



FEDERATION OF  
OBSTETRIC AND  
GYNAECOLOGICAL  
SOCIETIES OF INDIA

# TOG

## Times of Gynaecology™

Issue 1

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Gynaecology™

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## EDITORIAL

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# President Message

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## From the desk of Dr. Rishma Dhillon Pai – President FOGSI 2017



It gives me great pleasure to present to you the first issue of the "Times of Gynaecology" (TOG) series.

As FOGSI President this year, my focus is on improving communication between the FOGSIans spread across the entire country and to use every medium to hear about your achievements, successes, problems, and difficulties.

If we share our knowledge, we can enrich each other to learn and benefit.

The field of obstetrics and gynaecology is dynamic and constantly changing with new drugs and techniques and concepts. TOG will be easy reading and will help us to keep updated.

I wish the editors Dr. Nandita Palshetkar, Dr. Hrishikesh Pai and Dr. Pratik Tambe all the best. I am sure; TOG will be excellent.

*'A love affair with knowledge will never end in heartbreak'.*

*Michael Garrett Marino*

### **Dr. Rishma Dhillon Pai**

President 2017 - Federation of Obstetrics & Gynaecological Societies of India (FOGSI)  
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# Editorial Message

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## Dear Fellow FOGSIans,

It gives us immense pride to pen these few lines as the editors for the very first issue of the “Times of Gynaecology”.

The aim of this series is to have a mix of academic, scientific, and lifestyle-related articles to bring you up-to-date with developments in our field. With a view of offering a diverse range of reading material, we have scientific articles in this particular issue on the role of calcium supplementation, amino acids in pregnancy, and the bipolar resectoscope in operative hysteroscopy.

We also have vitamins and drugs during pregnancy and some insider travel information on Geneva, the venue for this year’s annual ESHRE meeting.

We hope you enjoy this laid-back new look series of Times of Gynaecology which is a little different from the standard scientific journals which we are all used to.

Do feel free to get in touch with us with your comments, remarks, recommendations for topics to be covered, and feedback you may wish to provide.

**Dr. Hrishikesh Pai**  
**Dr. Nandita Palshetkar**  
**Dr. Pratik Tambe**  
(Editors)





# #TOG-INSPIRE

**Dr. Rohit V Bhatt:** A legendary story that would inspire many



*Use your counseling abilities and cool temperament to interact with patients and their relatives, says Dr. Rohit Bhatt in a recent interview to TOG's executive editor Asma Parveen.*

Dr Rohit V Bhatt, Chief of Department of Obstetrics and Gynecology, BD Amin General Hospital, Baroda has been nominated for several prestigious awards including the Life-time Achievement Award by Harvard Medical School in 2010 for outstanding contribution to women health, Life-time Achievement Award by Federation of Obstetricians and Gynecologists of India (FOGSI) for contribution to women health, and Federation Activities & National Association of Reproductive and Child health (NARCHI) and has been conferred with the prestigious Dr BC Roy Award in the category of Eminent Medical Teacher last year.

Dr Rohit V Bhatt is the first doctor in his family. He was prompted to take up obstetrics and gynecology specialty by the sad incidence of the demise of his sister-in-law during child-birth, and his love for teaching and research prompted him to take up teaching assignments.

### **When asked about the current generation of Obs & Gynae's, he had the following to share:**

This generation has more opportunity to collect knowledge and information than earlier generation of obstetrics and gynecologists. You have greater access to technology like the internet and more access to endoscope, imaging science and endocrine lab. The newer technology should be used as your support. Let it not be your master and do not neglect your clinical touch and acumen.

Many young obstetrics and gynecologists feel, per vaginal examination is not necessary, do not believe this. Give more weightage to your clinical judgment and "remember information – knowledge and wisdom is not synonymous". Although more information and knowledge is available to you, do look for wisdom, and remember, knowledge comes but wisdom lingers. Keep room for wisdom. Young generation is restless and fast moving unlike earlier generation.

### **Asma: What do you think about the current state of doctor-patient relationship**

Doctor-patient relations have deteriorated in the last few years. Use your counseling abilities and cool temperament to interact with patients and their relatives."

During the interview, Dr. Bhatt also spoke about dress codes. He said "I find you have dispensed with white Apron and prefer to move in jeans and T-shirt in the hospital. This is not correct. You are at liberty to use informal dress like jeans when you are off duty, but you must maintain dignity and decorum of your position when on duty in the clinic/hospital."



# Calcium in women with osteoporosis

## Drug in Focus

“*The first-line therapy for the prevention of bone loss and osteoporotic fractures is the use of calcium with or without vitamin D. Supplementation with doses of at least 1,200 mg of calcium and 800 IU of vitamin D provides significantly greater reduction of fractures.*”



**Dr. Archana Verma**

MBBS, MD-Obstetrics & Gynaecology, DGO  
Ghaziabad

### Osteoporosis in women

The prevalence of osteoporosis is increasing among women in India. From prevalence studies conducted across the country, it is estimated that of the 230 million Indians over the age of 50 years in 2015, 20% (about 46 million) are women with osteoporosis. Several studies have reported that the prevalence of osteoporosis range from 8% to 62% in Indian women of different age groups. Hence, osteoporosis is a major public health problem among the Indian women.<sup>1</sup>

The causes of increasing incidence of osteoporosis include low calcium coupled with the prevalence of vitamin D deficiency, increasing longevity, sex inequality, early menopause, genetic predisposition, lack of diagnostic facilities, and poor knowledge of bone health. Osteoporosis is known as silent disease only until fractures occur; once fractures are caused there is resultant pain, disabilities, and economic burden.<sup>1</sup>

It has also been observed that during pregnancy and lactation, women have to form and maintain fetus and newborn skeleton which requires maternal hormonal and metabolic adjustments. In such women, calcium intestinal absorption rises, calcitonin levels increases and hypercalciuria can be detected until lactation is stopped. These changes can exceptionally lead to generalized or regional osteoporosis.<sup>2</sup>

### Treatment and prevention of osteoporosis in women

Creating an environment to achieve peak bone mass during adolescence, maintenance of healthy bone throughout the life cycle, and prevention of bone loss, postmenopausal bone health has to be optimized.<sup>1</sup>

