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# AOGD BULLETIN

Volume 21 I April 2022 I Monthly Issue 12

PROMOTE WOMEN'S HEALTH

STRONG WILL

QUALITY SKILL

***Dedicated Issue:***

***"Mixed Bag"***


**AOGD SECRETARIAT**

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# AOGD Bulletin

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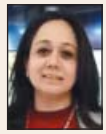

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# Foreword

I am immensely delighted to write the current issue's foreword. It's a mixed bag this month but pertaining to the crucial issues. Menopause is a vital transition in any woman's life and hence a major health milestone for women. As a gynaecologist it's important to provide Knowledge and awareness about the signs and symptoms of this phase and risks and benefits of various treatment options available. Estrogen deficiency during this period leading to osteoporosis can be very distressing to the woman. Preventive strategies include diet modification, exercise and smoking abstinence.

Obstetric care providers should routinely administer needed vaccines to pregnant patients including COVID vaccines keeping in mind that there is no risk of adverse fetal effects from inactivated vaccines. Regarding infections in pregnancy, exposure of non immune individuals to varicella in maternal and neonatal settings can cause serious illness. The most harmful HSV infection in pregnancy is primary genital herpes in third trimester therefore elective cesarean should be planned for such patients. On the other hand, rubella is a bigger problem if acquired in the first trimester.

In the end I would like to congratulate the AOGD secretariat at Safdarjung Hospital and editorial team for doing such a wonderful job this entire year and keeping us updated with all the CMEs and webinars even during the toughest times of pandemic!

**Dr Suneeta Mittal**
Advisor, AOGD

# From the President's Pen

Greetings to all AOGDians

It is time to bid adieu, secretariat at Safdarjung completed its tenure and handed over to Maulana Azad Medical College. We look back with a feel of satisfaction and pride at a very successful year of holding the AOGD Secretariat. I would like to extend my sincere gratitude to our Patrons, Advisors and the Executive Committee for their support and guidance throughout. With the active participation and enthusiasm of the subcommittee chairpersons the Association could hold number of CME'S, Public awareness programmes and workshops. I would like to congratulate Dr Asmita Rathore and her team and wish them all the best as they take over the AOGD secretariat. Our last flower in the bouquet, this issue of AOGD Bulletin covers some important topics, which could not be covered in theme based previous issues.

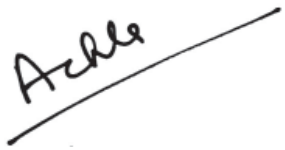
Hope this bulletin is as useful as the previous ones. We are humbled at your appreciation of each and every issue of AOGD bulletin.

Thank you all.

Long Live AOGD

***"Perfection is not attainable, but if we chase perfection we can catch excellence."***

***-Vince Lombardi***



**Dr Achla Batra**

President, AOGD (2021-2022)

# From the Vice-President's Pen

Dear AOGD Friends,

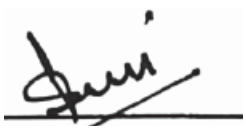
Seasons Greetings for the Indian New Year! May this Year bring lots of highs for all our members.

This is the last issue from the Secretariat of VMMC & Safdarjung Hospital. It is with mixed feelings that I pen this message. On one hand is the satisfaction of completing our tenure so successfully and on the other hand there is a feeling of nostalgia and sadness for the memorable times which have passed in such a jiffy. The entire year our Editorial Team led so ably by Dr Rekha Bharti, has worked overtime and each and every issue released is a masterpiece with a complete review of the theme topic. I have been told by many PG students not only from Delhi but from the entire India that they are revising for their exams from these Bulletins. I take this opportunity to acknowledge Dr Rekha and her Team and also to congratulate our most dynamic President Dr Achla Batra for leading from the front only as a true leader can! My compliments to the Secretarial Team led by the energetic Hon Secretary, Dr Monika Gupta for their perfect coordination with the Editorial Team.

I am sure our members will find this mixed bag issue most stimulating and interesting. In the end I would like to wish the MAMC Team all the success in taking our beloved AOGD to new heights.

Long Live AOGD!

So long friends!



**Dr Jyotsna Suri**
Vice President, AOGD (2021-2022)

# From the Secretary's Desk

Warm greetings to all!

We are glad to share with you all that Safdarjung AOGD secretariat has passed the baton on to the office bearers from Maulana Azad Medical college under the able leadership of Dr Asmita Rathore.

I once again place on record my gratitude for our beloved outgoing President Dr Achla Batra for entrusting me with the honour of being the secretary of this prestigious organisation. I thank my Safdarjung AOGD team and all AOGD members for supporting me during my tenure as AOGD Secretary. I am indebted to you all.

It has been an absolutely wonderful eventful academic journey through this last year. We left no stone unturned in putting up dedicated efforts towards our theme, 'Strong Will and Quality Skills- For Woman's Health'. We have always strived for bringing best of scientific programs on latest developments in Obstetrics and Gynaecology for our members at both state and national level. After successfully reaching out to you all via the telecommunication way, we even entertained our members with few interesting and long awaited physical programs as well. One of our major accomplishments has been bringing out the long awaited AOGD Constitution Amendment after a tedious process.

After presenting you with various dedicated bulletin issues round the year, feeling proud and content at the same time to present before you the last issue of AOGD bulletin from Safdarjung Hospital secretariat which deals with "Mixed Bag" covering important aspects of Obstetrics and Gynaecology. It deals with antenatal infections, latest with vaccination in pregnancy and important updates in management of menopausal issues. I am sure these interesting articles will be immensely useful for all our AOGD members.

Wishing you all a happy reading and the very best for future!

**Dr Monika Gupta**
Secretary, AOGD (2021-2022)

# From the Editor's Desk

Warm wishes to all of you from the Editorial Team!

We bring to you the April issue of AOGD bulletin which a mixed bag of academic bonanza with topics touching the important aspects of both Obstetrics and Gynaecology. This is also the last issue from Safdarjung Hospital as AOGD secretariat has been shifted to Maulana Azad Medical College and Lok Nayak Hospital.

We are grateful to Dr Suneeta Mittal for sparing her valuable time from her busy schedule to contribute foreword for this issue. Menopause is a natural phenomenon but it may not be normal for all women. It in-fact is an estrogen deficient endocrinopathy that may affect the quality of life of a large number of women. The gynaecology part of this bulletin includes articles on two major problems related to menopause, **"Genitourinary Syndrome of Menopause: Practical Treatment Considerations"** and **"Management of Postmenopausal Osteoporosis"**.

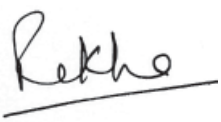
Immunisation is an essential part of care for adults, including pregnant women. **"Vaccination during Pregnancy and Lactation"** is especially important because of greater risk of maternal and neonatal morbidity and mortality.

Common infections that cause mild-to-moderate disease in healthy adults and children can cause serious maternal and fetal complications if acquired during pregnancy. A unique concern with maternal infection is the potential for mother-to-child transmission or congenital infection. Varicella zoster virus (VZV), rubella and herpes are common infections associated with moderate-to-severe fetal and infant complications when acquired congenitally. To update the current understanding of these infections during pregnancy we have included comprehensive articles covering **"Herpes in Pregnancy: Case Based Management", "Managing Varicella Infection in Pregnancy" and "Rubella in pregnancy: Prenatal diagnosis"**.

We hope this bulletin will enrich knowledge and skills of our readers.

The editorial team wishes you all success in all your endeavours!!

Happy Reading!



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# Genitourinary Syndrome of Menopause: Practical Treatment Considerations

**Pikee Saxena**
Director Professor, Obstetrics & Gynecology, Lady Hardinge Medical College & Associated Hospitals

## Introduction

Genitourinary syndrome of menopause (GSM) is a new terminology which includes a group of urinary, vulvovaginal and sexual symptoms and signs associated with menopause. Other terms used for this problem are vulvovaginal atrophy (VVA), atrophic vaginitis, and urogenital atrophy.

## Prevalence

GSM-like symptoms may be present in 15% of premenopausal women due to hypoestrogenic state. Younger women may suffer from GSM due to induced hypo-estrogenic states including surgical menopause, use of gonadotropin-releasing hormone (GnRH) agonists, hypothalamic amenorrhea or because of cancer treatments like chemotherapy, pelvic radiation, or endocrine therapy. However, majority of women suffering from GSM are of older age, with 50-70% of postmenopausal women being symptomatic at least to some degree.

## Estrogen Deficient Endocrinopathy

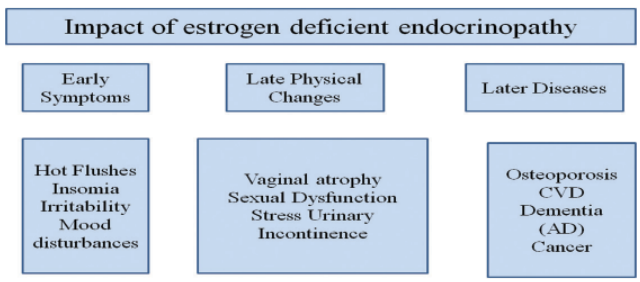
Due to estrogen deficiency after menopause, anatomic and histologic changes occur in female genital and urinary tissues, including reduction in the content of collagen and hyaluronic acid and in the levels of elastin, thinning of the epithelium, alterations in the function of smooth muscle cells, increase in the density of connective tissue, and fewer blood vessels. These changes reduce elasticity of the vagina, increase vaginal pH, lead to changes in vaginal flora, diminish lubrication and increase vulnerability to physical irritation and trauma.

GSM symptoms become more evident 5 years after menopause as the estrogen deficiency becomes more pronounced. It has been observed that GSM occurs in 84% of women six years after menopause as compared to 65% in women one- year post menopause.

Estrogens acts through estrogen receptors (ERs) present in the urogenital area, including the vagina, vulva, labia, urethra, and bladder trigone. Premenopausal estradiol levels range between 10 to 800 pg/mL while after menopause estradiol levels fall up to <30 pg/mL.

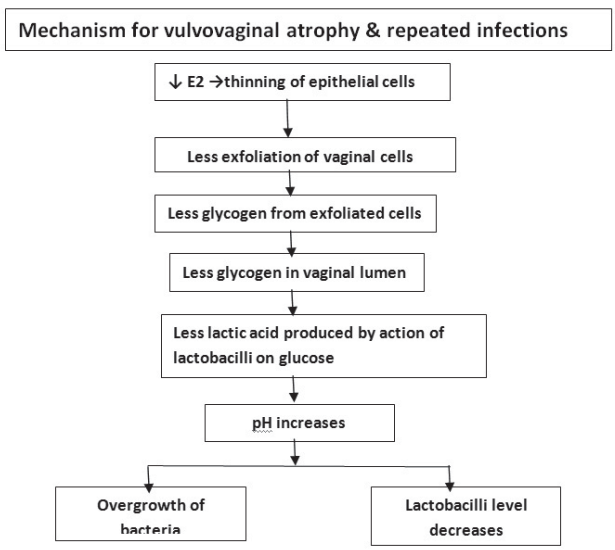
Three types of estrogens are present in the body. Estrone (E1) is the least potent while Estradiol (E2) is 80 times more potent than estriol (E3). In premenopausal women, Estradiol (E2) is predominant while after menopause estrone is predominant. There is a reversal of hormonal milieu after menopause. As estrogen deficiency progresses, presentation of menopausal symptoms changes (Fig. 1).

**Fig. 1**




Mechanism to explain development of vulvovaginal atrophy and associated repeated infections is shown in Fig 2. The common embryonic origin during fetal development of the lower urinary tract and external genitalia explains the pathophysiologic effects of the lack of estrogens on the urinary and genital tract anatomical structures.

**Fig.2**



## Symptoms of GSM

- Lack of lubrication during intercourse, vaginal pruritus, soreness, stinging pain → dyspareunia
- Vaginal spotting, due to small tears, thin yellow or grey watery discharge secondary to the rise in pH, urgency, frequency, nocturia, or urge incontinence
- Urinary symptoms like dysuria, urgency, frequency, nocturia, urinary incontinence, and recurrent UTI
- Stress incontinence is commonly found in this age group, but current evidence suggests it is not directly attributable to VVA

## Clinical Features of VVA

Diagnosis of GSM can be made by assessing the following features and severity can be calculated objectively by using the modified vaginal health index given in table 1.

- Atrophy of the labia majora and vaginal introitus.
- The labia minora may recede.
- Vaginal mucosae may appear pale, shiny, and dry; if there is inflammation, they may appear reddened or pale with petechiae.
- Vaginal rugae disappear, and the cervix may become flushed with the vaginal wall.
- Vaginal shortening and narrowing tend to occur.
- A thin watery yellow vaginal discharge may be observed.
- A urethral caruncle, a small, soft, smooth friable red outgrowth along the edge of the urethra, may develop

Clinicians should keep in mind and exclude other causes with similar symptoms like dermatological conditions of the vulva such as lichen sclerosus or planus, eczema, dermatitis, chronic vulvovaginitis, vaginitis and vaginosis, vulvodynia, malignancies, and chronic pelvic pain.

**Table 1:** Modified Vaginal Health Index

| Parameters | 1 | 2 | 3 |
|---|---|---|---|
| ph | >6.5 | 5-6.5 | < 5 |
| Moisture/ Consistency of fluid | No | Minimal | Minimal |
| Rugosity | None | Minimal | Good |
| Elasticity | Poor | Fair | Excellent |
| Length of Vagina | < 4 | 4-6 | > 6 |
| Thickness of Vagina | Papery thin | Thin | Normal |
| Epithelial Integrity | Petechiae | Petechiae after scraping | Normal |
| Vascularity | Minimal | Fair | Good |

## Management Strategy

### Non Hormonal

Lifestyle changes like maintenance of regular sexual activity, smoking cessation are recommended. Bladder drill and pelvic floor exercises are recommended for urinary incontinence.

