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ASRAJA/RAKTAYONI/PUTRAGHNI YONIVYAPADA W.S.R. TO SPONTANEOUS ABORTIONS UPTO 20 WEEKS OF PREGNANCY

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ABSTRACT
According to *Ayurveda*, spontaneous abortions occur in *Asraja/Raktyoni/Putraghni Yonivyapada*. Spontaneous miscarriage is clinically detectable loss of foetus occurring before 20 weeks of gestation. Recurrent pregnancy loss (RPL) is the occurrence of three or more consecutive spontaneous miscarriages before 20 weeks of gestation. Some however, consider two or more as a standard. *Ayurveda* places great emphasis on prevention and encourage the maintenance of health of women through close attention to balance *Dosha*, performing right deeds, taking proper diet, use of herbs, therapies like *Uttarbasti* etc. Prevention of disease is encouraged among women with history of recurrent abortions by counselling for avoiding misdeeds, tender loving care, proper nutrition etc.

KEYWORDS: *Spontaneous abortions, Recurrent pregnancy loss.*

INTRODUCTION

Asraja/Apraja/Raktyoni/Putraghni are explained as *Yonivyapadas*.

ASRAJA/ RAKTYONI YONIVYAPADA

रक्तपित्तकरैनार्या रक्तं पित्तेन दूषितं |
अतिप्रवर्तते योन्यां लब्धे गर्भेपि सासृजा ||
(च.चि.३०/१६).[1]

According to ***charaka*** due to excessive use of articles capable of aggravating *Rakta* and *Pitta*, the *Rakta* situated in reproductive organs of female gets vitiated by *Pitta*, and then, even after achievement of conception there is excessive bleeding per vagina. This condition is known as ***Asraja*/*Raktyoni.***

"यस्यां लब्धेपि गर्भे असृगतिप्रवर्त्ते, सा तादृशरक्तसृत्या **अप्रजा** भवति;
इयं च रक्त्योनिरुच्यते इति रक्त अति सृत्यैव लभ्यते".....||
(च.चि.३०/१६ की चक्र. टीका).[2]

Acharya Chakrapani has explained the excessive bleeding leads to abortion; thus, the woman remains without a progeny hence, it is also termed as ***Apraja*** (without progeny).

रक्त्योंयाख्या सृगति सुते:
(अ.स.उ. ३८/४५ एवं अ.ह्र.उ.३३/४३).[3,4]

Vagbhata has said excessive bleeding per vaginum is known as ***Rakt-yoni.***

Samprapti (Asraja/Raktyoni)

Pitta Vrdhak Aahar (Ushna, Katu, Vidahi Aahar) Avam Vihar
↓
Yonigata Rakta-Pitta Dushit
↓
Garbh Uplabdhi Ke Baad Bhi Atyadhik Pravratti
(असृजा/रक्तयोनि)

Treatment

1. Predominance or association of specific *Doshas* should be determined on the basis of colour of excreted blood and then haemostatic treatment keeping in mind of vitiated *Dosha* should be given.[5,6,7]
2. *Uttarbasti* with *Ghrita* medicated with the decoction of *Kaashmari* and *Kutaja* should be given.[8,9]
3. *Uttarbasti* with blood of deer, goat, sheep and pig mixed with *Amla* (sour substances or *kaanji*), curd, honey and *Ghrita* should be given.[6]

PUTRAGHNI YONI VYAPADA

रौक्ष्याद वायु यदा गर्भं जातं जातं विनाशयेत, दुष्ट शोणितजं नार्याः पुत्रघ्नी नाम सा मता| (च.चि.३०/२८).[10]

***Charaka* says**

That *Vaayu* aggravated due to predominance of *Ruksha* properties (due to consumption of dry diet and use of *Vaata-Kara* mode of life) in the body, repeatedly destroys the fetuses born from vitiated *Shonita* (abnormalities of *Shonita* produced by *Vaayu*). Though in this condition fetuses of both the sex are destroyed, however, destruction of male fetuses predominates hence the name *Putraghni*.

