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THEME: "MIXED BAG"

UPDATEKNOWLEDGEUPGRADESKILLSUPLIFTWOMEN'SHEALTH

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Modern medicine increasingly unfolds at intersections rather than within silos. Disorders of neurology, cardiology, transplantation, gender identity, and mental health often converge with the discipline that treats women demanding care that is updated, ethical, and deeply individualized. For our final issue of the NARCHI Delhi bulletin, we are proud to bring to you this curated kaleidoscope of articles.

We open with the brilliant article on Gender Identity by Air Commodore Dr. Sanjay Sharma. This article outlines the pivotal role of gynaecologists in providing evidence-based, gender-affirming care to transgender and gender-diverse adolescents, and takes us through the changing legal landscape of laws and landmark judgments grounded in gender identity issues in India. This is a must read for all gynaecologists since, post NALSA, "woman"no longer exclusively derives from the biological sex of the individual

From gender incongruence to the chapter on hypogonadotropic hypogonadism, we are informed of how disruptions of the hypothalamic–pituitary–gonadal axis shapes puberty, and fertility and outlines therapies for their management

Pregnancy, too, has become a crucible for complex decision-making. Women with neurological disorders or prior organ transplantation exemplify the shift from risk avoidance to risk balancing. Contemporary evidence shows that disease stability—achieved through carefully selected and monitored therapies—is frequently safer than medication withdrawal. Therefore, discerning reader, these two insightful articles by Dr. Sharmishtha and Dr. JayShree Sunder are absolutely indispensable to us.

Antenatal detection of congenital heart disease has transformed outcomes through multidisciplinary planning and structured perinatal pathways. However, not all heart diseases have the same prognosis and even the good ones may be marked by a measure of foreboding and extreme anxiety for involved parents. Not the least of them may be costs involved in a future corrective surgery. Therefore, delivering prognostic uncertainty with compassion, coordinating with teams, and guiding families through ethically fraught choices like termination versus continuation demand emotional labour. Dr. Neeraj Aggarwal's article guides us through this uncharted territory.

Dr Shweta Mittal's article on luteal phase support gives evidence based guidelines on luteal phase support after IUI, a procedure done commonly by Gynecologists across the world.

Overlaying all of this is a growing crisis within the profession itself. Burnout among Indian healthcare professionals—now formally recognized as an occupational syndrome—is alarmingly prevalent, fuelled by excessive workload, systemic inadequacies, and the near-total absence of mental health integration in medical education. The very clinicians expected to provide longitudinal, empathic, high-stakes care are doing so in environments that normalize exhaustion and silence distress. We thank Dr. Harsha Khullar for generously giving us insights on this very urgent issue.

Across these diverse clinical landscapes runs a common thread: the need for medicine that is interdisciplinary. And that dear reader, is what we have attempted to do with this last issue of the NARCHI Delhi bulletin that was so endearingly entrusted to us two years ago by Dr. Mala Srivastava, Dr. Chandra Mansukhani and Dr. Kanika Jain. As we sign off here, we thank all our past and present contributors without whom this deep diving into such diverse areas would have been impossible.

Sincerely,
The editorial team
Mamta Dagar, Ruma Satwik, Sakshi Nayar

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Warm Greeting & Happy New Year !

It is our pleasure & privilege to present a mixed bag bulletin during an air & aura of wonderful Delhi 68thAICOG 2026.

We all breathe & indulge in the success of a magnificent conference hosted by Dr. Ashok Kumar & Dr. Neerja Bathla. We fell so much a part of this conference. The comprehensive organisation, well planned scientific agenda, the ambience of Yashobhumi as well as the Gala culinary experience – all together added to the long lasting memories, & exceptional experience.

We have presented a Mixed bag bulletin. This time Dr. Harsha Khullar has written about "Mental Health Issues For The Health Care Professionals", a very important & burning topic of the modern times. Dr. Sharmistha Garg has expanded on "Safety of Neurological Therapeutic : Drugs in Pregnancy", whereas "Luteal Phase Support Is Less More ?", written by Dr. Shweta Mittal has nicely dwelled upon this topic with great responsibility.

Adenomyoma has always been a difficult condition to manage. It is not only affects the menstrual functions but also impacts upon the fertility of the women. Dr. Ruma Satwik has described here "Hypogonadotropic Hypogonadism". Thanks to advancement of modern medicine, now our transplant patients are living a near normal life & are aspiring for family & future fertility Dr. Jayashree Sunder has dealt with the burning topic of "Management of Pregnancy in A Renal Transplant Recipient". Caring & guiding the antenatal patients throughout their journey is an important responsibility of our obstetricians. Our Paediatric Cardiologist Dr. Neeraj Aggarwal has written about "Fetal Cardiac Anomalies What to do after Diagnosis". Last but not the least, Dr. Sanjay Sharma has presented a controversial & burning topic in a very comprehensive way - "Gender Identity in Adolescents & The Role of Gynaecologist".

Hope our young enthusiastic post graduate students senior residents & fellows will highly benefit from this mixed bag bulletin. The varied topics have added colour & flavour to this bulletin.

Every bulletin is knitted & crafted with great precision by our editorial team of Dr. Mamta Dagar, Dr. Ruma Satwik & Dr. Sakshi Nayar. We are sure all the readers will highly benefit & widen their knowledge by the scientific contents.

Festivities around the corner – after Makar Sankranti, we are enjoying Basant Panchami – While we indulge in colour & glamour of the atmosphere. We are also present scientific capsule in a glorious way.

Long Live NARCHI Delhi Chapter !!

Gender Identity in Adolescents and the Role of the Gynaecologist

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Abstract

Transgender and gender-diverse (TGD) adolescents represent a population whose healthcare needs have long been obscured by stigma and absent frameworks. The World Health Organization introduced the term "gender incongruence" in June 2018 when it released the ICD-11, moving this condition from "mental, behavioural, or neurodevelopmental disorders" to "conditions related to sexual health."[1] The ICD-11 became effective globally on January 1, 2022.[1] The WPATH Standards of Care, Version 8, affirm that gender-affirming care, when judiciously applied, reduces distress and improves psychological functioning and quality of life.[2]

Most significantly, in October 2025, the Supreme Court of India in **Jane Kaushik v. Union of India** delivered a landmark judgment affirming gender-affirming care as a constitutional right and directing the Union of India and States to implement the Transgender Persons (Protection of Rights) Act, 2019 with urgency and commitment.[3] The Delhi Transgender Persons (Protection of Rights) Rules, 2025, notified on July 10, 2025, operationalize this mandate through streamlined identity certification and integrated healthcare access mechanisms.[4] These developments represent a watershed moment: India's legal framework now explicitly mandates gender-affirming care aligned with international evidence.

Gynaecologists are uniquely positioned to lead multidisciplinary care for TGD adolescents, with expertise in reproductive and menstrual health, rapport with families, and role as primary care coordinators. While acknowledging the continuum of gender-affirming services, this review specifically restricts its scope to adolescent care—distinct from adult management protocols—to provide a comprehensive overview of the gynaecologist's pivotal responsibilities within the specific Indian healthcare setting.This article synthesizes WPATH SOC-8, ICD-11, India's legal framework (Transgender Persons (Protection of Rights) Act, 2019; Supreme Court directives; Delhi Rules, 2025), and peer-reviewed literature to define the gynaecologist's evolving role.

Keywords

Transgender adolescents; Assigned Female at Birth (AFAB); Assigned Male at Birth (AMAB); gender-affirming care; gynaecologist; menstrual health; WPATH SOC-8; ICD-11; Jane Kaushik judgment; Delhi Rules; Supreme Court; constitutional rights; gender incongruence

1. Introduction: The October 2025 Supreme Court Watershed

1.1 Epidemiology and the Indian Context

Gender diversity among adolescents is neither rare nor new. Population-based studies from high-income countries indicate prevalence rates of 1.2%

for explicit transgender identification and up to 2.7% for broader gender diversity, encompassing nonbinary and gender-questioning youth.[2] Notably, adolescents assigned female at birth (AFAB) initiate gender-affirming care 2.5–7.1 times more frequently than counterparts assigned male at birth (AMAB)—a differential reflecting both genuine epidemiology and help-seeking patterns.[2]

India has lacked robust epidemiological data on TGD adolescent prevalence, a gap reflecting decades of criminalization, pathologization, and social denial. Since the Supreme Court's 2014 judgment in National Legal Services Authority v. Union of India (NALSA) affirming the constitutional right to self-identify gender, and particularly following the October 2025 Jane Kaushik v. Union of India judgment, a paradigm shift has occurred. Anecdotal reports from gender clinics in metropolitan India document rising numbers of adolescents seeking care—a phenomenon reflecting unmet need finding voice through legal validation.

1.2 The Supreme Court Judgment: Jane Kaushik v. Union of India (October 17, 2025)

This landmark judgment fundamentally transformed India's legal landscape for transgender healthcare.[3]

Core holdings

Right to self-identification independent of medical proof: The Court affirmed that gender identity is a fundamental right under Articles 14, 15, 17, 19, and 21 of the Constitution, independent of medical, surgical, or psychological proof. Gynaecologists are not gatekeepers determining authenticity; the State must recognize self-identified gender.[3]

Prohibition of discrimination in employment and public institutions: The Court held that discrimination against transgender persons in employment, education, and public services violates fundamental rights. Both State and non-State actors bear positive obligations to prevent discrimination.[3]

Healthcare as a constitutional mandate: The Court directives affirmed that gender-affirming healthcare—including puberty suppression, hormone therapy, counseling, and surgical intervention—must be provided as a right. The judgment identified lack of implementation by the Union and States as a source of constitutional violation.[3]

Creation of institutional mechanisms: The Court directed constitution of:

- Welfare Boards in every State/Union Territory to coordinate services and advocate for transgender persons' rights[3]
- National Council for Transgender Persons (NCTP) to formulate comprehensive policies[3]
- Transgender Protection Cells under District Magistrates and police commissioners to monitor and prosecute discrimination cases[3]
- Equal Opportunity Policies and grievance redressal mechanisms in all establishments.[3]

Clinical implications: Gynaecologists providing gender-affirming care now operate within an explicit judicial mandate supported by fundamental rights and statutory law. The focus shifts from verifying authenticity to assessing clinical need and providing evidence-based care.

1.3 The Delhi Transgender Persons (Protection of Rights) Rules, 2025

On July 10, 2025, the Delhi Government notified comprehensive Rules operationalizing Supreme Court directives.[4]

Key provisions

Streamlined identity certification: Sections 4–5 of the Rules mandate that the District Magistrate shall issue a certificate of identity within 30 days of receiving a duly completed application, without any medical or physical examination—based solely on the applicant's affidavit and self-declaration.[4]

Institutional healthcare infrastructure: Rule 10(5) mandates that within two years of the Rules coming into force, at least one government hospital shall be equipped to provide safe, free gender-affirming surgery (MTF and FTM), counseling, hormone replacement therapy, separate HIV sero-surveillance centres, separate wards in hospitals, and separate washrooms for the transgender community.[4]

Transgender Welfare Board: Rule 14 constitutes the Transgender Welfare Empowerment Board, chaired by the Minister in-charge of the Department of Social Welfare. The Board comprises representatives from Home, Finance, Law, Labour, Health, Education, Revenue, Women and Child Development, and Transport Departments, as well as District Social Welfare Officers, three NGO representatives, and three representatives from the transgender community.[4]

Equal opportunity and grievance redressal: Rules 11–13 require all institutions to prevent

discrimination, provide safe facilities, and establish grievance redressal mechanisms with timelines.[4]

Insurance integration: The Rules mandate integration of gender-affirming services into Ayushman Bharat and state welfare schemes, ensuring coverage for menstrual management, fertility counselling, hormone therapy, and surgical interventions.[4]

For gynaecologists: The Rules provide legal frameworks for referral, insurance coverage, institutional support through the Welfare Board, and access to established healthcare infrastructure. Cost barriers are addressed through government mandates for free/subsidized care and scheme integration.

1.4 Why Gynaecologists Must Lead

Gynaecologists are, in many settings, the first and often sole point of contact for adolescent reproductive and sexual health. They possess expertise spanning menstrual health, contraception, fertility, and psychosocial dimensions of sexuality and identity. This positioning—access, credibility, knowledge—represents both an opportunity and an obligation.

The gynaecologist's role encompasses creating safe clinical spaces, conducting comprehensive biopsychosocial assessment, managing menstrual dysphoria, counselling on fertility preservation, and serving as the coordinator of multidisciplinary teams. For many TGD adolescents, the gynaecologist may be the first professional to affirm their identity and place their wellbeing at the centre of care.

2. Conceptual Foundations

2.1 Understanding Gender: Neurobiology, Development, and Diversity

Gender is the bedrock upon which the architecture of self is constructed. It is one's internal, deeply felt sense of self; what one perceives oneself to be; what one desires to communicate to the world; and how one navigates social, relational, and physical spaces. Gender is hardwired neurobiologically into the brain during fetal development, shaped by hormones, genes, and neural architecture—yet it is also expressed, negotiated, and lived within cultural and social contexts that vary across time, geography, and community.[2]

Importantly, gender is not synonymous with sex assigned at birth. Sex assigned at birth (SAAB) is a categorical designation based on genital anatomy at birth. Gender identity is one's internal sense of gender—which may be congruent with assigned sex or incongruent. Gender expression is the external presentation of gender through clothing, grooming, voice, movement, and mannerisms—which may or may not align with gender identity or SAAB.[2]

Gender is not binary. While many societies and medical systems have historically imposed a binary framework, the lived experiences of millions testify to a spectrum: nonbinary, genderqueer, agender, and identities yet unnamed. This spectrum reflects neurobiological diversity and deserves recognition and respect.[2]

2.2 Gender Identity Development in Adolescence: Variability and Stability

Adolescence is the crucible of identity formation—a bridge between childhood dependency and adult autonomy. For many adolescents, this is a time of gender exploration; for others, gender identity is fixed and has been so since early childhood; for still others, gender may remain fluid throughout adolescence and into adulthood.[2]

The trajectory of gender identity development is not uniform. For some young people, recognition of gender incongruity is sudden, arriving in late childhood or early adolescence. For others, the history stretches back to early childhood—a persistent, unwavering sense that their assigned sex does not match their inner sense of self. This variation reflects human development and is not pathology.[2]

Dutch longitudinal studies, considered the gold standard, followed adolescents with gender incongruence from early puberty into young adulthood. A landmark study by de Vries and colleagues (2014) found that adolescents who received comprehensive assessment and supportive care, deemed emotionally and cognitively mature, demonstrated high stability of gender identity over time. Of 70 adolescents followed from mean age 13.6 years through young adulthood (mean 20.7 years), participants demonstrated sustained gender identity, significant improvements in psychological functioning and life satisfaction, and low regret rates (1.9–3.5%).[2] This finding demolishes the myth that adolescent gender identity is necessarily unstable.

2.3 Gender Incongruence: ICD-11 Definition and Clinical Significance

The World Health Organization released the ICD-11 on June 18, 2018, introducing "gender incongruence" to replace outdated diagnostic language.[1] The World Health Assembly endorsed ICD-11 on May 25, 2019, and it became effective globally on January 1, 2022.[1]

Under ICD-11, gender incongruence appears in Chapter 17: "Conditions Related to Sexual Health"—not in mental disorders.[1] This reclassification is monumental, affirming that being transgender or gender-diverse is not a mental illness.[1]

ICD-11 Definitions:[1]

Gender Incongruence of Adolescence and Adulthood (HA60): A marked and persistent incongruence between an individual's experienced gender and assigned sex, lasting at least two years, associated with clinically significant distress or impairment in functioning.[1]

Gender Incongruence of Childhood (HA61): A marked incongruence between experienced or expressed gender and assigned sex in pre-pubertal children.[1]

Critical distinction: The diagnosis requires both incongruence AND clinically significant distress or impairment. A young person may experience incongruence without experiencing distress and without meeting diagnostic criteria.[1] Not every adolescent with gender diversity requires medical intervention.

2.4 Gender Dysphoria: Distress as a Distinct Clinical Construct

Gender dysphoria refers to clinically significant distress or impairment arising when a person's gender identity is incongruent with their assigned sex and lived social role. An adolescent may identify as transgender, may socially transition, may live authentically—and experience no clinically significant distress. Conversely, another may experience profound dysphoria manifesting as depression, anxiety, self-harm, or suicidality. Dysphoria, when present, is the target of clinical intervention; the identity itself is not.[2]

For gynaecologists, this distinction is crucial. An adolescent presenting with gender concerns may not require medical intervention; many benefit from affirmation, psychosocial support, menstrual management, and time. Others, whose dysphoria is severe and persistent, may benefit from pharmacological or surgical interventions.

3. Assessment and Affirming Clinical Care

3.1 Creating a Gender-Affirming Clinical Reception

A gender-affirming reception is a clinical necessity. It begins before the adolescent enters the clinic. Pre-appointment communication should inquire about preferred name, pronouns, and whether parents or guardians should be present. Reception staff should use the name and pronouns provided by the adolescent. Intake forms should separate "sex assigned at birth" from "gender identity," allowing space for nonbinary identities. Anti-discrimination policies should be visible and unambiguous.[2]

The confidentiality framework must be made explicit. Within legal and ethical bounds, gynaecologists must assure adolescents that gender identity concerns discussed in confidence will remain confidential unless safety is jeopardized.[2]

3.2 Essential Terminology and Language

Words matter profoundly. For gender-diverse adolescents, the language used by healthcare providers can mean the difference between affirmation and harm.[2]

Sex assigned at birth (SAAB): The designation based on genital anatomy at birth. This term is neutral and factual.

Gender identity: One's internal sense of gender. It may be binary (man, woman), nonbinary, or fluid.

Gender expression: The external presentation of gender through clothing, grooming, voice, and movement.

Gender incongruence: A marked incongruence between experienced gender and assigned sex. This is ICD-11 terminology—neutral and non-pathologizing.

Gender dysphoria: Clinically significant distress or impairment associated with gender incongruence. This is a clinical diagnosis when distress warrants treatment.

Transgender: A neutral descriptor for individuals whose gender identity differs from sex assigned at birth.

Language to avoid: "Real sex," "biological sex" (use "sex assigned at birth"), "transgenderism," "confused," "uncertain," mismatched pronouns, or "it."

3.3 Comprehensive Biopsychosocial Assessment

Before any medical intervention is contemplated, comprehensive biopsychosocial assessment is essential.[2] Assessment domains include:

1. **Gender identity and history:** When did incongruence arise? Has identity been stable or evolved? Current stability?
2. **Gender expression:** How does the adolescent present? Are there barriers to fuller expression?
3. **Social transition:** Has the adolescent changed their name, pronouns, or social role in any domain? Response from family and community?
4. **Distress and dysphoria:** What specific body characteristics cause dysphoria? How does it manifest? Impact on functioning?
5. **Mental health:** Screen for depression, anxiety, self-harm, suicidality, substance use. Comorbid conditions do not negate identity validity or contraindicate care.[2]
6. **Family and social support:** Response of family? Accepting or rejecting? Supportive peers or community organizations?
7. **Cultural and religious context:** Understanding perspectives without imposing judgment is crucial.
8. **Medical history:** Menstrual history, sexual activity, STI/HIV status, prior hormone use.
9. **Neurodevelopmental and cognitive factors:** Autism spectrum characteristics? ADHD? Cognitive functioning? Capacity for abstract reasoning?
10. **Strengths and protective factors:** Talents, interests, relationships, resilience.

