



# CONNECT

The Newsletter ♦ Issue 4, July 2021

## BE THE EXCEPTION

### NEWER INVENTIONS IN OBGYN



## She... The STAR

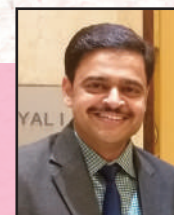
Sassy ♦ Talented ♦ Ageless ♦ Resilient



**Dr Vaishali Korde-Nayak**  
General Secretary, POGS



**Dr Sunita Tandulwadkar**  
President, POGS



**Dr Nilesh Balkawade**  
Clinical Secretary, POGS





She... The STAR

Sassy • Talented • Ageless • Resilient

# SHE - THE STAR

◆ Sassy ◆ Talented ◆ Ageless  
◆ Resilient

## EDITORIAL TEAM

“It’s hard to beat a person who never gives up.

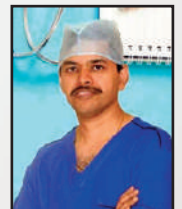
Babe Ruth”



Dr Hemant Deshpande



Dr Sabrina Bokil



Dr Amol Lunkad



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## PRESIDENT'S MESSAGE



Inventions are progressive and innovative methods of doing new things or doing the same things differently and more effectively.



**LEADERSHIP**  
is about **VISION**  
& **RESPONSIBILITY**  
not **POWER**

**Dear POGSians,**

Be a Trendsetter - Adopting Inventions in OBGYN

Obstetrics and Gynecology is a branch of medicine which is, metaphorically speaking, as old as the human race; but we have always been early adopters of new technologies and innovations, and have applied them to make our practice better, safer and easier. For example, Folic acid is a well known intervention to prevent NTD. Tweaking the technology to get Quatrefolic acid which is more effective molecule is an innovation.

This issue deals with exciting developments like fetal therapy, gene therapy, increasing use and applications of NIPT, use of lasers in TRAP sequence, etc.

Laparoscopy is believed to have changed the face of gynecological surgery forever and just as we have reached its threshold - robotic surgery comes as a new and exciting game changer!

In our series of interviews, with inspiring clinicians and teachers, comes another talk with a towering academician and doyen of OBGYN Dr. CN Purandare!

All our dreams can come true only if we have the courage to pursue them.

Happy reading.

**DR SUNITA TANDULWADKAR**  
**President, POGS 2021-22**



## GENERAL SECRETARY'S MESSAGE

Dear Friends,

### Greetings from Pune !

There is heavy rainfall everywhere. Hope you all are taking good care of yourself & your family. Let's Pray to lord Almighty to keep us safe.

In such vulnerable situations , 'Manache shlok' will guide us. Suggestions, recommendations, and instructions we should give to our mind for being in a healthy, happy, and peaceful state.

| Jai Shri Ram |

देहे त्यागिता कीर्ति मागे उरावी।  
मना सज्जना हेचि क्रिया धरावी।  
मना चंदनाचे परी त्वा झिजावे।  
परी अंतरी सज्जना नीववावे।। ८।।

Dehe tyagita kirti maage uraavi |  
Mana sajjana hechi kriya dharavi |  
Mana chandanache pari twa jhizave |  
Pari antari sajjana neevavave || 8 ||

Live an ideal life ....so that people remember you, after you depart from this world, for the good things you did throughout your life.

Oh my mind, always put such a goal before you, when you perform duties and do things for others in your life.

Oh my mind, live a life like sandalwood. Sandalwood gets worn out but keep giving its good fragrance to others.

Sandalwood gets completely destroyed but because of its properties it pleases and soothes the gentle and good people. || 8 ||

नको रे मना द्रव्य ते पुढिलांचे।  
अति स्वार्थ बुद्धी न रे पाप सांचे।  
घडे भोगणे पाप ते कर्म खोटे।  
न होता मनासरिखे दुख मोठे।। ९।।

Nako re manaa dravy te pudhilanche |  
Ati swarth buddhi na re paap saanche |  
Ghade bhogane paap te karm khote |  
Na hota mana sarikhe dukh mothe || 9 ||

Oh my mind, never hanker after the wealth or belongings of others or keep on expecting wealth from parents or ancestors.

Too much selfishness or thinking only about acquiring things for yourself results in accumulation of sins.

All your actions which ultimately make you suffer should be considered as sins and should be avoided.

Nothing is more painful when everything goes against you or nothing happens the way you want or the way you had planned. So do not plan too much or do not desire too much. || 9 || (English translation by Prof Kunte.)

Let's Pray we can conquer our minds.

Love

**DR VAISHALI KORDE-NAYAK**

**General Secretary, POGS 2021-22**



Yesterday I was clever,  
so I wanted to change the  
world.

Today I am wise, so I am  
changing myself.

**Rumi**



## BE THE EXCEPTION



“Man cannot Discover  
new oceans unless he  
has the courage to lose  
sight of the Shore”

Dear Friends,

***‘There is no exception to the rule that every rule has an exception.’***

Our future success is directly proportional to our Ability to understand adopt and integrate new technology into our work.

New technologies in obstetrics and gynaecology are coming up every day. Sky is the limit for any new invention in the form of newer approach to therapy, new Diagnostic technique, new drug, new machine, new molecular Technology and many more! Genetics, genomics, infertility, endocrinology and endoscopy are search fields where inventions are occurring every new day!

It is not possible to incorporate all the inventions in the field of obstetrics and gynaecology but this News Bulletin is an attempt to summarise various fields where inventions are taking place.

The vision of POGS President Dr Sunita Tandulwadkar is one such exception to the rule of common thinking. She has always thought out of the box not only in academics but also in practice. She has led different organisations effectively well with her novel ideas. I am thankful to her for allowing me to come up with these news bulletins.

I am also thankful General Secretary POGS Dr Vaishali Korde Nayak for her wholehearted support in this Endeavour.

The Editors for this News Bulletin Dr Hemant Deshpande, Dr Sabrina Bokil and Dr Amol Lunkad have worked tremendously hard to present what is the future and newer inventions in the field of obstetrics and gynaecology. Their untiring efforts have brought before you this excellent News Bulletin with crisp messages.

Modern medical advances have helped millions of people live a longer, healthier life. If this News Bulletin touches anyone heart and stimulates to dream about any new thing or invention, I feel the motive of this News Bulletin will be satisfied.

For any feedback on this News Bulletin kindly mail me on [nileshbap@gmail.com](mailto:nileshbap@gmail.com)

Happy Reading!

**DR NILESH BALKAWADE**  
**Clinical Secretary, POGS 2021-22**



## EDITORIAL TEAM'S MESSAGE

### Hello friends.

Hello friends and our dear colleagues.

This Covid19 pandemic has enforced various levels of restrictions on our social life but our thirst for knowledge and our endeavour to learn new things and do best for our patients is not restricted and still the same.

This Star Connect newsletter, an initiative by POGS, is to update each one of us on the various aspects of Obstetrics & Gynaecology. This newsletter aims at bringing the newer inventions and newer trends in OBGY practice. Remember where a new invention promises to be useful, it ought to be tried.

It is said Necessity is the mother of invention. An invention has to make sense in the world it finishes in, not in the world it started. In this newsletter we have brought to you some of the recent trends in Fetal therapy, gene therapy, prenatal testing, robotic gynaecology. We also discuss a newer drug on the block. We also share an unique case scenario.

This newsletter also brings you real life learning's of an iconic gynaecologist. This newsletter also focuses on social aspects by highlighting the work of an NGO in mother and child welfare. This newsletter will also update you regarding various POGS activities and the upcoming programs.

We hope to see you all soon personally and not virtually. Hope this newsletter finds you all in the best of the health and happiness. May you all enrich professionally and personally and contribute much more towards spreading health and happiness in the society. Have a great time ...

Happy Reading ...!!



Dr Hemant Deshpande



Dr Sabrina Bokil



Dr Amol Lunkad





# RENDEZVOUS WITH *Sunita*

## Zindagi-Ek Safar (Real Life Teachings)

At Pune's OBGYN society, today we're conversing with the legendary Dr. C.N Purandare who made us all proud by becoming the President Elect of the International Federation of Gynaecology and Obstetrics (FIGO).



RENDEZVOUS WITH  
*Sunita*

# Zindagi-Ek Safar (Real Life Teachings) Dr CN Purandare



## A BRIEF PROFILE OF THE MAN THAT IS A LEGEND - DR. CN PURANDARE

A dynamic leader, a medical marvel, an astute editor and an exemplary teacher — these are just a few words that can aptly describe Dr. CN Purandare. Known for transforming the face of obstetrics and gynaecology in India, he has forged alliances with the Health Department of the Government of India and State Governments, WHO, UNICEF, MacArthur Foundation, AMDD, IPAS, PSI and JHPIEGO. Internationally, Dr. Purandare has been conferred with Fellowship (Honoris Causa) by the RCOG (Royal College of Obstetricians & Gynaecologists) of the U.K. in 2009, Fellowship (Honorary) by the RCPI (Royal College of Physicians of Ireland) in 2013 and Fellowship (Hon) by the American College of Obstetricians and Gynaecologists 2014.

Along with this, he has over 80 peer-reviewed publications to his credit, countless contributions to international chapters and has honed the skills of over a thousand medical students. In honour of his contribution to the field, he has been presented with numerous national and international awards such as the Life Time Achievement Award by FOGSI, IFS of India, Rashtriya Gaurav Award, Laxmibai Adik Award, Ganatra Award and the B N Purandare Excellence Award among others.



***Dr. Sunita Tandulwadkar: Could you talk about your formative years in medical school?***

**Dr. C.N Purandare:** I joined medical college on a different note itself. My father wanted me to be-come an engineer and I was in an engineering school. When I was about 14 years old, my grandfa-ther was very seriously ill and we were very closely attached to him. A number of physicians from Bombay and the vicinity would often come to visit him and as a small child all I wondered was why wasn't anybody able to save him. Of course now when I look at it, he was already at the age of 87 and had enjoyed a great life. That was the time that I decided to change my field to medicine and become a doctor.

When I completed my S.S.C (Class XI in those days' time), I took up something known as 'Inter Science' with technical subjects such as electrical engineering, mechanical engineering et cetera. Af-ter the first year we were to choose a specialisation field — either engineering or medicine — I filled up all my forms at home to choose engineering and proceeded to St. Xavier's College to submit the papers. On my way, I changed my mind and shifted from A to B group. I came back home and told my father that I had chosen medicine as the field I wanted to pursue. He responded, "Well if that's what you want, then that's what you should do."

I joined Topiwala National Medical College which at that time was closest to our house in Bombay Central. If you ask about my formative years, medical school was really fun. For the first four and a half years, you are not determined to do anything in particular. With subjects like anatomy, physiolo-gy and a bunch of clinical ward work - it's great fun in the end with your group of friends. It's only when you complete your MBBS and move to do an internship and Res-idency is when you realise how much hard work goes into this field. It's no longer all fun and games like medical school.

When I completed my internship, I gave interviews for OB/GYN and was selected for this speciali-sation. I worked under Professor SS Thakur — I still have a picture of him. When I became the Pres-ident of FIGO, I gave the MOGS S S Thakur oration and he was sitting right there in the front row. It was a great sense of satisfaction to see my teacher sitting in front of me. I completed my MBBS and then MD from Nair College. I clearly remember during my MD, I was posted as a Registrar for one year at Bhagwati Hospital in Borivali. My boss was Dr. GB Belvi at that time and in the first month itself he told me, "You can go ahead and perform surgeries yourself, you don't have to wait for me. I think you're capable of handling it yourself."

At the end of one year, I had completed 150 major surgeries and that was something completely un-heard of for any resident doctor. In that time I did four radical Wertheims, he assisted me for the first one and later said, "You take it from here, I am waiting outside if you need any help." It gave me so much confidence to undertake various surgical techniques. We had so many house officers who were working with me and all of them did tremendously well in their respective careers. At the end of the day when you look at your life as a surgeon, you feel it is the volume of surgeries which makes you perfect, and makes all the difference.

***Dr. Sunita Tandulwadkar: After you completed your MD, instead of setting up a practice here, you chose to go to Ireland to study further despite having accomplished surgical skills. How was your experience in Ireland in the famous obstetric units ?***

**Dr. C.N Purandare:** Well, I went to Ireland purely by accident I would say. I was once at my in-laws place after completing my MD where I met Dr. Arun Mulgaonkar, one of the greatest obstetri-cians of our country — and one of the Mulgaonkar forcep fame. At that time, he was a consultant at Beijing Stoke Hospital close to London. He said to me, "Young man, you must come to the U.K to complete the remainder of your education. As soon as you finish your term, come to the U.K. and I will see that you get a job immediately." I went to London and started working under him as an ob-server. He asked me if I wanted to learn anything specific, at that time epidural analgesia was the 'in' thing, I told



him I wanted to work at a place where regional analgesia was being practised. He said, "There is only one person in the world who will teach you how to do analgesia during labour and you should learn from him — Dr. Fergus Meehan in Galway, Ireland."

So he wrote a letter to Dr. Meehan and unfortunately there was no reply because there was a postal strike in Ireland. So he told me, "Why don't you go to Ireland and meet him? I'll give you a copy of the letter. See what he can do to teach you, if not you can come back here." So I reached there on a Sunday morning. While I was waiting at the hospital, I saw an extremely dashing, well-dressed man driving a sports car walk in. I introduced myself and told him about what I had studied. He was sitting there in his armchair reading the letter I gave him and he said, "If Dr. Arun Mulgaonkar thinks you are good enough then you can start work tomorrow morning." That's how I ended up working in the University Hospital in Galway. I worked there for 5 years and didn't move out of that place before returning to India.

**Dr. Sunita Tandulwadkar:** *Sir you had a glorious career in Ireland and could have settled there very easily. How come you decided to come back to India?*

**Dr. C.N Purandare:** In 1982, times were very different back then and even though I had spent five years in Ireland, I wanted to return to my birth country. Although they were willing to give me a consultant job, I would always be like a second grade citizen in another country. In December, Dr. V.N Purandare was on his way to San Francisco for a conference, he stopped at Galway and told me, "Why don't you return to India? Why do you want to work in Ireland?" And that is how I came back to our country. Looking back, it was one of the most important decisions of my life. I would not have been a FIGO President if I would have remained in Ireland. Having said that, the Irish have a very similar mindset to Indians because they too were oppressed by the British. In fact, as luck would have it, my son travelled to India and became a doctor. Now, he is a consultant at the very hospital I worked at and he was born in Ireland. Sometimes, it's destiny that plays a very important role.



**Dr. Sunita Tandulwadkar:** *You have taken keen interest in FOGSI and are responsible to keep it growing at an international level. Could you highlight on the transformation of FOGSI and how you contributed to it?*

**Dr. C.N Purandare:** Well, I must give that credit to MOGS first. If I hadn't been to MOGS first, I would not have envisioned the growth of FOGSI. And of course to Dr. VB Patwardhan who was a consultant at JJ hospital at that time. I myself joined JJ Hospital one and a half year after coming back to India. He was a man of vision himself and promoted everybody. If he





would not have pro-moted me, I wouldn't have been in MOGS or FOGSI. Those days were again, of course, different. As you know, institutional rivalries were at its peak — you had KEM and Wadia on one side and JJ on the other. All the organisations were literally dominated and run by KEM and Wadia Hospital, other hospitals had no chance at all. It started off with MOGS where we all fought elections to even go into Pune OB/GYN society at various levels. Initially, we got the team of resident doctors together and I managed to get into the executive board of the MAGNICA committee of MOGS. It was Dr. PK Shah who came to me and said, "CN, we are on the periphery and nobody even looks at us." I told him, "Okay you join hands with me and I will see that you are in as well." That's how Sion Hospital got in as well. Now, you notice there is no such thing as lobbying, it is individual performance and capability that matters. Then, I moved into FOGSI because of Dr. Patwardhan who made me the Joint Secretary during his Presidentship. In one of the elections, I got elected as the Treasurer. I knew a lot about accounts. I managed my own accounts as well with my C.A when I was practicing. I realised that most of the treasurers of FOGSI were just blindly signing documents brought by the CA's without really understanding the paperwork. When I went into details, I found out that when I became the treasurer, FOGSI was actually in losses at -20,00,000 rupees. We had to pay the income tax which was accumulated, it would have wiped us out completely.

