IAP BPS

PEDISCAN ISSUE 5

MONTHLY NEWSLETTER OF

Indian Academy of Pediatrics Bangalore-BPS

Droplet

May - 2021

GREETINGS FROM THE EDITORIAL COMMITTEE OF PEDISCAN, YOUR MONTHLY NEWSLETTER

We have almost reached the midpoint of our sojourn for the year in perspective. The COVID saga continues to produce its MAYhem as we contemplate the sinister arrival of the third wave. Is there more in store for we Pediatricians as a substantial pediatric surge is anticipated. God forbid such a situation but in the eventuality of such a scenario are we prepared?

The IAP looks to be gearing up to take the bull by the horns in various spheres like advocacy, protocols, training etc for facing the situation. Our President Dr Mallikarjun.H.B has taken lead in constituting a Task Force of eminent pediatricians to suggest solutions of combating the same. We wish him and his team all success.

Thalassemia the inherited blood disorder of abnormal hemoglobin production is still a scourge and forms a large burden on the already stretched health resources. World Thalassemia Day is celebrated on the 8th of May to focus on this issue. The Thalassemia International Federation's (TIF) theme for 2021 is 'Addressing Health Inequalities Across the Global Thalassemia Community'. Pediscan addresses issues in thalassemia beyond chelation and transfusions.

Elsewhere a young budding intensivist gives us insight into the intriguing world of the dreaded covid saga in the ICU.

"DROPLET" of WATER in continuation of our Water theme is a tiny drop that when combined forms a large body of water filled with strength and vitality. We all members of this society as single droplets of water need to come together giving strength to each other in these turbulent times forming that ocean of water.

The vitiating atmosphere pervading our lives now is a consequence of sensational and many a times fallacious news items having a depressive impact on our Minds. These negative emotions and our reactions to these have disturbed many among us. Let us understand that "As is our thoughts so shall be the state of our mind". It is time for us to fill our minds with calm, peaceful and serene thoughts and putting out our negative emotions, for after all the mind is a faculty very much under our control if need be. Taking care of this mind should be our primary responsibility. A simple fivepoint

formula, of Observing the thoughts, of Detecting negative thoughts, of Eliminating these negative thoughts, of Substituting them with positive thoughts and lastly Strengthening the positive ones by reinforcing them would go a long way in overcoming the gloom. Beware that Thoughts turn to Words which convert to Actions forming Habits to build our Character and finally all of these leading to deciding our Destiny.

The Editorial Team thanks one and all members for the encouragement and goodwill showered on us. Let us all Pray and Wish that we all see the back of this Covid surge very soon.

Jai IAP, Jai Karnataka, Jai Hind.

Dr Kishore Baindur
Editor in Chief

Dr Ramitha Pai
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Editorial Team 2021 **(Drs Anil Sapare, Krithika MV, Pooja Chebbi, Rajanish KV, Vandana Bharadwaj)**

PICU- LIFE INSIDE 4 WALLS, BUT A BATTLEGROUND OF LIFE AND DEATH

Dr Apeksha Anand

IGICH:

Its been a year but it's still COVID everywhere! My exams got postponed and all my plans post MD exams got disrupted. So, I was stuck in the middle of a sea not knowing which direction to sail. Most of the people suggested that I stay back home and relax. But after a month I felt restless. I have always been interested in learning. I make up my mind to do a fellowship and I choose the toughest speciality - Pediatric intensive care. A lot of people discouraged me for various reasons but I was determined. I managed to get a fellowship in one of the best institutes of Bangalore and I was extremely excited.

I was all geared up for the new challenge. With a lot of confidence, I entered the ICU but in the very first week I realised that tough times are meant for everyone. A lot of things have changed post covid, but ICU is usually the same when it comes to work.

I was exposed to a variety of rare conditions which I hadn't come across in my residency. I got to see few conditions which I thought are only in books! Decision making was not as easy as I thought.

Reality started sinking in. I could see helplessness and fear in the eyes of families, I was counselling. Morbidity and mortality were affecting me mentally and I realised this is certainly not going to be easy for me. Life inside ICU is a different world. A place where we never give up, no matter what, because every effort counts and every life matters. It's the place where maximum battles are fought - medical/physical/emotional.

