09 - Smart Prescriptions: Safe Drugs, Safer Women

Gyan - Vahini

From

FOGSI, Food Drugs & Medicosurgical Equipment Committee September - 2025

"Safe drugs, safer women—every prescription matters."

Dr. Asha Jain

Editor & Chairperson, FOGSI FDMSE Committee

Message From Dr. Sunita Tandulwadkar

Dr. Sunita Tandulwadkar
President FOGSI-2025

It is with great satisfaction that I present to you the September 2025 edition of our e-magazine, “Smart Prescriptions: Safe Drugs, Safer Women.” The subject of drug safety in women’s health is of paramount importance and deserves continuous attention. As gynaecologists, we are entrusted not only with treating illness but also with ensuring that every prescription we write translates into benefit without avoidable harm.

This edition of the e-magazine reflects the collaborative efforts of experts who have examined different facets of drug safety—be it rational prescribing, awareness of drug–drug and food–drug interactions, understanding drug inserts and labels, or the importance of storage and formulation. The range of topics, from fertility medications to menopausal prescriptions, highlights the need to individualise treatment while upholding safety as our guiding principle.

The Food, Drugs, and Medicosurgical Equipment Committee has once again curated a highly relevant and thought-provoking issue. It is my hope that every FOGSI member will study these articles, discuss them in academic forums, and integrate the insights into practice. Safer women begin with smarter prescriptions, and our collective vigilance in this matter will shape healthier generations.

Dr. Sunita Tandulwadkar
President, FOGSI

Message from Dr Abha Singh

Dr. Abha Singh
Vice President FOGSI-2025

Dear Fogsians Greetings!

The September 2025 issue of our e-magazine, dealing with “Smart Prescriptions: Safe Drugs, Safer Women,” comes at a time when rationale use of drugs are important. Prescription writing remains one of the most fundamental clinical skills . Errors in this clinical decision making process account for significant proportion of adverse drug events and ethical implications. Smart Prescribing anchored with good clarity, rationality and safety, ensures that the therapeutic goals are met while protecting women from avoidable harm. By adopting systematic , evidence –based individualised approaches which are ethically based and physicians can transform prescription writing.

Smart prescription involves not only selecting the appropriate drug , but also correct dosage, duration & route, while minimizing the risk of polypharmacy , adverse drug reactions and teratogenicity. Women’s healthcare spans a wide spectrum—adolescence, reproductive years, pregnancy, menopause, and beyond .Each stage bringing unique challenges in terms of safety of medication. Therefore, Safe choices today shape healthier tomorrows.

It explores commonly encountered pitfalls such as silent food–drug interactions, the potential misuse of analgesics, and the nuances of emergency medications in the labour room. Equally valuable are discussions on alternative therapies, injectable contraceptives, and drug-device combinations, reminding us that innovation and safety must go hand in hand.

Every article here is not only a scientific update but also a tool to strengthen the prescribing practices ,which have been discussed at length by authors of Food, Drugs and Medicosurgical Equipment committee.
Moreover, Smart Prescribing with precision and safety around womens health should be our aim.

Happy Reading !

Dr Abha Singh

Message from Dr Suvarna Khadilkar

Dr. Suvarna Khadilkar
Secretary General FOGSI-2025

It gives me immense pleasure to introduce the September 2025 issue of our e-magazine, aptly titled "Smart Prescriptions: Safe Drugs, Safer Women." The safe use of drugs is not just a scientific necessity but a moral responsibility for every medical professional. In obstetrics and gynaecology, where our decisions often impact both mother and child, this responsibility becomes even greater.

This edition is a rich compilation of well-researched and thoughtfully written articles. It covers a wide range of themes—from pregnancy prescriptions, fertility treatments, and menopausal management, to antibiotic stewardship, adverse drug reactions, and the growing role of alternative medicines. Each contribution highlights practical take-home points that can be directly applied in daily clinical work. I am particularly appreciative of the focus on drug storage and labelling, which are often overlooked aspects but critical for patient safety.

I wish to thank the dedicated authors and the editorial team of the Food, Drugs, and Medicosurgical Equipment Committee for their hard work in shaping this issue. Their efforts have produced not just an academic resource but a handbook of safer practice.
As Secretary General, I urge all our members to actively use this knowledge to refine their approach to prescribing, to sensitise patients about safe drug use, and to mentor the next generation of doctors in making safety the cornerstone of women's healthcare.

With best and warm wishes,

Dr. Suvarna Khadilkar
Secretary General, FOGSI

Dr. Asha Jain
Chairperson
FOGSI FDMSE Committee

FOREWORD

It gives me great pleasure to present the September 2025 edition of our e-magazine, "Smart Prescriptions: Safe Drugs, Safer Women," prepared under the aegis of the Food, Drugs and Medicosurgical Equipment Committee of FOGSI. Drug safety remains one of the cornerstones of women's healthcare, and this issue has been curated with the aim of equipping practitioners with practical, evidence-based insights that can be readily applied in day-to-day practice.

This edition has been enriched by the contributions of a distinguished group of authors who have each addressed critical aspects of drug use in women's health. My heartfelt gratitude goes to Dr. Asha Jain (From Shelf to Self), Dr. Chitra Pandey (Beyond the Label), Dr. Sarita Kumari (Silent Interactions), Dr. Neetha George (Pill Power), Dr. Varuna Pathak (Pregnancy Prescriptions), Dr. Deepti Gupta (Fertility & Pharmaceuticals), Dr. Ginny Gupta (Menopause & Medicines), Dr. Monika Gupta (The Antibiotic Alarm), Dr. Priyanka Rai (Analgesics & Anti-inflammatories), Dr. Jyothi G.S. (Emergency Medications in the Labour Room), Dr. Sandhya Rani and Dr. Ragweshwar J. Mahajan (Injectables), Dr. Vandana Gupta (Device–Drug Duos), Dr. Urvashi (Adverse Drug Reactions), Dr. Archana Singh (From Herbal to High-Tech), Dr. Ruche Bhargava (Storage Stories), and Dr. V. Padmaja (Prescription to Prevention). Their collective expertise has transformed this edition into a comprehensive reference on the subject.

I extend my sincere thanks to our dynamic President, Dr. Sunita Tandulwadkar, our Vice President Incharge, Dr. Abha Singh, and our Hon. Secretary General, Dr. Suvarna Khadilkar, for their constant encouragement, guidance, and vision. A special word of appreciation goes to Mr. Bhupendra, whose thoughtful design and layout have given this e-magazine a professional and appealing presentation.

I hope this issue inspires all readers to reaffirm their commitment to safe prescribing and to share this knowledge widely, so that together we can ensure safer and healthier lives for the women we serve.

Dr. Asha Jain
Editor, FOGSI FDMSE Committee E-magazine

"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

FOGSI FOOD DRUGS & MEDICOSURGICAL EQUIPMENT COMMITTEE

ADVISORS

Dr. Narendra Malhotra
Past President Fogsi

Dr P C Mahapatra
Past President Fogsi

Dr Rishma Pai
Past President Fogsi

Dr Jaydeep Tank
Imm. Past President

Dr Ashok Khurana
Patron Society of SFM

Dr Ragini Agrawal
Past VP Fogsi

Dr, Rajendra Singh Pardeshi
Past VP Fogsi

Dr. Ameya Purandare
Joint Treasurer

Dr Vidya Thobbi
VP Elect Fogsi

Dr Ritu Khanna
Past CP FDMSEC

COMMITTEE - MEMBERS


Dr Arati Kulkarni
Aurangabad MH


Dr Archana Singh
Hyderabad Telangana


Dr Chitra Pandey
Prayagraj UP


Dr Dolly Mehra
Ratlam MP


Dr Durgadas Asranna
Tumkur Karnataka


Dr E S Usha
Erode TN


Dr Ginny Gupta
Ludhiana Punjab


Dr Himleena Gautam
Assam


Dr Jyothi GS
Bangalore Karnataka


Dr Kiran Chhabra
Delhi


Dr M Chandra Ponnusami
Namakkal Tamil Nadu


Dr Neetha George
Thrissur Kerala


Dr Nidhi Bajaj
Katni MP


Dr Okram Sarda Devi
Imphal Manipur


Dr.Padmaja Veeramachaneni
Vijayawada


Dr Prabhdeep Kaur
Bhilai CG

Dr Prerna Saigal
Pathankot Punjab

Dr Priyanka Rai
Deoghar Jharkhand

Dr Ragweshwar Jyoti Mahajan
Shimla Himanchal Pradesh

Dr Renu Jain
Gwalior

Dr Rimpi Singla
Chandigarh

Dr Ruche Bhargava
Jalandhar Punjab

Dr Sandhyarani Panigrahi
Berhampur Odisha

Dr Sarita Kumari
Jamshedpur Jharkhand

Dr Shikha Sachan
Varanasi UP

Dr Sonal Gupta
Faridabad Hariyana

Dr Sreedevi Vellanki
Vijaywada AP

Dr Sugandha Goel
Jodhpur Rajasthan

Dr Sujaysri Sangita
Bhimavaram AP

Dr Urvashi Barman Singh
Prayagraj UP

Dr Vandana Gupta
Delhi

Dr Vishnu Priya
Bangalore Karnataka

INDEX

01 From Shelf to Self: Ensuring Drug Safety in Women's Health

Author - Dr Asha Jain
Chairperson, Food, Drugs & Medicosurgical Equipment Committee, FOGSI &
President Raipur Menopause Society Raipur CG

Introduction

Medicines are an integral part of women's health care. From adolescence to menopause, and through pregnancy and lactation, women are prescribed a wide variety of drugs—ranging from iron and antibiotics to contraceptives, hormonal agents, and advanced biologics. Every prescription carries the potential for cure as well as harm. Ensuring drug safety is therefore not a one-time act but a continuous process—beginning with how medicines are manufactured and tested, moving through regulation and prescription, and finally reaching the woman who consumes them.

The concept of "From Shelf to Self" is particularly relevant in India, where access, awareness, cultural practices, and regulatory realities all shape how drugs are used. This chapter aims to examine the journey of drugs from their development and approval to their ultimate use by women, highlighting points where safety can be strengthened.

Drug Development and Clinical Trials

Historically, women—especially pregnant and lactating women—have been under-represented in clinical trials. This has led to significant gaps in knowledge regarding dosage, metabolism, and adverse drug reactions (ADRs) specific to women. Recent analyses have shown that women experience almost twice as many ADRs as men, partly due to differences in body composition, hormonal milieu, and drug metabolism【Singh K, Nature, 2025】.

In India, the Clinical Trials Registry of India (CTRI) has made progress in transparency, but reviews reveal that very few trials specifically address pregnant women or analyse outcomes by sex【Karekar SR, 2019】. Without this foundational evidence, clinicians often rely on extrapolated data, increasing the risk of unforeseen outcomes.

Regulatory Approval and Labelling

Once a drug moves from research to approval, regulators decide on its safety for public use. In India, the Central Drugs Standard Control Organization (CDSCO) plays this role. Updated guidelines emphasise Periodic Safety Update Reports (PSURs) and pharmacovigilance obligations for manufacturers【CDSCO, 2024】.

However, the information that eventually reaches the prescribing doctor is often inadequate. Drug inserts may be poorly worded, with pregnancy and lactation categories not updated to international standards. For example, many inserts still use the outdated FDA pregnancy risk categories rather than the narrative “Pregnancy and Lactation Labelling Rule” (PLLR) approach. This results in uncertainty and variability in interpretation.

For women, especially in rural India, the problem is compounded when information leaflets are not available in regional languages or when the literacy barrier prevents proper understanding. Thus, the regulatory approval process must be complemented with effective labelling, patient-friendly communication, and training for healthcare providers.

Prescribing Practices in Women’s Health

Safe prescribing requires individualisation. A drug that is appropriate for a healthy 25-year-old may be hazardous for a 45-year-old with diabetes and renal compromise. In gynaecological practice, common areas where prescribing needs particular care include:

- **Pregnancy**: Drugs must be chosen after balancing maternal benefit and fetal risk. For example, antihypertensives such as labetalol and nifedipine are safe, while ACE inhibitors are contraindicated. A recent Indian cross-sectional study showed that most antenatal prescriptions adhered to safer categories, but vigilance is always required【BRIMS Study, 2024】.
- **Contraceptives**: Combined oral contraceptives (COCs) are effective but may cause side effects such as weight gain, nausea, and headaches. A study comparing COCs with ormeloxifene, a non-steroidal contraceptive, found that ormeloxifene had better acceptability and continuation rates【Gupta et al., 2024】.
- **Menopause**: Hormone replacement therapy (HRT) remains underused in India, partly due to concerns about long-term risks. Safer prescribing demands that women are counselled on benefits, risks, and alternatives.
- **Common Gynaecological Complaints**: Analgesics, antifungals, and antibiotics are widely used. Over-the-counter availability often leads to misuse, particularly of antibiotics, contributing to resistance.

Post-Marketing Surveillance and Pharmacovigilance

Approval is only the beginning of a drug’s safety journey. Real-world use reveals adverse events that trials may miss. In India, the Pharmacovigilance Programme of India (PvPI) under the Indian Pharmacopoeia Commission has created ADR Monitoring Centres across the country. Yet, under-reporting remains a major challenge.

A 2025 study analysing serious ADRs in Indian hospitals highlighted that women were disproportionately affected, particularly by antimicrobials and NSAIDs【Singh P, 2025】. Another pharmacovigilance report from Karnataka documented self-medication during pregnancy, with women consuming iron, analgesics, and even antibiotics without supervision【Ahmad A, 2014】.

For drug safety to improve, clinicians must actively report ADRs, educate patients about early warning signs, and promote a culture of vigilance.

Special Populations

Pregnancy and Lactation

Pregnancy alters drug absorption, distribution, metabolism, and elimination. Drugs such as antiepileptics, anti-tuberculars, and antiretrovirals pose dilemmas. In India, parenteral iron preparations are widely used for anaemia. Case reports of severe reactions to ferric carboxymaltose highlight the need for careful monitoring【Pune Case Report, 2024】.

Adolescents

Adolescents may experiment with emergency contraception or acne medications without supervision. Education and counselling are critical to prevent misuse.

Menopause and Elderly Women

Polypharmacy is common in older women who may be on drugs for hypertension, diabetes, arthritis, and gynaecological conditions. Interactions and adverse events are frequent. Clinicians must periodically review medications and deprescribe where necessary.

Self-Medication and Traditional Remedies

In India, self-medication is common, particularly with antibiotics, analgesics, and traditional herbal preparations. While Ayurveda and herbal formulations are culturally accepted, they may interact dangerously with modern drugs. For instance, herbal galactagogues taken during lactation can alter metabolism of antiepileptics or antihypertensives.

A pharmacovigilance study from a teaching hospital revealed that a significant proportion of pregnant women consumed iron supplements obtained over the counter, without medical advice【ResearchGate, 2025】. While some of these were safe, others led to gastrointestinal upset or allergic reactions.

Storage, Access, and Patient Education

Drug safety is not ensured merely by correct prescribing. Storage conditions—temperature, humidity, and light exposure—directly affect potency. In India, where climatic extremes are common, medicines are often stored inappropriately. Dr. Ruche Bhargava's work on Storage Stories underlines the importance of educating women to keep medicines in cool, dry places and away from children.

Equally vital is patient education. Women must be encouraged to read labels, check expiry dates, and complete prescribed courses. Community health workers and pharmacists can play a pivotal role in reinforcing these messages.

Policy and System Interventions

Ensuring drug safety for women requires systemic changes:

1. **Strengthening PvPI**: Encouraging ADR reporting through digital platforms and integrating them into hospital electronic records.
2. **Updating Guidelines**: Aligning Indian drug labeling with international standards like the PLLR.
3. **Capacity Building**: Training doctors, nurses, and pharmacists in rational prescribing and pharmacovigilance.
4. **Public Awareness:** Campaigns to discourage self-medication and promote responsible use.
5. **Research:** Encouraging India-specific studies on drug safety in women, particularly in pregnancy and menopause.

Conclusion

The journey from shelf to self is complex, but it is also full of opportunities to improve women's health. Every stage—development, regulation, prescribing, dispensing, storing, and consuming—carries a responsibility. For clinicians, the challenge is not merely to treat disease but to ensure that treatment does no harm.

In India, where diversity of population and healthcare delivery poses unique challenges, drug safety must remain at the forefront of women's health. By strengthening pharmacovigilance, rationalising prescriptions, integrating traditional with modern medicine responsibly, and empowering women with knowledge, we can move towards the vision of "Safe Drugs, Safer Women."

References

1. Singh K. Women are poorly represented in clinical trials. Nature. 2025.
2. Karekar SR, et al. Clinical studies involving pregnant women in the Clinical Trials Registry of India. Indian J Med Ethics. 2019.
3. Central Drugs Standard Control Organization. Pharmacovigilance Guidance Document for MAHs. 2024.
4. Singh P, et al. Serious adverse drug reactions in Indian hospitals. Indian J Pharmacol. 2025.
5. Ahmad A, et al. Drug safety monitoring programme in India. Perspect Clin Res. 2014.
6. Gupta D, et al. Acceptability and side effects of ormeloxifene vs COCs. Int J Reprod Contracept Obstet Gynecol. 2024.
7. BRIMS Teaching Hospital. Drug pattern use during pregnancy. Int J Basic Clin Pharmacol. 2024.
8. Case Report: ADR to Inj. Ferenject in pregnancy. IJCRT. 2024.
9. ResearchGate. ADR to iron preparations among pregnant women. 2025.
10. Swain PK, et al. Adverse pregnancy outcomes in India. Indian J Community Med. 2024.

---xxxxxxxxxx--

02 Beyond The Label: Understanding Drug Inserts & Leaflets

Author: Dr. Chitra Pandey
M.D. FICOG, Consultant- Obs. & Gynae.
And Director Harsh Hospital, Prayagraj

INTRODUCTION

Drug inserts and leaflets are critical tools for communication to ensure safe, rational and effective utilization of medicines. They provide information to the healthcare professionals who rely on these inserts for accurate prescription, while the patients depend on the accompanying leaflets for proper administration and adherence to the treatment. (Ref.1) .

Both are legally binding documents and manufacturers are responsible for complete document, ensuring accuracy and safety. They not only safeguard patients from inappropriate use but also protect physicians and pharmaceutical companies by maintaining transparency and compliance with ethical guidelines.

DEFINITION

Drug insert or Patient Package Insert (PPI) can be defined as an officially approved technical document with scientific details. It is intended for healthcare professionals (doctors, nurses & pharmacists) and provide comprehensive, objective information for clinical decision making by doctors. Its content is highly detailed based on preclinical and clinical studies and its purpose is to ensure the safe and effective use of a medicine.

OBJECTIVE AND IMPORTANCE OF DRUG INSERTS

Drug inserts fulfil multiple purposes.

- Essential in cases when verbal means of communication are inadequate and sometimes to strengthen the verbal counselling.
- Patient's Health Education and awareness which helps in maintaining medication adherence.
- It is an effective means for conveying additional prescription drug information to the patients.
- It helps doctors and pharmacists to give additional information about the doses of Medicine, route of administration and side effects etc.
- Insert also provide information on storage and expiry date of medicine.
- If provided in regional language inserts help average people to read them easily.

Main objectives of drug leaflets and inserts are:

1. **Safety**: highlighting contraindications, potential interactions with other drugs and food, and adverse effects.
2. **Efficacy**: Ensuring that the drug is taken in the correct doses and at the appropriate interval.

3. **Informed consent**: allowing patients to make educated decisions about their treatment.
4. **Standardization**: providing consistent information across different healthcare settings.
5. **Legal protection**: safeguarding manufacturers and prescribers by disclosing risks.

CONTENTS OF PATIENT PACKAGE INSERT

Description - Proprietary name, dosage form, ingredient information, pharmacologic and therapeutic class of drug, chemical name and structural formula of drug.

Clinical Pharmacology – Mechanism of action of the medication, drug absorption, metabolism, elimination, findings of clinical trials. (Ref.2)

Indications and Usage – It includes uses for which drug has been approved, e.g. asthma, diabetes.
Contraindications – List of conditions in which medicine should not be used.

Warnings – Information on possible serious side effects.

Precautions – Information and guidelines for safe use of medicines e.g. to be taken empty stomach.

Adverse reactions - List of all side effects.

Non clinical toxicology- it provides information about carcinogenesis, mutagenesis, impairment of fertility, animal toxicology and pharmacology.

Drug abuse and dependence- information regarding prolonged use of drugs can cause physical dependence.

Storage and handling – Handling guidelines and special storage conditions.

Name and address of manufacturer
Date and revision of package insert
References- list of various print and digital resources, regulatory agencies websites, journals, etc used to collect information. As described by Hermann et al. minimum information PI should contain is how to take the drug, how to store the drug, how it is expected to help the illness, how to recognise problems (side effects) that can arise and what to do about them. (ref 3)

DIGITAL TRANSFORMATION OF DRUG INSERTS

With Digital Revolution, Traditional paper inserts are evolving:

- QR codes and apps: patients can scan codes for interactive videos or multilingual content.
- E leaflets: regulators in Europe are piloting electronic formats to reduce waste and enhance accessibility.
- Personalized medicine: future inserts may adapt content based on genetic profiles or Co morbidities.
- Digital formats also allow for real time updates overcoming the lag in imprinted revisions.
- PPI may be found online on drug manufacturer's website in a reference book called as the physician's desk reference PDR.

PATIENT INFORMATION LEAFLET (PIL)

PIL is a simplified consumer friendly version for patients.

Content of PIL is written in clear, concise and less scientific layman's language for the consumers. It emphasizes clear instructions on dosage, precautions, possible side effects and how to handle missed doses etc.

The core difference between Package Insert (PI) and patient information leaflet (PIL) lies in the complexity and intended user. A PI is the comprehensive scientific source for prescribers, while a PIL is a user- friendly guide for the consumer to understand and manage their treatment.

NATIONAL REGULATORY BODIES IN INDIA AND OTHER COUNTRIES

The Central Drugs Standard Control Organization (CDSCO) is the national regularity authority in India working under the Ministry of Health and family welfare, government of India. The CDSCO Performs multiple operations in India to safeguard and promote public health while assuring safety, quality and efficacy of drugs, cosmetics and medical devices

The Drug Controller General of India (DGCI) is the chairperson of CDSCO governing all these operations.

CDSCO's equivalent counterpart in United State of America is United States Food and Drug Administration (USFDA) which is responsible for regulating and supervising the safety of food, dietary supplements, drugs, vaccines, biological medical products, blood products, medical devices and cosmetics. Since 1999, every medicine distributed within the European Union (EU) has been required to include PPI. To ensure package insert uniformity in each EU member state, content

& layout are determined mainly by the European guidelines & recommendations. (Ref.4)

GUIDELINES FOR PACKAGE INSERTS

In India, the concept of package insert guidelines are regulated by the 'Drugs and Cosmetics Act (1940) and Rules (1945). Section 6.2 of schedule D, lists 8 parameters pertaining to therapeutic indications whereas section 6.3 indicates 8 parameters of pharmaceuticalinformation.(ref-5) Section 6.2 mandates that the package must be in 'English'. Rule 96 and 97 provide guidelines for labelling content and format of innermost and outermost container of drug.