First line treatment is use of simple non-hormonal remedies lubricants which are water or silicone or oil-based products which are not skin absorbed. They act immediately and provide temporary relief from vaginal dryness and dyspareunia. Xylocaine 5% jelly applied before coitus is also useful for women who have painful intercourse.

On the other hand, vaginal moisturizers need to be applied on a regular basis as they act as bioadhesives and can improve discomfort during intercourse and improve vaginal moisture. Moisturizers mimic vaginal secretions and lower the pH by altering the fluid content in the vaginal epithelium. However, both these products are useful mostly for women with mild to moderate symptoms

Other complementary therapies like oral vitamin D, vaginal vitamin E, phytoestrogens and probiotics which have also been proposed as alternative therapy to GSM although their efficacy data requires further validation.

## Menopausal Hormonal Therapy (MHT)

MHT covers therapies including estrogens, progestogens, combined therapies, androgens, and tibolone. Indications of MHT are specific which are recommended only for management of vasomotor symptoms, GSM, osteoporosis and surgical menopause resulting in diminished quality of life.

Contraindications include active endometrial and gynecological hormonedependent cancers, active breast cancer, high risk for breast cancer, severe active liver disease with impaired or abnormal liver function, venous thrombosis, established CVD and at severe increased risk of CVD, known or suspected pregnancy and undiagnosed and abnormal vaginal bleeding.

Treatment should be started early to prevent irreversible atrophic changes and may need long-term treatment to maintain benefits. MHT may be given to women below the age of 60 years or within 10 years of menopause, and the risks are rare.

**Hormonal Treatments** – Gold standard for treating GSM

***Vaginal MHT:*** It is most effective and relatively safe route of MHT. Preparations include estradiol, conjugated estrogens, and vaginal estriol. Recurrent attacks of atrophic vaginitis require the use of the smallest effective dose over a period of time. After control of acute symptoms, the dose of local estrogen can be tapered for longterm maintenance therapy. Cochrane Systematic Review: 19 RCT involving 4162 postmenopausal women: vaginal estrogen is an effective treatment for GSM and all forms, whether cream, ring, or tablet, appeared to relieve symptoms more effectively than non-hormonal gels and placebo.

North American Menopause Society (NAMS): Endorsed vaginal estrogen therapy. **Progestogen may not be prescribed in combination with low-dose vaginal estrogen to prevent endometrial cancer- Level IIIc.** Improvement has been noticed in many cases of recurrent urinary tract infections and overactive bladder (without any sign of microbial involvement), but not in women with stress incontinence- Level 1a. Intravaginal or transdermal Estrogen + Testosterone therapy may improve sexual dysfunction in selected women after proper evaluation and consent- Level1c.

Lowdose vaginal estrogen formulations reported no incidence of increase in CHD, stroke, and VTE. There are no contraindications for use in nonestrogendependent cancers.

*Systemic absorption of vaginal hormonal therapy:* Several studies comparing different doses and preparations of estradiol have found that systemic absorption occurs, but to a limited extent. Levels of estradiol increased on an average from a baseline (pretreatment) level of 3 pg/mL to 17 pg/mL on day 7 of treatment for both estradiol vaginal tablets (25 µg) and conjugated estrogen cream (0.625 mg). Some evidence shows that estradiol levels diminish over time when vaginal estrogens are used consistently.

***Systemic MHT****:* Systemic estrogen therapy, in the form of patches, oral agents, or a higher-dose vaginal ring, is sometimes used for GSM, especially when the patient also has hot flashes. However, 10% to 20% of women may have residual GSM symptoms even while taking systemic estrogen and may require administration of local vaginal estrogens alone or along with systemic therapy for relief of VVA symptoms. Few studies have shown that oral hormone therapy (HT) may worsen symptoms of urinary incontinence. In women with absent uterus, estrogen alone may be administered by vaginal, oral, transdermal, intranasal, subcutaneous routes. Different preparations available with some common brand names are shown in table 2. In women with intact uterus, estrogen needs to be combined with progestogens as a continuous or sequential regimen in order to protect the uterus from unopposed estrogen effect which may result in endometrial hyperplasia or malignancy.

## Screening & Follow Up

Pretreatment investigations: Complete physical and gynecological examination is mandatory. Investigations include complete haemogram, urine culture, blood sugar, lipid profile, Pap smear, TVS, mammography and DEXA scan.

Regular follow up is required for women on MHT and discuss the risk benefit ratio with the patient and the dose and duration of use of MHT should be individualized. First follow is planned after 3 months to confirm the compliance/ side effects. 2nd Follow up is done after 6 months and then yearly. Repeat biochemical test are done yearly. Two yearly mammography and TVS is carried out.

Safety data on EPT with CEE + MPA use are 3–5 years, and with ET, safety data are 7 years of treatment with 20 years followup. Role of extended use of HT should be a shared decision between the woman and the physician and may be considered only in cases of recurrence of symptoms after stopping therapy when other therapies are contraindicated (Grade A).

Stopping MHT may be abrupt or the dose and duration may be tapered off gradually (Grade C). Transdermal estrogen has a neutral effect on triglycerides, CRP, and sex hormonebinding globulin and is preferable for use in women with hypertriglyceridemia, obesity, glucose intolerance, high risk of deep vein thrombosis, and tobacco users.

## Other Preparations

**Tissue-selective estrogen complex:** Pairs conjugated estrogens with a SERM, bazedoxifene acetate (APRELA). It improves vasomotor symptoms, quality of life, vaginal atrophy and prevents fractures in healthy postmenopausal women. It is safer for the breast and uterus without increasing the risk of myocardial infarction, stroke, or venous thromboembolism. Dose of single tablet is once a day for 2 to 3 years. Endometrial safety is shown up to 2 years.

**Table 2:** Estrogen only Preparations as Vaginal and Other Routes

| Product type | Generic name | Strength | Treatment | Advantages | Disadvantages |
|---|---|---|---|---|---|
| Vaginal cream **Estrace** | Estradiol | 0.1 mg (100 µg)/g of cream; 1 g = applicator | ¼ to ½ applicator twice weekly | Lower in cost, flexible in dosing | Managing and cleaning applicator frequently, messy |
| Vaginal cream **Evalon** | Estriol | 0.5 mg (5mal cream in applicator) 1 g = applicator | 0.5 to 1 mg Daily for 3 wks followed by 1 wk off.For mailtainence twice a week | Lower in cost, flexible in dosing | Managing and cleaning applicator frequently, messy |
| Vaginal cream **Premarin** | Conjugated estrogens | 0.625 mg (625 µg)/g of cream; 1 g = applicator | ¼ to ½ applicator twice weekly | Lower in cost, flexible in dosing | Managing and cleaning applicator frequently ,messy |
| Vaginal tablets **Vagifem** | Estradiol hemihydrate | 25 µg | Insert twice weekly | Less messy | Higher in cost, preferred, less messy |
| Vaginal pessary | 17 beta Estradiol | 2 mg | weekly or biweekly | Less messy | Higher in cost, messy |
| Vaginal ring **Estring, Femring** | Estradiol | 7.5 µg/24 h | Replace every 90 d | Convenience (lasts 90 d) | Cost and acceptance of intravaginal device |
| Oral estrogen **Estrace** | Estradiol | 0.5,1,2mg | Daily | Ease of administration | Costly<br><br>Estrogen related systemic side effects<br><br>Less efficacy compared to vaginal route for GSM<br><br>Prescribed only in women where uterus is absent |
| Oral estrogen **Menest Evalon** | Esterified estrogen | 0.3,0.625,1.25mg | Daily | | |
| Oral estrogen **Estropipate** Generic (previously available as Ortho-Est) | Oral estropipate | 0.75,1.5,3mg estropipate (equivalent to 0.625,1,25,2.5mg conjugated equine estrogen) | Daily | | |
| Oral estrogen **Premarin Conjugase Espause** | Oral Conjugated Equine Estrogens (CEE) | 0.3 to 0.625 mg | Daily | | |
| Oral estrogen **Progynova Estrabet** | Oestradiol valerate | 1-2 mg | Daily | | |
| Transdermal Estrogens **Oestrogel** | Estradiol gel | 1mg | Daily | | |
| Transdermal Estrogens **Estraderm MX 50 ETS patch** | 17 beta Estradiol matrix patch 17 beta Estradiol reservoir patch | 1-1.5mg/patch 1.8mg/patch | Twice a week | Ease of administration | |
| Transdermal Estrogens **Estaspray** | Estradiol spray | 0.025 | Daily | | |
| Intranasal spray | Estradiol spray | 0.15mg/puff | Daily | | |

**Table 3:** Combined Estrogen and Progestogen Preparations

| **With uterus- EPT (oestrogen progestogen therapy)** | | | |
|---|---|---|---|
| **Cyclic** | | | |
| Oestrogen X 1-25 days | 17β estradiol | Transdermal | 0.025-0.1mg once or twice weekly |
| | | Oral | 1mg/ day |
| | Oestradiol valerate | Oral | 1-2 mg/day |
| | | Oral | 0.3 to 0.625 mg/ day + |
| + | CEE + | + | 10 mg/ day |
| progesterone X 10-14 | Dydrogesterone / | Oral | 100- 200mg/ day |
| days per month or every 3 | Micronized progesterone | Oral | |
| months | | | 1.25 -2.5mg/ day |
| OR | Medroxyprogesterone | Oral | |
| progesterone X 1-25 days | acetate | | |
| **Continuous** | | | |
| Oestrogen | 17β estradiol | Oral | 1mg/ day |
| + | + | | |
| Progesterone | Dydrogesterone | Oral | 5 -10 mg/ day |
| Oestrogen | 17β estradiol | Transdermal | 0.025-0.1mg once or twice weekly |
| | Oestradiol valerate | Oral | 1-2 mg/day |
| | CEE | Oral | 0.3 to 0.625 mg/ day + |
| + | + | + | 100mg/ day |
| Progesterone | Micronized progesterone | Oral | |
| Oestrogen/ LNG IUS | Oestrogen | | |
| | + | | |
| | LNG-IUS 20 | | 20 mcg released/day; effective for 5 years |
| Conjugated estrogen | CEE | Oral | 0.45 mg/ day |
| + | + | | + |
| SERM- mostly used for | Bazedoxifene | Oral | 20 mg/ day |
| osteoporosis | | | |

***Ospemifene:*** A third-generation SERM, approved for the treatment of dyspareunia and GSM, by the Food and Drug Administration in 2013. It is useful for women who cannot tolerate local or systemic estrogens. Dose: 60 mg tablets. Safety on endometrium demonstrated up to 52 weeks (Goldstein et al, Climacteric 2014), Not available in India

***Sulbutiamine:*** It is a thiamine derivative and has antiasthenic property. It is an oral selective estrogen receptor (SERM) and improves mental, physical, emotional and sexual asthenia. Dose is 100-200mg per day and it can be given continuously.

***Intravaginal testosterone:*** Studies suggest that intravaginal testosterone may lower vaginal pH, increase the proportion of vaginal lactobacilli and probably improves the vaginal maturation index, but its efficacy in GSM generally lacks robust evidence. It is used as daily intravaginal administration of 0.50% (6.5 mg) DHEA (Prasterone).

***Intravaginal dehydroepiandrosterone (DHEA):*** Studies have shown that DHEA, increases blood estrogen concentration, thereby leading to the improvement of sexual arousal and the return of lost libido. Vaginal DHEA 0.5% 6.5 mg is to be used daily for 52 wks. It improves Female sexual function index (FSFI).

***Tibolone:*** It is a synthetic steroid having two estrogenic, one progestogenic and one androgenic metabolite. Used for prevention of vasomotor symptoms and bone loss. It has an additional advantage of improving mood, libido and sexual desire. Brand names- Livial, Tibofem, Sibolone; Dose: 2.5 mg daily. Has controversial effect on breast cancer so it should not be given for longer period; It Increases the risk of stroke in women > 60 years of age.

**Microablative fractional CO2 and non-ablative**

**erbium: YAG (Er: YAG) lasers**

Recently, laser and radiofrequency devices have appeared as substitute treatment modalities for GSM. It is suggested that microablative fractional CO2 and non-ablative erbium: YAG (Er: YAG) lasers restore the tropism in the lower genitourinary tract with three to five sessions. In spite of the initial anticipation for this new therapeutic approach, it has not been fully implemented in the day-to-day practice to this day and its routine use is not recommended by some scientific societies.

## Conclusion

GSM is a common and often underreported condition, occurs in women who experience estrogen deficiency endocrinopathy. GSM is characterized by various symptoms like vaginal dryness, dyspareunia, dysuria, recurrent UTI thereby leading to a far-reaching influence on the QOL. Recently, different treatment alternatives have emerged to treat the condition's bothersome and life-changing symptoms. First-line treatment consists of non-hormonal therapies such as lifestyle changes, lubricants and moisturizers, while hormonal therapy with locally administered intravaginal estrogen products is considered the "gold standard" in more persistent cases. Systemic MHT is recommended only if GSM is accompanied with other menopausal symptoms like vasomotor symptoms but are not as effective as Novel therapeutic approaches with Silbutamine or laser technologies can be employed as alternative options, but further research is required to analyze their implementation in everyday clinical practice.