Though I was surrounded with very humble and helpful people around me, I felt lost and started questioning myself as to whether I was in the right place? Would I be able to handle all this? I began doubting my abilities during crisis times! Every day I was surrounded with sickness and sadness. Beeping monitors and CPRs were haunting me in dreams. Deranged blood reports were disrupting my sleep! For the first time in my life I had second thoughts about the field I chose!

It was almost the 3rd week since I joined when I came across a patient which was like ' twilight' for the mental battle I was going through!

PICU- LIFE INSIDE 4 WALLS, BUT A BATTLEGROUND OF LIFE AND DEATH

A 1year old boy with acute stroke with refractory seizures- was referred ventilated to our institute. The mother greeted me with tears, and I could see fear and hope in her eyes. I took a detailed history, examined, and started looking through the labs. I was in the middle of some calculations when I heard a soft voice asking in hindi ' Kya mera beta teek hojayega'? I knew I couldn't give false hopes, but my heart melted. I didn't let my emotions take over and firmly said we will try our best! My inner voice said I should not give up no matter what! Every morning the mother would greet me with a smile and ask about my where abouts. I generally stay neutral with my patients, smile and get back to work.

I did everything I could and successfully weaned off the child. The day I was shifting him out of ICU she said " I used to pray for my sons recovery everyday but I also prayed for your happiness and I wished u keep saving lives and become the best doctor ever" . She also said, ' I see u working hard every day, not only for my son but for all the children '. Allah will bless you. I felt numb for a few seconds. I couldn't control myself. I had tears of joy and accomplishment. I always doubted my capabilities, but her words just wouldn't stop buzzing in my mind!!

She continued to wish and thank me every morning till the child was in the hospital and I followed up until he recovered and was discharged! As an intensivist we can't let our emotions take over, but some things will have a very huge impact in our life.

Each of us are gifted with one or the other capabilities. We can't be masters of all.

Eventually I started enjoying my work. The stress started becoming a challenge. My fears started fading away gradually. The smile of a recovering child and ray of hope in the eyes of mothers made me a stronger person day by day. Every day I had few families thanking me and blessing me which made me feel delighted.

What keeps us moving is self-confidence and victories in the path. No matter how dark the night is, the Sun rises with a fresh ray of hope every morning.

It's rightly said we learn from our tough times. Learn from your mistakes. Our profession demands a lot of dedication. Our journey from a resident to consultant is always a roller coaster ride. Emotionally, mentally, physically we get exhausted, but we keep going no matter what. There are a lot of sacrifices. We know life is not as fancy as others think or feel. But I feel privileged and happy to have chosen this profession.

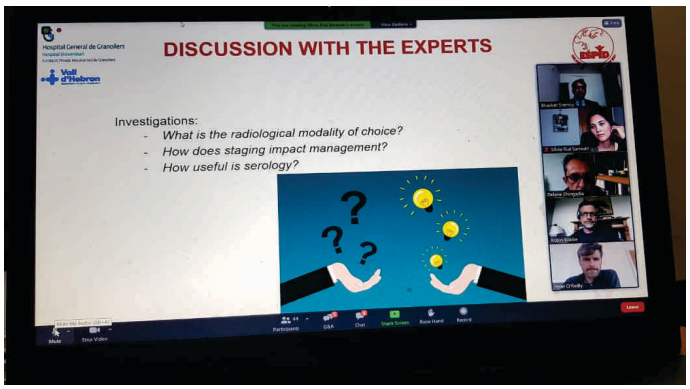
I am neither a senior consultant nor a very experienced Pediatrician. I am just a girl who wanted to be in this profession and worked hard for where I am. I have had a lot of ups and downs. But I have accepted my journey. Everything happens for the good. After I witnessed so many kids suffering with various complicated medical conditions, I feel we are privileged to be enjoying good health.

Let's make each day count. Let's cherish each moment. Thrive to be a better person every day. Let's set aside our egos, learn from our mistakes. Give the best of yourself and keep saving lives the way we always do.

