STEM CELL SOCIETY (INDIA)

2016 SCSICON 11th & 12th June, New Delhi

SCSICON - 2016

3rd Annual Conference of

Stem Cell Society (India)

11th and 12th June 2016
India Habitat Centre, Delhi (India)

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Scientific Program & Abstract Book

A Message from
Shri Jagat Prakash Nadda
Minister of Health & Family Welfare
Government of India

NATIONAL HEALTH MISSION
राष्ट्रीय स्वास्थ्य मिशन
जगत प्रकाश नड्डा
Jagat Prakash Nadda

सत्यमेव जयते

स्वच्छ भारत
एक कदम स्वच्छता की ओर

स्वास्थ्य एवं परिवार कल्याण मंत्री
भारत सरकार
Minister of Health & Family Welfare
Government of India

MESSAGE

It gives me great pleasure to know that Stem Cell Society is organizing its Third Annual Conference at New Delhi on 11th – 12th June 2016.

Stem Cell therapy is the latest and most promising development in the world medical sciences. Many incurable diseases that have no definitive treatments at present can be helped with Stem Cell Therapy. Recent scientific publications worldwide and from India as well show that in killer diseases like Duchenne muscular dystrophy and Motor neuron disease lives can be saved, that limb amputations can be prevented in ischemic limb diseases, that children with autism and cerebral palsy can be integrated back into mainstream society though improvements in their mental and physical states, that paralysed patients of Spinal cord injury and brain injury can be lifted out of wheelchairs, that our elder citizen suffering from osteoarthritis can be given relief and that lifestyle diseases such as diabetes and ischemic cardiac disorders can also be helped.

It is a matter of pride for us that India is playing a leadership role in this field with many of our doctors doing pioneering work and helping thousands of patients. The work of these doctors in Stem Cell Therapy is in alignment with the Government of India's and our Honourable Prime Minister Shri Narendra Modi's Vision of "Make in India" and "Skill India". I wish the Conference all success and hope that the deliberations of this Conference create greater awareness amongst the medical community about this field so that eventually the ordinary citizen of the country suffering from incurable diseases can benefit from Stem Cell Therapy.

(Jagat Prakash Nadda)

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A Message from
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Directorate General of Health Services
Central Drug Standard Control Organisation

Dr. G. N. Singh
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सत्यमेव जयते

स्वास्थ्य सेवा महानिदेशालय
सी. डी. एस. सी. ओ. (एच. क्यू.)
एफ. डी. ए. भवन, कोटला रोड़
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DIRECTORATE GENERAL OF HEALTH SERVICES
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MESSAGE

I am glad that the Stem Cell Society is organizing its Third Annual Conference in New Delhi on 11-12 June 2016. I had pleasant memories of the 2015 Annual conference where I had inaugurated the first issue of the Indian Journal of Stem Cell Therapy.

A lot of developments have happened on the regulatory framework on Stem Cell during the last one year globally including in USA, Japan and Korea etc. Regulators world over are realizing that safer stem cell therapies for older as well as newer clinical indications should be more easily available to patients needing them and are modifying their regulations accordingly. In our country, we are in the process of revisiting the Drugs and Cosmetics Act 1940 and rules 1945 with respect to Stem Cell.

The importance of Stem Cell therapy lies in the fact that it is able to treat diseases that were earlier considered incurable and for which there was no hope. These include some severely debilitating neurological, pediatric, orthopedic, cardiac, endocrine and other conditions.

I hope the Conference will provide a vital platform for discussion and knowledge dissemination to all the Society members. I wish the event a grand success and I convey my best wishes to the organizers.

(Dr. G. N. Singh)

Welcome Message From Organizing Committee of SCSICON 2016.

Dear friends & colleagues,

We welcome you all to the 3rd Annual Conference of Stem Cell Society (India).

From small beginnings of about a dozen members we have grown into a large society with members from almost all the states of the country, representing work done in different specialties in the field of stem cell therapy. We now have our own official journal "The Indian Journal of Stem Cell Therapy". The number of publications is increasing manifold and our members are making presentations in different conferences across the countries. Recognition for our work is also coming from all over the world.

During the last year, our single minded focus was on working with the regulatory authorities to create an environment and regulations that permit greater freedom in the Stem Cell Therapy work. We have met the health minister, secretaries from health ministry, heads of CDSCO/ DCGI as well as ICMR along with other senior officials from these agencies. We got a very favorable response from the health ministry as well from the DCGI and we are hopeful that they will support our ongoing efforts. Work with ICMR is still in progress since they still have many reservations about our point of view. We understand and respect the fact that there will always be two sides to a coin and there will be differing views at different levels. As senior office bearers of Stem Cell Society (India) we are committed to this work and will continue to engage and interact with all government agencies and regulatory bodies ,explaining our point of view whereas at the same time respecting their point of view too. We want to discuss and debate but not confront and be in conflict. All of us want the same thing that the ordinary citizen of the country should benefit from modern advances in the field of Stem Cell Therapy whereas at the same time be protected from unsafe treatments.

What has given us additional hope is that the global regulations worldwide are shifting to become more favorable towards regenerative medicine and Stem Cell Therapy. We believe that ICMR, CDSCO and ministry of health with appropriate inputs including those from our society, can come up with a new framework of guidelines and regulations that could become a landmark and which would be of overall benefit to the common man suffering from previously untreatable disease in which Stem Cell Therapy can help. Working together we believe that we can make regulations better than that of Japan, Korea and USA. We would like to end with this quote from Robert Frost.

"The woods are lovely, dark and deep,
But I have promises to keep,
And miles to go before I sleep,
And miles to go before I sleep."

