mg elemental Iron + 500 mcg Folic Acid, sugar-coated, red color

Form (tablet)	Formulation	Elemental iron	Adult dosage
Ferrous fumarate	325 mg	106 mg (33%)	1 tablet, once per day or once every other day
Ferrous gluconate	325 mg	38 mg (12%)	1-3 tablets, once per day or once every other day
Ferrous sulfate	325 mg	6 mg (20%)	1-2 tablets, once per day or once every other day
Haem iron polypeptide	398 mg	11 mg	1-3 tablets per day
Polysaccharide iron complex	150 mg	150 mg	1 tablet,once per day
Ferric citrate	1,000 mg	210 mg	1 tablet, once every other day

- Side Effects: Constipation, nausea, dark stools; mitigated by hydration and food intake.
- Caution: Avoid excess unless prescribed; may interact with antibiotics.

Calcium & Vitamin D

- Function: Supports fetal bone, teeth, heart, and muscle development.
- Recommended Intake:
- Calcium: 1,000 mg/day (ages 19–50); 1,300 mg/day (ages 14–18).
- Vitamin D: 600 IU/day.
- Side Effects: Generally safe; excess Vitamin D may be toxic. Excessive consumption of calcium (>3 gm/d) may increase the risk of urinary stones and Urinary Tract Infection (UTI) and reduce the absorption of essential micronutrients

Omega-3 (DHA) in Pregnancy: Indian Guidelines

- **Recommended Intake**: At least 200 mg DHA daily is advised to support fetal brain and eye development.
- **Dietary Sources**: Safe options include salmon, sardines, shrimp, and canned light tuna. Avoid high-mercury fish like shark, swordfish, and king mackerel.
- **Supplementation**: Often necessary due to low omega-3 intake among Indian women, especially vegetarians. Algae-based DHA supplements are preferred for plant-based diets. Cod liver oil is not recommended due to high vitamin A.
- **Timing**: DHA is crucial throughout pregnancy, especially in the third trimester, and beneficial during breastfeeding

Vitamin B6 & Ginger

- Function: First-line OTC treatments for pregnancy-related nausea.
- Dosage:
- B6: 25 mg 2–3 times/day.
- Ginger: ≤2 g/day from capsules or teas.
- Side Effects: Minimal; doxylamine may be added for enhanced effect.

Additional OTC Nutrients and Supplements

FDA Advisory: NSAID Use in Pregnancy

Medications to Avoid After 20 Weeks

- buprofen (Advil, Motrin)
- Naproxen (Aleve)
- High-dose Aspirin
- Diclofenac

Risks

- Oligohydramnios: NSAIDs may impair fetal kidney function, reducing amniotic fluid.
- Cardiac Impact: Risk of premature closure of the fetal ductus arteriosus after 30 weeks.

Safer Alternative

- Acetaminophen (Tylenol): Preferred for pain and fever relief when used as directed.

Common OTC Medications: Safety Overview

Antihistamines

- Safe Options: Diphenhydramine (Benadryl), loratadine (Claritin), cetirizine (Zyrtec).
- Uses: Allergies, sleep aid.
- Caution: May cause drowsiness; avoid combination products with NSAIDs.

Diphenhydramine and chlorpheniramine are the most commonly used antihistamines in cold preparations. These first-generation antihistamines are associated with drowsiness but have not been found to increase the risk of malformations above baseline

Cough & Cold Remedies
- Safe Ingredients: Dextromethorphan , guaifenesin (Mucinex).
- Avoid: Multi-symptom products with pseudoephedrine or phenylephrine.
- Caution: Use single-ingredient formulations; consult provider.

Antacids & Heartburn Relief
- Safe Options: Calcium carbonate (Tums), magnesium hydroxide (Milk of Magnesia), famotidine (Pepcid).
- Avoid: Sodium bicarbonate and aluminum-containing antacids.
- Caution: Monitor calcium intake to avoid excess.

Constipation Relief
- Safe Options: Fiber supplements, stool softeners (docusate sodium), osmotic laxatives (polyethylene glycol).
- Avoid: Stimulant laxatives (senna, bisacodyl) unless prescribed.

Hemorrhoid Relief
- Safe Options: Witch hazel pads, hydrocortisone creams, sitz baths.
- Caution: Limit use of steroid creams to short durations.

Topical Treatments
- Safe Options: Antibiotic ointments (Neosporin), antifungal creams (clotrimazole, miconazole).
- Avoid: Retinoids (e.g., tretinoin), high-dose salicylic acid.

General Safety Guidelines for OTC Use During Pregnancy
- Consult First: Always speak with your OB-GYN before using any OTC product.
- Read Labels Carefully: Avoid hidden NSAIDs, alcohol, or unlisted herbal ingredients.
- Follow Dosage Instructions: Overuse of vitamins (e.g., A, D, E) can cause birth defects or toxicity.
- Watch for Drug Interactions: Iron may reduce antibiotic effectiveness; magnesium may interfere with absorption of certain medications.
- Avoid Unproven Herbal Remedies: Black cohosh, St. John's wort, and certain essential oils may be unsafe.
- Use Single-Ingredient Products: Helps isolate effects and reduce risk of interactions.

Final Thoughts

Navigating OTC supplements and medications during pregnancy requires vigilance, clinical insight, and personalized care. While many products are marketed as safe, only a subset has been rigorously evaluated for use during pregnancy. The FDA and ACOG offer essential frameworks, but individualized guidance from a healthcare provider remains paramount.

For healthcare professionals, staying updated on evolving guidelines ensures optimal maternal and fetal outcomes. For expectant mothers, informed conversations with providers empower safer choices and healthier pregnancies.

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