Congratulations

Dr. Bhaskar Shenoy for being one of the panelist in a Panel discussion in "Meet the expert" session of **Annual conference of European society of Pediatric Infectious disease** on 26th May 2021 .

One of the panelists (Deline Singhadia) is current President of ESPID.



BETA THALASSEMIA :
THERAPEUTIC MODALITIES ON THE HORIZON BEYOND TRANSFUSION AND IRON CHELATION

Dr.Rajanish K.V.
Professor Pediatrics
RRMCH, Bangalore

Dr. Shobha Badiger
Consultant Pediatric Hematooncology and BMT,
Majumdar Shaw Medical Centre , NH health City, Bangalore

Dr.Adarsh.E
Prof and HOD, Pediatrics'
RRMCH, Bangalore

˝ mama mama, I want that red bottle˝
Demanded the girl playfully.....

The mother looked at the blood transfusion drip
And replied ˝ I wish you didn't.....

BACKGROUND:

Hemoglobinopathies are the most common monogenic diseases worldwide, and 1-5% of the global population are carriers for a thalassemia mutation. Beta thalassemia is a highly prevalent condition globally and their management and care is of increasing concern for health care systems.

Different conventional modalities for the management of thalassemia used today include blood transfusion, iron chelation, splenectomy, hydroxyurea and for a subgroup of patients' hematopoietic stem cell transplantation (HSCT).

Although being mainstay of management, these modalities are fraught with many challenges and limitations.

With increasing understanding of the basic pathophysiologic molecular mechanisms operating in thalassemia, newer therapies are emerging, which are under various phases of clinical trials and hold the promise of near optimal management of thalassemia

EMERGING THERAPIES :

These can be categorised into three major categories based on their efforts to address different aspects of pathophysiology of β-thalassemia.

1. Correction of globin chain imbalance
2. Addressing ineffective erythropoiesis
3. Addressing iron dysregulation

CORRECTION OF GLOBIN CHAIN IMBALANCE :

This is one of the basic mechanisms which contribute to decreased RBC survival. Intracellular accumulation of free α-globin-heme complexes on red cell membranes generates proteotoxicity, inhibits late-stage erythroid differentiation and causes hemolysis.

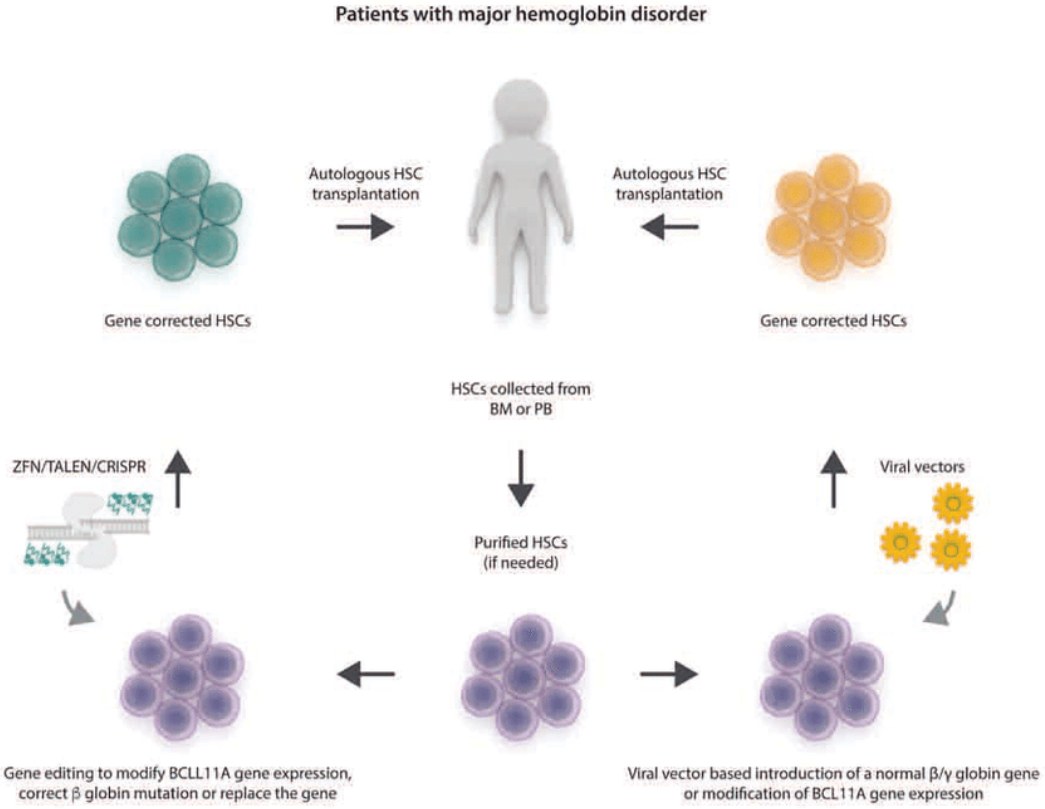
Allogenic hematopoietic stem cell transplantation (HSCT), potentially restores the tissue's capability of producing functional haemoglobin. Despite improving survival rates in these transplanted patients, limitations and concerns persist due to constrains in availability of suitable donors, patient fitness, procedure related toxicity, graft rejection and graft versus host disease(GVHD).