## Suggested Reading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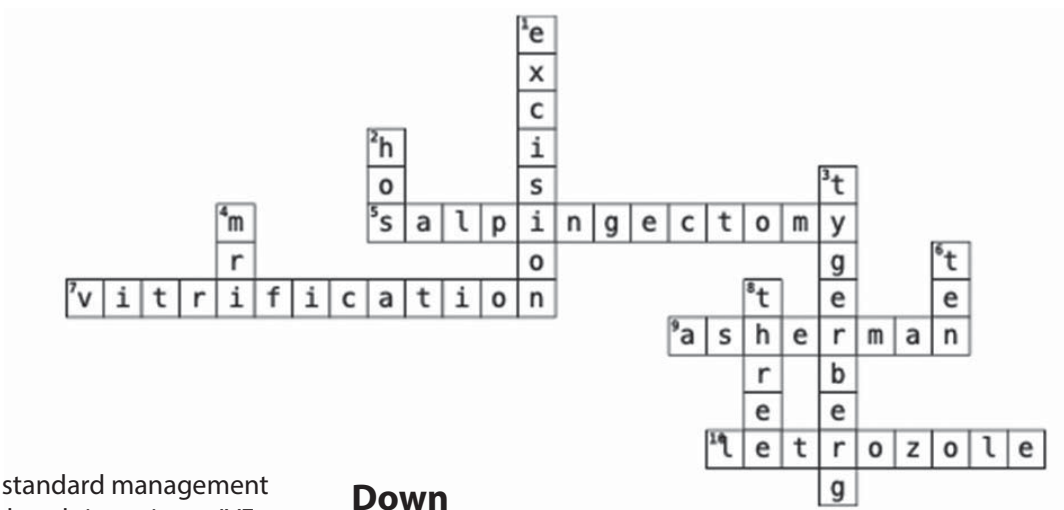
## Answers Crossword, March Issue



### Across

5. Gold standard management of hydrosalpinx prior to IVF
7. Preferred method of cryoprerservation of oocytes
9. Syndrome associated with thin endometrium
10. Ovarian stimulation drug used to lower estradiol levels in breast cancer patients

### Down

1. Preferred method of endometrioma capsule removal
2. The test used for sperm vitality
3. Name of strict criteria used for sperm morphology
4. The preferred modality for diagnosis of adenomyosis
6. Donor gametes can be stored for a maximum period of how many years
8. Poseiden group of a 30-year old female with poor ovarian reserve

# Management of Postmenopausal Osteoporosis

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Osteoporosis is an asymptomatic, silent disease which is associated with significant morbidity and mortality. The World Health Organization (WHO) has identified osteoporosis as an important noncommunicable disease with an impact on quality and quantity of life that affects adversely medical, social, and economic aspects.

## Why is Osteoporosis a major public health concern?

The National Osteoporosis Foundation (NOF) has estimated that there are 9.1 million women with osteoporosis and an additional 26 million with low bone mass. The lifetime risk of fracture for a 60-year-old woman is close to 44%, nearly double the risk for a man of the same age. Hip fractures occur at an earlier age in developing countries. The peak age for hip fractures in India is in the 60s compared to 80s in western countries. 20% of women with hip fracture die within 1 year of the fracture and 50% of them never regain their functional independence. There are > 130 million women in India who are in menopause.

## What is the definition of Osteoporosis?

The WHO defines osteoporosis as "a systemic skeletal disease characterized by low bone mass (measured as bone mineral density [BMD]) and micro-architectural deterioration of the bone tissue with a consequent increase in bone fragility and susceptibility to fractures, involving the wrist, spine, hip, pelvis, ribs, or humerus"

It is important to understand the term **Fragility Fractures.** Clinically, a fragility fracture can be defined as one which occurs as a result of minimal trauma, such as a fall from a standing height or less, or no identifiable trauma. The most common sites of fragility fracture are the hip, spine, and forearm. The other sites are pelvis, proximal femur, proximal humerus, proximal tibia, and fractures involving three ribs simultaneously

## How is the Fracture Risk assessed?

As osteoporosis is an asymptomatic disease, the Fracture Risk is assessed by identification of clinical risk factors and BMD score. In India for asymptomatic women, opportunistic screening should *start at 40 years*[1] which is ten years earlier than our western counterparts. In the absence of a validated population screening tool for PMO in India, a case-finding strategy utilizing clinical risk factors with the addition of DXA as needed is suggested. A detailed history, physical exam, and clinical fracture risk assessment with fracture risk assessment tool (FRAX®) or other fracture risk assessment tool should be included in the initial evaluation for osteoporosis

**Major risk factors defined by the WHO are:** Advancing age is a single most significant risk factor, Low body mass index (BMI), Prior history of a fracture, Parental history of hip fracture, Smoking, Alcohol, Use of glucocorticoid, and Rheumatoid arthritis.

## Osteoporosis Risk Assessment Calculators Available:

Risk assessment tools such as **The Osteoporosis SelfAssessment Tool (OSTA) for Asians** and Simple Calculated Risk Estimation Score (SCORE) are simple and costeffective to screen women at risk for osteoporotic fracture, Table 1.

**Table 1:** Osteoporosis SelfAssessment Tool (OSTA)

- Developed by the World Health Organization (WHO) to identify women at risk and is based simply on age and weight
- Developed based on data from 860 women from eight countries including Malaysia
- OSTA = 0.2[weight (kg) – age (year)]
- Patients are stratified into low, intermediate and high-risk groups.
- The risk of osteoporosis in the high, intermediate and low risk category was found to be 61%, 15% and 3% respectively.
- This risk index had a sensitivity of 91% and specificity of 45%,

**The WHO Fracture Risk Assessment Tool (FRAX)** is country specific and an online tool (http: www.shef.ac.uk/FRAX). It is not validated for India as yet.

FRAX is used to identify patients in the osteopenia group most likely to benefit from treatment. **It predicts the 10year absolute risk for a fracture in an individual.** 10-year major osteoporotic fracture probability (≥ 20%) or hip fracture probability (≥ 3%) is considered as high risk

## Dual X-ray absorptiometry

*Indications* (Indian Menopause Society 2020)[1]: All postmenopausal women more than 5 years of menopause, Postmenopausal women less than 5 years of menopause with risk factors, Women in menopause transition with secondary causes, Radiological evidence of osteopenia and the presence of vertebral compression fracture, Women with fragility fractures by radiology or DXA, Ideally, before initiating pharmacotherapy for osteoporosis, and Emerging indications are to measure total body fat and lean tissue mass.

*Best Practice Points for DEXA*

1. Axial dual-energy X-ray absorptiometry (DXA) measurement (lumbar spine, femoral neck and hip; 1/3 radius if indicated) should be used
2. The lowest BMD score obtained from all the sites is used for diagnosis
3. Screen women for secondary osteoporosis if history or examination shows systemic disease or Low Z scores on DXA

## How is Osteoporosis Diagnosed?

Diagnosis of osteoporosis can be based on WHO or American Association of Clinical Endocrinologists/ American College of Endocrinology Criteria, Table 2 & 3.

**Table 2:** World Health Organization Criteria for Classification of Osteopenia and Osteoporosis

| Category | T score |
|---|---|
| Normal | −1.0 or above |
| Low bone mass (osteopenia)a | Between −1.0 and −2.5 |
| Osteoporosis | −2.5 or below |
| Severe or established osteoporosis | −2.5 or below with fragility fracture |

## Evaluation for Osteoporosis

*Evaluate for causes of Secondary Osteoporosis:* Chronic glucocorticoid users, Patients with rheumatoid arthritis, Collagen vascular disease or inflammatory bowel disease, Hypogonadism, thyroid dysfunction, type 2 diabetes, and Use of aromatase inhibitors in breast cancer survivors

**Table 3:** 2020 AACE Diagnosis of Osteoporosis in Postmenopausal Women[2]

1. T-score −2.5 or below in the lumbar spine, femoral neck, total proximal femur, or 1/3 radius
2. Low-trauma spine or hip fracture (*regardless of bone mineral density*)
3. T-score between −1.0 and −2.5 **and** a fragility fracture of proximal humerus, pelvis, or distal forearm
4. T-score between −1.0 and −2.5 **and** high FRAX® (or if available, TBS-adjusted FRAX® - MOF>20% or Hip Fracture>3%)

*Laboratory Investigations:* Complete blood picture, ESR, Random blood sugar, Serum calcium, Fasting serum phosphorus, Serum creatinine, Serum albumin, Alkaline phosphatase, Serum TSH 25 hydroxy vitamin D, X ray of Thoracolumbar Spine (Lateral View), and PTH (based on clinical judgment).

Consider using bone turnover markers in the **initial evaluation and follow-up of osteoporosis patients**. Elevated levels can predict more rapid rates of bone loss and higher fracture risk

*Marker of Bone resorption*: Serum C-terminal telopeptide (CTX), used when patient is on anti-resorptive therapy. Sample taken at 9 am after overnight fasting.

*Marker of Bone formation*: Serum procollagen type 1 N-terminal propeptide (PINP), bone-specific alkaline phosphatase. Used for monitoring when on anabolic medications. Sample can be taken anytime.

## Measures for Bone Health[1]

*Life Style Modifications*: This includes a balanced diet, adequate physical activity and exposure to sunlight, and avoidance of bone-depleting agents. Limit alcohol intake to no more than 2 units/day, Avoid or stop smoking, Avoid and limit caffeine, tobacco, excessive salt (not more than 5 gm/day), Maintain an active lifestyle, including weight-bearing, balance, and resistance exercises and effective strategy for prevention of falls, and Ensure daily protein intake of 0.8 to 1 gm/day.

*Calcium Intake recommendations:* The recommended daily dietary allowance (RDA) of calcium intake for an adult Indian woman is >800 mg/day up to 1200 mg/day. Encourage dietary intake and supplements should be added to meet the daily allowance, Table 4. **Limit** *500 mg calcium at one time* from food and/or supplements. Dietary calcium restriction is no longer recommended for patients with hypercalciuria. *The risk of cardiovascular events and calculi are not observed with the recommended doses of calcium (<*

*2500 mg/day).*

**Table 4:** Quick Dietary Calcium Assessment Chart[1]

| Source | Calcium (mg)* | Number of servings | Total calcium (mg) |
|---|---|---|---|
| Diary source | 300-525/1 glass<br>300/1 katori curds | x | |
| Non diary | 200-300 | x | |

Total intake of calcium in mg. *Approximate estimates. Calculate the total daily dietary intake by entering the sources and the number of servings from diary and nondiary sources before supplementation

*Vitamin D Recommendations[1]:* Vitamin D can be obtained through sunlight by exposing 15%–30% of body surface area (face, neck, and both arms and forearms) without sunscreen for at least 30 min between 10 am and 3 pm. This is equivalent to consuming 340–490 IU of Vitamin D every day. It is preferable but difficult. Dietary sources are limited. Hence supplementations are essential. Vitamin D supplementation ((≥500–2000 IU/day) was favorable in the reduction of hip fracture or any non-vertebral fracture in a woman aged 65 years or more. Maintain serum 25-hydroxyvitamin D ≥30 ng/mL. Cholecalciferol is the preferred therapy, for deficiency: 60000 IU/orally once a week for 8 weeks or One IM injection of 600,000 IU. Maintenance dose: 2000 IU/day or injection of cholecalciferol 300,000 IU IM twice a year or 600,000 IU IM once a year is given. The dose for treatment should not exceed 4000 IU/day and hypercalcemia has been reported when the dose exceeds 10,000 IU/day

*Vitamin K Supplementation:* Both bone and cardiovascular health of women with osteoporosis would benefit from Vitamin K2–7 intake. For women of postmenopausal age, 180–350 µg/day of Vitamin K2–7 may need to be supplemented along with the recommended intake of calcium, magnesium, Vitamin D, and a balanced diet.

## Treatment plan according to the Risk stratification Pharmacotherapy[2]

*Bisphosphonates* with efficacy to reduce hip, nonvertebral, and spine fractures including alendronate, denosumab, risedronate, and zoledronate are appropriate as initial therapy for most osteoporotic patients with high fracture risk (Risk stratification, Table 5). Abaloparatide, denosumab, romosozumab, teriparatide, and zoledronate should be considered for patients *unable to use oral therapy and as initial therapy for patients at very high fracture risk*. Ibandronate or raloxifene may be appropriate initial therapy in some cases for patients requiring drugs with spine-specific efficacy.

**Table 5:** Risk stratification[3]

| Stratification of Risk | Treatment Advised |
|---|---|
| **Low risk of fracture (all must be present)**<br>• No fragility fractures<br>• DXA-derived *T*-score < -1 and > -2.5 standard deviations<br>• FRAX 10-year probability of fracture (adjusted for trabecular bone score):<br>• Any major osteoporotic fracture: < 20%<br>• Hip fracture: < 3%<br>• Or less than the country-specific threshold for intervention | **Low fracture risk**<br>Optimize calcium and vitamin D status<br>Bone-friendly lifestyle |
| **High risk of fracture (any one of the following)**<br>• Presence of fragility fracture<br>• DXA-derived T-score ≤ -2.5 standard deviations<br>• FRAX 10-year probability of fracture (adjusted for trabecular bone score):<br>– Any major osteoporotic fracture: > 20%<br>– Hip fracture: > 3%<br>– Or exceeding the country-specific threshold for intervention | **High fracture risk**<br>Optimize calcium and vitamin D status<br>Bone-friendly lifestyle<br>Falls prevention<br>**Start appropriate antiresorptive therapy** |
| **Very high risk of fracture (any one of the following)**<br>• Recent fracture<br>• Multiple fractures<br>• Severe fracture<br>• Fracture while on treatment<br>• Fracture while on bone-toxic drug such as corticosteroids<br>• *T*-score ≤ -3.0 standard deviations<br>• FRAX 10-year probability of fracture (adjusted for trabecular bone score):<br>– Any major osteoporotic fracture: > 30%<br>– Hip fracture: > 4.5%<br>– Or exceeding the country-specific upper threshold for high risk<br>– Other factors such as an extremely high risk for falls. | **Very high fracture risk**<br>Optimize calcium and vitamin D status<br>Bone-friendly lifestyle<br>Falls prevention<br>**Consider appropriate anabolic treatment for 12–18 months followed by antiresorptive therapy.** |

***Preparations Available:*** Alendronate: 70 mg weekly; Risedronate: 35 mg weekly or 150 mg monthly; Ibandronate: 150 mg PO monthly or 3 mg IV every 3 months; Zoledronate: 5 mg IV once a year. Duration of treatment depends on the risk factors, Table 6.