3.4 Capacity to Consent: Assessing Readiness for Medical Decision-Making

Adolescents are developmentally diverse. WPATH SOC-8 recommends assessment of capacity to consent rather than relying solely on age.[2] Capacity assessment involves four domains:[2]

1. **Understanding:** Does the adolescent comprehend the nature of the proposed intervention, its benefits, and its risks?
2. **Appreciation:** Can the adolescent relate this information to their own situation?
3. **Reasoning:** Can the adolescent weigh options and articulate a reasoned choice?
4. **Expression of choice:** Can the adolescent clearly and consistently communicate their decision?

The presence of mental health symptoms does not automatically preclude capacity. The clinician must discern whether the condition impairs decision-making regarding this specific decision, at this specific time.[2]

4. Non-Pharmacological and Pharmacological Interventions

4.1 Non-Pharmacological Approaches: Gender Expression Support

Among the most powerful yet underutilized therapeutic tools is support for gender expression—helping the young person explore and optimize clothing, grooming, voice, movement, and mannerisms to align with their gender identity.[2] This intervention is entirely non-invasive, fully reversible, and profoundly affirming. For many adolescents, gender expression support alone can significantly reduce dysphoria, improve self-esteem, enhance peer relationships, and improve school attendance and academic performance.[2]

Concrete examples

Binding and tucking: An AFAB adolescent may wish to flatten breast prominence through chest binders, sports bras, or compression vests, or to tuck genitalia. Gynaecologists should provide evidence-based education on safe binding and tucking, avoiding skin irritation, chest pain, or musculoskeletal strain.[2]

Voice and speech: Voice modulation—pitch, resonance, intonation, patterns of speech—is among the most gender-coded aspects of communication. This can be achieved through self-directed practice or speech pathologists trained in voice therapy.[2]

Grooming and appearance: Hairstyle, facial hair growth or removal, makeup, body hair management, tattoos, piercings—all are forms of gender expression. Gynaecologists should normalize this exploration and be alert to complications.[2]

Movement and mannerisms: Gait, posture,

gesture, patterns of social interaction—all are culturally and gender-coded. Supporting this process is powerful and affirming.

4.2 Menstrual Management: Addressing Dysphoria and Enabling Agency

For many AFAB adolescents—particularly those with male or nonbinary gender identity—menstruation is a profound source of distress and dysphoria.[2] The monthly reminder of female-typical body characteristics can trigger intense dysphoria, worsen depression and anxiety, impair school attendance, and precipitate self-harm. The ability to suppress or manage menstruation is not cosmetic; it is a clinical imperative.[2]

Gynaecologists have multiple evidence-based options for menstrual management in TGD adolescents:[2]

Levonorgestrel IUD (Mirena): Effective and long-acting (5 years), achieves amenorrhoea in 80%, improves dysmenorrhoea. Does not prevent ovulation entirely. Excellent for suppressing dysphoria-related menstruation in AFAB adolescents not on testosterone.

Combined oral contraceptive, continuous or extended regimen: Estrogen-progestin combination. Familiar, reversible, can be used continuously to minimize or eliminate menses. Requires compliance; estrogen may worsen dysphoria in some; increased clotting risk with smoking.

Progestin-only pill: Can suppress menses in 30% at lower doses. Useful for breakthrough bleeding. Requires adherence.

GnRH agonist (leuprorelin, goserelin): Suppresses pituitary gonadotropins. Highly effective, induces hypoestrogenic state, menses cease. Expensive, requires injections; bone health concerns with prolonged use without concurrent hormone replacement.

Clinical approach: Assess the degree of dysphoria. Discuss the full range of menstrual management options, including risks and benefits. Allow the adolescent to make an informed choice. Manage breakthrough bleeding if it occurs. Monitor long-term outcomes at each visit. Integrate with gender-affirming hormone therapy if the adolescent is receiving testosterone.[2]

4.3 Psychosocial Support and Family Engagement

Among the most robust findings in the literature: family acceptance is one of the strongest predictors of mental health outcomes in TGD youth.[2] Adolescents whose families are accepting show lower rates of depression, anxiety, self-harm, and suicidality.[2]

Yet many families enter the clinic confused, frightened, or conflicted. Gynaecologists have a unique opportunity and responsibility to engage families therapeutically.[2]

Strategies for family engagement:

1. Reframe affirmation as mental health intervention: Help families understand that gender affirmation—recognizing and supporting the adolescent's identity—protects mental health and resilience. Families who affirm their TGD children see improvements in mood, school attendance, and social functioning.
2. Provide psychoeducation: Many family members are simply uninformed. Educational conversations about gender identity development and why affirmation reduces harm are often transformative.[2]
3. Assess family dynamics and safety: Is the family's response placing the adolescent at risk of abuse, homelessness, or self-harm? What are the family's strengths and resources? Refer to social work or family therapy as needed.[2]
4. Involve schools and communities: Schools are the primary social context for adolescents. A gender-affirming school—through a Gender-Sexuality Alliance (GSA), staff training, inclusive policies—significantly buffers against discrimination.[2] Liaise with school counsellors and encourage advocacy for inclusive policies.
5. Connect to community: LGBTQIA+ youth organizations, community centres, and online support groups provide adolescents and families with belonging, role models, and mentors. Knowing other TGD adolescents and families can be profoundly affirming.[2]
6. Hold space for resistance and grief: Some families will not be ready to accept their adolescent's gender identity. Others will grieve the loss of the anticipated gender identity. These responses are human; they are not permanent. Gynaecologists can hold space for these emotions while gently encouraging understanding and acceptance over time.

5. Pharmacological Interventions: Puberty Suppression and Gender-Affirming Hormones

5.1 Puberty Suppression: Buying Time, Preventing Permanent Changes

Puberty is a relentless process. Once it begins, secondary sex characteristics emerge in a predictable sequence: breast development and menstruation in AFAB adolescents; testicular growth, penis enlargement, and facial hair in AMAB adolescents. These changes are driven by gonadal sex hormones and are largely irreversible.[2]

For many TGD adolescents whose gender identity is incongruent with developing characteristics, puberty is experienced as dysphoria—a cascade of distress moving them further from congruence.[2]

Puberty suppression—using gonadotropin-releasing hormone (GnRH) agonists—offers a compassionate alternative. GnRH agonists suppress the pituitary-gonadal axis, preventing release of FSH and LH, thereby suppressing gonadal sex hormone production. The result is a pause in puberty: menses cease, breast development halts, voice remains high, facial hair does not emerge. This pause is fully reversible; if the adolescent discontinues medication, endogenous puberty resumes within 6–12 months.[2]

Rationale and benefits

1. Time for exploration: Suppression allows time for gender exploration and identity crystallization without permanent physical changes.[2]
2. Prevention of dysphoria-inducing changes: For adolescents with stable gender identity and marked dysphoria, suppression prevents secondary sex characteristic development requiring later reversal through surgery or long-term hormone therapy.[2]
3. Improved psychological outcomes: Studies show that adolescents on puberty suppression who later receive gender-affirming hormones demonstrate significant improvements in mood, self-esteem, and body image satisfaction.[2]

WPATH SOC-8 eligibility criteria:[2]

1. Adolescent at Tanner stage 2 or beyond (early puberty begun)
2. Persistent, sustained gender incongruence ideally at least 12 months; longer observation in complex cases
3. Clinically significant distress or impairment related to gender incongruence
4. Capacity to consent (emotional and cognitive maturity sufficient to understand risks and benefits)
5. Access to ongoing mental health support and medical monitoring
6. Ideally, some degree of social transition or gender-congruent expression

Medications

Medication	Dosing
Leuprorelin (Lupron)	11.25 mg IM every 3 months, or 30 mg depot every 4 months
Goserelin (Zoladex)	3.6 mg SC every 4 weeks, or 10.8 mg depot every 12 weeks
Triptorelin (Trelstar)	3.75 mg IM every 4 weeks, or 11.25 mg every 12 weeks

Timeline of effects:[2]

Timeframe	Effect	Reversibility
Days to weeks	Suppression of gonadal hormone production begins	Fully reversible
1–3 months	Menses typically cease (AFAB); testicular growth slows (AMAB)	Fully reversible
3–6 months	Cessation of breast development (AFAB); prevention of voice lowering, facial hair growth	Fully reversible
Ongoing	Growth continues at pre-pubertal rate; skeletal maturation slows	Reversible; rapid catch-up after discontinuation

Monitoring during puberty suppression:[2]

1. Height and growth velocity: Measure every 6 months. Expect minimal growth during suppression (typically 2 cm/year).
2. Bone age: Assess via wrist X-ray every 1–2 years. Rapid catch-up in bone density occurs after resumption of hormones; this is generally not a contraindication to suppression.[2]

3. Metabolic markers: Lipid panel and fasting glucose at baseline and annually.
4. Tanner staging and genital examination: Assess progression or lack thereof. Obtain consent and ensure privacy.
5. Psychological assessment: Regular check-ins (every 3–6 months) to assess identity stability, mental health status, and ongoing need for the intervention.

Evidence base: The Dutch longitudinal studies provide the strongest evidence. A cohort of 70 adolescents who initiated puberty suppression at mean age 13.6 years and were subsequently treated with gender-affirming hormones, with follow-up into early adulthood (mean 20.7 years), demonstrated:[2]

- Significant improvement in gender dysphoria
- Improved psychological functioning, body image, and quality of life
- High gender identity stability in adulthood
- Low regret rates (1.9–3.5%)
- No negative cognitive or developmental effects

Recent studies from diverse settings consistently replicate these findings.[2]

5.2 Gender-Affirming Hormone Therapy

After approximately 12 months on puberty suppression, or in cases where suppression is not used, gender-affirming hormone therapy can be initiated. This involves administering hormones aligned with the adolescent's gender identity to induce secondary sex characteristics congruent with their identity.

For AFAB adolescents: Testosterone therapy

Testosterone induces virilization—development of male-typical secondary sex characteristics. It is among the most effective interventions for reducing dysphoria in AFAB TGD adolescents and is associated with marked improvements in mental health outcomes.[2]

Dosing and administration:[2]

Route	Formulation	Starting Dose	Maintenance Dose	Notes
Intramuscular injection	Testosterone enanthate	50 mg/week	50–100 mg/week	Most common; predictable levels
Intramuscular injection	Testosterone cypionate	50 mg/week	50–100 mg/week	Equivalent to enanthate
Transdermal gel	1% gel	25 mg/day	25–100 mg/day	Good for variable dosing; avoid skin contact
Transdermal patch	2–6 mg/24h	2 mg/day	2–6 mg/day	Applied to skin; less common
Sublingual pellet	Testosterone undecanoate	120–160 mg BID	120–240 mg BID	Newer option; variable absorption

Physiological effects and timeline:[2]

Timeframe	Effect	Reversibility
1–3 months	Voice deepening begins; increased libido/sexual function; clitoral enlargement 2–3 cm	Mostly reversible; voice may partially persist
3–6 months	Voice fully deep (male range); facial and body hair growth begins; increased muscle mass; fat redistribution	Facial/body hair permanent; others partially reversible
6–12 months	Continued hair growth; male-pattern baldness if genetically predisposed; continued muscle/fat changes	Hair and baldness permanent if genetic; fat changes partly reversible
1–2 years	Facial and body hair complete; clitoral growth plateaus; testicular atrophy; gonadal suppression	Hair and clitoral growth permanent; fertility compromised

Fertility implications: Testosterone suppresses ovulation in most AFAB individuals within 3–6 months. However, ovarian reserve may persist, and some do conceive while on testosterone (though uncommon). [2] Gynaecologists MUST discuss fertility preservation options before initiating testosterone. Options

include egg retrieval and freezing (expensive, invasive) or banking ovarian tissue (experimental). For many AFAB adolescents, dysphoria relief outweighs the risk of permanent infertility; however, the discussion is non-negotiable.[2]

Monitoring during testosterone therapy:[2]

1. **Clinical assessment:** Every 1–3 months initially, then every 3–6 months. Assess virilization progression, side effects, and mental health status.
2. **Laboratory monitoring:**
   - o Baseline: CBC, lipid panel, liver and renal function, glucose
   - o Ongoing: Repeat lipids and renal function every 6–12 months. Testosterone can elevate hemoglobin; monitor for polycythemia.
   - o Testosterone levels: Check 1–2 months after starting or changing dose. Target mid-male range, 300–1000 ng/dL.
3. **Screening:** Annual blood pressure, weight, and fasting glucose. Testosterone can worsen metabolic profile in some.

For AMAB adolescents: Estrogen and androgen suppression

While the primary focus of adolescent gender-affirming care has been AFAB individuals, AMAB adolescents also benefit from feminizing therapy. The approach involves reducing circulating testosterone through gonadotropin suppression or androgen blockade, while introducing estrogen to feminize secondary sex characteristics.

Medications

Medication	Class	Dose Range	Notes
Estradiol (oral)	Estrogen	1–4 mg/day	Divided doses; monitor for clotting
Estradiol (transdermal)	Estrogen	0.1–0.4 mg/day	Patches; lower clotting risk; preferred in some centres
Spironolactone	Androgen antagonist	100–200 mg BID	Common; monitor potassium, creatinine
Cyproterone acetate	Progestin/androgen antagonist	25–50 mg/day	Potent; less commonly used in some countries
GnRH agonist	Gonadotropin suppressor	Variable dosing	Suppresses testosterone production; used with low-dose estrogen

Timeline and effects:[2]

Timeframe	Effect	Reversibility
1–3 months	Softening of skin; decreased muscle mass; decreased libido/erectile function	Mostly reversible
3–6 months	Breast budding begins; fat redistribution (to hips, thighs, breast tissue)	Breast tissue partly permanent; fat redistribution partly reversible
6–12 months	Continued breast growth (may not reach adult size); continued body changes	Breast tissue permanent; hormone-dependent changes reversible
1–2 years	Breast growth complete; voice unchanged (estrogen does not feminize voice); continued fat redistribution and muscle loss	Breast tissue permanent; other changes partly reversible

Voice and hairiness: Estrogen does not lower voice pitch (that was done by testosterone at puberty). Voice therapy may be pursued. Facial and body hair already grown does not regress with estrogen; laser hair removal or electrolysis may be pursued. These are fully reversible considerations.[2]

Monitoring during feminizing therapy:[2]

1. **Clinical assessment:** Every 1–3 months initially, then every 3–6 months. Assess feminization progression, side effects, and mental health status.

2. **Laboratory monitoring:**
   - Baseline: CBC, lipid panel, liver and renal function, glucose, prolactin, electrolytes (if on spironolactone)
   - Ongoing: Repeat lipids every 6 months (estrogen increases clotting risk in some); electrolytes if on spironolactone; renal function annually
   - Testosterone levels: Check 1–2 months after starting. Target suppressed levels (< 50 ng/dL)
   - Estradiol levels: Check 1–2 months after starting. Target premenopausal range (40–200 pg/mL)
3. **Screening:** Annual blood pressure, weight, fasting glucose. Estrogen can increase clotting risk, especially with smoking or immobility.
4. **Bone monitoring:** Similar to puberty suppression; rapid recovery of bone density after discontinuation.

6. Multidisciplinary Care and Institutional Coordination

Optimal gender-affirming care for TGD adolescents requires coordination across multiple disciplines: mental health, endocrinology, primary care, surgery, social work, and community support. Gynaecologists serve as coordinators and advocates, leveraging India's evolving legal and institutional framework.

6.1 Institutional Mechanisms: Delhi Rules and Supreme Court Directives

The Delhi Rules, 2025, and the Jane Kaushik judgment establish specific institutional structures for coordination:

Transgender Welfare Board: Established under Rule 14 of the Delhi Rules, chaired by the Minister in-charge of Social Welfare. The Board comprises representatives from Health, Education, Labour, Women and Child Development, and other departments, as well as District Social Welfare Officers, NGO representatives, and transgender community members.[4] Functions include protecting rights, facilitating access to welfare schemes, and monitoring implementation.[4]

Gynaecologist role: Liaison with the Welfare Board to coordinate services, advocate for resources, and address systemic barriers affecting adolescents' care. The Board provides a forum for high-level advocacy and coordination across government departments.

Healthcare Infrastructure: Rule 10(5) mandates that within two years, at least one government hospital shall be equipped with gender-affirming surgical capacity, hormone therapy services, counseling, separate HIV centres, wards, and washrooms.[4]

Gynaecologist role: Coordinate referrals to equipped facilities, participate in capacity building, and liaise with surgical and endocrinology teams.

Grievance Redressal Mechanism: Rules 13 and the 2020 Rules mandate complaint officers in all establishments and a nation-wide toll-free helpline.[3] The Jane Kaushik judgment directed the Union to establish a comprehensive grievance redressal mechanism within one year.[3]

Gynaecologist role: Ensure adolescents are aware of these mechanisms; file complaints on behalf of minors if needed.

National Council for Transgender Persons (NCTP): Established under Sections 16–17 of the 2019 Act, mandated to formulate policies and coordinate implementation.[3] The Jane Kaushik judgment emphasized NCTP's role in evidence-informed policy development.[3]

Gynaecologist role: Engage with NCTP to ensure clinical evidence informs policy on adolescent care, puberty suppression, hormone therapy, and surgical care.

6.2 Addressing Systemic Barriers: 2025 Solutions

Limited specialist availability: The Delhi Rules mandate the Welfare Board to coordinate training, mentorship, and capacity building. AIIMS Delhi and state institutions serve as referral hubs. Gynaecologists can access mentorship through established networks and contribute to training others.[4]

Cost barriers: The Delhi Rules explicitly mandate free/subsidized gender-affirming care through government facilities.[4] Integration into Ayushman Bharat ensures insurance coverage. Gynaecologists should ensure adolescents are enrolled in relevant schemes and understand their entitlements.

Legal uncertainty: The Jane Kaushik judgment provides explicit legal authority for gender-affirming care as a constitutional right.[3] Medical Councils should develop guidelines aligned with the judgment. Gynaecologists operating within this framework have legal protection.

Provider stigma: The Delhi Rules mandate staff training on gender-affirming care.[4] Professional organizations (ICOG, Indian Society of Pediatrics) should develop position statements reinforcing constitutional and statutory mandates. Gynaecologists can champion such statements and ensure institutional implementation.

7. Legal and Ethical Foundations

The Jane Kaushik judgment affirms gender-affirming care as a constitutional imperative, not discretionary.3 The Transgender Persons (Protection of Rights) Act, 2019 (Section 16) mandates that the State provide gender-affirming healthcare through public health centres at free or concessional rates.5 The Mental Health Care Act, 2017 explicitly prohibits conversion therapy, affirming that gender-affirming care (not conversion) is appropriate.6

Ethically, the framework rests on autonomy (adolescents' right to self-determination), beneficence (evidence demonstrates improved mental health with gender-affirming care), non-maleficence (denial of care causes demonstrable harm), and justice (historical marginalization warrants affirmative action).