Dr. Alok Sharma
President
Stem Cell Society (India)

Dr. Rohit Kulkarni
Vice President
Stem Cell Society (India)

Dr. B S Rajput
Organizing Chairman
SCSICON 2016

Dr. Prabhu Mishra
Organizing Secretary
SCSICON 2016

Scientific Program

Day 1

Registration- 8:30 to 9:00 am

Session I		**Chairperson** – Dr. Kanchan Mishra, Dr. Sharda Jain, Dr. Pradeep. Mahajan
Time	**Speaker Name**	**Topic**
9:00-9:15 am	Dr. B.S. Rajput / Dr. Prabhu / Dr. Alok Sharma	Welcome and introductory remark
9:15-9:30 am	Dr. Nandini Gokulchandran	Stem cell Therapy in neurodevelopmental disorder
9:30-9:45 am	Dr. Anant Baqul	Adult MSCs in spinal cord injury
9:45-10:00 am	Dr. Mrinalini Chaturvedi	Cellular Therapy Accreditation (National & International Standards)
10:00-10:10 am	**Panel Discussion**	
Session II		**Chairperson –** Dr. Deepali Bhardwaj, Dr.Rupali Bassi, Dr. Shankar Narayanan
Time	**Speaker Name**	**Topic**
10:15-10:30 am	Dr. Sheilly Kapoor	Platelet rich plasma in hair regeneration
10:30-10:45 am	Dr. Karun Jain	Bone, cartilage, ligaments and tendon tissue repairing
10:45-11:00 am	Dr. Rohit Kulkarni	Stem cell treatment in Diabetes
11:00-11:15 am	Dr. Rimmy Singla	Mononuclear Cells & Poor Ovarian Reserve.
11:10-11:25 am	**Tea Break**	
11:25-11:40 am	**Lamping, Chief Guest**	
Session III		**Chairperson-** Dr. Ravi, Dr. Sanjay Mongia, Dr. Manish Khanna, Dr Varsha Baste
Time	**Speaker Name**	**Topic**
11:40-11:55am	Dr. B.S. Rajput	Musculoskeletal disease - Stem cell hype or hope
11:55-12:10pm	Dr. Pradeep Mahajan	MSC the changing Paradigm
12:10-12:25pm	Dr. Rubina	Stem cell in thin endometrium
12:25-01:15pm	Dr.Shivi Deol	Keynote Speaker - Clinical superiority of Ischemic tolerant immune privileged allogenic stem cells
1:15-2:00 pm	**Lunch & Networking**	

Session IV		**Chairperson-** Dr. Rajput, Dr. Ramesh Bhonde, Dr. Asha Sakolkar
Time	**Speaker Name**	**Topic**
2:00-2:30 pm	Dr. Alok Sharma	Stem cell regulation and current scenario
2:30-2:45 pm	Dr. Prabhu Mishra	Global scenario of stem cell industry
2:45-3:00 pm	Dr. Shankar Naraynan	Stem cells and tissue engineering- novel approach
3:00-3:15 pm	**Panel discussion**	
3:15-4:00 pm	**Poster Presentation-** Dr. Kanchan Mishra, Dr. Rachna Kapoor, Shagufta Parveen	
4:15-4:30 pm	**Tea break**	
Session V		**Chairperson-** Dr. Kamini Patel, Dr.Shakuntala Kumar, Dr. Hathi Bhusan
Time	**Speaker Name**	**Topic**
4:30-4:45 pm	Dr. Manish Khanna	Role of stem cells in Autoimmune Disease-1
4:45-5:00 pm	Dr. Sapna Jain	Role of Stem cells in cervical disease
5:00-5:15 pm	Dr. Subhadra Dravida	Stem cells & tissue banking
5:15-5:30 pm	**Closure Remarks**	

Day 2

Registration: 8:30 to 9:00 am

Session I		**Chairperson-** Dr. Yogesh Agarwal, Dr. Vishal Gour, Dr. Rucha Ponske
Time	**Speaker Name**	**Topic**
9:00-9:15 am	Dr. Vikram Pabreja	Role of stem cells in ILD
9:15-9:30 am	Dr. Senthil Tyagrajan	Role of Stem cells in Autoimmune disease.
9:30-9:45 am	Dr. Nayana Patel	Clinical advances in IVF
9:45-10:00 am	**Panel discussion**	
Session II		**Chairperson-** Dr. Shivani Gour, Dr. Manish Khanna, Dr. Manu Menon
Time	**Speaker Name**	**Topic**
10:00-10:15am	Dr. Sharda Jain	Ageing has no Mercy
10:15-10:30am	Dr. Deepali Bhardwaj	Role of Stem cells in skin rejuvenation
10:30-10:45am	**Panel discussion**	
10:45-11:00am	**Tea break**	
Session III		**Chairperson-** Dr. Alok Sharma, Dr. Prabhu Mishra, Dr. Kaberi Bannerjee
Time	**Speaker Name**	**Topic**
11:00-11:30am	Dr. Ramesh Bhonde	Keynote Speak- Stem cell-Bench to bedside
11:30-11:45am	Dr. Meghnad Joshi	Role of stem cells in hepatocyte regeneration
11:45-12:00	Dr. Ravi	Role of stem cells in CLI
12:00-12:15	**Panel discussion**	
Session IV		**Chairperson-** Dr.Ruby, Dr. Nandini, Dr. Rohit Kulkarni
Time	**Speaker Name**	**Topic**
12:15-12:30	Dr. Rajneesh Verma	IPSCs basics and clinical applications
12:30-12:45	Dr. Chandraman More	Stem cells in oral and maxillofacial surgery
12:45-1:00	Dr. Nedun Chezian	Stem cells in Haematology
1:00-1:15	Dr. Deepali Tiwari	Adipose stem cells– diabetic foot & limb salvage
1:15-1:45	**Lunch**	

Session V		**Chairperson-** Dr. Raman Singla, Dr. Alpa Chavda, Dr. Jyoti Agarwal, Dr Narendra Malhotra
Time	**Speaker Name**	**Topic**
2:00-2:15	Dr. Varsha Baste	Role of stem cells in female infertility
2:15-2:30	Dr. Shivani Sachdev Gour	Novel technologies in Asherman's & Male infertility
2:30-2:45	Dr. Radhika Thapar	Global regulation for stem cell application & clinical trial
Session VI		**Chairperson-** Dr. Kavita Agarwal, Dr. B.S. Rajput, Dr. V.K. Upadhyay
Time	**Speaker Name**	**Topic**
2:45-3:00pm	Dr. Kamini Patel	Case presentation in skin & face rejuvenation
3:00-3:15pm	Dr. Mayank Jain	Role of stem cells in OA and eye disorder
3:15-3:30pm	Dr. Vandana	Rehabilitation and sports injury
Session VII		**Chairperson-** Dr. Surendra Bapat, Dr. Abhijeet Bopardikar, Dr. Anshika Lekhi
Time	**Speaker Name**	**Topic**
3:30-3:45pm	Vipul Jain	Stem cells basic to advances
3:45-4:00pm	Deepika Kohli	Diet & supplements- age management
4:00-4:15pm	Dr. Deepak Verma	Role of stem cells in cardiac disease
4:15-4:30pm	**Tea break**	
4:30-5:30pm	**Panel discussion for future development** **Panelist-** Dr. B.S. Rajput, Dr. Pradeep Mahajan, Dr. Alok Sharma, Dr. Rohit, Dr. Bhonde **Closure Remarks-** Dr. Prabhu Mishra	

Regulations for Stem cell therapy - The current global scenario as compared to the present Indian scenario and the proposed way ahead.