Gene therapy and Gene editing, are strategies evolving to circumvent problems of HSCT.

In Gene therapy, the approach is to introduce a normal gene into AUTOLOGOUS hematopoietic stem cells through a Lentiviral vector. The process involves harvesting of AUTOLOGOUS hematopoietic stem cells from the receipient either from Bone marrow or peripheral blood, followed by ex vivo transduction of these cells with the Lentiviral vector carrying the transgene. Then a quality assessment to determine the number transduced and vector copy numbers per HSC is performed.

A myeloablative conditioning therapy is given to eliminate existing HSCs in the recipient, following which AUTOLOGOUS hematopoietic stem cells transduced with vector (carrying a functional β-globin gene) is transplanted. The transgenic expression then follows resulting in β-chain synthesis and HbA formation.

Gene editing involves strategy to switch on the γ-globin gene expression to reactive synthesis of fetal Hb (HbF).



Gene therapy product in phase 3 trials:

ZYNTEGLO: Autologous hematopoietic stem cells transduced with Lentiglobin vector encoding the human BA – T87Q – globin gene.

- **Targeting ineffective erythropoiesis:**

Erythropoiesis is a complex, life-long process where hematopoietic stem cells proliferate, differentiate and mature into red blood cells. It is a continuous process that can be conceptually divided into early and late stages. It is a tightly regulated steady-state process.

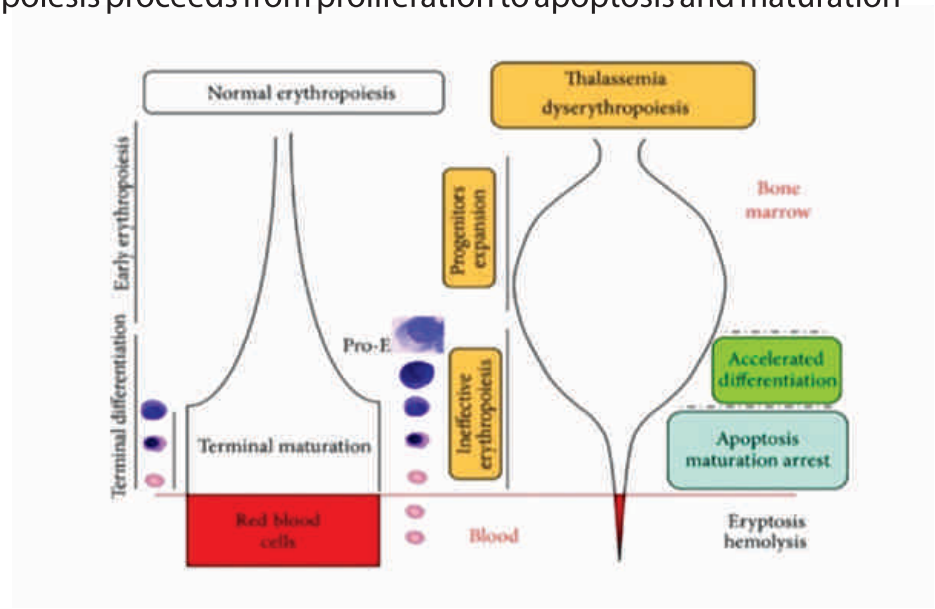
Ineffective erythropoiesis (IE) is defined as a suboptimal production of mature erythrocytes originating from a proliferating pool of immature erythroblasts.