पुत्रघ्नी-स्थितं स्थितं हन्ति गर्भं पुत्रघ्नी रक्तसंस्रवात् |
चतसृष्वपि चाद्यासु पित्तलिंगोच्छ्रयो ||

(सु.उ.त.३८/१३)

According to *Sushruta*, in this condition, fetuses after attaining stability are repeatedly destroyed due to bleeding besides there are other clinical features of disordered *Pitta*.i.e. Burning Sensation and Heat etc.

A clinical entity characterized by repeated pregnancy loss due to *Artava Dosha* (ovarian and hormonal disorders), *Rakta Dosha* (blood disorders) and due to excessive bleeding.

….जातघ्नी तु यदानिलः| जातं जातं सुतं हन्ति रौक्ष्याद दुष्ट आर्तवो उद्ध्वं ||

(अ.सं.उ.३८/३७ एवं अ.ह्र.उ.३३/३४).[11]

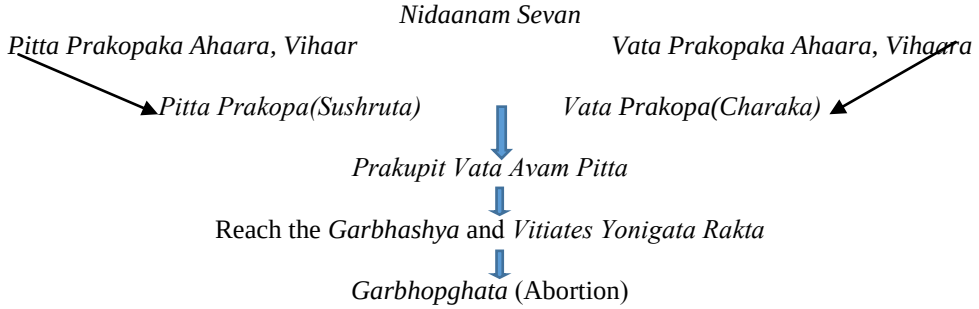
Both *Vagbhattas* opine that when *Vayu* due to dryness kills repeatedly the neonates immediately after birth, which have conceived and developed from vitiated *Artava*, then the entity is known as *Jataghni. Bhaava Prakaasha*[12], *Maadhava Nidaana*[13], *Yoga Ratnaakara*[14] have followed *Sushruta* and have given the cause as loss of *Rakta* or *Artava* due to *Vayu.*

NIDAAN

Table no. 3: *Nidaana* with probable modern co-relation.[15]

***Nidaana* described in texts**	**Modern co-relation**
Rakta Sam-Sraava	Excessive bleeding from female genital tract or due to other causes leading to anemia causing anemia related problems (abortion, I.U.D, I.U.G.R. with pregnancy loss and perinatal loss)
Garbhopaghaatkara Bhaavas* like *Krodha, Raatri-Jaagarana	Emotional imbalance
Dushta Shonita* or *Artav	Abnormalities of ovum leading to genetic and congenital abnormalities
***Dushta Shonita-Sambhoota* (*Dushta Rakta*)**	Rh incompatibility, infections including Toxoplasmosis, Rubella, Cytomegalovirus, Herpes etc. (TORCH), Syphilis or Thyroid deficiencies

Sampraapti: Vitiated *Vata (Charaka)* and *Vitiated Pitta (Sushruta)* destroys fetuses or newborn children.



Roopa- स्थितं स्थितं हन्ति गर्भं (Repeated destruction of fetuses)

रक्तसंस्रवात् (Excessive Bleeding per vaginum)

As *Putraghni* describes about consecutive repeated fetal loss it can be co-related with Habitual abortion.[16]

Treatment

- *Jivaneeya Gana Siddha Dugdha Pana.*
- Use of *Phala Ghrita* regularly(अ.ह्र.उ.३४/६३-६७).
- *Kaashmari* and *Kutaja Kwatha siddha Ghrita Uttarbasti.*[8,9]
- *Mriga, Aja, Avi Varah -Rakta, Dadhi* and *Amala-Phala Rasa Sidddha Ghrita Uttarbasti.*[9]
- *Mriga, Aja, Avi, Varah-Rakta, Dadhi and Amla Phala Rasa Siddha Ghrita Pana.*

In Ayurveda some of *Jaatharini* can be related to spontaneous abortions due to unknown causes. Unknown causes can be attributed to misdeeds and misacts of humans leading to health problems. In order to understand these *Jaatharini* we have to understand the concept of *Jaatharini*.