Dr. Alok Sharma
President - Stem Cell Society (India)

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The Current problem:

The main problem today is that we have a new treatment option in the form of Stem cell therapy that can help lakhs of patients suffering from incurable conditions but they cannot access these treatments easily because the current guidelines are not permissive enough for hospital and doctors all over the country to offer stem cell therapy for newer indications.

Many of us are practising Ethical stem cell therapy based on the Helsinki Declaration of the World Medical Association which clearly states *that "In the treatment of a patient, where proven interventions do not exist or have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgment it offers hope of saving life, re-establishing health or alleviating suffering"*. We are saving lives of hundreds of patients with our stem cell therapy, we are re-establishing health and easing suffering, giving mobility, giving greater consciousness, speech and vision, preventing limbs from getting amputated etc etc. How can it be unethical to save a human life or prevent a limb amputation with a treatment that has proven safety and whose results have been published in reputed medical journals?

Much of our work is published in peer reviewed and pub med indexed journals. Published work from Indian authors is now included in systemic reviews and metanalysis which is the highest form of medical evidence. Latest textbooks of medical specialities have chapters written by us on Stem cell therapy. We have made presentations across the country and the world on invitations and our work has been acknowledged and well received.

A few people from a committee with no direct clinical experience in Stem cell therapy for newer indications and a few lines written in a set of guidelines can't make all this work unethical. It would not be an exaggeration to say this and I say this with full responsibility: - that the well intentioned guidelines and regulations (by virtue of not being permissive enough) are in fact responsible for many patients dying that could otherwise have been saved had stem cell therapy been more easily available. No patient has died because of stem cell therapy but thousands of patients are dying because of non availability of stem cell therapy. We would like to ask the regulatory authorities just one question. Is it ethical to let patients die or have their limbs amputated or continue to suffer when there is a treatment option available that can save their lives and limbs or can ease their suffering? Who is responsible for these deaths? Denying life saving treatment is an infringement of the fundamental rights of a patient. According to the White paper published by the International society of Cellular Therapy :- "*Patients seeking medical treatment for cellular therapies have the following rights that must be respected by healthcare providers and all associated with their care. The right to seek treatment: patients and their families/partners have the right to seek treatments for their diseases. No entity should withhold this fundamental right unless there is a high probability of harm to the patients."* Regulatory authorities need to understand one simple fact. That just because something is not proven does not mean it does not work. People responsible for framing guidelines need to open their minds, engage and discuss with us openly about our clinical results and read what is being published in medical journals worldwide and in India. A big price is being paid by the ordinary citizen in terms of life and limb for this rigid non permissive attitude. This has to change and it has to change soon.

The Present Global Regulatory Scenario:

Worldwide countries have realized the need for newer regulations that are more permissive of Stem cell therapy. [1] The most dramatic transformation is happening in the USA where a completely new law called the Reliable and Effective Growth for Regenerative Health Options that Improve Wellness Act (REGROW Act) is under consideration by their Senate. This Act allows for a conditional approval of cellular or tissue therapeutic products if there is preliminary clinical evidence of safety and a reasonable expectation of effectiveness. They include minimally manipulated for non homologous or more than minimally manipulated for homologous or non homologous use etc. The conditional approval is to be for a period of 5 years. [2] Earlier Japan with its partial amendment of the older Pharmaceutical Affairs Law (PAL) which is now called Pharmaceutical, medical devices and therapeutic products Act (PMDA) to include regenerative medical products allowed for similar conditional approval for seven years. They have in addition passed the Act on Safety of Regenerative Medicine (ASRM) which applies to medical institutions that provide processed cells in clinical research and private practice. [3] The Korean Regulations have excluded minimally manipulated cells from their 'Review and authorization of Bio logical products'. [4] European medical agency (EMA) has also come up with the advanced therapy medical product (ATMP) laws, PRIME (PRIority MEdicines) act and Hospital Exceptions (HE) act that are also favorable to newer therapies such as regenerative medicines. [5] Many other countries such as China, United Arab Emirates and others are also coming with newer more favorable regulations.

New concepts and terms that are now becoming part of the more permissive regulations are [1] Conditional approval [2]Risk Stratification [3]Post-Hoc efficacy analysis [4] Presumed efficacy [5]Reasonable expectation of effectiveness [6] Patients' right to seek treatment [6] Distinction between cellular therapies [7] Distinction between a stem cell product and medical service.

The Present Indian Regulatory Scenario:-

In sharp contrast to this, in India the latest guidelines made by Indian Council of Medical Research (ICMR) in 2013 are moving backward and are in the process of trying to implement policies that will completely destroy the stem cell therapy field in India. The Major problems with the ICMR guidelines are that

[a] . The word therapy has been removed from the guidelines and there is a refusal to accept that is something like stem cell therapy (The Proposed American law accepts cellular therapies exist)

[b] The important distinction between a product and a medical service and the fact that that both these need to have separate regulatory pathways is not clearly specified. (The Japanese legislation clearly makes that distinction)

[c] There is a refusal to accept that safer forms of stem cell therapy should have more permissive regulations such as their being permitted with institutional committees oversight only. (The Korean and Japanese legislations clearly accept this)

[d] The current policies, which insist on only doing clinical trials for all types of cell types and that too after having an IC-SCR (Institutional Committee for Stem Cell Research) registered with NAC-SCRT (National Apex Committee for Stem Cell Research & Therapy) , registration with CTRI, having a data safety monitoring board and having a DCGI license for GMP facility, means that only heavily funded private corporates can fulfill their criteria. This is because doing the above takes several Crores of rupees. The current policy means that government/ semi government institutions, smaller private hospitals and individual doctors can never fulfill their criteria. Therefore this current ICMR policy clearly discriminates against the ordinary hospitals and practicing doctors in the country in favor of rich corporates.

[e] Even if institutions want to work in accordance with ICMR regulations, NAC-SCRT makes it extremely difficult for them to even begin the process. This is evidenced by the fact that out of 107 institutes that have applied for NAC-SCRT registration only 24 i.e 22% have actually got the NAC-

SCRT registration. By doing this ICMR is closing its doors at the very entry point. Also the process is extremely long and can take several months to years to complete. The result of this is a real life example in recent months wherein a semi government hospital in Gujarat doing wonderful limb salvage stem cell therapy free of cost (they had saved 57 limbs from amputation in the past few years) was made to stop their work whereas during the same period a private corporate was given permission to charge patients (US $ 2200) for similar type indication. Any regulatory policy that favors only large corporates and those who can spend large amounts of money and discourages or prevents those who cannot spend large amounts of money is not in the national and public interest of a country such as ours.