INDIAN CDSCO GUIDELINES	
Section 6.2: Therapeutic Indications	
1	Posology and method of administration.
2	Contra-indications
3	Special warnings and special precautions for use, if any.

4	Interaction with other medicaments and other forms of interaction.
5	Pregnancy and lactation, if contra-indicated.
6	Effects on ability to drive and use machines, if contra-indicated
7	Undesirable effects/side effects.
8	Antidote for overdosing
Section 6.3: Pharmaceutical Information	
9	List of excipients
10	Incompatibilities
11	Shelf life in the medical product as packaged for sale
12	Shelf life after dilution or reconstitution according to direction
13	Shelf life after first opening the container
14	Special precautions for storage
15	Nature and specification of the container
16	Instructions for use/handling

US FDA GUIDELINES

1. Highlights of prescribing information Product names, other required information Boxed warning
Recent major changes
Indications and usage dosage and administration Dosage forms and strengths
Contraindications Warnings and precautions Adverse reactions
Drug interactions
Use in specific populations

2. Full prescribing information: Contents

3. Full prescribing information

Boxed warning

1. Indications and usage
2. Dosage and administration
3. Dosage forms and strengths
4. Contraindications
5. Warnings and precautions
6. Adverse reactions
7. Drug interactions
8. Use in specific populations
9. Drug abuse and dependence
10. Overdosage
11. Description
12. Clinical pharmacology
13. Nonclinical toxicology
14. Clinical studies
15. References
16. How supplied/storage and handling
17. Patient counseling information

Changes needed in Indian package inserts

The Indian package inserts need to be more patient oriented having patient counselling information including advice about diet, lifestyle, side effects, directions for use etc.

India is a country with enormous variations in demographic characteristics of patients and several languages. Multi linguistic format of PI will help in reaching out to a greater number of patients as well as poorly educated patients.

Development of electronic databank is necessity now as India is the third largest producer of medicines in terms of volume.

CONCLUSION

PI and PIL are Important source of drug information for both the prescriber and user of the medication. Over the years, drug inserts and leaflets have evolved from brief technical notes to comprehensive evidence-based documents designed to meet international regulatory standards

The PI should be optimised and tested before marketing by regulatory bodies for lack of information.

The government should ensure pharmaceutical companies are complying with the current regulations.

Regulating bodies should invite suggestions from physicians to improve the format of PIs.

References:

(1)WHO. Patient information leaflets: guidance for development. 2019.

(2)Bennett PN, Brown MJ, Sharma P. Clinical Pharmacology. 12th ed Elseiver;2021.

(3)Hermann F et al. Package insert for prescribed medicines: What minimum information do patients need? Br MedJ.1978;2:1132-5. Doi:10.1136/bmj.2.6145.1132

(4)European Medicines Agency. Quality Review of Documents- Human. 2022.

(5)Guidance for drug package inserts in India and United States.Int.J.Pharm.Sci.Rev.Res.,67(2), March-Apr2021; Article No 10

03 Silent interactions: Food-Drug & Drug-Drug Pitfalls

Author: Dr. Sarita Kumari
Consultant at department of Obstetrics and Gynaecology at Tata Main Hospital. Jamshedpur Jharkhand

Author: Pooja Lal
Specialist at department of Obstetrics and Gynaecology at Tata Main Hospital.

Oral drugs may have interactions with food or other drugs taken simultaneously. The effect of a drug on a person may be different than what is expected because that drug can interact with another drug the person is taking (drug-drug interaction) or the food, beverages, dietary supplements the person is consuming (drug-nutrient/food interaction) Food drug or drug-drug interaction means when they change how the medicine works, either it can and change its pharmacokinetics or the pharmacodynamics. These interactions can decrease, increase or produce all together new effect. These interactions may occur if taken accidently or because of lack of awareness about its ingredients.
The majority of clinically relevant food-drug interactions are caused by food induced changes in the bioavailability of the drug.

Vegetable and fruit supplements have recently become increasingly popular for their roles in medicine and as staple foods. This has, however, led to the increased risk of interaction between prescribed drugs and the bioactive ingredients contained in these foods. These interactions range from pharmacokinetic interactions (absorption, distribution, metabolism, and excretion influencing blood levels of drugs) to pharmacodynamic interactions (drug effects).

The influence of dietary substances on drug effects depends on numerous variables ranging from physicochemical properties of the drug to host factors such as enzymes and transporters in the gastrointestinal tract [1] as well as in the entire body. Major side-effects of some diet (food) on drugs include alteration in absorption by fatty, high protein and fiber diets.

Drug interactions (DIs) represent an important and widely under recognized source of medication errors. The gastrointestinal absorption of drugs may be affected by the concurrent use of other agents that[2] have a large surface area upon which the drug can be absorbed[3] bind or chelate[4] alter gastric pH[5] alter gastrointestinal motility, or affect transport proteins such as P-glycoprotein.

The most important interactions are those associated with a high risk of treatment failure arising from a significantly reduced bioavailability in the fed state. Such interactions are frequently caused by chelation with components in food. In addition, the physiological response to food intake, in particular, gastric acid secretion, may reduce or increase the bioavailability of certain drugs.[4,5]

Analgesics and Antipyretics
Analgesics and antipyretics are the most commonly used drugs.Co-administration of acetaminophen with pectin delays its absorption and its onset of action therefore acetaminophen should be preferably taken in empty stomach for rapid action[6].

NSAIDs like ibuprofen, naproxen, ketoprofen and others can cause stomach irritation and thus they should be taken with food or milk. The Cmax and AUC0-alpha of ibuprofen were significantly increased after single and multiple doses of Coca-Cola, thereby indicating increased extent of absorption of ibuprofen

Warfarin

Warfarin is commonly used to treat or prevent thromboembolic events. It is widely used in pregnancy complicated by APLA syndrome.21 There is a possible interaction between warfarin and a high protein diet. The potential for increased dietary protein intake to raise serum albumin levels and/or cytochrome P450 activity has been postulated as mechanisms for the resulting decrease in international normalized ratio (INRs).[7]

Some vegetables (broccoli, Brussels sprouts, kale, parsley, spinach, and others) are high in vitamin K. Eating large quantities or making sudden changes in the amounts eaten of these vegetables, interferes with the effectiveness and safety of warfarin therapy.[8] The combination of warfarin administration and cranberry juice ingestion appeared to be associated with an elevated INR without bleeding in elderly patient.

A number of studies have been documented on the interaction of warfarin and cranberry juice.[9-11] Cranberry juice is a flavonoid, which has been shown to induce, inhibit, or act as a substrate for the biosynthesis of several cytochrome P-450 (CYP) isoenzymes. It was suggested that cranberry juice increased the International Normalized Ratio (INR) of patients taking warfarin, but neither clearly identified cranberry juice as the sole cause of INR elevation.[12] If warfarin sodium is ingested with leafy green vegetables, the hypoprothrombinemic effect of warfarin may be decreased and thromboembolic complications may develop.[13]

Antihypertensive Drugs

Propranolol serum levels may be increased if taken with rich protein food. A change in diet from high carbohydrates/low protein to low carbohydrate/high protein may result in increased oral clearance. Smoking may decrease its plasma levels by increasing its metabolism.[14]
The intestinal absorption of celiprolol (beta-blocker) is inhibited when it is taken with orange juice. Hesperidin, present in orange juice, is responsible for the decreased absorption of celiprolol.[15] The absorption of ACEs inhibitors is increased when taken on an empty stomach.[16]

Antibiotics

Food intake can influence the effectiveness of an antibiotic.Avoid coadministration of antibiotics with milk products which are rich sources of divalent ions, such as calcium and magnesium that complex with some antibiotics and prevent their absorption. A number of studies give evidence that fluoroquinolones forming slightly soluble complex with metal ions of food show reduced bioavailability.[17] Casein and calcium present in milk decrease the absorption of ciprofloxacin.47It was found that the absorption of ciprofloxacin (500 mg) tablets can be reduced by concomitant ingestion of the grape fruit juice.[18] Therefore, to avoid drug therapeutic failures and subsequent bacterial resistance as a result of sub-therapeutic level of the drug in the systemic circulation, ingestion of the juice with ciprofloxacin should be discouraged. Azithromycin absorption is decreased when taken with food, resulting in a 43% reduction in bioavailability.[19] Tetracycline should be taken one hour before or two hours after meals and taken with milk because it binds calcium and iron, forming insoluble chelates, and influencing its bioavailability.

Antihistamines

A study indicates that concomitant intake of food with a single 20 mg oral dose of rupatadine exhibits a significant increase in rupatadine bioavailability.[20] Cimetidine is given with food to assist the maintenance of a therapeutic blood concentration. A fraction of cimetidine is absorbed in the presence of food, allowing the remaining drug to be dissolved and maintain a prolong concentration.

Monoamnine Oxidases

However older monoamine oxidase inhibitors (MAOIs) are effective in the treatment of depressive disorders, they are under-utilized in clinical practice due to main concerns about interaction with tyramine-containing food(matured cheese, red vine, ripped bananas, yogurt, shrimp paste and salami) or so called cheese reaction, since they are capable of producing hypertensive crisis in patients taking MAOIs.[21] Tyramine is an indirectly acting sympathomimetic agent, it is degraded by MAO but in the presence of MAOIs, it escapes degradation and reaches the systemic circulation where it is taken up by the adrenergic neuron, leading to a hypertensive crisis.

Fruit Juices

Among all fruit juices, grape fruit juice (GFJ) possesses high interaction with almost all types of drugs. The juice modifies the body's way of metabolizing the medication, affecting the liver's ability to work the drug through a person's system.Numerous reports have documented drug interactions with GFJ that occur via inhibition of CYP3A enzymes.10 Furanocoumarins present in GFJ inhibit the intestinal CYP 3A4 and have been shown to increase the oral bioavailability of medications that are CYP 3A4 substrates like Felodipine, midazolam, cyclosporine and raise their concentrations above toxic levels.[22]

Thyroxine

Recent evidence pointed out the role of gastric acid secretion on the subsequent intestinal absorption of thyroxine in relation with the timing of food ingestion as well as with pH impairment associated to frequent gastric disorders like Helicobacter pylori infection and gastric atrophy.[23] Levothyroxine is a derivative of thyroxine. Grapefruit juice may slightly delay the absorption of levothyroxine, but it seems to have only a minor effect on its bioavailability.

Conclusion

Generally speaking, drug interactions are to be avoided, due to the possibility of poor or unexpected outcomes. Like food, drugs taken by mouth must be absorbed through the lining of the stomach or the small intestine. Consequently, the presence of food in the digestive tract may reduce absorption of a drug. Often, such interactions can be avoided by taking the drug 1 hour before or 2 hours after eating. Like drugs, foods are not tested as comprehensively so they may interact with prescription or over the-counter drugs. The authors would suggest patients to tell their doctors and pharmacists about their food intake and dietary supplements so that interactions can be avoided.

References:

1.Custodio JM, Wu CY, Benet LZ. Predicting drug disposition, absorption/elimination/transporter interplayand the role of food on

2. Frankel EH. (2003). Basic Concepts. In: Hand book of food-drug Interactions, McCabe BJ, Frankel EH., Wolfe JJ (Eds.) pp. 2, CRC Press, Boca Raton, 2003.

3. Ayo JA, Agu H, Madaki I. Food and drug interactions: its side effects. Nutr Food Sci 2005;35(4):243-252

4. Schmidt LE, Dalhoff K. Food-drug interactions. Drugs 2002;62(10):1481-1502.

5. Nekvindova J, Anzenbacher P. Interactions of food and dietary supplements with drug metabolising cytochrome P450 enzymes. Ceska Slov Farm 2007 Jul;56(4):165-173.

6. Miller B, Carthan N. (2003) Non-prescription drug and nutrient interaction. In: Hand book of food-drug Interactions, McCabe BJ, Frankel EH., Wolfe JJ.

7. Lacy CF, Armstrong LL, Goldman MP, Lance LL. (2005). Drug interaction handbooks. Laxicomp's Ohio. 13th edition. 706-708, 1269. (Eds.), CRC Press, Boca Raton, pp 251-258.

8. Holt GA. Food & Drug Interactions. Chicago. Precept Press 1998;1998:293.

9. Ansell J, McDonough M, Zhao Y, Harmatz JS, Greenblatt DJ. The absence of an interaction between warfarin and cranberry juice: a randomized, doubleblind trial. J Clin Pharmacol 2009 Jul;49(7):824-830.

10. Griffiths AP, Beddall A, Pegler S. Fatal haemopericardium and gastrointestinal haemorrhage due to possible interaction of cranberry juice with warfarin. J R Soc Promot Health 2008 Nov;128(6):324-326.

11. Aston JL, Lodolce AE, Shapiro NL. Interaction between warfarin and cranberry juice. Pharmacotherapy 2006 Sep;26(9):1314-1319.

12. Yamreudeewong W, Henann NE, Fazio A, Lower DL, Cassidy TG. Drug-food interactions in clinical practice. J Fam Pract 1995 Apr;40(4):376-384.

13. Walker SE, Shulman KI, Tailor SA, Gardner D. Tyramine content of previously restricted foods in monoamine oxidase inhibitor diets. J Clin Psychopharmacol 1996 Oct;16(5):383-388.

14. Uesawa Y, Mohri K. Hesperidin in orange juice reduces the absorption of celiprolol in rats. Int J Pharm 2008;355(1-2):93-99.

15.. Ismail (2009). Drug-Food Interactions and Role of Pharmacist. Asian Journal of Pharmaceutical and Clinical Research, vol 2(4):1-10.

16.. Stormer FC, Reistad R, Alexander J. Glycyrrhizic acid in liquorice–evaluation of health hazard. Food Chem Toxicol 1993 Apr;31(4):303-312.

17. Furedi P, Papai K, Budai M, Ludanyi K, Antal I, Klebovich I. In vivo effect of food on absorption of fluoroquinolones. Acta Pharm Hung 2009;79(2):81-87.

18. Akinleye MO, Coker HA, Chukwuani CM, Adeoye AW. Effect of Five Alive fruit juice on the dissolution and absorption profiles of ciprofloxacin. Nig Q J Hosp Med 2007 Jan-Mar;17(1):53-57.

19.Stormer FC, Reistad R, Alexander J. Glycyrrhizic acid in liquorice–evaluation of health hazard. Food Chem Toxicol 1993 Apr;31(4):303-312.

20.Solans A, Carbo ML, Pena J, Nadal T, Izquierdo I, Merlos M. Influence of food on the oral bioavailability of rupatadine tablets in healthy volunteers: a single-dose, randomized, open-label, two-way crossover study. Clin Ther 2007 May;29(5):900-908.

21.Volz HP, Gleiter CH. Monoamine oxidase inhibitors. A perspective on their use in the elderly. Drugs Aging 1998 Nov;13(5):341-355.

22.de Castro WV, Mertens-Talcott S, Derendorf H, Butterweck V. Grapefruit juicedrug interactions: Grapefruit juice and its components inhibit P-glycoprotein (ABCB1) mediated transport of talinolol in Caco-2 cells. J Pharm Sci 2007 Oct;96(10):2808-2817.

23.Centanni M, Franchi A, Santaguida MG, Virili C, Nardo S, Gargano L. Oral thyroxine treatment: towards an individually tailored dose. Recenti Prog Med 2007 Sep;98(9):445-451.

---xxxxx---

04 Pill Power: How Formulation Shapes Effectiveness

Author: DR.NEETHA GEORGE
MS DGO FMAS FICOG
Diploma in lap,hysteroscopy,urogynaec(Kiel),
Assoc.Prof in OBG ,JMMC ,Thrissur ,Kerala

Drug formulation (or pharmaceutical formulation) refers to the process of combining various pharmaceutical ingredients, both active and inactive, to produce a final drug product. The primary goal of drug formulation is to deliver the active pharmaceutical ingredient in a manner that ensures optimal stability, bioavailability, safety, and patient acceptability, thereby maximizing therapeutic outcomes.

The three primary types of formulations are solid formulations (e.g., tablets, capsules), liquid formulations (e.g., solutions, suspensions), and parenteral formulations (e.g., injections).

A pill's formulation fundamentally shapes its effectiveness by controlling its bioavailability, the rate and location of drug release, and its stability. The formulation combines an active pharmaceutical ingredient (API) with inactive substances called excipients to ensure the drug is delivered reliably to the body.

Impact on bioavailability and absorption
Bioavailability is the amount of a drug that enters the bloodstream to produce a therapeutic effect. A pill's formulation can manipulate this by addressing the drug's inherent properties and its interactions with the gastrointestinal (GI) tract.

Solubility enhancement: Many modern APIs have poor water solubility, which limits their absorption. Formulations can use excipients like surfactants or cyclodextrins to increase the drug's solubility, improving its absorption into the body.

Particle size: Smaller drug particles have a larger surface area, which can increase the dissolution and absorption rate. Formulations can reduce particle size through processes like micronization to speed up the drug's onset of action.

Amorphous vs. crystalline form: A drug can be formulated in different crystalline or amorphous solid-state forms, affecting its dissolution rate. While amorphous forms are often more soluble and dissolve faster, they can be less stable than crystalline forms.

Control over drug release profile
A pill's formulation can dictate when and where the active drug is released in the body, which is critical for the drug's therapeutic effect.
a)Immediate-release (IR) vs. modified-release (MR):

IR tablets are designed to disintegrate quickly in the stomach, exposing the drug for rapid dissolution and absorption. This provides a fast onset of action, for example, with pain relievers.

b)MR formulations (including extended-release and delayed-release) release the drug over a longer period. This provides a steady, prolonged effect and can improve patient compliance by reducing how often a pill must be taken.

c)Enteric coatings: Some drugs can be destroyed by stomach acid or irritate the stomach lining. An enteric coating, which is insoluble at the stomach's low pH but dissolves in the small intestine's higher pH, allows the pill to pass through the stomach intact. This ensures the drug is released only where it can be effectively absorbed.

D)Capsules vs. tablets: Different dosage forms can target different areas of the GI tract. Some medications may be formulated in capsules to avoid an acidic environment, while others in tablet form are designed to disintegrate in the stomach. The choice depends on the drug's stability and optimal absorption site.

Enhancement of stability and consistency
Proper formulation ensures that the medicine remains safe and effective throughout its shelf life.

Protecting from degradation: Excipients like antioxidants and preservatives protect sensitive APIs from degradation caused by environmental factors such as oxygen, light, and moisture. Buffering agents help maintain a stable pH to prevent chemical breakdown.

Compatibility: The manufacturing process must ensure that all ingredients are compatible. Incompatible excipients can cause the drug to degrade or release inconsistently, negatively impacting its effectiveness.

Shelf-life: Stability studies are conducted on formulations to determine the shelf-life and storage conditions necessary to guarantee the product's potency and safety over time.

Influence on patient adherence
Formulation also addresses how a medicine is accepted and used by patients, which directly impacts its real-world effectiveness.

Taste and appearance: Coatings and flavoring agents can mask the unpleasant taste or odor of an API, making the pill more palatable. The size, shape, and color can also make it easier to swallow and help patients distinguish their medications, reducing the chance of errors.

Specific populations:
Pediatric and geriatric formulations often require alternative forms, such as liquids, chewable tablets, or orally disintegrating tablets (ODTs), because many patients in these age groups have difficulty swallowing conventional pills.

How ingredients (excipients) influence absorption.
The "inactive" ingredients, or excipients, are crucial for a pill's performance. They can either enhance or hinder the drug's absorption.

Excipient Type	Role in Formulation	Effect on Effectiveness
Diluents/Fillers	Increase the bulk of the pill for proper sizing and ease of handling.	Can promote the solubility of poorly water-soluble drugs by coating them and making them hydrophilic.
Binders	Hold the active drug and fillers together to form granules and prevent the tablet from crumbling.	The quantity of binder can affect the tablet's hardness and, in turn, its dissolution rate. A tablet that is too hard may dissolve too slowly.
Lubricants	Reduce friction between the ingredients and manufacturing equipment.	Many are hydrophobic and can inhibit water from entering the tablet, potentially slowing dissolution.
Coatings	A polymer layer applied to the tablet, which can improve stability, mask taste, or control the location of drug release.	Affects the dissolution rate. The effect depends on the coating type, following this general order from fastest to slowest release: non-enteric film coat > sugar coat > enteric coat.

A drug's inherent properties play a key role in formulation design.
Solubility: For a drug to be absorbed, it must first dissolve. Many modern drugs are poorly water-soluble, which can limit absorption. Formulators address this with strategies like using co-solvents or surfactants to increase solubility.

Particle size: Smaller drug particles have a greater surface area, which increases the rate of dissolution. Reducing particle size can improve absorption, particularly for poorly soluble drugs.

Polymorphism: The solid-state crystalline structure of a drug can affect its solubility and dissolution rate. Amorphous (non-crystalline) forms generally dissolve faster than crystalline ones

Beyond a patient's clinical outcome, formulation also impacts commercial strategy and safety.
Extended patent life: Companies can extend market exclusivity by developing patented modified-release versions of older drugs as their original patents expire.

Improved market position: An easier-to-use, once-daily product can give a manufacturer a competitive edge.

Dose dumping risk: In the case of some modified-release formulations, especially those involving opioids, co-ingestion with alcohol can disrupt the delivery system, causing the entire dose to be released at once. This can lead to a potentially fatal overdose

The Role of Formulation in Innovation

Formulation is not just about following a recipe—it is also a field of innovation. Scientists are constantly developing new ways to improve how drugs work, such as:

Nano-formulations for targeted drug delivery
Controlled-release systems for better patient convenience
Taste-masked formulations for pediatric use
Combination formulations to treat multiple conditions with one pill
These innovations enhance patient experience and improve treatment outcomes.

Challenges in Pharmaceutical Formulation

Formulating a drug isn't always easy. Some common challenges include:

Poor solubility of the drug: Some drugs don't dissolve well in water, making it hard for the body to absorb them.

Unpleasant taste or smell: These must be masked using flavoring agents or coatings.

Drug-excipient interaction: Some ingredients may react with the drug and reduce its effectiveness.

Maintaining stability: Especially in tropical climates where heat and humidity can affect the drug.

Expert formulators carefully tackle these issues to ensure safe and stable medicines.