8. Key Takeaways

1. Gender incongruence was introduced by WHO in June 2018 in the ICD-11 and became effective globally on January 1, 2022. It is no longer classified as a mental disorder but as a condition related to sexual health.
2. The Supreme Court of India in October 2025 affirmed gender-affirming care as a constitutional right. This is a judicial mandate, not discretionary.
3. Self-identification is a fundamental right independent of medical proof. Gynaecologists are not gatekeepers determining authenticity.
4. The Delhi Rules, 2025 operationalize the Supreme Court mandate through streamlined identity certification, institutional healthcare infrastructure, and Welfare Board coordination.
5. Non-pharmacological interventions are powerful. Gender expression support, menstrual management, and psychosocial support are often sufficient.
6. Evidence strongly supports gender-affirming care. Low regret rates, improved mental health, decreased suicidality, and high satisfaction are well-documented.
7. Family acceptance is protective. Gynaecologists should engage families therapeutically.
8. Multidisciplinary care is standard. Institutional mechanisms now support coordination across departments and disciplines.
9. WPATH SOC-8 remains the gold standard for clinical guidance. All pharmacological protocols align with SOC-8 recommendations.
10. Training and capacity building are institutional priorities. State-level initiatives and established facilities provide opportunities.
11. The moment is now. Adolescents expect evidence-based care aligned with constitutional and statutory law. Gynaecologists must answer the call.

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Hypogonadotropic Hypogonadism

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Introduction

The initiation and maintenance of reproductive capacity in humans involves action at various levels. Pulsatile secretion of the hypothalamic Gonadotropin Hormone Releasing Hormone (GnRH) initiates synthesis and release of gonadotropins: Follicle Stimulating Hormone (FSH) and Luteinizing Hormone(LH) from the pituitary gland which in turn stimulates the gonads to complete gametogenesis and steroidogenesis. This hormonal axis from the brain to the gonads is often referred to as the Hypothalamic Pituitary Gondal axis (HPG axis). The gonadal steroids, testosterone in men and estrogen in women, are responsible for the maturation and maintenance of internal and external genitalia in form and function, whereas gametogenesis renders an individual fertile. The deficient production, secretion or action of GnRH or less commonly, FSH and LH, leads to the clinical condition of Hypogonadotropic Hypogonadism (HH) characterized by delayed puberty, infertility and loss of estrogenization and virilization in women and men respectively.

This chapter deals with the different types, etiology, clinical features, diagnosis and management of hypogonadotropic hypogonadism.

Prevalence, Types and Etiology

Hypogonadotropic Hypogonadism is a rare condition, prevalent in 0.3 -1 percent of men referred for infertility work-up, In women with amenorrhoea 3-4% would have HH.

It can be divided into the congenital type and the acquired type based on its etiological origins.

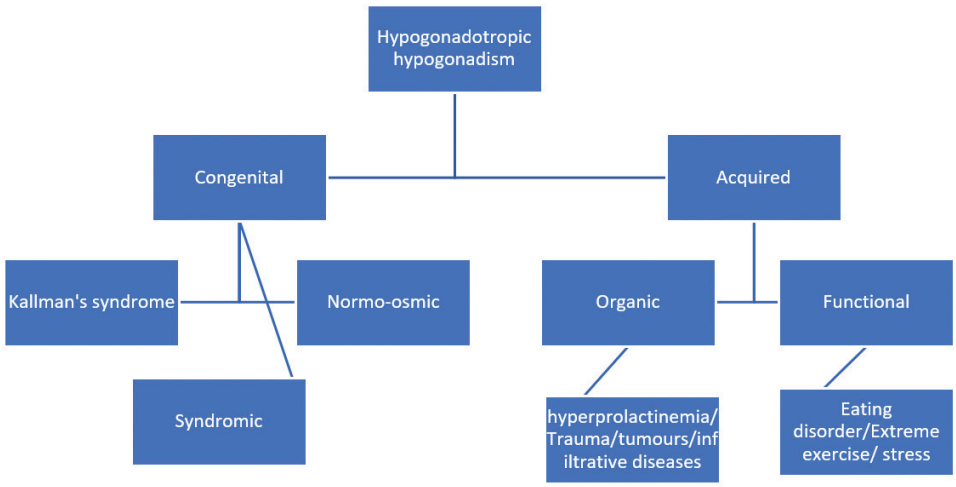

Figure 1: Etiological types of HH

Congenital hypogonadotropic hypogonadism (CHH) is a clinically heterogenous condition detectable in 1-10 newborns per 100,000 live births. CHH has a male predominance of 3-5 male:1 female. About two-thirds of CHH is associated with hyposia or anosmia in which case it is called Kallman's syndrome. This is a well characterized syndrome that may additionally be associated with midline facial defects such as cleft lip and palate, dental agenesis and less commonly with synkinesia, unilateral

renal agenesis, ear agenesis or neurosensory deafness. The remaining third have normo-osmic CHH and have variously been called Isolated GnRH Deficiency (IGD) or idiopathic CHH in the past.

Although rare in occurrence the reproductive endocrinologist should also be aware of the coexistence of HH state with some well characterized syndromes like Congenital pituitary hormone deficiency; CHARGE syndrome (coloboma, heart defects, choanal atresia, growth retardation, genital abnormalities and ear abnormalities); Adrenal hypoplasia Congenita (salt wasting, hyperpigmentation, muscular dystrophy, hypogonadism); Wardenberg Syndrome (congenital sensorineural deafness and abnormal pigmentation of the iris, hair, and skin); Bardett Biedel Moon syndrome (a rare autosomal recessive disorder associated with five fundamental characteristics: retinitis pigmentosa, polydactyly, obesity, hypogonadism and mental retardation); Gordon Holmes Syndrome (an autosomal recessive adult-onset neurodegenerative disorder characterized by progressive cognitive decline, dementia, ataxia and chorea) and others.

A genetic cause may be detectable in approximately 50% of individuals with CHH (both in syndromic and non-syndromic cases) when using the next generation sequencing platform. CHH is genetically heterogenous with approximately 40 genes identified at different loci to date. These genes encode for either a) GnRH neuronal migration from the olfactory placode to the preoptic hypothalamic nucleus during embryonal development, such as KAL1, FGF8, FGFR1, PROK2 or PROK2R gene; b) GnRH peptide synthesis such as the KISS1 or GNRH1 gene c) GnRH receptor synthesis or its action, such as GNRHR gene or d) synthesis of anterior pituitary hormones. CHH is mostly a monogeneic disorder, but digeneic or oligogeneic forms are known to exist too. Both sporadic (de-novo mutations) and familial cases are known. Familial cases have a mono-geneic alteration and transmission can be X-linked (most common) through the KAL 1 gene, autosomal dominant through the FGF8, FGFR1, CHD7 or the SOX10 gene, or autosomal recessive through the GNRH1R, KISS1R, PROK2 or PROKR2 gene. Variability in inheritance pattern is additionally introduced by variable gene penetrance and expressivity.

Acquired type of HH could arise due to exogenous steroid use, pituitary tumours such as prolactinomas (the most common cause), pituitary trauma, infiltrative diseases such as sarcoidosis, hemochromatosis or amyloidosis, iatrogenic causes such as surgeries or radiation, or developmental abnormalities like cysts, aneurysms etc. leading to panhypopituitarism. The cause could also be functional such as severe malnutrition due to an eating disorder, extreme stress or physical activity or a severe chronic illness.

Clinical Features

Although CHH is present from birth onwards, its diagnosis may be missed at birth. Most patients with CHH are diagnosed late in adolescence (15-19 years) or early in adulthood as CHH is challenging to differentiate from other causes of delayed puberty. The acquired causes may present before or during puberty but much more commonly present as an adult onset disorder.

Neonatal CHH: A history of crypto-orchidism or presence of a micropenis at birth may point to the diagnosis of CHH in male infants. No specific clinical signs of CHH are present in female neonates. Lack of mini-puberty; a physiological state that persists in young infants due to an active GnRH pulse generator from fetal period, could also point to the diagnosis of CHH. Reproductive hormones in normal infants at 2-4 months are in the normo-gonadotropic range for adults before settling into the hypogonadotropic range by age one. At months 2-4, gonadotropic hormones in the undetectable range point to a diagnosis of CHH. Genetic tests are initiated when clinical features and hormonal tests suggest presence of CHH or when infants are born to HH parents with identifiable genetic mutations.

Adolescent CHH: In adolescence, HH manifests as delayed, absent or incomplete puberty. A delay in puberty in boys is classically defined as lack of testicular enlargement by age 14 (testicular volumes less than 4ml). In girls, a lack of breast development (Tanner's stage 2 or less) by age 13 or amenorrhoea by age 15 would constitute delayed puberty. In addition, virilization, marked by voice change, facial hair and libido, is lacking in HH boys. In the absence of gonadal steroid induced growth spurts boys and girls continue to grow at steady rates. Similarly, in the absence of gonadal steroid induced epiphyseal closure their long bones gain eunuchoidal proportions with arm spans being longer than their vertical heights. These adolescents in later life manifest infertility in the absence of therapy due to their anovulatory and azoospermic states. Adolescents and young adults with CHH often have low self-esteem, distorted body image, and, in some cases, problems with sexual identity.

Adult onset HH: is less common and attributable to acquired causes. It manifests as secondary

amenorrhoea, infertility and loss of libido in women and with increasing severity of oligozoospermia, infertility and libido loss in men. In long standing cases there may be regression of signs of virilization and estrogenization and bone mineral density loss in both sexes.

Differential Diagnoses and Work Up

A complete diagnostic work-up is presented in Table 1.

Table 1: Diagnostic workup in a suspected hypogonadotropic hypogonadal individual

Diagnostic modality	What to look for	Additional features
History	1. Symptom details (with a focus on menstruation in women) and onset. 2. Symptoms of headache, visual and olfactory defect 3. Past history: brain surgeries, radiation or chemotherapy, trauma, chronic illnesses 4. Family history of similar syndromes 5. Current or past medicines 6. Exercise schedule and present eating habits	Sexual history, questions on libido Shaving frequency in men Reproductive history Questions to identify low self esteem, depression
Examination	Height, Weight, arm span, facies, palate, secondary sexual characteristics, systemic and local exam, testicular volume in men	Visual, olfactory and hearing tests where indicated
Ultrasound	Small size uterus with normal morphology, small volume ovaries, low antral follicle count.	If cryptorchidism, ultrasound to locate testes
Seminogram	low volume ejaculate, azoospermia, pH> 7.2, and positive fructose	
Hormones	Low estrogen and low testosterone Low to normal gonadotropins Normal prolactin and TSH High Prolactin and low TSH in acquired causes of HH	-GAST to distinguish between pituitary and hypothalamic causes of HH. -AMH and Inhibin B are low but not used for diagnosis in isolation
Brain MRI	Macro or microadenoma of the pituitary fossa, Granuloma, abscesses, tumours, other SOLs	Olfactory placode hypoplasia
Genetic Tests	HH gene panel	Whole exome sequencing

A careful history of symptoms, its onset, symptoms of headache, visual and olfactory defects, personal history of exercise, eating disorder, presence of chronic illness, drug intake, prior brain surgeries, radiation or chemotherapy and family history of similar syndromes or delayed puberty should be elicited from the affected individual. A sexual history, questions on libido, fertility and menstrual history should additionally be elicited from adults. An examination to rule out morphological defects involving the lip, palate, teeth and ears along with an assessment of height, weight, arm span, testicular volume using orchidometer, secondary sexual characteristics and a perineal, pelvic and systemic examination is essential to the cause of making a diagnosis. The sense of smell, hearing and peripheral field vision should be checked using olfactometry, hearing tests and visual field tests respectively when indicated by history.

Ultrasonography of the abdomen with specific focus on the pelvic organs and kidneys will help identify an infantile uterus, small volume ovaries in women with reduced antral follicle count and any coexisting renal defects in both sexes. Ultrasound pelvis may also be able to locate testes in cryptorchidism.

The reproductive hormones in hypogonadotropic hypogonadism are at levels less than the fifth centile for normal. Typically, in complete forms of CHH, the gonadotropic hormones would be at

FSH< 1.2mIU/mL and LH< 0.65mIU/ml. Another study finds higher cut-off for females with Serum basal LH <0.85 IU/L and basal FSH <2.43 IU/L showing moderate sensitivity (80.0% or 100.0%) and specificity (75.0% or 50.0%) in the diagnosis of HH in females. Basal Inhibin B is low, typically <30ng/dL in both sexes. Basal AMH is low as well though it cannot be used for diagnosis in isolation. Low basal AMH does not reflect a poor ovarian reserve as pre-antral and small antral follicular pool that generates AMH is non-existent and AMH value is likely to improve with FSH therapy as more and more FSH regulated preantral and small antral follicles are recruited into the pool. The gonadal hormones would be at estradiol <20pg/ml, progesterone <1ng/ml in women and total testosterone less than 100ng/dL in men. It is essential to run a prolactin test to rule out a prolactinoma or other pituitary macro- or micro-adenomas, and a thyroid profile to test anterior pituitary function.

A GnRH agonist stimulation test (GAST) helps in distinguishing between a hypothalamic (more common) or a pituitary origin (less common) for this condition. An intravenous injection of 100 µg/m2 or 2.5 µg/kg of GnRH agonist Buserelin or Leuprolide or 1mcg/Kg of Naferelin is administered and blood is tested for FSH and LH at baseline and half hourly for 4-8 samples till peak FSH and LH levels are reached. The levels of FSH and LH should typically rise in healthy individuals with an intact hypothalamic pituitary axis, in the first couple of hours before falling. Individuals with a pituitary cause for HH will not respond to GnRH agonist whereas those with a hypothalamic cause will respond.

Additionally, GnRH agonist stimulation test can also help distinguish between CHH and Constitutional delay in growth and development (CDGP), a more common cause of delayed puberty. Making this distinction at adolescence is a challenging task since both conditions present with delayed puberty and similar basal hormonal characteristics. On follow-up CDGP adolescent will go through a normal puberty albeit at a later age than a normal adolescent. An HH adolescent will not go through puberty at all. Hence it is necessary to distinguish between these similar profile individuals to be able to take the right management decision. (reassure the former and start steroidal therapy in the latter).

The gonadotropin rise seen after GAST is typically to a mean of 22 miu/ml for LH and to a mean of 12 mIU/ml for FSH in adolescents with CDGP. In CHH, LH peaks remain under 9mIU/ml. . FSH peaks as a rule are lower in CHH than in CDGP, but there is a considerable overlap in values between the two groups and hence FSH peaks post GAST cannot be used to discriminate between CDGP and CHH. Towards the same cause, using radiographs for bone age as a key part of the workup helps in differentiating between CDGP adolescent (bone age < 13) and HH adolescent (bone age > 13)

Once a diagnosis of HH has been made based on clinical profile and hormonal testing, the next step is to establish a cause for this state. For if the cause is correctable, attention is focused on its alleviation following which the HH state auto corrects itself.

A brain MRI reliably rules out a pituitary micro or macroadenoma, craniopharyngioma, aneurysms, Rathke pouch cysts, CNS tumours, granulomas, abscesses, infiltrative lesions of the pituitary. It may also identify olfactory placode aplasia or hypoplasia where these exist.

Genetic tests have a high yield in cases with normal MRI scans. The purpose of genetic tests is to be able to counsel individuals about heritability of the condition and its transmission risks. This is best done by ordering an HH gene panel or in recent years by Whole genome sequencing using the NGS platform.

Management of the hypogonadotropic hypogonadal male

There are two states of concern to the individual: delayed puberty and infertility. Both have separate management algorithms and are discussed separately.

Induction of Puberty and maintenance of secondary sexual characteristics

The aim of treatment is to induce virilization and normal sexual function, to stimulate statural growth, to promote bone health and to address psychological and emotional wellbeing.

Typically, testosterone replacement therapy (TRT) is utilized to achieve these aims. The dosage and preparation chosen is appropriate to the sexual developmental stage the individual is in and the target stage aimed at. For young boys between 12 to 16 years with the right diagnosis and after ruling out other causes, treatment begins with low dose testosterone (Table 2). This is gradually increased in dose and frequency every six to nine months over 24 months. Once the boy enters Tanner's stage IV development, full adult dose may be commenced. Such regimen helps mimic natural puberty and maximize statural growth while affording time for psychosexual development and minimizing the risk of precocious sexual activity.

Table2: Hormone therapy for induction of puberty and maintenance of reproductive maturation in males

Preparation	Dose	Frequency	Route
For boys between 12-16 yrs. (Puberty induction)			
Testosterone Enanthate	50mg	4 weeks	Intramuscular
Transdermal Testosterone	10mg	Every other day	Transdermal
Testosterone Undecanoate	40mg	Daily	Oral
For adults (Induction or Maintenance)			
Testosterone Enanthate	150-200mg	2-4 weeks	Intramuscular
Testosterone Undecanoate	750mg	10-14 weeks	Intramuscular
Testosterone Gel	50-100mg (1%) 25-50mg (2%)	Daily	Transdermal
Testosterone Patch	4mg	Daily	Transdermal

For young adults presenting for the first time for TRT, a more aggressive approach may be adopted with starting dose being higher than in boys and stepped up more frequently at 3-6 monthly interval to reach the final adult dose over one year. Dosing frequency is guided by trough serum testosterone measurement (pre injection testosterone levels) targeting the lower end of the normal range typically 350 – 400ng/dL. Long acting injections cause a huge difference between peak testosterone values seen usually in the first week post injection and trough values, seen at the end of injection interval. These huge fluctuations in serum testosterone levels cause alternate states of hypergonadism and hypogonadism. Smaller more frequent dosing can avoid this issue but introduces the issue of frequent needle pricks. Transdermal patches and gels may be the best in maintaining steady levels of testosterone but are limited by their huge costs and skin allergies in some men. The choice of preparation and dosing should be individualized in every case.

Side effects associated with TRT include gynecomastia, weight gain, acne, erythrocytosis, hepatotoxicity, and development/worsening of obstructive sleep apnoea, worsening of lower urinary tract symptoms and increased risk of prostate cancer with long-term usage.

Monitoring patients on TRT as per the Endocrine Society Guideline 2018, should be with assessment of change in voice, testicular size, facial and body hair growth, shaving frequency, change in libido, erection and ejaculation frequency, sleep patterns. Pre-injection total testosterone levels, CBC and LFT should be ordered at each visit to monitor response to therapy and development of development of adverse effects. Bone densitometry for changes in osteoporotic status every 1-2 years after initiation of TRT. Prostate specific antigen is ordered for older hypogonadal individuals above 40 years of age. Additional tests may be ordered as per the clinical situation.

TRT ideally is administered lifelong to attain optimal benefit and does not lead to gonadal size increment or improvement in fertility. The patient and their relatives need to be informed of these facts. If while on testosterone therapy, men report an increase in testicular size, the physician should consider two possibilities: testicular tumour or a spontaneous reversal of CHH with return of HPG axis activity. A reversal has been seen in 10-20% of individuals. In either case, the physician should stop the TRT and investigate through appropriate tests.

Contraindications to testosterone replacement therapy as per the Endocrine Society are untreated prostate or breast cancer, uninvestigated prostate nodule or a PSA >4, congestive heart failure grade 3-4, hematocrit more than 54%, severe obstructive sleep apnea, myocardial infarction or stroke within the past six months and a current desire for fertility. Pulsatile GnRH or a combination of HCG and FSH may be used to induce or maintain virilization in such patients.