MODERN REVIEW

Abortion

Definition: According to W.H.O Abortion is the expulsion or extraction from its mother of an embryo or fetus weighing 500 gm or less when it is not capable of independent survival. This 500 gm. of fetal development is attained approximately at 22 weeks (154 days) of gestation. The expelled embryo or fetus is called abortus.[1]

Abortion is classified as spontaneous abortion and induced abortion.

Spontaneous Abortion- The term miscarriage is the recommended terminology for spontaneous abortion. When abortion occurs without medical or mechanical means to empty the uterus, it is referred to as spontaneous abortion.

Incidence: Spontaneous abortion is the most common complication of early pregnancy. The frequency decreases with increasing gestational age. The incidence of spontaneous abortion (miscarriage) in clinically recognized pregnancies up to 20 gestational weeks is 8 to 20%. However, the incidence among women who have previously had a child is much lower (5 percent). The overall risk of spontaneous abortion after 15 weeks is low (0.6 percent) for chromosomally and structurally normal foetuses, but varies according to maternal age and ethinicity.[2]

Mechanism of abortion: 80% of diagnosed abortions occur during the second and third months of pregnancy. Before the 12th week, the conceptus tends to be extruded from the uterus in one mass. After that time, the process more often resembles labour in that the membranes rupture at some stage during the dilation of cervix and the fetus and placenta are then born separately. In either case, the process is not likely to be as smooth as it is in labour at term because the uterus is not properly sensitized and its muscular action is less efficient. Some part of the chorion is therefore often retained and excessive haemorrhage is common.

Aetiology: There are many possible causes for abortion and more than one may operate at a time.

1. Genetic Factors-Majority (50%) of early miscarriages are due to chromosomal abnormality in the conceptus. Autosomal trisomy is commonest (50%) Polyploidy (22% of abortuses), monosomy (20%), structural chromosomal rearrangements (2-4%), other chromosomal abnormality (4%).

2. Anatomical Factors-It includes (a) Cervical incompetence (common cause of mid-trimester abortions and RPL) (b) Congenital malformation of uterus (bicornuate, septate uterus etc.) (c) Uterine fibroid (d) Intra uterine adhesions.

3. Endocrine and metabolic factors-Luteal phase Defect (LPD) results in early miscarriage as implantation and placentation are not supported adequately.

Deficient progesterone secretion from corpus luteum or poor endometrial response to progesterone is the cause.

Thyroid abnormalities -Hypothyroidism or Hyperthyroidism are associated with increased fetal loss. Diabetes Mellitus-in poorly controlled cases increases miscarriage.

4. Infections: (5%) They are the accepted causes of late as well as early abortions. Transplacental fetal infections occur with most micro-organisms. Fetal losses could be caused by any of the micro-organic infections.
(1) Viral: Rubella, Cytomegalo, Variola, Vaccinia or H.I.V.
(2) Parasitic: Toxoplasma, Malaria
(3) Bacteria: Ureaplasma, Chlamydia, Brucella. Spirochetes hardly cause abortion before 20th week because of effective thickness of placental barrier.