Quality and Regulatory Compliance

Pharmaceutical formulation must comply with strict quality standards set by regulatory bodies like the FDA, WHO, or local drug control authorities. This includes:
Good Manufacturing Practices (GMP)
Documentation and validation
Batch testing and quality control

REFERENCES

1.Effect of shape on the physical properties of pharmaceutical tablets
Author links open overlay panelTipu Sultan [a], Xiaochi Xu [a], Enamul Hasan Rozin [a], Joona Sorjonen [b], Jarkko Ketolainen [b], Håkan Wikström [c], Luis Martin de Juan [d], Pirjo Tajarobi [c], Cetin Cetinkaya
International Journal of Pharmaceutics
Volume 624, 25 August 2022

2.The shape of the pill: Perceived effects, evoked bodily sensations and emotions
Olesya Blazhenkova 1,*, Kivilcim Dogerlioglu-Demir 2
Editor: Gilles van Luijtelaar3 PMCID: PMC7478620 PMID: 32898184

05 Pregnancy Prescriptions: Balancing Benefit and Risk

Author: Dr Varuna Pathak
Professor and Head Department of Obstetrics and Gynaecology
Ram Krishna Medical College Hospital and Research Centre Bhopal

Co-Author :Dr Neelu Sontakke
Assistant Professor Department of Obstetrics and Gynaecology
Ram Krishna Medical College Hospital and Research Centre Bhopal

1.1 Introduction

Pharmacotherapy in pregnancy and lactation presents a dual challenge: optimizing maternal treatment while minimizing fetal and neonatal risk. This necessitates a rigorous understanding of altered maternal pharmacokinetics, placental drug transfer, teratogenic potential, and postnatal exposure through human milk. The World Health Organization (WHO) has emphasized rational prescribing within antenatal care to improve maternal and perinatal outcomes.[1] Nonetheless, epidemiological studies demonstrate that a substantial proportion of pregnant women receive prescription drugs, many with potential embryotoxic or teratogenic risk.[2]

1.2 Maternal Physiological and Pharmacokinetic Modifications[3,4]

Pregnancy induces complex physiological adaptations that alter drug absorption, distribution, metabolism, and excretion. Key modifications include:

1. **Expanded plasma volume and increased total body water** → increases volume of distribution for hydrophilic drugs, lowering plasma concentrations.

2. **Reduced serum albumin concentration** → increases free fraction of protein-bound drugs, enhancing pharmacological activity.

3. **Increased glomerular filtration rate (GFR)** → enhances renal clearance of drugs excreted through kidney.

4. **Altered hepatic enzyme activity:**
   - CYP3A4 and CYP2D6: activity increased, leading to accelerated metabolism of substrates.
   - CYP1A2: activity decreased, reducing clearance of relevant drugs.

5. **Gastrointestinal changes (delayed gastric emptying, altered pH)** → may influence absorption kinetics.

These cumulative modifications necessitate individualized dose adjustments to maintain therapeutic efficacy and prevent maternal or fetal toxicity.

1.3 Placental Transfer and Fetal Pharmacodynamics

Placental drug transfer is governed by molecular weight, lipid solubility, protein binding, ionization state, and placental blood flow. Agents with molecular weight <1000 Da readily cross; however, lipophilic and weakly protein-bound compounds traverse more efficiently. Placental permeability increases with gestational age.[3] Fetal drug disposition is further influenced by immature metabolic pathways and limited renal clearance.

Table 1: Timing of drug exposure and fetal outcomes

Trimester	Developmental Stage	Potential Outcomes of Drug Exposure
First trimester	Organogenesis	High susceptibility to structural malformations
Second trimester	Growth and functional maturation	Risk of functional deficits and growth restriction
Third trimester	Late fetal maturation, preparation for birth	Risk of neonatal adaptation syndromes, withdrawal, or direct pharmacological toxicity

1.4 Teratogenic Mechanisms

Teratogenesis results from disruption of cell proliferation, migration, or differentiation. Mechanisms include folate antagonism (methotrexate), endocrine disruption (diethylstilbestrol), oxidative stress, and receptor-mediated signaling interference. The severity of anomalies depends on dose–response dynamics, maternal–fetal pharmacogenomics, and temporal window of exposure. For instance, isotretinoin exposure in the embryonic period induces craniofacial, cardiac, and central nervous system malformations.[3]

1.5 Risk Classification Frameworks

1.5.1 FDA Categories

While widely used, these categories oversimplified risk. Andrade et al. demonstrated that nearly half of pregnant women received medications classified as C, D, or X, underscoring ambiguity in safety interpretation.

Table 2. FDA Pregnancy Risk Categories

Category	Definition
A	Controlled human studies show no risk.
B	No evidence of risk in humans, animal data reassuring.
C	Risk not excluded; animal data positive or lacking.
D	Positive evidence of human fetal risk, benefits may outweigh risks.
X	Contraindicated due to proven teratogenicity.

1.5.2 Pregnancy and Lactation Labeling Rule (PLLR)

The FDA replaced the traditional A–X pregnancy risk categories with the Pregnancy and Lactation Labeling Rule (PLLR) in 2015.[5] The PLLR requires narrative sections in drug labeling that provide more clinically useful information. These sections include:

1. **Pregnancy:** Summarizes risks based on human and animal data, disease-associated maternal and fetal risks, and dosing adjustments during pregnancy.
2. **Lactation**: Details the presence of drug in human milk, effects on the breastfed infant, and effects on milk production.
3. **Females and Males of Reproductive Potential**: Provides information on pregnancy testing, contraception, and infertility when relevant.

The PLLR system allows clinicians to weigh evidence more accurately, supporting individualized risk–benefit assessments.

1.5.3 WHO Framework

WHO advocates restriction of unnecessary prescribing, prioritization of essential medicines, and application of evidence-based non-pharmacologic alternatives.[3]

The WHO's 2016 ANC model stresses that **rational prescribing** is part of quality maternal care. It highlights the following principles:

1. Prescriptions must be justified by clear maternal or fetal benefit.
2. Providers should explain drug safety in culturally sensitive ways.
3. Medicines with strong evidence of benefit (iron, folic acid, tetanus vaccination, intermittent preventive malaria treatment) should be universally recommended.

1.6 Epidemiology of Drug Exposure in Pregnancy

Large-scale pharmacoepidemiologic analysis (152,531 deliveries) demonstrated 64% of pregnant women were prescribed non-vitamin/mineral medications. Of these, 37.8% received category C, 4.8% category D, and 4.6% category X agents. Notably, 1.1% were prescribed category X medications post-recognition of pregnancy, underscoring persistent gaps in prescribing vigilance.[2]

1.7 Principles of Rational Prescribing in Pregnancy[1,4]

1. **Therapeutic justification:** Prescribe only when maternal benefit outweighs fetal risk.
2. **Minimal effective dose:** Limit exposure while achieving efficacy.
3. **Evidence-based drug selection:** Prefer drugs with established safety profiles; avoid novel or data-deficient agents.
4. **Avoidance of polypharmacy:** Minimize pharmacodynamic and pharmacokinetic interactions.
5. **Gestational timing:** Restrict teratogenic agents in embryogenesis; consider trimester-specific risks.
6. **Therapeutic drug monitoring (TDM)**: Apply plasma level monitoring for drugs with narrow therapeutic indices.

Table 2. Safer alternatives vs contraindicated drugs for common pregnancy conditions.

Indication	**Preferred Agents**	**Contraindicated Agents**
Hypertension	Labetalol, Methyldopa	ACE inhibitors, ARBs
Epilepsy	Levetiracetam, Lamotrigine	Valproate
Infection	Penicillins, Cephalosporins	Tetracyclines, Fluoroquinolones
Nausea/vomiting	Doxylamine, Pyridoxine	Thalidomide
Diabetes	Insulin, Metformin	Glimepiride
Thyroid disorder	Levothyroxine	Radioactive iodine
Pain management	Paracetamol, limited short-term use of opioids	NSAIDs in third trimester

1.8 Prescribing in Lactation

Most drugs appear in breast milk, typically at sub-therapeutic concentrations for infants. However, neonates, especially preterm infants, have immature metabolic clearance, increasing susceptibility.[3]

Drug excretion into breast milk depends on:

1. Molecular weight (<300 Da cross more easily)
2. Lipid solubility (lipophilic drugs accumulate in milk fat)
3. Plasma protein binding (low binding increases transfer)
4. Maternal serum concentration

1.9 Clinical Strategies

1. Utilize drugs with short half-lives and minimal milk penetration.
2. Dose post-feeding to minimize infant peak exposure.
3. Monitor infants for adverse pharmacological effects, particularly sedation or feeding difficulties.

1.10 Practical Implementation Strategies

1. **Preconception medication review**: Optimize therapy prior to conception.
2. **Patient-centered counseling:** Provide transparent risk–benefit discussions to facilitate informed consent.
3. **Non-pharmacological interventions:** Implement lifestyle modifications, behavioral therapy, and nutritional support when feasible

1.11 Conclusion

Safe prescribing in pregnancy and lactation requires integration of maternal physiology, pharmacokinetics, teratology, and neonatal pharmacology into therapeutic decision-making. Evidence-based selection, trimester-specific risk stratification, therapeutic drug monitoring, and reliance on established safety profiles are central tenets. The overarching principle is that maternal therapeutic benefit must clearly outweigh potential fetal or neonatal harm. Rational prescribing, informed by global guidelines, epidemiological evidence, and pharmacological science, remains essential to optimize outcomes across the maternal–fetal dyad.

References

1.World Health Organization. WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience. Geneva: WHO; 2016. Available from https://www.who.int/publications/i/item/9789241549912.

2. Andrade SE, Gurwitz JH, Davis RL, Chan KA, Finkelstein JA, Fortman K et al. Prescription drug use in pregnancy. Am J Obstet Gynecol. 2004;191:398–407.

3. Briggs GG, Freeman RK, Towers CV, Forinash AB. Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk. 12th ed. Philadelphia: Wolters Kluwer; 2021.

4. James DK, Steer PJ, Weiner CP, Gonik B, editors. High Risk Pregnancy: Management Options. 4th ed. Philadelphia: Saunders Elsevier; 2011.

5. U.S. Food and Drug Administration. Pregnancy and Lactation Labeling Resources [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; [cited 2025 Sep 05]. Available from: https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-resources.

06 Fertility And Pharmaceuticals

Author :- Dr. Deepti Gupta
Associate Professor, Department of Obstetrics & Gynaecology, NSCB MCH Jabalpur
Consultant & Unit Head, Ankur Fertility Clinic and IVF Centre Jabalpur

Introduction

The relationship between pharmaceuticals and human fertility represents a complex paradox in modern medicine. On one hand, pharmaceutical advancements have revolutionized the treatment of infertility, enabling millions of couples to conceive through assisted reproductive technologies (ART). On the other hand, certain medications have been implicated in contributing to the growing global burden of infertility, with unintended adverse effects on reproductive health. This dual role of pharmaceuticals reflects the intricate balance between therapeutic benefit and potential harm in the delicate realm of human reproduction. The significance of this topic has intensified against the backdrop of declining fertility rates worldwide and increasing exposure to pharmaceutical compounds through medical treatment, environmental contamination, and lifestyle factors.

The modern era of fertility pharmaceuticals began in the 1930s with the isolation of reproductive hormones and evolved dramatically with the development of the first oral contraceptives in the 1960s. Today, the global market for fertility drugs is valued at over $4 billion annually, reflecting the substantial demand for medical assistance in conception. Simultaneously, growing scientific evidence suggests that non-fertility medications—including common drugs like analgesics, antidepressants, and chemotherapy agents—may exert negative effects on reproductive function. This article comprehensively examines the multifaceted impact of pharmaceuticals on fertility, exploring both therapeutic applications and adverse effects, while considering the ethical, economic, and regulatory dimensions of this critical healthcare issue.

Fertility impairment

A patient maybe consuming prescribed or over the counter medications for myriad reasons. Few of them and possible impairment on fertility are as follows.

NSAIDs- In our country, it is very common for women to consume over the counter NSAIDs. By interfering with prostaglandins, they may interfere with ovulation. The pharmacological target of NSAIDs is cyclo-oxygenase (COX), which catalyses the first rate-limiting step in the production of prostaglandins. COX-2, one of two isoenzymes, is active in the ovaries during follicular development. Its inhibition is thought to cause luteinised unruptured follicle (LUF) syndrome.

Antidepressants- There are several types of antidepressants, each with its own mode of action & potential side effects. The following are some of the most common antidepressant medicines are:

- Selective Serotonin Reuptake Inhibitors (SSRIs): SSRIs are the most effective antidepressant medicines.
- Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)
- Monoamine Oxidase Inhibitors (MAOIs)
- Atypical Antidepressants

SSRIs use is associated with possible reduced infertility treatment efficacy as well as higher rates of pregnancy loss, preterm birth, pregnancy complications, neonatal issues and long-term neurobehavioral abnormalities in offspring. SSRI also shown to negatively impact semen quality in in vitro, animal and human studies. Fluoxetine, in particular, has been the subject of multiple studies and has been associated with gonadotoxic effects, including decreased sperm concentration and motility, increased deoxyribonucleic acid fragmentation, and decreased reproductive organ weights.

Drug induced hyperprolactinemia as cause of infertility- many common medications are known to cause hyperprolactinemia with varying frequencies. Few medicines known for high risk of hyperprolactinemia include first generation anti- psychotics (Chlorpromazine, haloperidol), 2nd generation anti psychotics like risperidone/ sulpiride, D2 receptor blockers like Domperidone/ metoclopramide, morphine, reserpine, gonadotropins and GnRH agonists (transient change) and fenfluramine. Hence it is imperative to ask for medication history in detail.

Anabolic steroids and fertility- When combined with a proper diet and an intense training program, anabolic steroids are able to increase strength and muscle mass in some people. Exogenous administration of testosterone synthesis derivatives induces negative feedback on the hypothalamic-pituitary axis and therefore inhibiting the secretion of both FSH and LH. Infertility after AAS abuse commonly presents as oligozoospermia or azoospermia, associated with abnormalities in sperm motility and morphology.

Chemotherapy and fertility- treatment for malignancies involving chemotherapy/ radiotherapy has gonadotoxic effect which depends on multiple variables like type of agent, area of irradiation, age of patient, duration of treatment etc. fertility preservation options must be offered to every patient undergoing cancer treatment. Women who receive abdominal or directed pelvic radiation at high doses are at greater risk for subsequent infertility. The most damaging chemotherapies include alkylating chemotherapies, such as cyclophosphamide, busulfan, melphalan procarbazine, and chemotherapeutic combinations that include alkylating chemotherapies.

Radiation markedly reduces the numbers of spermatocytes up to the leptotene (L) stage at 2 weeks after exposure; marked depletion of pachytene spermatocytes (P) occurs as expected by 25 days after irradiation. Dramatic declines in ejaculated sperm counts occur at about 10 weeks after irradiation, as predicted considering the epididymal and vas transit time of about 12 days. However, azoospermia is not achieved until 18 weeks. In humans, following treatment with chemotherapy agents that do not kill stem spermatogonia, there is usually a return of normal sperm count and potential fertility in many individuals within 12 weeks after the cessation of chemotherapy.

Fertility enhancement

The development of pharmaceuticals to enhance fertility represents one of the most significant achievements in reproductive medicine. Gonadotropin-based therapies have formed the cornerstone of ovarian stimulation protocols since the early days of assisted reproductive technology. The delivery systems for fertility medications have evolved alongside the drugs themselves. The transition from lyophilized powders requiring reconstitution to pre-filled pen devices has dramatically improved the patient experience.

Diet supplements and female fertility

Many preparations have been used in varying combinations in an attempt to enhance female fertility. DS for female infertility mainly contains ingredients with poor evidence of efficacy. Notably, about 80% of DS contained one or more ingredients with no evidence of effects. Five effective ingredients, respectively **melatonin, folic acid, myo-inositol, N-acetyl cysteine (NAC) and carnitine, had evidence of efficacy.** Inositols facilitate the ovulatory processes through insulin-sensitizing action. periconceptional use of folic acid was shown to reduce the incidence of non-NTD birth defects including cleft palates, upper limb reduction deficits, and genitourinary defects. effects of vitamin D3 supplementation on female fertility are still unknown. melatonin supplementation was found to exert a positive effect on oocyte quality, embryo quality and luteal function. NAC supplementation has been demonstrated to enhance spontaneous ovulation in women with polycystic ovarian syndrome, as well as to improve oocyte and embryo quality in infertile women undergoing IVF. supplementation was associated with an improvement of oocyte quality in both animal and human studies, suggesting a potential role for this molecule as adjuvant in the prevention of post-ovulatory aging in infertile women.

Endocrine disruptor chemicals & fertility

"An endocrine disruptor is an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations." Endocrine disrupting chemicals, which can be found in agriculture, industry, drugs or food chain, comprise a wide variety of exogenous chemicals including synthetic compounds able to affect hormones synthesis, metabolism, and function. Bisphenol A and phthalates are some of the chemicals that can be found frequently in food packaging industries and can be easily identified in contamination processes. Another vast group is pesticides, more specifically organophosphate and organochloride compounds that are also very linked to adverse reproductive effects. Finally, we have dioxin and dioxin-like compounds that emerge very frequently from uncontrolled incinerations, accidental fires, and waste burning, where the principal source of human contamination is through food and through environment.

BPA can disrupt at many levels, the feedback control system including hypothalamic–pituitary–gonadal (HPG) axis is one of them. this chemical can alter the levels of Gonadotropin-releasing hormone (GnRH), regulating kisspeptin expression. This alteration traduces in the release of Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), and sex hormone, which results in adverse effects on the reproduction system via irreversible impairment of the HPG axis.

Phthalates are used to make the plastic more malleable, more transparent, and with larger durability. They are considered endocrine disruptors since they have the capacity to interfere with biosynthesis, metabolism, and hormonal activity, changing the natural way of our hormonal system.

Dioxins are dangerous environmental pollutants that belong to a group called persistent organic pollutants (POPs). DDT (isomers and metabolites), as an organochlorine pesticide that has reported endocrine disruptive activity, has demonstrated its dangerous activity when binding with hormone receptors, such as AR, where displays an antagonistic role, and its capacity to increase the progesterone receptor in the ovary and uterus, also raises concerns.

The Role of Pharmaceutical Industry: Innovation, Marketing, and Influence

Beyond research, pharmaceutical companies influence clinical practice through marketing activities and educational programs for healthcare providers. These activities shape prescribing patterns and contribute to the adoption of new technologies but may also encourage the use of more expensive medications without clear evidence of superiority over established alternatives. Research into the long-term effects of pharmaceutical exposures on reproductive health must be prioritized. Current understanding of how medications affect fertility across the lifespan remains incomplete, particularly for drugs commonly used during childhood or reproductive years. Prospective cohort studies incorporating detailed exposure assessment and standardized fertility endpoints would strengthen the evidence base guiding clinical practice. Additionally, improved preclinical screening models for identifying pharmaceutical hazards to reproduction could enable earlier detection of potential risks during drug development .

Suggested reading.

1. Vitagliano A, Petre GC, Francini-Pesenti F, De Toni L, Di Nisio A, Grande G, Foresta C, Garolla A. Dietary Supplements for Female Infertility: A Critical Review of Their Composition. Nutrients. 2021 Oct 11;13(10):3552. doi: 10.3390/nu13103552. PMID: 34684554; PMCID: PMC8541636.

2. Silva ABP, Carreiró F, Ramos F, Sanches-Silva A. The role of endocrine disruptors in female infertility. Mol Biol Rep. 2023 Aug;50(8):7069-7088. doi: 10.1007/s11033-023-08583-2. Epub 2023 Jul 4. PMID: 37402067; PMCID: PMC10374778.

3. Stone S, Khamashta MA, Nelson-Piercy C. Nonsteroidal anti-inflammatory drugs and reversible female infertility: is there a link? Drug Saf. 2002;25(8):545-51. doi: 10.2165/00002018-200225080-00001. PMID: 12113640.

4. El Osta R, Almont T, Diligent C, Hubert N, Eschwège P, Hubert J. Anabolic steroids abuse and male infertility. Basic Clin Androl. 2016 Feb 6;26:2. doi: 10.1186/s12610-016-0029-4. PMID: 26855782; PMCID: PMC4744441.

5. Waimey KE, Smith BM, Confino R, Jeruss JS, Pavone ME. Understanding Fertility in Young Female Cancer Patients. J Womens Health (Larchmt). 2015 Oct;24(10):812-8. doi: 10.1089/jwh.2015.5194. Epub 2015 Jun 15. PMID: 26075731; PMCID: PMC4623984.

6. Meistrich ML. Effects of chemotherapy and radiotherapy on spermatogenesis in humans. Fertil Steril. 2013 Nov;100(5):1180-6. doi: 10.1016/j.fertnstert.2013.08.010. Epub 2013 Sep 4. PMID: 24012199; PMCID: PMC3826884.

07 Menopause & Medicines

Author-- Dr Ginny Gupta
MBBS, MD, FICOG
(Ex-PGI Chandigarh)

Menopause is the permanent cessation of menstruation due to declining ovarian hormone production, leading to somatic symptoms disturbing day to day life and some having serious health implications for later years .

Menopause is a natural biological process when a woman's ovaries stop producing estrogen and progesterone, leading to the end of menstruation. (It is called premature if occurring before 30 yrs) This hormonal shift causes various symptoms, including:

Vasomotor symptoms: Hot flashes and night sweats. Genitourinary symptoms: Vaginal dryness, irritation, and urgency. Other symptoms: Fatigue, trouble sleeping, mood changes, brain fog and weight gain.
Myalgias caused by sarcopenia and worsened by osteoporosis due to accelerated bone loss in absence of oestrogen decrease mobility making the women injury prone and increase fall risk .

What is Menopause Hormone Therapy (MHT)?
MHT involves taking medications containing hormones to alleviate symptoms and prevent some long-term complications of estrogen deficiency.
Types: Treatment can involve estrogen, progestogen (to protect the uterus), or combined forms, delivered via oral pills, patches, or gels.

Effects:
MHT eAectively reduces hot flashes, improves sleep, alleviates vaginal dryness, and helps prevent bone loss and fractures.

Risks and Benefits of MHT
The benefits and risks of MHT depend on individual factors, including age, health conditions, and the type, dose, and route of administration.
Benefits: The benefits are most pronounced for healthy women initiating therapy within 10 years of menopause or before age 60.

Risks:
Risks, such as an increased risk of heart disease, stroke, and blood clots, are higher for women starting MHT more than 10 years after menopause or who are over 60.
(Some younger women are also predisposed to blood clots due to habits or constitution) Women with estrogen dependent cancers or with a high risk of such are to be carefully excluded from MHT .

Transdermal estrogens: These may be preferred as they avoid the liver, reducing the risk of blood clots and other negative eAects, especially for women with cardiovascular risk factors or thrombophilic disorders.

Key Considerations in patient selection for MHT

1. ESTABLISH INDICATION for usage then INDIVIDUALISATION of therapy

MHT is not a one-size-fits-all treatment; therapy should be tailored to each woman's needs and risk factors.

2. Rule out the contraindications.

3. Shared Decision-Making

Discussing the potential benefits and risks with a healthcare provider is essential for making an informed decision.

4. Periodic Reevaluation

The benefits and risks of continuing therapy should be reviewed periodically, and treatment should be for the shortest duration with the lowest dose needed for the documented indication.

THE DRUGS IN USE

Various oestrogen formulations available for menopausal women to oAset symptoms are :
Conjugated equine estrogens Estradiol valerate (newer low dose liver friendly) Estradiol hemihydrate (newer….) Estrogen patch / gel (by passing the liver)

The estrogen therapy needs addition of progesterone for endometrial protection of uterus if present (or any endometriotic deposits) (Estrogen alone is for woman with absent uterus) Progesterone formulauions :

LNGIUS Micronised progesterone Dydrogesterone MPA - methyl progesterone acetate) Drospirenone **A Synthetic non sex hormone steroid :** Selective estrogen receptor modulator SERM Tibolone Benefits vasomotor , bone friendly , uterus friendly .