Treatment of infertility in males

Irrespective of HH etiology, it is one of the most medically treatable causes of non-obstructive azoospermia. Identifiable acquired causes need to be addressed separately. Hyperprolactinemia responds to dopamine agonist therapy or in intractable cases to surgery. Anabolic steroid induced hypogonadal state responds to cessation within three to six months. Functional causes like eating disorders, extremely low weight and

excess stress respond to appropriate behavioral interventions. Pituitary tumours, abscesses, sarcoidosis and hemochromatosis can respond to appropriate medical or surgical intervention. In those with idiopathic HH or those with an acquired cause not responsive to specific therapy, the treatment protocol to induce fertility in men as specified by the European Consensus on management of CHH is shown in Figure 2.

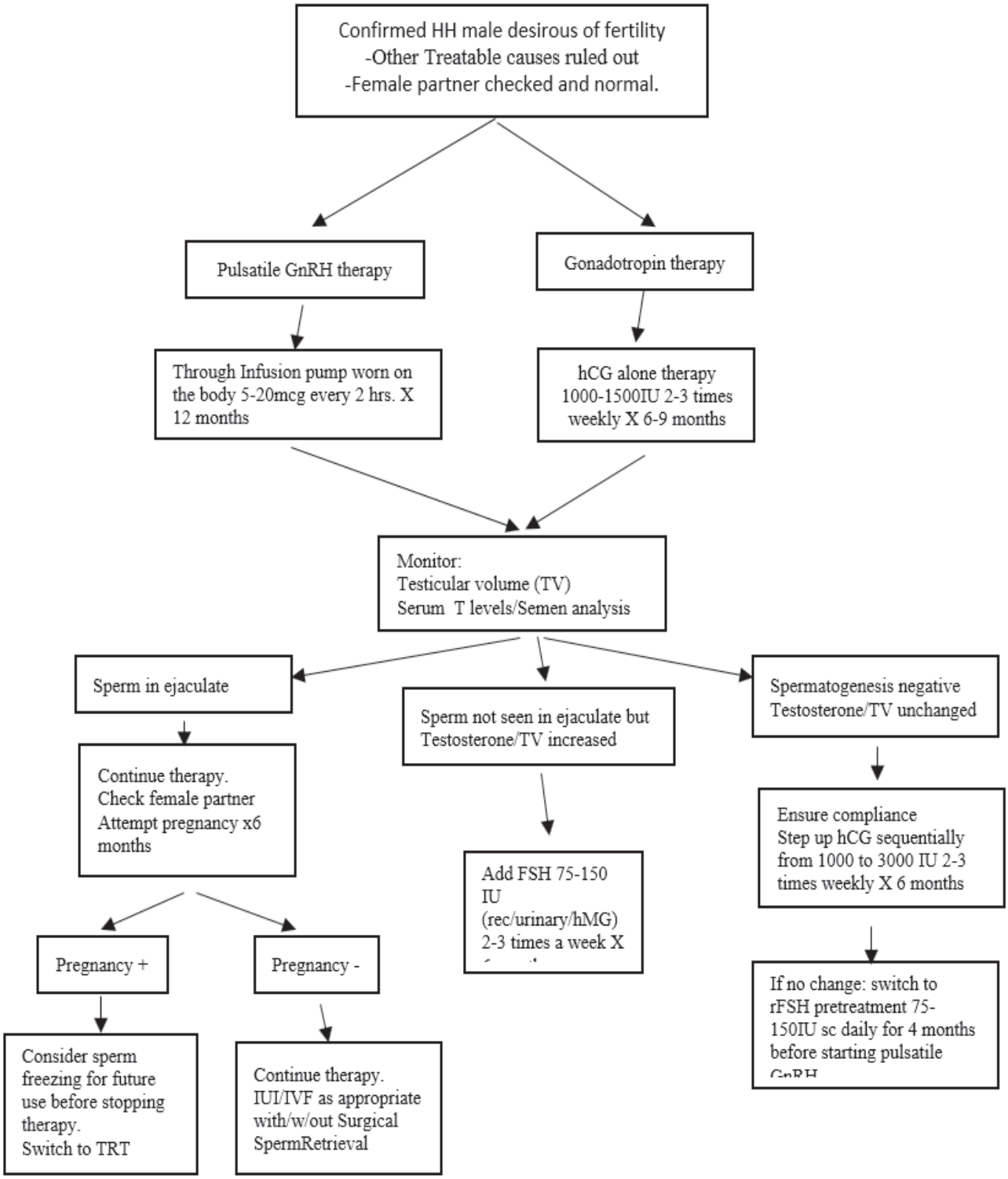

Figure 2: Infertility management in the hypogonadotropic hypogonadal male

wed by pulsatile GNRH for 18-24 months has been tried successfully.

Clomiphene citrate 25 mg daily has been tried in select men with idiopathic HH and with intact pituitary function with two pregnancies resulting in partners of 10 men treated this way. However, there are inconsistencies in literature with respect to the effect of Clomiphene and cannot be recommended for routine use in men with idiopathic HH men.

GnRH therapy is as effective as gonadotropin therapy in achieving spermatogenesis and pregnancy in patients with hypothalamic disorders who have intact pituitary function. However, due to its cumbersome nature and its ineffectiveness in men with panhypopituitarism, pulsatile GnRH is less likely to be used than gonadotropin therapy. Dose titration should be guided by mean testosterone levels. Response to therapy is quicker in men who have signs of puberty at the time of treatment initiation. Those with a history of cryptorchidism and pre pubertal onset of HH usually have less response rates and may take up to two years to respond. In severe cases, a reversal of treatment order involving FSH pre-treatment for four months follo

About 75% of patients initiated on Gonadotropin therapy will have a response in the form of sperm in ejaculate at twelve months. Clinicians should remember that even with long term therapy, sperm counts rarely return to normal with mean sperm count of 5.9 × 106/ml (range: 4.7–7.1 × 106/ml) for gonadotropin therapy and 4.3 × 106/ml (range: 1.8–6.7 × 106/ml) for GnRH therapy reported in a 2014 meta-analysis. And yet, this low mean sperm count does not preclude natural fertility. The pregnancy rates for the gonadotropin and GNRH therapy are between 30-50%. Only a minority of the pregnancies require ART. Sperm may be obtained through the ejaculate or in the face of persisting azoospermia but testicular volume and hormone improvements, through surgical retrieval.

Management of the hypogonadotropic hypogonadal female

Induction of Puberty and maintenance of secondary sexual characteristics

The aim of treatment is to induce estrogenization: normal breast and uterine growth, establishment of menses, promote bone and cardiovascular health and to address psychological and emotional wellbeing. The treatment guidelines as per the Expert European Consensus on treatment of CHH female are as given in Table 3.

Table 3: Hormone therapy for induction puberty and maintenance of reproductive maturation

Estradiol preparation	Dosage	Frequency	Progesterone	Purpose	Period
Young girls (10-13 years with no prior breast development)					
Transdermal Estradiol	0.05-0.07mcg/Kg Stepped up every six months to 0.08-1.2mcg/Kg Max daily dose 50mcg/day	Daily at bed time	- -	Induction of puberty Breast development	12-24 months Till Full breast development or till first menstrual bleed
Oral Estradiol	0.1-0.2mg Stepped up every six months by 0.1mg/day To a max of 1-2mg/day	Daily	-		
After growth spurt and breast development to atleast tanner's stage 3 (Choose a combination of any one estrogen and any one progesterone)					
Transdermal Estrogen	50-100mcg	Daily	Medroxyprogesterone acetate 2.5-5 mg daily continuously or 10 mg for 12 days a month	Maintenance of reproductive maturation Maintaining cyclic menstrual bleeding Bone health Reducing Cardiovascular risk Psychosexual well-being	Till age of natural menopause Or As per symptoms of woman after risk-benefit assessment.
Oral estrogen	1-2mg	Daily	Micronized progesterone 100mcg daily continuously or 200mcg for 12 days a month		
Conjugated equine estrogen	0.625-1.2mg	daily	LNG intrauterine device		
Estradiol Gel	1-2 pumps of 0.06%	daily	,,		

Puberty can be induced by oral or preferably transdermal estradiol using low dose preparations with the goal of mimicking estradiol levels during gonadarche. The estradiol dose is slowly increased over 12–24 months, after which time cyclic progesterone is added or after the first menstrual bleed whichever is earlier, in order to maximize breast development. In adulthood, higher estradiol doses are used and progesterone is added either continuously or sequentially to avoid endometrial hyperplasia. Estrogen treatment increases uterine size and combined estrogen and progestin therapy induces monthly withdrawal bleeding, but does not induce ovulation.

Another common approach is the use of combined hormonal contraceptives, which may allow for ease of administration compared with a HRT regimen. However, the dose of estrogen and progestin in combined hormonal contraceptives is not replacement dosage; these hormonal preparations are significantly more potent than the aforementioned HT options.

Data on HT use in hypogonadal women and its link with breast cancer is scarce and indirect. Based on the premise that HT uses low doses meant to attain physiological levels of steroids in the body, the adverse cardiovascular event risk and cancer risk should not be affected. Hence the confidence in prolonged usage of HT is high. However, COCs which use supraphysiological doses of hormones and not in a physiological order, prolonged use of COCs especially when given to post-menopausal women may be thought to be detrimental. A 2017 prospective nationwide cohort involving more than 10 lakh women between 15-49 years of age revealed that, the overall relative risk of invasive breast cancer among women who were current or recent users of any hormonal contraception was 1.20 (95% confidence interval [CI], 1.14–1.26) compared with women who never used hormonal contraception. Relative risk increased with duration of use, ranging from 1.09 (95% CI, 0.96–1.23) for less than 1 year of use to 1.38 (95% CI, 1.26–1.51) for use longer than 10 years. In general, risk was similar among different formulations or preparations of combined oral contraceptives.

Treatment of infertility in females

GnRH deficiency leads to incomplete development of follicles especially from stages that are FSH dependent such as pre-antral, small and mid-antral follicular stage. A histopathological examination of HH ovaries would reveal the ovarian cortex studded with primordial, primary and secondary follicles but having a lack of antral follicles. This leads to the combination of small ovaries, decreased antral follicular count, and low circulating AMH concentrations observed in women with CHH.xxii It could wrongly suggest an alteration in ovarian reserve and a poor fertility prognosis and the woman should be made aware that this is not the case. With adequate duration GNRH or gonadotropin therapy, follicular growth and maturation commences and ovarian sizes, antral follicular counts and AMH start to rise. Fertility is usually not an issue.

The algorithm for management of the infertile hypogonadotropic hypogonadal female is given in Figure 3.

Prior checking of uterine morphology, adnexal pathology, tubal patency and partner seminogram is advisable before commencing ovulation induction. Acquired causes need attention and treatment as per cause as detailed in the section on male hypogonadotropic hypogonadism.

Women respond equally well to pulsatile GnRH therapy as to gonadotropin therapy.

Pulsatile GnRH therapy in women mimics physiological pulses of GNRH with frequency and amplitude set as per the menstrual phase. Typically a dose of 75ng/Kg per pulse is given through an intravenous infusion pump/ The dose for subcutaneously administered pulsatile GNRH therapy is twice as high as the intravenous route. A pulse frequency of 90 minutes is set in the early follicular phase and this is reduced to 60 minutes in the peri-ovulatory (late follicular, ovulatory and early luteal) period. These pulses increase to 120 minutes in the mid and late luteal phase. The major advantage of pulsatile GnRH therapy compared with gonadotropin treatment is the physiological way of causing folliculogenesis and ovulation, absence of a need for exogenous ovulatory trigger or luteal phase support, decreased risk of multiple pregnancy and ovarian hyperstimulation and reduced need for monitoring. The disadvantages are the inconvenience of having to wear these pumps over the body during the course of treatment sometimes for periods as long as 1-2 years, complications of phlebitis or cellulitis and lack of easy availability of these pumps.

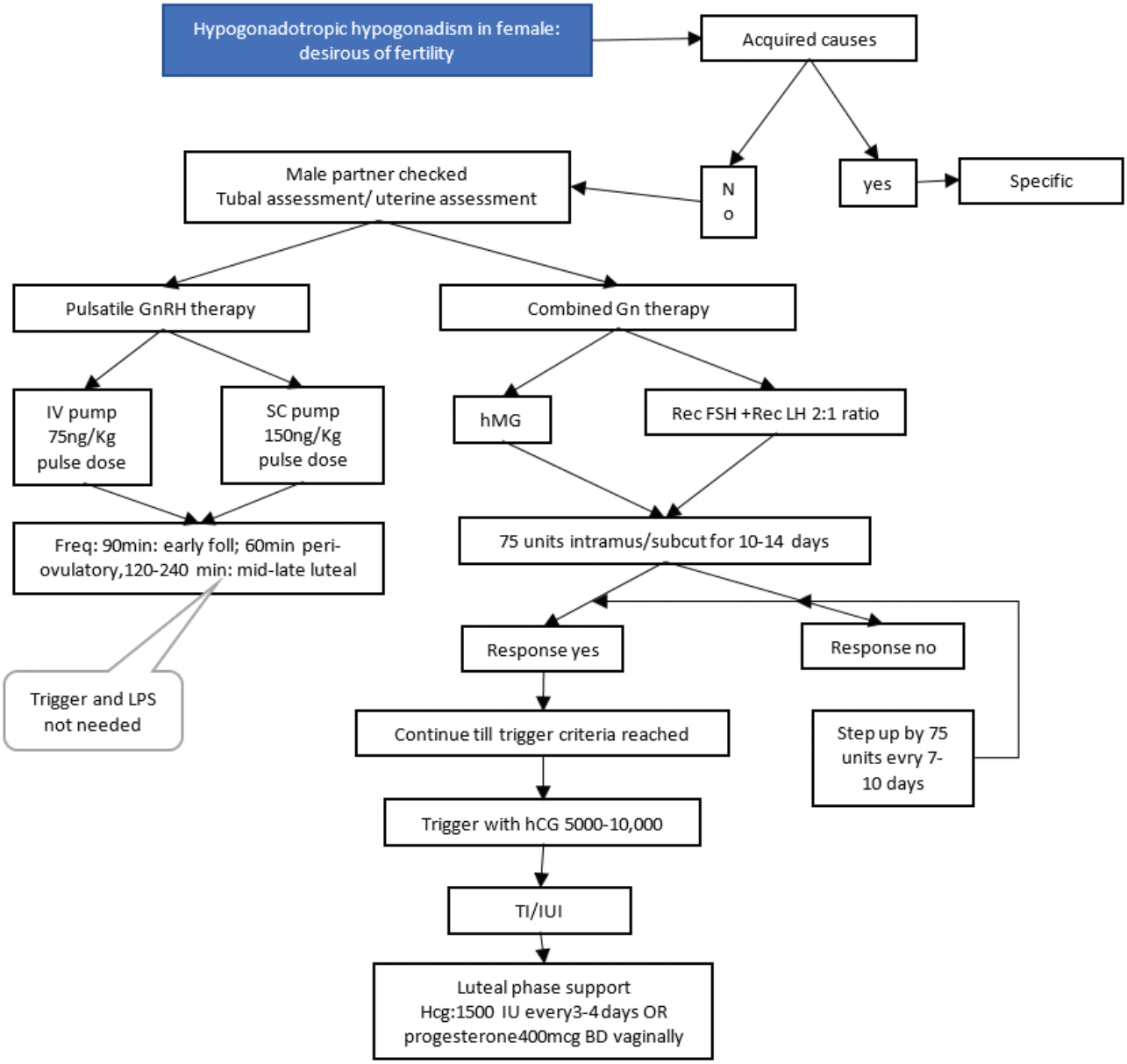

Figure 3: Infertility management in the hypogonadotropic hypogonadal female

Gonadotropin therapy is the preferred therapy for its easier availability and convenience of usage. GnRH deficiency leads to absence of both FSH and LH and hence a preparation having LH activity is preferable over pure FSH alone. Both Human Menopausal Gonadotropins (hMG) and recombinant FSH + recombinant LH preparations in ratios of 2:1 have been used. In a two arm randomized controlled trial involving 70 HH women, 70% of r-FSH/r-LH treated patients achieved ovulation vs 88% in hMG-HP group (p=0.11). However, pregnancy Rates in r-hFSH/r-hLH group was 55.6% compared to 23.3% in hMG-HP group (p=0.01). . Other retrospective studies have not shown this benefit with hMG outperforming recombinant gonadotropins in terms of pregnancy rates. .

When using hMG, it is normal practise to start with 75IU IM of hMG and response monitored with ultrasound folliculometry at 7-10 days. Dose is titrated up after 14 days if ovaries remain non-responsive or titrated down if a hyper-response is seen. It is not unusual to see long follicular phase lengths with typical durations being between 15-20 days. A duration of 60 days to achieve follicular dominance has also been described during the first stimulation and physicians and women should have this knowledge to persist with treatments patiently. Subsequent cycles seem to require fewer injections. xxxix

After follicular sizes of 18 mm or more are achieved, final ovulation trigger is given with an hCG injection (5000-10,000IU urinary or 250mcg of recombinant). GnRH agonist trigger may be used as well but would not work with pituitary causes of HH. Luteal phase needs to be supported with hCG injection 1500-2000IU twice weekly if there is no risk of OHSS or with exogeneous progesterone either given vaginally (400mcg twice daily) or intramuscularly (100mg once daily) when there is an OHSS risk. The ovulatory response rates are to the tune of 90% and pregnancy rates per cycle of about 12-27% have been achieved. xxviii, xxxix. Cumulative pregnancy rates of 89% after six treatment cycles have been reported in two small series of hypogonadotropic women.xl

If pregnancy occurs, luteal phase needs to be supported with exogenous progesterone till luteo-follicular transition, typically occurs at 8 weeks of pregnancy. Rates of multiple pregnancy are high, at about 30% and this fact alone can make HH pregnancies at high risk for preterm labour. There is no evidence to suggest however, that the course of a singleton pregnancy in the HH female is any different from a normally ovulating female.

Key Points

1. Hypogonadotropic hypogonadism is a rare cause of infertility in men and women.
2. It can be congenital or due to acquired causes.
3. The congenital form manifests as absent puberty in both sexes. The acquired form manifests most commonly in adults as secondary amenorrhoea in women and azoospermia and regression of signs of virilization in men.
4. When fertility is not the issue, age-appropriate doses of sex steroidal hormones are the treatment of choice in men and women.
5. When fertility is the primary concern, gonadotropin or pulsatile GnRH therapy is used.
6. Gonadotropins are more easily acceptable and available though could lead to multiple pregnancies and OHSS in women.
7. Pulsatile GnRH therapy is a physiological way of inducing ovulation and spermatogenesis and is devoid of the side effects of multiple pregnancies and OHSS, but its use is limited by its availability and the inconvenience of having to have a pump worn over the body.

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Safety of Neurological Therapeutic Drugs in Pregnancy

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Introduction

Neurologic conditions are among the concurrent medical conditions encountered during pregnancy. They constitute a significant proportion of chronic medical illnesses affecting women of reproductive age. Conditions such as epilepsy[7-8/1000], migraine [1in 5-6], multiple sclerosis [1-2 in 5000], movement disorders, cerebral venous thrombosis [1-2 in 10,000 deliveries], intracranial haemorhage [1-30in 100,000 deliveries], myasthenia gravis [1-2 in 5000], neuromuscular diseases, and neuropathic pain often require long-term pharmacotherapy, which may extend into pregnancy. The overlap of common pregnancy symptoms, limitation of clinical expertise in diagnosis and management of neurological disease can lead to serious maternal and fetal outcomes. The management of these disorders during pregnancy presents a complex clinical challenge, as both the disease itself and the medications used for treatment may adversely affect maternal and fetal outcomes.

