

# Unexplained Recurrent Pregnancy Loss: Decoding the Enigma and Exploring Pathways to Hope

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## Abstract

**Introduction:** Unexplained recurrent pregnancy loss (URPL) is a complex and distressing condition defined by the loss of two or more pregnancies before 24 weeks of gestation, without identifiable causes despite comprehensive evaluation. Affecting approximately 1% of reproductive-aged women, URPL poses significant diagnostic and therapeutic challenges.

**Causes & Mechanisms:** Potential contributing factors include genetic anomalies, uterine structural abnormalities, hormonal imbalances, and immune system dysregulation, particularly involving regulatory T cells (Tregs) and natural killer (NK) cells.

**Diagnosis:** Diagnostic approaches encompass genetic testing, hormonal and metabolic screening, immunological assessments, and advanced uterine imaging.

**Management:** Management strategies range from lifestyle modifications and medical interventions to supportive care and emerging immunological treatments.

**Conclusion:** This article provides a detailed overview of the current understanding, diagnostic techniques, and treatment options for URPL, emphasizing the importance of a multidisciplinary approach in improving pregnancy outcomes for affected women.

## 1. Introduction

Recurrent pregnancy loss (RPL) is a distressing condition defined by the loss of two or more pregnancies before 24 weeks of gestation. When no specific cause can be identified after comprehensive evaluation, it is termed unexplained recurrent pregnancy loss (URPL). Despite advances in reproductive medicine, URPL remains a significant challenge, affecting about 1% of reproductive-aged women.

**Potential Causes and Mechanisms**  
**Genetic Factors** Chromosomal abnormalities in embryos are a known cause of pregnancy loss, but in URPL, typical genetic tests often return normal results. Subtle genetic mutations or variations that standard testing may not detect can still play a role.

**Uterine Anomalies**

Structural issues like a septate uterus, fibroids, or polyps can sometimes be identified and corrected, but in URPL, these factors are typically ruled out.

## Hormonal Imbalances

Conditions such as thyroid dysfunction, uncontrolled diabetes, or elevated prolactin levels can disrupt pregnancy, yet many women with URPL have normal hormonal profiles.

## Immune System Dysregulation

Increasing evidence suggests that immune system anomalies significantly contribute to URPL. Regulatory T cells (Tregs), which help maintain immune tolerance to the fetus, are often found in abnormal proportions in women with URPL. Studies indicate both high and low levels of Tregs can adversely affect pregnancy outcomes, highlighting the delicate balance required for a successful pregnancy.

## Diagnostic Approaches

Comprehensive evaluation for URPL typically includes:

- **Genetic Testing:** Both parents might undergo karyotyping to detect chromosomal abnormalities, while products of conception from miscarriage tissue are analyzed for genetic defects.
- **Immunological Assessments:** Tests for antiphospholipid syndrome and other immune markers help identify immune-related causes.
- **Hormonal and Metabolic Screening:** Assessments for thyroid function, glucose metabolism, and other hormonal factors are standard.
- **Uterine Imaging:** Advanced ultrasound or MRI scans evaluate the uterus for structural abnormalities.

## Management and Treatment Options

1. **Lifestyle Modifications:** Addressing factors like smoking, alcohol consumption, obesity, and exposure to environmental toxins can improve overall reproductive health.
2. **Medical Interventions:** Depending on the findings, treatments may include hormonal therapies, anticoagulants for thrombophilic disorders, or immunomodulatory treatments to correct immune imbalances.
3. **Supportive Care:** The "tender love and care" (TLC) approach, involving frequent monitoring and emotional support, has been shown to improve pregnancy outcomes in many cases

[oai\_citation:11,Recurrent Pregnancy Loss > Fact Sheets > Yale Medicine]

(<https://www.yalemedicine.org/conditions/recurrent-pregnancy-loss>) [oai\_citation:12, Recurrent pregnancy loss]([https:// www.eshre.eu/Guidelines-and-Legal/Guidelines/Recurrent-pregnancy-loss](https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Recurrent-pregnancy-loss)).

### Emerging Research and Future Directions

Recent studies are exploring the role of the maternal immune system, specifically Tregs and natural killer (NK) cells, in maintaining pregnancy. Understanding the intricate balance of these cells could lead to targeted therapies for URPL. Additionally, ongoing research into genetic and molecular markers promises to improve diagnostic accuracy and individualized treatment plans

[oai\_citation:13, Frontiers | Overexpression of regulatory T cells in patients with unexplained recurrent pregnancy loss: friend or foe?] (<https://www.frontiersin.org/articles/10.3389/fmed.2023.1244424/full>).

### Conclusion

Unexplained recurrent pregnancy loss remains a complex and multifaceted challenge. While significant progress has been made in understanding its potential causes, much remains to be discovered. A multidisciplinary approach involving geneticists, immunologists, endocrinologists, and reproductive specialists is essential for managing and supporting women experiencing URPL. With ongoing research and advanced medical interventions, the outlook for affected couples continues to improve, offering hope for successful pregnancies in the future.

### References

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