What should be the way ahead:-

{A} There is a very simple road map that Indian regulators should take. Broadly speaking there should be 3 categories; [I] Researchers :- should follow ICMR guidelines [II] Corporate manufacturers:- should follow CDSCO guidelines [III] Clinical stem cell therapists should be divided into 3 categories. (a)Those using low risk cell therapies such as autologous and minimally manipulated therapies should be permitted to do therapy subject to their IEC approval only. (b) Those using medium risk cell therapy such more than minimally manipulated allogenic would in addition need approval from IEC and CDSCO and (c) Those using high risk cell therapies such as embryonic and iPSCs would need IEC, CDSCO and ICMR approval.

{B} The membership of NAC-SCRT should be expanded to include more members from the clinical side having experience and expertise in Stem cell therapy so that a more balanced view is taken. The Chairmanship of NAC-SCRT should be changed by rotation every year so that fresh insights are available to the committee.

Conclusion:

We conclude that the Ministry of Health along with ICMR and CDSCO need to study the REGROW Act of USA as well as the Japanese and Korean legislations for regenerative medicine and come up with a definitive set of regulations which are permissive of medical practitioners offering safer forms of cellular therapies like autologous and minimally manipulated therapies and stricter regulations for more unsafe cellular therapies and corporate producing and selling stem cells as a product. This will result in only safe treatments being available as therapy and at the same time ensure that patients suffering from serious medical conditions are not deprived of stem cell therapies that can help them.

Stem Cell Therapy in Neurodevelopmental Disorders

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Neurodevelopmental disorders represent one of the leading causes of disability in children throughout the world. Very few of these conditions have a cure and they patients often deteriorate over time. Recently, stem cell therapy has emerged as a potential therapeutic strategy for these disorders. Stem cells carry out the repair by multiplying and differentiating into the host tissue cells. They also secrete paracrine factors which stimulate the endogenous cells to carry out repair and regeneration and halt further neuronal damage. They carry out neuroprotection, neurogenesis, angiogenesis, etc and reverse the pathology of the neurodevelopmental disorders. To demonstrate the efficacy of the intervention, we administered autologous bone marrow mononuclear cells intrathecally in patients with neurodevelopmental disorders. Stem cell therapy was combined with neurorehabilitation as a part of our protocol. Evidence suggests that neurorehabilitation facilitates neuroplasticity, which may enhance the outcome of our intervention. 371 patients were included in this study, out of which 149 were autism,193 cerebral palsy and 29 intellectual disability.

At a minimum 6 months follow up, 338 out of 371 (91.6%) showed overall improvement, wherein 22.2% showed significant improvement, 39.7% moderate, 89.8% mild improvement. On further analyzing the data based on the disorders, in autism, 134 out of 149 (89.93%) showed overall improvement. In which 36% showed significant improvement , 30.6% moderate improvement and 23.3% mild improvement. Improvements were observed in social interaction, eye contact, attention, stereotypical behaviour, hyperactivity, aggressive behaviour, communication, self stimulation and speech. In cerebral palsy, 177 out of 193 (91.7%) showed overall improvement. 17.2% showed significant improvement, 41.4% moderate, 34.5% mild improvement in oromotor activity, balance, trunk, LL movement, UL movement, muscle tone and ambulation. Out of 29 children with Intellectual Disability, 27 (93.1%) showed overall improvement. 17.2% showed significant improvement, 41.4% moderate, 34.5% mild improvement. Majority of the cases showed marked improvement in cognition, remote memory, social inhibition and toilet training. No major adverse events were reported in the duration of the follow up.

The results of this study indicate a positive outcome of stem cell therapy in neurodevelopmental disorders. Use of autologous bone marrow mononuclear cells is safe, feasible and efficacious and may help restore functions and improve the quality of life of these patients.

Adult MSC in Spinal Cord Injury

Dr. Anant Bagul, (MS, Ortho)
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The term 'spinal cord injury' refers to damage to the spinal cord resulting from direct trauma or compression by disc herniation or damage caused by occurred spinal arteries. Every year, around the world, between 250 000 and 500 000 people suffer a spinal cord injury (SCI) in which approximately 1,00,000 New spinal cord cases arises in India . Spinal cord injury (SCI) develops primary and secondary damage to neural tissue and this often results in permanent disability of the motor and sensory functions.

Current treatment of SCI is limited to early administration of high dose steroids to mitigate the harmful effect of cord edema that occurs after SCI and to reduce the cascade of secondary delayed SCI. Stem Cell transplantation, as a therapeutic intervention for spinal cord injury (SCI), has been extensively studied by researchers in recent years. . Scientists have been trying all efforts to improve various experimental methods which contribute to the reconstruction of histological impaired tissue structure, and to the restoration of neural function eventually .Stem cell transplantation is promising option for regeneration in SCI.

Here we have studied the effect of Adult stem cell (BMMSCs) in case of spinal cord injury patient,showed sign of recovery ,Improvement of sensation below the lesion and significant movement in affected limbs was also noted. Stem cells and their therapeutic potential have been mainstay of discussions controversies but definitely a new ray of Hope in various intractable diseases. This BM-MSC shows significant regeneration pattern in this case, along with quality of life .Today hundreds of millions of people live in pain suffering due to spinal cord injuries and will eventually die .We stand within reach of alleviating all this death and anguish, preventing it from occurring again ever. We should rise to the challenge!

Cellular Therapy Accreditations (National & International Standards)

Dr. Vikas Verma [1], Dr Mrinalini Chaturvedi[2]
1. Head Lab Operations, Cryoviva Biotech Private Limited
2. Medical Director, Cryoviva Biotech Private Limited
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Cellular therapy (Cell Therapy or cytotherapy) is a therapy in which the human cells, tissues & cellular & tissue based products consists of human cells or tissues intended for implantation, transplantation, infusion or transfer into a human recipient. These therapies have grown dramatically in power & scope in the recent years. They are regulated with WHO GMP & GTP guidelines. The accreditations (AABB, CAP, NABL, GMP, FACT-JACIE)are important for patient/donor safety, safe &effective procurement,processing, testing, storage,distribution & administration of cellular therapy products, plays an important roles in pitching the International markets i.e. creating uniform quality management system & in promoting the medical tourism in Indian market. In India, the Drug Controller General of India within Central Drugs Standards Control Organization (CDSCO) is the regulatory authority; it issues four categories of licenses/ approvals. There are three categories of stem cells for research-permitted (adult stem cells), restricted (ES Cell & iPSC) & prohibited (therapeutic cloning, breeding of genetically manipulated animals). As per the current ICMR-DBT national guidelines for stem cell research (2013), in accordance with the stringent definition, every use of stem cells in patients outside an approved clinical trial shall be considered as malpractice.Although these requirements will present significant challenges for clinician- Investigators & laboratories producing HCT/Ps, the regulations fundamentally support good clinical care by increasing safety & control & enable good science by improving the quality & reliability of data.