I went into depth and told the committee that if we are a charitable organisation then why do we have to pay income tax for all these years? So I went to the income tax office and recovered the money which was paid in the previous years and cancelled the current dues. Eventually, we modified the whole system of working — right from Treasurer to Deputy General et cetera. I transformed the entire system wherein people were just coming into office to warm their chairs. It was then nurtured into an extremely viable and financially strong organisation. Look at how much it has grown today. It is now worth crores of rupees!

We even moved from Purandare to Cama Hospital and eventually bought the office space in Parel. During that time, we faced so much opposition for buying that premises. Some of the comments that came our way were actually 'nau-seating', for lack of other words. It was Dr. P.K Shah and myself who insisted on buying that place. From that premises

then into Kamla Mills Compound, the organisation was growing from strength to strength. Look where we are today! It is now worth a fortune, one of the best and most organised systems in medical associations.

**Dr. Sunita Tandulwadkar: From FOGSI, how did your journey to FIGO happen?**

**Dr. C.N Purandare:** Before becoming President of FOGSI, I was the Secretary General there. It was Dr. Behram Anklesaria who was the FIGO representative from India on the board there. He said to me, "Ranjan (as I was called by close family and friends), I am not interested in pursuing my position at FIGO, why don't you go in my place if you are interested? Your experience there as a Committee Member and Council Chair would help you further. You are more likely to grow there as compared to me at this age." And that's how I attended many of the meetings in his place. In today's time, nobody else would vacate their place to give someone else a chance to go there. He was such a great man and saw potential in me.

I kept attending the meetings and then the Treasurer job came up. We went to South Africa with me as the Indian nominee, knowing very little about the international politics that goes into play. All I knew was that there was a job coming up and do you know who was my Lieutenant there? Handing our brochures to 40 people saying 'Vote for Dr. CN Purandare' was Dr. Shantakumari. This was way back in 2009. Unfortunately, I lost that election by three votes, and that was due to poor political manoeuvring. When I filed my papers, someone else from India had also filed their papers for another position and some people wondered how can two people stand from the same country? We both lost and realised this was one of the major blunders that happened.

Although I lost that election, when the President's position came up, I decided to apply. Many people wondered why my name was being proposed. Anyway, I went through a lot of hurdles in those days. So when I applied for the post of President, the Asia Oceania Secretary General called asking me to withdraw my nomination. I asked why, he replied, "India has already had 2 Presidents in the past, you have no business to apply." I said at the most I would lose, why should I withdraw. At that time they were supporting China. The Chinese people were very moneyed and each and every president, 130 in total, received a bone china set from the Chinese nominee as a gift. People asked me what are you going to send. I told them, "Nothing, we cannot afford such a thing. If I get elected - it would be great, and if I don't - that's also okay."

At an international level, there are so many things involved in politics — right from religion to colour. The election results were so close, it was down to the Chinese nominee and myself, eventually I won by a 60:40 ratio. It was absolutely phenomenal. People still remember when the screen showed a 60:40 ratio it was Dr. PK Shah who stood up overjoyed to







say hurray! All the members started looking at the Indian contingent and wondered who this gentleman was who was screaming with joy. That's how it all happened.

While I know previous Indian Presidents who were very illustrious did well, they didn't get the chance like I did to go further on in the organisation. I got 10 more people in the committee and our presence was felt widely. Our hard work was shown to everybody. We had the Scientific Committee Chair who did a phenomenal job at the Rio Congress. We had people like Dr. Sanjay Gupte, Dr. Jaideep Malhotra, Dr. Hema Diwakar or even Dr. Shantakumari - so many of them. Everybody who I thought could portray India's capability was chosen to be a part of the organisation. They did a fantastic job and I am very proud of them.

**Dr. Sunita Tandulwadkar:** *Just liked you changed the financial status of FOGSI, what was the role you played in FIGO as President?*

**Dr. C.N Purandare:** Before being the President, I was the President Elect for three years and I realised one thing – the organisation was completely dominated by non-Asians and Africans. The organisation was supposed to work for the underdeveloped, but none of the Third World countries had representation — nobody was in the Chair. Out of the 10 or 15 committees that were there, they were distributed between the US, some parts of Europe and the U.K. The first thing I said was a new rule we will follow is that if there are 10 positions to be filled, they will be equally distributed between the five zones. If there are 6 people in each committee, which makes about 60 in total, they too will be

equally distributed between all the regions of FIGO which is Europe, America, Latin America, Asia Oceania and Africa. I got the best talent from around the world to become the Chairperson and Committee Members at various positions. They did phenomenal work and believe me, in three years we changed the face of FIGO.

When these kinds of changes takes place, you develop enemies as well because you have a dislodged a system that belonged only to them. As Winston Churchill says though, 'You have enemies? Good. That means you've stood up for something, sometime in your life.' Eventually, I got this rule passed as a constitutional requirement that committee members need to be equally distributed from all regions and across genders. We had to give women an equal opportunity to grow. Unless it is enshrined in the rules and bylaws, nobody would follow it. Today so many people from Asia and Africa want to make their way through the organisation, because they now feel that they have a chance which was never there before.

**Dr. Sunita Tandulwadkar: Apart from these organisations, you have played a key role in women's health. Could you highlight the impact you created?**

**Dr. C.N Purandare:** If you take the example of FOGSI, there has been a sea of change when it comes to leadership roles. Earlier, it was only dominated by men and there were very few women at that point of time. From my Treasurer days till now, maybe more than half positions are taken on by women. It's not that men don't want to do a good job, it's just that the opportunity needs to be given to everybody.

I am of the belief that when you treat your juniors as colleagues or friends, it makes a world of difference. I remember my first day of surgery in Ireland, a major one was given to me because of the kind of work I had already done. Afterwards I went to my boss who was having a cup of tea, he asked me if I wanted some too. I told him, "Sir, I will make it myself," to which he replied, "No you were the one in surgery, you must be tired. I will make you some. And please don't call me 'sir,' my name is Fergus — you will call me Fergus from tomorrow. And remember one thing, I am Irish - I have no intention of getting knighted, so don't address me as 'sir'."

When I joined JJ Hospital as a consultant, I would treat all my resident doctors or even the junior most ones as friends. Every single day I would take them to the canteen and treat them to some good food and relax. It created such a good bond that even today they come to me when they need any kind of help or advice.

**Dr. Sunita Tandulwadkar: As Editor Emeritus, what's your take on Evidence vs Experience vs Expertise in the medical practice today. Dr. PC Mahaptra said, "Those who practice, cannot publish and vice versa," - what is your take on it sir?**

**Dr. C.N Purandare:** In 1982, I was at an oncology conference and Sir John Stallworthy who was Head of the Department as a Nuffield Professor of Obstetrics at Oxford. He was the boss's boss at Oxford and I was introduced to Dr. Stallworthy.







He looked at me and the conversation went this way:

Sir John Stallworthy: Hold on! Are you from India?

Me: Yes sir

Sir John Stallworthy: You're from Bombay?

Me: (quite taken aback) Yes

Sir John Stallworthy: You're a Purandare

Even my boss was shocked.

Sir John Stallworthy :Young man, you have a stamp on your face."

I wondered why he had not written a monogram, Sir John Stallworthy was by then a legendary name and therefore asked him.

Sir John Stallworthy: Does B.N Purandare have a monogram? Those who work have no time to write and those who write have no time to work.

This is the same thing that PC said, but situations are different. Today evidence-based medicine becomes the basis of a lot of things. Unfortunately there are bad sides of that as well. I have been a part of a number of WHO meetings where I have noticed that a lot of times people generate evidence. It is falsely generated by the help of pharmaceutical companies or instrument companies. These are then published in a number of journals to prove something that may be incorrect. Look at hysterectomies or mesh and see how things have changed over the years. You have to look at it with a pinch of salt. In places like India where evidence is so vast one cannot say that I did this and this is the way you must look at it. You must publish what you have done. If you have done 10,000 hysterectomies, show the evidence for it.

For example, let's look at allylestronol, the tablet which was said to treat repeated or threatened miscarriages and to prevent premature birth in pregnant women was said to be administered to a number of women. A number of journals published evidence based practices that said it would help in prolonging pregnancy which meant innumerable doctors started prescribing it. Over the last 20 years, the pharmaceutical company made millions. Only now has the medical fraternity realised that these tablets are worse than drinking a glass of water and don't make any difference. Recently, you have also heard about statins wherein the company did three trillion dollars of

business by prescribing it in America. Even the editor of the New England Journal of Medicine said that evidence that is being published like this is destroying the very fabric of medical care.

**Dr. Sunita Tandulwadkar:** *Do you think sir at our JOGI level you made a difference by not allow-ing such malprac-tices to come into the picture?*

**Dr. C.N Purandare:** I must give this credit to those who trained me as to how to look at the articles, understand and evaluate them - Dr. VN Purandare and Dr. RD Pandit. Both of them were so meticu-lous and they really trained me right from the junior level to evaluate the papers and understand the truth behind the publication. Good editors really make a lot of difference – no one should be sitting on that chair and certifying anything without verification — it would be injustice to medicine. Sub-sequent to me being there, there are number of editors who have done a com-mendable job such as Suvarna. I think JOGI is on the right path - we are producing very good quality content. I have time and again said that Indian surgeons are doing very well in their field. I have travelled all over the world,

but you cannot compete with the kind of surgeries we are doing in India. It is some-thing of which we should be proud of. It's time that we let our international peers know our value.

**Dr. Sunita Tandulwadkar:** *Apart from these associations and being a doctor par excellence, did you ever take time out for your hobbies? Could you please tell us about them?*

**Dr. C.N Purandare:** Cricket is something that is imbibed in me from the very beginning, whether there is a match at 2:00 am or 3:00 pm I will definitely watch it. If a wicket fell at 3:00 am, I would wake my son up we both would be really excited, while my wife would complain that we should go to sleep, it is the middle of the night. A lot of sport came into my family because of Nita, my wife, she has played badminton and excelled at it. Our children too love exercising — going to the gym or practicing yoga. But I must admit that besides medicine I have not really taken time out for anything else. It is after all a 24 hour job that we did — being there for every delivery, looking out for every patient – it gave its own kind of satisfaction.

**Dr. Sunita Tandulwadkar:** *Our last question sir, how would you describe Dr. CN Purandare?*

**Dr. C.N Purandare:** You are asking me a very difficult question, this is something someone else can answer — it would be rather difficult for me to describe myself. But I believe in one thing that suc-cess doesn't come just like that, it's a lot of hard work. It is your dedication to your profession that makes you succeed. Hard work, hard work and hard work – is the basis of everything. If you think that you are so-and-so's relative and your life will be made, it is never like that — people who are sons and daughters of great surgeons and obstetricians, sometimes wither away as non-entities.

Personally, for me, I would attribute my success to my three teachers – Dr. Thakur, Dr Belvi and Dr. Patwardhan who were all from GMC at JJ Group of Hospitals. In fact, JJ Hospital further nurtured me for 20 years to become what I am. Today, I would say that my students have been my greatest teachers. What I learnt from them in life has been tremendous and it has helped me grow as an indi-vidual. When I became FOGSI President, in my inaugural speech I put up the names of all my resi-dents. Someone then said, "It is for the first time that someone of this stature has shown his gratitude to resident doctors." So I think they are the ones who have made me what I am today.

**Dr. Sunita Tandulwadkar:** *So hard work, success, passion is one part. Do you think the blessings of God have helped you go ahead? Are you a spiritual person?*

**Dr. C.N Purandare:** I believe that everything is destiny. Everything is written on your forehead. I don't believe in God, but as a doctor I must say, sometimes we work really hard and save lives but there are other times when we work equally hard and we lose the patient. We are all only tools in the hands of the Almighty. Doctors are not God themselves, if someone tells me that you are God, I ab-solutely disagree - I am just a tool in His hand. I do my best, and if it succeeds then I'm happy about it. It's not something I can guarantee and that is the way life is.







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## Recent Advances In Fetal Therapy And Gene Therapy



### ABSTRACT

Recent advances in the molecular diagnostics like next generation sequencing, imaging modalities, procedure related instrumentations and robotics has provided much needed impetus in the field of fetal diagnostics and management of congenital disorders and malformations in utero. Recent success in treating hemoglobinopathies by gene therapy has opened new avenues for fetal therapies. Here we discuss specific fetal therapy modalities in context to recent advances in fetal gene therapy and fetal surgery and other intervention techniques.

**Keywords:** fetal therapy, gene therapy,

### INTRODUCTION

Pregnancy and childbirth is an important phase in the life of a couple. Unfortunately, not all pregnancies end in a healthy baby. The prevalence of congenital anomalies in India is 6-7% which translates to around 1.7 million birth defects annually <sup>(1)</sup>. Congenital anomalies may be structural or functional in nature pertaining to the organ system involved. If untreated, such congenital anomalies may perpetuate and compromise the outcome of pregnancy.

Over years Prenatal diagnosis of congenital diseases has advanced with the advent of high resolution ultrasonography, fetal MRI, and innovations in molecular genetic testing in form next generation sequen-



cing<sup>(2)(3)</sup>. Fetal whole exome sequencing (WES), coupled with imaging – ultrasound/MRI and molecular testing of cell-free DNA present in maternal blood, has unlocked the potential to diagnose and thus treat congenital disorders in utero.<sup>(4)</sup>

Fetal therapy can be defined as all interventional modalities viz medical, surgical, lesser or non invasive procedures performed on fetus (in utero) or administered to the pregnant mother with the intention to prevent, correct or treat fetal anomaly or a medical disorder. Evolution of Fetal Therapy can be traced to late 1900s. It involved early interventions performed during pregnancy prior to birth of baby to prevent or treat life-threatening birth defects. Such therapies comprise open surgeries or a less invasive methods like fetoscopy, blood transfusions or specific medication given to the mother. Spina bifida and lower urinary tract obstruction (LUTO) are two types of birth defects that can be treated with fetal therapy or surgery.

Specific Fetal therapy approaches have shown to curb fetal morbidity and mortality and to improve fetal outcome. With recent advances, research and development of sophisticated instruments Fetal therapy is evolving and certain procedures have become more feasible. For example, antenatal magnesium sulfate treatment may reduce the risk of cerebral palsy associated with preterm delivery.

Broadly interventions under fetal therapy can be categorised as:

1. Fetal medical therapies
2. USG guided fetal therapy
3. Fetal endoscopic therapy
4. Fetal surgical interventions
5. Fetal (in-utero) gene/stem cell therapy

Here we outline the recent advances in various forms of fetal therapies, newer techniques of fetal surgical interventions, in utero gene therapy components and highlight advancements in viral and non-viral delivery platforms that could be utilized to achieve fetal gene transfer.

## **FETAL INTERVENTIONS AND SURGERY**

Surgical interventions are often performed on fetus with specific congenital anomalies in utero to help improve the long-term outcome of baby. Due to the advances in technical field, robotics and instrumentation of sophisticated surgical equipment many fetal congenital anomalies are now amenable to various surgical and less invasive or non-invasive modalities of management. Various case reports and studies have highlighted the utility of such interventions to improve fetal outcome in conditions like spina bifida, meningomyelocele, bladder outlet obstruction, fetal tumors etc. Study done at Mayo clinic showed that spina bifida repair done in utero triggers the fetal body's ability to restore normal brain structure and anatomy along the course of development during pregnancy.<sup>(5)</sup>

Few conditions amenable to fetal surgery and interventions are listed below.