Drugs reserved for local eAect for genitourinary syndrome of menopause : Ospemiphene Estrogen vaginal cream Drug reserved for careful use in female sexual disorder of menopause :

Testosterone (patch) The various menopause specific drugs are listed above but to be used with careful patient selection according to symptoms and detailed risk evaluation . Use lowest dose for the shortest time .A shared decision making is vital to get the maximum benefit out of these agents to improve the woman’s health and decrease all cause mortality and morbidity from heart disease , atherosclerosis , cancers , osteoporosis , congnitive dysfunction . Other health improving medications : Calcium , Vitamin D , macro and micronutrients are vital supplements in menopause. Black cohosh , Soya Isoflavonnes used for oestrogen like action but do not give reliable concentration of hormone . These are not endorsed by international Menopause bodies .

08 Antibiotic Alarm: Fewer Prescriptions Today, Fewer Superbugs Tomorrow

Author-- Dr. Monika Gupta
West Zone Coordinator, PAC committee FOGSI

Co-Author- Dr. Purvi Agarwal
DGO, DNB, FETAL MEDICINE.
RAIPUR.

Introduction — Why This Matters Now

Antibiotics have been a cornerstone of modern obstetrics and gynecology, saving millions of lives since the mid-20th century. They have prevented puerperal sepsis, reduced postoperative infections, and treated conditions from pelvic inflammatory disease (PID) to urinary tract infections (UTIs) with remarkable success.

However, the same miracle drugs are now facing an existential threat — antimicrobial resistance (AMR). The World Health Organization lists AMR among the top ten global public health threats. Resistant infections are rising in both community and hospital settings, and in OBGYN, the consequences can be devastating.

The stakes in our specialty are doubled — we often treat two patients at once: the mother and her fetus. Resistant infections jeopardize both, and our prescribing decisions have far-reaching implications for maternal health, neonatal outcomes, and community resistance patterns.

Part 1: Understanding Antibiotic Resistance — The Science Behind the Crisis

Antibiotic resistance refers to the capacity of bacteria to survive, adapt, and continue multiplying even in the presence of antibiotics that would normally kill them or halt their growth, a phenomenon rooted in natural evolution but greatly accelerated by the misuse and overuse of these drugs in humans, animals, and agriculture. Resistance can develop through genetic mutations—spontaneous changes in bacterial DNA that alter cellular processes—or via horizontal gene transfer, in which bacteria exchange resistance genes directly, sometimes even across unrelated species, rapidly spreading survival advantages within microbial communities. Once acquired, these resistance mechanisms manifest in several ways: bacteria may neutralize antibiotics by producing enzymes such as β-lactamases that chemically degrade or modify the drug; expel antibiotics through efflux pumps that actively transport the drug out of the cell; alter their own target sites by changing the structure of proteins or enzymes so the antibiotic can no longer bind effectively; or block antibiotic penetration by modifying their cell membranes to reduce permeability. Collectively, these strategies not only render standard treatments ineffective but also fuel a global public health crisis, making once-routine infections harder, costlier, and sometimes impossible to treat.

Why Resistance Matters in OBGYN

Antimicrobial resistance in obstetrics and gynecology is far from being a distant laboratory statistic—it has direct, daily implications for patient safety and clinical decision-making.

Resistant pathogens complicate common scenarios such as post-cesarean surgical site infections, which can lead to prolonged hospitalization, repeated interventions, and delayed maternal recovery; postpartum endometritis caused by multidrug-resistant organisms, which often necessitates escalation to costlier and more toxic second-line drugs; recurrent urinary tract infections in pregnancy due to ESBL-producing E. coli, where limited oral treatment options increase the risk of pyelonephritis, preterm labor, and low birth weight; and pelvic inflammatory disease caused by resistant Neisseria gonorrhoeae or Mycoplasma genitalium, threatening reproductive health and fertility. In India, the challenge is amplified by some of the world's highest resistance rates to cephalosporins, fluoroquinolones, and aminoglycosides in key pathogens like E. coli, Klebsiella pneumoniae, and Staphylococcus aureus, severely narrowing effective therapeutic choices. Alarmingly, resistant strains are now increasingly detected in cases of neonatal sepsis, often traced back to maternal genital tract colonization, highlighting the intimate link between maternal and newborn health and underscoring the urgent need for targeted infection prevention, rational antibiotic use, and strengthened microbiological surveillance in obstetric and gynecologic practice.

Part 2: Why OBGYN Must Lead the Stewardship Effort

Obstetrics and gynecology is one of the highest antibiotic-utilizing specialties, placing the field in a unique position to lead antimicrobial stewardship efforts. Cesarean sections, which rank among the most frequently performed surgeries worldwide, almost universally involve prophylactic antibiotic administration, and additional common interventions—such as miscarriage management, mastitis treatment, postpartum fever evaluation, and a wide spectrum of gynecologic surgeries—frequently result in antibiotic prescriptions, often initiated without culture confirmation. Despite clear evidence-based recommendations, prescribing patterns in many hospitals still reflect habit rather than protocol, with extended post-operative antibiotic courses being administered "just in case," even when both WHO and ACOG guidelines advocate for single-dose prophylaxis in most OB-GYN surgical procedures. Complicating this is the "safety paradox" of pregnancy: the clinical instinct to avoid missing even a single potential infection leads to early, broad-spectrum, or sometimes unnecessary prescribing, driven by the understandable desire to protect both mother and fetus. However, while this caution is well-intentioned, it must be carefully balanced against the long-term consequences of antimicrobial resistance, the principles of rational antibiotic use, and considerations of fetal safety, making it imperative for OB-GYN practitioners to model disciplined, evidence-based prescribing practices.

Part 3: Where Overuse Happens Most in OBGYN

Clinical Area	Recommended Practice	Common Misuse	Risk of Resistance
Cesarean Section	Single dose cefazolin before incision; add azithromycin in high-risk laboring patients	Post-op antibiotics for 3–5 days without indication	MDR Klebsiella
Uncomplicated Vaginal Delivery	No antibiotics unless GBS prophylaxis, chorioamnionitis, or complex tears	Routine antibiotics in normal delivery	Community MRSA
Mild Mastitis	Breastfeeding, warm compress; antibiotics if bacterial	Empirical antibiotics for all mastitis	Resistant *S. aureus*
Clean Laparoscopy	No prophylaxis unless entering vagina/bowel	Blanket prophylaxis	Gram-negative resistance
Asymptomatic Bacteriuria	Treat only if culture positive	Empiric therapy without culture	ESBL *E. coli*

Part 4 – The 5 – R Stewardship framework for gynecologists

The 5-R Stewardship Framework provides gynecologists with a structured, evidence-based approach to minimize unnecessary antibiotic use while ensuring optimal patient outcomes. Right Indication means prescribing antibiotics only when there is clear evidence of a bacterial infection or a strong clinical suspicion supported by relevant tests, avoiding their use for viral or self-limiting conditions. Right Drug emphasizes selecting an antibiotic guided by culture results and the hospital's local antibiogram, starting with narrow-spectrum agents whenever possible to minimize collateral damage to normal flora and slow resistance development. Right Dose requires tailoring the antibiotic dose to the patient's weight, renal and hepatic function, and specific pharmacokinetic considerations to ensure therapeutic levels are achieved without underdosing that fosters resistance. Right Duration stresses limiting therapy to the shortest effective course supported by guidelines and clinical evidence, thereby reducing the risk of adverse effects and resistance from prolonged exposure. Finally, Right Review involves systematically reassessing the patient's condition and laboratory results at 48–72 hours, then de-escalating to a narrower agent, switching to oral therapy, or stopping antibiotics altogether if the initial suspicion is not confirmed. Together, these five principles create a disciplined prescribing culture that preserves antibiotic effectiveness for the future while safeguarding maternal and neonatal health in obstetric and gynecologic practice.

Part 5: Evidence-Based Prophylaxis & Treatment Surgical prophylaxis.

Procedure	Regimen	Notes
Cesarean Delivery	Cefazolin 2 g IV (3 g if ≥120 kg) pre-incision; ± azithromycin	No post-op antibiotics unless indicated
Hysterectomy	Cefazolin ± metronidazole (for vaginal approach)	Single dose only
Clean Laparoscopy	None unless contaminated	Diagnostic cases need none
Operative Vaginal Delivery	Single prophylactic dose if high-risk	High risk: prolonged rupture, instrumentation

Common OBGYN Infections

Common infections encountered in obstetric and gynecologic practice require targeted, evidence-based management to ensure efficacy while minimizing resistance risk. Urinary tract infections in pregnancy should be treated with first-line agents such as nitrofurantoin (avoiding use near term due to the risk of neonatal hemolysis) or cephalexin, while ampicillin and amoxicillin are generally avoided because of high resistance rates among E. coli in many regions. Pelvic inflammatory disease (PID) management follows CDC recommendations, combining intramuscular ceftriaxone with doxycycline and metronidazole to cover Neisseria gonorrhoeae, Chlamydia trachomatis, and anaerobes, with concurrent partner testing and treatment to prevent reinfection. Sexually transmitted infections (STIs) demand organism-specific therapy: uncomplicated gonorrhea is treated with a single intramuscular dose of 500 mg ceftriaxone, while chlamydial infection in pregnancy is best managed with a single oral dose of 1 g azithromycin, which is safe and effective for both mother and fetus.

Postpartum endometritis—a common post-cesarean complication—requires broad coverage, typically clindamycin plus gentamicin for aerobic and anaerobic pathogens, or ampicillin-sulbactam as an alternative regimen, with prompt initiation critical to reducing morbidity. Careful adherence to these regimens ensures optimal outcomes while aligning with antimicrobial stewardship principles.

Part 6: Antibiotic Safety in Pregnancy & Lactation

Antibiotic safety in pregnancy and lactation is a crucial consideration in obstetric and gynecologic practice, as both maternal well-being and fetal or neonatal safety must be safeguarded. Generally safe options during pregnancy include penicillins, cephalosporins, clindamycin, nitrofurantoin (avoided at term due to the risk of neonatal hemolysis), and fosfomycin, all of which have reassuring safety profiles when used appropriately. Certain agents, such as tetracyclines, aminoglycosides, and fluoroquinolones, should be avoided unless there is no suitable alternative, given their potential risks—tetracyclines can affect fetal bone and teeth development, aminoglycosides carry ototoxicity and nephrotoxicity risks, and fluoroquinolones have been linked to cartilage toxicity in animal studies. During breastfeeding, most penicillins, cephalosporins, and macrolides are considered compatible, but clinicians should remain alert for possible infant gastrointestinal disturbances, such as diarrhea or candidiasis, and advise mothers accordingly. By combining knowledge of drug safety profiles with judicious prescribing, clinicians can ensure effective infection control while minimizing potential harm to the developing fetus or nursing infant, thereby aligning clinical care with both stewardship and perinatal safety principles.

Part 7: Implementing Stewardship in Practice

Implementing antibiotic stewardship in everyday obstetric and gynecologic practice requires a structured, team-based approach that combines clinical discipline with ongoing education. The use of surgical prophylaxis checklists ensures that antibiotics are given only when indicated, in the correct dose, at the correct time, and for the correct duration, reducing unnecessary exposure while maintaining surgical safety. Regular education of junior doctors and nursing staff on updated guidelines reinforces best practices, addresses common misconceptions, and empowers frontline providers to confidently prescribe—or withhold—antibiotics in line with evidence-based protocols. A monthly audit of antibiotic prescriptions helps identify patterns of overuse, deviation from guidelines, or missed opportunities for de-escalation, creating a feedback loop for continuous improvement. Incorporating local antibiogram data into prescribing decisions ensures antibiotic choices are tailored to the most prevalent and resistant pathogens in the specific hospital or community setting, maximizing effectiveness and minimizing resistance risk. Finally, patient counseling plays a critical role—explaining to women why “no antibiotic” may sometimes be the safest choice not only builds trust but also reduces pressure on clinicians to prescribe unnecessarily, fostering a culture of shared responsibility in combating antimicrobial resistance.

Part 8: The Ethical Imperative

The ethical imperative in antibiotic stewardship for obstetricians and gynecologists stems from a dual responsibility that extends beyond the immediate clinical encounter. We owe it to current patients to provide treatment that is both effective and safe, ensuring that they receive antibiotics only when truly necessary, in the right dose, and for the right duration—thereby protecting them from avoidable side effects, drug interactions, and the long-term consequences of resistance. Equally, we bear a duty to future patients, safeguarding the effectiveness of antibiotics for the next generation by preventing the unnecessary use that accelerates the spread of resistant organisms.

Every unwarranted prescription, however small it may seem, incrementally erodes our therapeutic arsenal, inching us closer to a grim reality reminiscent of the pre-antibiotic era, when postpartum sepsis, endometritis, and wound infections were leading causes of maternal death and disability. Upholding this responsibility is not merely a matter of clinical prudence—it is a moral obligation to preserve life, protect public health, and honor the trust that patients place in our profession.

Final Takeaway

The final takeaway for obstetricians and gynecologists is clear: antibiotic stewardship is not an optional add-on to clinical practice—it is a core responsibility that blends clinical excellence, ethical duty, and public health leadership. In a specialty where antibiotics are among the most frequently prescribed drugs, every prescribing decision carries weight, influencing not only the immediate outcome for the woman in front of us but also the broader resistance patterns that will determine treatment options for future mothers and newborns. By strictly adhering to evidence-based guidelines, tailoring therapy to culture results, limiting prophylaxis to the correct timing and duration, and actively engaging in patient education, OB-GYN practitioners can directly slow the spread of resistant organisms. The guiding principle is simple yet powerful: fewer prescriptions today mean fewer superbugs tomorrow. This is not just about preserving drug efficacy—it is about ensuring that childbirth, miscarriage care, gynecologic surgeries, and postpartum recovery remain safe in the decades to come, sparing future generations from returning to an era when preventable infections claimed countless maternal and neonatal lives.

References

1. Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States. Atlanta: CDC; 2023.

2. World Health Organization. Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report. Geneva: WHO; 2024.

3. Indian Council of Medical Research. Annual Report: Antimicrobial Resistance Surveillance and Research Network (ICMR-AMRSN). New Delhi: ICMR; 2024.

4. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 199: Use of Prophylactic Antibiotics in Labor and Delivery. Obstet Gynecol. 2018;132(3):e103–19.

5. Sheehan SR, Montgomery AA, Carey M, et al. Oxytocin for preventing postpartum haemorrhage. Cochrane Database Syst Rev. 2014;(10):CD001808.

6. World Health Organization. Global Guidelines for the Prevention of Surgical Site Infection. Geneva: WHO; 2018.

7. National Institute for Health and Care Excellence. Surgical site infections: prevention and treatment. NICE Clinical Guideline CG74. London: NICE; 2019.

8. Centers for Disease Control and Prevention. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1–187.

9. World Health Organization. WHO AWaRe Classification Database of Antibiotics. Geneva: WHO; 2023.

10. World Health Organization. Global Action Plan on Antimicrobial Resistance. Geneva: WHO; 2015.

11. Zaidi AK, Huskins WC, Thaver D, Bhutta ZA, Abbas Z, Goldmann DA. Hospital-acquired neonatal infections in developing countries. Lancet Infect Dis. 2005;5(10):651–60.

12. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70(3):195–283.

13. Davies J, Davies D. Origins and evolution of antibiotic resistance. Microbiol Mol Biol Rev. 2010;74(3):417–33.

14. Allen HK, Donato J, Wang HH, Cloud-Hansen KA, Davies J, Handelsman J. Call of the wild: antibiotic resistance genes in natural environments. Nat Rev Microbiol. 2010;8(4):251–9.

15. Bush K, Bradford PA. Epidemiology of β-lactamase-producing pathogens. Clin Microbiol Rev. 2020;33(2):e00047-19.

---XXXXX---

09 Analgesics & Anti-inflammatories in Gyn Practice

Author-- Dr Divya M B
Assistant Professor, Department of Obstetrics and Gynaecology, AIIMS Deoghar, Jharkhand.

Co- Author :- Dr Priyanka Rai
Additional Professor and HOD, Department of Obstetrics and Gynaecology, AIIMS Deoghar, Jharkhand.

Introduction

One of the most prevalent complaints in gynaecological practice is pain. It may present as chronic pain, as in endometriosis and pelvic congestion syndrome, or as acute pain, as in ovarian torsion, haemorrhagic cyst, or pelvic inflammatory disease. Gynaecological malignancies and postoperative patients also experience pain. Over 50% of women of reproductive age suffer from dysmenorrhea alone, which frequently lowers their quality of life. Similarly, early ambulation and recovery are still significantly impacted by postoperative pain.

Gynaecological pain is still mostly managed with analgesics and anti-inflammatory medications, especially non-steroidal anti-inflammatory medicines (NSAIDs). An improved quality of life, patient comfort, and symptom relief all depend on the proper use of analgesics and anti-inflammatory drugs. However, if they are used irrationally, whether through overprescription, improper combinations, or insufficient dosage, it may result in negative side effects and low patient satisfaction. The World Health Organisation (WHO) promotes the concept of rational medicine usage, which suggests that patients should be prescribed drugs suitable for their clinical needs and in dosages that meet their requirements.

The Principles of Rational Use of Analgesics

1. Individualization of therapy – The subjective sensation of pain differs depending on its cause. For rational prescribing, the medication selection must be tailored to the particular illness (e.g., neuropathic modulators for chronic pelvic pain and NSAIDs for dysmenorrhea). The kind, severity, comorbidities, and patient characteristics of the pain should all be taken into consideration while choosing a medicine.

2. Stepwise approach (ERAS guidelines) –

Start with non-opioids → add opioids if needed → use adjuvants for chronic pain.

- Non-opioids (NSAIDs, paracetamol) for mild pain
- Weak opioids (tramadol) ± non-opioids for moderate pain
- Strong opioids (morphine, fentanyl) ± adjuvants for severe pain.

3.Multimodal analgesia – Combining drugs with different mechanisms to maximize relief and minimize toxicity. The use of agents with complementary mechanisms, such as paracetamol + NSAIDs + regional anaesthesia, is now standard in postoperative care.

4. Shortest effective duration & lowest effective dose – Avoid prolonged NSAID or opioid use. Rational use requires prescribing the lowest effective dose for the shortest necessary time.

5. Safety monitoring – Check renal, hepatic, gastrointestinal, and cardiovascular risks. NSAIDs are associated with gastrointestinal, renal, and cardiovascular risks, while opioids may cause dependence and constipation.

Types of Common Analgesics

I. Non-Opioid Analgesics

- **NSAIDs (Non-steroidal anti-inflammatory drugs)**
  - Mechanism: Inhibit cyclooxygenase (COX) → ↓ prostaglandin synthesis.
  - Role: First-line in dysmenorrhea, endometriosis-related pain, pelvic inflammatory disease, and postoperative pain.
  - Common agents: Ibuprofen, Naproxen, Mefenamic acid, Diclofenac.
  - Dosage – Ibuprofen 200 to 400mg 6^{th} hourly, Naproxen 500mg 12^{th} hourly, Mefenamic acid 500mg followed by 250mg 6^{th} hourly, Diclofenac 100mg/day
  - Usage is limited due to the side effects.
  - Considerations: Gastric irritation, renal impairment, cardiovascular risk.

- **Paracetamol (Acetaminophen)**
  - Analgesic & antipyretic, weak anti-inflammatory.
  - Useful in mild-to-moderate pain, safe in pregnancy, and has fewer gastrointestinal side effects.
  - Highest oral dose is 100mg/kg and intravenous dose of 4g/day.
  - Hepatotoxicity risk in overdose.

- **Metamizole**
  - Has spasmolytic effect.
  - It has high tolerability and low organ toxicity.
  - Dose – 500mg 6^{th} to 8^{th} hourly.
  - Can cause agranulocytosis.

II. Opioid Analgesics

- Reserved for moderate-to-severe acute pain (e.g., postoperative, advanced malignancy).
- Examples: Tramadol, Morphine, Fentanyl.
- Dosage – Tramadol 50mg 8^{th} hourly, Morphine 4mg 6^{th} or 8^{th} hourly, Fentanyl 25 to 50mcg i.m/i.v.
- Considerations: Dependence, constipation, nausea, sedation.

III. Other Adjuvant Analgesics

- Used in chronic pelvic pain syndromes.
- For example: Neuropathic pain modulators: Gabapentin, Pregabalin, Amitriptyline.
- Dosage – Gabapentin 300mg od, Pregabalin 25mg od, Amitriptyline 10 to 25mg od.

NSAIDs in Gynaecological Pain

NSAIDs are the cornerstone of gynaecological pain management due to their ability to inhibit prostaglandins, which play a central role in uterine contractility, inflammation, and nociceptor sensitization.

- NSAIDs remain the mainstay due to anti-prostaglandin effects.
  - Primary dysmenorrhea: Reduce uterine prostaglandins, relieve pain, decrease menstrual blood loss.
  - Endometriosis: Partial relief of pain.
  - PID: Symptomatic relief alongside antibiotics.
  - Post-surgery: Reduce inflammation and pain, facilitate early ambulation.

Advantages

- Rapid onset of action
- High efficacy in dysmenorrhea
- Opioid-sparing effect in surgery
- Widely available and cost-effective

Contraindications

- Gastrointestinal toxicity (ulcers and bleeding)
- Renal impairment
- Increased cardiovascular risk in predisposed patients
- Contraindicated in late pregnancy (because of risk of ductus arteriosus closure, oligohydramnios)

Analgesics Choices in Specific Gynaecological Conditions

a) Dysmenorrhea

- Pathophysiology: Excess prostaglandin F2α → strong uterine contractions and ischemia.
- First-line treatment: NSAIDs (Mefenamic acid, Ibuprofen).
- Rational approach:
  - Start 12–24 hours before menstruation in severe cases.
  - Continue for 48–72 hours.
  - If ineffective, consider hormonal therapy (OCPs, LNG-IUS).

b) Endometriosis

- Pain results from ectopic endometrial implants, inflammation, and adhesions.
- NSAIDs provide symptomatic relief but do not alter disease progression.
- Rational approach: Use as adjuncts with definitive therapies (surgery, hormonal suppression).

Pelvic Inflammatory Disease (PID)

- Pain is inflammatory and infectious.
- NSAIDs relieve pain but should never replace antibiotics.
- Rational approach: Symptomatic relief only, along with antimicrobials.

Ovarian Cysts and Benign Masses

- Ruptured or haemorrhagic cysts may cause acute pain.
- NSAIDs or paracetamol may suffice in stable patients.
- Opioids are reserved for severe pain or in emergency settings.

e) Chronic Pelvic Pain

- Often multifactorial: endometriosis, adhesions, neuropathic pain, psychosocial factors.
- Rational management requires a multidisciplinary approach:
    - NSAIDs for the inflammatory component.
    - Neuropathic agents (Gabapentin, Pregabalin, Amitriptyline).
    - Psychological support, physiotherapy.
    - Avoid long-term opioids unless in a palliative setting.

f) Gynaecological Malignancies

- Pain is multifactorial—tumour infiltration, post-radiation fibrosis, nerve compression.
- Rational use follows the WHO analgesic ladder:
    - 1st step - Paracetamol/NSAIDs.
    - 2nd step - Weak opioids (tramadol, codeine).
    - 3rd step - Strong opioids (morphine, fentanyl).