5. Immunological disorders: (5 to 10%)

1) Autoimmune Factors-Antinuclear antibodies (ANA's), Anti DNA antibodies, Anti phospholipid antibodies includes Lupus anticoagulant (LAC) Anticardiolipin antibodies(aCL).
2) Allo-immune factors- It is assumed that histoincompatibility particularly in human leucocyte antigen is essential for stimulation of the immune system to produce blocking factors which prevent rejection of the fetus.
3) Anti-fetal antibodies-are deleterious to cause fetal loss as found in cases with Rh-negative women with anti-D antibodies.
4) Maternal medical illness-Cyanotic heart disease, Haemoglobinopathies are associated with early abortion.
5) Blood group incompatibility: Incompatible ABO group mating may be responsible for early pregnancy wastage and often recurrent but Rh incompatibility is a rare cause of death of the fetus before 28th week. Couple with Group A husband and Group O wife have a higher incidence of abortion.[3]
6) Premature rupture of membranes.
7) Environmental Factors-Cigarette smoking increases the risk due to formation of carboxy haemoglobin and decreased oxygen transfer to the fetus. Alcohol consumption should be avoided or minimized during pregnancy. X-ray exposure and antineoplastic drugs are known to cause abortion. Contraceptive devices increase the risk. Drugs, chemicals, noxious agents - anaesthetic gases, arsenic, aniline, lead, formaldehyde increase the risk.
8) Unexplained (40 – 60%).
9) Trauma-External to abdomen or during abdominal or pelvic operations.

Types of Spontaneous Abortions

1) Threatened Miscarriage
2) Inevitable Miscarriage
3) Incomplete Miscarriage
4) Complete Miscarriage
5) Delayed Miscarriage
6) Missed Miscarriage
7) Septic Miscarriage

Types of Spontaneous Abortions

Type	Characterstics
Threatened Miscarriage	It is a clinical entity where the process of miscarriage has started but has not progressed to a state from which recovery is impossible.
Inevitable Miscarriage	It is a clinical type of abortion where the changes have progressed to a state from where continuation of pregnancy is impossible.
Incomplete Miscarriage	When the entire products of conception are not expelled, instead a part of it is left inside the uterine cavity, it is called incomplete miscarriage.
Complete Miscarriage	When the products of conception are expelled all together, it is called complete miscarriage.
Missed Abortion	When the fetus is dead and retained inside the uterus for a variable period, it is called missed mi scarriage or early fetal demise.
Septic Abortion	Any abortion associated with clinical evidences of infection of the uterus and its contents.

RECURRENT MISCARRIAGE/RECURRENT PREGNANCY LOSS/HABITUAL ABORTION

Recurrent miscarriage/Recurrent pregnancy loss/ Habitual abortion has been defined as the "occurrence of three or more clinically detectable consecutive Spontaneous abortion before 20 weeks". Some however consider two or more as a standard.

Recurrent miscarriage of unknown aetiology presents a challenge to the clinician since the psychological impact for affected couples can be profound, with increased depression, anxiety and lowered self-esteem being reported.

A variety of potential therapeutic interventions have been explored, although the evidence base remains equivocal, warranting further research into the pathophysiology of recurrent miscarriage.

An abortion is a personal and emotional loss to a young couple who is planning to start a family. When this problem occurs repeatedly the emotional trauma is compounded manifold. Evaluation for these abnormalities usually begins after two or three miscarriages. Reproductive endocrinologists are specifically trained to evaluate and treat patients with recurrent abortions.

Symptoms: Three main symptoms are

1. Bleeding per vagina
2. Labour pains
3. Premature rupture of membranes

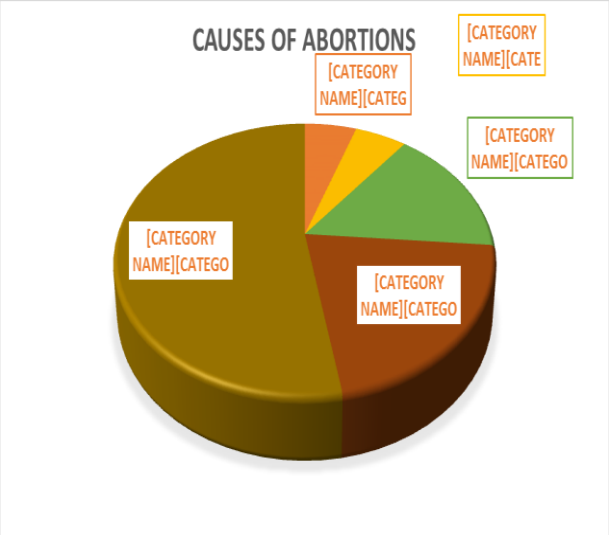
Bleeding may lead to the detachment of the implanted embryo from the uterus. It now acts as a foreign body in the uterus, which stimulates uterine contraction and the conceptus is thrown out.