*Contraindications:* Active oesophageal disease, Presence of anatomic or functional esophageal abnormalities, Presence of documented or potential GI malabsorption, Drug hypersensitivity or hypocalcaemia, and Creatinine clearance less than 35 mL/min and in those with evidence of acute renal impairment

*Precautions while administering Drug:* Must be taken

after a **prolonged fast** (usually fasting overnight and taken in the morning soon after arising); Swallowed with a full glass of water (with at least a 30-minute wait after ingestion before other medications, food, or beverages other than water); and to remain upright for 30 to 60 minutes

*Side Effects:* Acute-phase reactions in up to 30% of patients receiving their first dose. These reactions are characterized by fever and muscle aches—a flu-like illness—lasting several days. Bone, joint, or muscle complaints that may be severe but usually resolve on discontinuation. Osteonecrosis of the jaw (ONJ) and atypical femoral fractures (AFFs) are safety concerns

*Treatment Monitoring:* Obtain a baseline axial (lumbar spine and hip; 1/3 radius if indicated) DXA and *repeat DXA every 1 to 2 years* until findings are stable. Follow-up of patients should ideally be conducted in the *same facility with the same DXA system***.** BTM should be evaluated initially and then after 6 months**.** *Significant reductions in BTMs are seen with antiresorptive* therapy and have been associated with fracture reduction, and *significant increases indicate good response to anabolic therapy.*

**Table 6:** Duration of Pharmacotherapy

| | **Oral Biphosphonates** | **Zolendronate** | **Denosomab** | **Romosozumab** | **Abaloparatide and teriparatide** |
|---|---|---|---|---|---|
| High Risk | 5 years | 3 years | 2-10 years | | |
| V. High Risk | 6-10 years | 6 years | | 1 year | 2 years |
| Remarks | Ending of a holiday should be based on individual patient circumstances such as an increase in fracture risk, a decrease in BMD Increase in BTM | | Transit to Biphosphonate | Follow with a bisphosphonate or denosumab | |

## Role of MHT in prevention and management of Osteoporosis[2]

Although once considered the treatment of choice for postmenopausal osteoporosis**,** *estrogen was never specifically approved for this use.* Estrogen is approved by the FDA for prevention of postmenopausal osteoporosis with the added caveat, "when prescribing solely for the prevention of postmenopausal osteoporosis, *therapy should only be considered for women at significant risk of osteoporosis and for whom non-estrogen medications are not considered to be appropriate*". MHT can be prescribed for postmenopausal women at risk of osteoporosis if *they are < 60 years of age and < 10 years menopausal and have VMS.*

## Factors Determining the Success of Treatment

- Stable or increasing bone mineral density, with no evidence of new fractures or vertebral fracture progression as a response to therapy for osteoporosis
- Bone turnover markers at or below the median value for premenopausal women as a target for response to therapy for patients taking antiresorptive agents.
- Significant increases in bone formation markers as a pharmacologic response to anabolic therapy

**Motto of Indian Menopause Society**

Fit @ Forty, Strong @ 60, Independent @ 80

## References


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# Vaccination during Pregnancy and Lactation

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## Introduction

Immunization is a key component of primary health care and an unquestionable human right. It's one of the most cost-effective health investments. Vaccines are critical to prevent and control outbreaks of infectious diseases. Pregnancy is an immune tolerant state and makes pregnant women susceptible to infectious diseases with resultant maternal and perinatal morbidity and mortality. Pregnant women, however, build up a good response to vaccines.

The antibodies developed by pregnant women in response to vaccines not only protect them, but also help protect their babies from serious diseases early in life. The new-borns take about six months after birth to build their own immune response following vaccination. Vaccination during pregnancy also helps protect a mother from getting serious diseases and passing it to her new-born.

It is ideal to vaccinate women preconceptionally. Obstetric health care providers should routinely assess the vaccination status of pregnant women at their registration visit. Based on this they should recommend and administer desired vaccines which are safe during pregnancy. All pregnant women should be evaluated for immunity to rubella and varicella and be tested for the presence of HBsAg. Those susceptible to rubella and varicella should be vaccinated immediately after delivery.

## Types of vaccines

Various types of available vaccines include live attenuated, killed inactivated, purified macromolecules like polysaccharides, toxoids, cellular fractions, and recombinant vaccines (Table 1). Of these the use of inactivated and toxoid vaccines is safe in pregnancy. Live attenuated vaccines are contraindicated except in conditions where there is a substantial risk of exposure to the pregnant woman as in case of exposure to yellow fever or polio. Whenever immunisation is performed during pregnancy, the benefits to the mother and the foetus should outweigh the risks.

Nonpregnant women who are administered live attenuated vaccines are advised against pregnancy for at least 4 weeks after being vaccinated. However, if a pregnant woman is inadvertently administered a live attenuated vaccine or if a woman conceives within 4 weeks of receiving the vaccine, she should be counselled about the lack of any published reports on vaccine related adverse effects on the foetuses born to mothers who received the vaccine in pregnancy. Termination of pregnancy is not warranted due to lack of robust evidence of any harmful effects on the foetus.

**Table 1:** Types of available vaccines

| Type of vaccine | Name of vaccine |
|---|---|
| Live attenuated | Measles, Mumps, Rubella, Influenza (Intranasal), Varicella, BCG |
| Killed inactivated | Typhoid, Pertussis, Rabies, Influenza (Intramuscular), Japanese Encephalitis, Covid, Hepatitis A, HPV, COVID |
| Toxoids | Tetanus, Diphtheria |
| Cellular fraction | Meningococcal polysaccharide, Pneumococcal polysaccharide Hepatitis B polypeptide |
| Recombinant | Hepatitis , Covid |

## Induction of immunity

Immunity is defined as resistance to infectious diseases. Immunity may be induced in an individual by infection or vaccination. Active immunisation involves the administration of an antigen to stimulate production of antibodies and provide long term immunity. Passive immunity involves the administration of an antibody to confer short-term immunity.

## Recommended vaccination schedule during pregnancy (MOHFW 2018)

***Td (tetanus and diphtheria toxoid) Vaccine*:** Tetanus is a life-threatening bacterial disease that is caused by the toxin of a bacterium called Clostridium tetani which is often found in soil. Tetanus bacteria enter the body through an open wound. Tetanus is prevented only through vaccination. The tetanus

vaccine contains non-infectious toxoids.

Conventional tetanus toxoid TT vaccine was replaced by Td vaccine, a combination of tetanus and diphtheria by MOHFW in 2018 to curtail the outbreaks of diphtheria. It is a heat and freeze sensitive vaccine. The schedule is as follows:

Td 1 (first dose): early in pregnancy

Td 2 (second dose): 4 weeks after Td1

Td B (booster): If pregnancy occurs within 3 years of last pregnancy and 2 doses of Td were received in that pregnancy.

Some experts recommend that the second dose of the vaccine should be given 4 weeks prior to the expected date of delivery. The WHO also recommends that a third vaccine be given 6 months after the second one to provide protection for at least 5 years.

This provides active immunization to the mother and extended passive immunization to the new-born for 3-6 months after birth by transplacental transfer of IgG antibodies to the foetus. In June 2018, ACOG recommended replacement of TT vaccine with TdaP, which contains tetanus toxoid, acellular pertussis, and diphtheria toxoid. The live pertussis vaccine is contraindicated in pregnancy.

Health-care personnel should administer a dose of Tdap during each pregnancy irrespective of the patient's prior history of receiving Tdap. To maximize the maternal antibody response and passive antibody transfer to the infant, optimal timing for Tdap administration is between 27 and 36 weeks of gestation although Tdap may be given at any time during pregnancy. Currently available data suggest that vaccinating earlier in the 27 through 36–week period will maximize passive antibody transfer to the infant. For women not previously vaccinated with Tdap, if Tdap is not administered during pregnancy, Tdap should be administered immediately postpartum.

## Optional immunization

***Influenza Vaccine*:** The goal of the vaccine is to prevent seasonal influenza. The flu comes around each year and antenatal women and children are among some of the most vulnerable populations. Each year the viral strain changes hence a new vaccine is released by WHO around July depending upon the prevalent strain. This vaccine offers protection both to the mother and new-born who cannot be vaccinated for first 6 months of life. Studies have demonstrated significant reduction in influenza illness among infants up to 6 months whose mothers were immunized during pregnancy. Two types of influenza vaccines are available: inactivated and live attenuated. Inactivated vaccine 0.5 ml intramuscular is recommended after 26 weeks of pregnancy. However, during pandemic, it can be given at an early period of gestation. Live attenuated vaccine given via intranasal route is contraindicated during pregnancy due to a theoretical teratogenic risk.

## Specific vaccines used in pregnancy

***COVID-19 Vaccine:*** COVID vaccine is validated by WHO for emergency use. Evidence continues to build showing that COVID-19 vaccination before and during pregnancy is safe and effective. It suggests that the benefits of receiving a COVID-19 vaccine outweigh any known or potential risks of vaccination during pregnancy. In a recent population-based study of over 18,000 pregnant women in Scotland it was observed that in the pregnant patients with COVID-19, unvaccinated individuals had a significantly higher proportion of COVID-19-associated hospital admissions (77%), critical care admissions (98%) and perinatal deaths including stillbirths and neonatal deaths (100%). The perinatal death rate in the vaccinated cohort was similar to historical background rates and the rates in pregnant women without COVID-19.

Various vaccines are available in India using various platforms. None of these contain a live SARS Cov 2 virus. These include Covaxin (Inactivated), Covishield, Johnson and Johnson (Non replicating viral vector adeno virus, Corbevax (Protein subunit recombinant platform), Moderna (mRNA), Pfizer (mRNA), Sputnik light and Sputnik V (Non replicating viral vector) and Zydus Cadila (DNA based). All have been approved for use by Drug Controller General of India (DCGI).

COVID vaccine can be administered in any trimester. Any available vaccine can be prescribed however most of the safety data available is with respect to Moderna. COVID vaccine can be administered at the same time with other vaccines advised during pregnancy but at a different anatomic site. Anti D can be administered simultaneously with COVID vaccine, and breast feeding should not influence its administration. The dose schedule of primary vaccination and boosters is the same as in nonpregnant women.

The counselling must include minor side effects

such as soreness of arm, fever and flu like symptoms for which she can safely take tablet paracetamol. She must be informed about rare danger signals like a new, severe headache which is not helped by usual painkillers or is getting worse, an unusual headache which seems worse when lying down or bending over or may be accompanied by blurred vision, nausea and vomiting, difficulty with speech, weakness, drowsiness, or seizures, a new onset, unexplained pinprick bruising or bleeding, and shortness of breath, chest pain, leg swelling or persistent abdominal pain. She must be counselled to report to the hospital at the earliest in case of any danger signal.

***Hepatitis B Vaccine:*** Hepatitis B infection is a serious infection that causes inflammation of the liver. It can cause severe morbidity in the pregnant woman and increase the risk of preterm birth. The biggest concern is its vertical transmission i.e transmission of infection from mother to child. About 70% to 90% of babies will remain chronically infected with hepatitis B into adult life and can develop liver cirrhosis and hepatocellular carcinoma later. Pregnancy is not a contraindication to vaccination. Limited data suggest that developing foetuses are not at risk for adverse events when hepatitis B vaccine is administered to pregnant women. Available vaccines contain non-infectious HBsAg and should cause no risk of infection to the foetus. It has a seroconversion rate of 90-100%.

Pregnant women who are identified as being at risk for HBV infection during pregnancy that is those having more than one sex partner during the previous 6 months, been evaluated, or treated for an STD, with history of recent or current injection drug use, or having had an HBsAg-positive sex partner should be vaccinated. Moreover, any woman who becomes pregnant while getting immunized with Hepatitis B vaccination can complete the remaining doses in pregnancy as well.

***Hepatitis A Vaccine:*** The safety of hepatitis A vaccination during pregnancy has not been determined; however, because hepatitis A vaccine is produced from inactivated HAV, the theoretic risk to the developing foetus is expected to be low. The risk associated with vaccination should be weighed against the risk for hepatitis A in pregnant women who might be at high risk for exposure to HAV. In may be considered for women with chronic liver disease and in those travelling to endemic areas.

***Meningococcal Vaccine:*** Pregnancy should not preclude vaccination with meningococcal quadrivalent conjugated (inactivated) vaccine, if indicated. However, serogroup B is avoided during pregnancy.

***Pneumococcal Vaccine:*** Pneumococcal Polysaccharide (Inactivated) can be administered before, during and after pregnancy safely. It is indicated in high-risk women such as Sickle cell disease, splenectomy, Chr. liver disease, immunocompromised, DM, Chr. lung disease. This is best administered before pregnancy.

***Haemophilus influenzae Vaccine:*** Hemophilus influenzae type B Hib (Inactivated) is safe in third trimester and after pregnancy. It is indicated in pregnant women with Sickle cell disease, splenectomy, HIV +ve, and leukaemia. This is best administered before pregnancy.

***Rabies:*** Because of the potential consequences of inadequately managed rabies exposure, pregnancy is not considered a contraindication to postexposure prophylaxis. Certain studies have indicated no increase in incidence of abortion, premature births, or foetal abnormalities associated with rabies vaccination. If the risk of exposure to rabies is substantial, pre-exposure prophylaxis also might be indicated during pregnancy. Rabies exposure or the diagnosis of rabies in the mother should not be regarded as a reason to terminate pregnancy.

***Polio (IPV):*** Although no adverse effects of IPV have been documented among pregnant women or their foetuses, vaccination of pregnant women should be avoided on theoretical grounds. However, if a pregnant woman is at increased risk for infection and requires immediate protection against polio, IPV can be administered in accordance with the recommended schedules for adults.

***Yellow fever:*** As compared with most other live vaccines, which are contraindicated in pregnancy, it is a precaution for yellow fever vaccine. If travel is unavoidable, and the risk of exposure to yellow fever virus outweighs the vaccination risks, a pregnant woman should be vaccinated.

***Typhoid:*** No data have been reported on the use of either typhoid vaccine in pregnant women. In general, live vaccines like Ty21a are contraindicated in pregnancy. Vi polysaccharide vaccine should be given to pregnant women only if clearly needed.