Analgesics Use in Post-Surgical Care

Goals of Postoperative Pain Management

- Relieve suffering.
- Enable early mobilization and deep breathing, reducing risks of pneumonia, venous thromboembolism, and ileus.
- Facilitate early discharge.
- Prevent transition to chronic pain.

Postoperative Pain Mechanisms

- Tissue injury → inflammatory mediators (prostaglandins, cytokines) → nociceptor sensitization.
- Central sensitization may lead to exaggerated pain responses.

Analgesic Options

1. **Paracetamol** – baseline analgesia; safe, opioid-sparing.
2. **NSAIDs** – reduce inflammation and opioid requirement; caution in bleeding risk.
3. **Opioids** – for breakthrough pain; rational use mandates low dose, short course, and monitoring for side effects.
4. **Regional anaesthesia and local infiltration** – Trans-abdominis plane blocks, epidural analgesia, paracervical blocks reduce systemic analgesic requirement.

Multimodal Analgesia and ERAS Protocols

- Enhanced Recovery After Surgery (ERAS) protocols emphasize opioid-sparing multimodal strategies:
    - Pre-emptive paracetamol + NSAID before incision.
    - Intraoperative regional blocks.
    - Postoperative scheduled non-opioids with opioids reserved for rescue.

- Benefits: reduced hospital stay, reduces requirement of opioids, faster ambulation, improved patient satisfaction.

Special Considerations

- **Pregnancy:**
  - Paracetamol is safe.
  - NSAIDs avoided in 3rd trimester (risk of ductus arteriosus closure, oligohydramnios).
  - Opioids with caution (risk of neonatal withdrawal, respiratory depression).

- **Breastfeeding:**
  - Ibuprofen and Paracetamol are safe.
  - Avoid codeine due to the risk of neonatal toxicity.

- **Comorbidities:**
  - GI disease → prefer COX-2 inhibitors or combine with PPI.
  - Renal/hepatic impairment → dose adjustments needed.

- **Elderly:** Lower doses, cautious use of opioids due to fall risk.

Adverse Effects and Monitoring

NSAIDs

- Gastrointestinal bleeding, peptic ulcers.
- Renal dysfunction, fluid retention.
- Hypertension, thrombotic events (selective COX-2 inhibitors).

Paracetamol

- Hepatotoxicity in overdose.

Opioids

- Constipation, nausea, vomiting.
- Sedation, respiratory depression.
- Dependence and withdrawal syndromes.

Rational use requires patient education, periodic monitoring, dose adjustments, and prophylactic measures (e.g., Proton pump inhibitors with NSAIDs).

Conclusion

Rational use of analgesics and NSAIDs in gynaecological practice is essential for effective pain management, patient safety, and improved outcomes. NSAIDs remain the mainstay for inflammatory pain such as dysmenorrhea and endometriosis, while paracetamol offers a safe alternative across populations, including pregnancy. Opioids should be reserved for severe or cancer-related pain, always with caution regarding dependence and side effects.

In postoperative care, multimodal analgesia and ERAS protocols emphasize opioid-sparing strategies, combining paracetamol, NSAIDs, and regional techniques. It also requires consideration of comorbidities, pregnancy status, and patient preference, along with vigilance for adverse events. The fundamental principles are right drug, right patient, right dose at the right time.

Learning points

- Rational analgesic use in gynaecology emphasizes NSAIDs as first-line for inflammatory pain, paracetamol for safety, and opioids only when essential.
- In postoperative care, multimodal opioid-sparing analgesia is the standard of care.
- The ultimate goal: effective pain relief, reduced side effects, early recovery, and improved quality of life.

References

1. Ohnesorge H, Günther V, Grünewald M, Maass N, Alkatout İ. Postoperative pain management in obstetrics and gynecology. Journal of the Turkish German Gynecological Association. 2020 Dec 4;21(4):287.

2. Ballantyne JC, Kalso E, Stannard C. WHO analgesic ladder: a good concept gone astray. Bmj. 2016 Jan 6;352.

3. Ireland LD, Allen RH. Pain management for gynecologic procedures in the office. Obstetrical & gynecological survey. 2016 Feb 1;71(2):89-98.

4. Livshits A, Seidman DS. Role of non-steroidal anti-inflammatory drugs in gynecology. Pharmaceuticals. 2010 Jul 5;3(7):2082-9.

5. Toledano RD, Kodali BS, Camann WR. Anesthesia drugs in the obstetric and gynecologic practice. Reviews in Obstetrics and Gynecology. 2009;2(2):93.

6. Ismail S, Siddiqui AS, Rehman A. Postoperative pain management practices and their effectiveness after major gynecological surgery: An observational study in a tertiary care hospital. Journal of Anaesthesiology Clinical Pharmacology. 2018 Oct 1;34(4):478-84.

--xxxxx---

10 Emergency Medications in the Labour Room

Author-- Dr. Jyothi G. S.
MBBS, MD OBG, PGDMLE, FICOG, FICMCH
Professor and Head,
Department of Obstetrics & Gynaecology,
Ramaiah Medical College & Hospitals,
Bengaluru 560054

Co- Author :- Dr. Varsha G.
MBBS, MS OBG Senior Resident
Department of Obstetrics and Gynaecology,
Ramaiah Medical College and Hospitals,
Bengaluru 560054

When Every Second Feels Like an Hour

It's 2:13 a.m. The room is warm with the hum of monitors and the soft cries of a newborn in the next cot. The delivery was smooth, until now. A nurse's voice cuts through the stillness: "Doctor, she's bleeding!"

You glance at the blood-soaked pads, the postpartum uterus boggy under your hand. Your mind shifts into emergency mode. "PPH! Oxytocin, stat." In less than a breath, the first-line uterotonic is drawn, checked, and injected. The bleeding slows, the uterus firms. Another life is steered away from the brink.

If you've been in a labour room long enough, you know these scenes aren't rare. Obstetric emergencies don't wait for a consultant's arrival or the pharmacy's opening hours. They arrive unannounced, often at the worst possible time, and demand one thing: immediate, precise drug intervention.

Why a Ready List Saves Lives

Every obstetric unit should have a pre-packed, labelled, and routinely checked emergency drug tray. This is not about convenience - it's about survival.

WHO's Managing Complications in Pregnancy and Childbirth (2017) states that lifesaving medications for maternal emergencies should be:

- Stored in a single, standardised location in every labour room.
- Checked at the start of each shift for stock and expiry.
- Clearly labelled with dose charts to avoid errors under pressure.

A delay of even 2-3 minutes in retrieving and preparing a drug can change an outcome from recovery to catastrophe. Every ampoule in the tray has a purpose, and knowing when and how to use each is as critical as having them.

The Big Five Emergencies- and Their Life-Saving Medications

1. Postpartum Haemorrhage (PPH)

PPH remains the leading cause of maternal death worldwide, responsible for up to 27% of maternal deaths according to WHO. In most cases, uterine atony is the culprit and uterotonics are our first weapon.

Primary drug:

- Oxytocin- 10 IU IM after birth or 20-40 IU in 1 L NS over 60 drops/min.

1. Why it matters: Oxytocin acts quickly on uterine smooth muscle, enhancing rhythmic contractions and reducing bleeding.
2. Safety tip: Avoid undiluted IV bolus- rapid infusion can cause hypotension and arrhythmias.

If bleeding persists:

- Methylergometrine- 0.2 mg IM; may repeat q2–4h.

1. Why it matters: Potent, sustained uterine contraction.
2. Safety tip: Contraindicated in hypertension and pre-eclampsia- can cause dangerous vasospasm.

Misoprostol- 800-1000 µg PR or 600 µg SL/oral.

1. Why it matters: Heat-stable, low-cost, excellent for low-resource settings.

Carboprost tromethamine (15-methyl $PGF_2\alpha$)- 250 µg IM q15-90 min (max 8 doses).

1. Safety tip: Avoid in asthmatics due to bronchospasm risk.

Adjunctive therapy:

- Tranexamic Acid (TXA)- 1 g IV over 10 min within 3 hours of PPH onset; repeat after 30 min if bleeding continues.

1. Evidence: WOMAN Trial (2017)- early TXA reduced death from bleeding without increasing thromboembolic events.

2. Hypertensive Crisis & Eclampsia

A woman in labour with a blood pressure of 170/115 mmHg and blurred vision is a ticking time bomb. Stroke, organ damage, fetal distress- all can unfold within minutes.

The goal: lower BP safely and prevent seizures.

Antihypertensives:

Labetalol- 20 mg IV over 2 min; escalate in increments to max 300 mg.

- Benefit: Dual α- and β-blockade without major maternal tachycardia.

Hydralazine- 5-10 mg IV every 20-40 min.

- Benefit: Direct vasodilator, good for acute BP drops.

Nifedipine- 10 mg oral capsule (bite and swallow); repeat after 20-30 min.

- Benefit: Fast, effective oral option when IV access is delayed.

Seizure prophylaxis & treatment:

Magnesium Sulphate (Pritchard regimen)- 4 g IV over 5 min + 10 g IM (5 g in each buttock), then 5g IM q4h for 24 h after last seizure or delivery.

- Why it matters: Gold standard for preventing recurrent eclampsia.
- Safety tip: Monitor respiratory rate (>12/min), patellar reflexes, and urine output (>25 mL/h).
- Antidote: 10 mL of 10% calcium gluconate IV slowly.

3. Sepsis & Septic Shock

Infections in pregnancy and postpartum can spiral into septic shock alarmingly fast. The golden hour is literal here- every hour's delay in antibiotics increases mortality.

Empiric antibiotic therapy:

- Ampicillin 2 g IV every 6 hours + Gentamicin 5 mg/kg IV once daily- good initial coverage for Gram-positive and Gram-negative organisms.
- Ceftriaxone 2 g IV once daily- convenient broad-spectrum alternative.
- Piperacillin Tazobactam 4.5 g IV every 6-8 hours- for suspected resistant Gram-negative infections or hospital-acquired sepsis.
- Metronidazole 500 mg IV every 8 hours- add if anaerobic coverage is needed (e.g., pelvic abscess, septic abortion).

If hypotension persists despite fluids:

- Norepinephrine- start at 0.05–0.1 μg/kg/min, titrate to maintain MAP ≥65 mmHg.

Why it matters: First-line vasopressor in pregnancy-compatible septic shock.

4. Anaphylaxis

Whether triggered by antibiotics, latex, or oxytocin, anaphylaxis is a race against airway collapse.
First-line:

- Epinephrine- 0.5 mg IM (1:1000) into mid-thigh; repeat q5-15 min if no improvement.

Why it matters: The only drug that reverses airway swelling and circulatory collapse fast enough.

Adjuncts:

- Chlorpheniramine 10 mg slow IV.
- Hydrocortisone 200 mg IV.
- High-flow oxygen until recovery.

5. Cardiac Arrest in Pregnancy

Thankfully rare, but devastating if unprepared.

- Adrenaline- 1 mg IV every 3–5 min during CPR.
- Amiodarone- 300 mg IV for refractory VF/pulseless VT.
- Special note: Manual left uterine displacement during resuscitation relieves aortocaval compression and improves outcomes.

Safety in the Storm

In the heat of an obstetric emergency:

- Colour-coded trays save seconds.
- Dilution charts prevent dose errors.
- Daily checks avoid expired or missing drugs.
- Mock drills keep the team sharp- because no one rises to the occasion; they fall back on training.

Quick-Glance Reference Table

Emergency	First-line	Dose & Route	Key Safety Point
PPH	Oxytocin	10 IU IM or 20–40 IU IV infusion	Avoid IV bolus
Eclampsia	Magnesium sulfate	4 g IV + 10 g IM, then 5 g IM q4h	Monitor reflexes & respiration
Hypertensive crisis	Labetalol	20 mg IV	Escalate gradually
Sepsis	Broad-spectrum antibiotics	Per local protocol	Give within 1 hr
Anaphylaxis	Epinephrine	0.5 mg IM	Repeat if needed
Cardiac arrest	Adrenaline	1 mg IV q3–5 min	Maintain CPR & LUD

Closing Thoughts

Labour room emergencies don't respect timetables. They happen at 3 a.m., in the middle of handover, or when your hands are already full.

When that moment comes, there is no time to look up doses or search drawers. You must know where your drugs are, how much to give, and when to give it- by heart.

Because in obstetrics, seconds matter- and knowing your life-saving drugs can turn chaos into survival.

References

1. WHO. Managing complications in pregnancy and childbirth. Geneva: World Health Organization; 2017.

2. Lalonde AB. Prevention and treatment of postpartum hemorrhage. J Obstet Gynaecol Can. 2018;40(12):e841-e855.

3. FOGSI. Labour Room Emergency Drug List. Federation of Obstetric and Gynaecological Societies of India; 2021.

4.Cunningham FG, et al. Williams Obstetrics. 25th ed. McGraw-Hill; 2018. Ch. 41: Obstetric Emergencies.

5. WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality... Lancet. 2017;389(10084):2105–2116.

6. Magee LA, et al. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. Pregnancy Hypertension. 2022;27:148–169.

11-A Injectables for Cancer Care in Gynaecology

Author :Dr Ragweshwar Jyoti Mahajan Assistant Professor,
KNSHM&C, IGMC,
Shimla (Himachal Pradesh)

Introduction

Injectable therapies are central to modern gynaecologic oncology. They include cytotoxic intravenous (IV) chemotherapeutic agents, intraperitoneal (IP) delivery, targeted biologics (e.g., monoclonal antibodies), immune checkpoint inhibitors and supportive-care injectables (growth factors, antiemetics, etc.). Proper selection, dosing, route, monitoring and toxicity management of injectables directly determines treatment efficacy, patient safety and quality of life. We will review commonly used injectable agents in gynaecologic malignancies (ovarian, endometrial, cervical and rarer sites), routes of delivery, clinical evidence for key approaches (including IP and intraoperative heated chemotherapy), administration precautions, adverse-event management and principles for multidisciplinary delivery and documentation.

1. Classes of injectable agents used in gynaecologic cancers

1.1 Cytotoxic chemotherapeutics (intravenous ± intraperitoneal)

The backbone regimens for epithelial ovarian cancer and many gynaecologic malignancies are platinum and taxane combinations: carboplatin (IV) plus paclitaxel (IV) is standard first-line therapy for ovarian and many endometrial cancers; cisplatin remains useful in cervical cancer and some ovarian protocols. Several formulations exist (e.g., liposomal doxorubicin for recurrent ovarian cancer). Intraperitoneal (IP) delivery of cisplatin or paclitaxel has been used to improve peritoneal drug exposure in optimally debulked ovarian cancer. Randomized trials demonstrated survival benefit for IP cisplatin/paclitaxel in selected patients.

1.2 Targeted biologics (monoclonal antibodies, VEGF inhibitors)

Bevacizumab, a monoclonal antibody to VEGF, is an established IV targeted agent in gynaecologic oncology. It has demonstrated improvements in progression-free survival (and in some settings overall survival) when added to chemotherapy for advanced ovarian cancer, and improved survival for recurrent, persistent or metastatic cervical cancer when added to chemotherapy. Bevacizumab requires vigilance for hypertension, proteinuria, impaired wound healing and bleeding/thrombotic events.

1.3 Immune checkpoint inhibitors (ICIs)

PD-1 inhibitors such as pembrolizumab (IV) have increasingly important indications in gynaecologic cancers — for example in MSI-high or PD-L1–positive tumours and in combination with chemotherapy for selected advanced endometrial cancers. ICIs are administered IV and can produce durable responses but carry a unique toxicity profile (immune-related adverse events, irAEs) that affects multiple organs (skin, gut, liver, endocrine) and requires rapid recognition and often corticosteroid therapy.

1.4 Other injectables and locoregional therapies

- **Intraperitoneal (IP) chemotherapy:** direct peritoneal instillation of cytotoxics (single or multiple agents).
- **HIPEC (hyperthermic intraperitoneal chemotherapy)**: intraoperative heated perfusion of platinum or other agents at time of cytoreductive surgery—an evolving adjunct in selected ovarian cancer cases. Recent meta-analysis suggests benefit in specific settings, though patient selection and centre experience are critical.

1.5 Supportive-care injectables

Essential injectables to allow safe delivery of anti-cancer therapy include:

- **Antiemetics (IV 5-HT3 antagonists, NK1 antagonists, dexamethasone)** for prophylaxis of chemotherapy-induced nausea and vomiting (CINV). Guideline-directed prophylaxis reduces early and delayed CINV.
- **Colony stimulating factors (G-CSF; filgrastim, pegfilgrastim)** to prevent or treat neutropenia and febrile neutropenia according to risk stratification.
- **Bisphosphonates/denosumab (injectable)** when treating bone metastases or managing treatment-related bone loss (adjunctive).
- **IV fluids, electrolytes, parenteral nutrition and transfusions** as needed during cytotoxic therapy.

2. Evidence summary and standard regimens (selected highlights)

Ovarian cancer

- **First-line:** Carboplatin AUC 5–6 IV + paclitaxel 175 mg/m² IV q3weekly (or dose-dense weekly paclitaxel regimens in some settings). IP cisplatin/paclitaxel regimens demonstrated survival benefit in randomized trials for optimally debulked stage III disease and remain an option in selected patients; more contemporary analyses and trials have refined indications and supportive measures. Patients with BRCA mutations or HRD may also receive PARP inhibitors (oral) as maintenance — though PARP inhibitors are non-injectable, their interplay with chemo timing is important.

Cervical cancer

- Recurrent/metastatic: Platinum-based doublets (e.g., cisplatin or carboplatin + paclitaxel) are commonly used. Addition of bevacizumab to chemotherapy improved overall survival in the GOG-0240 trial and is a recognized option where available and appropriate. ICIs now have approvals in PD-L1–positive disease or in later lines depending on region.

Endometrial cancer

- **Advanced/recurrent:** Carboplatin + paclitaxel is widely used; pembrolizumab (IV) has shown benefit in selected populations and in combination with chemotherapy has regulatory approvals in certain indications for advanced endometrial carcinoma. Molecular profiling (MMR/MSI, POLE, p53, HER2) increasingly guides injectable therapies (e.g., trastuzumab in HER2-positive serous endometrial cancer — IV trastuzumab combined with chemo).

3. Routes of injectable delivery: practical considerations

Intravenous (peripheral vs central venous access)

- Peripheral IV is suitable for many agents but repeated cycles, vesicant drugs, or poor peripheral access favor central venous catheters (PICC, tunneled port). Central access lowers risk of extravasation but carries catheter-related infection/thrombosis risk; strict insertion, maintenance and dressing protocols are required.

Intraperitoneal (IP) chemotherapy

- IP administration achieves high peritoneal drug concentrations with lower systemic exposure. Candidates: optimally debulked epithelial ovarian cancer with limited residual disease. Risks include catheter complications, abdominal pain, neuropathy, and increased hematologic toxicity; careful patient selection, centre experience and patient counselling are paramount. Recent trials/meta-analyses have revisited IP strategies and HIPEC adjuncts; institutional multidisciplinary discussion is advised before offering IP strategies.

Intraoperative HIPEC

- HIPEC is delivered under general anesthesia after cytoreduction; centres performing HIPEC must have surgical, anesthetic and critical-care expertise and specific protocols for perfusion, chemotherapy choice and temperature management. Evidence suggests benefit in selected neoadjuvant interval debulking settings, but randomized evidence and long-term safety data continue to evolve.

4. Administration, premedication and safety

Premedication

- **Paclitaxel:** premedicate with corticosteroid (e.g., dexamethasone), H1/H2 blockers to reduce hypersensitivity reactions (standard practice).

- **Antiemetic prophylaxis:** follow emetogenicity-based guidelines — high-emetic-risk regimens deserve a three- or four-drug approach (5-HT3 RA + NK1 RA + dexamethasone ± olanzapine). ASCO antiemetic guidelines provide regimen-specific recommendations.

Extravasation and vesicant management

- Vesicant agents (e.g., anthracyclines) can cause tissue necrosis if extravasated. Institutions must have extravasation antidote kits, protocols for immediate limb immobilization, aspiration, local antidote (e.g., dexrazoxane for anthracyclines), and documentation. Early recognition and prompt management reduce morbidity.

Infusion reactions and anaphylaxis

- Be alert for infusion-related reactions (e.g., with paclitaxel, monoclonal antibodies). Premeds reduce risk for some agents; infusion should be slowed or stopped at first sign of severe reaction and emergency protocols followed.

Organ-specific toxicities: monitoring

- **Renal:** cisplatin — baseline and periodic creatinine, ensure hydration protocols.
- **Hematologic:** all cytotoxics — CBC monitoring; use G-CSF per risk guidelines.
- **Cardiac:** anthracyclines — baseline and periodic LVEF assessment.
- **Hepatic:** many agents require dose adjustments for hepatic impairment.
- **Hypertension/proteinuria:** bevacizumab — monitor BP, urine protein; withhold around surgery.
- **Immune-related adverse events (irAEs):** ICIs — baseline endocrine tests, LFTs, and low threshold for investigating new symptoms; treat moderate-severe irAEs with corticosteroids and specialist referral.

5. Supportive injectables: principles and practice

G-CSF (filgrastim/pegfilgrastim)

- Use for primary prophylaxis when risk of febrile neutropenia from chemotherapy regimen or patient factors is high (commonly ≥20% risk), and for secondary prophylaxis to maintain dose intensity. Timing is typically 24–72 hours after chemotherapy (guideline dependent). Appropriate use reduces FN, hospitalizations and chemotherapy dose reductions.

Antiemetics

- Match antiemetic regimen to chemotherapy emetogenicity (high, moderate, low). NK1 receptor antagonists plus 5-HT3 antagonists and dexamethasone are core components for highly emetogenic regimens; add olanzapine where indicated. Proper prophylaxis improves adherence and patient comfort.

Management of other supportive needs

- IV fluids and electrolyte correction, blood product support, growth factors for anaemia (erythropoiesis-stimulating agents in select scenarios), and thromboembolism prophylaxis (risk must be balanced against bleeding) are integral to delivering complex injectable regimens.

6. Special situations and sequencing

Perioperative timing (bevacizumab, wound healing)

- Anti-angiogenic therapies (bevacizumab) impair wound healing — therapy is generally withheld several weeks before elective surgery and resumed only after adequate wound healing. Communication across teams (surgeon, medical oncologist) is essential.

Combination with radiotherapy

- Certain systemic injectables are radiosensitizers (e.g., cisplatin in concurrent chemoradiation for cervical cancer). Dosing, timing and toxicity profiles must be planned in a multidisciplinary setting with radiation oncology.

Molecular testing guiding injectables

- Routine tumour testing (MMR/MSI, PD-L1, HER2, BRCA/HRD) should inform the use of injectables (e.g., PD-1 inhibitors for MSI-high cancers, trastuzumab for HER2-positive uterine serous carcinoma). Molecularly guided use optimizes benefit and avoids ineffective therapy.

7. Toxicity recognition and management — practical checkpoints

- Educate patients and caregivers about red flags: fever, severe diarrhoea, new-onset dyspnoea, chest pain, severe skin rash, jaundice, or neurological symptoms (possible severe irAEs). Early telephone triage protocols and rapid access to oncology services reduce complications.
- Document baseline status (comorbidities, prior neuropathy, hearing loss) to anticipate cumulative toxicities (e.g., platinum neuropathy, ototoxicity).
- Use dose modification algorithms for hematologic or organ toxicities; consult institutional protocols and drug monographs.