The Role of Stem Cells In Bone, Cartilage, Ligament & Tendon Regeneration

Dr. Karun Jain
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Regenerative Orthopedic Specialist,
Stemgenn Therapeutics & Life Care Hospital, Delhi

Application of 'regenerative medicine' in orthopaedic practice has aroused a new ray of hope among surgeons. Myriads of orthopaedic conditions with limited therapeutic options could be benefited with technologies developed in regenerative medicine. In Orthopedics, considerable benefits have resulted from the biomechanical solutions in the past 50 years, with better biomaterials and implants for joint replacements, more precise instrumentation and computer-aided navigation techniques. However, implants have a finite lifespan owing to loosening or other modes of failure and may require further surgery involving increased morbidity for the patient. The future lies in regenerative medicine, with the potential to grow new tissues and organs to replace damaged or diseased ones by utilising stem cells, which have the capacity to self-renew and differentiate into many different types of tissue. Although this area of research holds infinite promise, it is also influenced by scientific, ethical, moral and political controversies. The bone and cartilage regeneration ability of stem cells have been demonstrated clinically, but the tendon regeneration capability is still in the experimental stage. Most common use of stem cell therapy in current orthopaedic scenario is in fracture non union& delayed union, Gap union, avascular necrosis, cartilage defects, arthritis of knee & Rheumatoid arthritis, tendon & ligament injuries, spinal fusion & disc lesions and few congenital orthopedic anomalies. Stem cell therapy looks to be an appealing new option but the studies documented so far have shown failures as well as successes. This is an evolving aspect of Orthopaedics& many more long-term prospective randomised human trials need to show good results before the use of these cells can be recommended to all.

Diabetes and Stem Cells

Dr. Rohit Kulkarni
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Diabetes mellitus (DM) is a group of metabolic disorders characterized by a chronic hyperglycemic condition resulting from defects in insulin secretion, insulin action or both. Diabetes is a serious chronic disease without a cure, and it is associated with significant morbidity and mortality, both acute and chronic. Acute complications are due to severe hyperglycemia. Chronic complications are characterized by damage, dysfunction, and eventual failure of various organs, especially the eyes, kidneys, nerves, heart, and brain. The common denominator is vascular damage. Type 1 diabetes is caused by an autoimmune destruction of the beta cells of the pancreas due to an interplay between genetic susceptibility and environmental modifiers. Type 2 diabetes, the most prevalent form of diabetes, is characterized by a combination of insulin resistance and insulin deficiency.

Apart from using anti diabetic drugs, diabetes researchers have been searching for ways to replace the insulin-producing cells of the pancreas that are destroyed by a patient's own immune system, Researchers have tried whole organ pancreas transplantation in large number of patients with type 1 diabetes, but however due to lack of organs and intense immune suppression it is difficult to control undesirable morbidity. The transplantation of isolated pancreatic islets into the livers of diabetic patients also been largely tried and is unsuccessful for many years due to limited availability of donor islet cells.

Stem cell therapy holds immense promise for the treatment of patients with diabetes mellitus. Research on the ability of human embryonic stem cells to differentiate into islet cells has defined the developmental stages and transcription factors involved in this process. However, the clinical applications of human embryonic stem cells are limited by ethical concerns, as well as the potential for teratoma formation. As a consequence, alternative forms of stem cell therapies, such as use of induced pluripotent stem cells, Fetal Stemcells, adult stemcells from umbilical cord, placenta and bone marrow-derived mesenchymal stem cells have been tried. Bone marrow transplantation as a Therapeutic approach for ß-cell Replacement and as Immune Therapy for Type 1 Diabetes have become an area of intense study. With all the recent advances in stem cell research, Stem cell therapy will turn this into a realistic treatment for diabetes in the near future.

Poor Ovarian Reserve

Dr. Rimmy Singla, MBBS, DGO, FICOG, DRME, Germany
Director - IVF Centre, Ivy Hospital, Mohali

Ovarian reserve is the pool of eggs present in the ovaries at any given time. Low ovarian reserve is when there is a physiological decrease in the number of eggs, resulting in an insufficient number to ensure a reasonable chance of pregnancy.

Bologna Criteria
(Ferraretti et al. ESHRE Consensus, Hum Reprod 2011)

At least 2 of the following:

1) Advanced maternal age (≥40 years or risk factor for POR)

2) Previous POR (≤3 oocytes with conventional stimulation)

3) Abnormal ovarian reserve biomarker

AFC<5-7; AMH <0.5-1.1ng/Ml

Or:

Two episodes of POR after maximal stimulation

POOR RESPONDER (ESHRE)

- Two of the following three features must be present:
- Advanced maternal age (≥40 years) or any other risk factor for POR;
- A previous POR (≤3 oocytes with a conventional stimulation protocol);
- An abnormal ovarian reserve test (i.e. AFC <5–7 follicles or AMH <0.5–1.1 ng/ml).
    - Patient age
    - USG: ovarian measures and number of secondary follicles (3^{th} day)
    - basal FSH (3^{th} day)
    - basal E_2 (3^{th} day)
    - β-inibina (3^{th} day)
    - MIF (3^{th} day)
    - Clomiphene Challenge test (CCCT)
    - Gn-RH-a test
    - FSH test

Role of stem cells in the management of Musculoskeletal diseases

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Intro Musculoskeletal diseases affect the abilities of the person greatly, it may render them bedridden or may prove fatal also like in muscular dystrophies. So the role stem cell transplantation, in the management of musculoskeletal diseases like Degenerative arthritis of knee, Rheumatoid polyarthritis, Ankylosing spondylitis, Muscular dystrophies, spinal muscular atrophy, spinal cord injuries, AVN hip, Delayed union and non union of fractures, osteochondral lesions of knee, Critical Limb ischaemia, Diabetic foot and non healing ulcers, is of great significance.