“ Calcium intake is essential for bone development and maintenance throughout life. It is especially crucial during pregnancy and lactation because of the potential adverse effect of depleted maternal calcium stores on maternal bone health. Calcium intake should be encouraged, especially during pregnancy and lactation, through the diet or by supplementation with calcium-containing supplement products.<sup>3</sup>”

In Indian women, calcium, vitamin D, and bisphosphonates are the common first-line therapies. The first-line therapy for the prevention of bone loss and osteoporotic fractures is the use of calcium with or without vitamin D. According to the researchers, reduction of fractures is significantly greater with supplementation with doses of at least 1,200 mg of calcium and 800 IU of vitamin D. The use of other drugs, such as hormone replacement therapy, estrogen agonists, calcitonin, parathyroid hormones, and denosumab, are some other treatment options.<sup>1</sup>

### Calcium supplement in clinical practice

The human body requires calcium to maintain the strength and structure of bones and teeth, along with certain critical metabolic functions. The serum levels

of calcium is tightly controlled by the parathyroid hormone, calcitonin, and vitamin D.<sup>2</sup> Food is the best source of calcium; however, postmenopausal women do not consume enough calcium may require supplements to achieve the recommended daily allowance of calcium.<sup>4</sup>

Calcium administered during pregnancy and the early postpartum period was associated with reduced bone resorption in women with adequate intakes. Thus, calcium supplementation may be a practical intervention to prevent transient skeletal loss associated with childbearing.<sup>5</sup>

Supplemental calcium is available in a variety of different forms, such as calcium carbonate, calcium citrate, coral calcium, calcium ascorbate, calcium lactate, and calcium phosphate. Coral calcium consists of parts of coral that have broken off coral reefs.

### Calcium supplementation and prevention of osteoporosis

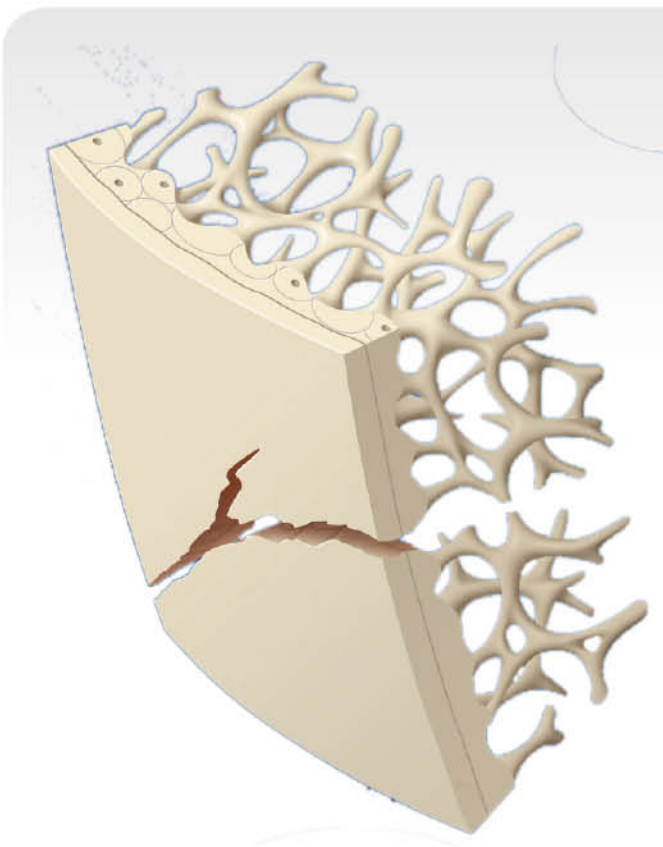
In a meta-analysis of 15 studies involving 1,806 individuals, researchers reported that calcium alone caused a positive mean percentage bone mineral density change from baseline of 2.05% for total body bone density, 1.66% at the lumbar spine, 1.6% at the hip, and 1.9% at the distal radius. The study also indicated

a trend toward reduction in vertebral fractures [relative risk reduction: 0.79 (95% CI: 0.54- 1.09)]. According to the study, calcium was more effective compared to placebo in reducing the rates of bone loss after >2 years of treatment.<sup>6</sup> Calcium supplements produce repeated sustained increases in serum calcium concentrations after each dose. And also, calcium supplements effectively suppress bone turnover.<sup>7</sup>

According to the researchers, bone loss is reduced in healthy, older postmenopausal women when the calcium intake is increased with 400 to 800 mg/day.<sup>8</sup> Also, postmenopausal women (n=118) who were supplemented with 1700 mg/day for 3 to 6 years of menopause reduced bone loss from the femoral neck and improved calcium balance.<sup>9</sup>

### Conclusion

The prevalence of osteoporosis is increasing among women in India, and is a major health concern. This calls for improved, effective, and economical supplementation of calcium in this population. The first-line therapy for the prevention of bone loss and osteoporotic fractures is the use of calcium with or without vitamin D. Supplementation with doses of at least 1,200 mg of calcium and 800 IU of vitamin D provides significantly greater reduction of fractures.



### Coral calcium

Coral calcium typically contains over 70 trace minerals, which assist in effectiveness and absorption.<sup>10</sup> A study published in the *Journal of Nutritional Science and Vitaminology* has reported on the different absorption rates of coral calcium and calcium carbonate, and that calcium of coral origin was better absorbed in the intestines than calcium carbonate.<sup>11</sup> In this study, calcium absorption was determined from the ingestion of crackers into which the coral powder or calcium carbonate was added. The study included 12 participants who were divided into two groups; one group ingested coral-added crackers first (group A) and those of the other group ingested calcium carbonate-added crackers first (group B). The researchers determined the degree of intestinal absorption of calcium from coral-added crackers and that from calcium carbonate-added crackers by assessing



Coral calcium has been reported to have calcium and minerals that improve bone health. It contains over 70 trace minerals, which assist in effectiveness and absorption. Coral calcium is better absorbed from the intestine than the calcium of calcium carbonate