8. Consent, documentation and quality/safety systems

- Informed consent must include intended benefit, alternative options, principal toxicities (short- and long-term), route and the necessity of supportive injections. For off-label or investigational uses, clearly document rationale and regulatory/ethical approvals.
- Institutions should maintain standard operating procedures for injectable chemotherapy: order verification (indication, dose, cycle day), bedside barcode checks, infusion pump safety, extravasation kits, and emergency protocols. Multidisciplinary morbidity review for severe adverse events helps quality improvement.

9. Resource and access considerations (relevance to low-middle income settings)

- Injectable regimens vary in cost and infrastructure needs (central lines, infusion suites, monitoring). Where resources are limited, choose evidence-based, affordable options while ensuring safety (e.g., outpatient carboplatin/paclitaxel with robust antiemetic and infection-control measures). Biosimilars for biologics and long-acting G-CSF may improve accessibility, local procurement and national cancer control policies influence availability.

10. Future directions

- Integration of immunotherapy and targeted agents with standard chemotherapy is reshaping systemic injectable therapy in gynaecologic cancers (e.g., pembrolizumab combinations). Novel locoregional approaches (optimized IP regimens, HIPEC protocols) and antibody-drug conjugates (injectable targeted cytotoxics) are active research areas. Precision oncology (molecular selection) will continue to refine who benefits most from specific injectable agents.

Conclusion

Injectables remain indispensable in gynaecologic oncology. Optimal outcomes depend not only on choosing the right agent but on appropriate route selection (IV vs IP), meticulous administration, guideline-based supportive care (antiemetics, G-CSF), rapid recognition/management of toxicities and multidisciplinary coordination. Institutional protocols, informed consent and patient education are key to delivering safe, effective injectable cancer therapy. As targeted and immune therapies expand, molecular profiling and careful toxicity surveillance will further individualize injectable regimens for gynaecologic cancer patients.

References

1. Intraperitoneal Cisplatin and Paclitaxel in Ovarian Cancer. Armstrong DK, et al. N Engl J Med. (Seminal randomized data for IP chemo).
2. Primary ovarian cancer chemotherapy: current standards of care (review). (Overview of carboplatin-paclitaxel regimens).
3. Bevacizumab in advanced cervical cancer (GOG-0240). Tewari KS, et al. N Engl J Med. (Bevacizumab + chemo improved survival in recurrent/metastatic cervical cancer).
4. Pembrolizumab plus chemotherapy in advanced endometrial cancer. NEJM (recent pivotal data supporting ICI combinations).
5. ASCO Clinical Practice Guideline: Antiemetics for acute and delayed chemotherapy-induced nausea and vomiting. (Guideline basis for antiemetic injectable use).

11-B Injectables for Cancer Care in

Co-Author :Dr. Sandhya Rani Panigrahy FICOG MICOG FICMCH FAIOG FCGP CIPMS
Berhampur Odisha

The contraceptive injection is an effective form of contraception that is given to prevent pregnancy. It contains a progestogen hormonecalled depo medroxyprogesterone acetate (DMPA).Progestogen hormones arevery similar to a woman'sown hormone called progesterone. Depo-Provera the brandused most oftenand it is given every12 weeks. Sayana Press is very similar to Depo-Provera and also contains
DMPA. Noristerat is a brand which is rarely used as it is limited to very short-term use.

The contraceptive injection is sometimes called a LARC.This stands for long-acting reversible contraceptive. LARCs that containprogestogen in separateleaflets called Contraceptive Implantand Intrauterine System(IUS).
There is alsoa separate leafleton the LARCwhich doesn't containany hormone called the Intrauterine Contraceptive Device(The Coil). Injectable contraceptives like Depo- Provera, are hormone-based birth control methodsadministered via a shot typically every three months.

Mechanism of Action
1. They work by preventing ovulation.
2. Thickening cervical mucus to reduce the chance of pregnancy.This stops sperm getting through to uterusto fertilise an egg.
3. Thinning the lining of the uterus the endometrium. This makes unfavorable for implantation of fertilised egg.

Types of Injectable Contraceptives Type
-Administration Method
-Duration of Effect
-Frequency of Injection

1. Depo-Provera (DMPA-Antara)
It is to be admintered Intramuscular route. Repeat every 3 months. Dose is 150mg. Free supply by Govt of Odisha.
2. Depo-SubQ Provera 104(Antara) - It is to adminstered Subcutaneous route.
Repeat every 3 months. Dosage is 104mg. It is available in prefilled syringe. Many
Centre choosen for Pilot Project previously and now available at all Health facilities.
3. Combined Injectable Contraceptives (CICs) - Intramuscular route. To repeat 1 month

Benefits and Considerations

Benefits– Highly effective in preventing pregnancy when administered on schedule. Reduces menstrual cramps and bloodflow. Does not require daily action makingit convenient for users. Free supply.Cheap. Available plentiful. One shot free of pregnancy for 3months.

Non- contraceptive benefitslike improve HB level in sickle cell disease, improvesPMS, use in AUB,usein Endometrial Hyperplasia, conserve uterus, endometriosis, Irregular cycles

Effectiveness – It is 99.8% effective at preventing pregnancy if used correctly. Research shows it is 94% effective at preventing pregnancy.

Advantages

1.Women do not remember to take a pill every day. Only to think about contraception every 2-3 months.
2. It does not interfere with sex.
3. It can be used when breastfeeding.
4. Periods oftenstop completely whichis perfectly safe.
5.May help some of the problems people get with periods, such as premenstrual tension, heavy, painful periods and endometriosis.
6.It can be used by many of the women who cannot take the combined pill. It is not harmful to women with sickle cell disease and may even reduce the pain of a sickle crisis.
7.It may be taken by women who are on medication that would interfere with other forms of hormonal contraception - for example,medications for epilepsyor HIV.
8. It may reduce the chances of getting cancer of the ovary or endometrial cancer
9. If want to stop using it women don't have to go back to doctor or nurse to have it removed; just have to wait for it to wear off.

Limitation of uses – May cause sideeffects such as weight gain,irregular bleeding and potential delays in returning to fertility after discontinuation. Does not protectagainst sexually transmitted infections (STIs). Recommended not to be used for longer than two years due to potential risks like osteoporosis.

Usage Guidelines – The first injection can be given at any time if pregnancy is not suspected. If given outside the first seven days of the menstrual cycle backup contraception is needed for the first week. Women who are breastfeeding can start Depo-Provera within five days postpartum. Injectable contraceptives are a reliable option for many, but it's essential to consult a healthcare provider to determine the best method based on individual health needs and circumstances.

PROGESTOGEN ONLY INJECTABLES SIDE EFFECTS

a)Menstrual irregularities

1) DMPA and NET-EN are associated with disruptions of the menstrual cycle including amenorrhoea, prolonged menses,spotting between periods, and heavy bleeding. Less than one-thirdof women receiving DMPA report having normal menstrual cycles during the first year of use.

2) Amenorrhoea is the most common side-effect and its occurrence increases with durationof use from about 50 % of DMPA users by the end of one year to 80%by the end of 5 years. Womenusing NET-EN areless likely to experience amenorrhoea. Heavy bleeding is uncommon(occurs in 1-2%ofusers), and prolongedbleeding is seldom heavy enough to be a threatto health. Any woman who reports prolonged or heavy bleeding may need to be evaluated for anemia. Anaemiatreatments include nutritional advice C an appropriate dosage of oral iron tablets.

Treatments for heavy bleeding include non-aspirin anti-inflammatory drugs such as ibuprofen,short-term use of combinedoral contraceptives or estrogen or early administration of thenext injection (notsooner than 4 weeks afterthe previous injection).

After menstrual changes,weight gain, headache, anddizziness are the next most common side-effects reported. Most users of POIs put on weightand this is a common reason for discontinuation. The average DMPA user gains 1.5-2.0kg in the first year and some userscontinue to gainweight thereafter at about the same rate.In clinical trials, between 3% and 19% of users of injectables have reported headache or dizziness. Few women discontinue for these reasons.

Possible Carcinogenicity – Clinical studieshave found no association betweenDMPA use and cervical, ovarian, or livercancers, and haveconfirmed a substantial protective effect against endometrial cancer.

Studies have foundno overall increasein risk of breast cancer.Although some studies have indicated a smallno of women following initialexposure, the studiesshow no trend towardincreased risk among more long-termusers.

Bone density – Findings to date suggesta relatively smalland reversible effect,with no serious health risk for womenof any age. At presentmedical experts recommend no restriction on useof injectables by adolescents over age 16. Changes in calcium uptake

by bone and decreases in urinary calciumexcretion have beendocumented and thereis a suggestion of a relationbetween long term use of DMPA and low bone mass.
Effect on fetal exposure – There are no knownadverse effects of fetal exposure to injectables. Studies of teenage children who were exposed to DMPA in utero show no significant differences in health,growth,or sexualdevelopment compared to other children.

Progestogen-only injectables can be used by breastfeeding women at 6 weeks postpartum withoutadverse effects on nursing infants.
Effect on Metabolism – The only metabolic effect of undoubtedclinical
importance is weight gain. Minor alterations of lipid metabolism,
fluid/nitrogen balance, glucosetolerance, steroid metabolism and immune function have been recorded but seem to be of no clinical significance. Fewer datahave been published on the metabolic effects of NET-ENbut its effect on most biochemical functions appears to be similarto that of DMPA. Data are insufficient to indicate whether there is any relation betweenDMPA use and cardiovascular
complications. Resultsof a WHO study suggestthat there is little or no increased risk of cardiovascular disease associated with the useof progestagen-only injectable although further investigation is needed into a possibleincreased risk of stroke among women with high blood pressure.

RETURN OF FERTILITY

Fertility is not impaired after discontinuation of DMPA or NET-EN although its return is delayed.Theaverage time betweenthe last DMPA injection and conception is about nine months,including the three months during which the injection is effective.

More than 80%of women become pregnant within one yearof discontinuing DMPA and 90%within two years. The few data on NET-EN suggest that fertility returns more quickly with this agent

Eligibility Criteria for Use of a Contraceptive Method

World Health Organization (WHO) developed eligibility criteria for the use of various contraceptive methods

- Category 1:A condition for which thereis no restriction for the use of the contraceptive method.
- Category 2:A condition where the advantages of using the method generally outweigh the theoretical or proven risks.
- Category 3: A condition where the theoretical or proven risks usually outweigh the advantages of using the method.
- Category 4:A condition whichrepresents an unacceptable health risk if the contraceptive method is used.

Contra-indications: Category 4 POIs shouldnot be used in thepresence of:

1.Confirmed or suspected pregnancy

POIs should generally not be used in the presence of:

1.Diabetes with vascular disease or of >20 years duration

2.Cerebrovascular or coronary artery disease

3. Acute liver disease

4. Benign or malignant liver tumours

5. Severe hypertension/(BP>180/110 mm Hg)

6.Hypertension with vascular disease

7. Focal migraine

8. severe cirrhosis

Adolescents – Injectable contraceptives have important advantages in Adolescents however in those under16 years of age thereare concerns regarding the hypo- oestrogenic effects of Pols which may affectthe post-menarche increaseof bone mineral density.

Women Over 35 – POIsand CICs can be usedby most healthywomen over 35. Any increase in risk of cardiovascular disease will be minimal forthese women if they do not smoke and have no other risk factorssuch as hypertension or diabetes.

Postpartum in Breast feeding Women- If a woman wishes to start injectable contraception during breastfeeding a POI shouldbe recommended.

DMPA and NET-ENhave no apparent negative influence on milk production or the duration of lactation and infants whosemothers have receivedDMPA while breastfeeding seem to developnormally both physically and mentally. The amounts of steroid transmitted in the milk and absorbed by the infant are known to be small. Short- term follow-up studiesof children breastfedby mothers usingprogestagen-only contraceptives have givenreassuring results butlonger-term studies are yet to evaluated.0

Mesigyna- Not suitable for women who are fully breast feeding until 6 months postpartum.
Postpartum in Non-Breast feeding Women- To avoid increasing the risk of used during the first three weeks after delivery. After 21 days blood coagulation and fibrinolysis are essentially back to normal.POIs can be started at any time afterdelivery.

Drug Interaction - Drugs that induce liver enzymes may lessen the efficacy of hormonal contraceptives. Such drugswhich are commonlyused in long-term treatments include the antibiotics rifampicin and griseofulvin and the anticonvulsants phenytoin, carbamazepine and barbiturates.

Prevention of STD/HIV Transmission- Strict aseptic techniques should be maintained whengiving the injections to avoid the risk of transmitting any infection including
HIV. Injectable contraceptives do not protect against STD/HIV infection.Therefore,when there is a risk of sexual transmission of infection condomsshould always be used in addition to injectable contraceptives.

Counselling - It's to be clearly informed about the advantages and disadvantages of the agents and theirside-effects, their cost and the alternative contraceptive options.
Where once-a-month injectables are available, clientsshould be toldabout the differences between these injectables and POIs.

Follow up- A card must be issued to the womenwith all data entry for easy followup and future references. She can continue her Injection any where she wants by showing that card. Womenwho desire a rapid returnto fertility on discontinuation of their contraceptive should be advised to use CICs where availableor another method.

LNG IUCD-
The levonorgestrel-releasing intrauterine system (LNG-IUS) is a safe,effective and acceptable form of contraception used by over 150 millionwomen worldwide. This contraceptive method is safe,extremely “low maintenance” contraceptives. They are second only to femalesterilization as these are long acting contraceptive benefits. Duration of action for 5yrs. They also come in a wide variety of sizes and shapes including T-shaped and “frameless” devices.

These are medicated IUCDand marketed as Mirena by Bayer pharmaCompany. The LNG-IUS provideshighly effective contraception for up to five yearswith potential for approval for up to seven years in the near future. The mechanisms of action of the LNG- IUS are similar to that of levonorgestrel implantsor mini pills.

PROGESTERONE IMPLANT-
A progesterone implant, commonly knownas a contraceptive implant, is a smallrod- like device insertedunder the skin of the upper arm that releasesthe hormone progestin to prevent pregnancy. It is effective for up to three years and is over 99% effective in preventing pregnancy. This contraceptive implant is a flexible rod under the skin of thearm that releasesprogestin to preventpregnancy. These are also knownas long acting reversible contraceptive. @ LARC.Once implanted they act for 3 to five years. A contraceptive implant is a flexibleplastic rod about the size of a matchstick that is placed under the skin of the upperarm. These subdermal implant releases a low, steady dose of the hormoneprogestin.

Etonogestrel -

Brand and Other Names: Implanon, Nexplanon

Classes: Progestins

Dosage Forms G Strengths
Implant 68mg

Contraception
Insert 1 implant subdermally. May be used for up to 3 years and then requires replacement. Specialdevise is requiredfor loading and implantation is required. Insertion procedure and technique differsbetween brands.

Nexplanon: Radiopaque. May use X-ray, CT, ultrasound or MRI to locate once implanted.
]Implanon: Nonradiopaque may use ultrasound or MRI to locate once implanted.

--xxxxx--

12 Drug Device Combinations

Author-- Dr Vandana Gupta MS (ObGyn) (Gold Medalist),FICOG,CCGDM
Senior Consultant ObGyn Max Hospital Patparganj, Delhi

Introduction

DDCs represent an emerging sector in healthcare industry, comprising a heterogeneous group of different products, which combine a medical device with a medicinal product

Increasing collaboration between pharmaceutical companies and medtechs to provide better products that incorporate both medical devices and medicinal products in the same item has led to an increase in complex hybrid products that can range from drug-administering (e.g. pre-filled pens and injectors) to drug-eluting (e.g. drug-eluting stents (DES)) medical devices (Cyphert and von Recum, 2017, Quarterman et al., 2021

The last European Medicines Agency (EMA) Annual Report, published in 2019, showed that approximately one in four centrally-approved medicines included a medical device component (EMA, 2019). This is concurrent with the evolution of materials science which, combined with medicinal products, has fuelled the development of more sophisticated therapies (Alvarez-Lorenzo and Concheiro, 2019, Cohn et al., 2019, Sadeghi et al., 2021)

A drug-device combination product integrates a medical device with a drug or biologic substance to create a single unit, such as pre-filled syringes or drug-eluting stents, which are
designed to enhance treatment by improving drug delivery, targeting specific areas, or reducing side effects and controlled release for improved patient outcomes

Drug-Device Combinations are Important as they offer

1. Enhanced efficacy:
Can deliver treatments more precisely, leading to better clinical outcomes.

2. Improved patient compliance:
A single, integrated product can simplify the treatment regimen, making it easier for patients to follow.

3. Controlled drug release:
Devices can control the rate and location of drug delivery, optimizing treatment and reducing side effects.

Challenges and Regulation

- Complex classification:
  Because they blend the characteristics of drugs and devices, these products present unique regulatory challenges.
- Hybrid regulatory approach:
  Regulatory agencies have developed frameworks to address these products, considering their dual nature.

- Collaborative development:
  Successful development requires close collaboration between drug and device experts and thorough consideration of human factors and user interface design
- Nomenclature and applicable legislation
  DDC's always combine a medical device with a medicinal product leading to applicability of two different legislations. In Europe, those legislations are the EU Medical Device Regulation (Regulation 2017/745) on one hand and the Medical Products Directive (Directive 2001/83/EC) on the other.

• The nomenclature is not yet used consistently in Europe; Basically, it is often differentiated between integral and non-integral DDC products

• Non-integral DDC products:

There are cases where a medicinal product and a medical device are placed on the market in the same secondary packaging (= co-packed) but do not form an integral product, for example, a vial containing a medicinal product solution, with an (empty) CE marked sterile syringe. This product is NOT considered a drug-device-combination

• Irrespective of the nomenclature, the applicable "leading" legislation is always unequivocal and depends on the principle mode of action of the product. Provided the principle mode of action is provided by the medical device part, leading leading legislation is the EU-MDR .When drug provides the principal mode of action, the Medical Products Directive (MPD = Directive 2001/83/EC) is the primary applicable legislation

Integral DDC products:

These comprise mainly the following 2 product groups:

1.Integral DDCs, in which the Medical Device (MD) has the primary mode of action

2.Integral DDCs, in which the pharmaceutical component (PC) has the primary mode of action

Integral DDCs / MD primary mode of action

• This product group comprises devices that are MDs, incorporating as an integral part a medicinal product. The principal mode of action is achieved by the MD part. The Medicinal Product has an ancillary mode of action to that of the MD.

• Examples:

1. Devices containing an integral ancillary medicinal substance
2. Catheters coated with heparin or an antibiotic agent
3.Bone cements containing antibiotic
4.Root canal fillers which incorporate medicinal products with ancillary action to that of the device
5.Soft tissue fillers incorporating local anaesthetics
6.Bone void filler containing growth factors
7.Condoms coated with spermicides
8.Electrodes with steroid-coated tip
9.Wound dressings, surgical or barrier drapes (including tulle dressings) with antimicrobial agent
10.Intrauterine contraceptives containing copper or silver
11.Ophthalmic irrigation solutions principally intended for irrigation which contain components that support the metabolism of the endothelial cells of the cornea

12.Drug eluting coronary stents
13.Blood bags containing substances which, if used separately, would be considered to be a medicinal product
14.Liquid wound dressing with antimicrobial agent

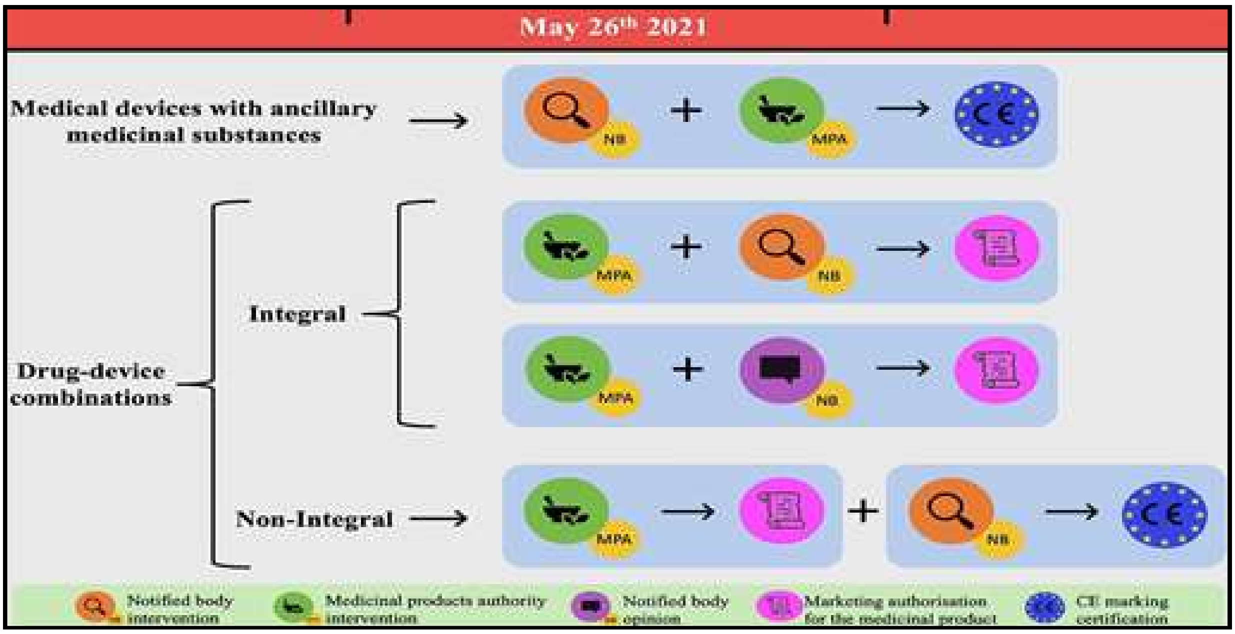
Integral DDCs / PC primary mode of action

Products, falling into this category, are products acc. to article 1(8) 2nd paragraph of the EU-MDR. I.e. Devices are MDs, incorporating as an integral part a PC, whereas the principal mode of action is achieved by the PC.

Examples for integral DDCs

1.Syringes prefilled with a medicinal product
2.Aerosols containing a medicinal product
3.Nebulisers pre-charged with a specific medicinal product
4.Patches for transdermal drug delivery
5.Implants containing medicinal products in a polymer matrix whose purpose is to release the medicinal product, for example plastic beads containing antibiotic for treating bone infections, or a matrix to release osteoinductive proteins into the surrounding bone
6.Intrauterine contraceptives whose purpose is to release progestogens
7.Single-use disposable iontophoresis devices incorporating a medicinalproduct, whose purpose is to deliver the medicinal product for the treatment of a medical condition
7.Wound treatment products comprising a matrix whose purpose is the administration of medicinal products, for example wound dressings containing an antimicrobial agent where the primary action of the dressing is to administer the agent to the wound for the purpose of controlling infection
8.Temporary root canal fillers incorporating medicinal products, whose purpose is to deliver the medicinal product
9.Tablets containing a medicinal product with embedded sensor to monitor adherence to treatment

Authorities to be notified



•Key Aspects of Drug-Device Combinations in Contraception

Drug-Eluting Devices:

- A major category includes non hormonal Cu containing Intra uterine device which are T-shaped devices placed in the uterus that release Cu to prevent pregnancy. (IUCD)
- Another major category includes hormonal intrauterine systems (IUSs), which are T-shaped devices placed in the uterus that release progestin to prevent pregnancy.