- Fetal shunts for fetal bladder outlet obstruction
- Cord occlusion (bipolar, radiofrequency ablation (RFA) and interstitial laser).
- Myelomeningocele repair
  - ♦ Amniotic band syndrome – release of band
  - ♦ Bronchopulmonary sequestration of the lung
  - ♦ Congenital cystic adenomatoid malformation (CCAM) of the lung
  - ♦ Tracheal occlusion for Congenital diaphragmatic hernia (CDH)
  - ♦ Congenital high airway obstruction syndrome (CHAOS)
  - ♦ Twin reversed arterial perfusion (TRAP) sequence (Photocoagulation of planetary vessels)
  - ♦ Twin-twin transfusion syndrome (TTTS) by laser therapy

The survival rate has been shown to be significantly higher in fetuses treated with the Intra-Uterine-Shunt due to LUTO (lower urinary tract obstruction) than with the pigtail solution. Also the shunts showed a significantly lower rate of early dislocation. Renal function reported normal in 72% of the newborns in the study.<sup>(6)</sup>

Open maternal-fetal surgery for in utero closure of myelomeningocele (MMC) is now a standard management for prenatally diagnosed open neural tube defects. Further studies have shown utility irrespective of maternal BMI which was thought as a deterrent previously.<sup>(7)</sup>





Fetal surgeries are invasive with risk to mother and fetus, in form of preterm delivery, chorioamnionitis, chorioamniotic membrane separation, placental abruption, uterine rupture, and all subsequent pregnancies to be delivered via caesarian delivery. Importantly fetal surgery is intrinsically limited to the correction of congenital structural abnormalities and does not address the root cause ie. underlying genetic diseases. Fetal therapy is ultimately performed on two patients: the mother and her fetus so ethical considerations are essential for such studies and clinical implementation.

### **IN UTERO GENE THERAPY AND STEM CELL THERAPY**

Gene therapy is defined as the insertion, alteration, or removal of genes within individual cells and biological tissues to treat a disease. Gene or genome editing technologies allow genetic material to be added, removed, or altered at particular locations in the genome

The delivery of genetic material to target cells in a developing fetus has several advantages viz small size of the fetus, maximizes delivery vector titer per weight of recipient, hence facilitating efficient gene transduction. Also reducing the dosage of delivery vectors required per recipient.<sup>(8)</sup> Fetal permeability of the blood-brain barrier (BBB) permits potential treatment of central nervous system(CNS) disorders with gene therapy which may not be possible postnatal. via systemic delivery The fetal immunologic immaturity allows introduction of antigens (e.g. vector materials, transgenes) without a limiting immune response and with the induction of antigen-specific immune tolerance<sup>(9)</sup>. Chan et al., utilized viral vectors to achieve curative levels of human factor IX in a fetal macaque model of Hemophilia B, while demonstrating a high degree of immune tolerance and no long-term adverse effects of vector or transgene expression after four years<sup>(10)</sup>. The abundant population of fetal stem cells are easily accessible as ideal targets for therapeutic genetic correction. Also due to the enhanced potential for expansion of fetal stem cells with propagation of the genetic correction, migration, and distribution in the fetal microenvironment can lead to a long term therapeutic effect. Direct access to fetal circulation via ultrasound-guided puncture of the umbilical vein in the late second trimester or even direct intracardiac injections earlier in gestation may assist in delivery of transgenes to specific fetal tissues during pregnancy.

Fetal gene delivery platforms must also achieve a delicate balance of transduction between its two recipients, maximizing transfer to the fetus and minimizing transfer to the mother To avoid unintended effect to other tissues, delivery of the gene therapy vector should be tightly regulated. The vector genome must sustain transcriptional expression in light of epigenetic modifications to achieve lifelong expression.

### **The various approaches to In Utero Gene Therapy are listed as-**

- a) Viral delivery platforms for In Utero Gene Therapy
  1. Retroviruses
  2. Lentiviruses.
  3. Adenoviruses
  4. Adeno-associated viruses(AAVs)
- b) Non-viral delivery platforms for In Utero Gene Therapy
  1. Physical methods
  2. Inorganic nanoparticles
  3. Polymer-based nanoparticles
  4. Lipid-based nanoparticles
- c) Gene editing techniques
  1. CRISPR-Cas9 Gene Editing
  2. Restriction Enzymes
  3. Zinc Finger Nucleases (ZFNs)
  4. Transcription activator-like effector nucleases (TALENs) Gene Editing



### **Advantages in delivery of gene therapeutics to the fetus <sup>(11)</sup>:**

- (1) Significant dose advantage due to small fetal size;
- (2) long-term proliferation of transduced cells is possible due to highly accessible population of progenitor cells;
- (3) Tolerogenic immune system limits a robust immune response to exogenous genetic material and delivery vehicle;
- (4) Fetal shunts maximize bioavailability of transgenes in the systemic circulation;
- (5) Permeable blood brain barrier (BBB) permits treatment of postnatally inaccessible central nervous system disorders

Use of plasmids is probably the oldest gene therapy technique. However the effects of such plasmid mediated gene therapy are often transient, with effects diminishing after every cell replication. In addition, plasmids are an inefficient method of actually delivering the gene product due to low cell uptake rates of the plasmid.<sup>(12)</sup> Viral vectors have good genomic integration profile, but again off target effects and genotoxicity is an issue encountered. Non-viral vectors have better safety profile, good transfection efficacy but few concerns of efficacy of delivery systems exist.

Recently CL11A inhibition following infusion of autologous CD34+ cells transduced with gene therapy by CRISPR-CAS9 and lentiviral vector, has shown to be an effective target for HbF induction thus decreasing the clinical manifestations of sickle cell disease in adults and teenage patients.<sup>(13) (14)</sup> Using an adenoviral delivery approach to excise the mutant Sftpcl73T gene via CRISPR-mediated Non Homologous End Joining (NHEJ) in fetal mouse model of surfactant protein C deficiency Alapati et al. were able to demonstrate rescuing its neonatal lethal phenotype in a subset of mice<sup>(15)</sup>. However, immunogenicity of adenovirus vectors is an issue of concern limiting the clinical translation in the current scenario. AAV and novel non-viral delivery platforms can be the potential alternatives, need to be investigated.

**Nanoparticle Based Gene Therapy** is another interesting field in development. With the rapid advancement in the field of nanotechnology, nano sized materials were identified to be the perfect candidate for non-viral vectors in gene delivery. The biggest advantage of nanoparticles is that their surface can be engineered in many possible ways to deliver the drugs/vectors directly to the target site<sup>(16)</sup> This was shown by R S Riley et al group who developed a library of ionizable lipid nanoparticles (LNPs) for in utero mRNA delivery to mouse foetuses and demonstrated that LNPs can deliver mRNAs to induce hepatic production of therapeutic secreted proteins<sup>(17)</sup>

**CRISPR-CAS** [clustered regularly interspaced short palindromic repeats- CRISPR-associated protein (Cas)]

Much constraints in the viral and non viral gene therapy were addressed by the genome editing techniques. Nuclease-independent systems (TALENs, ZFNs) have lesser drawback profile such as off-target effects, immunogenicity, and cytotoxicity. CRISPR-CAS has overcome many major limitations compared to TALENs, ZFNs and Restriction Enzymes. With Researchers developing CRISPR-Cas9 therapies for a wide range of diseases, CRISPR-Cas9 is poised to revolutionize medicine. CRISPR-Cas9 therapies under development include inherited eye diseases, neurodegenerative conditions such as Alzheimer's and Huntington's disorders, and non-inherited diseases such as cancer and HIV. CRISPR human trials are underway for many of these diseases.

Using the CRISPR system, researchers can precisely edit any target DNA locus which was not possible using other gene editing tools. Precise editing a disease mutation to correct genetic errors creates opportunities for treating disease conditions that have long eluded the medical research community. Advances in CRISPR – CAS and CRISPR/Cas-derived editing systems, have transformed the gene therapy landscape. Their ability to edit genomic sequences with versatility and facilitate gene correction/insertion/disruption have broadened the spectrum of potential gene therapy targets. This has accelerated the development of potential curative therapies for many rare diseases treatable by transplantation or modification of HSCs

The first cases treated and cured of beta thalassemia and sickle cell disease after their own genes were edited with CRISPR-Cas9 technology, with this approach were recently published. The two researchers Dr. Damiano Rondelli, the Michael Reese Professor of Hematology at the UIC College of Medicine, who invented this technology received the Nobel Prize in Chemistry in 2020. The researchers by using CRISPR-Cas9 gene editing modified the DNA of stem cells by deleting the gene BCL11A, the gene responsible for suppressing fetal hemoglobin production. Stem cells started producing fetal hemoglobin so that patients with congenital hemoglobin defects (beta thalassemia or sickle cell disease) make enough fetal hemoglobin to overcome the effect of the defective hemoglobin that caused their disease.<sup>(18)</sup>





### USFDA APPROVED GENE THERAPIES

Recently USFDA has approved license for gene therapies for genetic disorders like spinomuscular atrophy, Duchenne muscular dystrophy, Beta-Thalassemia, retinitis pigmentosa, Retinal Dystrophy, certain forms of acute lymphoblastic leukemia (ALL), Large B-cell Lymphoma etc. for use in eligible patients<sup>(19)</sup>. In utero gene therapy thus will receive further impetus for further research and advancement. Many studies and clinical trials are currently underway at various stages for gene therapy targeting different genetic disorders.

### In utero stem cell transplantation (IUSCT)

Amongst all the likely prenatal treatments available or under trial, in utero stem cell transplantation (IUSCT) is probably the most promising. It doesn't involve myeloablation or immunosuppression hence avoids various associated risks and complications. Safer postnatal management is another advantage.

IUSCT confers advantage over postnatal stem cell management. Due to Fetal immunologic immaturity, engraftment of allogeneic cells sets in before fetal immune system maturation, thus enhancing donor-specific tolerance and life-long chimerism<sup>(20)</sup>. Despite host cell competition within the fetal and maternal immune systems, as well as practical aspects of IUSCT, progress is being made—preclinical studies are underway to overcome these barriers and achieve successful clinical implementation.

Before 14 weeks' gestation sites for hematopoiesis has not yet developed in the fetal bone marrow, also the Thymic processing of self-antigens has not yet started, and differentiated T cells have not yet been released into the circulation and hence fetus is receptive to the engraftment of circulating hematopoietic stem cells. At this stage, foreign HSCs without myeloablation should engraft without inducing an immune rejection or graft-versus-host disease. Human leukocyte antigen (HLA) matching is not required. Additional cells or bone marrow from the same donor may be transplanted postnatally as specific tolerance for donor antigen is induced in the fetus.

### IUSCT can be therapeutically utilised as:

- A single IUSCT resulting in levels of engraftment adequate to treat monogenic conditions as sickle cell disease (SCD)
- IUSCT that induces donor-specific tolerance, allowing for a second same-donor (non-myeloablative, non-immunosuppressive) transplant postnatally to boost engraftment to clinically relevant levels.

IUSCT is a promising approach for treating conditions like Haemoglobinopathies, Sickle cell disease and other conditions amenable to stem cell therapy. In future the onus will be to develop gene and stem cell therapies targeting the fetus so as to prevent the onset of pathogenesis of such disorders in the fetus in the first place.

### Other miscellaneous approaches towards fetal therapies

Apart from stem cell and gene therapies various other modalities of fetal intervention are also simultaneously being evaluated with mixed response. Animal and in vitro studies have shown encouraging results. Castleman JS et al showed that Intravenous immunoglobulin (IVIg) and novel monoclonal antibody (Nipocalimab) treatments, if started at the end of the first trimester, may attenuate the transplacental passage and fetal effects of IgG antibodies and to improve fetal survival in severe presentation of haemolytic disease of fetus and new born due to maternal red cell alloimmunisation when early in utero transfusion was performed.<sup>(21)</sup> Combination of Ig fetal therapy (FT) and neonatal therapy (NT) with antiviral drugs has been found to be more effective in improving neurological outcomes of newborns with symptomatic congenital CMV as compared to NT alone in study done by Tanimura K group.<sup>(22)</sup> Recently Livingston J et al reported a first safe and effective in-utero therapy with rapamycin for a rapidly enlarging, obstructive, fetal cervical lymphatic malformations (LMs)<sup>(23)</sup>

A few recent studies on gene therapy in animal and humanised models across various medical conditions have been listed in **table 1**. These approaches have the potential of being utilised for in utero gene therapy.

**Table 1. List of some of the recent therapeutic gene editing studies in in vivo preclinical and clinical models**

Disease	Target organ	Gene editing tool	Delivery system	Therapeutic modality	Reference
SCD	Humanized mouse and SCD disease model	CRISPR/Cas9 and transposase system	Intravenous injection of a bimodular HDAd5/35 <sup>++</sup> vector	Combined transposase-based integration and CRISPR/Cas9-mediated gene disruption	(24)
HBV	Mouse liver	TALEN	Hydrodynamic injection of two plasmids encoding the editing machinery	Gene disruption of HBV sequences	(25)
HTI	Mouse liver	CRISPR/Cas9	Hydrodynamic injection of ssDNA donor template	HR-mediated point mutation correction	(26)
Hunter's syndrome	Mouse liver	ZFN	Systemic injection of AAV2/AAV8	NHEJ- or HDR-mediated integration into albumin locus	(25)
Hemophilia A and B	Mouse liver	ZFN	Systemic injection of AAV8	HDR- and HITI-dependent gene insertion	(27)
HTI	Mouse hepatocytes	CRISPR/Cas9	Hydrodynamic tail-vein injection of Cas9 and sgRNAs	NHEJ-based gene disruption	(28)
DMD	Cranial tibialis muscles in dogs	CRISPR/Cas9	Intramuscular injection of AAV9	DMD gene restoration in ΔEx50 DMD canine model by exon 51 skipping	(29)
LCA type 2	Young adult eye	Human retinal pigmented epithelium-specific 65(RPE65) complementary cDNA under RPE65 promoter	Subretinal injection of rAAV2/2	AAV-mediated transduction	(30)
Age-related macular degeneration	Adult mouse eye	CRISPR/Cas9	Subretinal injection of specific Cas9 RNP	NHEJ-based gene inactivation	(31)
Retinitis pigmentosa	Transgenic mouse model with human <i>Rhodopsin</i> gene	CRISPR/Cas9	Electroporation of Cas9 and dual gRNAs in mouse retina	NHEJ-based gene knockdown	(32)
Huntington disease	Mouse brain	CRISPR/Cas9	Stereotactic injection of AAV1	SNP-based allele-specific editing of <i>Htt</i> gene	(32)
Rett syndrome	Mouse brain	CRISPR/Cas9	Stereotactic injection of AAV1/2	NHEJ-based disruption of multiple genes	(33)
β-Thalassemia	Mouse model of human β-thalassemia	Triplex forming PNA	Intravenous injection of nanoparticles containing donor DNA	PNA-mediated gene editing	(34)
β-Thalassemia	Humanized mouse and thalassemia mouse blood cells	Transposase	Intravenous injection of HDAd5/35 <sup>++</sup> vector	Transposase-based gene integration	(35)(36)
β-Thalassemia	Rhesus macaques	Transposase	Intravenous injection of HDAd5/35 <sup>++</sup> vector	Transposase-based gene integration	(37)

## CONCLUSION

While fetal surgery and IUSCT have shown to have specific clinical applications, they are limited in scope and utility. In contrast, in utero gene therapy offers a promising and a minimally invasive solution to prevent pathogenesis of a variety of monogenic congenital genetic disease. A fetus is uniquely poised for gene therapy given the physiological barriers but various vectors viral and non viral have shown to overcome such limitations in various studies. Given the strong gene transfer profiles but also potential genotoxicity in viral vectors, non-viral vectors CRISPR-CAS in particular has proved to be advantageous. With success of gene therapy in patients recently demonstrated for spinomuscular atrophy, hemoglobinopathies etc, in utero fetal gene therapies will certainly receive a much needed boost in arm.