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urinary calcium excretion per decilitre of glomerular filtrate (GF) (coral calcium vs calcium carbonate) and increase in urinary calcium excretion per milligram creatinine (vs control value).<sup>12</sup> Researchers observed a significant difference (from control value) in the increase of urinary calcium excretion per milligram creatinine ( $p=0.0008$ ). This data suggested that the coral calcium is better absorbed from the intestine than the calcium of calcium carbonate.<sup>12</sup>

Women with osteoporosis have lower serum magnesium levels when compared to women with osteopenia and those without osteoporosis or osteopenia.<sup>13</sup> Hence, magnesium deficiency may be a risk factor for osteoporosis. Studies have suggested that increasing magnesium intakes from food or supplements increases bone mineral density in postmenopausal women. Similarly, magnesium supplementation during pregnancy was associated with lower frequencies of fetal growth retardation and preeclampsia.<sup>14</sup> Coral calcium has been widely used in Ayurveda as calcium supplement from time immemorial due to the advantage of easy absorption from the intestine.<sup>15</sup> Coral calcium (praval prasti) has been used in women with recurrent abortions and during pregnancy.<sup>16</sup>



# Bipolar resectoscope

## Scientific review

“*Hysteroscopic bipolar resectoscopy should be considered a minimum standard of care in today's world where patient safety, shorter operating times and efficient surgical technique is required.*”



**Dr. Pratik Tambe**  
MD, FICOG  
Mumbai

### Introduction

The bipolar resectoscope was introduced about a decade ago and has revolutionized the field of hysteroscopic surgery. Prior to the availability of the bipolar resectoscope, the available instruments were unipolar/monopolar in design and required non-ionic distension media, for example glycine. This entailed accepting the complications associated with fluid overload, absorption of the media via open blood vessels under pressure, and the consequences thereof including cerebral oedema, hepatic encephalopathy, and, in extreme cases, convulsions, coma, and death.

The bipolar resectoscope uses simple, easily available media such as normal saline (NS) or Ringer's lactate; ensures good vision owing to less turbidity, is associated with a lower complication rate, and does away with the need for using high current settings used in monopolar electrosurgery, which may have a long term impact on the endometrium and fertility potential.

### Operative procedure

The standard 4 mm, 30 degree Hopkins II telescope may be used in conjunction with the operative sheath having a 9 mm outer diameter. This requires a cervical dilatation of at least 9.5 mm, which may occasionally be difficult in infertile nulliparous women. Inserting a misoprostol tablet 200 mg per vaginam overnight may facilitate the process of cervical dilatation when usage of a 9 mm operative sheath is expected.

The outer sheath with the attached suction and irrigation tubes and the obturator are introduced, following which the obturator is withdrawn and the inner working element with the appropriate electrode and the telescope-camera system is introduced. The seals are then re-checked to ensure a water tight assembly of the system and the fluid distension medium is introduced.

Distension may be achieved by using two standard Medex C-Fusor pressure bags of 1 L capacity, each attached via a Y connector or disposable TUR set to ensure optimum intrauterine pressure without allowing the cavity to collapse when one fluid pint has been exhausted. Three L capacity bags are also available but have scant utility today as availability of 3 L fluid pints is almost non-existent. Alternatively, a Hysteromat pump which digitally displays the pressure and flow rates of fluid or the more recent Karl Storz EASI fluid management system may also be used.

### Instrumentation

The bipolar resectoscope is equipped with a working electrode and an inactive, return electrode. Both of these are placed close to each other that is 1–2 mm apart, which ensures no current leakage and a predictable path of current from one electrode, through the tissue to which it is applied and back via the return electrode to the electrosurgery generator.

NS or Ringer's lactate may be used as a distension medium. Bipolar electrodes need an electrolytic solution to conduct electric current and when the activated electrode is not in contact with tissues, the solution dissipates it, adding to the safety.



When close to the tissue being dissected, the high bipolar voltage spike arc between the two electrodes converts the conductive sodium chloride solution into a non-equilibrium vapour layer or “plasma effect” containing energy-charged sodium particles. This can be maintained at lower voltages once initiated. When in contact with tissues, the tissue disintegrates via molecular dissociation.

## Technique

For intrauterine polyps and fibroids, the principle is to introduce the resectoscope system along the wall which is free from pathology and reach above the tissue to be resected. The electrodes are applied to the base of the tissue and the foot pedal activated, while withdrawing the working element towards the operator. This ensures that the electrode movement is always under vision towards the surgeon and minimises the risk of inadvertent uterine perforation. In case of intrauterine adhesions and Asherman syndrome, particularly if the anatomical landmarks are not visible and the cavity is distorted, preventing the electrode from reaching above the adhesions, it may be necessary to cut in a direction away from the operator, but exercising maximum caution to prevent complications.

### Hazards of distension media

The AAGL Practice Guidelines for the Management of Hysteroscopic Distending Media (2007) provides clinicians with evidence-based information about commonly used and available hysteroscopic distending media to guide them in their performance of both diagnostic and operative hysteroscopy.

The guidelines note, that while necessary for the performance of hysteroscopy and hysteroscopically-directed procedures, distending media, if absorbed systemically in sufficient amounts, can have associated adverse events, including life-threatening complications. Consequently, understanding the physical properties and the potential risks associated with the use of the various distending media is critical for the safe performance of hysteroscopic procedures.

### Choice of distension medium

Low-viscosity media can vary in their osmolality and electrolyte content. Traditionally, urologic endoscopic surgery featured the near ubiquitous use of monopolar electrosurgical instruments. Such instruments require a nonconductive medium to facilitate completion of the radiofrequency (RF) electrical circuit between the

active and remotely located dispersive electrode. If such instruments are used in saline, the media disperses the current from the active electrode, thereby preventing the creation of a surgical effect.

If absorbed in volume systemically, one of the risks was that of hemolysis. Consequently, the addition of solutes such as glucose, sorbitol, and glycine increased the medium's osmolality to a degree that hemolysis was largely prevented. Occasionally, the systemic absorption of large volumes of these (usually) hypotonic and electrolyte-free solutions led to TURP (transurethral resection of the prostate) syndrome, characterised by hyponatremia, hypoosmolality, nausea, vomiting, and neurologic symptoms including muscular twitching, grand-mal seizures, and coma.