Preventive measures

Prevention of another miscarriage in a future pregnancy will depend in part on the diagnosis and treatment of any underlying problem. After attaining pregnancy early prenatal care should be scheduled with more frequent prenatal visits and medical advice.

Expected outcome

In about half of the couples, the cause is undetermined, but even without treatment; there is chance of future successful pregnancy. The prognosis of successful pregnancy depends on the cause of the repetitive miscarriages. Multiple factors may be involved in some couples.



Aetiology[4]

1) Genetic Causes - 2-5%
2) Anatomic causes- 10-15%
   - Congenital Uterine malformation
   - Cervical insufficiency
3) Infections-.5-5%
4) Autoimmune /blood clotting- 15-20%
5) Endocrinal Factors- 15-20%
6) Psychological Factors

7) Unknown Causes/Unexplained causes- 40-50%

GENETIC CAUSES (2-5%)
The most common cause of sporadic spontaneous abortion is a chromosomal abnormality of the fetus. More than 60% of first trimester fetal losses show some type of cytogenetic abnormality.

- **Defective germ plasms:** Pathological sperms or oligospermia
- Defective ova

Chromosomal Abnormality

- Sperm chromosomal abnormalities in men with normal karyotype could occur during spermatogenesis.
- Structural chromosomal abnormalities may pass from parent to child; therefore, when a structural anomaly (balanced or unbalanced) is found in a fetus or in an individual, Karyotype analysis of parents and possibly other relatives is indicated.
- Translocations, which occurred at a greater rate than in the general population. These can be diagnosed by cytogenetic study (karyotype analysis) of virtually any tissue type.

ANATOMIC CAUSES (10-15%)
It can be of two types
1. Congenital defects of the uterus
Mullerian fusion defect predisposes women to Habitual Abortion secondary to poor blood supply to the endometrium and placenta. Congenital malformations include Arcuate uterus, Unicornuate uterus, Bicornuate uterus, Septate uterus and Didelphis uterus, Diethylstilbestrol -exposed uterus, a midline uterine depression indicating a Mullerian fusion defect.

The anatomic variants of septum, thick or thin, entirely fibrous or vascular and of variable length from the fundus as well as the site of pregnancy cause either first or second trimester spontaneous abortion or pre-term labour, or may not present a problem.

2. Acquired Defects of Uterus
Myomas-These are benign solid tumors made of fibroid tissue of the uterus. They can be submucosal, intramural or subserosal. Myomas are usually asymptomatic but they have been associated with abnormal uterine bleeding, infertility, recurrent pregnancy loss.

Polyps-Endometrial polyps are benign localized hyperplastic overgrowths of the endometrium that contain both endometrial glands and stroma.[5] It was also suggested that by inducing chronic inflammatory changes in the endometrium, polyps cause the endometrial tissue to be less receptive and hence impair implantation.[6]

Intrauterine Synechiae
Intrauterine synechiae are the intra-uterine adhesions resulted due to previous infections and operative procedures on uterus and constitute an uncommon cause of habitual abortion.

Investigations: Hystero-salpingogram with honeycomb appearance or direct visualization of adhesions in hystero-sonography.

Treatment
Lysis of the intra-cavitary adhesions may be performed under direct vision during hysteroscopy.

INFECTIONS (.5-5%)
1) Occult or subclinical intrauterine infections include Chlamydia, Mycoplasma, Cytomegalovirus, Listeria mono-cytogenes and Toxoplasma gondii.

2) Sexually transmitted diseases (STDs) Active infectious causes of HA are uncommon. Cervical and endometrial cultures and viraltiters should be pursued in the evaluation only after other possible causes have been investigated.

There are several STDs
Gonorrhoea and syphilis are particularly important because of their high prevalence and are well-recognized causes of fetal death in utero, low birth weight and severe diseases in neonates.