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# THE FUTURE OF MEDICINE



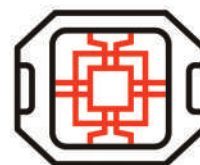
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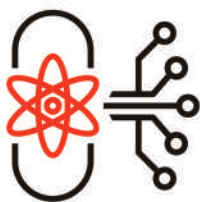
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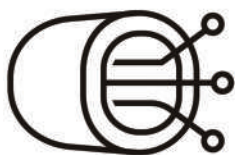
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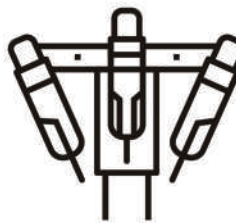
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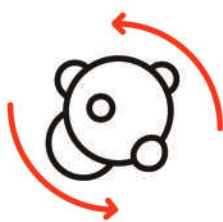
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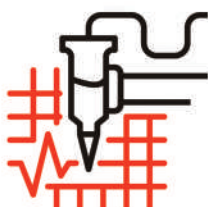
ROBOTIC SURGERY



NEURAL  
INTERFACE



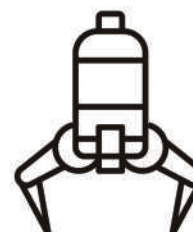
METABOLISM



BIOPRINTING



CONVERSATIONAL  
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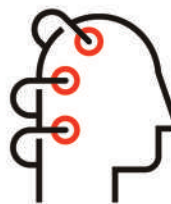
NANOROBOTICS



BIOINFORMATICS



ENERGY  
DEVELOPMENT



NEUROPROSTHETIC  
DEVICES



OCIMETICS  
BIONIC LENS

# QUATREFOLIC ACID... A MAGIC BULLET

*-“An undernourished mother inevitably gives birth to an undernourished baby perpetuating an intergenerational cycle of undernutrition.”*

Pregnancy is a time of rapid and profound physiological changes from the time of conception until birth. Nutritional requirements increase during pregnancy to maintain maternal metabolism and support foetal growth and development. Poor maternal nutrition status is associated with poor maternal and fetal outcomes.<sup>1</sup>

Quatrefolic is a glucosamine salt of (6S) -5-methyltetrahydrofolic acid and is structurally analogous to a biologically active form of folic acid. It is a metabolized form of folic acid that is no longer dependent on the MTHFR enzyme, and it can be used directly by the organism, even in people with the MTHFR mutation.

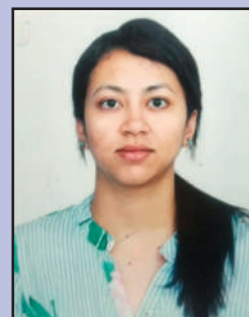
Folate is a generic name for a naturally occurring family of B-group vitamins. Folates are widely distributed in nature and are essential for the maintenance of cellular functions and health. As humans (and other mammals) cannot synthesize folates, they must be obtained via diet. However, natural folates (the first generation) are susceptible to oxidation, they rapidly lose activity in foods and have a bioavailability range of 25- 50%, depending on kind of food.

## GENERATION OF FOLIC ACID:

Generation	Folate
1 <sup>st</sup>	Refers to the various tetrahydrofolate derivatives naturally present in foods
2 <sup>nd</sup>	Folic acid: synthetic oxidized molecule, that does not occur in nature but can be utilized by the human body as a precursor to form natural folates that are biologically active
3 <sup>rd</sup>	Reduced folate - Calcium salt of 5-methyltetrahydrofolate
4 <sup>th</sup>	(6S)-5-methyltetrahydrofolate glucosamine salt

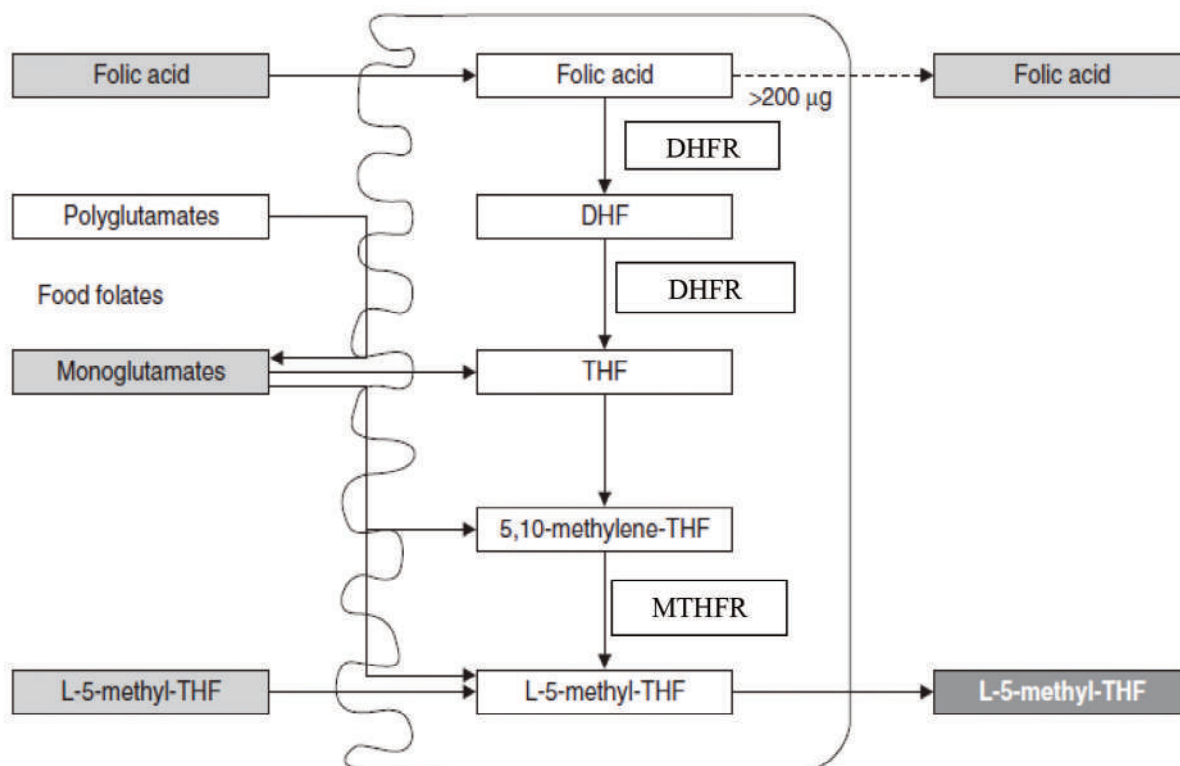


**Dr Hemant G. Deshpande**



**Dr Alisha Das**





On the contrary, folic acid, the synthetic form of monoglutamyl folate, is almost completely stable for months or even years and can be considered as a “second generation of folate, the stable one”<sup>(8,9)\*</sup>. In order to diffuse all cells into body through the circulatory system, the folate monoglutamate must be transformed in the 5-methyl-tetrahydrofolate form, which passes by diffusion from blood into all body cells. Oral supplementation with folic acid increases the body’s pool of 5- methyltetrahydrofolate in healthy and diseased individuals.

Folate-requiring reactions, collectively referred to as “one-carbon metabolism”, include those involved in

- amino acid metabolism
- purine and pyrimidine synthesis
- formation of the primary methylating agent, S-adenosyl- methionine (SAM)<sup>2</sup>.

Folate (vitamin B9) is widely accepted to protect against fetal neural tube defects. The main sources of dietary folate are folic acid-fortified foods and folic acid-containing dietary supplements. Folic acid is inactive in the human body and must be converted into methionine, the biosynthesis of glycine from serine, and the biosynthesis of DNA precursor molecules. Therefore, folate is fundamental for growth, especially in the embryonic and fetal stages.. Some of the risks can be avoided by supplementation with 5-MTHF rather than folic acid. Because 5-MTHF does not require activation, it is immediately available to mother and fetus and does not accumulate in blood like folic acid does in cases of reduced hepatic transformation.<sup>5</sup>

- Most commonly used folate supplement is folic acid, a synthetic oxidized form of folate, which is more stable and more readily absorbed than naturally occurring folates

#### **DISADVANTAGES OF 1ST , 2ND AND 3RD GENERATION FOLIC ACID:**

- Bioavailability of folic acid is lower than that of (6S)5-MTHF

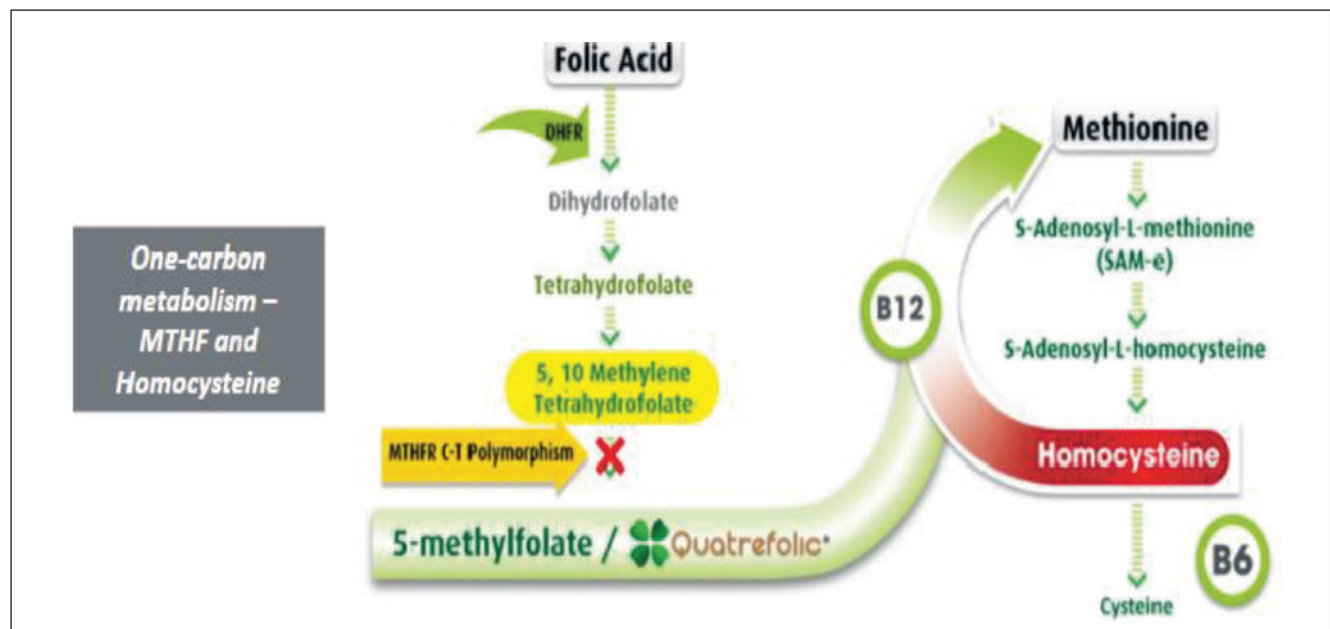
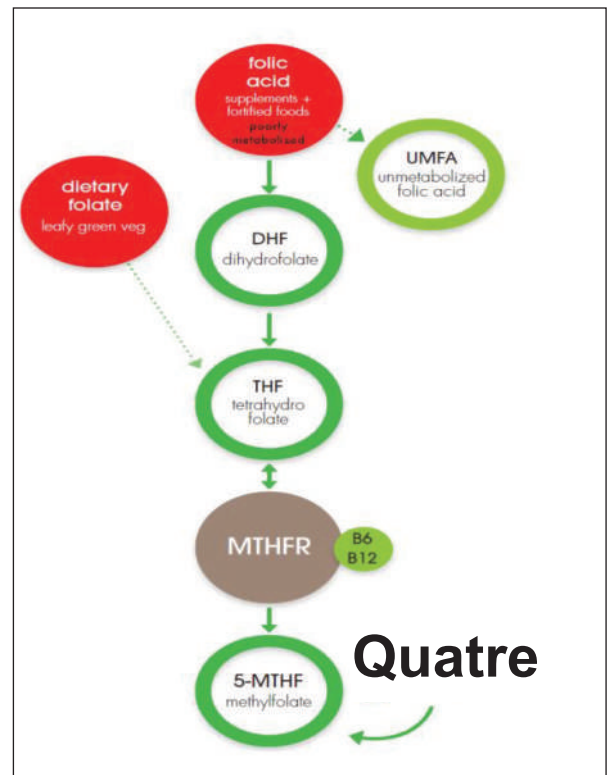


- Enzymatic conversion of folic acid into (6S)5-MTHF is a saturable process
- UMFA can be incorporated in tissues and be reduced in a vitamin B12 independent pathway to THF so masking a vitamin B12 deficiency. If not correctly diagnosed, vitamin B12 deficiency can result in irreversible neuropathy
- MTHFR gene mutations affect over 40% of the world population – being unable to convert folic acid to its active form
- 5-methyltetrahydrofolate calcium salt (the third generation) however,
  - ♦ Has low solubility
  - ♦ Only stable at 2 – 8 degrees

#### QUATREFOLIC ACID

- 4th generation folic acid
- A novel, patented folic was developed by Gnosis i.e. glucosamine salt of (6S)5-MTHF
- Structurally analogous to the reduced and active form of folic acid
- Delivers a “finished” folate the body can immediately use without undergoing any kind of metabolism
- (6S)5-MTHF glucosamine salt represents the fourth generation folate
  - ♦ long lasting stability as well as a peculiarly high water solubility
  - ♦ Improved bioavailability and
  - ♦ Well established safety

Quatrefolic passes through the gastric barrier and is absorbed mainly in the small intestine by a process facilitated by a glucosamine salt carrier, which ensures the extremely high water solubility of Quatrefolic® and therefore higher folate absorption and better bioavailability.





#### **CLINICAL EVIDENCE OF QUATREFOLATE:**

- Administration of [6S]-5-MTHF is more effective than folic acid supplementation at increasing red blood cell folate concentrations in women of childbearing age
- Supplementation with [6S]-5-MTHF might be an adequate alternative to folic acid for increasing folate status and, thus, for reducing the risk of having an NTD-affected pregnancy<sup>9</sup>
- A physiological dose of 5-MTHF bypasses the MTHFR block and is suggested to be an effective treatment in patients with MTHFR polymorphism. It also avoids potential adverse effects of the UMFA syndrome<sup>10</sup>
- Couples with a long history of infertility should be analysed for MTHFR and homocysteine and should be treated with physiological doses of 5-MTHF instead of high doses of folic acid
- [6S]-5-methylTHF appears to be as and perhaps more effective in preserving maternal folate stores during lactation than an equimolar amount of folic acid<sup>11</sup>

#### **PHARMACOLOGY:**

- Dose: 527.25mg of 9(6S)- 5 MHTF  
(527.25 mcg of 5MTHF- glucosamine(Quatrefolic) = 570 mcg of Dietary Folate = 285 mcg of Folic acid )<sup>12</sup>
- (6S)5-MTHF glucosamine salt showed
  - ♦ 1.8 times higher bioavailability than Ca salt
  - ♦ Upto 3.1 times higher bioavailability than folic acid
- AUC<sub>8h</sub>
  - ♦ 1.12 times higher than Ca salt
  - ♦ Upto 10 times higher than folic acid<sup>13</sup>
- AUC and C<sub>max</sub> were significantly higher, and t<sub>max</sub> significantly shorter for [6S]-5-MTHF compared with FA
- [6S]-5-MTHF was more effective at increasing total plasma folate concentrations compared with FA
- As [6S]-5-MTHF is not known to have any potential adverse effects, this natural and biologically active form of folate could be an alternative to FA supplementation<sup>14</sup>

#### **MOST COMMON USES OF FOLATE / QUATREFOLIC® FOLATES APPLICATION AREAS :**

- Neural-tube Defects, Irritable bowel disease Male and female infertility
- Cognitive impairment in elderly Spontaneous abortion Lifestyle putting people at risk of low folate levels: Smoking
- Alcohol
- Excess Eating disorders Low vegetables intake Chronic dieting Coronary heart disease Epilepsy
- Macrocytic anemia Mood
- Elevated homocysteine levels MTHFR SNPS4