NS and other isotonic electrolyte-rich solutions are useful and safer media, for even if there is absorption of a substantial volume of solution, NS does not cause electrolyte imbalance and, consequently, is a good choice for minor procedures performed in the office. While electrolyte-containing solutions are not suitable for RF surgery with monopolar RF systems, the development of bipolar RF instrumentation for hysteroscopic surgery has allowed the application of saline as a distending medium in even more advanced and complex procedures. Ringer's lactate possesses similar properties as NS but is even more “physiologic,” and consequently would be expected to have a similar risk profile.

### Fluid overload and consequences

The principal reason for the use of electrolyte-free solutions is their suitability for the performance of RF electrosurgery with monopolar instrumentation. However, hypotonic and electrolyte-free media can create fluid and electrolyte disturbances if absorbed in excess amounts. Included in the sequelae are hyponatremia and related issues as well as heart failure, which can also be caused by absorption of conductive media such as NS and pulmonary and cerebral edema.

Under conditions of hyponatremia, water moves into brain cells, causing cerebral edema, which can lead to pressure necrosis and progression to brain stem herniation and rarely death. This issue may be even more important for premenopausal women because the  $\text{Na}^+/\text{K}^+$ -ATPase pump is inhibited estrogens. This unique impact may explain why, in the context of hyponatremic encephalopathy, premenopausal women are 25 times more likely to die or have permanent brain damage than men or postmenopausal women.



These circumstances make low osmolality a more risky proposition in premenopausal women, at least in those who undergo resectoscopic surgery. A number of deaths have been reported associated with the use of hypotonic glycine or sorbitol at the time of operative hysteroscopic surgery. Hypo-osmolality and hyponatremia are more likely to induce the greatest degree of morbidity, but neurologic morbidity from hyponatremia in the absence of hypo-osmolality has not been described as associated with resectoscopic intrauterine surgery. The impact of fluid imbalance also varies according to the patient's age and comorbid conditions including cardiovascular and renal function. While low or even modest volumes of absorbed fluid can be accommodated by most healthy individuals, excessive absorption can result in fluid overload, and if non-physiologic fluids are used, electrolyte disturbances typically result.

These issues have important practical considerations, and the evolving availability of bipolar resectoscopic systems that function in electrolyte-containing solutions provides the opportunity to reduce the risk of hyponatremia as a consequence of excess absorption of distending media.

### Management of excess fluid absorption

It is apparent that the best "management" of fluid overload is to prevent its occurrence by constantly and accurately monitoring the distending medium input and output. Prevention requires that the team have a protocol for responding to escalating absorbed volume that stipulates the thresholds for action.

Every time a fluid pint is changed, the output in the suction bottle and if used, the fluid leakage from around the cervix and resectoscope system into a specially designed disposable pouch should be monitored. A difference between input and output between 500–1,000 mL should prompt a decision whether to continue the procedure or to abandon it in the interests of patient safety.

It has been shown with routine postoperative CT imaging of the brain that cerebral oedema can occur with as little as 500 mL of hypotonic solutions. Such low thresholds may be appropriate for those who are older and/or medically compromised, but for healthy individuals, absorption of up to 1,000 mL can generally be tolerated. A decrease in serum sodium of 10 mmol corresponds to an absorbed volume of around 1,000 mL.

Consequently, if a threshold of 1,000 mL is reached in healthy women free of cardiovascular disease, the patient should be carefully evaluated for signs of

pulmonary oedema before continuing the procedure. In addition, if absorption of electrolyte free media is a concern, an indwelling catheter should be placed, and intraoperative measurement of serum electrolytes and osmolality is suggested.

If overload has occurred, the use of intravenous furosemide is appropriate. The onset of action of intravenous furosemide is 5 minutes, and clinical improvement occurs in 15 to 20 minutes. Significant fluid overload if not quickly corrected by a diuretic, should be managed by a team approach of experts including the gynaecologist, anesthesiologist, nephrologist, cardiologist, and specialist in intensive care.

### Advantages over traditional monopolar surgery

Having made the case for bipolar electro-surgery, it must be recognised that there are many advantages of bipolar versus traditional monopolar surgery:

In bipolar electro-surgery, the current flow is restricted to the area between the two electrodes which are under vision of the endoscopic camera. In monopolar surgery, the current passes through several tissues via the pathway of least resistance to the patient plate (neutral electrode) placed on the patient's skin.

The risk of injuries to other organs, distant tissues, and areas not under visual control are higher. The risks of current leakage due to imperfect insulation or current leakage are higher with monopolar current. Monopolar current has a higher risk of interfering with other electrical equipment in the OR, including the multipara monitors, defibrillator, pacemakers etc. The risk of fluid absorption, volume overload, hyponatraemia, hypervolaemia, glycine toxicity, and hepatic encephalopathy are all significantly higher with monopolar electro-surgery.

Most of the morbidity and mortality is related to hypotonic non-electrolyte solutions rather than pure fluid overload. On the other hand, NS is less expensive, easily metabolised, is non-toxic, can be used in higher quantities, and is vastly superior in terms of patient safety.

### Evidence in recent literature

In a recent prospective randomised study by Roy KK et al., 70 women underwent hysteroscopic septal resection using either unipolar or bipolar resectoscope. Intraoperative parameters (operation time, fluid deficit, and complications) and pre- and postoperative serum sodium levels were compared between the two groups. A second-look hysteroscopy was performed after 6 weeks.



There was no statistically significant difference between the two groups in terms of operation parameters and second-look hysteroscopy findings. Six patients in the unipolar group were found to have hyponatraemia in the postoperative period compared to none in the bipolar group ( $p=0.025$ ). The authors concluded that the use of bipolar resectoscope is associated with a lesser risk of hyponatraemia compared to the unipolar resectoscope. Bipolar resectoscopy is a safe alternative to unipolar resectoscopy with similar reproductive outcome.