## Vaccines contraindicated during pregnancy

All live attenuated vaccines such as MMR (measles, mumps, and rubella), varicella, meningococcal, HPV, OPV, typh-oral, cholera, Japanese encephalitis and plague are contraindicated during pregnancy as they can cross placenta and pose risk to the fetus.

Any woman who becomes pregnant after initiating the series of HPV vaccination the remaining doses can be delayed till after pregnancy. However, a pregnancy testing is not needed before vaccination. If inadvertently a dose of HPV vaccine has been administered during pregnancy, no intervention is needed.

**Vaccines during lactation**

Inactivated, recombinant, subunit, polysaccharide, and conjugate vaccines, as well as toxoids, are safe for the mothers who are breastfeeding their infants. Live vaccines (except smallpox and yellow fever) may be administered to breast feeding mother if indicated. Breastfeeding does not adversely affect success or safety of vaccination. Smallpox and yellow fever vaccines are avoided in nonemergency situations because breastfed infants of vaccinated nursing caregivers are at risk of developing vaccinia and meningoencephalitis. Vaccines such as MMR, Varicella, HPV, Tdap, LAIV may be safely offered.

## Passive Immunization during Pregnancy

There is no known risk of passive immunization of pregnant women with immune globulin preparations to the fetus.

## Conclusion

MOHFW recommends universal immunization with tetanus and diphtheria (Td), and COVID vaccine of all pregnant women. This is safe and effective and provides immunization to both the pregnant woman and her newborn. All women should preferably be immunized preconceptionally, however those who are not immunized and are at an increased risk of vaccine preventable diseases should be administered non-live vaccines safely during pregnancy. After delivery, all women who have not been immunized against diseases like rubella, varicella, HPV etc. should be immunized in the postpartum period. All live attenuated vaccines should be avoided in pregnancy except in conditions like increased risk of exposure to yellow fever.

**Table 2:** Summary of vaccinations during pregnancy and lactation

| Vaccine | Before pregnancy | During Pregnancy | After pregnancy |
|---|---|---|---|
| Tdap (Toxoid/ Inactivated) | Yes | Yes, ideally between 27-36 weeks | Yes |
| COVID | Yes | Yes | Yes |
| Influenza IIV (Inactivated) | Yes | Yes | Yes |
| Influenza LAIV (Live attenuated) | Yes | No (delay till after birth) | Yes |
| Hepatitis B | Yes | Yes | Yes |
| Hepatitis A | Yes | Yes | Yes |
| Pneumococcal (Polysaccharide inactivated) | Yes | Yes | Yes |
| Meningococcal Quadrivalent conjugate inactivated | Yes | Yes | Yes |
| Hemophilus influenzae type B Hib (Inactivated) | Yes | Yes, safe in last trimester | Yes |
| Typhoid Vi polysaccharide (Inactivated) | Yes | Yes | Yes |
| Rabies post exposure (live attenuated) | Yes | Yes | Yes |
| MMR mumps, measles, rubella | Yes, delay pregnancy for 4 weeks | No | Yes |
| Varicella (live attenuated) | Yes, delay pregnancy for 4 weeks | No | Yes |
| HPV | Yes | No delay till 4 weeks after pregnancy | Yes |

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# Herpes in Pregnancy: Case Based Management

**Bijoya Mukherjee[1], Sumitra Bachani[2]**
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## Introduction

Herpes Simplex Virus (HSV) is a DNA virus belonging to alpha Herpesviridae family. Infection in pregnancy can be caused by two types: HSV 1 which is responsible mainly for herpes labialis, gingivostomatitis and keratoconjunctivitis, while HSV 2 is the primary etiologic agent of genital herpes. However, HSV1 is also emerging as important agent of oral and genital herpes, specifically in young and adolescent women. The prevalence of HSV in India is 7.5-8.5%. The incidence of new episode of HSV infection in pregnancy is 2%, while 75% of patients with history of genital herpes develop recurrence in current pregnancy.

## Mode of transmission

It occurs mainly by sexual contact, also by contact with mucosa or abraded skin. Vertical transmission occurs mainly during delivery (85%) resulting in neonatal herpes, followed by postpartum transmission (25%) through contact with mother, health care worker or family member. Transplacental transmission rarely occurs (5%), which can cause scarring or blisters on skin, hydrocephaly, calcification in brain, chorioretinitis, micro-ophthalmia or even fetal growth restriction or death.

## Maternal infection

**First episode primary infection:** HSV 1 or 2 is isolated from a lesion but there are no HSV 1 or HSV 2 antibodies seen. It is asymptomatic in almost 70% women. Vesicular lesions are common with painful genital ulcers, pruritis and dysuria along with systemic effects like fever, headache and inguinal lymphadenopathy.

**First episode non primary infection:** One HSV type is isolated from the lesion and antibody of other HSV type is present. Prodromal symptoms like pruritis and dysuria occur before appearance of local lesions, which may be non tender and atypical (fissures, vulvar irritation). This type usually lacks systemic findings and duration of viral shedding is shorter than primary infection.

**Recurrent disease:** Isolation of HSV type 1 or 2 from a lesion and isolation of same serotype antibody. Recurrent lesions occur at the same site in this type of infection.

## Fetal infection

Infection during 2nd trimester is associated with a very low risk (5%) of transplacental transmission & congenital anomaly. Evidence suggests that infection in 3rd trimester may lead to low birth weight, preterm labour and stillbirth. Neonatal herpes is caused by HSV 1 in 50% cases and rest by HSV 2. Neonatal HSV infections can be classified as disseminated disease (25%); central nervous system disease (30%); and disease limited to the skin, eyes, or mouth (45%). Mortality is highest for disseminated disease (30%) and lowest for local lesions, and long term neurological sequelae are noted in 20% of survivors.

**Case**: A 30 year old G3P1L0 came at $12_{+5}$ weeks period of gestation (POG) with HSV IgM positivity and HSV IgG positivity for both 1 and 2 at 9 weeks POG. She had no clinical symptoms of herpes infection. In her first pregnancy, she had history of herpes labialis and genital herpes in the 3rd month which continued on and off throughout pregnancy, had normal level II USG, but had intrauterine death with severe fetal growth restriction and bilateral pleural effusion at 34 weeks. Serology for herpes infection was not done and she did not receive any antiviral treatment during her antenatal period or labour. She was however given Valacyclovir after her delivery. In her second pregnancy, she again had herpes labialis and Genital herpes at 5 weeks POG and had a missed abortion at 11 weeks. She did not undergo any serology test and did not receive any antiviral treatment in her second pregnancy also.

*Case Outcome:* This was a case of recurrent herpes infection in pregnancy with positive IgG serology for both types of HSV. She was asymptomatic and IgM was likely falsely raised. She was counselled regarding very low risk of perinatal transmission to the fetus and offered Acyclovir 400 mg TDS from 36 weeks to prevent perinatal shedding and infection though a very rare possibility existed. She did not take Acyclovir and had spontaneous labour and

vaginal delivery at 38 weeks of pregnancy. Both mother and baby were unaffected.

## Discussion

She had adverse pregnancy outcomes in her previous pregnancies due to lack of treatment as first episode HSV infection. She needed antiviral treatment with Acyclovir.

There was no increased risk of congenital malformation, preterm labour, fetal growth restriction or stillbirth in current pregnancy as it was a case of recurrent HSV and has very low risk of perinatal transmission (0-3%).

Since it was a case of recurrent herpes infection, she did not need PCR testing from lesions at term or during labour (if they developed) to confirm asymptomatic shedding.

Antiviral treatment with Acyclovir 400mg TDS from 36 weeks of gestation till delivery should be continued and patient should be encouraged for vaginal delivery. However, if active genital lesions developed during labour, she could be offered for LSCS to reduce the viral shedding.

## Diagnosis of HSV infection in pregnancy

Routine screening of HSV in pregnant women is currently not recommended. Those with suspicion of infection can undergo testing by two basic modalities: 1) viral detection techniques and 2) antibody detection techniques. Those presenting with genital ulcers or mucocutaneous lesions are subjected to HSV detection by Polychromase chain reaction (PCR) technique (sensitivity 96-98%) and cultures (sensitivity 80% for primary lesions and 40% for secondary lesions). As most primary infections can be asymptomatic hence serology should also be done in all cases suspected to be HSV as it may be a non primary, recurrent or asymptomatic primary case. The sensitivity of ELISA for HSV 1 and 2 antibody testing is 90-100%.

## Management in pregnancy and labour

According to GTG and British Association for Sexual Health and HIV (BASHH) guidelines, HSV infection in pregnancy is managed as follows:

## First episode genital herpes

- *During 1st and 2nd trimester* (upto 27+6 weeks): Diagnosis of suspected lesions is confirmed by PCR testing. Treatment started with Acyclovir 400 mg TDS for 5 days (has good safety profile, only associated with transient neonatal neutropenia). Along with it, local treatment with paracetamol and 2% lidocaine is advocated. From 36 weeks, Acyclovir 400mg TDS given daily till delivery. Pregnancy managed expectantly and vaginal delivery is preferred.
- *During 3rd trimester:* Treatment started with Acyclovir 400mg TDS daily till delivery. Caesarean section is recommended mode of delivery, especially if infection is acquired within 6 weeks of delivery as neonatal transmission is 41% during this period.
- *At onset of labour:* Clinical history taking is the only way to determine first episode infection at labour. However, swabs should be taken from the lesion site to influence the neonatal management. Caesarean section is recommended mode of delivery if active genital lesions are present or delivery occurs within 6 weeks of infection. If vaginal delivery is opted for, then Intravenous acyclovir given intrapartum to the mother (5 mg/kg every 8 hours) and subsequently to the neonate (intravenous acyclovir 20 mg/kg every 8 hours) may be considered. In such cases, invasive procedures like application of fetal scalp electrodes, artificial rupture of membranes and instrumental delivery to be avoided. In active non-genital lesions, vaginal delivery is allowed with occlusive dressing of the active lesions.

## Recurrent genital herpes

*Any trimester:* The risk of neonatal herpes is 0-3% only if active genital lesions are present at time of delivery and 0.02-0.05% if lesions are absent during delivery. There is no increased risk of congenital abnormalities, preterm labour, prelabour rupture of membranes and fetal growth restriction in recurrent HSV infection. Sequential PCR testing or culture not required to determine viral shedding at term in such cases. Conservative management with paracetamol and saline bathing is sufficient. The lesions subside within 7-10 days even without antiviral treatment. Acyclovir 400 mg TDS given daily from 36 weeks till delivery, however evidences regarding this are insufficient.

*At the onset of labour*: Vaginal delivery is advocated, even in presence of active genital lesions. However, the decision of vaginal delivery verses caesarean section should be finalised by the mother in consultation with the obstetrician, keeping in mind

the very low risk of neonatal transmission versus the risks of caesarean section itself.

## Preterm pre labour rupture of membranes (PPROM) with HSV

### Primary infection with PPROM

There is limited evidence regarding time of delivery.

If immediate delivery is warranted, caesarean section should be offered.

If delivery occurs within 6 weeks of primary infection, caesarean section is indicated inspite of prolonged rupture of membranes.

If conservative management is undertaken, IV Acyclovir 5mg/kg TDS and prophylactic steroids should be considered.

### Recurrent infection with PPROM

The risk of neonatal herpes is very less.

Expectant management is carried out at less than 34 weeks of gestation along with Acyclovir 400mg TDS daily till delivery.

After 34 weeks gestation, management is not influenced by herpes infection and is carried out in line with routine management of preterm prelabour rupture of membranes.

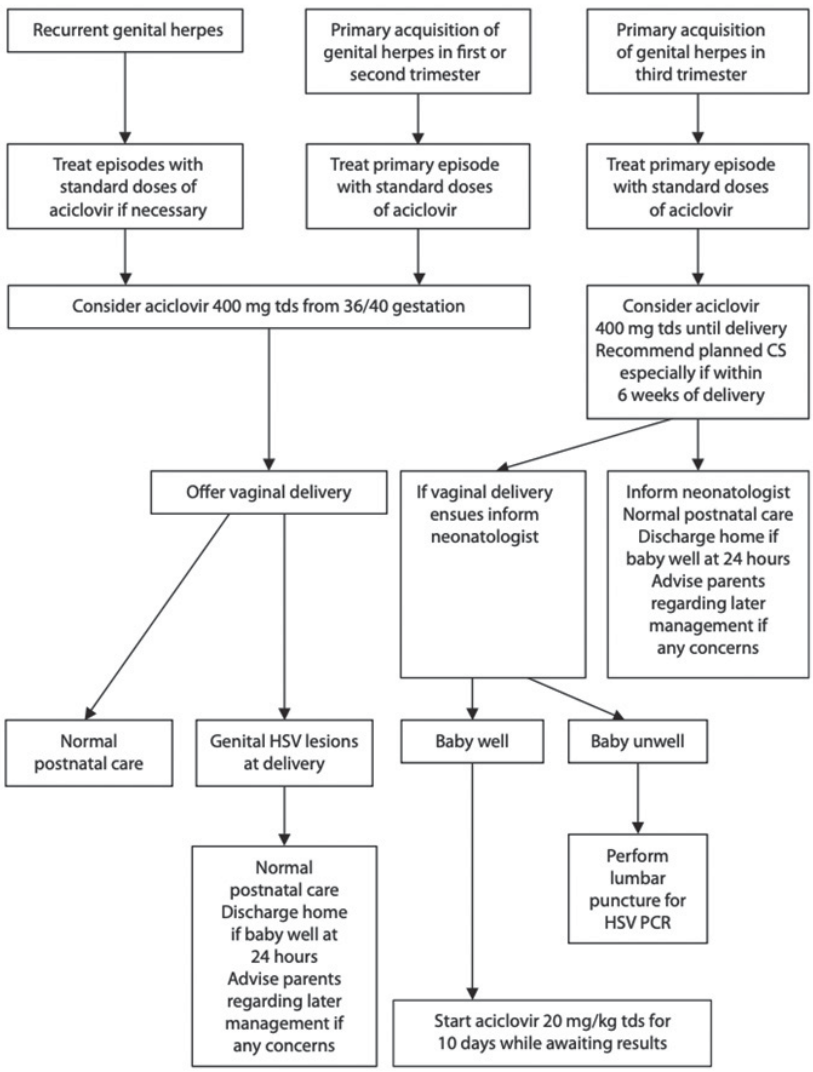
### Postnatal management

Prevention of neonatal infection of HSV is practiced by maintaining proper hand hygiene by the mother or staff associated who may come in contact with herpetic lesions.