Pregnancy introduces unique physiological changes that alter drug pharmacokinetics and pharmacodynamics, thereby influencing efficacy and safety. Moreover, the developing fetus is particularly vulnerable to drug exposure during organogenesis in the first trimester. Historically, fear of teratogenicity led to unnecessary discontinuation of essential neurological medications, resulting in disease exacerbation, maternal morbidity, and adverse perinatal outcomes. Contemporary evidence emphasizes that **optimal maternal disease control is often the safest approach for the fetus,** provided drug selection is evidence-based and individualized.

This chapter provides a detailed review of the **safety profile of commonly used neurological medications during pregnancy,** with emphasis on teratogenic risks, neurodevelopmental outcomes, pharmacokinetic considerations, and guideline-based recommendations. It aims to equip postgraduate trainees with a rational framework for decision-making in this complex area of clinical practice.

Physiological Changes in Pregnancy Relevant to Neurological Pharmacotherapy

Pregnancy induces substantial anatomical, physiological, and biochemical changes that significantly influence drug handling.

Pharmacokinetic Changes

Absorption

- Reduced gastric motility and increased gastric pH may alter absorption.
- Nausea and vomiting in early pregnancy can reduce drug bioavailability.

Distribution

- Plasma volume increases by approximately 40–50%, leading to dilution of water-soluble drugs.
- Serum albumin levels decrease, increasing the free (active) fraction

of protein-bound drugs such as phenytoin and valproate.

Metabolism

- Hepatic enzyme activity is altered:
  - Increased activity: CYP3A4, CYP2D6
  - Decreased activity: CYP1A2
- Drugs such as lamotrigine undergo increased glucuronidation, leading to reduced serum concentrations.

Excretion

- Renal plasma flow and glomerular filtration rate increase by 30–50%, enhancing clearance of renally excreted drugs such as levetiracetam and gabapentin.

These changes necessitate **therapeutic drug monitoring (TDM)** for several neurological medications during pregnancy.

Placental Transfer and Fetal Drug Exposure

Most neurological drugs cross the placenta to some degree. Factors influencing placental transfer include:

- Molecular weight (<500 Da crosses readily)
- Lipophilicity
- Degree of ionization
- Protein binding
- Placental transporter activity

The fetal liver has limited metabolic capacity, increasing susceptibility to drug toxicity. Exposure during weeks 3–8 of gestation carries the highest risk for major congenital malformations.

General Principles of Neurological Drug Use in Pregnancy

1. Preconception counseling should be offered to all women of childbearing age with neurological disorders.
2. Use monotherapy wherever possible.
3. Prescribe the lowest effective dose.
4. Avoid drugs with known high teratogenic potential.
5. Avoid abrupt discontinuation of therapy.
6. Supplement high-dose folic acid (4–5 mg/day) in women on antiepileptic drugs.
7. Employ a multidisciplinary approach, involving neurologists, obstetricians, and pediatricians.
8. Individualize treatment based on disease severity, previous response, and patient preferences.

Antiepileptic Drugs (AEDs)

Epilepsy and Pregnancy

Epilepsy affects approximately 0.3–0.5% of pregnant women. Approximately one third of patients will have an increased frequency of seizures while the remainder will experience no change or a decrease in seizure frequency. The factors affecting seizure frequency involves increased steroid hormone levels, sleep deprivation, and metabolic changes, Patient non compliance due to fear of fetal drug effect is another common reason of discontinuation of drugs. The lower the number of seizures frequency in 9 months before conception, the less are the chances of worsening during pregnancy Seizure control during pregnancy is crucial, as seizures—especially generalized tonic–clonic seizures—can result in maternal trauma, hypoxia, placental abruption, miscarriage, and fetal demise.

Teratogenicity of AEDs

The effect of AEDs on the fetus are complex . The four most commonly used agents i.e carbamazepine, phenobarbital, phenytoin and valproate are known to cross placenta and all are believed to cause teratogenic effects. The rate of congenital malformations in patients using these drugs is approximately two to three times higher than the infants of nonepileptic mothers [i.e 6-8 %in epileptic pregnancies]. However there are evidence of in utero exposure to valproate on long term cognitive potential of babies.

The risk of major congenital malformations (MCMs) varies significantly among AEDs:

- General population: 2–3%
- AED monotherapy: 3–7%
- AED polytherapy: 6–10%
- Phenytoin, primidone and carbamazepine are associated with patterns of malformation that are similar including mildly dysmorphic face and fingers, with stubby distal phalanges , hypoplastic fingernail suggestive of ' fetal antiepileptic drug syndrome'.. A genetic predisposition might be responsible leading to decrease in enzyme epoxide hydrolase in amniocytes of fetuses developing hydantoin syndrome.

Individual AED Safety Profiles

Valproate

- Highest teratogenic potential
- MCM risk: 9–15%
- Neural tube defects, cardiac defects, limb anomalies, spina bifida [1-2%]
- Increased cognitive impairments and strong association with autism spectrum disorder, intellectual disability, and reduced IQ
- Dose-dependent risk
- Contraindicated in pregnancy except in exceptional circumstances

Carbamazepine

- Moderate risk
- Neural tube defects especially spina bifida (~1%)
- Craniofacial defects, hypospadias
- Generally safer than valproate

Phenytoin

- Fetal hydantoin syndrome
- Cleft lip and palate, cardiac and urogenital defects
- Growth restriction, craniofacial anomalies, hypoplasia of nails and distal phalanges

Phenobarbital

Similar malformation patterns as phenytoin

- Increased risk of cardiac defects and cleft lip/palate
- Neonatal withdrawal syndrome
- Decrease in blood levels of coagulation factors [vitamin k dependant clotting factors]

Lamotrigine

- Low teratogenic risk
- Clearance increases by up to 300% during pregnancy
- Requires dose adjustment and serum level monitoring
- Considered first-line therapy

Levetiracetam

- Initially used as adjunctive therapy in partial onset seizures in adults and children aged 4 years and older and then it was approved for treatment of myoclonic seizures in adults and adoloscents aged 12 years or older. Now its use as monotherapy for generalsed tonic clonic seizures in increasing as it has a favorable safety profile
- Low MCM rates
- Increasingly preferred for women of childbearing age

Topiramate

- Increased risk of clefts lip and palates
- Avoid if possible, especially in first trimester

Migraine Medications in Pregnancy

Migraine is common in women of reproductive age. Many experience improvement during pregnancy, particularly in the second and third trimesters. Migraines are divided into those with aura and those without aura. Course of migraine in pregnancy is variable. The women who experience migraine during menstruation and are not associated with aura are likely to shoe improvement in third trimester and the headaches tend to worsen in postpartum. There are no demonstrable fetal adverse outcomes associated with migraines.

Acute Migraine Treatment: therapy are usually divided into abortive therapy and prophylactic measures. The prophylactic measures are reserved for patients with debilitating headaches or those with frequency more than 3 migraine episodes per month e.g beta blockers and tricyclic antidepressants.

- Paracetamol and low dose caffeine: First-line and safe
- NSAIDs: Use with caution; contraindicated in third trimester due to risk of premature ductus arteriosus closure and oligoamnios
- Triptans (Sumatriptan): Increasing evidence supports safety
- Ergot alkaloids and benzodiazepines[category D] : Contraindicated due to uterotonic effects, benzodiazepine can cause neonatal withdrawal and depression if used in latter part of pregnancy
- Opioids [morphine, meperidine and hydromorphone] category B drugs
- Glucocorticoids: generally safe

Preventive Therapy

- Propranolol: First-line preventive agent

- Amitriptyline: Acceptable
- Valproate and topiramate: Contraindicated
- CGRP monoclonal antibodies: Insufficient data; avoid

Movement Disorders and Pregnancy

Parkinson's Disease

It is an idiopathic hypokinetic disorder typically seen after 40 years of age but 5% of cases can present earlier. The condition is a degenerative disorder of unknown etiology related to deficiency of dopamine secreting neurons in substantia nigra of the brainstem mesencephalon. Symptoms include slowed movement, increased tone, resting tremors, loss of postural reflexes, masked faces and transient akinesia. Many medications like methyldopa, disulfuram, dopamine recptor antagonist, lithium, methanol, reserpine and tetrabenazine may lead to parkinsonism.

- Levodopa/ carbidopa:mainstay of treatment[category C] :they are associated with malformations in animals but adequate human data not available but most evidence supports relative safety
- Amantidine [category C] overall malformation rate is reported to be higher but no specific pattern is documented
- Bromocriptine[category C]:considered safe in pregnancy
- Selegiline and pergolide: relatively newer drugs and lacks safety data
- MAO-B inhibitors: Avoid
- Anticholinergics: Use cautiously

Dystonia and Tremor

- Botulinum toxin: Limited but reassuring data for focal use
- Propranolol: Useful for essential tremor

Demyelinating Disorders

Multiple Sclerosis (MS)

Multiple sclerosis is a demyelinating disease that affects the central nervous system at different levels and time. Relatively common neurologic disease affecting young adults at around 30 years of age. Women are affected twice as men.. Common symptoms include acute onset of diplopia, vertigo, gait instability, bladder incontinence, loss of vision and fatigue. The disease course in an individual is unpredictable. One pattern is relapsing and remitting with an identified onset and resolution of symptoms. The chronic progressive pattern follows a protracted curse with worsening of symptoms over a prolong period of time. Finally a relapsing progressing course displays identifiable exacerbations with no clear return to baseline neurologic functions. Poor prognostic factors include prominent weakness, poor response to steroids and older age of onset. Pregnancy is associated with reduced relapse rates, followed by increased postpartum relapse risk.

Disease-Modifying Therapies (DMTs)

Drug	Recommendation
Interferon-β	Increasing evidence of safety
With slightly increased risk of preterm labour Glatiramer acetate	Safe
Fingolimod, mitoxantrone	Contraindicated
Natalizumab	Use in high-risk cases
Teriflunomide	Contraindicated
Ocrelizumab	Limited data; avoid

Relapse treatment with short courses of corticosteroids is generally safe after the first trimester. However maternal and neonatal adrenal suppression and maternal glucose intolerance are reported.

Neuromuscular Disorders

Myasthenia Gravis

Myasthenia gravis is an autoimmune condition affecting neuromuscular transmission, resulting in variable weakness and fatiguability of skeletal muscles. Increasing weakness with repetitive use of muscles is the characteristic feature. It occurs in 2-10 per 100,000 individuals and affects women twice more than men. The cause is identified as antibody mediated autoimmune attack on acetyl choline receptor complex of neuromuscular junction. 10-20% infants born to women with MG show signs of neonatal MG because of transplacental passage of antibodies from mother to child.

Management requires careful balance to avoid maternal respiratory compromise and neonatal myasthenia.MG is treatable but not curable. Tymectomy is indicated in patients with thymoma. Glucocorticoids are the mainstay of treatment causing immunosuppression and can be continued in pregnancy though at lowest possible doses.

Azathioprine is used in some cases. Rituximab can be used with good results. In refractory cases IVIG and plasmapheresis are used.

Safe medications:

- Pyridostigmine: works by impeding degradation of acetylcholine and is relatively safe
- Prednisolone
- Azathioprine (relative safety)
- IVIG and plasmapheresis

Contraindicated:

- Mycophenolate mofetil
- Methotrexate
- Cyclophosphamide

Neuropathic Pain and Psychotropic Medications

Neuropathic Pain

- Gabapentin: Limited but reassuring data
- Pregabalin: Emerging data suggest possible risk; avoid if possible
- TCAs: Acceptable

Psychotropic Drugs

- SSRIs: Generally safe
- Benzodiazepines: Risk of neonatal withdrawal and floppy infant syndrome
- Antipsychotics: Use lowest effective dose

Lactation and Postpartum Considerations

Most neurological drugs are excreted into breast milk to varying degrees. Drugs with high protein binding and low oral bioavailability are safer.

Compatible with breastfeeding:

- Lamotrigine
- Levetiracetam
- Carbamazepine

Infant monitoring is recommended for sedation, feeding difficulties, and weight gain.

Conclusion

The management of neurological disorders during pregnancy requires a nuanced understanding of drug safety, disease-related risks, and physiological changes of pregnancy. While certain medications pose significant teratogenic risks, uncontrolled neurological disease may be equally or more harmful. Advances in pregnancy registries and pharmacovigilance have greatly improved knowledge, enabling safer therapeutic choices. Postgraduate trainees must adopt an individualized, evidence-based, and multidisciplinary approach to optimize outcomes for both mother and fetus.

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Management of Pregnancy in A Renal Transplant Recipient

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Introduction

The first successful pregnancy in kidney transplant recipient occurred in 1958 to 23-year-old Edith Helm who received a kidney from her identical twin sister in 1956 and delivered a healthy full term baby boy of 3.3 kg by cesarean section. Since then, there have been many successful pregnancies which have been reported. Pregnancy following renal transplant represents a unique clinical scenario in which maternal physiological adaptation to pregnancy occurs in the context of chronic kidney disease, immunosuppression, and a functioning allograft. Although fertility often improves after transplantation, pregnancy in renal transplant recipients is complicated by underlying maternal pathology, the health and function of the transplanted kidney, the effects of pregnancy on graft survival, and the impact of maternal disease and immunosuppressive therapy on the fetus. In addition, concerns regarding teratogenicity, infection risk, and obstetric complications necessitate careful multidisciplinary management.

With advances in transplantation medicine, immunosuppressive regimens, and obstetric care, pregnancy outcomes in renal transplant recipients have improved substantially. Nevertheless, rates of adverse maternal and fetal outcomes—including pre-eclampsia, fetal growth restriction, preterm delivery, and operative birth—remain higher than in the general obstetric population.

Adaptation in pregnancy

During pregnancy, a woman's body undergoes many changes to support the growing baby. One of the most significant areas of change is the renal system. Understanding these changes is crucial for managing both normal pregnancies and those complicated by renal disease.

1. **Increased Blood Volume and Cardiac Output**

   As pregnancy progresses, the mother's blood volume increases by up to 50%. This helps supply enough blood to the placenta and the baby. With more blood in circulation, the heart pumps more blood each minute, a process called increased cardiac output. The extra blood flow reaches the kidneys, leading to changes in how they function.

2. **Increased Renal Blood Flow and Glomerular Filtration Rate (GFR)**

   The kidneys receive more blood i.e renal plasma flow increases by 60-80% which increases the Glomerular Filtration Rate (GFR)—the rate at which the kidneys filter blood. An increased GFR means that waste products and extra fluid are cleared from the mother's blood more efficiently. As a result, normal laboratory values for kidney function, like creatinine and blood urea nitrogen (BUN), are lower in pregnant women. Renal vasodilation and increase plasma flow leads to increase renal size. Renal hyperperfusion and hyperfiltration causes increase urine output, frequency and nocturia.

3. **Hormonal Changes Impacting the Kidneys**

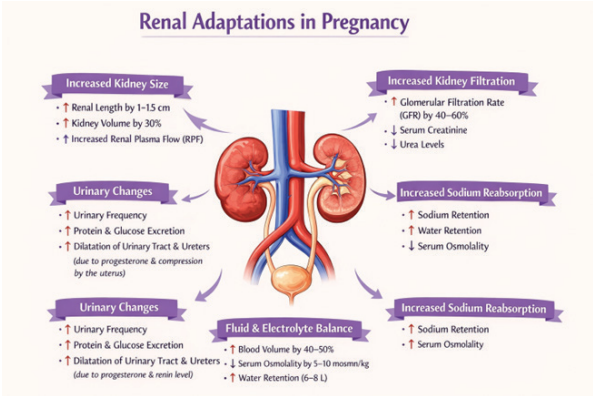
   Hormones like oestrogen, progesterone, Renin-Angiotensin-Aldosterone System (RAAS) become more active during pregnancy. These hormones cause the kidneys to retain more sodium and water, which contributes to the increased blood volume. This is crucial for maintaining a healthy pregnancy but can also lead to swelling (oedema) and a lower concentration of sodium in the blood (hyponatraemia).

4. **Sodium and Water Retention**

   The kidneys, under the influence of pregnancy hormones, retain more sodium and water than non-pregnant state. This retention is necessary to support the increased blood volume and ensure that the baby has enough nutrients. However, it can sometimes lead to oedema in the legs and feet.

5. **Lower Serum Creatinine and BUN Levels**

   As the kidneys are working more efficiently, normal blood levels of waste products like creatinine and BUN decrease. Lower levels of these substances are normal in pregnancy. This means what is considered "normal" for kidney function differs for pregnant compared to non-pregnant women. Creatinine values of 80 micromol/l or more during pregnancy suggest renal dysfunction and should prompt further evaluation. Health care providers need to be aware of these differences to assess kidney health during pregnancy.



Epidemiology and Incidence

The prevalence of renal transplantation among women of reproductive age in the UK is estimated at 2–6 per 10,000 women, with approximately 30–40 pregnancies in renal transplant recipients reported annually. Pregnancy is estimated to occur in around 12% of transplanted women of childbearing age, and the number of kidney transplant recipients conceiving is steadily increasing. Registry data demonstrate that the majority of pregnancies in renal transplant recipients result in live births, with success rates exceeding 90% in well-selected cohorts. However, transplant recipients remain at increased risk of maternal and perinatal complications compared with non-transplant populations.

Pre-pregnancy Counselling and Contraception

Maternal morbidity and mortality are increased in women with medical comorbidities who do not receive appropriate pre-pregnancy counselling. Consequently, all women with renal transplants should receive specialist pre-pregnancy counselling before conception. Effective contraception should be used until counselling is complete and pregnancy is optimally timed. Pre-pregnancy counselling should include discussion of:

- Risks of maternal complications of hypertension, pre-eclampsia, infection, and gestational diabetes
- Potential fetal risks of prematurity and fetal growth restriction
- Effect of pregnancy on graft function and long-term graft survival
- Medication safety, including teratogenicity and breastfeeding considerations
- Referral to a clinical geneticist for women with inherited renal disease
- Check on Rubella serology
- Advice and support with smoking cessation
- Folic acid supplementation

Timing of Pregnancy

Conception is not advised within the first year following renal transplantation. During this period, immunosuppressive doses are higher, graft function may be unstable, and the risk of acute rejection—estimated at 10–15%—is greatest, particularly in women under 45 years of age.

Criteria for considering a pregnancy (European best practice guidelines):

- Good general health for 12–24 months post-transplantation
- Good stable allograft function (serum creatinine preferably below 1.5mg/dl and urine protein excretion < 500mg/24 hrs)

- No recent episodes of acute rejection and no ongoing rejection
- Normotensive or minimal antihypertensive requirement
- Normal allograft ultrasound (no graft pelvicalyceal dilation)
- Stable maintenance immunosuppression and compatible with pregnancy (e.g. prednisolone ≤15 mg/day, azathioprine ≤2 mg/kg/day)
- Absence of active infections
- Optimally controlled comorbidities such as diabetes

Graft Function and Maternal Risk Stratification

For women with stable graft function one year after transplantation, pregnancy risks depend largely on baseline renal function, hypertension, and proteinuria. Women with graft function equivalent to a normal estimated glomerular filtration rate can generally be reassured that pregnancy does not appear to increase the risk of graft rejection or accelerate long-term graft loss.

However, renal disease etiology remains important. Women transplanted for diabetic nephropathy may have coexisting microvascular complications, while those with lupus nephritis may have persistent autoantibodies that influence pregnancy risk.