Material and methods We enrolled 162 patients of MSK diseases for stem cell transplantation, over a period of 3 years from march 2013 to march 2016, out of which patients of OA knee were 32,rheumatoid poly arthritis -8 , ankylosing spondylitis -5, Duchenne muscular dystrophy -45, Becker muscular dystrophy -5, Limb girdle muscular dystrophy- 12, Facio scapulohumeral muscular dystrophy-4, spinal muscular atrophy-6, Spinal cord injury-24, Avascular necrosis of hip-4, Delayed and Nonunion of fractures-3, Critical limb ischaemia-2 ,Diabetic foot and non healing ulcers -12.

Procedure All patients were subjected to stem cell transplantation with specified protocols. Patients with genetic mutation diseases received cord derived allogenic stem cells while patients with rest of the diseases received autologous stem cells , prepared from patients own bone marrow or peripheral blood.

Results 80% of the Patients suffering from Degenerative arthritis of knee improved while more than 90% patients of Rheumatoid polyarthritis improved but only 40 % patients of ankylosing spondylitis improved. Similarly more than 80% patients of DMD and BMD improved while only 60% patients of LGMD responded positively and less than 25% in FSHD.

Spinal cord injury patients had region specific response. So the SCI patients with Lumbar spine injuries had best response in about 80% patients, while in thoracic spine patients it was only 60 to 65% patients. Cervical spine injury patients were worst responders, who responded in less than 10% patients.

Patients with delayed union of fractures, critical limb ischaemia, diabetic foot and non healing ulcers responded in excellent manner, while patients of AVN hip and spinal muscular atrophy responded very poorly

Conclusion Stem cell transplantation is not only effective in the management of most of MSK diseases but also proved to be life saver in deadly diseases like DMD and LGMD

Mesenchymal Stem Cells as Drug Molecules

Dr. Pradeep Mahajan
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Conventional medications are known to treat a disease and not cure an individual. The concept of mesenchymal stem cells (MSC) being proposed as a medicinal signaling agent is based on the fact that cells are not single molecular agents. Mesenchymal stem cells are adaptive agents capable of complex functions involving many bioactive factors. These multi-potent cells may be called injury-specific drug stores that home to the site of injury and secrete considerable levels of immunomodulatory and trophic factors. These properties aid in cell replacement, enhancement of organ function etc. by harnessing their innate regenerative potential. MSCs are now proving to be promising candidates in regenerative medicine owing to their availability in various tissues of the body, ease of isolation and rapid expansion. Stem cells may be converted into products, behaving as regulated delivery vehicles, to treat various conditions. Stem cell therapy, when considered as a drug, requires management logics and regulatory policies that are different than those existing for conventional drug molecules.

Global Scenario of Stem Cells

Prabhu Mishra
CEO, StemGenn Therapeutics

Stem cells have basic cells of all multicellular organisms having the potency to differentiate into wide range of adult stem cells. The basic characteristics of stem cells are self- renewable and potency. Recently several new avenues or paradigms in mobilization have emerged from ever-expanding work in humans subjected to granulocyte- colony stimulating factor (G-CSF) mobilization, as well as from studies in normal and gene deficient mouse models. Stem cell therapy is the new future of medical technology and has the capability of curing any type of medical condition. This has been proved by research, and researchers are still engrossed in exploring the potential of stem cell therapy.Stem cell treatment is sprouting rapidly in South Asia, and even in western countries, some approved stem cell therapies have made their way into clinics and are helping patients suffering from degenerative diseases. Stem cell Therapeutic applications is developing very fast as haematopoetic stem cell transplant is well established clinical practice and other source are experimental. For use in therapy purpose stem cell require strategic clinical trials and studies. This novel technology of mesenchymal stem cells have huge potential to capture the market of regenerative medicine in cosmetics, orthpedic and other auto immune diseases. This displays the steep rise in market of stem cell therapy across the globe.

Cell Based Therapy, Tissue Engineering - Application in Dentistry.

Dr. S. Sankaranarayanan
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In the new millennium, where biology and biotechnology have replaced chemistry, we are exploring "biological solutions to biological problems. Even though the stem cells have been studied for decades, only during the past few years has there been an overwhelming proliferation of publications covering isolation, cultivation and utilization of the body's master cells. Stem cell therapies also provide alternative solutions for the repair and regeneration of various tissues and organs. Regenerative medicine using human stem cells is one of the new and promising fields for treating various intractable diseases and damaged organs. Transplantation of MSC stem cells for treatment of alveolar bone defects appears safe and accelerates bone regeneration, enabling jawbone reconstruction with oral implants. DPSC shows highest osteogenic potential then compared bone marrow cells, and periosteal cells. We have treated alveolar bone regeneration using dental pulp stem cells, bone regeneration for implant placement and also an oral condition called osteoradionecrosis & ameloblastoma. My lecture will bring new focus on dental pulp stem cell and evidence in periodontal regeneration and for bone pathology in tissue engineering.

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Neural Stem Cell Isolation and Characterization from Brain of Embryonic Rats (*Sprague Dawley*) and Pups

Kanchan Kumar Mishra* & Sakshi Gupta**

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Background: Throughout the process of development and continuing into adulthood, stem cells function as a reservoir of undifferentiated cell types, whose role is to underpin cell genesis in a variety of tissues and organs. In the adult, they play an essential homeostatic role by replacing differentiated tissue cells "worn off" by physiological turnover or lost to injury or disease. As such, the discovery of such cells in the adult mammalian central nervous system (CNS), an organ traditionally thought to have little or no regenerative capacity, was most unexpected. Reynolds and Weiss (1992) first demonstrated the presence of neural stem cells in both the adult and embryonic mouse brain.

Materials and methods: Neural stem cells have been isolated and cultured from nearly all regions of the embryonic mouse CNS, by employing a novel serum-free culture system termed the neurosphere assay, we demonstrated the presence of neural stem cells in both the embryonic rat brain and pups that not only can self-renew but also can generate various CNS cell lineages (*Neurons*, *Astrocytes* and *Oligodendrocytes*).

Results & Conclusion: Here we describe how to generate, serially passage, and differentiate neurospheres derived from both the developing and adult brain, and provide more technical details that will enable one to achieve reproducible cultures, which can be passaged over an extended period of time. We have standardized a method for isolation and culture of multi-potent neural stem cells from rat foetal cortex (NSCs) and rat neonatal pups in the form of neurospheres. These NSCs were capable of giving rise to the three major differentiated neural lineages, *neurons*, *astrocytes*, and *oligodendrocytes*. Neurons were about 40%, astrocytes about 50% and oligodendrocytes were about 9% after 4 days of differentiation. These neurospheres could be passaged repeatedly.