Ineffective erythropoiesis (IE) characterised by:

1. Accelerated erythroid differentiation
2. Maturation blockade at the polychromatophilic stage
3. Death of erythroid precursors

The process of erythropoiesis is tightly regulated and effected through different transcription factors and signalling pathways, the players that control erythropoiesis.

Erythropoiesis proceeds from proliferation to apoptosis and maturation



Proliferation during early erythropoiesis is mediated through the influence of erythropoietin (EPO). During late stage erythropoiesis, a fine balance is achieved between maturation and apoptosis, so that marrow output matches the physiological requirement. In β-thalassemia this balance is disturbed, which is characterised by disproportionately increased proliferation (under influence of erythropoietin), increased apoptosis and inhibited maturation (ineffective erythropoiesis) leading to anemia. This process contributes to anemia in both transfusion dependent and non-transfusion dependent thalassemia.

The process of Apoptosis is mediated by molecular ligands on the cell membrane and its intracellular signalling pathway. ACTIVINS are one such ligands and its intracellular signalling is mediated by SMAD 2/3 molecule. ACTIVIN/SMAD 2/3 pathway work to inhibit erythroid maturation and promote Apoptosis, acting as 'Agents in the game of cell death'.

ACTIVIN II RECEPTOR TRAPS, are Novel recombinant fusion proteins, which act by blocking this SMAD 2/3 signalling and consequently improving anemia by inhibiting negative regulators. LUSPATERCEPT and SOTATERCEPT are drugs in this category currently in phase 3 trials. LUSPATERCEPT has been recently approved by FDA for treatment of TDT (Transfusion dependent thalassemia). Given once in 3 weeks by subcutaneous injection, it was overall very well tolerated and associated with a dose-dependent increase in Hb levels. Of note,75% of patients had 33% reduction in transfusion burden and transfusion independence was attained in 11% of patients in LUSPATERCEPT group

- **modulating iron metabolism:**

  There are two main mechanism by which iron overload develops in thalassemia: increased iron absorption due to ineffective erythropoiesis and blood transfusions. Iron overload could lead to development of organ damage and increased mortality.

  Iron metabolism in body is mainly regulated through hepcidin-ferroportin axis. HEPCIDIN, a molecule synthesised by liver acts by inhibiting iron transport by binding to the iron export channel FERROPORTIN, which is located on the basolateral surface of gut enterocytes and plasma membrane of reticuloendothelial cells. In β-thalassemia despite the presence of iron overload, hepcidin levels are low.

  MINIHEPCIDINS, synthetic human hepcidin-These molecules code named LJPC-401 and PTG-300 are under phase 2 clinical trials.

  FERROPORTIN INHIBITOR, VIT-2763- also in phase 2 trials currently, holds the promise of decreasing iron overload by decreasing gut iron absorption.

  TMPRSS6 inhibitors-TMPRSS6(transmembrane protease serine 6) is a gene which suppresses hepatic synthesis of hepcidin. TMPRSS6 inhibitor-IONIS TMPRSS6-LRx SLN124 is a molecule which aims to increase hepatic synthesis of hepacidin, currently under phase 1 study, but withdrawn due to COVID pandemic.

CONCLUSION:

The improvement in the understanding of β-thalassemia pathophysiology has paved the way for new therapeutic approaches that aim to directly correct the globin chain imbalance through gene therapy and correct ineffective erythropoiesis acting on different molecular pathways.

Among the new options activin receptor ligand trap molecules are so far, the most promising, with significant Hb improvements and reduction in transfusion requirements.

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Poem:
MAYHEM IN MAY ----A CRUSADE AGAINST COVID

A thousand salutations to all those thousand warriors ,
A chiliad adulations to all those chiliad victors ,
A myriad acclamations to all those myriad conquerors ,
A multitude of laudations to the multitude of vanquishers .