Higher pre-pregnancy serum creatinine levels are consistently associated with poorer pregnancy outcomes, including pregnancy loss, extreme prematurity, neonatal death, and congenital anomalies.

Medication Management and Teratogenicity

Immunosuppressive Therapy

Teratogenic medications must be discontinued before conception. Mycophenolate mofetil is associated with an increased risk of first-trimester pregnancy loss and characteristic fetal malformations, particularly affecting the ears and face. It should be replaced with azathioprine, which is considered safe in pregnancy. A minimum wash-out period of three months is recommended following conversion, during which graft stability should be confirmed and folic acid supplementation commenced.

Calcineurin inhibitors (tacrolimus and ciclosporin), corticosteroids, azathioprine, and hydroxychloroquine are considered compatible with pregnancy. There is limited safety data on sirolimus, everolimus, and rituximab, and these agents should generally be avoided.

Antihypertensive and Adjunctive Medications

Angiotensin-converting enzyme inhibitors and angiotensin receptor antagonists are contraindicated in pregnancy due to fetotoxicity and should ideally be discontinued before conception. In women with significant proteinuria, these agents may be continued until pregnancy is confirmed, with close monitoring thereafter.

Statins should be stopped prior to conception. Low-dose aspirin is recommended for pre-eclampsia prophylaxis unless contraindicated.

Effects of Renal Transplantation on Pregnancy

Hypertension and Pre-eclampsia

Hypertension predates pregnancy in up to 70% of renal transplant recipients and persists in more than half during pregnancy. An additional proportion of women develop gestational hypertension. Chronic hypertension significantly increases the risk of superimposed pre-eclampsia, fetal growth restriction, preterm delivery, and perinatal mortality.

Diagnosing superimposed pre-eclampsia is challenging in the presence of baseline hypertension and proteinuria. Rising blood pressure, escalating antihypertensive requirements, doubling of proteinuria, thrombocytopenia, elevated liver enzymes, fetal growth restriction, and low placental growth factor levels support the diagnosis.

Proteinuria

Proteinuria often increases during pregnancy and may double even in uncomplicated pregnancies. While proteinuria alone does not reliably predict pregnancy outcome, levels exceeding 1 g/day are associated with postpartum decline in renal function and increased thromboembolic risk.

Gestational Diabetes Mellitus

The risk of gestational diabetes mellitus is increased due to the diabetogenic effects of corticosteroids and calcineurin inhibitors. Meta-analyses suggest approximately double the risk compared with the general population, although UK data show comparable rates, possibly reflecting lower steroid exposure or demographic differences.

Obstetric and Neonatal Outcomes

Renal transplant recipients have higher rates of:

- Pre-eclampsia (20–30%)
- Caesarean delivery (up to 60%)
- Preterm delivery (<37 weeks in up to 45-60%)
- Fetal growth restriction: 20–40%
- Increased risk of infection due to immunosuppression
- Anaemia
- Neonatal unit admission

Despite these risks, live birth rates exceed 90% in contemporary cohorts. Congenital anomaly rates are similar to the general population when teratogenic medications are avoided. Ectopic pregnancy is more common due to prior abdominal surgery and dialysis-related adhesions.

Effect of Pregnancy on the Renal Allograft

Matched cohort studies and registry data demonstrate no significant difference in long-term graft survival between women who become pregnant and those who do not. Acute rejection during pregnancy is uncommon, occurring in less than 5% of women, and under 2% in UK cohorts.

A rise in serum creatinine during pregnancy is most often attributable to pre-eclampsia rather than rejection. If rejection is suspected, renal graft biopsy should be performed, as it is technically feasible and diagnostically valuable.

Rejection can be treated with corticosteroids and optimization of calcineurin inhibitors. Biological agents have been used in pregnancy, though placental transfer necessitates avoidance of live vaccines in exposed infants during the first six months of life.

Antenatal Management

Pregnant renal transplant recipients require consultant-led multidisciplinary care involving obstetricians, specialist in feto-maternal medicine, nephrologists, transplant surgeons, neonatologist and specialist midwives.

Key elements of antenatal care include:

- Regular monitoring of renal function and immunosuppressant levels (at least monthly, preferably 2-4 weekly)
- Blood pressure control (<140/90 mmHg). Office blood pressure monitoring complemented by home blood pressure monitoring, allows early detection and treatment of pre-eclampsia
- Screening for gestational diabetes (Offer glucose tolerance testing for women with risk factors for diabetes and those taking tacrolimus or steroids at 24–28 weeks of gestation.)
- Serial fetal growth surveillance
- Vigilance for infection, particularly urinary tract infection and opportunistic pathogens. Monthly urine analysis and culture for detection of asymptomatic bacteriuria should be advocated
- Periodic monitoring of calcineurin inhibitor levels (tacrolimus/ciclosporin) to ensure that adequate immunosuppression is maintained
- Timing of birth needs to take into account maternal and fetal wellbeing. In the absence of any complication ,delivery should be attempted at term.

Calcineurin inhibitor levels require close monitoring, as pregnancy increases drug metabolism while free drug concentrations may rise.

Intrapartum Care

Vaginal birth in an obstetric unit is recommended where no contraindications exist. The transplanted kidney lies extraperitoneally and does not obstruct labour. Continuous fetal monitoring is advised. Maternal fluid balance, temperature and cardiovascular status has to be monitored closely.Caesarean delivery should be reserved only for obstetric indications. When required, careful surgical planning is essential to minimize graft trauma and the technique of surgery needs to be discussed with transplant surgeon to avoid allograft injury. The transplanted kidney should be located before surgery and renal transplant surgeon should ideally be present during caesarean. During labour and delivery prophylactic antibiotics should be administered and stress-dose steroids should be considered for women on long-term corticosteroids.

Postpartum Care and Contraception

Postpartum management focuses on stabilizing blood pressure, monitoring fluid balance, rechecking calcineurin inhibitor levels, reassessing renal function, and rationalizing medications compatible with breastfeeding. Enalapril is the ACE inhibitor of choice for breastfeeding women when indicated. Breastfeeding is not contraindicated but it is advisable to have a discussion regarding the benefits of breastfeeding with the mother and clarify the doubts associated with the transfer of immunosuppressive medications in breast milk. A prolonged course of postnatal thromboprophylaxis

should be considered for women with heavy proteinuria. Follow-up with the transplant team should be individualized. Effective contraception is essential, with progesterone-only methods and intrauterine systems considered safe and effective.

Alarming signs of acute rejection (Occurs in 9–14% of pregnancies)

- Deteriorating Renal Function
- Fever
- Oliguria (Low urine output)
- Graft Swelling & Tenderness
- Altered Echogenicity & Blurring of Corticomedullary Junction on ultrasound

Conclusion

Pregnancy after renal transplantation is increasingly common and frequently successful. Optimal outcomes depend on careful patient selection, pre-pregnancy counselling, avoidance of teratogenic medications, and coordinated multidisciplinary care at a tertiary care centre. While women with stable graft function and minimal comorbidity generally fare well, those with impaired renal function, hypertension, or proteinuria face significantly higher risks and require intensified surveillance

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Fetal Cardiac Anomalies. What to do after diagnosis?

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Abstract

Early detection of fetal cardiac anomalies offers critical window for perinatal planning and informed parental decision-making. This obstetric guidance outlines a pathway for obstetric teams following a fetal congenital heart disease (CHD) diagnosis. Core elements include multidisciplinary coordination and delivery planning at tertiary centres equipped for neonatal and pediatric cardiac services.

Introduction

CHD is the most common congenital anomaly, affecting 8–10 per 1,000 live births. With widespread use of high-resolution ultrasound, fetal echocardiography, and improved prenatal screening, a significant proportion of cardiac defects are detectable antenatally. Early and accurate diagnosis enables structured counselling, optimized perinatal planning, and timely neonatal intervention when needed.

Understanding the Diagnostic Pathway

When to advise Fetal Echocardiogram

Routine anomaly screening at 18–22 weeks is crucial for identifying structural abnormalities. Suspicion of fetal CHD arises from:

- Abnormal four-chamber view, outflow tract view or three vessel tracheal view on routine ultrasound
- Increased nuchal translucency
- Extracardiac anomalies
- Abnormal ductus venosus or tricuspid regurgitation in first-trimester screening
- Maternal risk factors: diabetes, phenylketonuria, autoimmune disease, maternal infections like TORCH, bad obstetric history, Assisted reproductive technology
- Family history of CHD
- Fetal arrhythmias or hydrops
- Multiple pregnancy especially monochorionic twins Any suspicion should prompt referral for detailed fetal echocardiogram.

Why do we need Fetal Echocardiography

- Precise anatomical definition and hemodynamic assessment
- Prognostic clues and guidance for follow-up intervals
- The necessity, timing, and frequency of serial assessment should be guided by the nature and severity of the lesion along with anticipated timing and mechanism of progression

What should be done once fetal cardiac anomaly is detected ?

Immediate Steps After Diagnosis

Delivering the Diagnosis: The way a diagnosis is communicated greatly influences parental coping and decision-making. Essential principles include - provide information in simple, compassionate, non-technical

language and discuss with a pediatric cardiologist about potential outcomes before discussing with family. Parents should clearly understand about cardiac defect, expected prognosis, Possible interventions (prenatal, perinatal, postnatal), Any risks including hydrops, fetal demise, or neonatal surgery, delivery requirements and expenses involved .

Activate Immediate Multidisciplinary Involvement

Core team should include Obstetrician managing the pregnancy, fetal medicine specialist, pediatric cardiologist and pediatric cardiac surgeon, neonatologist and genetic counsellor. Early involvement of core team improves parental confidence, reduces uncertainty, and streamlines planning.

Genetic & Syndromic Evaluation - Up to 10–20% of major CHD may be associated with chromosomal or genetic abnormalities. The main indications for genetic testing may be as following -

- Increased nuchal fold thickness or cystic hygroma
- Major structural defects – cardiac or extracardiac
- Conotruncal anomalies (Tetralogy of Fallot, Truncus arteriosus, interrupted aortic arch)
- AV canal defect
- Left-sided lesions or Pulmonary stenosis
- Absent Thymus/reduced Thymic-thoracic ratio

Genetic Testing Options may include Invasive testing like Chorionic villus sampling (11–14 weeks),Amniocentesis (15+ weeks) for Karyotype, Microarray, Targeted FISH for 22q11.2 deletion, Whole exome sequencing and Non-invasive prenatal testing (NIPT)

We should categorise Fetal cardiac lesions based on severity and expected outcome -

Category 1: Defects where benign findings are present, but no cardiac intervention is needed - Intracardiac Echogenic focus (ICEF), isolated right aortic arch, PLSVC (persistent left superior vena cava), Aberrant right subclavian artery (ARSA).

Category 2: Defects which are mild and do not need fetal or neonatal interventions, need only follow up as they may resolve spontaneously over time - Small VSD, Mild tricuspid regurgitation (TR) in late gestation, isolated mild Pericardial effusion.

Category 3: Defects which are likely to require intervention and have good outcomes –Large VSD, Discrete Coarctation of aorta, Pulmonary and aortic valve stenosis with preserved ventricular function, Prolong PR interval, complete heart block (CHB) with ventricular rate >55/min and no Hydrops (Please note that prolong PR interval and CHB should be discussed for trans-placental therapy).

Category 4: Defects which are severe and will certainly require neonatal or infantile intervention, few of these may need multiple interventions - Cyanotic CHD like d-Transposition of great arteries (d-TGA), Total anomalous pulmonary venous connection (TAPVC), Tetralogy of Fallot (TOF)

AV canal defect, Vascular Ring, Arch anomalies like arch hypoplasia /interrupted aortic arch Critical aortic or pulmonary valve obstruction with ventricular dysfunction (may need intervention immediately after birth)

Multistage surgical repair – Pulmonary atresia variants, Truncus arteriosus, Few variants of TOF/ Double outlet right ventricle (DORV), severe forms of Ebstein anomaly.

Fetal Tachyarrhythmia (will need Transplacental drug therapy)

Cardiomyopathy, significant pericardial effusion, Severe TR Antenatal Ductal Narrowing /Foramen ovale restriction

Category 5: Defects which have poor prognosis and family may be given option of termination -

Univentricular cardiac disorders like Tricuspid Atresia, Hypoplastic left heart syndrome (HLHS), Double inlet left ventricle (DILV), DORV with non-routable aorta CHB <55 /min with hydrops.

Category 6: CHD with expected hemodynamic instability in delivery room where immediate intervention may be needed in first few hours of life - HLHS with restrictive foramen ovale, d-TGA with restrictive foramen ovale, Obstructed TAPVC,Ebstein anomaly with hydrops, TOF with absent pulmonary valve (APV) and severe airway obstruction,Uncontrolled arrhythmias with hydrops, CHB with low ventricular rate <55/min, Endocardial fibroelastosis (EFE) and/or hydrops

Fetal Interventions: When Are They Considered ?

Fetal cardiac interventions currently are in developing phase; indications and outcomes remain limited. Commonly Attempted Procedures include-Fetal aortic valvuloplasty for severe aortic stenosis with evolving HLHS, Pulmonary valvuloplasty for pulmonary atresia with intact ventricular septum, Atrial septoplasty for restrictive atrial septum in HLHS.

Criteria for Consideration

- Unambiguous evidence of evolving physiology
- Absence of major extracardiac anomalies
- Absence of severe hydrops
- Experienced fetal intervention team Fetal therapy improves outcomes only in carefully selected cases; parental expectations must be aligned realistically.

Fetal transplacental therapy in certain situations is required and need to be in collaboration with core team

- Maternal corticosteroids for immune-mediated heart block
- Antiarrhythmics for fetal arrhythmias
- Avoidance of teratogenic drugs

Follow-up During Pregnancy

Follow-up with fetal echocardiography typically depends on severity:

- Mild lesions: Neonatal evaluation
- Moderate lesions: every 4–6 weeks
- Severe or evolving lesions: every 1–3 weeks

Assessing Progression by Fetal echocardiogram is required for worsening valvular stenosis or regurgitation,ventricular dysfunction/myocardial performance index (MPI), fetal arrhythmias, signs of hydrops and doppler changes (ductus venosus, umbilical artery), Premature constriction of the ductus arteriosus or restriction of the foramen ovale.

Delivery Planning

Timing of Delivery

Most pregnancies should continue to term unless obstetric indications exist. Preterm delivery may worsen outcomes in most CHDs; Elective induction for foetuses with CHD before 39 weeks is not recommended unless there are obstetric issues or evidence of fetus compromise.

Place of Delivery

Delivery planning depends on defect severity:

- Primary/Secondary Centres: mild or isolated defects (e.g., small VSD, mild pulmonary stenosis,TR, primum ASD etc.)
- Tertiary Neonatal and Cardiac Centre: defects likely requiring immediate postnatal assessment or intervention (e.g., all cyanotic CHD like TGA, HLHS, TAPVC etc., duct Dependent lesions like arch anomalies and pulmonary atresia/ critical stenosis and all types of fetal arrhythmia)

Mode of Delivery

Vaginal delivery is safe in most cases. Caesarean delivery is reserved for obstetric indications or defects with unstable fetal hemodynamics requiring controlled timing.

Delivery Room Preparedness

Neonatal team must be briefed about anticipated resuscitation needs, prostaglandin E1 infusion, early postnatal echocardiography, and potential need for mechanical ventilation.

Neonatal Management Pathway

Immediate Postnatal Steps

- Clinical evaluation for cyanosis, respiratory effort, shock
- Pulse oximetry screening
- Echocardiography for confirmation
- Prepare prostaglandin E1 for duct-dependent lesions
- Early referral to pediatric cardiology

Prognosis

With modern surgical techniques, survival for CHDs has significantly improved; children with mild to moderate defects like VSD have near-normal long-term outcomes. High-risk groups with guarded outcomes typically include single-ventricle physiology, fetal hydrops, and those having associated syndromes.

The short term data, collected at Pediatric Cardiology unit, Sir Gangaram Hospital,Delhi from 2011- 2020 where fetus diagnosed with CHD were followed up; shows good short-term outcomes.

Parameters	Numbers (%)	Comments
Total	14561	
Normal	14020 (96.3 %)	Includes intracardiac echogenic focus and persistent left SVC
Abnormal	541 (3.7 %)	

Fetal CHD	Cases (n)	Medical termination of pregnancy (n)	Intrauterine death (n)	Neonatal follow up (available)	Outcome/follow up
Small Ventricular septal Defect (VSD)	105	0	0	72	VSD not found at birth - 30 Small VSD at birth - 40 surgical repair in childhood = 2 (no mortality)
Moderate to large VSD	26	0	0	20	16 pts advised surgical repair in infantile period and 4 pts were advised only medical follow up as VSD had reduced in size; (surgical repair in 13 pts)-no mortality; 3/16 pts lost to follow up
Tetralogy of Fallot(TOF)	21	03	0	12	Surgical repair (n=12)- no mortality
Double outlet right ventricle (DORV)	09	04	0	05	Complete repair (n=03)-no mortality Multistage repair in 02 pts (1 mortality)
TOF with Absent pulmonary valve	05	01	0	04	Surgical repair (n=4) - no mortality
Pulmonary atresia with or without VSD	07	03	0	04	03 pts underwent surgical repair –(multistage) BT shunt and followed by complete repair (01 mortality)
AV canal defect	10	07 (Trisomy 21 related)	0	03 (normal karyotype)	All 3 pts underwent surgical repair (no mortality)
Isolated mild TR (2nd or 3rd trimester)	110	0	0	86	All 86 pts - normalized
Pulmonary stenosis	11	0	0	07	6 underwent successful Balloon dilatation at birth one pt. had mild PS–on medical follow up
Aortic stenosis	02	0	0	01	Underwent successful Balloon dilatation at birth
Transposition of great artery (TGA) with intact ventricular septum	07	0	0	06	All 6 pts had neonatal surgery -no mortalit
TGA with VSD	03	0	0	03	All 3 pts had Surgery -no mortality
TGA.VSD and Arch anomaly	03	1	0	02	two staged surgery (n=2) -no mortality
Total anomalous pulmonary venous connection (TAPVC)- unobstructed	03	0	0	03	All 3 had surgical repair - no mortality
TAPVC - obstructed	03	0	0	03	All 3 had surgical repair - no mortality

Coarctation of aorta	11	0	0	09	All 9 pts had neonatal surgical repair- no mortality
Arch interruption with VSD	03	02	0	01	underwent successful surgical repair
Vascular ring	02	01	0	01	underwent successful surgical repair
Isolated right aortic arch	05	01	0	04	No surgery /normal neonate
Aberrant right subclavian artery(ARSA)	09	01	0	08	No surgery /normal neonate
Truncus arteriosus	05	04	0	01	underwent successful surgical repair- future conduit replacements required
Ebstein anomaly	05	03	0	02	Both pts underwent successful surgical repair
Single ventricle anomalies like Tricuspid atresia,non-routable DORV, Double inlet left ventricle	15	06	0	09	Multistage surgery (n=07) Mortality –nil Parents refused surgery (n=02)
Hypoplastic left heart syndrome	15	13	0	02	Parents refused surgery (n=2)
Miscellaneous complex anomalies like situs ambiguous, unbalanced AVCD etc.	16	10	1	05	Palliative surgery (n=03) Mortality -nil Parents refused surgery(n=02)
Rhabdomyoma	05	0	0	03	Normalized / decreased in size in all cases
Intracardiac calcifications – septa,aortic root, pulm root	02	2	0	0	Maternal SLE confirmed and family decided not to continue
Tachyarrhythmia like AF/SVT	09	0	1	08	Controlled with medications – stable (n=8)
Complete Heart Block	24	09	01	14	Permanent pacemaker (n=14) - no mortality
Prolonged PR (SLE mother)	05	0	0	05	Controlled with steroids and HCQS (n=4) one pt. needed Permanent pacemaker due to CHB
Atrial ectopic	35	0	0	35	30 pts resolved in fetal life and 5 normalized during neonatal period
Long QT syndrome with fetal bradycardia	02	0	0	02	Stable on medical follow up

Recurrence Risk in Subsequent Pregnancy

General recurrence risk ~3–5%, higher if one parent has CHD or child has syndrome. Risk increase to as high as 10% if both parents had CHD or one parent with one sibling had CHD. Preconception counselling and starting Folic acid 3 months preconception is advisable.