Regenerative Science in Auto Immune diseases

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Former Consultant, Sanjay Gandhi Post Graduate Institute of Medical sciences, Lucknow
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Progenitor cells applications has got a promising role in management of Autoimmune diseases . Autoimmune diseases are a family of more than 100 heterogeneous conditions that affect 5 to 8% of the world's population. Although conventional immunosuppression and new biological agents can provide disease control in severely affected patients, such treatments are rarely curative and alternative strategies are needed.Hematopoietic stem cell transplantation has been used since 1996 for the treatment of severe autoimmune diseases refractory to approved therapies. Hematopoietic stem cell therapy has got a promising role in Sero Negative/positive Arthritis,spondyloarthropathies, various Connective tissue diseases as Systemic Sclerosis,Systemic Lupus Erythrometosus (SLE),Polymyosistic etc. Various clinical trials done in Multiple sclerosis and uncontrolled Ulcerative colitis have shown significant positive role of Haemtopoietic stem cell therapy. In RA ,bone marrow stromal cells (BMSc) initiate the repair process by differentiating into chondrocytes or by inducing proliferation and differentiation of the remaining healthy chondroprogenitor cells into mature chondrocytes.

The largest cohort studied worldwide shows that autologous hematopoietic stem cell transplantation can induce sustained remissions for more than 5 years in patients with severe autoimmune diseases refractory to conventional therapy. The type of autoimmune disease, rather than transplant technique, was the most relevant determinant of outcome. The progression-free survival varied according to the type of autoimmune disease. In the majority of RA patients, the effect of autologous HSCT was rather limited. Indeed, the introduction of new, targeted biological treatments has modified the therapeutic panorama in the past few years with a decrease in the use of transplantation for inflammatory arthritis due to wider use and efficacy of anti-tumor necrosis factor drugs,while the standard treatment of Systemic sclerosis has not improved significantly in the last 10 years for poor prognosis patient. It seems that hematopoietic stem cell transplantation is better than Biological drugs in RA as Biological drug acts on one cell type or soluble cytokine only, HSCT affects all immune effector cells involved in AD, notably B and T lymphocytes, monocytes, natural killer (NK) cells, and dendritic cells (DCs). These factors contributed to changes in the distribution of the type of autoimmune disease for which autologous HSCT has been used since 2000. Systemic sclerosis and hematologic immune cytopenia (HIC) patients were referred for autologous HSCT more rather than RA, MS and SLE patients.

Role of stem cells in Interstitial lung disease

Dr Vikram Pabreja
PabCyte

Objective To determine role of stem cells in treatment of interstitial lung disease and pulmonary fibrosis

Methods We treated 27 patients with ILD, ILD leading to pulmonary fibrosis, and idiopathic pulmonary fibrosis with IV stem cell stimulation, ex-vivo growth factors and mixed population of bone marrow derived stem cells both by nebulized and intravenous route. Patients on steroids underwent SNMC therapy.

Results Patients improved in their dyspnea, 6minute walk test, oxygen saturation drop on exertion, heart rate, ABGs (pO2 levels) , radiological appearances (disappearing of honeycombing) HRCTs , coarse crepitations, and co morbid situations like hypothyroidism and knee OA.

Conclusion It is hereby concluded that stem cells (haematopoietic) under influence of growth factors have a definitive role to play in decreasing symtoms and disease per se of ILD and PF patients. And that human lung has a regenerative potential.

Role of Stem cells in Autoimmune disorders

Dr. Senthil Thyagarajan
Laboratory and Operations Director for NCORD Biotech Limited, India,

Mesenchymal stem cells (MSCs) are known to display not only stem cell multi potency, but also robust anti-inflammatory and regenerative properties. Following numerous in-vitro and in-vivo studies, MSCs are being used in a range of immune mediated conditions including graft versus host disease, Crohn's disease, multiple sclerosis, refractory systemic lupus erythematosus and systemic sclerosis. However, the processes involved in the pathogenesis of human diseases are more complicated and treatment cannot be administered before disease induction.

This talk will review on the use of Stem cells in autoimmune disorders, mode of action and clinical outcome. Additionally, this talk will try to address the need to perform controlled studies and proof of concept studies which would help in successfully evaluating the stem cells as a mainstream therapeutic module for ailments.

Clinical Advances in IVF

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Successful IVF should have only one meaning i.e. " Take Home baby" rate of one infant per pregnancy**.** New techniques offer the possibility of improving a patient's odds of having a baby through in-vitro fertilization. Louise Brown was the first human born from IVF in 1978. IVF techniques have come a very long way in the last 30 years. Throughout this time there have been many advances across all aspects of fertility treatments. Bad gamete quality or other genital organ related malfunction or abnormalities now no longer have remained cause for infertility.

This talk on "Clinical Advances in IVF" will provide information to the audience about the history of IVF, Factors affecting on success of IVF, Steps involved in IVF, Ooplasm transfer, detection of sperm DNA fragmentation for assessment of sperm quality and Y micro deletion as predictor of sperm retrieval, techniques of surgical retrieval of sperm in case of ejaculation failure and NOA, advance technique like IMSI and Polscope for selection of better sperm, Embryoscope for in vitro growth of embryo and its application in embryo selection based on morphokinetics of embryo development events, Technique of laser assisted hatching of embryo, Preimplantation genetic testing (PGS & PGD) for embryo selection of chromosomally normal embryo. This talk will also cover advanced techniques of preimplantation genetic screening by Next Genome sequencing and Fertility preservation by vitrification of oocytes, ovarian tissue and embryo freezing.

In-vitro fertilization (IVF) and its derivatives in pre-implantation diagnosis, stem cells and the ethics of assisted reproduction continue to attract immense attention scientifically and socially.

Role Of Stem Cell In Skin Rejuvenation - Dermatologist Experience

Dr Deepali Bhardwaj, MBBS, DVDL, MD(USA.IM),M.Phil, F IADVL, F ACSI, F EADV(Munich), F ISD (Iran)
The Skin & Hair Clinics*
Honorary Dermatologist to the- President Estate Clinic

Skin Rejuvenation is a very common demand and for many a necessity in today's day and age.

By skin rejuvenation we mean, rejuvenating and giving skin glow and its natural shine in more abundance to leave it radiant and smooth.