Other infectious diseases, acquired through sexual contact are Gardenella vaginalis, Chlamydia trachomatis, Trichomonas vaginalis and Candida, which are recognized as causes of abortion and pre-term labour. The transplacental infection leads to chorioamnionitis, release of prostaglandins and preterm uterine activity. Failure to give adequate and prompt care to those cases may result in considerable pregnancy loss.

Toxoplasmosis commonly occurs in adults, usually in a mild or asymptomatic form. Women with five or more abortions had the highest prevalence rate of toxoplasma antibodies. Therefore, the method of choice in the diagnosis is by the detection of specific antibodies in the patient serum.[7]

TORCH Complex
Is also known as STORCH, TORCHES, TORCH infections.

It is a medical acronym for a set of perinatal infections (i.e. infections that are passed from a pregnant woman to her fetus). TORCH infections can lead to severe fetal anomalies or even fetal loss. They are a group of viral, bacterial and protozoan infections that gain access to the fetal bloodstream transplacentally via the chorionic villi. Hematogenous transmission may occur at any time during gestation or occasionally at the time of delivery via maternal to fetal -transfusion.[8]

The TORCH Complex was originally considered to consist of 4 conditions with the

1. T referring to - Toxoplasmosis /Toxoplasma gondii
2. O referring to - Others
3. R referring to - Rubella
4. C referring to - Cytomegalovirus
5. H referring to - Herpes simplex virus – 2.

The "other agents" included under O are Coxsackie virus, Syphilis, Varicella – Zoster virus, HIV and Parvo virus B19. Hepatitis B may also be included among "other agents"

AUTOIMMUNE /BLOOD CLOTTING (15-20%)

Autoimmunity-presence of auto antibodies causes rejection of early pregnancy (15%) in the second trimesters mainly. Antibodies responsible are- Antinuclear antibodies, Anti DNA antibodies and Antiphospholipid antibodies (Lupus anticoagulant, anticardiolipin antibodies) APA positive women demonstrate a tendency to miscarry at progressively lower gestational ages. Spiral artery thrombosis, placental vascular atherosis, intervillous thrombosis and decidual vasculopathy with fibrinoid are the immediate pathology for fetal loss.

Alloimmunity- There is failure of maternal recognition of trophoblast lymphocyte cross reactive antigen (TLX). Consequently, there is lack of production of bloacking antibodies by the mother. This is due to sharing of (HLA) Human leucocyte Antigen between the partners. Parental HLA typing is not recommended.

Hemorrhagic defects

Recurrent fetal loss associated with rare haemorrhagic disorders is due to interference with adequate Fibrin formations, thereby disrupting implantation of the fertilized ovum into the uterine lining.

Thrombosis of early placental vessels.

The haemorrhagic defects associated with recurrent fetal loss include factor XIII, factor X, factor VII, factor V and factor II (Prothrombin) deficiencies, as well as Fibrinogen defects including Afibrinogenemia and those Dysfibrinogenemias associated with hemorrhage, Vitamin C deficiency, Antithrombin deficiency, Heparin cofactor II deficiency, and Fibrinolytic defects.

Management is generally plasma-substitution therapy

Anti-phospholipid syndrome is the most common thrombotic defect leading to RPL.

Multiple placental thrombi, as in placenta from woman with Antiphospholipid syndrome, are commonly associated with fetal wastage.

Treatment

Not to treat vigorously with pre-conception Antithrombotic therapy but rather with low-dose Aspirin.

Use of pre-conception low-dose of Heparin for in vitro fertilizations techniques. They continue to recommend caution, however, advocating low dose.

Aspirin as the preconception antithrombotic therapy of choice.

The post-conception addition of fixed low-dose Heparin is empirical, as higher doses are associated with bleeding and a lower success rate. Corticosteroid use may lower anti-phospholipid antibody titers, but they fail to stop thrombotic events.

ENDOCRINAL FACTOR (15-20%)

Insufficiency of oestrogen, progesterone, chorionic gonadotrophin, human placental lactogen is considered to be responsible.

Hypothyroid state may be responsible not only for infertility but for abortion.