Breastfeeding is recommended unless the mother has herpetic lesions around the nipples.

### Algorithm of management of herpes in pregnancy and neonatal management (RCOG GTG)

Abbreviations: CS- caesarean section, HSV- herpes simplex virus, PCR- polymerase chain reaction, TDS- three times daily




GTG: Green top guidelines, BASSH: British Association for Sexual Health and HIV

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# Managing Varicella Infection in Pregnancy

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## Introduction

Varicella Zoster Virus (VZV), a DNA virus of Herpesvirus family, is the causative agent of varicella or chicken pox and herpes zoster or shingles. It spreads by respiratory droplets, direct contact with vesicular fluids or secretions of nasopharynx. The incubation period is 14 days. The viral replication takes place in regional lymph nodes and tonsils and continues for 4-6 days. It is highly contagious, from a day prior to rash until lesions are crusted. Symptoms are characteristic vesicular rash, which appear in crops, highly pruritic and centripetal in distribution. There is malaise, fever, headache or myalgia. Secondary streptococcal or staphylococcus skin infection is the most common complication. Other rare complications can be pneumonia, arthritis, myocarditis, glomerulonephritis, ocular disease, adrenal insufficiency and Central nervous system (CNS) abnormality. Varicella infection is more severe in pregnant females than non-pregnant individuals. Varicella pneumonia can complicate 20% of infected pregnancies. It is rapidly progressive and in untreated cases mortality can be up to 40%. With aggressive treatment mortality can be brought down to less than 15%. Rarely 1% of women can develop encephalitis. Immunity is lifelong but in immunocompromised and elderly reactivation of virus causes shingles without any additional risk of fetal infection.

**Fetal infection:** In the first trimester the risk of fetal infection is 0.4%, between 13-20 weeks its 2% and beyond 20 weeks there is hardly any risk of infection. Maternal infection after 36weeks is associated with a 50% fetal infection and a 25% clinical varicella infection in the neonate. Fetal varicella syndrome may include any of the following features: polyhydramnios (due to decreased movement or digestive-tract atresia), limb defects and dermatomal skin scarring (due to fetal herpes zoster), soft-tissue calcification and damage to the eyes and CNS. Neurological defects include cortical atrophy, microcephaly, limb paresis, spinal cord atrophy, encephalitis, seizures and Horner's syndrome. In around half of fetuses/infants, the eyes will be affected by microphthalmia, chorioretinitis, cataracts or optic atrophy and limb defects are present in around 50% cases. FGR may be diagnosed on ultrasound imaging and developmental delay may occur.

**Neonatal infection:** Neonatal infection is high when mother develops acute varicella five days prior and two days after delivery. Since there is no opportunity for the protective antibodies to cross placenta in this short period the neonate gets affected. The features are disseminated mucocutaneous lesions, visceral infection, pneumonia and encephalitis. Mortality is up to 30% in untreated neonates. Immuno-prophylaxis can be administered with Varicella zoster Immunoglobulin (VZIG) and neonate can be treated with Acyclovir or Valacyclovir.

**Case: A** 27 years old Primigravida with history of chicken pox presented to Antenatal OPD two weeks after the appearance of vesicles (at POG- 14 weeks 1 day), and she had been treated with Acyclovir. The couple was counselled regarding 2% possibility of transmission of infection to fetus and they opted for invasive testing.

**Investigation:** Amniocentesis was performed after 6 weeks of clinical illness. Polychromase chain reaction (PCR) test for Varicella was negative.

**Follow up:** The couple was counselled about no risk of fetal infection. Pregnancy was continued, anomaly scan and growth scans were normal. She delivered vaginally at term, baby and mother were well.

## Discussion

All pregnant women should be asked about prior infection at first prenatal appointment. When there is:

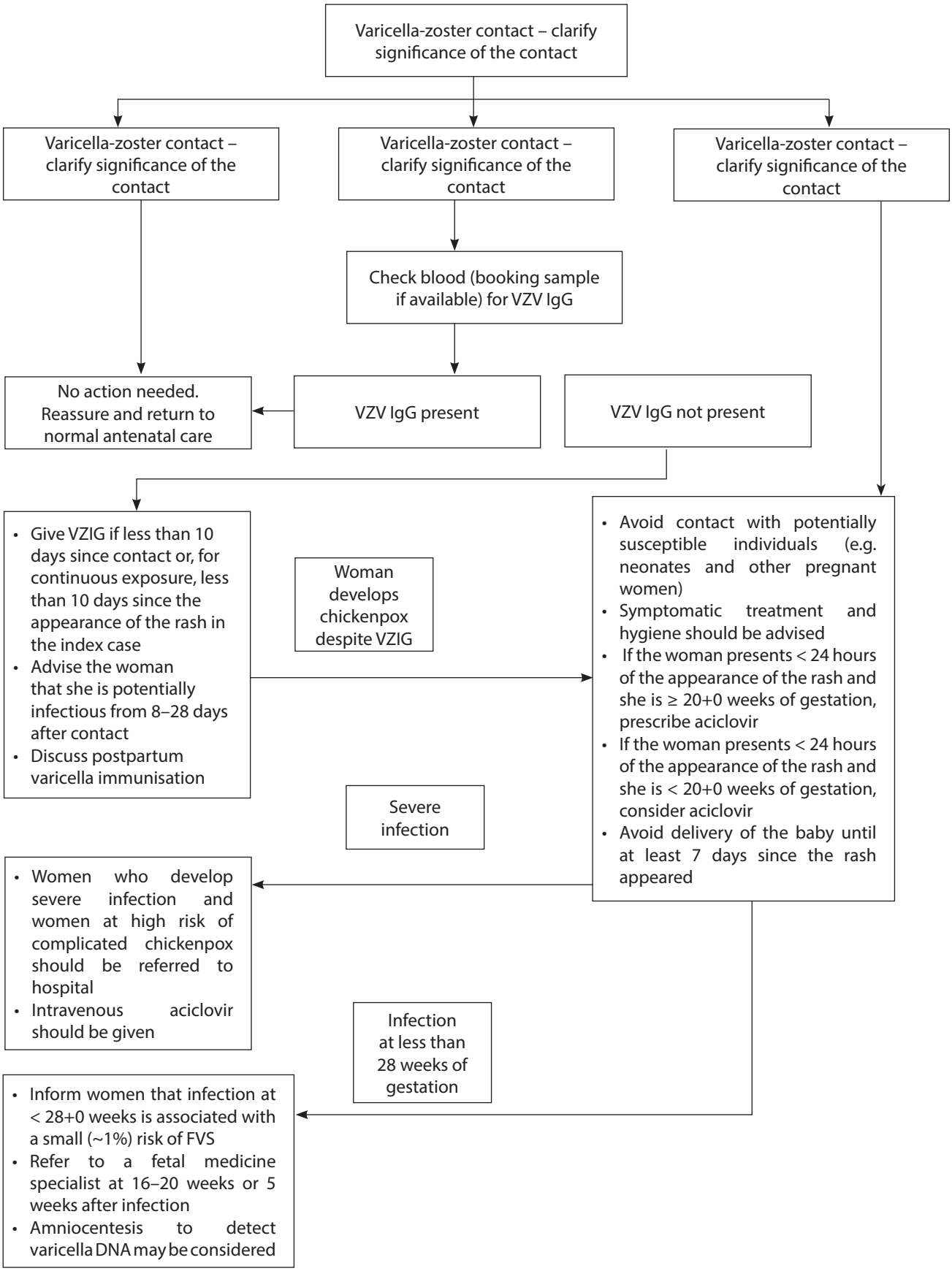
Definite history- reassurance, chance of second infection extremely unlikely.

Not certain of prior infection- anti-VZV IgG assay is done. 75% of such have definite serological evidence of immunity

Non-immune individuals are cautioned to avoid exposure

**Diagnosing maternal infection:** The diagnosis

**Algorithm for the management of varicella-zoster contact in pregnancy**



of VZV is based on the clinical findings of chickenpox of a classic pruritic, vesicular rash hence laboratory testing is not usually needed. Maternal serology testing for VZV in pregnancy is usually performed following contact with a known case of chickenpox.

## Diagnosing fetal infection

- Fetal infection can be confirmed by amniocentesis
- PCR can be used to detect VZV DNA.
- Diagnosis of fetal infection (i.e. as confirmed by positive PCR analysis following amniocentesis) does not confirm that the fetus will be affected by varicella syndrome. A close ultrasound follow up has to be done in all cases to identify any stigma of CVS.

## Treatment

- Supportive: Analgesics, Local application of Lidocaine jelly/ Emollients
- Severe chicken pox: Hospitalization
- Oral acyclovir 800mg 5times/day or
- Oral valacyclovir 1gm three times/day or
- Intravenous acyclovir 10mg/kg over 1hr x 8 hourly
- Varicella zoster immunoglobulins: given to newborn if maternal infection occurs 5 days prior and 2 days following delivery
- Infant should be isolated from mother until all vesicles have crusted

## Prevention

**VZV vaccine:**

- prior to pregnancy and postpartum if women are seronegative
- 2 doses subcutaneously 4-8 weeks apart
- Contraindicated in pregnancy
- Pregnancy should be deferred for 3 months post vaccination

## Varicella zoster immunoglobulins: (post-exposure)

- Effective when given upto 10 days after exposure. Recommended dose 125 units/10kg of body weight upto maximum of 625 units
- Only to be given in seronegative women and should not be given to women who have developed chicken pox lesions.

**Acyclovir: (post-exposure)**

- 800mg 5times/day for 7 days within 9 days of exposure (85% reduction in infection)

**Valacyclovir: (post-exposure)**

- 1gm 3 times/day for 7 days

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# Rubella in pregnancy: Prenatal diagnosis

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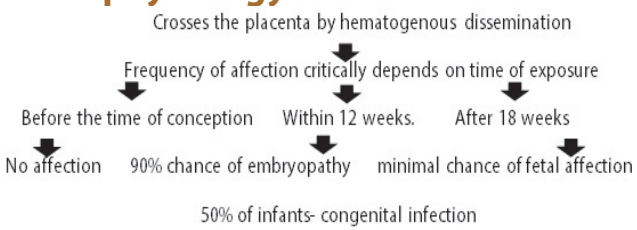
## Introduction

Rubella (German measles), a single stranded RNA virus of togavirus family spreads by respiratory droplets.[1] The incubation period is 2-3 weeks. Viremia occurs 7-9 days after exposure. Symptoms are characteristic maculopapular rash which starts from face, then involves the trunk, lasting for 3 days. There is malaise, fever, headache, conjunctivitis and occasionally post auricular, suboccipital and posterior cervical lymphadenopathy. Overt clinical symptoms manifest only in 50-75% women, hence clinical history may not always suggest prior illness.[2]

## Pathophysiology




**Fetal infection:** Rubella is one of the most teratogenic viruses. The risk of fetal infection decreases with increasing gestational age at maternal infection; it is around 90% before 12 weeks' gestation, 55% from 12 to 16 weeks and 45% after 16weeks. However the risk of an infected fetus being affected i.e. risk of developing congenital rubella syndrome (CRS) is greatest when infection occurs earlier in gestation: it is 97% when infection is prior to 12 weeks and 20% between 12 to 16 weeks, while infection from 16 to 20 weeks is associated with a minimal risk of sensorineural deafness only.[3-6] The risk of the fetus being affected as a result of primary maternal infection after 20 weeks gestation or recurrent infection is very less.

The four most common anomalies in CRS are

- Sensorineural deafness (60-70%)
- Eye defects: cataract, retinopathy, microphthalmia, chorioretinitis (10-30%)
- CNS defects: microcephaly, mental retardation (10-25%)
- Cardiac defects:Patent Ductus Arteriosus (PDA), Pulmonary artery stenosis (10-20%)

There can be fetal growth restriction, hepatospleenomegaly, jaundice, thrombocytopenic purpura, meningoencephalitis. Gregg's triad is a classical presentation where the baby has microcephaly, PDA and congenital cataract. Baby can have characteristic blueberry muffin rash.

**Case:** A 36 years old G2P1L1 presented at 14 weeks period of gestation. with report of high Rubella IgM titre. She had history of febrile illness around 10 weeks of pregnancy, without rash and had been advised a TORCH test.