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<b>Folic acid</b>	<b>6S-5-MTHF glucosamine salt</b>
Itself is not active and must be metabolized through several steps in order to enter the folate cycle	Main folate form in blood and cord serum. It is already the biologically active form. It can enter directly the folate cycle
Unmetabolized folic acid is found in blood at doses >200 µg /day	No unmetabolized folic acid with 5MTHF
Lesser bioavailability	Higher bioavailability: Pre-clinical study in vivo showed a plasmatic (6S)-5-MTHF concentration peak about 3 times higher than folic acid
High doses of folic acid can mask vitamin B12 deficiency and delay its diagnosis by correcting haematological signs	As it is already the biologically active form, it doesn't mask the vitamin B12 deficiency
Folic acid upper tolerable limit is 1mg /day	No upper tolerable limit in US dietary reference intakes
Metabolism affected by MTHFR polymorphism	As it is already the biologically active form, the problem of people with MTHFR polymorphisms doesn't exist anymore
Not soluble in water	Totally soluble in water

<b>6S-5-MTHF calcium salt</b>	<b>6S-5-MTHF glucosamine salt</b>
Lesser bioavailable	Study has shown that it is 10% more bioavailable than 5MTHF Ca salt
100 times less soluble in water than 5MTHF Glucosamine salt	Totally soluble in water
Stable only at temperature between 2-8°C	Is lyophilized and is stable at room temperature 25°C



**Dr Supriya Nair**

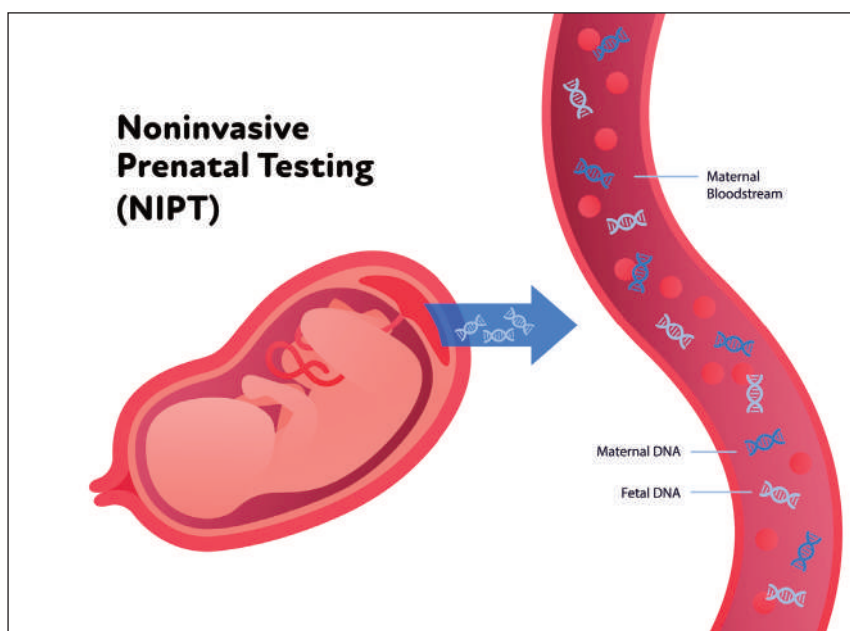


**Brinderjit Singh Buttar**



**Dr Sunita Polampalli**

## NIPT: A Quantum Leap in Genomic Solution



Non-invasive prenatal testing (NIPT) is an emerging pregnancy screening option that offers early genetic screening for chromosomal conditions as early as 10 weeks into pregnancy, utilizing just one tube of blood. Among the many benefits of noninvasive testing, NIPT stands out since it is totally

safe with no risk to mother and baby, provides high detection rates, and low false-positive results. Other prenatal screening and diagnostic tests may require multiple blood draws leading to more than one visit to the laboratory and carries a higher risk of false-positive results<sup>1-4</sup>. NIPT even outdoes diagnostic tests, such as chorionic villus sampling (CVS) or amniocentesis which provide definite results for most chromosome conditions but have an associated risk of miscarriage.

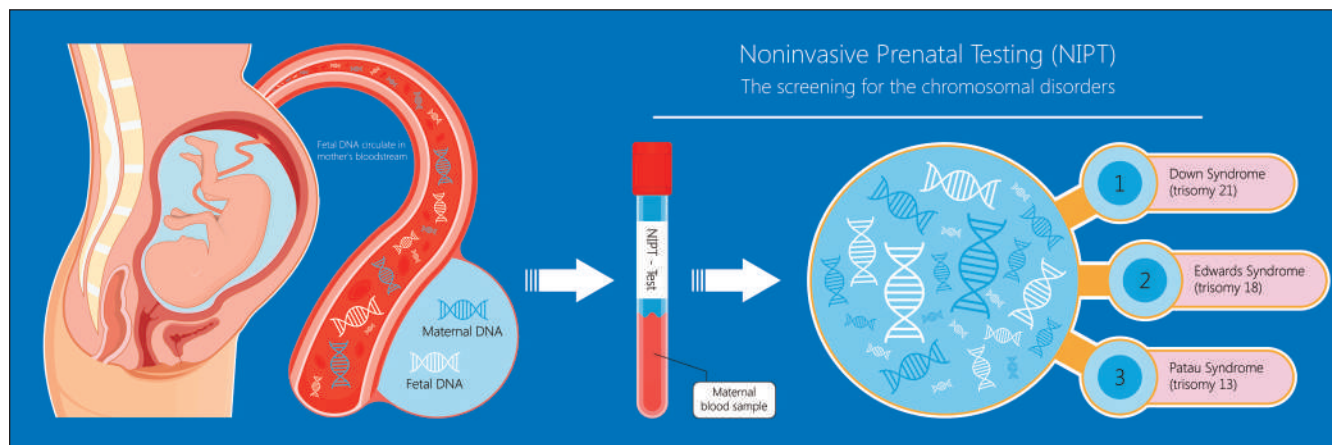
### How Does NIPT Work?

NIPT screens for common chromosomal conditions including trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome), and trisomy 13 (Patau syndrome) by analysing cell-free DNA (cfDNA) from maternal blood sample which is a mixture of fetal and maternal DNA.

A typical NIPT workflow begins by isolating plasma from maternal blood and further extracting cfDNA from this plasma for analysis. Sophisticated analysis is then applied to the data which is constructed from the extracted cfDNA.

**Prenat-Next (NIPT)** uses whole-genome sequencing with next-generation sequencing (NGS) technology to analyse cfDNA fragments across the whole genome. This methodology has established advantages over other NIPT methodologies including targeted sequencing and array-based methods. Whole-genome sequencing surpasses other methodologies considering the fact that test failure rates are substantially lower<sup>4, 7-8</sup>.

NGS, with its high levels of accuracy and sensitivity, produces quality data that is needed for reliable analysis of the trace amounts of cfDNA found circulating within blood plasma.



### Positioning NIPT – To be used in all pregnant women regardless of age or risk factors

Previous guidelines recommended use of NIPT only in high-risk women with singleton pregnancies. cfDNA use on twin pregnancies was not recommended. According to the American Congress of Obstetricians and Gynecologists (ACOG) 2016, risk factors included:

- 1) Maternal age 35 years or older at delivery
- 2) Fetal USG findings indicating an increased risk of aneuploidy
- 3) History of a prior pregnancy with a trisomy
- 4) Positive test result for aneuploidy, including first trimester, sequential, or integrated screen, or a quadruple screen
- 5) A parental balanced Robertsonian translocation with increased risk of fetal trisomy 13 or trisomy 21

The new joint committee guidelines issued by ACOG and Society of Maternal Fetal Medicine (SMFM) 2020 expands prenatal aneuploidy screening to all pregnant women regardless of their age or risk factors and highlights that cfDNA-based testing can be performed in twin pregnancies. It also concludes that NIPT is the most sensitive and specific screening test available for common fetal aneuploidies. The guideline also highlights unique aspects of SNP-based NIPT technology, including detection of triploidy, use as early as 9 weeks, and the ability to assess zygosity and individual fetal fraction when testing twins.

SMFM continues to recommend the following as important points to consider regarding the use of cfDNA and other tests for aneuploidy:

- 1) cfDNA is a screening test, and both false positive and false negative results occur. This is particularly true in lower risk women, in whom a positive test is more likely to be a false positive.
- 2) Women who desire definitive information about chromosomal conditions in their pregnancy should be offered the option of amniocentesis or CVS.
- 3) Diagnostic confirmation with CVS or amniocentesis is recommended for women with abnormal cfDNA results, particularly if clinical decision-making will change depending on the presence of aneuploidy.
- 4) Irreversible decisions such as pregnancy termination should NOT be undertaken based solely on cfDNA results.
- 5) A negative cfDNA result indicates a decreased risk and does not definitively rule out trisomy 21 or other chromosome conditions.
- 6) Women with failed cfDNA tests are at increased risk for aneuploidy, and therefore need careful counseling about further testing, including the offer of diagnostic testing.

### Sensitivity and Specificity

The advantages of NIPT is its low false positive rate (1–3%). Fewer positive findings may allow women to avoid unnecessary invasive procedures to confirm an inaccurate screening result. Miscarriage rates for invasive procedures may be elevated in low resource situations where skilled providers are less prevalent.

The new joint committee guidelines issued by ACOG and Society of Maternal Fetal Medicine (SMFM) 2020 ex-





Aneuploidies	Sensitivity (true positive rate)	Specificity (true negative rate)
Down syndrome (47,+21)	>99%	>99%
Edward syndrome (47,+18)	97–99%	>99%
Patau syndrome (47,+13)	87–99%	>99%
Turner syndrome (45,X)	92–95%	>99%

pands prenatal aneuploidy screening to all pregnant women regardless of their age or risk factors and highlights that cfDNA-based testing can be performed in twin pregnancies. It also concludes that NIPT is the most sensitive and specific screening test available for common fetal aneuploidies. The guideline also highlights unique aspects of SNP-based NIPT technology, including detection of triploidy, use as early as 9 weeks, and the ability to assess zygosity and individual fetal fraction when testing twins.

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### Limitations

- 1) Fetal fraction (the amount of fetal DNA among total circulating cell-free DNA in maternal serum) can be greatly influenced by maternal body mass index, ethnicity, gestational age, type of aneuploidy, singleton pregnancy versus multiples, and mosaicism. A low fetal fraction can presumptively lead to a false negative result.
- 2) NIPT is not diagnostic; reports in literature confirm examples of both false positives and false negatives.
- 3) In the case of twins, surviving placenta from a demised twin can release cfDNA, leading to a false positive result (or in theory, a false negative result). Although the test failure rate is higher in twins and the detection rate may be lower, it's crucial to note that most NIPT assays are validated for twin pregnancies. Higher order multiples are not usually tested by NIPT.
- 4) Maternal chromosomal abnormalities can lead to a false positive result viz. mosaic constitutional chromosomal abnormalities or copy number variants, presence of a bone marrow or tissue transplant and, in rare cases, maternal malignancy.
- 5) Different genotype of the fetus and the placental trophoblast, either 'confined placental mosaicism' or 'true fetal mosaicism' with feto-placental discordance, can lead to a false positive or false negative result respectively.

- 6) NIPT may not detect rare mosaic or partial trisomies of the targeted chromosomes.
- 7) Given that NIPT can produce false positives, there is also a concern that reliance on NIPT will increase the number of healthy fetuses aborted.
- 8) Invasive tests also detect chromosome abnormalities, like translocations, inversions, and Mendelian genetic conditions that are not currently included in commercial NIPT.

### **The Way Forward**

Future advances in NIPT technology holds the promise to expand the range of conditions that can be detected, including common Mendelian conditions, a broader range of sub-chromosomal conditions and single gene disorders which may provide families with accurate information about these conditions within the legal abortion timeframe. The inclusion of single gene disorders like thalassemias or sickle cell disease may be particularly useful in India.

Genetic counseling remains the focus of attention in NIPT. It will be pivotal to train more genetic counselors and to educate clinicians on how to lead the way for women going through the perplexing and emotional decisions they will stumble upon as prenatal testing options expand.

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## Robotic Surgery-Next Frontier In Minimal Invasive Surgery



### OVERVIEW:

Minimally invasive surgical procedures avoid open invasive surgery in favour of closed or local surgery with less trauma. These procedures can often be done vaginally or involve use of laparoscopic instruments. Laparoscopy allows observation of the surgical field through an endoscope or similar device, and is carried out through small incisions in the skin to allow access into the pelvis or abdomen. This may result in shorter hospital stays, or allow outpatient treatment.

The da Vinci system is a robotic operating system, approved by the U.S. Food and Drug Administration for gynaecologic surgery in 2005, is one of the newest technologies available for the treatment of gynaecologic problems including hysterectomy and ovarian surgery for cancer and other conditions such as pelvic organ prolapse.

For most patients, robotic surgery can offer numerous potential benefits over traditional approaches to vaginal, laparoscopic or open abdominal hysterectomy, particularly when performing more challenging procedures like radical hysterectomy for gynaecologic cancer or sacrocolpopexy for pelvic organ prolapse. Potential benefits include:

- Significantly less pain
- Less blood loss
- Fewer complications





- Less scarring
- A shorter hospital stay
- A faster return to normal daily activities

It enables gynaecologists to offer an effective minimally invasive approach for benign gynaecologic conditions requiring surgery. Compared to conventional laparoscopic surgery, robotic assistance minimizes conversions as well as the need for total abdominal hysterectomy. The excellent visualization (3D HD vision), dexterity (Endowrist instrumentation) and control (intuitive motion) provide surgeons with a surgical option to approach pathology minimally invasively, safely, reproducibly & even in high risk patients with adhesive disease, obesity.

In gynaecology robotic surgery has many applications:

1. Benign hysterectomies (fibroids, AUB)
2. Surgeries for prolapse, SUI (sacrocolpopexy, hysteropexy, burch colposuspension)
3. Endometriosis
4. Gynaecological oncology
5. Tubotubal recanalisation

Success in adoption of a surgical modality is highly dependent of the learning curve associated with acquisition of the necessary skills to comfortably and efficiently perform it. For the surgeon, robotic surgery overcomes some problems of conventional laparoscopic surgery. Muscular efforts are minimized because improved ergonomics when sitting at a console separate from the patient. Furthermore, combination of improved imaging and instrument control could allow for a faster surgical learning curve compared with conventional laparoscopy, which includes two-dimensional imaging and counterintuitive hand movements. However, even if the use of robot-assisted technology is believed to shorten the learning curve of complex minimally invasive procedures, the number of cases required for proficiency in robotic-assisted gynecological surgery is not clear.

Surgeons should be skilled at abdominal and laparoscopic approaches for a specific procedure before undertaking robotic approaches.

## **ROBOTIC-ASSISTED SURGERIES**

### **• PATIENT SETUP : POSITIONING**

As with conventional gynecologic laparoscopy, patients are placed in a modified dorsal lithotomy position. It is imperative to place the patient with her sacrum as close to the edge of the operating table as possible in order to ensure adequate space for uterine manipulation; recognizing that Trendelenburg often results in cephalad movement of the patient.. Since most robotic surgeons prefer that the arms are tucked and adducted to the patient's sides, proper arm placement and cushioning are necessary to help prevent nerve compression and subsequent injury.

### **UTERINE MANIPULATION**

Depending on the procedure, a uterine manipulator is not only useful but essential for successful execution and completion of the surgery. Since the surgeon sits some distance from the bedside and is unable to control uterine manipulation without leaving the console, it is essential to have an experienced professional at this position. The choice of manipulator is dependent on surgeon preference and availability.

### **• ROBOTIC COMPONENTS**

The da Vinci system is composed of three components that work together: the patient cart, the da Vinci vision tower, and the surgeon console.

### **PATIENT CART**

The patient cart has three or four arms that dock onto the camera and robotic trocars placed at the bedside (Figure ). The robotic instruments are placed through these trocars and are manipulated by the surgeon seated at the console.