Significant factors –

- Hyper-secretion of LH as seen in PCOS cases is associated with subfertility and higher miscarriage. This is due to adverse effects of LH on
- ❖ The oocyte
- On the endometrium via excess androgen secretion.
- Luteal phase defect with less production of progesterone is too often related but weather the diminished progesterone level is the cause or effect is not clear.
- Deficiency of Progesterone
- Poorly controlled diabetic patients do have an increased incidence of early pregnancy failure.
- Presence of thyroid auto antibodies is often associated with an increased risk.
- Idiopathic causes

PSYCHOLOGICAL CAUSES

To have a pregnancy loss is regarded as the failure of the woman, failure of man and also the failure of doctor-the failed common project. Miscarriage has been associated with profound emotional responses such anxiety, sadness, dejection, worthlessness, depression, guilt, revenge, denial, anger and a sense of loss which eventually leads to marital disharmony[9] etc. of the patient**.** From the moment a woman becomes pregnant she can start to bond with her unborn child. When the child turns out not to be viable, dreams, fantasies and plans for the future are disturbed roughly and a phase of grief continues for varying period.

UNKNOWN CAUSES/UNEXPLAINED CAUSES (40-50%)

- ❖ Inspite of the numerous factors mentioned, it is indeed difficult, in majority, to pinpoint the exact cause of abortion. Too often, more than one factor is present. However, risk of abortion increases with increased maternal age. Number of previous abortions and the aetiology are also important.

Several studies have attempted to find factors responsible for RPL which are not known till now. However, when all known and potential causes for RPL are accounted for, almost half of patients will remain without a definitive diagnosis. The optimal management of these patients is often as unclear as the etiology of their RPL.

- Progesterone has been shown to be beneficial in decreasing the miscarriage rate among women who have experienced at least 3 losses.[10]
- Low Dose Aspirin has also been investigated as a potential therapy for unexplained RPL. Its use prior to and during pregnancy has only been proven to increase live birth rates among those women with previous miscarriages beyond 13 weeks of gestation.[11,12]
- In fact, the most effective therapy for patients with unexplained RPL is often the most simple: antenatal counselling and psychological support. These measures have been shown to have subsequent pregnancy success rates of 86% when compared with success rates of 33% in women provided with no additional antenatal care.[13]
- **Recent researches** have attempted to find immunologic dysfunctions in unexplained RPL. One of these is immunologic treatments has been explored is that of lymphocyte immunotherapy (LIT). The lymphocyte is considered to act as an immunogen enhancing the maternal immune response by producing various antibodies to tolerate the pregnancy. Lymphocyte immunotherapy has been found to induce the production of-

- Antipaternal cytotoxic antibodies (APCA),
- Asymmetric antibodies (AAb),
- Mixed lymphocyte reaction blocking antibodies (MLR-Bf) in women with RPL and consequently improved their chances of a successful pregnancy. Studies have also shown decrease in (natural killer) NK cell levels and activity after immunotherapy.

- Several studies have shown significant benefits of intravenous immunoglobulin (IVIg) treatment (either standard dose 400-500mg/kg or low dose 200-250 mg/kg) in women with recurrent miscarriages. A study showed overall pregnancy success rate in IVIG treated group to be 80-88% and it appeared to be safe and effective in older women. The results of larger controlled clinical trial are still awaited.
- Other Researches have shown that oxidative stress is a cause of infertility and sub fertility. Oxidative stress is a redox state that favors oxidative reactions and promotes the generation of reactive oxygen species. Reactive oxygen species consists of highly reactive molecules with unpaired electrons and cause permanent structural damage to numerous cell components.
- Antioxidant vitamin E maintains oxidative balance in tissues. It may play a role in treating RPL.
- Vitamin D lipid soluble antioxidant and immune modulator that plays a role in implantation and to synthesis and secretion of human placental lactogen.

History and examination for causative or associated factors

- History of Repeated Pregnancy Loss:
- The period of gestation till which pregnancy continued.
- Confirmation of pregnancy (bio technically, ultrasonographically or histologically) on each occasion.
- Observation of a live embryo or foetus by ultrasound.