I know that your service is unparalleled, corresponding to the unfathomed misery from the holocaust ,

I realize that your service is unsurpassed , equivalent to the infinite devastation and tribulations from the immeasurable lives lost ,

I cognize that your selfless act is unrivaled , analogous to the boundless misfortune and monetary loss that this debacle has cost ,

I perceive that your kind gesture is proportionate to the abysmal anguish that this catastrophe has brought and left many as orphans and made many mourners distraught.

But Oh boy ! Don't you worry, for your crusade against the calamity will pay dividends one day,

But Oh girl! Don't you bother, for your mission against the adversity will fetch rewards one day,

Oh boy! Don't you brood, for your struggle against this depravity will yield rich returns one day,

Oh girl! Don't you ponder , for your battle against this iniquity will bring accolades one day .

This unseen virus may now be creating a mayhem in May but it's not invincible,

This diminutive creature may now be unbridled but it's not infallible ,

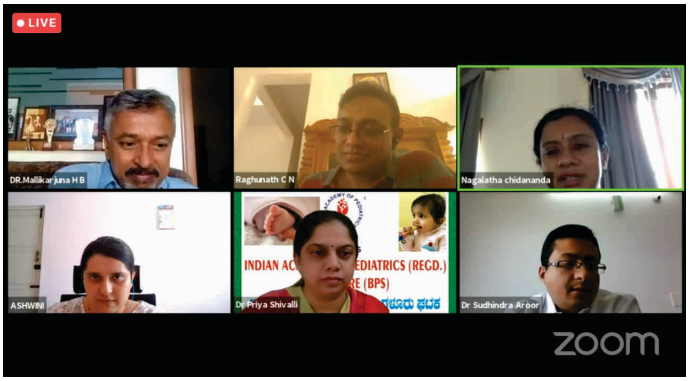
This miniscule being may now be omnipresent but it's not insurmountable ,

This tiny structure may now be unfettered but it's not noncollapsible !

Dr. Kalpana Praveen
Asst Prof Pediatrics
Bowring Hosp,
BMCRI Blore.

(Dedicated to all the peerless and fearless COVID WARRIORS for risking their own lives , for being away from their families , for losing out on the joy of the childhood of their own growing tiny tots and losing out on the fatherly / motherly touch and cuddling of their children , for losing on the secured touch of their parents , for losing their own near and dear ones and still sweating it out tirelessly in Personal Protection Equipment PPE and for losing their own lives and turning MARTYRS)

PHOTO GALLERY

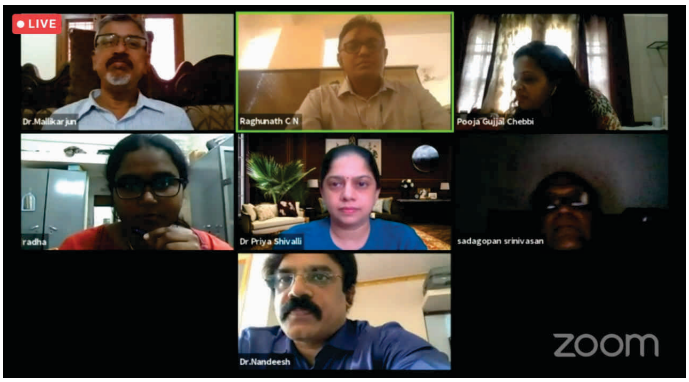


PG Teaching Program on CNS

Talk on Covid Caution and Care

PG Teaching program on Resp Infections

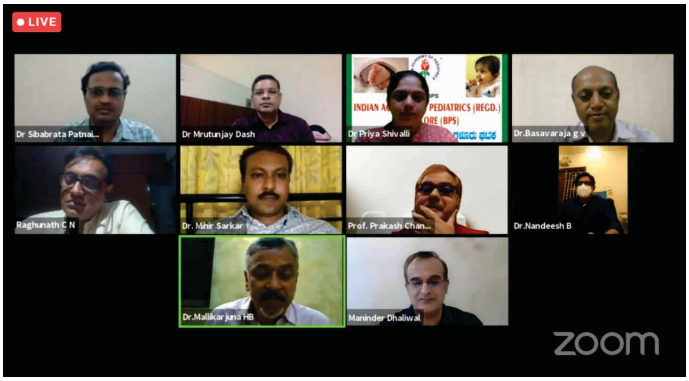
Dr. M A Chandrasekhar Addressing the Press