User-Controlled Systems:

New developments include user-controlled systems like the Annovera vaginal system, which combines a drug (segesterone acetate) with a vaginal ring that the user inserts and removes themselves & Nuvaring

IUCD Cu-T

Copper T (or Copper IUD) highlights its high effectiveness (>99%) for long-term contraception, lasting 5-10 years depending on the type

Effectiveness & Duration

1. Highly Effective: Copper IUDs are over 99% effective at preventing pregnancy.
2. Long-Lasting: Depending on the specific device, a Copper T can last for 5 to 10
3. Reversible: Fertility returns quickly after the device is removed.

Key Advantages

1. Non-Hormonal: .
2. Safe with Breastfeeding:
3. Rapid Action: It starts working immediately after insertion.
4. Emergency Contraception: It can be used as a highly effective emergency contraceptive within 5 days of unprotected sex.
5. Reversible

Complications

1. Perforation(in less than 1 in 1,000 cases)
2. Expulsion
3. Infection
4. Pregnancy

Caution- IUDs don't protect you from sexually transmitted infections (STIs) or HIV/AIDS.Not given

1. - An active pelvic, vaginal or uterine infection (including STIs).
2. Uterine fibroids or tumors.
3. Cervical or uterine cancer.
4. An allergy or intolerance to copper

Common Types of Copper IUDs:

-Cu 380A: T-shaped IUD with 380 mm² of exposed copper surface area,Effective up to 10 years

-Cu 380Ag (Silver IUD):

-Cu 380A, incorporates a silver core within the copper wire on the stem to prevent fragmentation and extend the device's lifespan, for 5 years.

-Cu 250: contraceptive protection for up to 3 years and contains less copper than the 380A.

-Multiload 375: Contains 375 mm² of copper wound around its stem, with flexible arms to minimize expulsion.

Cu 380 Slimline: Features copper sleeves flushed at the ends of the horizontal arms, which makes insertion easier.

Factors Differentiating Copper IUD Types:

1. Amount of Copper:
2. The surface area of the copper on the device directly affects its efficacy and lifespan.
3. Copper Wire or Sleeves: Early IUDs used wound wire, while modern devices often use solid copper sleeves, which can improve performance.

Silver Core: The inclusion of a silver core in the copper wire helps prevent the copper from breaking apart over time.

Frame Design:

Some designs incorporate features like flexible arms to reduce the risk of the IUD being pushed out of the uterus

Newer Models & Considerations

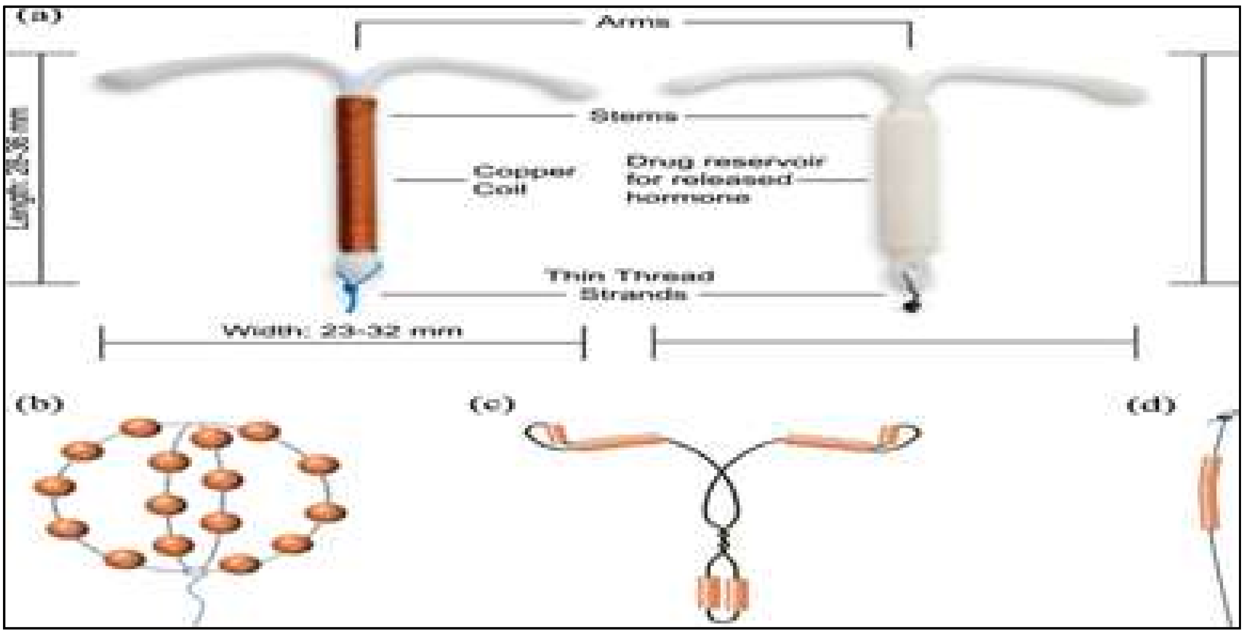
- **Flexible Designs:**

-Frameless GyneFix and the

-Shape-memory Nitinol frame of Miudella offer greater flexibility and can adapt todifferent uterine sizes and shapes.

- **Reduced Copper:**

-Some newer devices have less copper than the traditional TCu 380A model but are designed for effectiveness over a long lifespan



a Images of the non-hormonal Cu-IUD (left) and hormonal IUD (right). Obtained from iStock.com/lalocraclo. Illustrations of flexible Cu-based IUDs b intrauterine ball (IUB)[26], c Veracept[24], and d Gynefix

Mirena- The LNG-IUS is a long-acting, reversible contraceptive and a treatment for heavy menstrual bleeding, endometrial hyperplasia, and other gynecological conditionsdevice releasing the synthetic progestin levonorgestrel

-Duration - minimum of 5 years and, although absorbed systemically, cyclic function is maintained.

-The system is one of the most effective methods of contraception available today: a Pearl index of 0.1 per 100 woman-years.

-Although a postfertilization effect cannot be excluded, in a majority of cases, intrauterine systems act as true contraceptives, preventing fertilization

•Mechanism of Action:

-It works by releasing LNG directly into the uterus, which thickens cervical mucus to prevent sperm penetration and suppresses the growth of the uterine lining (endometrium).

Uses:

1.Contraception:

2.Menstrual Bleeding ;reducedbleeding,Amenorrhoea

3.Endometrial Protection:

Kristina Gemzell-Danielsson- a researcher and has helped to establish the LNG-IUS

NuvaRing –

-A medicated birth control device, the vaginal ring delivers prescription medicine that effectively prevents pregnancies.

-clear plastic ring placed in vagina for three weeks at a time. After one week without it, insert a new one.

-Effectiveness. These are the Synthetic hormones same asin other birth control medications, such as the pill or hormonal IUDs.

The ring releases daily doses

• 120 micrograms of etonogestrel, a hormonal birth control progestin

• 15 micrograms of Ethinyl estradiol, a semisynthetic estrogen compound

NuvaRing Effectiveness

-Prevents pregnancies 99.7 percent of the time if you use it as directed. Even with "typical use," which includes making mistakes in the four-week cycle, it still has 91 percent effectiveness

Advantages

- Convenient; insert it once every four weeks.
- If not taken out after three weeks, it continues working for another week.
- Neither partner feels the NuvaRing during sex..
- Lighter periods.
- Fewer cramps caused by menstruation.
- Lesser prone to acne
- contributes to stronger bones

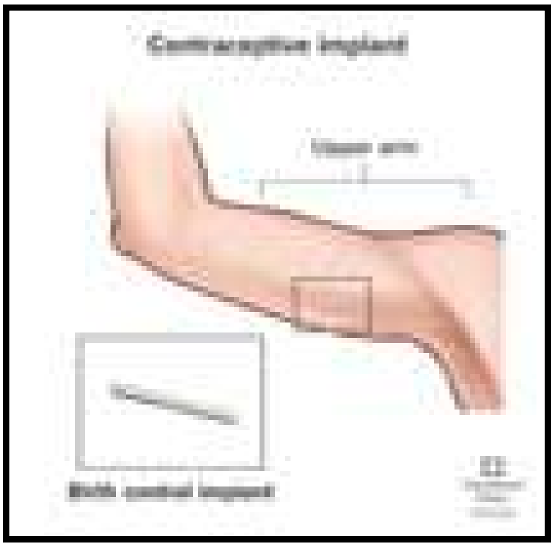
Some possible side effects include:

- increase chances of developing blood clots, heart attacks, or strokes.. Obese women are at higher risk.
- There is a slightly higher possibility of suffering from toxic shock syndrome, a complication from a bacterial infection. If one develops a fever, with or without vomiting and diarrhea, seek medical attention.
- May cause some vaginal discomfort or mild irritation
- Mood changes can occur
- headaches, including migraines.
- Rarely, irregular bleeding, but it isn't severe.
- nausea that may include vomiting.
- weight gain.
- increased discharge.
- It cannot, protect from STDs (sexually transmitted diseases) or infections
- ring may come out can be reinserted till 3 hours later after washing

ANNOVERA vaginal ring - Can be reused for a year

-Annovera uses a unique, lower-dose estrogen and a different progestin, segesterone, which allows it to be reused

- **Duration**: One uses the same Annovera ring for 13 cycles, or one year.
- **Hormones**: Contains ethinyl estradiol (estrogen) and segesterone acetate (progestin). Segesterone is a newer hormone that mimics the body's natural hormones.
- **Use**: Insert the ring for 21 days, remove it for a week (during your period), then wash, dry, store, and re-insert the same ring for another cycle.
- **Convenience**: No monthly trips to the pharmacy for a new ring.
- **Storage**: Comes with a case and needs to be washed with mild soap and stored at room temperature when not in use



IMPLANTS NEXPLANON

It's a small, flexible rod inserted under the skin of the upper arm that releases progestin to prevent pregnancy for up to 3 years

•Mechanism of action
-Hormonal Action: slowly releases the hormone progestin.
-Ovulation Prevention
-Cervical Mucus Thickening
-Uterine Lining Thinning

Effectiveness
-Highly Effective: 99% effective
-Long-Lasting: 3 years.

Insertion and Removal
•Insertion:
-local anesthetic used to numb the arm before inserting the flexible rod under the skin in a brief procedure.

•Removal:
-The implant can be removed at any time by a healthcare provider, with fertility quickly returning.

•Common Side Effects & Risks
-Irregular Bleeding: The most common side effect is changes to the menstrual cycle, which can include irregular periods, very frequent or infrequent bleeding, or no periods at all.

-Other Side Effects: You may feel the implant under your skin, and there might be some bruising or soreness after insertion.

•**Risks**: While rare, there's a small risk of infection at the insertion site.
•Benefits
-Highly Effective and Reliable
-**Convenient**: Eliminates the need to remember daily pills.
-**Reversible**: Fertility returns quickly after removal.
-Safe During Breastfeeding.

Side effects
•The birth control implant isn't known to have many side effects. Most side effects subside within a few months. Some of the potential side effects are:
-Spotting or changes in normal menstrual bleeding.
-Headaches.
-Acne.
-Sore breasts.
-Mood swings.

•Advantages of the birth control implant
-It's currently approved for three years, but effective for up to five years.
-Daily reminder & weekly change not required
-It doesn't interfere with sexual spontaneity.

-It’s hidden
-It’s safe for people who can’t use estrogen-containing birth control.
-Can be used use it while breastfeeding.
-It can reduce heavy menstrual bleeding.
•Reversibility immediate after removing the implant.

Disadvantages of the birth control implant
- Has to be inserted in office.
- Periods may become irregular, heavier, lighter, longer or shorter.
- Acne mar worsen.
-No protection against sexually transmitted infections (STIs).
-Has to remove it once you’re done with it.
-It may interfere with certain medications and antibiotics.
-Small risk of skin infection at the site of the implant.

Contraceptive patch
-Its a transdermal skin patch that releases estrogen and progestin hormones to prevent pregnancy by stopping ovulation and altering cervical mucus and the uterine lining. The patch is applied weekly for three weeks, followed by a patch-free week, and is a convenient, effective, but non-preventative-of-STIs method of hormonal contraception similar to birth control pills.

How does the birth control patch work?
• It’s a small bandage that you stick on your skin., it releases the hormones estrogen and progestin into your system.
-“They are the same two hormones found in most birth control pills,” says Dr. Patterson. “With the patch, they’re just delivered through the skin instead of in a pill form.”
- Can be applied overlower back, arm or abdomen and it releases a steady dose of the hormones
-Body absorbs the hormones, and they prevent your ovaries from releasing any eggs. The patch also thickens cervical mucus so that if an egg does manage to slip through (unlikely), sperm would have trouble reaching it.

Birth control patch effectiveness
Highly effective , when used correctly, it prevents pregnancy in more than 99 of every 100 cases. That’s about as effective **as the pill**.

Side effects
All forms of hormonal birth control — including the patch, pill and ring — can cause similar side effects, including:
•Nausea
•Breast tenderness
•Irregular bleeding or spotting
•Increased risk of blood clotting problems

Who is at risk of blood clots?

-The risk of blood clotting is a bigger concern. Overall, the risk is quite low when using the patch, Dr. Patterson says. In fact, the risk of blood clots is much greater during pregnancy than it is in those using the patch to prevent pregnancy.

-However, the patch does have a slightly higher risk of clots compared to the pill.

Avoid if you:

-Smoke
- Diabetes
-History of blood clots
-Had a heart attack or stroke
-Have a body mass index (BMI) over 30

Good" side effects

Not all side effects of the birth control patch are negative. In fact, some use the patch mainly for the other benefits that go along with it, like:

-Less acne
-Milder cramps
-More stable moods
-Shorter, lighter periods
-Less incidence of iron-deficiency anemia

Ovaprene

A new drug-device combination for non-hormonal contraception

Sabrina Johnson at Daré Bioscience is redefining contraception with Ovaprene, a non-hormonal, monthly option for safe and effective birth control

Ovaprene is a monthly, non-hormonal birth control method that acts as both a barrier and a drug-releasing device to block sperm from passing through the cervix

Its a small ring that has a physical barrier in the center made of a knitted polymer. It's a three-dimensional weave that is designed to inhibit sperm's progression through it. The ring also releases an active pharmaceutical ingredient that's a form of iron that interferes with sperm motility through a lipid peroxidation reaction. Women would replace the device with a new one every month.

Ovaprene, has had a small human proof-of-concept study showing that it could block progressively motile sperm from getting into the cervix

Conclusion

This brief review of DDC 's being used for contraception gives insight into a successful use of combining drug with devices effectively and safely with higher effectiveness and acceptability

Referrences

1. WHO. Contraceptive Technology Update. 2020.

2. Gemzell-Danielsson K et al. LNG-IUS in contraception and gynaecology. Hum Reprod Update. 2020;26(5):748-760.

3. Cutlip DE et al. Drug-eluting stents: a clinical update. Circulation. 2018;138:197-206.

4. Wild RA, Kaunitz AM. Contraceptive Technology. 22nd ed. Ayer Company; 2021. Ch.

5.1.NuvaRing vs. Annovera: Which birth control option is better for you? Esther Bell, Review Wed, July 6, 2022 at 9:42 PM GMT+5:30

6.The combination of medical devices and medicinal products revisited from the new European legal framework
Pau Antich-Isern[1], Julia Caro-Barri 2, Juan Aparicio-Blanco

7.Emerging trends in drug-device combination for advanced disease diagnosis and therapy
Author links open overlay panelZhe Liu [a b], Yu Shi [a b], Chenxi Liu

8.A new drug-device combination for non-hormonal contraception-Stephaine Demarco,Phd

--xxxxxx--

13 Adverse Drug Reactions in Women

Author-- Dr. Urvashi Barman Singh
Prof. & HOD Dept. of OBGY United Institute of Medical Sciences, Prayagraj

1. Introduction: The Forgotten Half of Pharmacovigilance

For decades, pharmacology operated on a silent assumption—that the male body could stand as the universal reference for drug testing, safety, and efficacy. Women were deliberately excluded from early-phase clinical trials, largely due to concerns about teratogenic risks, potential liability from pregnancies, and the belief that hormonal cycles introduced "unnecessary variability." Researchers presumed that results obtained in men could be generalized to women.

This exclusion created critical blind spots in drug development and safety surveillance. The consequences became strikingly clear only after widespread drug use. Between 1997 and 2001, eight out of ten drugs withdrawn from the U.S. market posed greater risks to women than to men. Such withdrawals underscored the cost of overlooking sex differences in pharmacology.

Corrective steps have since been introduced. The **NIH Revitalization Act of 1993** mandated inclusion of women in Phase III clinical trials, and the **FDA issued guidelines** requiring sex-specific analyses in clinical data. Yet, despite progress, many modern studies still fail to report sex-disaggregated outcomes, leaving clinicians without sufficient evidence to guide prescribing in women.

These persistent gaps highlight the need for **sex-specific pharmacovigilance**—a system that recognizes women not as "subsets" of men but as equally complex biological entities whose drug responses warrant independent study.

2. Why "Same Dose, Different Body" Matters

2.1 Pharmacokinetics: Disposition Matters

Pharmacokinetics (PK)—how the body absorbs, distributes, metabolizes, and eliminates a drug—differs systematically between men and women. Women often experience **higher systemic drug exposure** when given the same dose as men. These variations extend beyond simple differences in body weight or size.

- **Absorption**: Women generally have slower gastric emptying and higher gastric pH, which alters the dissolution and bioavailability of certain medications. Weak acids like aspirin may show reduced absorption, while weak bases and proton-pump inhibitors may be absorbed more readily.
- **Distribution**: Women typically have higher body fat percentages and lower total body water compared to men. Lipophilic drugs (e.g., benzodiazepines, antidepressants) accumulate more in fat stores, prolonging half-life, whereas hydrophilic drugs (e.g., aminoglycosides) reach higher plasma concentrations.

- **Metabolism**: Hepatic enzyme activity differs by sex. CYP3A4 activity is often higher in women, leading to faster metabolism of some drugs (e.g., midazolam, certain HIV protease inhibitors), while CYP2D6 and CYP1A2 may act more slowly. Hormonal modulation further complicates metabolism.
- **Excretion**: Women have lower **glomerular filtration rates (GFR)** and slower renal clearance (when normalized for body surface area). Drugs such as digoxin and aminoglycosides may therefore accumulate more readily in women, raising the risk of toxicity.

The case of **zolpidem** (a sedative-hypnotic) illustrates these principles vividly. Women were found to have up to 50% higher blood concentrations the morning after dosing, increasing the risk of impaired driving and accidents. This led the FDA in 2013 to mandate **sex-specific dose reductions**—halving the recommended starting dose for women.

2.2 Pharmacodynamics: Tissues React Differently

Pharmacodynamics (PD)—how drugs exert their effects at receptors and tissues—also varies between sexes. Even when plasma drug concentrations are equal, women may exhibit stronger or weaker therapeutic responses and side effects.

- **Cardiovascular drugs:** Women are more prone to drug-induced **QT prolongation and torsade de pointes**, partly due to longer baseline QT intervals and hormonal influences on cardiac repolarization. Medications such as sotalol, erythromycin, and haloperidol increase arrhythmia risk disproportionately in women.
- **Analgesics**: Women often report stronger analgesic responses to opioids like morphine, but also experience greater rates of adverse effects such as nausea and pruritus.
- **Psychotropics**: Women may respond more favourably to SSRIs but also exhibit higher rates of hyponatremia, sedation, and weight gain at equivalent doses.

These differences highlight that **similar plasma levels do not guarantee similar clinical outcomes**—a central challenge in tailoring safe therapy.

2.3 Sociocultural Factors and ADR Reporting

Biology alone cannot explain sex differences in adverse drug reactions (ADRs). Gender-related behaviours and healthcare engagement patterns amplify disparities:

- Women generally have more frequent healthcare interactions, increasing both drug exposure and opportunities to report side effects.
- They may be more vigilant in noticing subtle bodily changes and more likely to report them.
- However, physician biases can undermine detection—women's symptoms are often dismissed as "psychosomatic," delaying recognition of genuine ADRs.

Importantly, when adjusted for actual **drug usage rates**, women's higher ADR reporting decreases, indicating that differences in drug exposure play a major role.

Nevertheless, the interplay of **biology and gendered health behaviours** magnifies risk in women.

3. Evidence from Pharmacovigilance and Real-World Data
Pharmacovigilance systems consistently reveal higher ADR reporting in women worldwide.

- **Meta-analyses** confirm that women face a **1.5–2× higher risk of ADRs** than men, especially with cardiovascular, antimicrobial, and psychiatric drugs.
- Women's reports are often more frequent but less severe, whereas men's reports—though fewer—tend to be more severe.
- Drug classes with significant sex differences include:

    - **Cardiovascular agents:** Women experience higher bleeding risk with anticoagulants and stronger QT prolongation.
    - **Analgesics:** Women report more opioid-related side effects.
    - **Psychotropics:** Greater risks of arrhythmia, sedation, and hyponatremia are documented in women.

Such findings illustrate that **sex-specific drug safety concerns are not theoretical**—they manifest in everyday prescribing and outcomes.

4. Physiological Insights
Pregnancy and reproductive physiology dramatically alter pharmacology. Plasma volume expansion, increased cardiac output, altered protein binding, and hormone-driven changes in hepatic enzyme activity modify drug handling. For example, pregnancy **accelerates lamotrigine clearance** (necessitating higher doses) but reduces lithium clearance (raising toxicity risk). These examples highlight the need for **dynamic dose adjustments in reproductive-age women. (Williams Obstetrics)**

Renal clearance disparities explain higher accumulation of renally excreted drugs in women.
Examples include slower clearance of digoxin and altered metabolism of antidepressants—clear demonstrations that PK must account for sex. **(Goodman & Gilman's The Pharmacological Basis of Therapeutics)**

Receptor sensitivity: Women show different β-adrenergic receptor responses, influencing cardiovascular drug outcome, **Signal transduction:** Hormonal modulation alters intracellular signalling pathways, shaping sex-specific efficacy and toxicity. **Clinical outcomes**: At equivalent exposures, women more often experience drug-induced arrhythmia, sedation, and metabolic disturbances. **(Katzung's Basic and Clinical Pharmacology)**

Collectively, these authoritative texts affirm that **sex differences are not peripheral details—they are central to pharmacology.**

5. Strategies for Sex-Specific Pharmacovigilance
The path forward requires structural, clinical, and regulatory reforms:

1. **Enhanced Clinical Trial Design**
    - Mandate balanced inclusion of women across all trial phases.
    - Require sex-stratified analysis of efficacy and safety outcomes.
2. **Dose Optimization**
    - Adjust labelling to reflect PK/PD differences.
    - Use lower starting doses for drugs with narrow therapeutic indices (e.g., zolpidem, digoxin).
3. **Pregnancy-Focused Guidelines**
    - Implement dynamic monitoring frameworks for pregnant women.
    - Establish pregnancy drug safety registries to capture real-world evidence.
4. **Healthcare Provider Education**
    - Train clinicians to recognize sex-related ADR patterns.
    - Address gender biases that lead to under-recognition of ADRs in women.
5. **Regulatory Frameworks**
    - Strengthen post-marketing surveillance to ensure sex-disaggregated ADR reporting.
    - Require prompt label modifications when sex-specific safety signals emerge.
6. **Summary**
    - Women's physiology, hormonal patterns, and sociocultural contexts mean that same dose does not mean same effect. Higher systemic exposure, slower clearance, receptor sensitivity differences, and gendered health behaviours converge to influence drug safety in women. Integrating classic pharmacology (2,3), obstetric medicine (1), and modern pharmacovigilance data (4–9) shows that sex-specific approaches in research, regulation, and clinical care are essential to reduce ADR risk and optimize treatment outcomes.