Compared to conventional laparoscopy, these instruments have 7° of freedom versus 4°, scaled down motion, and tremor filtration. Robotic-assisted surgery also eliminates the fulcrum effect of laparoscopy, in which the instrument moves in the opposite direction of the hand movement, thus providing the surgeon the ability to operate as if performing open surgery in a minimally invasive manner. Docked to the patient cart is the camera trocar, through which the da Vinci vision system is placed.

## DA VINCI VISION TOWER



The Vision Tower represents the brain of the robot (Figure ). This system is composed of two cameras, each with a separate light source, that provide three-dimensional, high- definition images to the surgeon console. On the Si system, there are two cameras available in different sizes, 8.5 and 12 mm. There is a 0° lens and a 30° lens for each size, which can be placed up or down depending on the location of the surgical anatomy. For the newer Xi system, there is only a 8 mm camera option.

## SURGEON CONSOLE

The surgeon console is placed away and in direct line of site from the patient cart and operating bed. The console houses the binocular viewer, and camera and instrument controls that are manipulated through the use of pedals and hand controls (Figure). Through these controls the surgeon is able to manipulate all of the instruments and camera to magnify the view up to 15-fold. The ability to sit while operating provides multiple ergonomic advantages, both physical and cognitive, compared to conventional laparoscopy.

Available for the da Vinci Si and Xi systems is the option for a dual console. This enables two surgeons to operate at the console together, and is useful when training residents and new robotic surgeons.

## • DOCKING & PORT PLACEMENT



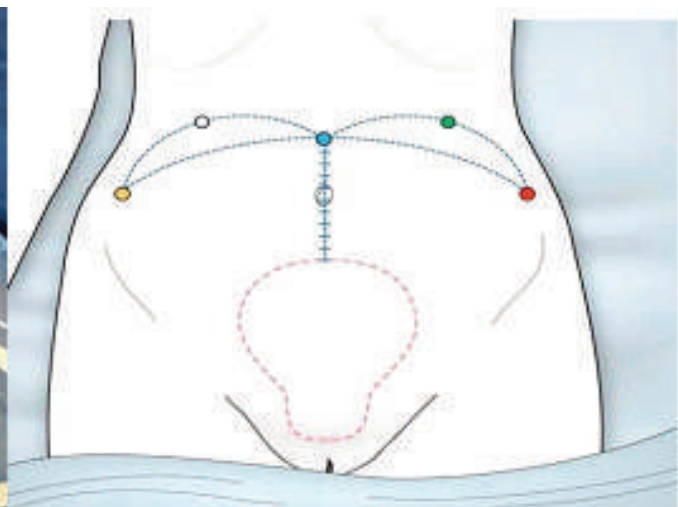
Accurate port placement is essential in a robotic-assisted procedure. If the robotic ports are placed incorrectly, either operative arm collision will occur or the wristed instruments will not achieve their full dexterity. The robotic endoscope enters the abdominal cavity through a 8mm cannula placed at or above the umbilicus usually 20 cm above pathology to be treated. Robotic instruments enter 8 mm steel cannulas. The placement of the accessory ports varies with the type of procedure planned. Procedures involving structures in the pelvic cavity, such as hysterectomy have similar port placements.

Two or three 8 mm steel trocars are then placed 8 cm lateral to central port in same line. If the fourth robotic arm, is used, the steel trocar can be placed in either the right or left lower or upper quadrant, inferior and lateral to the other robotic instrument port, at least 8 cm apart (Figure 1). Such placement enables optimal movement of the robotic arms, minimizes the risk of collisions, and enables access to the pelvic floor. Robotic monopolar scissors, hook, or spatula, and bipolar forceps may be placed through the bilateral lower quadrant trocars. The electrosurgical scissors allow for dissection and resection, while the bipolar forceps are used for traction and electrodesiccation (Figure). A non-energized instrument such as a forceps or retractor may be placed through the upper quadrant port. A 5–12 mm assistant port is also placed 1–2 cm above the camera port, between the camera port and one of the 8 mm trocars. Through this port, the assistant can introduce suture, instrumentation used for retraction, a suction-irrigator, vessel-sealing device, surgical clip applicator, or laparoscopic specimen bag.

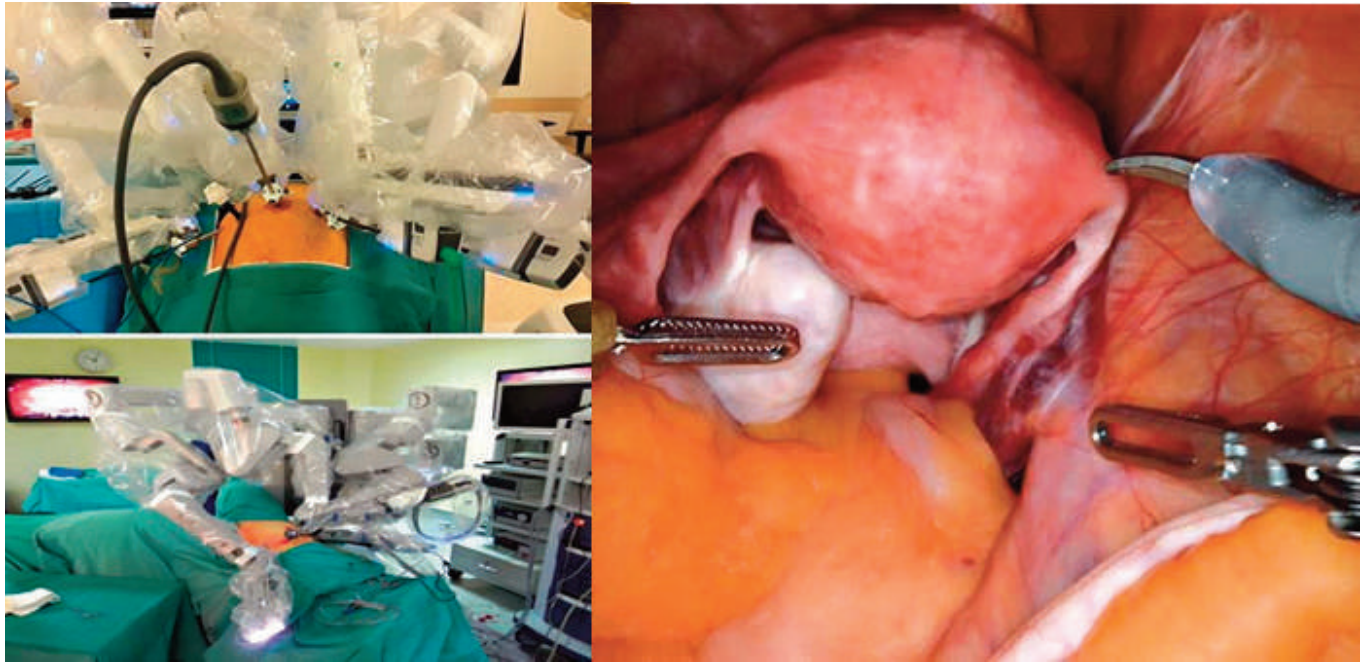
The docking of the da Vinci patient cart is often the most cumbersome and precise part of the procedure. The side-docking method has been incorporated into gynecologic surgery to aid in vaginal surgery, uterine manipulation, cystoscopy, or accessing the rectum. The parallel side-docking method has been used, where the base of the patient-side cart is directly adjacent to the base of the operating table. The column of the patient side cart is advanced to the level of the midhigh if the camera port is inserted through the umbilicus. It may be adjusted accordingly if the camera port is moved superiorly to accommodate upper abdominal procedures. The camera arm is then aligned to the midline of the patient, and the remaining arms are attached systematically.

#### • OPERATING TECHNIQUE

After docking the robot, any gynecological procedure can then be performed in the manner described with conventional laparoscopy.







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# Trap Sequence In An IVF Pregnancy Successfully Treated With Laser Coagulation - A CASE REPORT

## INTRODUCTION

Twin reversed arterial perfusion (TRAP sequence) is a rare condition of monochorionic twin pregnancies in which one twin does the work of supplying blood for both twins. Twin supplying blood is known as 'Pump twin', the other twin is known as 'Acardiac twin' - lacks a heart or has one that is not fully formed. Incidence is 1/35000 births & 1/100 monochorionic twin pregnancies. A 36 year old female with previous history of one IVF failure with adenomyosis conceived in IVF cycle with self embryos diagnosed antenatal with Monochorionic Diamniotic twin pregnancy with TRAP sequence, successfully treated with LASER coagulation at 14 weeks.

## CASE SUMMARY

### History

36 year old female from Pune with previous one IVF failure with k/c/o Adenomyosis. She was a case of primary infertility married for 10 years, her menses were regular with history of moderate dysmenorrhea. No history of any medical illness. She had a history of Myomectomy with right ovarian endometriotic cystectomy done in 2018. She had done 1 IVF cycle outside with self eggs but that was failure.

### Initial Evaluation / Investigation findings

WIFE Investigations: Hb: 11.4, Blood group: A Positive, RBS: 111gm/dl, TSH: 1.83, PRL: 13.68, AMH: 2.49, HIV: NEG, HBsAg: NEG, VDRL: NEG, HCV: NEG, Rubella IgG - Immune, Hb Electrophoresis - normal. BP: 130/70mmHg, BMI: 29.

USG: Bulky uterus with posterior & fundal wall adenomyosis, Endometrial cavity normal, endometrial thickness 8mm, AFC Right - 5, Left - 5.

HUSBAND: Semen Analysis count: 20million/ml, Total Motility: 20%, Morphology: NORMAL -1% - Asthenoteratozoospermia.

Husband : HIV: NEG, HBsAg: NEG, VDRL: NEG, Blood Group : B Positive.

### Treatment Details

Tab. Antioxidant with multivitamin 1OD for 1 month, Tab folic acid 5mg 1OD for 1 month, Antagonist stimulation protocol : Inj. rFSH 225 IU for 12 days, Inj. HMG 75 IU for 12 days with Inj. rHCG 250mcg for trigger .



**Dr Amol  
Lunkad**



**Dr Amit  
Magdum**



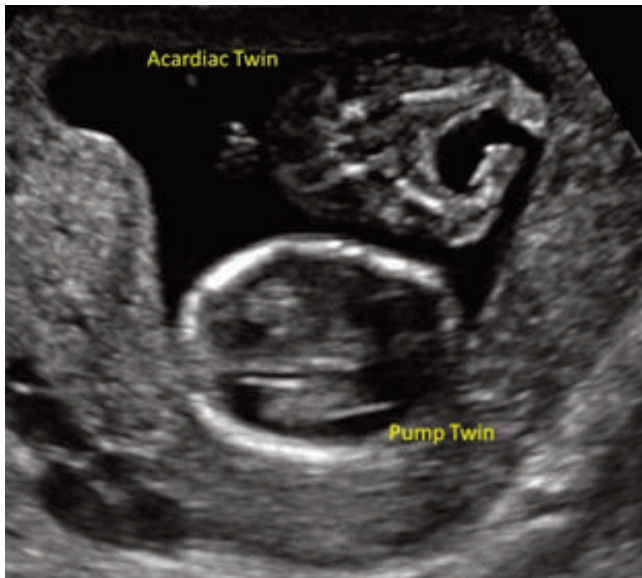
**Dr Ishita  
Lunkad**



**Dr Ramesh  
Gaikwad**

**Response to Stimulation at Ovum pickup-** 10 Oocyte Cumulus Complex, 9 Mature Oocytes, 2 Blastocysts 4AA formed. Both Blastocysts Vitrified on day 5.

**Post Ovum Pickup** – down regulation done with 2 Injections of GnRH Agonist depot 3.75mg given 28 days apart. Frozen embryo transfer done in a down regulated HRT cycle. Both Blastocysts were transferred. Beta HCG levels were 2200 mIU/ml. Her sonography at 7 wks confirmed a diamniotic monochorionic twin pregnancy with single live fetus. At 12 weeks sonography a diagnosis of monochorionic twin pregnancy with Trap Sequence was done with one partially developed acardiac fetus and the other normal fetus acting as the pump twin. The acardiac fetus had an incompletely formed skeleton, with no head, upper limbs, or heart (as shown in fig 1 below). On color Doppler imaging, the umbilical artery in the abnormal fetus showed reversal of flow. This appearance was typical of a TRAP sequence with an acardiac parabolic twin (acardius acephalus / acardius chorioangiopagus parasiticus). Normal fetus that is the pump twin had normal nuchal translucency and nasal bone at 12 weeks sonography. Couple was counseled and the decision for laser coagulation of the cord of the acardiac twin was decided.



**Figure 1.** Ultrasound picture of the monochorionic twin pregnancy with TRAP Sequence. Showing the Acardiac twin & the Pump Twin.

LASER Coagulation (Interstitial LASER) of umbilical vessel of Acardiac Twin done successfully at 14weeks under trans abdominal sonography guidance with aseptic precautions. As shown in the figure 2 while doing the laser coagulation. AMNIOCENTESIS with Fetal Karyotype & Microarray done of first Twin which was normal.



**Figure 2.** Ultrasound picture during doing of the laser coagulation of the umbilical cord of the Acardiac twin in TRAP sequence.





Early Anomaly scan done which was normal. High risk pregnancy care was given to her during her pregnancy. She was diagnosed with Gestational diabetes at 24wks and was started on Metformin and her sugars were monitored and well controlled on Metformin 500mg thrice a day. She underwent an elective LSCS at 37 weeks and delivered a healthy female baby of 2.6 kg.

## DISCUSSION

TRAP sequence represents a variant of conjoined Twins in which chorionic circulation is shared. Organogenesis defect due to anastomosis in the placenta during early embryonic period is suggested in the pathogenesis of TRAP sequence. In Acardiac fetus placental blood circulation between Acardiac fetus & donor fetus is provided by artery-artery & vein-vein anastomosis. In the TRAP sequence, the normal twin 'pumps' or 'donates' blood to the abnormal twin, which is called the 'recipient' or 'perfused' twin through abnormal artery-to-artery or venous-to-venous communications in the placenta. There is a reversal of flow in the recipient twin, with relatively oxygenated blood flowing from the abnormal anastomosis to the umbilical artery; the flow then proceeds cranially, leaving the fetus via the umbilical vein; hence the term, TRAP sequence. This finding can be confirmed by pulsed Doppler of the umbilical artery of the recipient twin, which will reveal reversal of flow on the spectral waveform. Antenatal diagnosis made by absence of heart on ultrasonography & revealing placental vascular anastomosis with Doppler diagnosis can be made by ultrasound at the end of the first trimester. Congenital anomalies are present in about 9% of pump twins. The overall perinatal mortality of pump twins is 50-55%, being usually due to either polyhydramnios leading to premature delivery or secondary to congestive cardiac failure; high-output cardiac failure develops due to the increased cardiac output secondary to the abnormal interfetal circulation. Goal of therapy is salvage of Pump Twin. Invasive methods towards eliminating Acardiac Twin are selected. Discontinuation of blood flow to Acardiac Twin is the method.

1. Coagulation of umbilical cord
2. Endoscopic umbilical cord ligation.
3. Sclerosis of umbilical cord with alcohol.
4. Thermo-coagulation of umbilical cord & Aorta under USG guidance.

Mortality for Acardiac Twin is 100% and Pump Twin is 50%

## CONCLUSION

TRAP sequence is a complication that is seen in Monochorionic Twin pregnancy & it has a poor prognosis. Early selection of proper treatment modality by making the diagnosis with typical ultrasonography and Doppler finding is of great importance for a successful pregnancy outcome.