PG Teaching Program on Childhood Anemia

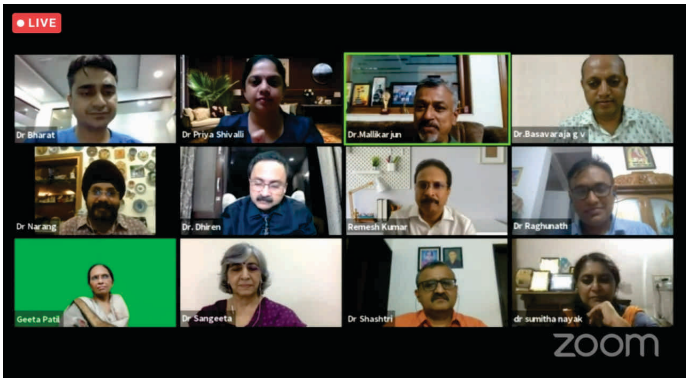
Dr. Asha Benkappa Addressing the Press

PHOTO GALLERY

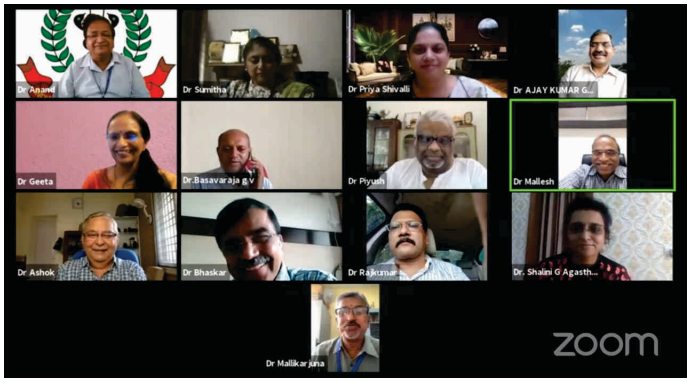


Scientific Session - Poisoning in Children

CADE Module Workshop



Scientific Session - Covid Management in Kids



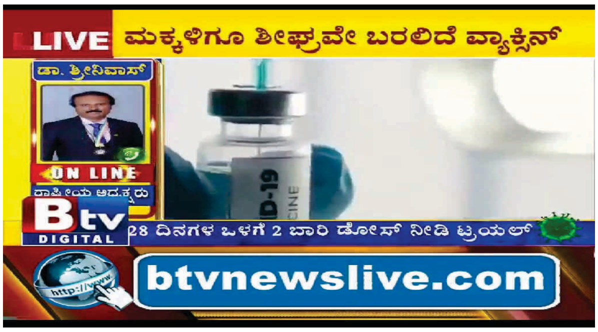
Mission Co-Win Uday Module Workshop

Scientific Session Monthly Meet - May

Scientific Session Monthly Meet April

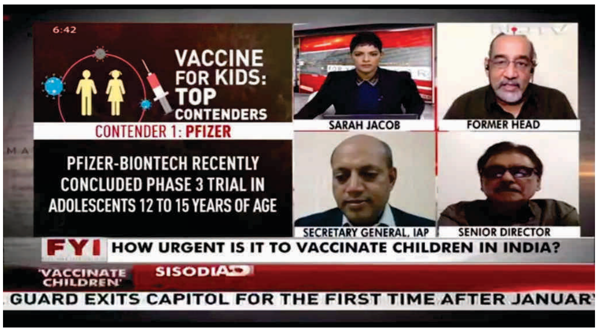
PHOTO GALLERY

Dr. Bhaskar Shenoy Addressing the Press



Dr. Srinivasa Addressing the Press

Dr. Adarsh Addressing the Press



Dr. Basavaraj Addressing the Press