A multicenter-observational-case-control study was conducted on premenopausal women affected by menorrhagia, pelvic pain, or infertility because of submucous uterine myoma by Litta P et al. The authors considered eligible: single G1 or G2 submucous uterine myoma, at least 0.5 cm ultrasound 'myometrial-free-margin,' and two months GnRH pre-surgical treatment (myoma > 3 cm). Group A patients were treated by bipolar resectoscope and Group B by monopolar resectoscope. The primary endpoint was to compare the groups in term of complete or incomplete myomas resection ("second-step-procedure" rate). The secondary endpoint was to compare two treatments in term of surgical time and intraoperative complications rate.

Group A (60 patients) and Group B (216 patients) were homogeneous for general features and myomas location, but they differed for G2 type prevalence (73.3% vs 50.5%), mean myomas diameter (33.17 +/- 11.93 vs 29.45 +/- 9.63), and surgical time (29.43 +/- 12.6 vs 23.2 +/- 8.2 minutes). In Group A patients, both G1 and G2 myomas were completely removed in a single step without intraoperative/postoperative complications; in Group B, surgical outcomes of G1 myomas were similar to those of Group A, while G2 myomas required procedure termination in 12% of cases because of slight electrolyte disturbance (22 cases) and severe hyponatraemia in four cases. All intraoperative complications occurred when procedure time exceeded 30 minutes and when myomas diameter was greater than 37.5 millimeters.

They concluded that in the era of mini-invasive surgery, hysteroscopic approach by bipolar device, should be considered as a useful, safe, and large-scale feasible procedure for submucosal myoma treatment, particularly when G2.

## Conclusion

Hysteroscopic bipolar resectoscopy should be considered a minimum standard of care in today's world where patient safety, shorter operating times, and efficient surgical technique is required. In case of

polyps and fibroids, it represents a great leap forward with the use of simple, inexpensive, clear, and effective distension media like NS. The incidence of complications with intravasation of large fluid volumes is low and can be prevented by constant vigilance and the use of a monitoring systems.

Figure 1. Bipolar Resectoscope with electro-surgical generator unit



Figure 2. Bipolar Resectoscope system

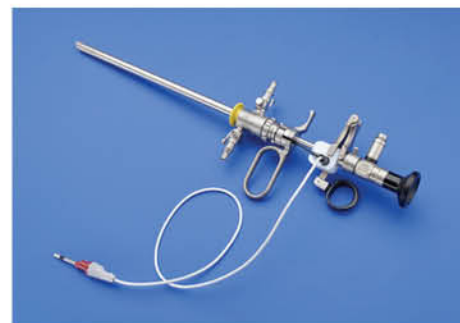
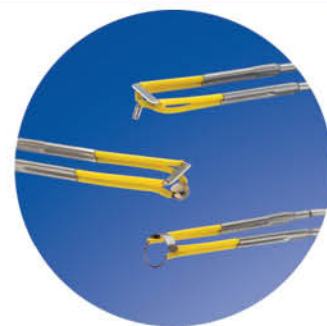


Figure 3. Bipolar electrodes



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# Role of amino acid supplementation in pregnancy

## In Focus



**Dr. Charmila Ayyavoo**  
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Trichy

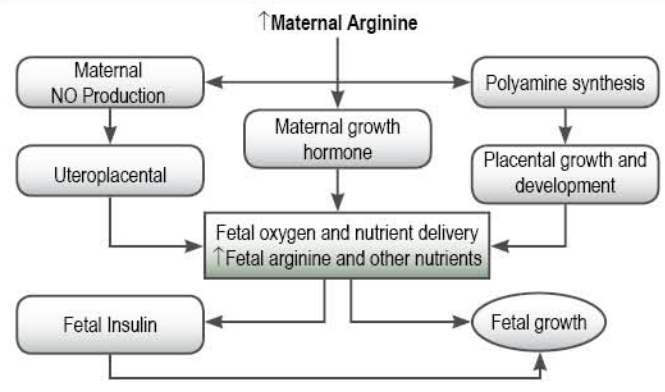
**D**uring pregnancy, appropriate fetal growth can be attained with adequate transport of nutrients through the placenta. The maternal body undergoes several metabolic and endocrine changes essential for intrauterine growth and placental development. Amongst these alterations, a significant change is observed in the maternal plasma amino acid concentrations during the first trimester which is normalized within 1 or 2 days after delivery. Therefore, the changes occurring in plasma concentration of amino acids may be responsible for determining appropriate fetal growth. Maternal plasma amino acids are generally observed to be altered in pathological conditions such as in intrauterine growth restriction (IUGR) and diabetes.<sup>1</sup> Eventually, alteration in the maternal plasma amino acid profile during pregnancy is reported to affect the fetal plasma amino acid profile. Hence, the composition and timing of supplementation during pregnancy, maternal amino acid profile and sufficiency of the placenta will impact the placental transport and amino acid delivery to the fetus.<sup>2</sup>

## Beneficial effects of amino acid supplementation during pregnancy

Amino acids supplementation improves the perinatal outcome in IUGR cases

Millions of pregnancies are affected with IUGR which is reported to range from 4–8% of total births. The child affected with IUGR may develop diseases such as coronary artery disease or diabetes in later life. IUGR occurring due to inadequate maternal nutrition hampers the fetal growth and prevents it reaching its full growth potential. Impaired placental exchange of amino acid is observed to be one of the main causes for retarded fetal development in cases of IUGR.<sup>1</sup> The mechanisms by which arginine supplementation might improve fetal growth is shown in Figure 1.<sup>2</sup> Taurine supplementation is also reported to cause an improvement in  $\beta$ -cell function and insulin secretion, thereby increasing the fetal anabolic hormones to improve fetal growth. The ability of leucine to independently stimulate muscle protein synthesis may promote lean mass growth in the IUGR fetus during pregnancy.<sup>2</sup>

**Figure 1.** Mechanisms by which arginine improves fetal growth.<sup>2</sup>



A study was conducted to compare the perinatal outcome in IUGR with or without oral amino acid supplementation. The study consisted of a treatment group which included mothers with IUGR who were administered amino acid supplementation (Group 1) and control group mothers with IUGR (Group 2). Findings showed:<sup>3</sup>

Around 88% of mothers in group 1 continued pregnancy beyond 36 weeks compared with 48% in group 2 who delivered in between 34 and 36 weeks.