References

1. Cunningham FG, Leveno KJ, Bloom SL, Dashe JS, Hoffman BL, Casey BM, Spong CY. Williams Obstetrics. 25th ed. McGraw-Hill Education; 2022.
2. Brunton LL, Hilal-Dandan R, Knollmann BC, editors. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 14th ed. McGraw-Hill Education; 2022.
3. Katzung BG, Vanderah TW, editors. Basic and Clinical Pharmacology. 16th ed. McGraw-Hill Education; 2021.
4. Zucker I, Prendergast BJ. Sex differences in pharmacokinetics predict adverse drug reactions in women. Biol Sex Differ. 2020;11(1):32.
5. Soldin OP, Mattison DR. Sex differences in pharmacokinetics and pharmacodynamics. Clin Pharmacokinet. 2009;48(3):143–157.
6. Clayton JA, Tannenbaum C. Reporting sex, gender, or both in clinical research? JAMA. 2016;316(18):1863–1864.
7. Zopf Y, Rabe C, Neubert A, Janson C, Brune K, Hahn EG, Dormann H. Women encounter ADRs more often than do men. Eur J Clin Pharmacol. 2008;64(10):999–1004.
8. Martin RM, Biswas PN, Freemantle SN, Pearce GL, Mann RD. Age and sex distribution of suspected adverse drug reactions in newly marketed drugs. Br J Clin Pharmacol. 1998;46(5):505–511.
9. National Institutes of Health (NIH). NIH Revitalization Act of 1993: Inclusion of Women and Minorities in Clinical Research. Bethesda (MD): NIH; 1993.

14 From Herbal to High Tech: Integrating Alternative Medicines Safety

Author - Dr Archana Singh
FICOG Fellowship in reproductive medicine (Germany),
Fellowship in Day Care Endoscopy
Hyderabad Telangana

Alternative, complementary, and traditional medicines (ACTM) — referred to as "alternative medicines" — remain widely used globally. Integration of their safe use into contemporary clinical practice requires understanding regulatory frameworks, evidence appraisal, known and potential harms (adverse events, contamination, interactions) [12].

1. Introduction and scope

Patients commonly use alternative medicines alongside conventional therapies. These range from herbal remedies and traditional formulations to dietary supplements, homeopathy, and physical/manual complementary therapies. Many patients do not disclose use unless explicitly asked. Consultants — by virtue of coordinating care, advising about specialist therapies, and writing institutional policies — must lead safe integration efforts [2].

2. Definitions and terminology

- **Alternative, complementary and traditional medicine (ACTM)**: Practices and products not usually part of conventional Western medical curricula; includes herbal medicines, traditional systems (Ayurveda, Traditional Chinese Medicine, Unani), dietary supplements, homeopathy, and manual therapies.
- **Dietary supplement:** In many jurisdictions, a category that includes vitamins, minerals, botanicals, amino acids and other substances consumed to supplement the diet [3].
- **Herb–drug interaction (HDI)**: A pharmacokinetic or pharmacodynamic interaction between a botanical product and a conventional pharmaceutical agent [4].
- **Adulteration vs contamination:** Adulteration indicates intentional addition of undeclared pharmaceutical agents; contamination refers to unintended presence of heavy metals, pesticides, mycotoxins, or microbial contaminants [4].

3. Epidemiology and drivers of use

Global and national surveys consistently show that a substantial portion of the population uses alternative medicines — often to manage chronic symptoms, improve well-being, or complement conventional therapies [2]. Drivers include cultural traditions, dissatisfaction with conventional care, perceived "natural" safety, accessibility, and cost. Non-disclosure remains high: studies report between 30–70% of patients using supplements or herbal remedies failing to inform clinicians unless specifically asked [2]. Consultants must therefore proactively seek full medication histories that include non-prescription products.

4. Regulatory frameworks and standards

Regulatory control over alternative medicines varies widely by country. Key paradigms include:

- **Food-based regulation (e.g., DSHEA in the United States)**: Dietary supplements are regulated as foods; manufacturers are responsible for safety; pre-market approval is not required for many products, and claims are restricted. Post-market surveillance and adverse event reporting are primary mechanisms for enforcement [3].
- **Medicinal product regulation:** Some jurisdictions regulate certain traditional herbal products as medicines with specified monographs and quality standards.
- **WHO policy guidance:** World Health Organization (WHO) published a Traditional Medicine Strategy (2014–2023) encouraging Member States to develop regulatory frameworks, promote safety, and integrate evidence-based traditional practices into health systems [1].

Implications for consultants: regulatory heterogeneity means clinical decisions should rely on product-level quality checks, independent third-party testing where available, and local regulatory guidance.

5. Evidence appraisal: efficacy and quality of studies

The evidence base for many alternative medicines is mixed: high-quality randomized controlled trials (RCTs) exist for some preparations (e.g., certain herbal extracts), whereas many products are supported only by observational data, small trials, or traditional/empirical use [2].

Practical guidance:

- Prioritize evidence from systematic reviews and well-conducted RCTs where available.
- Ensure the studied product matches the marketed product (same species, extract type, standardization, dose).
- Use validated clinical outcomes, not surrogate markers alone, when assessing benefit for patients.

6. Safety risks: adverse events, contamination, adulteration, and interactions

6.1 Direct toxicities and idiosyncratic reactions

Herbal products can cause organ-specific toxicity (e.g., hepatotoxicity from certain Chinese herbs), allergic reactions, or dose-related toxicities. Risk rises with unstandardized dosing, concentrated extracts, and prolonged or high-dose use [4].

6.2 Contamination and adulteration

Product analyses have repeatedly found heavy metals (lead, mercury, arsenic), pesticides, microbial contamination, and sometimes intentional adulteration with undeclared pharmaceuticals (e.g., corticosteroids, NSAIDs). These pose serious safety risks and complicate attribution of adverse events [4].

6.3 Herb–drug interactions (HDIs)

HDIs can be pharmacokinetic (changing absorption, metabolism, excretion) or pharmacodynamic (additive/synergistic or antagonistic effects). Examples of clinically important HDIs include:

- St John's wort — induces cytochrome P450 enzymes and P-glycoprotein causing reduced plasma levels of many drugs (oral contraceptives, immunosuppressants, anticoagulants, psychotropics) [45].

- Ginkgo biloba, garlic, ginseng — reported to affect platelet function and interact with anticoagulants (warfarin, DOACs) increasing bleeding risk [4].
- Green tea extracts — can reduce effect of certain beta blockers and interact with statins [5].

Risk factors for clinically significant HDIs include narrow therapeutic index drugs (e.g., warfarin, immunosuppressants, antiepileptics), polypharmacy, hepatic or renal impairment, and high-dose botanical preparations [5].

7. Clinical practice guidelines

7.a. Medication history and disclosure

- Use open, non-judgmental language to encourage disclosure [2].
- Collect details: product name (brand), scientific/botanical name if known, dose, route, frequency, duration, source/vendor, reason for use, and whether a practitioner guided use.
- Make it routine: ask, "Do you use any herbal products, vitamins, traditional medicines, or supplements?"

7.b. Risk stratification

Classify use into low, moderate and high-risk categories:

- **Low risk:** Single ingredient vitamin/mineral supplements at recommended daily doses in otherwise healthy individuals on no interacting medications [3].
- **Moderate risk:** Herbal products with some evidence of pharmacological activity taken with limited polypharmacy; products of uncertain quality.
- **High risk:** Use alongside narrow therapeutic index drugs, in pregnancy or breastfeeding, frail elderly patients, or when product quality is suspect [4].

7.c. Counselling and shared decision-making

- Be evidence-informed and transparent about benefits and risks; explain uncertainty openly [2].
- Offer safer alternatives when appropriate (e.g., certified products, lifestyle interventions).
- Negotiate treatment plans rather than demanding immediate cessation, especially where cultural or psychological reliance exists.

7.d. Monitoring and follow-up

- Baseline labs: for patients on high-risk combinations, consider baseline and periodic monitoring (e.g., LFTs for hepatotoxic herbs, INR for warfarin users) [5].
- Adverse event surveillance: instruct patients to report new symptoms promptly and stop product use if serious symptoms occur.

7.e. Documentation and consent

- Document discussion, risk stratification, agreed plan, and any educational materials.

For high-risk use, consider written informed consent noting uncertainty of benefit and risks.

8. Institutional and system-level interventions

8.a. Formularies and approved product lists

- Maintain an institutionally approved list of botanical preparations meeting quality standards (GMP, third-party testing).
- Prohibit unapproved or high-risk products in inpatient settings, especially peri-operative, oncology, and transplant care [13].

8.b. Pharmacovigilance and adverse event reporting

- Establish reporting systems for suspected herb-related adverse effects.
- Contribute to national or WHO pharmacovigilance programs [1].

8.c. Integration with electronic health records (EHRs)

- Build prompts for documenting ACTM in medication lists.
- Implement HDI alerts using curated databases [5].

8.d. Education and training

- Train staff in recognition of ACTM, potential HDIs, and cultural sensitivity.
- Provide quick-reference resources at point of care [2].

9. High-tech solutions

- **Blockchain** to track product authenticity and reduce adulteration.
- **Clinical decision support (CDS)** embedded into EHRs for real-time HDI alerts [5].
- **Big-data analytics** to detect adverse event patterns.

10. Special populations

- **Pregnancy/lactation:** limited safety data; avoid unless essential.
- **Oncology patients:** high risk for HDIs; monitor closely [5].
- **Transplant recipients:** avoid unverified ACTM due to immunosuppressant interactions [4].
- **Pediatrics/geriatrics:** altered pharmacokinetics heightens risks.

11. Policy recommendations

- Harmonize global regulatory approaches [1].
- Strengthen labeling and quality assurance [3].
- Expand pharmacovigilance reporting [1].
- Prioritize rigorous clinical trials for widely used ACTM [2].

12. Conclusion

Safe integration of alternative medicines requires vigilance, consultant leadership, and systemic reforms. Evidence-based use, regulatory awareness, and proactive monitoring can minimize risks while respecting patient preferences [12].

References

1. WHO. WHO Traditional Medicine Strategy 2014–2023. Geneva: World Health Organization; 2013.
2. National Institutes of Health. National Center for Complementary and Integrative Health. Complementary, Alternative, or Integrative Health: What's In a Name? Bethesda: NIH; 2023.
3. Food and Drug Administration. Dietary Supplement Health and Education Act of 1994 (DSHEA). Silver Spring: FDA; 1994.
4. Izzo AA. Interactions between herbs and conventional drugs: overview of the clinical data. Med Princ Pract. 2012;21(5):404-28.
5. Posadzki P, Watson L, Ernst E. Herb–drug interactions: an overview of systematic reviews. Br J Clin Pharmacol. 2013;75(3):603-18.

15 Storage Stories : Why Where You Keep Your Drugs Matters

Author - Dr. Ruche Bhargava
MD, D.N.B Jalandhar

Good storage practice is essential for maintaining drug quality and potency. This includes controlling environmental factors , maintaining proper segregation and following a robust documentation process.

Why is proper storage important ?

- To maintain the safety , efficacy and quality of the medicine .
- To prevent deterioration from environmental factors like temperature and light .
- To avoid cross contaimination and mix ups .
- To ensure compliance with legal and regulatory standards .

General Storage Conditions

Indian Guidelines for medicine storage emphasize maintaining proper temperature, light, humidity and sanitation conditions in a secure and organized manner.

1. Temperature Control : Maintaining appropriate temperature range for different medications is crucial. Some medications require refrigeration, while others need to be stored in a cool, dry place. The best place to store most medications is away from heat sources, a drawer in a climate controlled room, or any other location with a stable temprature and low humidity. Regular power supply should be available for cooling devices and dehumidifiers.

2. Light protection : Medications should be protected from direct sun light. This can be achieved by using shaded windows, curtains or keeping medications in the original packaging.

3. Humidity control-Maintaining a low humidity level (below 60%) is important. Proper ventilation, including the use of fans and screens on windows helps to control humidity. Dehumidifiers , air conditioners or desiccants are used whenever required.

4. Sanitation : The storage area should be kept clean and disinfected regularly to prevent contamination. It should be free from any water penetration, rodent and pests. It should have fire safety equipment in place.

5. Segregation and Organization : Medicines should be organized logically, often alphabetically by generic name and segregated based on their expiry dates. Look - alike and Sound - alike (LASA) medications should be stored separately.

6. Security : Access to the storage area should be restricted to authorized personnel and measures should be in place to prevent loss or theft.

7. Compliance with laws and regulations : Storage practices must adhere to relevant laws and regulations, such as Drugs and Cosmetics Act.

8. Emergency Medicine : Essential medicines should be readily available in emergency situation.

9. Proper Shelving : Shelves should be positioned to allow for adequate air circulation and prevent seepage. Similar boxes should be stored adjacent to each other and stacked as per their expiry dates.

10. Pest Control : The storage area should be free from pests and rodents.

11. Special Storage : Cytotoxic drugs should not be stored in advance and should be only ordered after specific patient or doctor requests. Special Bio-safety cabinet should be available for Chemotherapy

References

1.International Journal Of Community Medicine
www.ijcmph.com

2.pmc.ncbi.gov

16 Prescription to Prevention:

Author-- Dr. Padmaja Veeramachaneni
Vijayawada

Preventive care has long been the cornerstone of public health, traditionally emphasizing diet, exercise, lifestyle modifications, and environmental safeguards. However, a transformative approach is gaining prominence in women's health: preventive pharmacology. This field involves the proactive and strategic use of medications—including vitamins, minerals, drugs, and vaccines—to prevent diseases before they manifest. From the rapid growth of adolescence to the unique physiological demands of pregnancy and the health challenges of menopause, targeted pharmacological interventions can safeguard a woman's health throughout her lifespan, marking a shift from prescription for treatment to prescription for prevention.

Laying the Foundation in Adolescence

Adolescence is a critical period of physical, emotional, and social development. The immaturity of the hypothalamic-pituitary-ovarian axis often leads to abnormal uterine bleeding, making anemia a common concern. The proactive use of iron and folic acid supplements is essential to combat this, aiming for a hemoglobin level of at least 12 g% by age 12, a crucial step toward a healthy adulthood. When heavy bleeding does occur, medications like tranexamic acid and mefenamic acid serve as the first line of defense, followed by hormonal regulation with progesterone until the bleeding pattern stabilizes.[1]

This is also the time of peak bone mass accrual. If dietary intake and lifestyle are insufficient, supplementing with vitamin D and calcium is vital to help young women achieve optimal bone mineral density, reducing the risk of osteoporosis later in life. Furthermore, with the onset of sexual activity, the appropriate prescription of contraceptive pills not only prevents unintended pregnancies but also offers significant non-contraceptive benefits. These include regulating menstrual cycles, alleviating heavy or painful periods (menorrhagia and dysmenorrhea), managing premenstrual syndrome (PMS), and reducing the risk of ovarian cysts and anemia.

Vaccination is another pillar of preventive care in adolescence. A single dose of the MMR (measles, mumps, rubella) vaccine and two doses of the HPV (human papillomavirus) vaccine between the ages of 9 and 14 are strongly recommended to protect against viral infections with long-term health consequences, including cervical cancer.[2]

Nurturing Health: Preconception and Pregnancy

The period before and during pregnancy demands meticulous attention to nutritional and prophylactic needs to ensure the health of both mother and child.

Folic Acid: It is universally recommended that all women of childbearing potential consume 400 to 800 micrograms of folic acid daily. This simple intervention, continued through the first trimester, can dramatically reduce the risk of neural-tube defects in the developing fetus. For women with a history of a child with such a defect, a higher daily dose of 4 mg can lower the recurrence risk by over 70 percent. [3] **Vitamin B12 and Iron**: Vitamin B12 deficiency, a risk particularly for strict vegetarians, can also contribute to an elevated risk of neural-tube defects. Meanwhile, the iron requirements of pregnancy are substantial, with nearly 7 mg per day needed in the latter half to support the expanding maternal blood volume and provide for the fetus and placenta. A daily supplement of 30-60 mg of elemental iron is typically sufficient to meet these needs and protect the mother's own stores. **Calcium and Vitamin D:** A pregnant woman retains approximately 30 grams of calcium, most of which is transferred to the fetus late in gestation for bone development. While this represents a small fraction of the mother's total calcium, ensuring adequate intake is important. Concurrently, an adequate intake of 600 IU per day of vitamin D is recommended, as deficiency is common, especially in women with limited sun exposure or darker skin.

Preventing Complications: Beyond nutritional support, specific medications can prevent serious pregnancy complications. Low-dose aspirin, initiated before 12 weeks of gestation in women identified as high-risk for pre-eclampsia. In recent dueling metaanalyses, Roberge and colleagues (2017) found that
aspirin prophylaxis initiated before 16 weeks' gestation was associated with a
significant risk reduction—about 60 percent–for preeclampsia and fetal-growth
restriction. Moreover, they found a dose-response effect . [4]

Prophylactic Strategies in the Peripartum Period

The time surrounding childbirth presents unique risks that can be mitigated with targeted preventive pharmacology.

- **Rh Isoimmunization:** For Rh-negative women with an Rh-positive partner, the administration of anti-D immunoglobulin both during pregnancy and after delivery is a critical intervention that prevents the development of antibodies that could harm a future Rh-positive fetus.[5]

- **Blood Clots and Hemorrhage:** Low-molecular-weight heparin (LMWH) is recommended for deep vein thrombosis (DVT) prophylaxis in high-risk women, especially after a cesarean section. To minimize blood loss during a C-section, administering tranexamic acid before the incision has proven effective.[6] . The use of uterotonic agents like carbetocin and oxytocin has dramatically reduced rates of postpartum hemorrhage (PPH), a leading cause of maternal mortality.

- **Infections**: Prophylactic antibiotics are essential for preventing sepsis in cases of premature rupture of membranes (PROM) or in women with conditions like rheumatic heart disease. The use of probiotics is also being actively investigated as a way to prevent recurrent urinary tract infections and vulvovaginitis.

- **Unsafe Abortion:** The availability of medications for medical abortion plays a crucial role in preventing maternal morbidity and mortality associated with unsafe procedures.

Lifelong Protection: Adulthood and Beyond

As women age, the focus of preventive pharmacology shifts toward mitigating the risk of chronic diseases.

- **Cardiovascular Disease**: Statins remain the cornerstone for managing dyslipidemia, while low-dose aspirin is recommended for primary prevention of cardiovascular events in high-risk women, particularly those over 65.[7]

- **Osteoporosis:** Following menopause, the decline in estrogen accelerates bone loss. Bisphosphonates are the most common medications used for both the prevention and treatment of osteoporosis. Raloxifene, a Selective Estrogen Receptor Modulator (SERM), mimics estrogen's protective effects on bone. Menopausal Hormone Therapy (MHT) can also prevent osteoporosis, though it is typically considered when a woman also requires treatment for menopausal symptoms.

- **Breast Cancer:** For women at high risk of estrogen receptor-positive breast cancer, SERMs like Tamoxifen and Raloxifene can significantly reduce their risk. In postmenopausal women, Aromatase Inhibitors (AIs) such as Anastrozole and Exemestane are also effective preventive options.

- **HIV Prevention:** Post-exposure prophylaxis (PEP) is a critical and strongly recommended intervention following a potential exposure to HIV to prevent infection. PEP should be initiated immediately—ideally within 2 hours of an exposure but no later than 72 hours after an exposure—because the effectiveness of PEP decreases over time after 2 hours. Bictegravir 50 mg/tenofovir alafenamide 25 mg/emtricitabine 200 mg (BIC/TAF/FTC; Biktarvy) as a fixed-dose single tablet once per day [8]

The Guiding Principles of Preventive Pharmacology

The effective implementation of preventive pharmacology hinges on several key considerations. A **personalized approach** is paramount; the decision to start a preventive medication must be based on a woman's individual risk factors, health history, and personal values. This requires a thorough **risk-versus-benefit analysis**, weighing the potential to prevent a future disease against the potential side effects and costs of the medication. Finally, for any preventive strategy to be successful, patient **adherence** is vital.

Ongoing research continues to refine risk assessment tools, identify novel medications, and optimize prevention strategies tailored to the unique biological and physiological needs of women. By embracing the proactive power of preventive pharmacology, healthcare can move beyond simply treating illness and actively build a foundation for lifelong health and well-being for women everywhere.

Ref :

1. Srivaths LV, Dietrich JE, Yee DL, Sangi-Haghpeykar H, Mahoney D Jr. Oral tranexamic acid versus combined oral contraceptives for adolescent heavy menstrual bleeding: a pilot study. J Pediatr Adolesc Gynecol. 2015;28:254–257. doi: 10.1016/j.jpag.2014.12.012

2. Pingali C, Yankey D, Elam-Evans LD, et al. Vaccination Coverage Among Adolescents Aged 13–17 Years — National Immunization Survey-Teen, United States, 2024. MMWR Morb Mortal Wkly Rep 2025;74:466–472. DOI: http://dx.doi.org/10.15585/mmwr.mm7430a1

3.MRC Vitam. Study Res. Group. 1991. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. Lancet 338:131–37

4. Roberge A, Nicolaides K, Demers S, et al: The role of aspirin dose on the prevention of preeclampsia and fetal growth restriction: systematic review and meta-analysis. Am J Obstet Gynecol 216(2):110, 2017

5. McBain RD, Crowther CA, Middleton P. Anti-D administration in pregnancy for preventing Rhesus alloimmunisation. Cochrane Database Syst Rev. 2015 Sep 3;2015(9):CD000020. doi: 10.1002/14651858.CD000020.pub3. PMID: 26334436; PMCID: PMC7061251.

6. Hemapriya L, More G, Kumar A. Efficacy of Tranexamic Acid in Reducing Blood Loss in Lower Segment Cesearean Section: A Randomised Controlled Study. J Obstet Gynaecol India. 2020 Dec;70(6):479-484. doi: 10.1007/s13224-020-01351-3. Epub 2020 Sep 3. PMID: 33417631; PMCID: PMC7758378.

7. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: Donna K. Arnett, Roger S. Blumenthal, Michelle A. Albert, Andrew B. Buroker, et al.

8. Cowan E, Kerr CA, Daniel J, et al. PEP to Prevent HIV Infection [Internet]. Baltimore (MD): Johns Hopkins University; 2025 May. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562734/

---xxxxx---