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Recurrent Early Pregnancy Loss

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Recurrent Early Pregnancy Loss

Spontaneous abortion or miscarriage is defined as the involuntary termination of

pregnancy before 20 weeks of gestation (dated from the last menstrual period) or below

a fetal weight of 500 g.

Recurrent Early Pregnancy loss

There is no specific number of miscarriages or firmly established criterion that justifies evaluation for recurrent pregnancy loss or defines the scope of investigation.

Decisions must be individualized and consider the female partner's age, the timing and circumstances surrounding earlier pregnancy losses, elements of the personal and family medical history, and the couple's level of anxiety

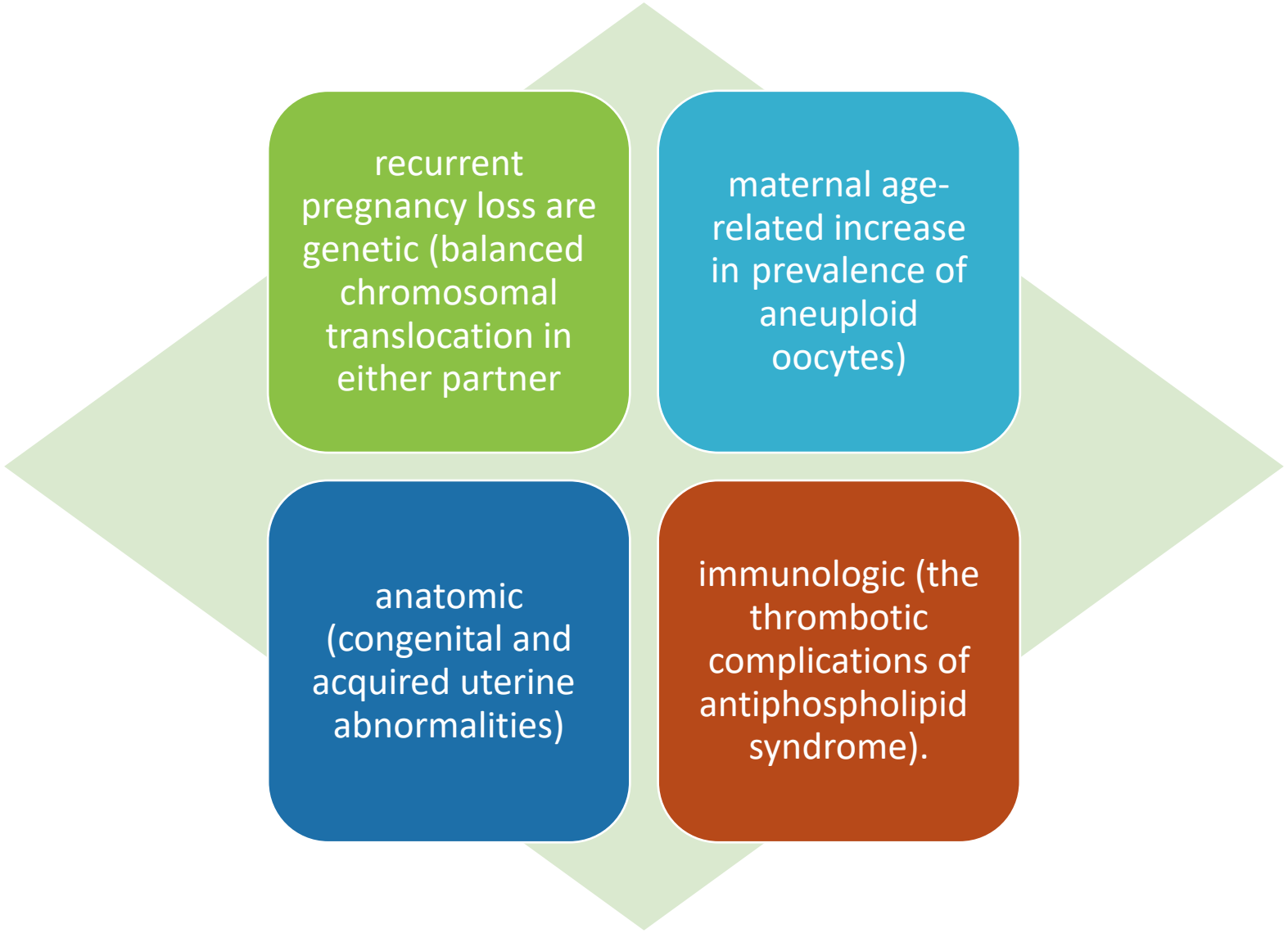
Today, recurrent pregnancy loss is usually defined as three or more pregnancy losses (not necessarily consecutive).

Evolving View (in 2020): Many experts and societies (like ESHRE) considered evaluation after 2 losses, especially in women over 35, to be justified.0

Recurrent Early Pregnancy Loss

- Embryonic heart activity observed before any earlier pregnancy loss.
- Normal karyotype on products of conception from an earlier loss.
- Female partner age over 35 years.
- Infertility.