Specific history

- Maternal age
- Consanguineous marriage or known genetic problem in either of the partners.
- Characteristics mid-trimester painless spontaneous rupture of membranes followed by expulsion of live foetus is suggestive of cervical incompetence.
- History of uterine curettage.
- History suggestive of PCOS e.g. oligomenorrhoea, obesity and hyperandrogenic features.
- History of known diabetes or thyroid disorders.

Family history

A detailed family history should be obtained, including information about the Partner's family. The family history may provide a clue to the presence of a familial chromosome derangement. A history of any congenital anomaly, mental retardation, infertility, spontaneous abortion, or perinatal death is significant because each is characteristic of chromosomal anomaly diagnostic procedures to consider in pinpointing the problem, such as cytogenetic studies, blood coagulation protein/platelet tests, hysterosalpingography, sonography, and magnetic resonance imaging.

Symptoms

- Recurrent history of missed abortions at progressively lower gestational age is suggestive of Anti-Phospholipid Syndrome.
- Skin rashes or joint symptoms are suggestive of autoimmune disorders.
- Family history of hereditary Thrombophilias, PCOS and NIDDM.

Physical examination

All the cases should be clinically evaluated by taking detailed history and doing a thorough general, systemic and vaginal examination at the initial visit.

Signs of endocrine disease like Goitre, dry skin, obesity, Hirsutism, Galactorrhoea etc. should be identified.

Per speculum examination
Speculum examination should be done to check for vaginal infections, tears of the cervix, double cervix or fibroid polyp protruding out through the os.

Per vaginal examination
Vaginal examination should be done for any pelvic mass like uterine fibroid, bicornuate uterus.

Investigations
- Baseline investigation include
- Hb, TLC, DLC (Differential leukocyte count) and ESR.
- Blood Sugar -Fasting and Postprandial
- VDRL of both partners
- Blood grouping and Rh-typing
- Urine routine examination for any proteinuria and reducing substances and microscopy
- Pelvic ultrasound to assess uterine anatomy and morphology, two dimensional pelvic ultrasound is good enough. The diagnostic value of three-dimensional ultrasound has been explored and appears promising for diagnosing uterine malfunctions, to assess the cervical status (internal diameter of internal os when exceeds 8-9mm in a nulliparous woman may suggest cervical incompetence).

Special Tests
- Peripheral blood karyotyping of both partners to be screened. For translocation and mosaics. For the finding of an abnormal parental karyotype should prompt referral to a clinical geneticist, Karyotyping of the abortus, Lupus anticoagulant (LA) and Anti-cardiolipin antibodies (ACA), Antiphospholipid antibodies (APA), Semen Analysis of male partner, Hysterosalpingography [HSG] or hysteroscopy, Hystero-scopy (before conception), Laproscopic evaluation of the pelvis and abdomen (optional), MRI (Magnetic resonance imaging for anatomical defects of the uterus or cervix, Tests for cervical incompetence (Hegar's dilator test), Glycosylated haemoglobin (HbAlc), Thyroid function tests and TSH screening, HLA typing and APCA testing, TORCH screening, Reproductive tract infections screening by vaginal cultures, Cervical cytology with pap smears for screening of precancerous and early cancerous lesions observed, Hormonal Profile.

MANAGEMENT
- Counselling: Psychological support (tender loving care) and constant reassurance about successful pregnancy will alleviate anxiety.
- General advice like quitting smoking and reducing alcohol intake, avoiding excessive coffee consumption, losing weight, balanced diet.
- Folic acid starting at least two months before planned pregnancy should be given to prevent neural tube defects.
- Vitamin supplements, alone or in combination with other vitamins prior to pregnancy or in early pregnancy, does not prevent miscarriage.
- Women with unexplained R.P.L. have excellent prognosis for future pregnancy without pharmacological intervention if offered supportive care alone in a dedicated early pregnancy assessment unit.
- Use of empirical treatment like Progesterone or H.C.G. supplementation, prophylactic antibiotics for vaginal infections, thrombo-prophylaxis with Aspirin and Heparin and immunotherapy are necessary if needed. Immunotherapy includes paternal cell immunization, transfusion reactions, anaphylactic shock and hepatitis vaccine.

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