Checklist for obstetric team

- Confirm fetal CHD with expert imaging; assess for additional anomalies
- Initiate genetic counselling/testing as indicated
- Convene a multidisciplinary obstetric–fetal cardiology-neonatology planning meeting and establish a care plan including delivery options
- Engage families in counselling; discuss prognosis, options, and interventions
- Arrange postnatal coordination with pediatric cardiology and neonatology team

Brief analysis of commonly encountered benign fetal cardiac conditions

Anomalous origin of right subclavian artery (arsa)

ARSA is a benign vascular aortic arch anomaly where right subclavian artery arises from left sided aortic arch distal to left subclavian artery. It courses posterior to trachea and esophagus best seen on three vessel trachea view.

Isolated ARSA with no other risk factors or extracardiac anomaly does not need any screening for aneuploidy. Association with Trisomy 21 and 22q11 deletion are rare.

Postnatally babies with isolated ARSA are mostly asymptomatic and no intervention required in majority of cases. Very few cases need to be referred for surgery for compressive symptoms.

Isolated right aortic arch(raa) with mirror image branching neck vessels

Right aortic arch is a benign and commonest aortic arch anomaly where aortic arch courses to right of trachea instead of left.RAA with right ductus arteriosus usually does not form vascular ring.

RAA with left ductus arteriosus usually forms incomplete vascular ring. As ductus arteriosus regresses after birth, it does not cause any compression symptoms(stridor/dysphagia) after birth. RAA with left ductus arteriosus is often mistaken as double aortic arch. Hence detailed scan by fetal and pediatric cardiology expert is a must to differentiate between two.

Isolated RAA is benign condition and does not need further evaluation. 22q11 deletion is seen in approximately 10 % of cases of RAA with no intracardiac anomaly, hence it is advisable to have genetic opinion in such cases.

Persistent Left SVC

Most common venous anomaly detected in fetal life due to non-regression of left cardinal vein. It is seen as extra vessel on left of main pulmonary artery in three vessel view. Dilated coronary sinus in 4 chamber view also gives a clue for presence of persistent left SVC. It is the common cause responsible for right-left discrepancy in chamber size in second and third trimester of pregnancy.

Persistent left SVC has high association with coarctation of aorta (approximately 20 %) and other congenital heart defects, hence referral for detailed fetal echocardiography is recommended. If persistent left SVC is detected in early trimester, follow up scan should be repeated at 32 weeks of gestation to rule out development of coarctation of aorta. Genetic association with persistent left SVC is rare.

Small Venricular Septal Defect

Isolated small VSDs are hemodynamically insignificant, benign lesions and carry high chances of spontaneous closure either prenatally or postnatally. Isolated small VSD with no extracardiac anomalies; does not need further management and should be reassured. Post-natal echo at 4-6 weeks is advised to assess further course of management.

Intracardiac Echogenic focus (ICEF)

Intracardiac echogenic focus is a small bright hyperechoic spot seen in fetal heart more commonly in left ventricle. It is seen in 3-5 % of normal pregnancies and more so in asians. ICEF represents micro-calcification of papillary muscle/ chordae and does not affect mitral valve or cardiac function. It is a soft marker for Trisomy 21 and in isolation, does not carry any additional risk. IECF is often isolated and with "low-risk triple marker" screening; it does not have any clinical significance. It becomes relevant only when other markers for trisomy 21 are seen on USG or there is high risk triple marker test. Isolated ICEF with structurally normal heart does not need any treatment or follow up with pediatric cardiologist.

Tricuspid Regurgitation (TR)

Isolated Mild tricuspid regurgitation (small jet Vmax<2.5m/s, brief and no chamber dilatation) seen in first and second trimester with normal

cardiac anatomy is often benign finding. It is more commonly seen at 18-22 weeks scan and often resolves on follow up. There is high risk for trisomy 21 only when first trimester mild TR is associated with increase Nuchal translucency, absent nasal bone or abnormal ductus venosus doppler.

Moderate to severe TR (large jet Vmax >2.5m/s and chamber dilatation) needs regular follow up. If it persists beyond 24 weeks, it is likely pathological. One should rule out fetal anemia, fetal arrhythmia or myocarditis when no obvious cause is found.

- Early gestation + trisomy 21 risk factors → TR frequently accompanies chromosomal or major cardiac disease
- Mid to late gestation echo referrals with otherwise normal cardiac anatomy → TR is usually functional, benign and resolves on follow up.

Conclusion

A structured, multidisciplinary approach improves short and long term outcomes in fetus through early detection, comprehensive counselling, multidisciplinary care, and meticulous delivery planning.

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Luteal phase support in an IUI cycle

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Introduction

Luteal phase is the post-ovulatory phase of the menstrual cycle characterized by progesterone secretion from the corpus luteum, which prepares the endometrium for implantation. Luteal phase support (LPS) refers to the administration of progesterone or other agents to optimize endometrial receptivity aiming to improve pregnancy outcomes.

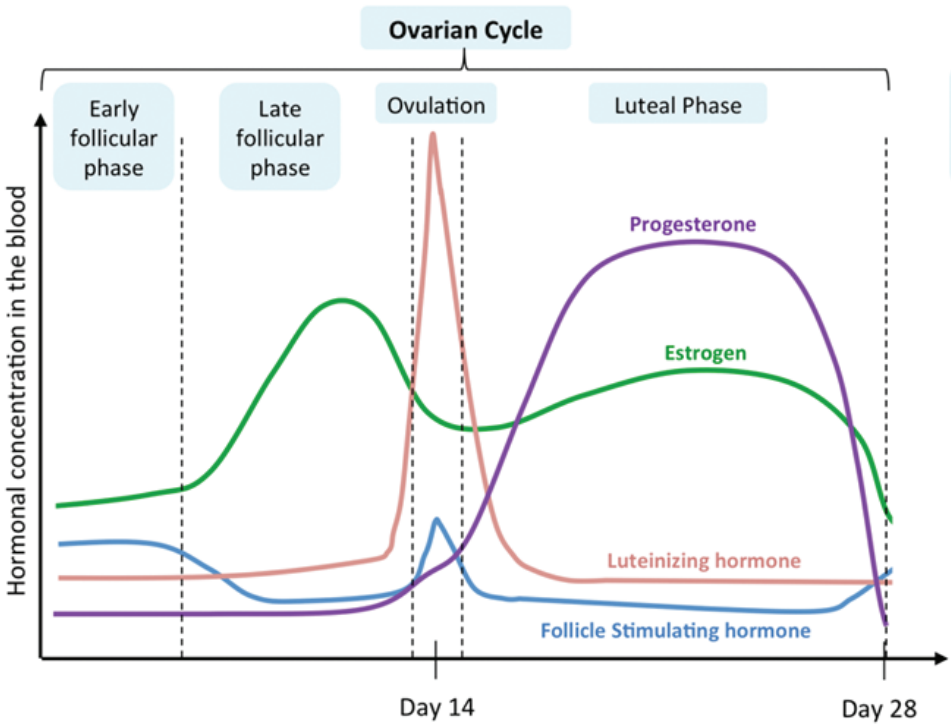
While LPS is well-established in IVF cycles, its role in intrauterine insemination (IUI) cycles remains an area of discussion, particularly in stimulated cycles.

Physiology of the Luteal Phase

After ovulation, luteinized granulosa cells produce progesterone under LH stimulation. Progesterone:

- Converts the proliferative endometrium into a secretory endometrium
- Supports implantation
- Maintains early pregnancy until placental progesterone production begins

Any disruption in progesterone production or LH support can lead to luteal phase insufficiency (LPI).



Physiology of ovulation in a menstrual cycle

Why Luteal Phase May Be Compromised in IUI Cycles

1. Ovarian Stimulation

- Clomiphene citrate: Anti-estrogenic effect → thinner endometrium, altered progesterone feedback
- Gonadotropins: Supraphysiologic estradiol → LH suppression → reduced luteal progesterone.

These mechanisms are likely to exert a greater impact in gonadotropin-stimulated cycles than in cycles using clomiphene citrate (CC), as CC competitively binds hypothalamic estrogen receptors and thereby attenuates the negative feedback of elevated estradiol levels. Nevertheless, mild ovarian stimulation with gonadotropins has been shown to result in higher live birth rates following IUI compared with CC stimulation in couples with unexplained infertility . Addressing a potential luteal phase defect in gonadotropin-stimulated cycles may therefore further enhance the success of OS-IUI treatment.

2. hCG Trigger

- hCG supports corpus luteum initially, but its effect may wane before placental takeover. A single-dose injection of human chorionic gonadotropin (hCG) used to trigger ovulation induces a more potent luteinizing hormone (LH)–like signal than the physiological endogenous LH surge. During the early luteal phase, the corpus luteum is adequately supported by this exogenous stimulus until hCG is gradually cleared from circulation, typically within 5–6 days. In the absence of additional luteal support, progesterone levels tend to decline earlier and more markedly than in a natural cycle. Both an early progesterone peak and subsequent inadequate secretion may result in premature or suboptimal endometrial receptivity, as well as impaired maintenance of endometrial function.

3. Multiple Follicular Development

- Leads to altered hormonal milieu and asynchronous endometrial development.

Indications for Luteal Phase Support in IUI

LPS is recommended in the following situations:

- Stimulated IUI cycles (clomiphene, letrozole, gonadotropins)
- History of luteal phase defect
- Recurrent pregnancy loss
- Thin endometrium
- Use of GnRH analogues
- Unexplained infertility with repeated IUI failures

Natural IUI cycles:

Routine LPS is generally **not required** unless specific risk factors exist.

Agents Used for Luteal Phase Support

1. Progesterone (Mainstay)

Routes of Administration

- Vaginal (preferred)
- Gel, suppositories, tablets
- Dose: 200–400 mg/day (micronized)
- Oral
- Oral Micronized progesterone is less effective due to first-pass metabolism. Dydrogesterone can be administered orally (20 mg divided doses)
- Intramuscular
- Rarely used in IUI due to pain and inconvenience

Advantages of Vaginal Progesterone

- Direct uterine effect (first uterine pass)
- Fewer systemic side effects
- Better patient compliance

2. hCG

- Mimics LH to support corpus luteum
- Not routinely recommended due to risk of OHSS and multiple pregnancy

3. GnRH agonist versus vaginal progesterone

The evidence for the effect of GnRH agonist injection on clinical pregnancy is very uncertain

3. Estrogen Supplementation

- Limited evidence in IUI cycles
- Occasionally used if endometrium is thin

Timing and Duration of LPS

Initiation

- Day of ovulation or day after IUI

Duration:

- Until pregnancy test (14 days post-ovulation)
- If pregnant, continue until 8–10 weeks of gestation

Evidence and Guidelines

At present, there is no clear consensus regarding the routine use of progesterone supplementation following IUI cycles. A 2017 meta-analysis by Green et al. reported that luteal phase support (LPS) may be beneficial in IUI, particularly in mildly stimulated cycles using low-dose FSH as compared to CC or CC with FSH. In this analysis, live birth rates were significantly higher among women receiving exogenous progesterone compared with controls (random-effects model: RR 1.76, 95% CI 1.29–2.40; $p < 0.001$; number needed to treat = 11).

An updated and expanded meta-analysis by Casarramona et al., which included four additional studies beyond those evaluated in the 2017 review, demonstrated similar findings. In single-cycle analyses, progesterone supplementation was associated with a higher live birth rate (RR 2.47, 95% CI 1.37–4.44; three randomised controlled trials [RCTs], 678 participants). Furthermore, cumulative live birth rates across up to six treatment cycles were also improved (RR 1.49, 95% CI 1.17–1.90; five RCTs, 1027 participants). In both reviews, the overall quality of evidence was graded as low to moderate.

Meta-analyses show improved clinical pregnancy rates in stimulated IUI cycles with progesterone support.

- No significant benefit demonstrated in natural IUI cycles.
- Most fertility societies support LPS in stimulated IUI cycles, especially with gonadotropins.

The first prospective randomized controlled trial (RCT) evaluating luteal phase support (LPS) in OS-IUI cycles was published by Erdem et al. in 2009 . In rFSH-stimulated IUI cycles for unexplained infertility, vaginal progesterone significantly improved clinical pregnancy rates (CPR) and live birth rates (LBR) per cycle and per patient, without increasing multiple pregnancy rates (MPR).

Two subsequent meta-analyses (20,21), including five RCTs (19,22–25), confirmed significantly higher CPR and LBR with LPS, with benefits restricted to gonadotropin-stimulated cycles. No differences were observed in MPR or miscarriage rates . Vaginal progesterone was used in all trials, although follicle numbers were not reported.

Two later double-blind RCTs from Iran yielded mixed results. Hossein Rashidi et al. found no benefit of vaginal progesterone LPS in COS-IUI cycles using CC and hMG, whereas Khosravi et al. reported comparable outcomes between vaginal progesterone and oral dydrogesterone (20 mg), with higher mid-luteal progesterone levels and lower miscarriage rate in the dydrogesterone group

Study (Author & Year)	Total No. of Patients	No. of Treatment / Control Cycles	Stimulation of Ovulation	Luteal Support, Dosage, Duration	Outcomes
Erdem et al.(19), 2009	214	223/204	rFSH	Vaginal progesterone gel, 90 mg/24 h, once daily, until 12th wk.	CPR, BPR, LBR, MPR, MR
Kyrou et al.(22), 2010	468	196/204	Clomiphene citrate	Vaginal progesterone suppositories, 200 mg/8 h, until 7th wk.	CPR, BPR, MPR, MR
Ebrahimi et al.(23), 2010	200	252/259	Clomiphene citrate + hMG	Vaginal progesterone suppositories, 400 mg/24 h, once daily, until 10th wk.	CPR, BPR, LBR, MPR, MR
Maher(24), 2011	71	132/126	rFSH	Vaginal progesterone gel, 90 mg/24 h, once daily, for 14 days.	CPR, BPR, LBR, MPR, MR
Agha-Hosseini et al.(25), 2012	300	148/142	Clomiphene citrate, Clomiphene citrate + hMG, Letrozole, Letrozole + hMG	Vaginal progesterone suppositories, 400 mg/24 h, once daily, until 12th wk.	CPR, BPR, MPR, MR
Hossein Rashidi et al.(26), 2014	253	NA	Clomiphene citrate + hMG	Vaginal progesterone suppositories, 400 mg/12 h, twice daily, until 8th wk.	CPR, BPR, MR
Khosravi et al.(27), 2015*	150	NA	Clomiphene citrate + rFSH	Vaginal progesterone suppositories, 400 mg/24 h, once daily.	CPR, MR

Study (Author & Year)	BPR (%) (p)	CPR (%) (p)	LBR (%) (p)
Erdem et al.(19), 2009	25.1%-13.7% (0.002)	21.2%-12.7% (0.028)	17.4%-9.3% (0.016)
Kyrou et al.(22), 2010	-	7.3%-8.7% (NS)	-
Ebrahimi et al.(23), 2010	13.5%-11.2% (NS)	11.5%-10% (NS)	7.5%-5.7% (NS)
Maher(24), 2011	37.1%-20.6% (0.004)	29.5%-19.8% (0.07)	18.9%-5.5% (<0.001)
Agha-Hosseini et al.(25), 2012	29%-21.8% (NS)	24.3%-14.1% (0.02)	-
Hossein Rashidi et al.(26), 2014	30.8%-22.2% (NS)	15.8%-12.7% (NS)	-
Khosravi et al.(27), 2015*	-	25.7%-29.7% (NS)	-

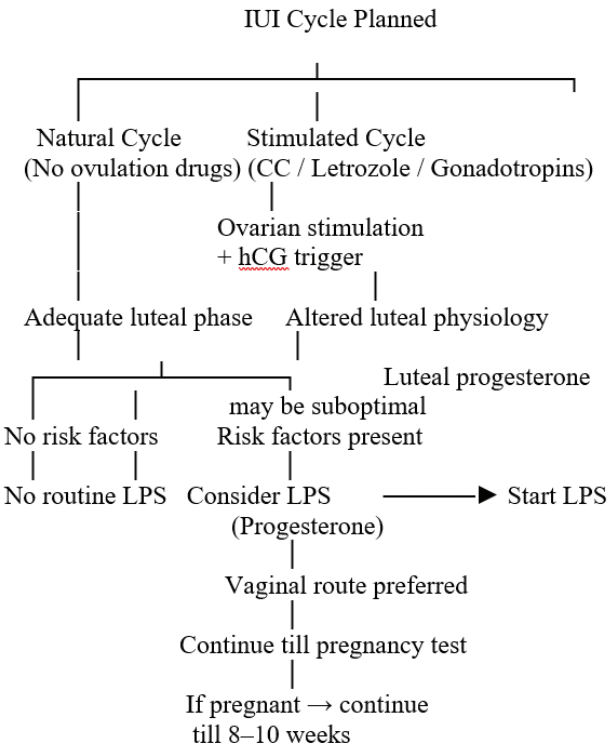
Side Effects of Progesterone

- Vaginal discharge
- Breast tenderness
- Bloating
- Mild drowsiness (oral)

Overall, progesterone is safe and well tolerated.

Key Take-Home Messages

- LPS is beneficial in stimulated IUI cycles
- Progesterone is the agent of choice
- Vaginal route is preferred
- Not mandatory in natural IUI cycles
- Individualization based on stimulation protocol is essential



Key Practice Points (Flowchart Summary)

- Natural IUI cycles → LPS not routinely required
- Stimulated IUI cycles → LPS recommended
- Progesterone is first-line
- Vaginal route preferred
- Individualize based on patient risk factors

Conclusion

Current evidence suggests that luteal phase support (LPS) may improve pregnancy outcomes in IUI cycles, particularly in gonadotropin-stimulated or mild ovarian stimulation protocols. Progesterone supplementation appears to increase clinical pregnancy and live birth rates without significant adverse effects. However, benefits are less consistent in natural or clomiphene-only cycles. Given the heterogeneity of available studies, routine use of LPS in all IUI cycles cannot be universally recommended, and treatment should be individualized based on stimulation protocol and patient characteristics.

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Mental Health Issues For The Health Care professional

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"It is said that when ambition overtakes performance, the gap is called frustration but if performer overtakes ambition it is called success".

Health systems are experiencing increasing pressure with many doctors & nurses reporting poor mental health and working conditions. These challenges are contributing to burnout and professionals leaving the workplace. The well being of doctors and nurses is critical to the future of health system. Protecting their mental health risk is a moral obligation.