Recurrent Early Pregnancy Loss



Recurrent Early Pregnancy Loss

Alloimmunopathology, inherited thrombophilias (factor V Leiden andothers)

endocrinopathies (thyroid disorders, diabetes, luteal phase deficiency)

infections (genital mycoplasmas)

environmental exposures (smoking, heavy alcohol, or caffeine consumption) have been implicated but are not established causes of recurrent pregnancy loss.

EPIDEMIOLOGY OF PREGNANCY LOSS

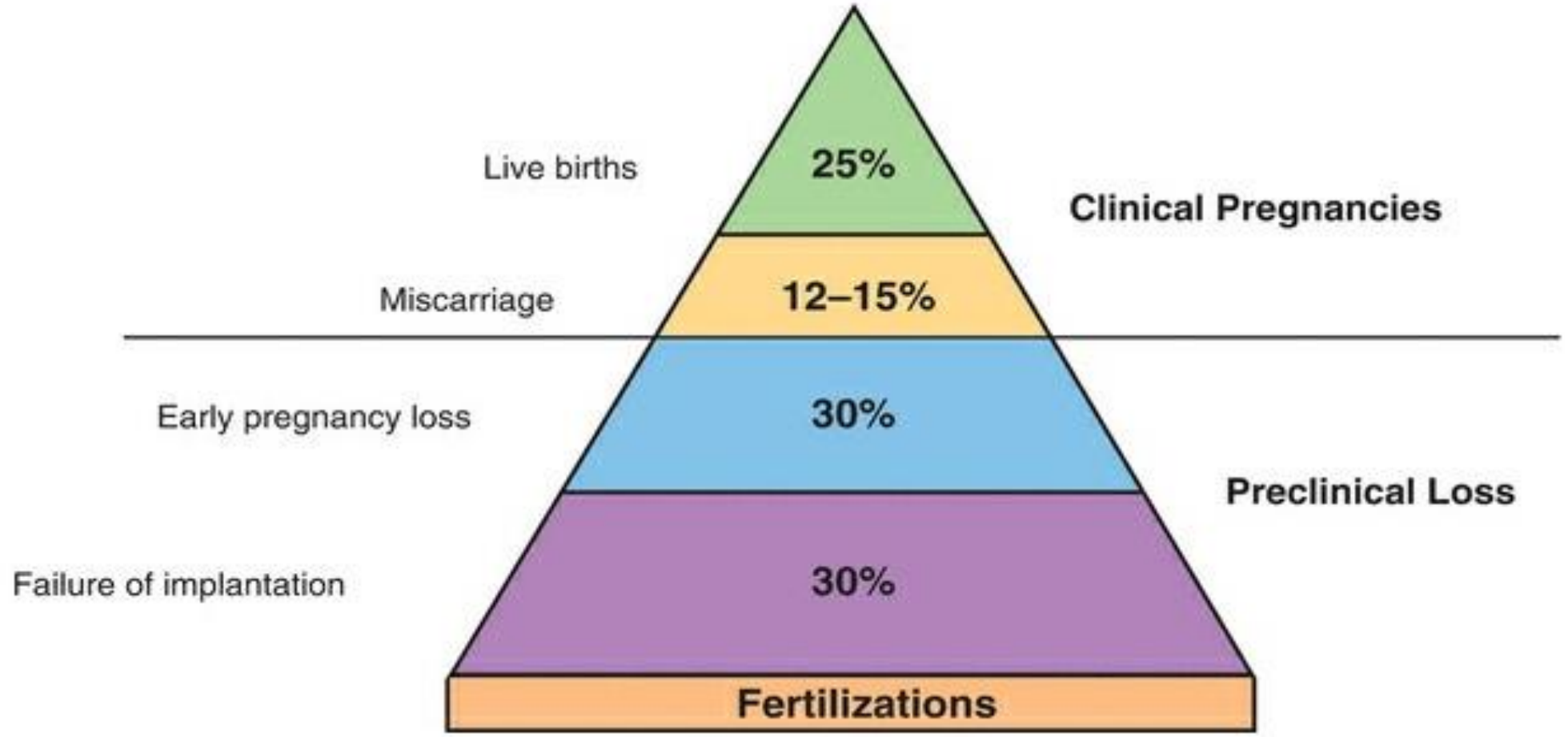


FIGURE 30.1

Recurrent Early Pregnancy Loss/RIF

- In summary, approximately 12–15%of all clinically recognized pregnancies end in miscarriage, but the true incidence of miscarriage, including unrecognized early pregnancy losses, is 2–4 times higher (30–60%).
- Miscarriage risk increases with the number of previous pregnancy losses but rarely exceeds 40–50%.
- Risk for pregnancy loss also rises with increasing maternal age, moderately after age 35

and more rapidly after age 40

Etiologic Category

- **Anatomic Factors:**
- Congenital Uterine Malformations
- Uterine Leiomyomas
- Intrauterine Adhesions (Asherman Syndrome)

- Transvaginal Ultrasound, Sono hysterography, Hystero salpingogram (HSG), Hysteroscopy.
- Focus on congenital (septate uterus) & acquired (Asherman's syndrome, fibroids) issues.
- **Genetic Factors:**
- Parental Karyotyping (both partners) for balanced translocations.
- Products of Conception (POC) Karyotyping/CMA (Chromosomal Microarray) for aneuploidy.