## Investigation

| Parameters | At 13 weeks | At 15 weeks | Normal range |
|---|---|---|---|
| IgM | 49.55 U/ml | 0.18 U/ml | PI >1.1- positive<br><0.9- negative<br>0.9-1.1- equivocal |
| IgG | 18.72 U/ml | 21.79 U/ml | Seropositive 0-15 U/mL<br>Seronegative 15.1-73.5 U/mL |
| IgG Avidity | | 86.5% | <47%- low avidity<br>47-60%- equivocal<br>>60%- high avidity |

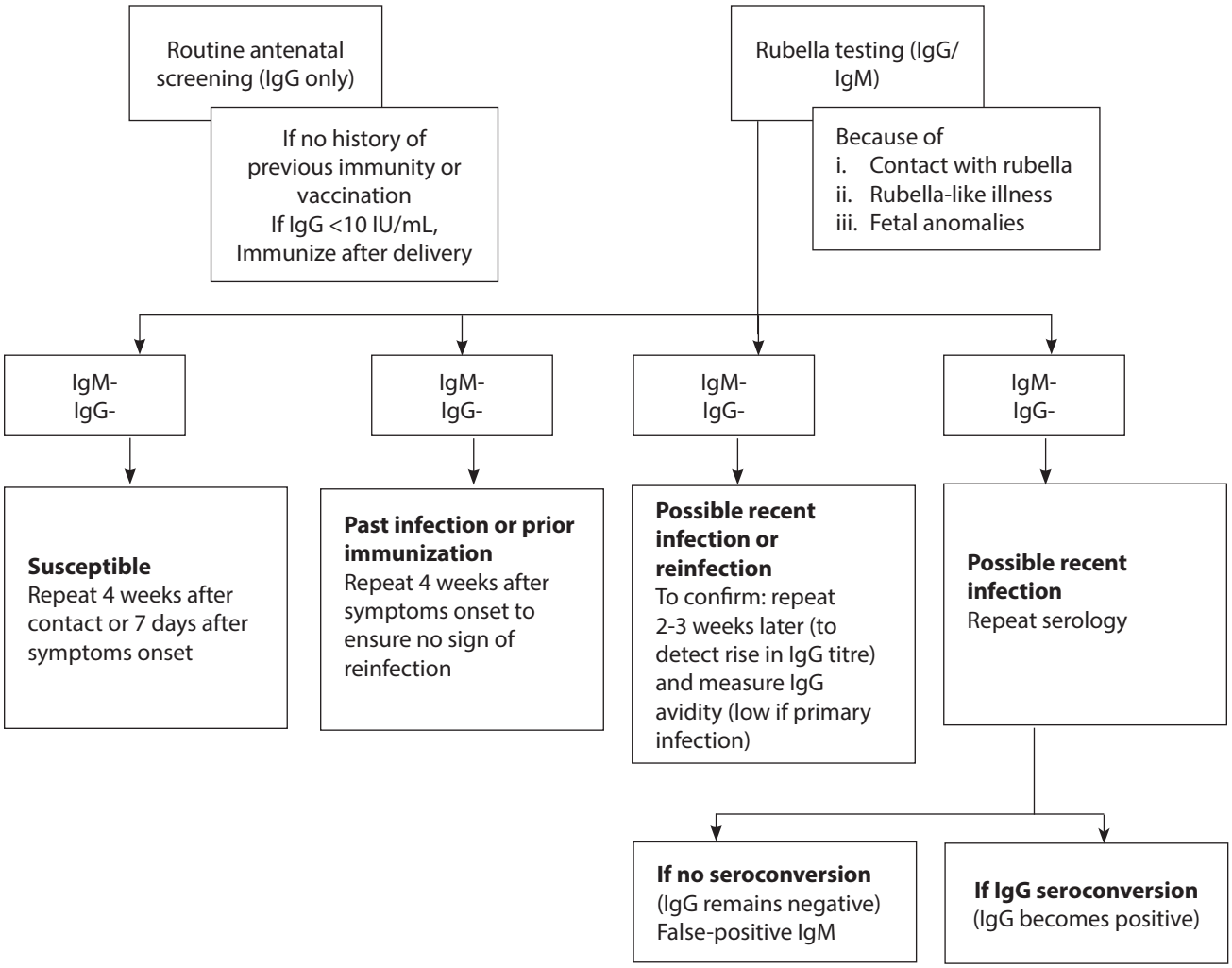
Since in this case based on high avidity time of infection was likely periconception period the couple opted for Amniocentesis which was performed after 18 weeks of POG. PCR test for Rubella was negative.

**Follow up:** The couple was counselled about no risk of fetal infection and falsely high IgM during the febrile illness. Pregnancy was continued, anomaly scan and growth scans were normal. She delivered vaginally at term, baby and mother both doing well currently.

## Discussion

1. Routine screening for Rubella is currently not recommended. Serology can be offered in following conditions
2. Exposure to Rubella positive person, face to face contact or presence in same room for 15 minutes or more.
3. Presence of symptoms suggestive of infection.
4. Ultrasound features such as cardiac anomalies, microcephaly, ventriculomegaly, placentomegaly or unexplained growth restriction.
5. Unexplained still birth.
6. Rubella IgG ideally in preconception period and if not done then in pregnancy to confirm immune status.

**Diagnosing maternal infection:**




## Diagnosing fetal infection:

- Infection of the fetus can be confirmed by amniocentesis. This is usually delayed until after 18–20 weeks' gestation, when fetal urination is established.
- Invasive testing is usually performed for primary maternal infections occurring between 12 and 16weeks of gestation, the risk to the fetus of infection after that time being small.
- The viral nucleic acid can be detected in the amniotic fluid using PCR; this test has high sensitivity and specificity. (87% and 99% respectively)
- Amniocentesis performed within 6weeks of the primary maternal infection carries a risk of being false-negative, so a negative result in these circumstances may justify repeat invasive testing later.
- Total and viral-specific IgM in fetal blood obtained by cordocentesis can be done only after 20 weeks and carries a 2-4 % risk of fetal loss.
- When primary infection occurs before 12 weeks' gestation, given the risk of fetal infection and the risk of an infected fetus developing severe abnormalities, it is reasonable to consider termination of pregnancy when appropriate, even without invasive testing.[7]

**Prevention:** Although being the most teratogenic virus, rubella infection can be preventable with vaccination. Trivalent preparation of measles-mumps-rubella (MMR) became available in US 1969, after 10 years the annual incidence of rubella infection including CRS decreased by 99.6%. It gives the long-term immunity in 95% individuals. It is a part of our national immunization schedule. It should be administered to all children between 12-15 months, 2nd dose to be administered at least 1 month after 1st dose but before 6 years. Susceptible adolescent girls and all women of reproductive age group should receive vaccine (RA 27/3 vaccine, subcutaneously,

0.5ml). Pregnancy should be deferred for 1 month after the vaccine. However, termination is not advised in cases of conception within a month as no adverse outcome is reported on follow-up studies. Susceptible pregnant women should be offered vaccination immediately after delivery.

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# Calendar of Virtual Monthly Clinical Meetings 2021-22

| | |
|---|---|
| 28th May, 2021 | B L Kapoor Hospital |
| 25th June, 2021 | All India Institute of Medical Sciences |
| 30th July, 2021 | Sitaram Bhartia Hospital |
| 3rd September, 2021 | Army Hospital (Research & Referral) |
| 24th September, 2021 | Deen Dayal Upadhyay Hospital |
| 29th October, 2021 | PGIMSR & ESI Hospital |
| 19th - 21st November, 2021 | 43rd Annual Conference |
| 26th November, 2021 | MAMC & Lok Nayak Jai Prakash Narayan Hospital |
| 7th January 2022 | Sir Ganga Ram Hospital |
| 28th January, 2022 | ABVIMS & Dr Ram Manohar Lohia Hospital |
| 25th February, 2022 | UCMS & Guru Tek Bahadur Hospital |
| 1st March, 2022 | VMMC & Safdarjung Hospital |
| 29th April, 2022 | LHMC & Smt. Sucheta Kriplani Hospital |
| 27th May, 2022 | Apollo Hospital |

# Events Held in March 2022

| S. N. | Date | Events |
|---|---|---|
| 1 | 01.03.2022 | CME on "I care for Contraception" with FOGSI Family Welfare Committee Association |
| 2 | 01.03.2022 | Public Forum on "Polycystic Ovary" |
| 3 | 05.03.2022 | Webinar on "Anorectal Physiology for the Gynecologist" by Urogynaecology Committee |
| 4 | 08.03.2022 | Women's day Celebration by AOGD & DGF |
| 5 | 9.03.2022 | "Adolescent Health Medical Concerns" by SGRH under aegis of AOGD |
| 6 | 10.03.2022 | Case Based Discussions in Fetal Medicine by Fetal Medicine and Genetics Committee |
| 7 | 12.03.2022 | Physical Workshop by AOGD at Safdarjung Hospital |
| 8 | 12.03.2022 | CME by MAMC with Fet & Gen Committee, SFM |
| 9 | 19.03.2022 | CME on"Towards Elimination of Cervical Cancer-Translating Guidelines to Practice" by Oncology Committee |
| 10 | 21.03.2022 | PG Forum Class on " Endometriosis" |
| 11 | 22.03.2022 | CME on "Rh Negative Pregnancy" by Multidisciplinary Committee |
| 12 | 23.03.2022 | CME on "PCOS" by FOGSI Endocrinology Committee in association with AOGD |
| 13 | 24.03.2022 | "Robotics in Gynaecology: A Masterclass by Endoscopy Committee |
| 14 | 29.03.2022 | Physical CME by Infertility Committee AOGD |
| 15 | 31.03.2022 | "Fetomaternal Infections : Prevention and Care" by AOGD & SFM Delhi Chapter |

# Events to be Held in April 2022

| S no | Date | Events |
|---|---|---|
| 1 | 01.04.2022 | **AOGD monthly clinical Meeting, GBM & Handing Over at VMMC & Safdarjung Hospital** |
| 2 | 05.04.2022 | Workshop on "Breast and Cervical Cancer Screening" by Sharda University in association with AOGD & Breast and Cervical Cancer Screening Committee |
| 3 | 16.04.2022 | Webinar on "Transitions in Adolescence" by Rural Health Committee with IAP |
| 4 | 18.04.2022 | PG forum on "Hypertensive Disorders in Pregnancy" |
| 5 | 23.04.2022 | Webinar on "Towards Elimination of Cervical Cancer, Translating Guidelines to Practice- Part 2" by AOGD Oncology Committee |
| 6 | 25.04.2022 | "Induction of Labour", a Webinar by Safe Motherhood Committee, AOGD |

# Journal Scan

**Saumya Prasad[1], Sheeba Marwah[2]**
[1]Consultant, Obstetrics, Gynaecology & IVF Center, Primus Super Speciality Hospital
[2]Associate Professor, Obstetrics & Gynaecology, VMMC & Safdarjung Hospital, New Delhi

## Early Menopause May Associate With a Higher Risk of CKD and All-Cause Mortality in Postmenopausal Women: An Analysis of NHANES, 1999-2014

***Qian D, Wang ZF, Cheng YC, Luo R, Ge SW, Xu G.*** *Early Menopause May Associate With a Higher Risk of CKD and All-Cause Mortality in Postmenopausal Women: An Analysis of NHANES, 1999-2014. Front Med (Lausanne). 2022 Mar 18;9:823835.*

**Background:** Chronic kidney disease (CKD) in women is often accompanied by hormone disorders such as sex hormones, and most women with CKD are in the post-menopausal age group. Due to the close relationship between menopause and sex hormones, we aimed to explore the association between early menopause and CKD in post-menopausal women, and the influence of early menopause on longevity in the CKD population. **Methods:** Information regarding 4,945 post-menopausal women was extracted from the database of the National Health and Nutrition Examination Survey (NHANES) 1999-2014, and then divided into 4 groups according to the type of menopause (natural or surgical) and early menopause (menopause at age <45) or not. The association between early menopause and CKD prevalence was examined using multivariable logistic regression, while we used multivariable Cox proportional hazards models to investigate the possible relationship between early menopause and all-cause mortality in CKD and non-CKD populations. The differences in the levels of sex hormones between women with and without CKD were also explored. **Results:** Compared with women with natural menopause at age ≥45, women experiencing early natural menopause had a higher risk of CKD [OR = 1.26 (1.01-1.56)]. Similarly, as compared to women with surgical menopause at age ≥ 45, women in the early surgical menopause group were more likely to have CKD [OR = 1.38 (1.05-1.81)]. In addition, early surgical menopause was associated with higher mortality in the non-CKD group [HR = 1.62 (1.06-2.49)], but not in the CKD group. Women with CKD had a higher level of luteinizing hormone and follicle-stimulating hormone, combined with a lower level of testosterone and estradiol than the non-CKD women. **Conclusion:** Both early natural and surgical menopause were associated with a higher risk of CKD. Early surgical menopause was a hazard factor for survival in the non-CKD group, but not in the CKD group. Further research is required to understand the mechanisms.

## Association between lymphadenopathy after toxoplasmosis seroconversion in pregnancy and risk of congenital infection

***Donadono V, Saccone G, Sarno L, Esposito G, Mazzarelli LL, Sirico A, et al.*** *Association between lymphadenopathy after toxoplasmosis seroconversion in pregnancy and risk of congenital infection. Eur J Clin Microbiol Infect Dis. 2022 Jan;41(1):45-51.*

**Objective:** The aim of the study was to describe the pregnancy outcome of a large cohort of women with toxoplasmosis seroconversion in pregnancy and to investigate the relation between maternal lymphadenopathy and risk of congenital toxoplasmosis (CT). **Methodology:** This was a retrospective study involving women with confirmed toxoplasmosis seroconversion in pregnancy between 2001 and 2017. Women were clinically evaluated for lymphadenopathy and classified as follows: lymphadenopathy absent (L-) or lymphadenopathy present (L+). The mothers were treated and followed-up according to local protocol, and neonates were monitored at least for 1 year in order to diagnose CT. **Results:** A total of 218 women (one twin pregnancy) were included in the analysis. Pregnancy outcome was as follows: 149 (68%) of children not infected, 62 (28.3%) infected, 4 (1.8%) first trimester termination of pregnancy, 2 (0.9%) first trimester miscarriages, and 3 (1.4%) stillbirths (of which one already counted in the infected cohort). 13.8% of women were L+ , and they were nearly three times more likely to have a child with CT compared to L- women (aOR, 2.90; 95%CI, 1.28-6.58). Moreover, the result was still statistically significant when the analysis was restricted to 81 children whose mothers were clinically examined and received

treatment within 5 weeks from estimated time of infection. **Conclusion:** There is a positive association between L+ status in pregnant women, and risk of CT also confirmed when restricting the analysis to women with early diagnosis of seroconversion and treatment. This data could be very useful in counselling pregnant women with toxoplasmosis seroconversion and lead to direct a more specific therapeutic and diagnostic protocol.