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**Dr Amol  
Lunkad**

## #Social Initiative

### **SURAJYA SARVANGIN VIKAS PRAKALP- NGOs for URBAN SLUMS – Changing Lives!**

**Surajya Sarvangin Vikas Prakalp** (run under the aegis of Swargiya Nana Palkar Smruti Samiti, Pune) a social organization is working for the upliftment of the downtrodden society living in the slums of PUNE (Yerwada, Vishrantwadi, Viman Nagar, Wadgaonsheri, Chandan Nagar, Wagholi and Koregaon Park) for the last 20 years. Surajya commenced its operations in May, 2001 in six slums and today after 20 years it has its footprints in 54 slums. The main objective of the above projects is to improve the quality of lives of the slum dwellers and make them better citizens. They have focussed on women and child welfare with education and health being the main areas of upliftment work. The various projects which it has embarked during the last 20 years are as follows –

1. Education including computer literacy.
2. Women Empowerment including Micro Financing Initiatives (Mahila Bachat Gat).
3. Self- Employment Courses.
4. Adolescent Girl's Education.
5. Youth Development.
6. Health.
7. Value Education.
8. Personality development of school going children.
9. Educational Tours and Camps.

During the present pandemic situation, Surajya Sarvangin Vikas Prakalp, engaged in conducting regular health camps for the slum dwellers. Besides, keeping in mind the impending third wave, they are conducting health camps for the slum children in a big way. Dr. Sunanda Agashe Medical Practitioner from Vishrantwadi and Dr Amol Lunkad Gynaecologist (POGS MC Member) have been actively helping and guiding these health initiatives. They both are also the part of the trustee team of this NGO.

#### **FREE HEALTH CAMPS IN OUR SLUMS**

During the second wave of Pandemic, since going to nearby doctors and hospitals was becoming difficult due to curfew measures and also difficulty in getting doctors, Surajya embarked on this project of conducting free health camps right at the door steps of slums with the help of Doctors from PMC and few private medical practitioners.



Also, effective 1st March, 2021, at the Swatantrya Veer Gangaram Karne Hospital, Near Maharashtra Housing Board, Yerwada, through Pune Municipal Corporation, a COVID vaccination centre and a general health check-up initiative has been also started. The Corporation has given the licence/registration to run this hospital to Swargiya Nana Palkar Smruti Samiti.

With the help of PMC Doctors and private medical practitioners, we have so far conducted 26 free health camps in our slums. 2492 Slum residents including children to date have taken advantage of these health camps. At the hospital to date 200 citizens have gone through their health check-ups. To date, 720 eligible citizens have been vaccinated against the Corona virus. All these activities are an on-going process.



During the second wave of COVID-19 Surajya Sarvangin Vikas Prakalp also created a oxygen concentrator bank for free home use of oxygen concentrator for the needy people across Pune. This involved its volunteers and doctors going home of the patient explaining them how to use the oxygen concentrator and its cleaning. This helped many Covid patients in home care.

Surajya Sarvangin Vikas Prakalp has also conducted Health exhibitions, scientific exhibitions across all the slum areas of Pune on various occasions. Dr. Amol Lunkad has also conducted some Pradhan mantri Matrutawa Abhiyan camps for Surajya Sarvangin Vikas Prakalp. In these camps free Antenatal checkup of needy pregnant patients with dispensing of free hematinics have been done. It is also running free evening education classes or coaching classes for the poor students in the slum across Pune. Before Covid pandemic it had such free evening coaching classes at more than 20 locations across pune for the needy students.

Those POGS members interested in doing some social activity can contribute to this NGO which is doing very good work in Pune. POGS members and other individuals in your circle can help them by volunteering in various activities of this NGO or by donating medicines, PPE kits, etc or can also help financially. Below are some details of this NGO. –

**SURAJYA SARVANGIN VIKAS PRAKALP  
RUN UNDER THE AEGIS OF**

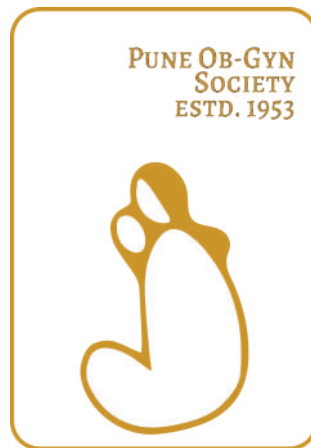
**SWARGIYA NANA PALKAR SMRUTI SAMITI, PUNE**

Reg. No. MAH 768 Pune (Act XXI of 1860) - F-598 Pune (Bom. XXIX of 1950)

E-mail: [vijay.surajya@gmail.com](mailto:vijay.surajya@gmail.com) Website: [www.surajyaprakalp.org](http://www.surajyaprakalp.org)

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# POGS *in*



## GENERAL SECRETARY'S REPORT - JUNE 2021

Team POGS is been working hard for our members & PG students in these hard times. Maintaining our academic saga, in June also we had a lot of good programmes virtually, let's have a look at them.

### 1. POGS Connects Karnataka:

Star Connect is a brainchild of President POGS Dr. Sunita Tandulwadkar. It's an initiative through which we are rekindling our friendship with other societies and sharing knowledge with them. POGS connected with the societies of Bidar, Bagalkot, Bijapur, Gulbarga and Raichur on 18 June 2021. Dr Hema Divakar and Dr Sunita Tandulwadkar, President POGS gave deliberations on "GDM what's new in management" and "Simplifying TLH" respectively. The STAR Award for the contribution in the field of Obstetrics and Gynecology was given to Dr Hema Divakar Past President, FOGSI. The program was a huge success with more than 250 delegates participating on different platforms online.



### 2. POGS virtual Masterclass on 23 June 2021 we had a case discussion



on "Abdominal mass in elderly patient." The case was presented by Dr. Aditi Prakash Kolhe and Dr. Kiran Khemani, postgraduate students from Smt. Kashibai Navale Medical College, Pune. Discussing abdominal mass is like opening Pandora's Box, but these girls did a fairly good job. The examiners for this PG study session were Dr. Pushpa Junghare (Prof. & HOD, PDMMC Amravati), Dr. Savita Mehendale (Prof. Emeritus BVMC Pune), Dr. Shilpa



Chaudhari (Prof. & HOU, SKN Medical college Pune), Dr. Fessy Louis. T (Assoc. Prof AIMS, Cochin). 250 participants attended this class which included postgraduate students and consultants from all over Maharashtra. Dr Ketaki Junnare was the co-convenor with general secretary Dr Vaishali Korde Nayak. President POGS Dr Sunita Tandulwadkar gave her valuable inputs.

**3. FOGSI Girl Child Day** celebration on 1st July 2021: On 1st July we celebrated “FOGSI Girl Child Day” to create awareness about gender equality. If girls get equal opportunities, our society will progress, thus leading to the progress of our nation. President POGS Dr Sunita Tandulwadkar released a beautiful video with our POGS member’s photos depicting various roles of a girl child in our lives like daughter, friend, wife, mother, grandmother etc. We shared ‘She... the Star’ brooch & a beautiful card with all our POGS members on this occasion. We had Radio bytes aired on Big FM radio channel the whole day. It included elaborate interview with President Dr Sunita Tandulwadkar regarding POGS role in upliftment of girl child. We also had radio messages by Convener Dr Meenakshi Deshpande & General Secretary Dr Vaishali Korde-Nayak. All together it was a wonderful celebration.

**4. POGS Star Connect with Uttar Pradesh on 2nd July** - POGS, under the visionary and dynamic leadership of Dr Sunita Tandulwadkar, witnessed a brainstorming CME - POGS CONNECT: The UP series Part 2, Dr Narendra Malhotra was bestowed upon by the STAR AWARD in appreciation for his magnanimous contribution towards Obstetrics and Gynecology. Respected and most loved Dr Chandravati madam was the chief guest. President POGS Dr Sunita Tandulwadkar unveiled the mystery of E=MC<sup>2</sup>. Her talk was very well received. The program concluded with an illustrious panel on ‘Multifetal Gestation’ moderated by Dr Chaitanya Ganpule. Special thanks to our enthusiastic panel of experts – Dr Rita Mittal, Dr Sumati Saxena, Dr Priyanka Garg, Dr Jyoti Aggarwal, Dr Manju Barik and Dr Pooja Lodha. POGS is thankful to the society members of Allahabad, Mathura, Khora-Makhanpur, Kanpur & Meerut.

Happy Monsoon... Enjoy!

**Dr Vaishali Korde-Nayak**  
**General Secretary, POGS**



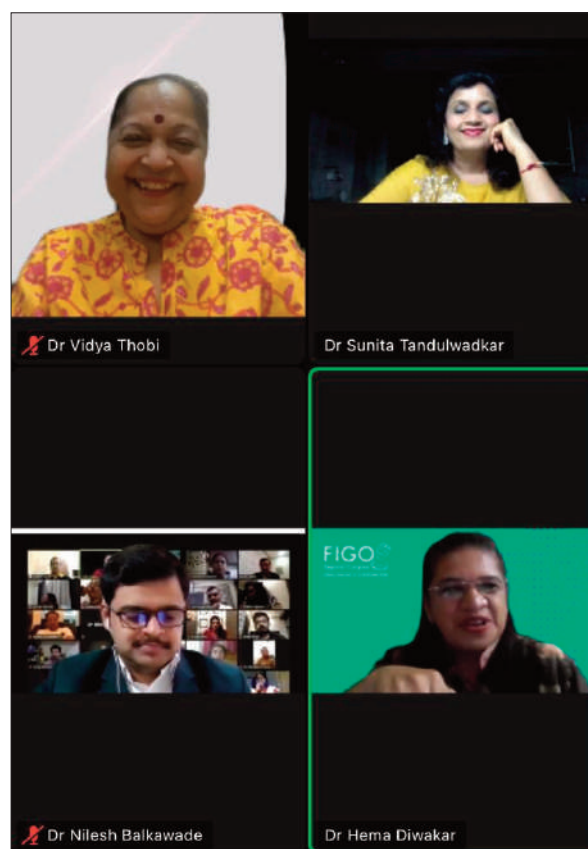
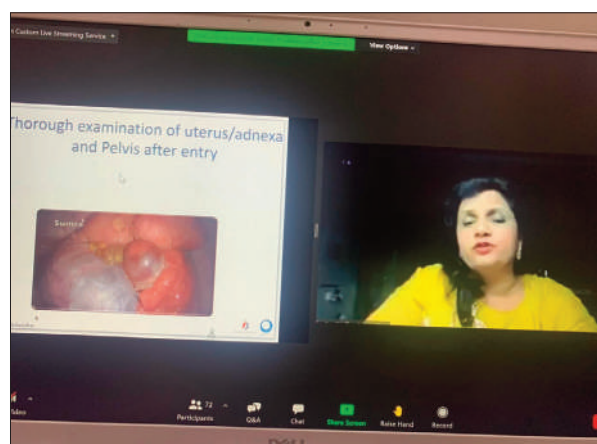
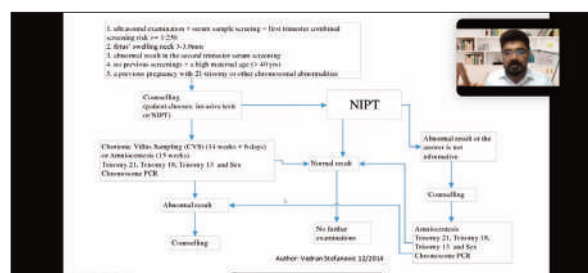
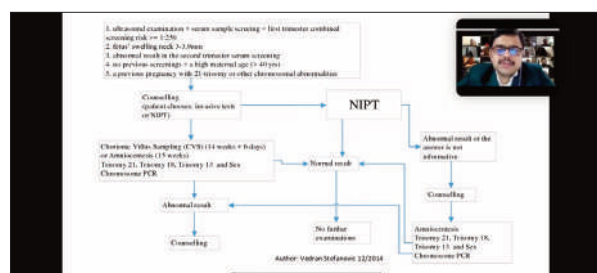
## Report of Star Connect Karnataka

POGS decided to go National by connecting with societies all over India. The first POGS star connect with the societies of Karnataka was conducted on 18th June at 8 p.m. virtually.

POGS connected with the societies of Bidar, Bagalkot, Bijapur, Gulbarga and Raichur. The coordinators were Dr Nilesh Balkawade, Dr Amey Chugh and Dr Vidya Thobi. Dr M G Hiremath, Past Vice President, FOGSI graced the occasion as the Chief Guest.

The STAR Award for the contribution in the field of obstetrics and gynaecology social work, academics was given to Dr Hema Divakar past president FOGSI. The award was physically sent to Madam by post and it was celebrated Virtually too. Dr Hema Divakar and Dr Sunita Tandulwadkar gave deliberations on GDM what's new in management and simplifying TLH. Chairpersons were Dr Sarita Bhadbhade, Dr Rohini Manvikar, Dr Ashalata Mallapur, Dr Vidya Thobi, Dr Rajshree Paladi, Dr Subhash Mudanyur who were the presidents of respective societies of Karnataka.

The talks were highly appreciated by all the chairperson and the participating delegates. It was followed by a panel discussion on pregnancy after 40 and was moderated by Dr Kasturi Donimath and Dr Nilesh Balkawade. The program was a huge success with more than 250 delegates participating on different platforms online.



## Mask India

*In the light of the troubles, we have today  
There's just a little POGS wants to say  
Although these days seem long  
As a country, we ought to stay strong*

POGS released ' MASK INDIA', its Public Awareness Campaign video, in an effort to spread awareness about preventing the 3rd wave of Covid. When we have the vision of a visionary President Dr Sunita Tandulwadkar, and the efforts and creative skills of Mr Shamsheer Singh (Song writer, Music composer) and young dynamic director Ms Mayuri Walke, magic is bound to happen! This awareness video, which has reached over lakhs of viewers is doing waves in the social media and has gone globally viral!

Heartfelt gratitude to Zydus for their unconditional support in our journey of awareness! We urge you all to spread the word, and join hands in an effort to fight the Covid crisis!

Please find the link below –[https://www.instagram.com/tv/CPv564YpZeo/?utm\\_medium=share\\_sheet](https://www.instagram.com/tv/CPv564YpZeo/?utm_medium=share_sheet)

### Facing all adversities

अब हमारा बस एक ही है TASK इंडिया '

MASK INDIA'

'MASK INDIA'

'MASK INDIA'

Stay tuned for more.. the STAR POGS Marathon has just begun!



## WORLD ENVIRONMENT DAY



5th June is celebrated as World Environment Day. In FOGSI 5th June is celebrated as FOGSI INFERTILITY DAY. PUNE Ob-Gyn Society celebrated both these days together in a unique way. It was a tree plantation drive with the sole purpose of returning something back to the mother earth for what all the privileges and love she gives us wholeheartedly.

The idea was not to plant the trees for the sake of celebrations or pics but to take ahead this motive years ahead by the team of each year. The incharge of the activity was Dr. Leena Patankar. Dr. Vaishali Korde-Naik guided for the event. Our president, Dr. Sunita Tandulwadkar supported hugely by offering a place, giving suggestions, taking care of every minute detail. The

uniqueness was an area was selected with such a thought that the trees will not only planted but also looked after, cultivated and nurtured so that we contribute our bit to preserve the nature.

We selected mango trees for plantation and taking care of huge trees is a task and a huge responsibility. Realising this very well our President, Dr.Sunita Tandulwadkar, suggested that we generate a separate corpus and a separate account just for that so that there should not be lack of funds in looking after the plants. She also offered the place near her farmhouse so as to ensure that the trees are not abandoned and taken care of properly. Also,a separate team is selected which will take take of the plants throughout the year and for the years together. For any activity to be successful apart from meticulous planning and efficient execution, active participation is utmost important.

And this exactly was seen during the celebrations of FOGSI INFERTILITY DAY and WORLD ENVIRONMENT DAY. Everyone reached on time at the venue which was Panshet, opposite Sunita M'am's Farm house. Each individual was looking nice n fresh in the predecided dress code , blue jeans and white shirt/top. The preparations were ready well in advance like the mango trees had reached a day before, the pits were already dug for each tree along with the bamboo railing for protection, the flex board for the display of the activity and the laminated photos of this year's team to be hung on the branches and also the photographer. Because of this everything went on very smoothly saving not only the time but also the last minute hassles.