Around 80% of babies had a birth weight between 2.5 and <3 kg in group 1, in comparison to 84% of babies weighing between 2 and <2.5kg in group II.

Moreover, 80% of babies had Apgar score in between 7 and 10 in group I and 92% of group I cases did not require any NICU admission.

Therefore, oral amino acid supplementation from the second trimester of pregnancy significantly improved the perinatal outcome in IUGR cases.<sup>3</sup>

Another study by Sieroszerski et al, showed that an oral arginine supplement of three grams per day for 20 days around the 32<sup>nd</sup> week of gestation increased the fetal growth. The mean birth weight evaluated post-delivery was increased in the arginine supplemented group (2.823 vs. 2.495 kg) compared with the placebo group.<sup>4</sup>

### L-arginine supplementation improves amniotic fluid volume and prolongs pregnancy

Amniotic fluid is essential for proper development and growth of the fetus. Oligohydramnios, reduced amniotic fluid, is associated with various complications such as impaired lung development, chronic placental insufficiency, and restricted space for fetal growth. However, long-term oligohydramnios may cause umbilical cord compression, fetal hypoxia, and pressure-induced deformities.<sup>5</sup>

A study by Hebbar et al. demonstrated that L-arginine supplementation during pregnancy (mean gestational age of 33.4±1.9 weeks) in women with decreased liquor [amniotic fluid index (AFI) <8] led to an improvement in the mean AFI from 6.9 [standard deviation (SD) 0.8] to 9.3 (SD 1.7) at the end of therapy. The pregnancy was also observed to be prolonged from 33.4 weeks to 36.3 weeks. The overall improvement in AFI according to the type of intervention was found to be statistically significant as shown in Table 1. Therefore, a significant, improvement in liquor and prolongation of duration of pregnancy by around 3 weeks was observed with L-arginine supplementation.<sup>5</sup>

### L-arginine supplementation reduces the incidence of pre-eclampsia during pregnancy

Pre-eclampsia/eclampsia is reported to be among the leading causes of maternal and neonatal morbidity and mortality. Abnormal placentation due to remodelling of the uterine vasculature and defective invasion of trophoblast cells may decrease utero-placental perfusion and may activate mechanisms that promote maternal vasoconstriction and damage of endothelial cells. In this case, L-arginine provides a source of substrate for nitric oxide synthesis which promotes vasodilatation.<sup>6</sup>

Supplementation of pregnant women with L-arginine plus antioxidant vitamins significantly reduced the incidence of pre-eclampsia ( $\chi^2=19.41$ ;  $p<0.001$ ) compared with placebo (absolute risk reduction 0.17 (95% confidence interval 0.12 to 0.21). L-arginine plus antioxidant vitamins resulted in a significant effect ( $p=0.004$ ; absolute risk reduction 0.09, 0.05 to 0.14) compared with antioxidant vitamins alone.<sup>6</sup>

### Amino acid intake recommendations during pregnancy

The amino acid intake recommendation during pregnancy is given in Table 2.<sup>7</sup>

TABLE 2. Amino acid intake recommendations during pregnancy<sup>7</sup>

	EAR <sup>1</sup>	RDA <sup>2</sup>
Amino acid	mg/kg/d	mg/kg/d
Histidine	15	18
Isoleucine	20	25
Leucine	45	56
Lysine	41	51
Methionine + cysteine	20	25
Phenylalanine + tyrosine	36	44
Threonine	21	26
Tryptophan	5	7
Valine	25	31

EAR: Estimated average requirement, RDA: Recommended dietary allowance  
<sup>1</sup> Factorial estimates based on adult amino acid requirements 3.1.33 to take into account increased protein demands of pregnancy. <sup>2</sup> Factorial estimate based on 24% variability from the EAR.

TABLE 1. Maternal intervention and improvement in amniotic fluid index (AFI)<sup>5</sup>

Type of intervention	n (%)	Pre-treatment AFI	Post treatment AFI	Increase in AFI	p value
		Mean (SD)	Mean (SD)	Mean (SD)	
L-Arginine and maternal hydration	39 (78)	6.7 (0.8)	9.2 (1.7)	2.5 (1.4)	0.004 (HS)*
L-Arginine	11 (22)	7.4 (0.4)	9.2 (1.1)	1.8 (1.3)	0.0001 (HS)*
Overall outcome	50 (100)	6.9 (0.8)	9.3 (1.7)	2.4 (0.8)	0.0001 (HS)*

\*HS: highly significant; SD: standard deviation.



## Summary

- Adequate transport of nutrients through the placenta helps in appropriate fetal development. Several metabolic and endocrine changes occurring during pregnancy leads to alteration in the maternal plasma amino acid concentrations, which may determine fetal growth. Therefore, maternal amino acid profile, composition and timing of supplementation, and sufficiency of the placenta will have an effect on the placental transport to the fetus.
- One of the reasons of IUGR is the impaired placental exchange of amino acid during pregnancy.
- Amino acids such as arginine, taurine, and leucine act through multiple mechanisms and improve fetal growth during pregnancy.
- Arginine supplementation increased the mean birth weight of the infant and prolonged the period of pregnancy.
- Arginine supplementation also improved the volume of amniotic fluid, which can prevent various complications associated with reduced amniotic fluid.
- L-arginine is reported to significantly reduce the incidence of pre-eclampsia during pregnancy.
- Therefore, amino acid supplementation during pregnancy provides various protective effects on the fetus, and should be considered as a promising option for preventing several complications during pregnancy.

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## TRAVEL

## Geneva

Geneva remains one of the most sought after European destinations. This year, the ESHRE Annual Meeting will be held in this historic city from 2-5 July, 2017.

A gateway to the Alps and European headquarters for the United Nations, Geneva has a rich and colourful history of religious turmoil and revolution, and a handful of fascinating museums and grand monuments.

This higher part of the city is now Geneva's Old Town and is classed as a national heritage site. The 330 ft-long Reformation Wall built into the old city wall nearly a century ago to mark the 400th anniversary of Calvin's birth commemorates the key role Geneva played in the religious tumult of 16th-century Europe. You can get to grips with the polemics and examine rare copies of the Bible at the International Museum of the Reformation, housed in the 18th-century Mallet House built on the site where the people of Geneva voted to adopt these new religious ideas in 1536.