## First-line noninvasive management of cytomegalovirus primary infection in pregnancy

***Denef M, Noel L, Bruck G, Gudelj J, Tebache M, Vielle-levoye R, et al.*** *First-line noninvasive management of cytomegalovirus primary infection in pregnancy. J Perinat Med. 2021 Dec 20;50(3):270-276.*

**Objectives:** To introduce a first-line noninvasive antenatal management of maternal cytomegalovirus (CMV) primary infection based on ultrasound (US) and magnetic resonance imaging (MRI). Amniocentesis (AC) is used as a second-line tool in cases of abnormalities compatible with fetal CMV infection on US and/or MRI screening. **Methods:** Between January 2011 and October 2018, pregnant women referred with a CMV primary infection on antibody screening were followed up by monthly US scans and a brain MRI at approximately 32 weeks. In cases with US and/or MRI abnormalities compatible with congenital CMV infection, AC was performed to confirm the diagnosis. **Results:** Ninety pregnant women with a primary CMV infection were included (89 singleton and one twin pregnancy). The first-line screening by US and/or MRI was normal for 72 of 91 fetuses (79%). At birth, 19 of these 72 neonates (26%) had a positive urine sample for CMV but were asymptomatic. US and/or MRI abnormalities were identified in 19 fetuses (21%). AC confirmed a fetal CMV infection in 16 fetuses (84%); 12 pregnancies were terminated, and four were continued, with three symptomatic neonates at birth and one poor neurodevelopmental outcome at postnatal follow-up. **Conclusions:** First-line noninvasive management of maternal CMV primary infection based on serial US scans and brain MRI can be offered to identify fetuses with severe symptomatic congenital CMV infection and reduce the number of ACs without compromising the fetal outcome.

# AOGD Monthly Clinical Meeting Held at VMMC & Safdarjung Hospital on 1st March 2022

## Interesting Case of Hemoperitoneum in a young Girl

**Zeba Khanam, Rekha Bharti, Jyotsna Suri, Sumitra Bachani, Divya Pandey**

**Background:** Distal vaginal atresia (DVA) is a rare Mullerian anomaly that may present as hematocolpos during puberty. Rarely does a hematocolpos cause hydroureteronephrosis and never does it rupture spontaneously into the abdomen. We describe here the management of such an exceptional case of hematocolpos in DVA. **Case report:** An adolescent girl with DVA presented to emergency with acute abdomen in shock. She had a backdated MRI reporting a massive hematocolpometra and bilateral hydroureteronephrosis. On laparotomy, the hematocolpometra was seen draining into the abdominal cavity through two posterior vaginal wall rents. A pull-through vaginoplasty was performed. Later she developed vaginal re-stenosis for which a revision vaginoplasty was performed. She had a wide patent vagina at her six-month follow-up visit. **Conclusion:** Hematocolpos in DVA may rupture spontaneously into the peritoneal cavity requiring a multidisciplinary treatment approach. Such patients need thorough counselling on the importance of regular follow-ups and self vaginal calibration post-operatively.

## Challenges of Ovarian Malignancy in the Young

**Renu Arora, Sarita Singh, Sumedha Gupta, Nalini H**

25 year nulligravida woman, married for 3 years came with Abdominal discomfort for 4 months, Abdominal distension for 2 months, Dyspepsia and loss of weight for 1 month. On examination, GPE is normal. Abdomen is uniformly distended along with fullness of flanks. A large mass, filling both flanks, about 24*26 cms, cystic in consistency is palpated. No shifting dullness present. On PV, Uterus couldn't be felt separately from mass, B/L fornices are full. Her Routine investigations were WNL. Tumor markers were as follow CA125-151, CEA-101, CA19.9-248. On USG, Abdominopelvic cystic structure of size 15.5*14*7.2 cm, abutting the uterine fundus and right ovary with multiple linear echogenic septations within noted. No obvious lymphadenopathy/ascites seen. MRI confirmed USG findings s/o Cystadenoma. A repeat USG after 2 months showed a large abdominopelvic predominantly cystic mass with multiple internal septations within seen to show Arborization Pattern with a central core showing internal vascularity with arterial flow on spectral doppler. B/L ovaries were not seen separately. CT perfusion scan shown multiple internal septations with no increased vascularity within. Upper GI endoscopy and colonoscopy are normal. Staging Laparotomy done. On opening abdomen, there was abundant gelatinous mucinous peritoneal material occupying the whole abdomen and pelvis. Large multicystic right ovarian cyst~22*26 cm filled with gelatinous viscid material removed with multiple sites of capsule rupture removed and sent for frozen section. Frozen section and scrape cytology shown *mucinous cystadenoma*. Left sided ovarian cyst 10*11 cm noted filled with gelatinous material, multiple sites of capsular rupture present. Cyst removed leaving behind remnants of about 4*3 cm of left ovary to preserve fertility as frozen section shown benign condition. On exploration, Appendix of 6*3 cm, enlarged, tensely cystic with mucinous deposits over it seen. Appendicectomy was performed. Multiple deposits were seen over POD, uterosacral ligaments, omentum. Infracolic omentectomy was done. Rest of the abdominal organs inspected. Found no visible nodules. Postoperative period was uneventful.

Her final HPE report is Primary Appendix Tumor-pT4b, Nx, well differentiated grade 1 mucinous cystadenocarcinoma with metastases to B/L ovaries and omentum. Post surgery, PETCT shown No other hypermetabolic lesions in the body. Tumor markers post 1 month of surgery shown CA125- 31.6, CA19.9 -42.7, CEA- 96.78. Final diagnosis is Primary appendiceal mucinous cystadenocarcinoma with B/L ovarian metastatic cystadenocarcinoma with pseudomyxoma peritonei. She is now planned for CRS (right hemicolectomy) with HIPEC.

## Challenges of Ovarian Malignancy in the Young

**Shivani Verma[1], Saritha Shamsunder[1], Sunita Malik1 Archana Mishra[1], Sheeba Marwah[1], Sachin Kolte[2],**
[1]Department of Obstetrics and Gynaecology,
[2]Department of Pathology

**Background:** Malignancy is seen in 2% to 5% of all ovarian neoplasms found in pregnancy. One in 18,000 pregnancies is complicated by an ovarian malignancy. **Case:** A 29-year-old lady G2P1L1 came to ANC OPD at Safdarjung Hospital with 6 months of amenorrhea and loss of appetite, nausea & vomiting for 7 days, and pain lower abdomen for 2 days. On per abdomen examination, uterus corresponded to 30 weeks period of gestation with mild tenderness infraumbilical region. Imaging (USG and MRI) was suggestive of bilateral ovarian cystic neoplasm with features of malignancy with raised CA 125 (50.6 U/ml) and Serum LDH values (523 U/L). Surgical staging was done, frozen section revealed ovarian malignancy; hence bilateral salpingo-oophorectomy and infracolic omentectomy was done. Histopath revealed bilateral papillary serous cystadenocarcinoma FIGO Stage IIA. As she refused chemotherapy, she was kept on follow-up, and delivered a healthy child spontaneously at 39 weeks following which six cycles of chemotherapy (Inj Paclitaxel + Inj Carboplatin) were given. Completion surgery i.e. TAH revealed no evidence of residual disease. She is well on FU with CA125 of 20 U/ml. She is on estrogen only HRT as she had vasomotor symptoms. She has been referred for genetic testing to hereditary cancer clinic at AIIMS.

## An Unusual Cause of Ovarian Cyst in an Adolescent Girl

**Anshul Tripathi, Harsha S Gaikwad, Aprajita Chawla, Nishi Choudhary, Sonam Topden**

Endocrinological disturbances during the pubertal age in females can have varied clinical presentation. A young 15 years old girl presented with menstrual irregularities for one year when she reported to our hospital. On laboratory, imaging and clinical findings a case of spontaneous bilateral large ovarian cysts mimicking ovarian hyperstimulation syndrome was made. Her TSH was very high (more than 400 micro international units ). Symptomatic and hormonal treatment with thyroxine led to complete regression of her signs and symptoms which was highly remarkable. Review of literature did not show similar case presentation and so this case was presented.

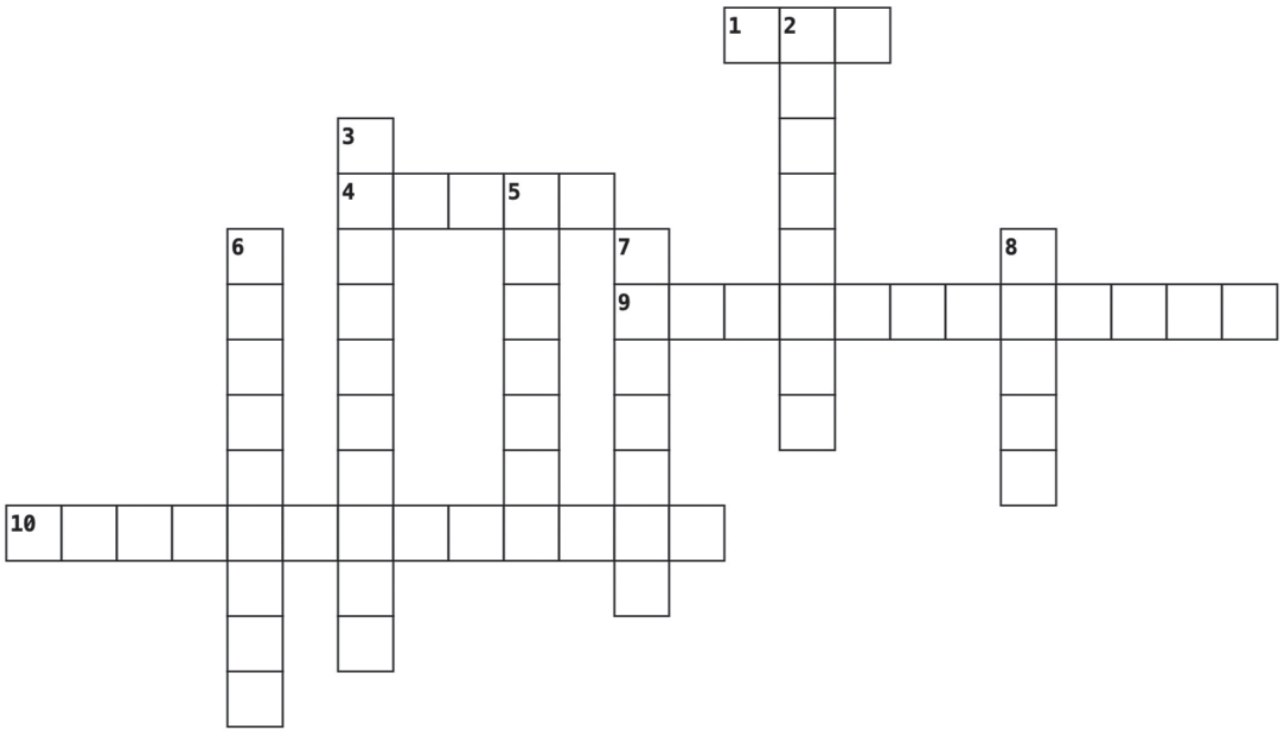
## Fetal autopsy- A Piece of the Jigsaw Puzzle

**Suchandana Dasgupta, Sumitra Bachani, Renu Arora**

The term autopsy is derived from Greek autopsia, meaning "to see for oneself". It aids in diagnosing the aetiology in nearly half of the cases of pregnancy terminations done for anomalous fetus and in unknown still births. It becomes important when there is suspicion of any genetic aetiology or where prenatal samples are not available or parents do not consent for any prenatal testing. After an informed consent, the fetus is placed upon a clean sheet; the length and weight are measured. Any external anomaly is looked for. Photographs of front, back and sides are taken and preserved. A "Y" shaped incision is given over chest and abdomen. The abdomen is opened first, all viscera are examined regarding position, size and anatomy and affected organs are retrieved for histopathology. Three cases were discussed. First was a case with recurrent hydrops fetalis with hydrops in current pregnancy and no previous records. After termination fetal autopsy was performed. Histopathology of heart and great vessels suggested possibility of mucopolysaccharidosis. Two other cases presented with ultrasound features suggestive of cystic kidneys with one couple having the same recurrent anomaly. In both the cases autopsy was done and histopathology report suggested possibility of polycystic kidney disease. Further clinical exome based on autopsy findings could clinch the diagnosis of MPS VI, ARPKD and ADPKD in these cases respectively. In era of advanced imaging in obstetrics much information regarding structural anomaly can be obtained. But, autopsy gives the opportunity to confirm them by seeing. Counselling regarding future pregnancy is more directed and precise after doing targeted genetic testing.

# Cross Word Puzzle

**Niharika Guleria[1], Rekha Bharti[2]**
[1]Senior Resident, [2]Professor, Obstetrics & Gynaecology, Vardhman Mahavir Medical College & Safdarjung Hospital, New Delhi




## Across

1. Test of choice for diagnosis from genital herpes ulcers
4. In VZV infection delivery should be delayed by how many days after the appearance of rash?
9. T score -2.5 and below is diagnosed as?
10. The procedure used to diagnose fetal varicella-zoster infection

## Down

2. Preferred mode of delivery if the patient has active genital herpetic lessions
3. Third generation SERM used in the treatment of dyspareunia?
5. Predominant estrogen in postmenopausal female
6. DOC for treatment of varicella-zoster infection in pregnancy
7. Inactivated virus COVID vaccine available for use in pregnancy and lactation
8. Name of triad associated with congenital rubella syndrome

**Mail the answers to editorsaogd2021@gmail.com. The correct answers and names of the three winners will be announced in the next issue.**

# Events Held in March 2022


"Anorectal Physiology for the Gynaecologist"

International Women's Day celebration


International Women's Day celebration

Webinar "Adolescent Health"


"Critical Care Obstetrics" Physical Workshop

CME on "Endometriosis",

CME on "PCOS"

Webinar on "Rh negative pregnancy"


"Respectful Abortion Care" Training


"Contraceptive Update"


"Ovarian & Breast Cancer Conclave"

Women's Cancer screening Fortnight


"Robotics in gynaecology"

CME "Fetomaternal Infections"


AOGD GBM and Secretariat Handing Over to MAMC & Lok Nayak Hospital

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# Association of Obstetricians and Gynaecologists of Delhi

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