We got divided in groups at each tree to be planted and Sunita m'am along with Vaishali personally went at each tree for planting the tree. Then a group photo was taken.This was followed by beverages (different types of tea & coffee) and sumptuous snacks at madam's farm house. It was so well organised that at every step automatically all the norms of COVID were being followed. All this is just another example of our President, Dr. Sunita's vision as well as generosity.

















## OUR THEME THIS YEAR

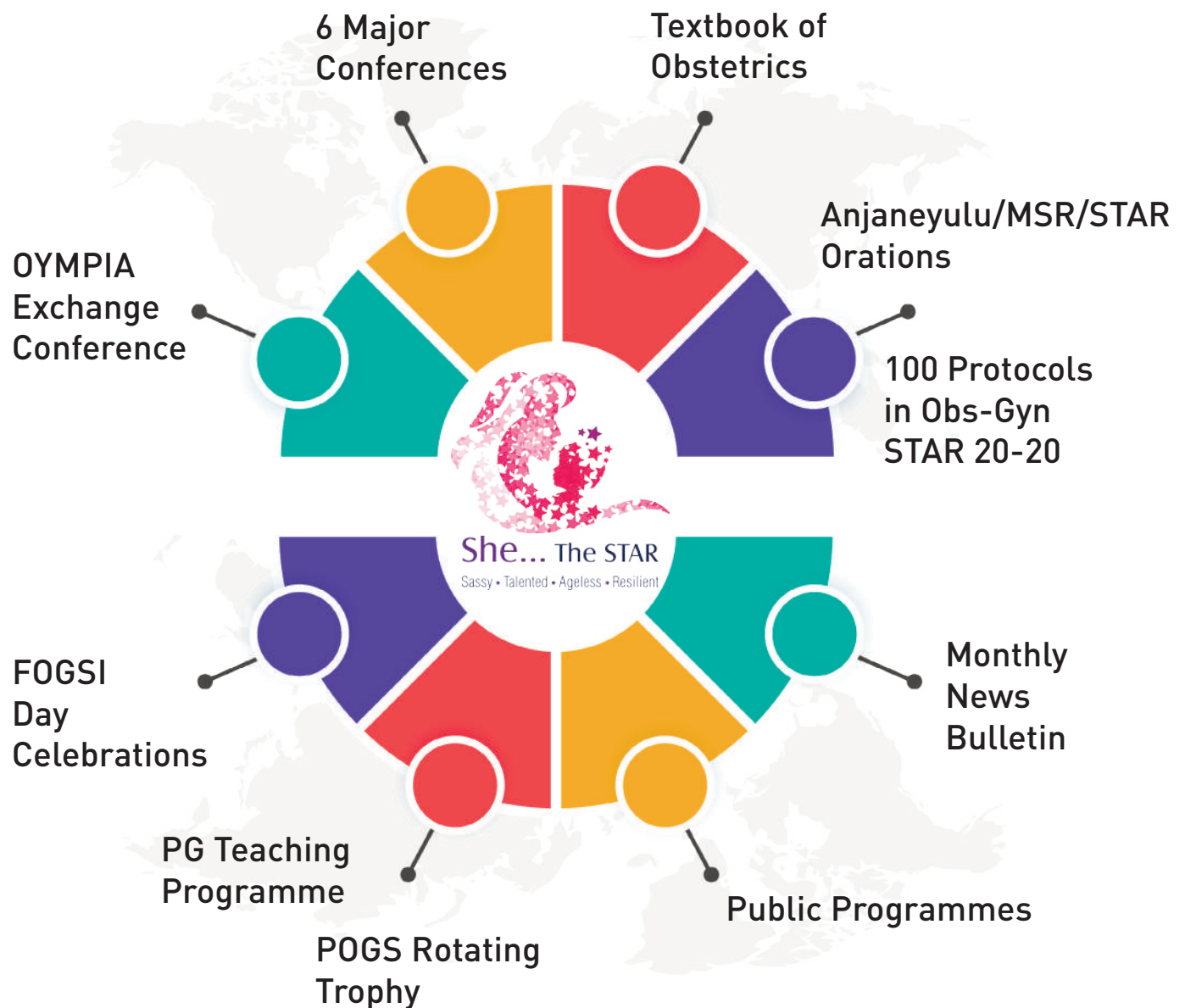


# She... The STAR

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## CALENDER OF THE YEAR





## 2021-2022 ACTIVITIES

### 6 MAJOR CONFERENCES

**APRIL  
2021**

16<sup>th</sup> - 18<sup>th</sup>

POGS STAR-OG  
Global Virtual  
Conference on  
**Recent Trends**

**AUGUST  
2021**

7<sup>th</sup> & 8<sup>th</sup>

POGS-FOGSI IOI -2  
International  
Conferences on  
**Ovulation Induction**

**OCTOBER  
2021**

8<sup>th</sup> - 10<sup>th</sup>

POGS- AMOGS  
Zonal Conference  
on - **Critical Care  
Obstetrics**

**OCTOBER  
2021**

22<sup>nd</sup> - 24<sup>th</sup>

POGS-FOGSI  
STAR - LEGAL  
**National Medicolegal  
Conference**

**DECEMBER  
2021**

11<sup>th</sup> & 12<sup>th</sup>

POGS-ISUOG  
FETOPANISHAD  
International  
**Fetal Medicine  
Conference**

**FEBRUARY  
2022**

18<sup>th</sup> - 20<sup>th</sup>

POGS  
**Endoscopy  
Conference**





## 2021-2022 ACTIVITIES

**Jan  
2022**

Exchange Conference "Olympia" organized by POGS in association with AMOGS and will be endorsed by many more societies from Maharashtra at DY PATIL Stadium, Navi Mumbai.



**CONNECT** Monthly Newsletter

- POGS Rotating Trophy
- Orations – Anjaneyulu , MSR & STAR Oration
- Social Programmes & Public Awareness
- PG teaching programs once in 3 months
- Text Book of Obstetrics
- STAR 20-20 - A practical book on 100 protocols in OBGY



## FOGSI DAY CELEBRATIONS

**April  
11<sup>th</sup>**

**FOGSI SAFE  
DELIVERY DAY**

Dr Shubhlaxmi Kurtkoti



**June  
5<sup>th</sup>**

**FOGSI INFERTILITY  
DAY (PLANT A TREE  
TODAY)**

Dr Leena Patankar



**July  
1<sup>st</sup>**

**FOGSI GIRL  
CHILD DAY**

Dr Meenakshi  
Deshpande



**Oct  
18<sup>th</sup>**

**FOGSI MENOPAUSE  
DAY**

Dr Parag Biniwale

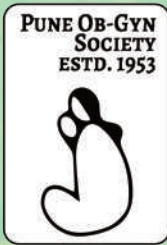


**Nov  
7<sup>th</sup>**

**FOGSI PAP  
SMEAR DAY –  
PREVENT  
CANCER DAY**

Dr Harshad Parasnis





# POGS 2021 IOI-2

INTERNATIONAL CONFERENCE OF OVULATION INDUCTION

EXCEL IN STAR FERTILITY



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**DATES: 7<sup>TH</sup> & 8<sup>TH</sup> AUGUST 2021**

**VENUE: JW MARRIOTT, PUNE**



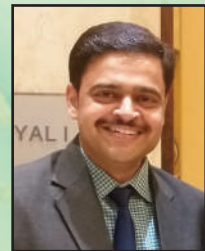
**Dr Vaishali Korde-Nayak**  
General Secretary, POGS



**Dr Sunita Tandulwadkar**  
President, POGS  
Organizing Chairperson

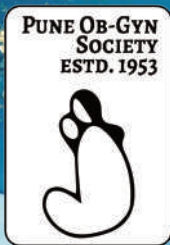


**Dr Kundan Ingale**  
Organizing Chairperson  
Chair, Infertility Committee  
FOGSI



**Dr Nilesh Balkawade**  
Clinical Secretary, POGS





HOSTED BY PUNE OBSTETRICS  
& GYNAECOLOGICAL SOCIETY



**ZONAL CONFERENCE OF THE ASSOCIATION OF  
MAHARASHTRA OBSTETRICS & GYNAECOLOGICAL  
SOCIETIES**

**AMOGS**

**2021**

**DATES:**

**8<sup>TH</sup>, 9<sup>TH</sup>, 10<sup>TH</sup>**

**OCTOBER 2021**

**VENUE:**

**HOTEL JW MARRIOTT,  
PUNE**



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**Dr Pankaj Sarode**  
Organising Chairperson



**Dr Nandita Palshetkar**  
President, AMOGS



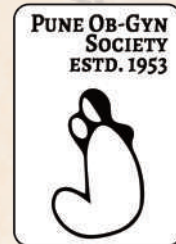
**Dr Sunita Tandulwadkar**  
Organising Chairperson-  
President, POGS



**Dr Kiran Kurtkoti**  
Organising Chairperson



**DATES:**  
**22<sup>ND</sup> - 24<sup>TH</sup> OCTOBER 2021**  
**VENUE:**  
**JW MARRIOTT, PUNE**



# POGS STAR LEGAL



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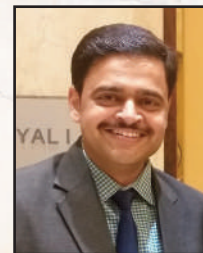
Dr Vaishali Korde-Nayak  
General Secretary, POGS



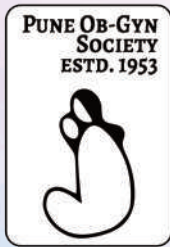
Dr Sunita Tandulwadkar  
President, POGS  
Organising Chairperson



Dr Manish Machave  
Chairperson Ethics &  
Medicolegal Committee FOGSI  
Organising Chairperson



Dr Nilesh Balkawade  
Clinical Secretary, POGS



**DATES:**  
11<sup>TH</sup>, 12<sup>TH</sup> DECEMBER 2021  
**VENUE:**  
JW MARRIOTT, PUNE

# Fetopanishad

## THE FETAL CONGRESS FOR ALL



## She... The STAR

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### HIGHLIGHTS

**International Accreditations**

**Two Parallel Halls**

**Minus3Nine:**

Fetal Medicine for Obstetricians

**Fetus+:**

Fetal Medicine for Practicing Fetal  
Medicine Clinicians

**Hands-On Fetal Interventions**

**For Minus3Nine:**

Aminocentesis, CVS

**For Fetus+:**

Fetal Shunt, Radio-Frequency  
Ablation, Bipolar Cord Coagulation,  
Laser for TTTS



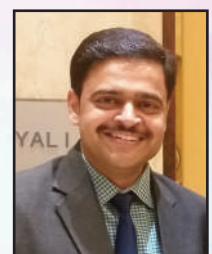
Dr Vaishali Korde-Nayak  
General Secretary, POGS



Dr Sunita Tandulwadkar  
President, POGS  
Organising Chairperson

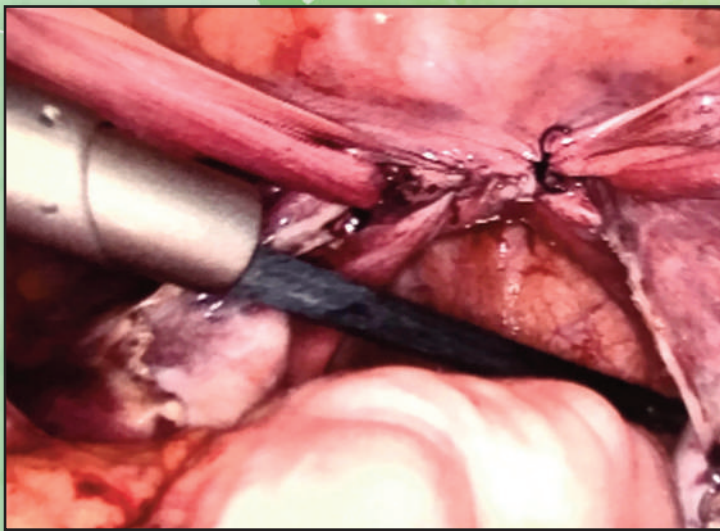
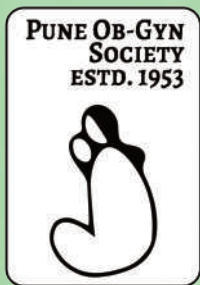


Dr Pooja Lodha  
Conference Director



Dr Nilesh Balkawade  
Clinical Secretary, POGS





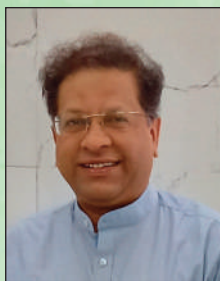
**DATES:**  
**18<sup>TH</sup>, 20<sup>TH</sup>**  
**FEBRUARY 2022**  
**VENUE:**  
**DR DY PATIL**  
**MEDICAL**  
**COLLEGE, PIMPRI,**  
**PUNE**

# **POGS-Star**

## **Endoscopy Conference**



**Dr Sunita Tandulwadkar**  
President, POGS  
Organizing Chairperson



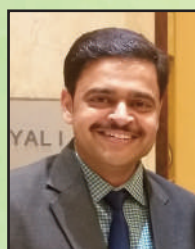
**Dr Kiran Kurtkoti**  
Organising Chairperson



**Dr Hemant Deshpande**  
Organising Chairperson



**Dr Vaishali Korde-Nayak**  
General Secretary, POGS



**Dr Nilesh Balkawade**  
Clinical Secretary, POGS



**Dr Meenu Agarwal**  
Organizing Secretary



**Dr Chaitanya Ganpule**  
Organizing Secretary

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<sup>#</sup> Mirza F. et al. Dydrogesterone use in early pregnancy. *Gynecol Endocrinol*. 2016;32(2):97-106. <sup>†</sup> Schindler AE. Progestational effects of dydrogesterone in vitro, in vivo and on human endometrium. *Maturitas*. 2009;65(1):S3-S11.  
<sup>^</sup> Novel-Estradiol hemihydrate first time in India. <sup>+</sup> Safer<sup>+</sup> As compared to conjugated equine estrogens. Smith NL et al Lower risk of cardiovascular events in postmenopausal women taking oral estradiol compared with oral conjugated equine estrogens. *JAMA Intern MED*. 2014; 174(1):25-31. <sup>\*</sup> As Prescribing Information of Solfe, version 1; Dated: 25th July 2013

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General Secretary, POGS



**Dr Parag Biniwale**  
President-Elect



**Dr Pankaj Sarode**  
Vice President



**Dr Kundan Ingale**  
Executive Vice President



**Dr Nilesh Balkawade**  
Clinical Secretary



**Dr Laxmikant Behele**  
Treasurer



**Dr Madhav Kankawale**  
Joint Secretary



**Dr Pooja Lodha**  
Joint Clinical Secretary



**Dr JP Rath**  
Joint Treasurer

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**Dr Aarti Nimkar**



**Dr Amey Chugh**



**Dr Amol Lunkad**



**Dr Anita Gavali**



**Dr Archana Pungliya**



**Dr Chaitanya Ganapule**



**Dr Kapil Kanade**



**Dr Kiran Kurtkoti**



**Dr Leena Patankar**



**Dr Manjiri Valsangkar**



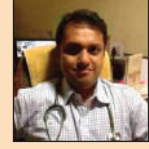
**Dr Meenakshi Deshpande**



**Dr Milind Dugad**



**Dr Nitin Sangamnerkar**



**Dr Rahul Argade**



**Dr Sabrina Bokil**



**Dr Shubhalaxmi Kurtkoti**



**Dr Uma Wankhede**



**Dr Vaishali Biniwale**



**Dr Veena Todkar**

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## Ex-Officio



**Dr Ashwini Kale**



**Dr Prakash Kothavale**

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**Dr Kundan Ingale**



**Dr Manish Machave**



**Dr Nilesh Balkawade**

## AMOGS 2<sup>nd</sup> Vice President



**Dr Kiran Kurtkoti**

## Past Presidents



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**Dr Dilip Walke**



**Dr Bharti Dhore Patil**



**Dr Nishikant Shrotri**



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