- On arrival at your hotel, pick up a Geneva transport card which are free for guests and can be used on all public transport in the city.
- Explore the city and surroundings by bike. Bikes are available to hire from the Genève Roule Association ([geneveroule.ch](http://geneveroule.ch)). For recommended cycling routes see [veloland.ch](http://veloland.ch).
- Take to the water on a yellow taxi-boat. The Mouettes Genevoises (Geneva Gulls) are free to use with a transport card and, depending on the line, depart every 10 to 30 minutes from city centre stops. See [mouettesgenevoises.ch](http://mouettesgenevoises.ch).
- Make the most of good value, set-price lunch menus. Top city restaurants offer excellent two- or three-course options from around £32 or more simple plats du jour from £11.
- Buy a Geneva Pass if you're planning a full-on program of sightseeing. These are available for 24, 48, or 72 hours and cost from £18. See [geneva-pass.com](http://geneva-pass.com).





# UPCOMING EVENT

## India Day 2017

A Joint Meeting of FOGSI, RCOG & AICC  
Friday 30 June 2017  
Venue: RCOG, London



Royal College of  
Obstetricians &  
Gynaecologists

### OVERVIEW

The Royal College of Obstetricians and Gynaecologists (RCOG) and Obstetricians and Gynaecologists from the Indian subcontinent have shared a special relationship for a long time. The maximum number of members of the RCOG outside the United Kingdom are currently based in India. With globalisation of medicine, it is essential that policy-makers and clinicians from major associations and colleges have open discussions on important issues in the speciality. This will enhance standardisation of care, development of guidelines, and help innovate ideas. The meeting will provide an opportunity to exchange ideas, share, and learn from experiences. This can only have a positive impact on women's health.

To ensure this occurs, the Federation of Obstetric and Gynaecological Societies of India (FOGSI), the All India Co-ordinating Committee (AICC), and the Royal College of Obstetricians and Gynaecologist (RCOG) have organised a joint meeting.

### Why attend?

- Hear discussions on the latest controversies and advances in Obstetrics and Gynaecology that span the two countries
- Listen to debates and round table discussions on issues such as method of delivery, ultrasound and pregnancy screening and endometriosis, infertility, gynaecological issues such as fibroid and Endometriosis
- Meet colleagues from India and UK
- Claim a maximum of 7CPD credits for full attendance at this meeting

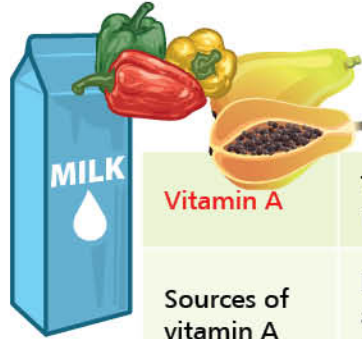
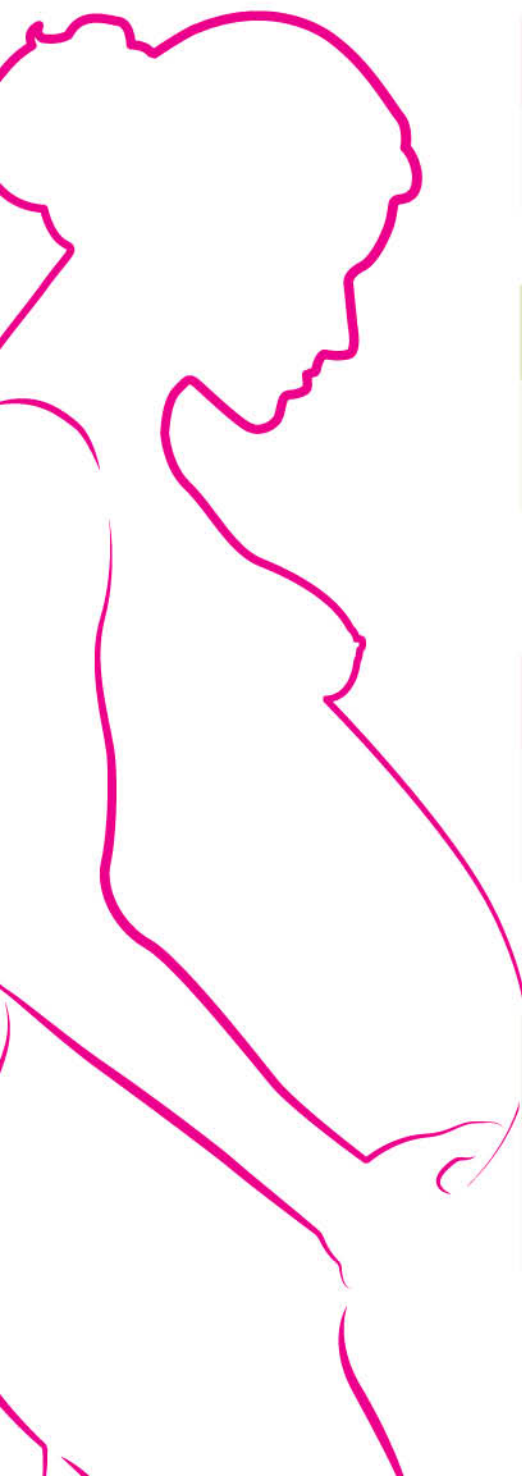
### Who should attend?