In India more than one million doctors are there. Every year more than 80,000 medical students graduate as doctors from 529 medical colleges. Medical profession is considered as more stressful but mental health is still a subject of taken in medical profession. The new medical curriculum has not incorporated single skill in Psychiatry as mandatory in examination for M.B.B.S Students to become doctors in India. This adversely affects mental health awareness among budding doctors.

Many individual factors result in adverse effects associated with reduced workplace productivity and efficiency, reduced practice revenue and greater probability of ordering unnecessary tests or procedure leading to patient burden. So burnout is a widespread cancer among medical profession.

Burnout is not a symptom but it is a syndrome as a result of ongoing emotional demands associated with this occupation. Burnout is included in international classification of diseases - 11th revision as an occupational phenomenon. It is not a classified medical condition.

The difference between stress and burnout is that stress may kill you prematurely when as burnout may make life seem not worth living.

Work related causes of burnout are :

- Feeling like you have little or no control over you work.
- Lack of recognition or rewards for good work.
- Unclear or overly demanding job expectation.
- Doing work that is monotonous or unchallenging.
- Working in an unrecognised or high pressure environment.

Sometimes lifestyle causes also add to burnout

- Working too much without enough time for relaxing & socializing.
- Being expected to do too many things to too many people
- Taking too many responsibilities
- Lack of enough sleep and lack of close supportive relationships.

Personality traits :

- Perfectionist tendencies
- Passimistic of yourself & world
- Need to be in control
- Type A personality

In a survey from portal regional referal hospital prevalence of burnout among healthcare professionals (Published on 06/05/2024) : -

Among Doctors	High Burnout 25% Low Burnout 75%
Among Nurses	High Burnout 6% Low Burnout 25% Moderate 69%
Among allied health professionals	High Burnout 9% Low Burnout 18% Moderate Burnout 73%

Low burnout was seen in all females between 40-49 years. Moderate Burnout 37.5%, 40-49 years whereas in 30-39 years it was 62.5%.

Possible causes of Burnout

- Unbalanced duty allocation 38.7%
- Physical exhausting work 35.5%
- Emotional exhaustion 32.3%
- Getting blamed for other's mistake 35.5%
- Nothing to do for a patient 50.1%

Burnout by specialities:

- Emergency medicine 68%
- General internal medicine 55%
- Obstetrics & Gynaecology 52%
- General Surgery 42%
- Dermatology 30%

Times of India newspaper dated 24th Feb 2024 reported 122 medical student suicides & 1270 dropouts in past 5 years according to National Medical Council.

Consequences of Physician Burnout

- Medical errors
- Impaired professionalism
- Reduced patient satisfaction
- Depression and suicidal ideation
- Anxiety disorder
- Motor vehicle crashes and near-misses

Prevention Strategies against Burnout among Doctors

- Modifying the organizational structure and work processes.
- Improving the satisfaction between the organization and the individual doctor so that better adaption to the work environment occurs.
- Individual-level actions to reduce stress and poor health symptoms through effective coping and promoting healthy behaviors.

Coping with Job Burnout

Dealing with Job Stress

- In order to avoid job burnout, it is important to reduce and manage stress at work. Start by identifying what factors are stressful. Then you can take steps to deal with the problem either by changing your work environment or changing the way you deal with the stressor.

Actively address problems

- Take a proactive approach - rather than a passive one to issues in your workplace. You'll feel less helpless if you assert yourself and express your needs. If you don't have the authority or resources to solve the problem, talk to a superior.
- In a developing country India with enormous population, huge expectations from medical professionals day to day stress borne by Obst & Gynae is never considered and their concerns take a back seat.
- Most common triggers of work place are long duty hours, over worked, inadequately skilled support staffs, scarcity of resources, no supportive colleagues and unfavorable events.
- Indirect factors contribute like:
  - Keeping oneself calm under all circumstances
  - Maintaining interaction with patient and relative
  - External factors like family, children, financial issues.

Burnout Prevention Tips

- Start the day with a relaxing ritual jumping out of bed as soon as you wake up, spend at least fifteen minutes meditating, writing in your journal, doing gentle stretches, or reading something that inspires you.
- Adopt healthy eating, exercising, and sleeping habits. When you eat right, engage in regular physical activity, and get plenty of rest, you have the energy and resilience to deal with life's hassles and demands.
- Set boundaries. Don't overextend yourself. Learn how to say - no to requests on your time. If you find this difficult, remind yourself that saying - no allows you to say yes to the things that you truly want to do.

- Take a daily break from technology. Set a time each day when you completely disconnect. Put away your laptop, turn off your phone, and stop checking email.
- Nourish your creative side. Creativity is a powerful antidote to burnout. Try something new, start a fun project, or resume a favorite hobby. Choose activities that have nothing to do with work.
- Learn how to manage stress. When you're on the road to burnout, you may feel helpless. But you have a lot more control over stress than you may think. Learning how to manage stress can help you regain your balance.

Coping with Job Burnout

Clarify your job description.

- Ask your boss for an updated description of your job duties and responsibilities. Point out things you're expected to do that are not part of your job description and gain a little leverage by showing that you've been putting in work over and above the parameters of your job.

Take time off.

- If burnout seems inevitable, take a complete break from work. Go on vacation, use up your sick days, ask for a temporary leave of- absence - anything to remove yourself from the situation. Use the time away to recharge your batteries and take perspective.

Relaxation Response

- Step 1: Calming focus- small prayer or breath in and out
- Step 2: Let go relax – Meditation, Yoga, religious prayer

  It courses physiological shifts on the body just opposite of the stress response

Work Place Stress In Obstetric & Gynaecology in India

- Stress word is derived from Latin word stringer which means starvation, string, pain and physical hardship.
- Most stressful type of work is that which value excessive demands and pressure that are not matched to workers knowledge and abilities.
- In a Dutch study of Obst & Gynae out of 683 participants 12.6% experienced work related traumatic event with an estimated prevalence of 1.5%.
- It is estimated that 40-75% obgy currently suffer from professional burnout, making the lifetime risk a virtual certainty.

Stress Related Symptoms

Cognitive	Emotional	Physical	Behavioral
Memory	Short tempered	Pain, diarrhea	Sleep deprivation
Concentration problem	Labile	Constipation, tachycardia	Eating disorder, drug abuse

De Stress Guide

1	**Chalk down common stressors**
	Getting up late
	Unsure to regain OPD /OT on time
	Unsure of abilities
	Overworked, burned out
	Tense, pessimistic
2	**Mini relaxation technique**
	Breath focus
	Body image
	Yoga
	Meditation
3	**Use of mindfulness to reduce work stress**
4	**Power of mind**
5	**Feel grateful**

In a study from Rohtak by M. Chauhan et al. 2024 the primary stressors faced by obgy residents brief COPE assessment showed :-

Relationship Status of Residents	
Age in Years	N=45
20 – 25 years	18 (40%)
26 – 30 years	25 (62.5%)
30 – 35 years	2 (4.44%)
>35 years	0
Age distribution of residents of Obstetrics & Gynaecology	

Obstetrics & Gynaecology residents who pursued or did not pursue their hobbies

	n = 45
Residents who pursued their hobbies	5
Residents who did not/ could not pursue their hobbies	40

The reason behind stress experienced by residents of Obstetrics & Gynaecology

Reason of stross	**n=45**
Too much poperwork	42 (93.33%)
Long working hours	37 (82.22%)
Less time for friends and family	22 (48.88%)
New learnings of subject	31 (68.88%)
Expectation to perform well in clinics	38 (84.44%)
Experiencing complication of birth, death of a patient	40 (88.89%)
Others	2. (4.44%)

Coping techniques for stress among the obstetrics & gynaecological residents

	n = 45
Talk with friends/family/partner	45 (100%)
Usten to music/movies	37 (82.22%)
Login to social media	42 (93.33%)
Exercise	15 (33.33%)
Eat junk food	29 (64.44%)
Sleep or relax	30 (66.66%)
Shopping (Offline or Online)	39 (86.66%)
Substance Abuse	0
Others	6 (13.33%)

Distribution of Obstetrics & Gynaecology residents having colloquial or clinical depression

	n = 45
Residents with colloquial depression	10 (22.22%)
Residents with clinical depression	0

In a study done on 41 DNB students at Sir Ganga Ram Hospital Psychiatry department showed

(Two assessments were conducted – within the first 2 months of training, and again at 8±1 months).

- Exhaustion remained consistently high throughout the year.
- Modest downwards shift was observed showing nearly half continued to experience alienation from work.
- Married and Muslim showed a general downwards trend in stress and burnout, suggesting a protective effect of social/family structures.
- Unmarried and Hindu residents displayed rising scores, as above buffers were missing.
- Higher burnout was seen due to financial stress and family psychiatric history.
- Surgical resident experienced rising burnout over time.

National mental health program (NMHP) was launched in 1982 in India and in 1996 district mental health program (community level) was originated. In 2017 mental health care act to provide for mental health care and services for persons with mental illness and to protect from related matters.

WHO / Europe launches first of its kind survey on mental health of health care professionals.

This underscores burnout as a systemic and clinically significant challenge, demanding institutional attention and preventive strategies rather than expecting natural resolution.

JOURNAL SCAN

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Mid-trimester patch repair of a large cesarean scar dehiscence in an incarcerated gravid uterus with successful pregnancy outcome – A case report and review of literature

Int J Gynaecol Obstet. 2025 Dec;171(3):1075-1080. doi: 10.1002/ijgo.70296. Epub 2025 Jun 10.

Background

Cesarean scar dehiscence during an ongoing pregnancy is rare but potentially catastrophic, especially when associated with uterine incarceration. There is limited guidance on optimal management, particularly in mid-trimester when continuation of pregnancy is desired. This report describes surgical repair using a patch technique with a favorable maternal and fetal outcome.

Case Summary

A pregnant woman in the mid-trimester with a history of prior cesarean delivery presented with pain and was diagnosed with a large cesarean scar dehiscence in an incarcerated retroverted gravid uterus. Imaging confirmed thinning and defect at the previous scar site with risk of rupture. Given ongoing viable pregnancy and risk of catastrophic rupture, a decision for surgical repair was made.

Intervention

The patient underwent laparotomy. After careful release of the incarcerated uterus, a large anterior uterine wall defect at the cesarean scar was identified. The defect was repaired using a 15 × 15-cm polyvinylidene fluoride patch (DynaMesh) to restore uterine integrity and reduce tension. Hemostasis was secured and the pregnancy was preserved.

Outcome

Postoperative recovery was uneventful. The pregnancy progressed without major complications till 34+5 weeks, and the patient ultimately delivered a healthy baby boy by planned cesarean section.

Discussion

Uterine incarceration with cesarean scar dehiscence in pregnancy is a rare but potentially life-threatening condition with risk of progressive scar stretching and catastrophic uterine rupture. Normally, a retroflexed uterus ascends by 14–16 weeks; however, when the fundus remains trapped in the pouch of Douglas, ongoing enlargement directs mechanical stress toward the weakest area—the dehiscent scar. Diagnosis is often challenging because the elongated cervix obscures the anterior uterine wall, and the dehiscent area may resemble a "new fundus." Urinary complaints are the most common presentation, although some women remain asymptomatic.

Management remains controversial due to the rarity of the condition. Early repositioning maneuvers may be attempted before 20 weeks, but later in pregnancy these are often unsuccessful and may cause complications, necessitating close surveillance for preterm labor,

membrane rupture, and fetal growth restriction. The distinction between uterine rupture and dehiscence is important, as dehiscence represents incomplete disruption with intact serosa, yet may progress to rupture in high-risk settings such as incarceration.

Review of available literature enlisted 14 cases till 2014 that underwent surgical repair of uterine defects during the second and third trimesters—using single, double, or triple-layer suturing, sometimes reinforced with mesh or patch—can prolong pregnancy with favorable fetal outcomes. The present case highlights that timely repositioning and reinforced repair may successfully preserve pregnancy in carefully selected patients.

Conclusion

Repair of uterine dehiscence/rupture during an ongoing pre-viable pregnancy is feasible and may allow continuation of pregnancy with good outcomes. Early recognition, individualized surgical management, and close surveillance are essential, though standardized guidelines are lacking due to rarity.

QUIZ TIME

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1. Pregnancy after renal transplant is safest when conception occurs:
   A. Within 3 months of transplant
   B. 6 months after transplant
   C. After 1–2 years with stable graft function
   D. After 5 years only
2. Which immunosuppressant is contraindicated in pregnancy?
   A. Tacrolimus
   B. Azathioprine
   C. Mycophenolate mofetil
   D. Prednisolone
3. The primary defect in hypogonadotropic hypogonadism is:
   A. Ovarian failure
   B. Pituitary/ hypothalamic deficiency of GnRH or gonadotropins
   C. Hyperprolactinemia only
   D. Endometrial resistance
4. First-line fertility treatment in women with hypogonadotropic hypogonadism:
   A. Clomiphene citrate
   B. Pulsatile GnRH or gonadotropin therapy
   C. Letrozole only
   D. Progesterone therapy
5. Main purpose of luteal phase support:
   A. Induce ovulation
   B. Improve follicular growth
   C. Support endometrial receptivity and implantation
   D. Prevent OHSS
6. Gender identity refers to:
   A. Biological sex at birth
   B. Sexual orientation
   C. Internal sense of being male, female, both or neither
   D. External genitalia
7. Gender dysphoria is:
   A. Psychotic disorder
   B. Distress due to mismatch between assigned sex and gender identity
   C. Personality disorder
   D. Mood disorder only

8. Most common mental health issue among healthcare workers:
   A. Schizophrenia
   B. Burnout syndrome
   C. Bipolar disorder
   D. Substance intoxication only

9. Key preventive strategy for burnout:
   A. Increased work hours
   B. Ignoring stress
   C. Work-life balance and institutional support
   D. Social isolation

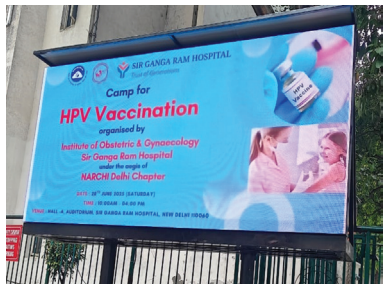
10. Valproate use in pregnancy is associated with:
   A. Neural tube defects
   B. Cleft palate only
   C. Renal agenesis
   D. No fetal risk

Answer : 1. C 2. C 3. B 4. B 5. C 6. C 7. B 8. B 9. C 10. A

Activities Under NARCHI

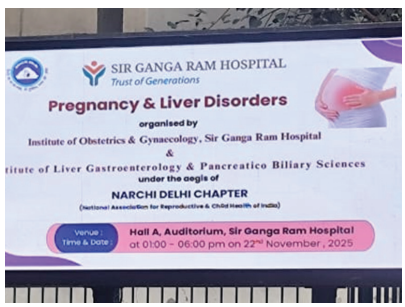
Camp Held on 1st November 2025

- "Public Awareness & Camp for HPV Vaccination" on 1st November 2025 under the aegis of NARCHI Delhi Chapter organized by Institute of Obstetrics & Gynaecology, Sir Ganga Ram Hospital.
- Free HPV vaccines were given to more than 95 girls less than 26 years of age.
- We were blessed by our chief guests Dr. Jayashree Sood, Guest of Honor Dr. Kanwal Gujral, Dr. Geeta Mediratta. Dr. Mala Srivastava, Dr. Chandra Mansukhani & Dr. Kanika Jain. About 150 delegates participated in this camp. This endeavor was highly appreciated and requests came for more such activities in future.



CME on "Pregnancy & Liver Disorder" Held on 22nd Nov, 2025

- NARCHI Delhi chapter organized CME on Pregnancy & Liver Disorder on 22nd Nov 2025 at Sir Ganga Ram Hospital, New Delhi.
- We were lucky to have star speakers who enlightened us on topics of "Pregnancy in Liver Transplant Recipient" by Dr. Parveen Sharma", "Portal Hypertension & Pregnancy" by Dr. Monika Jain" & "Liver SOL & Pregnancy : Special Consideration" by Dr. Anurag Yadav.



- Case based Panel Discussion on "Liver Disorder Specific to Pregnancy" under expert guidance of Dr. Harsha Khullar & Dr. S. Shingvi, moderated by Dr. Geeta Mediratta & panelists were Dr. Kanika Chopra, Dr. Sheeba Marwah, Dr. Sakshi Nayar, Dr. Sandeep Bhagat & Dr. Renu Chawla. Case based Panel Discussion on "Viral Hepatitis in Pregnancy" under expert guidance of Dr. Achla Batra & Dr. Ushat Dhir, moderated by – Dr. Anil Arora & panelists were Dr. Parveen Sharma, Dr. Sharmistha Garg, Dr. Sumita Mehta, Dr. Ashmita Jawa & Dr. Neeti Tiwari. Case based Panel Discussion on "Gall Stones in Pregnancy" under expert guidance of Dr. Manju Puri & Dr. S.K. Kalhan, moderated by – Dr. Shrihari

Anikhindi & panelists were Dr. Geetha Balsarkar, Dr. Deepa Gupta, Dr. Rekha Bharti, Dr. Mukund Khetan & Dr. Naresh Bansal. Case based Panel Discussion on "IHCP" under expert guidance of Dr. Abha Singh & Dr. S. S. Trivedi, moderated by – Dr. K. Gujral and panelists were Dr. Munish Sachdeva, Dr. Nishtha Jaiswal, Dr. Huma Ali, Dr. Renuka Brijwal & Dr. Purvi Khandelwal.

- The CME was attended by approximately 50 delegates. It was an interactive session with lots of take home messages.

Camp Held on 27th December 2025

- "Public Awareness & Camp for HPV Vaccination" on 27th December 2025 under the aegis of NARCHI Delhi Chapter organized by Institute of Obstetrics & Gynaecology, Sir Ganga Ram Hospital.
- Free HPV vaccines were given to more than 220 girls less than 26 years of age.
- We were blessed by our chief guests Dr. Jayashree Sood, Guest of Honor Dr. Kanwal Gujral, Dr. Geeta Mediratta. Dr. Mala Srivastava, Dr. Chandra Mansukhani & Dr. Kanika Jain. About 150 delegates participated in this camp. This endeavor was highly appreciated and requests came for more such activities in future.

World Cancer Day on 4th February 2026

- "Public Awareness Lectures on World Cancer Day" were organized by Institute of Obstetrics & Gynaecology, Sir Ganga Ram Hospital & Clinical Research Committee of FOGSI on 4th February 2026 under the aegis of NARCHI Delhi Chapter.
- We were blessed to have as chief guests Dr. Jayashree Sood, Guest of Honor Dr. Kanwal Gujral & Dr. Geeta Mediratta, Dr. Mala Srivastava, Dr. Chandra Mansukhani & Dr. Kanika Jain. About 100 delegates participated in this event. This endeavor was highly appreciated and requests came for more such activities in future.
- The speakers were Dr. Deepika Gupta; who spoke on "Prevention of Breast Cancer" & Dr. Purvi Khandelwal who's talk was on "Prevention of Cervical Cancer". Poster competition was organized for the Nursing Students & Staff Nurses on the Topic "Prevention of Cancer in Women". The Judges Dr. Kanwal Gujral & Dr. Harsha Khullar, had a tough time deciding the winners as all the posters were excellent. Prizes were given to winners and others got participating certificates.

World Cancer Day on 4th February 2026

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