Etiologic Category

- **3. Antiphospholipid Syndrome (APS) :**

Requires two positive tests, 12 weeks apart.

Lupus Anticoagulant (LAC)

Anticardiolipin Antibodies (IgG/IgM)

Anti-β2-glycoprotein I Antibodies (IgG/IgM)

- **4. Endocrine & Metabolic:**

Thyroid Stimulating Hormone (TSH) & Thyroid Peroxidase Antibodies.

Prolactin Level.

HbA1c / Fasting Glucose (for uncontrolled diabetes).

Controversial: Progesterone level / Luteal Phase defect testing.

- **5. Thrombophilias HEREDITARY:**

Factor V Leiden, Prothrombin Gene Mutation, Protein C/S, Anti thrombin III.

Screening was controversial and not universally recommended for RPL alone.

Management strategies

- **Anatomic:** Hysteroscopic septum resection for septate uterus. Myomectomy for submucosal fibroids.
- **Genetic:** Preimplantation Genetic Testing for Aneuploidy (PGT-A) for parental translocations or advanced maternal age. Gamete donation is an option.
- **Antiphospholipid Syndrome (APS):** Combination therapy with Low-Dose Aspirin (LDA) and Prophylactic Heparin/LMWH starting with a positive pregnancy test. Gold standard treatment.

Management strategies

- **Endocrine:** Treat underlying disorders (e.g., Levothyroxine for hypothyroidism, Metformin for PCOS with insulin resistance).

- **Progesterone Supplementation**: Evidence (from the PRISM and PROMISE trials) showed a small but significant benefit in women with early pregnancy bleeding and/or ≥ 3 prior miscarriages.

- **Thrombophilias:** No clear evidence supports anticoagulation for hereditary thrombophilias in RPL. Treatment is typically reserved for APS or a separate VTE histor

Recurrent Early Pregnancy Loss

- INFECTIOUS CAUSES

- Routine serologic testing, cervical cultures, and endometrial biopsy to detect genital infections in women with recurrent pregnancy loss cannot be justified.
- **Evaluation should be limited to women with clinical cervicitis, chronic or recurrent bacterial vaginosis, or other symptoms of pelvic infection**.
- Empiric antibiotic treatment in women suspected of harboring a genital mycoplasma infection is less costly and less complicated than serial cultures.

Recurrent Early Pregnancy Loss

ENVIRONMENTAL FACTORS

Smoking increases the risk of miscarriage and should be discouraged.

Alcohol consumption exceeding two drinks per day and caffeine consumption exceeding 30 mg/day may increase risk for pregnancy loss and are best avoided.

Women who have experienced a miscarriage should be cautioned regarding know environmental toxins.

An increased risk of miscarriage is one more reason to vigorously confront obesity

Recurrent Early Pregnancy Loss

- Unexplained RPL & Supportive Care
- ~50% of cases remain unexplained after a full workup.
- Empirical treatments (IVIG, intra lipids, TNF-alpha blockers, glucocorticoids) are NOT recommended due to lack of evidence and potential harm.
- The cornerstone of management is empathetic, supportive care: Close monitoring, early ultrasounds, and psychological support. The live birth rate in subsequent pregnancies with supportive care alone can be > 60-70%.

Recurrent Early Pregnancy Loss

- Even thorough evaluation will reveal no evidence for a predisposing factor in more than half of all women with recurrent pregnancy loss.
- Under such circumstances, the longer term prognosis for achieving a successful pregnancy is very good.
- Emotional support and careful monitoring during early pregnancy help to improve pregnancy outcomes.
- Empiric treatments with exogenous progesterone or aspirin in women with unexplained recurrent pregnancy loss have no proven value

Category	Evaluation	Treatments
Genetic	**Karyotype, both partners** Ovarian reserve test Comparative genomic hybridization	**Counseling** **Donor gametes where appropriate** Preimplantation genetic diagnosis
Anatomic	**Sonohysterography or HSG** Magnetic resonance imaging IVP or renal ultrasound	**Hysteroscopic septoplasty** **Hysteroscopic myomectomy** **Hysteroscopic adhesiolysis** Abdominal metroplasty Abdominal myomectomy Cervical cerclage
Immunologic	**Lupus anticoagulant** **Anticardiolipin antibody** **Anti–β2-glycoprotein 1 antibody**	**Aspirin and heparin**
Thrombophilias	Factor V Leiden Prothrombin gene mutation Activated protein C resistance Homocysteine Protein C Protein S Antithrombin III	Heparin
Endocrine	**TSH** **Luteal phase duration** Blood glucose, Hgb A1c Prolactin	**Thyroxine** **Clomiphene citrate** **Metformin** **Dopamine agonists**
Infectious	**As indicated by symptoms**	Empiric antibiotics
Environmental	**History**	Behavior modification

Recurrent Early Pregnancy Loss/RIF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