- All Consultants and Trainees in Obstetrics and Gynaecology
- Staff Doctors, Staff Grades, Trust Doctors and Associate Specialists
- MRCOG and Non MRCOG Obstetricians and Gynaecologist

### Course Organisers:

Dr Rishma Pai, FRCOG, Mumbai  
Miss Raneer Thakar MRCOG, Croydon  
Dr Ameet Patki FRCOG, Mumbai  
Honorary Director of Conferences: Mr Nick Panay FRCOG, London  
Honorary Deputy Director of Conferences: Mr Philip Tooze-Hobson FRCOG, Birmingham

# VITAMINS IN PREGNANCY

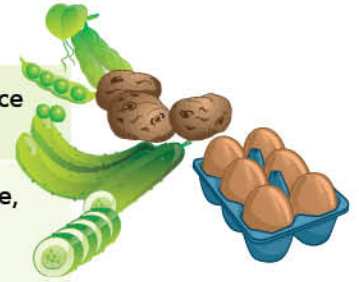


**Vitamin A**

The recommended dietary allowance is 800 IU

Sources of vitamin A

Dark green leafy vegetables, orange, sweet potato, papaya, and dairy products such as milk and eggs



**Vitamin D**

The recommended daily intake of vitamin D is 5 mg cholecalciferol or 200 IU

Sources of vitamin D

Fortified milk, egg yolk, and sunlight



**Folic acid**

The recommended daily intake is 0.4 mg per day

Sources of folic acid

Beans and legumes, citrus fruits and juices, whole grains, dark green leafy vegetables, poultry



**Vitamin B complex**

The recommended intake is increased

Sources of vitamin B complex

Dairy products, whole cereals, meat, and legumes



**Ascorbic acid (Vitamin C)**

The recommended daily intake of vitamin C is 85 mg

Sources of ascorbic acid

Oranges, berries, kiwifruit, cabbage, broccoli, cauliflower, brussels sprouts, capsicum, and tomato as it helps in absorbing iron





# DRUGS IN PREGNANCY

Sometimes drugs are essential for the health of the pregnant woman and the fetus. In such cases, doctors should consider and discuss the risks and benefits of the drugs with the women. For some disorders, it may be possible to change to a different category of drug prescribed. The following broad principles are useful while prescribing drugs to pregnant women.

1. Consider non-pharmacological treatment whenever possible
2. Analyze risks *vs.* benefits
3. Discuss the risk of a particular drug that cannot be avoided during pregnancy
4. Educate patient about the available antenatal screening to detect abnormalities in the fetus.

#### Drugs associated with fetotoxic effects when taken after the first three months

Drug taken by the mother	Possible effect on the infant
ACE inhibitors and angiotensin II receptor	Oligohydramnios (deficiency of amniotic fluid), growth retardation, antagonists lung and kidney hypoplasia, hypocalvaria, neonatal convulsions, hypotension, anuria
Aminoglycosides	Deafness, vestibular damage
Antidepressants	Neonatal withdrawal symptoms
Antiepileptics	Mental retardation, possibly autism/ Asperger's syndrome
$\beta$ -adrenoceptor antagonists	Possibly intrauterine growth retardation, neonatal bradycardia, hypoglycemia
Benzodiazepines	Floppy infant syndrome, neonatal respiratory depression, withdrawal symptoms
Cytotoxic drugs	Intrauterine growth retardation, stillbirth
Diethylstilbestrol	Vaginal adenocarcinoma transplacental carcinogen
Drugs of abuse	CNS dysfunction, intrauterine growth retardation
Narcotics	Neonatal respiratory depression, withdrawal symptoms
Non-steroidal anti-inflammatory drugs	Possible prolongation of gestation and labour, premature closure of ductus arteriosus, neonatal pulmonary hypertension
Phenothiazines	Neonatal withdrawal symptoms, impaired thermoregulation, extrapyramidal effects
Retinoids	CNS dysfunction
Salicylates	Fetal/neonatal hemorrhage
Sex hormones	Virilization of female fetus/feminization of male fetus
Sulfonamides	Hyperbilirubinemia, kernicterus
Tetracyclines	Staining of deciduous teeth, impaired bone growth
Warfarin/coumarins	Fetal hemorrhage, CNS abnormalities

#### References:

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3. Safer Prescribing 4th Ed Linda Beeley
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5. ABPI Data Sheet compendium 1993-94



## Maternal anxiety and depressive disorders is associated with early infant diseases

Maternal mental health during and prior to pregnancy is associated with gastrointestinal complaints and inflammatory diseases in the offspring. Researchers conducting a study reported that severe psychopathological symptoms during pregnancy were associated with inflammatory diseases and anti-infective medication, whereas symptoms during and prior to pregnancy include anxiety and depression diarrhea and colic complaints in infants.

Early Hum Dev. 2017 Apr 8;109:7-14.

## Physical activity in healthy pregnant and postpartum women: A beneficial approach

Regular physical activity during and after pregnancy is reported to provide beneficial effects in mother and child. Recent German recommendations have suggested that pregnant women without contraindications should be encouraged to remain active. Exercise for at least 150 min per week (analogically 20–30 min per day on most or all days of the week) in moderate to vigorous aerobic intensity has been recommended in healthy pregnant and postpartum women.

Gesundheitswesen. 2017 Mar;79(S 01):S36-S39.

## Local endometrial injury during ovulation induction improves chances of pregnancy in infertile women

Endometrial injury before ovulation induction has been reported to improve chances of pregnancy and its outcomes. A study was conducted to investigate the effect of endometrial injury on pregnancy outcomes among infertile women taking clomifene citrate. The clinical pregnancy rate was found to be significantly higher in those who received endometrial injury on cycle day 15-24 (37%) than in the control group (13%;  $p=0.006$ ).

Int J Gynaecol Obstet. 2017 Apr 11. doi: 10.1002/ijgo.12178. [Epub ahead of print]

## QUIZ Whiz

### 1. Risk of preterm delivery is increased if cervical-length is:

- A. 1.5 cm
- B. 2 cm
- C. 2.5 cm
- D. 3cm

### 2. Most common cause of the primary postpartum hemorrhage is:

- A. Uterine atonicity
- B. Coagulopathy
- C. Trauma
- D. Infection

### 3. The most common cause of tubal block in India is:

- A. Gonorrhoea infection

- B. Bacterial vaginosis
- C. Tuberculosis
- D. Chlamydia infection

### 4. Initial treatment of rectovaginal fistula should be:

- A. Colostomy
- B. Colporrhaphy
- C. Anterior resection
- D. Primary repair

### 5. Pregnancy should not be allowed in which of these conditions:

- A. ASD
- B. Aortic stenosis
- C. Mitral stenosis
- D. Eisenmenger's complex





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