Various methods as a qualified Dermatologist I have in my armanterium for skin rejuvenation like Dermaroller, CO2 Laser, Erbium Yag Laser, Thulium Laser, Peels, PRP (near to stem cells extract with high content of platelets with alpha granular secretions of Pdgf, Vegf, Tegf, etc) and latest is stem cells both plant origin and individual origin.

In my experience plan origin don't work at all and are like placebo and its result is based on delivery system in skin! Besides, individual stem cells in aesthetic science can be a totally new high for the doctors and consumers both and is quite relatively untouched by many still though there is a continuous research in the field of aesthetics.

Role of Stem Cells In Hepatocyte Regeneration

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Stem cell therapy holds promises for treatment of acute and chronic liver diseases, however extensive research forthe last 2 decades could not improve the outcome of hepatocyte transplantation. Major limitation are the availability of good quality hepatocytes for transplantation. Orthotopic liver transplantation has been the only available therapy for patients with end-stage liver failure. Unfortunately, the availability of donor organs is inadequate and many patients die each year on transplant waiting list.We have identified a defined population of human liver progenitor cells (HLPC) expressing the markers CD117+/CD34+/Lin- that could be successfully expanded *ex vivo*. These cells could be maintained with stable morphology and phenotype for several passages. When cells in various passages were transplanted into animals with acute liver injury they exhibited functional differentiation into hepatocytes, cholangiocytes and sinusoidal cells. The achievement of positive outcomes in many clinical protocolsinvolving liver progenitor cells has been handicappedby the limited numbers of liver repopulating cells availableto actually bring about therapy. Currently, only 30% or less of transplanted hepatocytes stem/progenitor engraft. This suggests a great loss of the total transplanted cells. If human liver progenitor cells (HLPC) are to be used as an alternative to organ transplantation, it is very important to better understand factors that allow HLPCs integration and engraftment. This will help to reduce the need for repeated cell infusions and large numbers of cells for transplantation.

Thus, development in the strategies of generating hepatocytes, banking of hepatocytes, hepatocyteengraftment, therapeutic cell number, and functionality of hepatocytes will change the present scenario of cell transplant.

CLI - Our Experience and Expectation

Dr. V. R. Ravi* MS (Ortho.), Dr. S. Sankaranarayanan MDS,
Dr D. Avinash Gandi Ph.D.
* Director
Mothercell Regenerative Centre Pvt. Ltd., Trichy, Tamilnadu, India
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Chronic critical limb ischemia (CLI), defined as > 2 weeks of rest pain, ulcers, or tissue loss attributed to arterial occlusive disease, is associated with great loss of both limb and quality of life. The medical management in treating patients with CLI include reducing cardiovascular risk factors, relieving ischemic pain, healing ulcers, preventing major amputation, improving quality of life and increasing survival. These aims may be achieved through medical therapy, revascularization, or amputation but the results were mostly unsatisfactory. Even after stent and ballooning procedures the revascularisation obtained was limited. Hence the term "Therapeutic angiogenesis" originated two decades back and were mainly focused on neo-angiogenesis. From persistent basic research and publications it is evident that cell based angiogenesis for CLI is possible.

My presentation will be about the results of two case reports on CLI treated with autologous Bone Marrow Mononuclear cells where the patient showed evidence of ABI index improvement, Development of new collaterals and claudication distance was improved.

iPSC A "New" Hope for Animals and Humans

Dr. Rajneesh Verma BSc, MSc and PhD
Scientific Director
Stem Cells 21 Pvt. Ltd and Intelli-health, Thailand and U.A.E

Most of species are classified as threatened, vulnerable and endangered due to poaching and habitat loss. These species are often difficult to breed both in captivity and under natural conditions.

While stem cell biology and assisted reproduction technologies can prove invaluable in understanding development in endangered animals and providing conservation alternatives, the critical limitation to date has been the scarcity of gametes and embryos. The seminal discovery by Shinya Yamanaka's team that it was possible to revert first mouse and then human somatic cells back to an Embryonic Stem Cell (ESC) equivalent, termed Induced Pluripotent Stem Cells (iPSC), by forced expression of as few as 4 pluripotency associated genes, raised potential opportunities for other species. Despite numerous publications on generation of iPSC in rodents and primates, such cells have only been generated in only a handful of large animal species to date. The resulting iPSC have the same properties as of ESC isolated from fertilized eggs, and so have the potential to develop into all cell types of body in the laboratory-including sexual reproductive cells as shown in mice.

The great promise offered by iPSC is studying human cells, which may reflect a disease phenotype more accurately than previous cellular models or animal models, will make therapeutic drug discovery faster, more efficient, and eventually, customizable to individual patients. High quality iPS cell lines must be systematically generated from a diverse patient population and from appropriate control individuals for each disorder, and these lines must be made broadly available to the research community.

In conclusion, efficient production of iPSC from endangered species creates an opportunity for species preservation through gamete production, nuclear transfer, embryo complementation and future novel technologies.

Since iPSC technology is still in its infancy, different aspects of the process will need to be optimized in humans before iPSC can become reliable tools for therapeutic drug development. Reprogramming protocols need to be systematically compared; storage, culturing and expansion procedures need to be streamlined; and cellular characterization must be standardized. Rigorous and dynamic attention to these details, possibly through a centralized resource such as an iPSC banking facility, could prove an invaluable asset for furthering the therapeutic potential of iPSC.

Stem cells in Haematology

Dr. Nedun Chezhian

The practice of stem cells (Haematopoietic stem cells) application in Haematologyis used to treat marrow and immune function in patients with a variety of acquired and inherited malignant and non-malignant disorders.

Hematopoietic stem cell transplantation is a process which includes mobilization, harvesting, and transplant of stem cells after the administration of high dose chemotherapy and/or radiotherapy.

High dose of chemotherapy is accompanied by a re-infusion of hematopoietic stem cells, which are primitive cells capable of replication and formation into mature blood cells.

Haematopoietic stem cells transplants are classified in to four types

Autologous: Stem cells are harvested from an individual's own bone marrow or Peripheral blood.

Allogeneic: Stem cells are harvested from a HLA Matched donor/ Cord Blood.

Syngeneic: **Stem cells are harvested** from identical twin.

Haplo Identical: Stem cells harvested from parents or child or siblings.

The most applicable stem cell source for a specific individual depends upon the disease, treatment history, and the availability of a compatible donor. The most appropriate source of stem cells for each individual must poise the risks of graft failure and re-infusion of malignant cells in autologous procedures, the risks of graft rejection, and graft versus host disease in allogeneic procedures.

Use of SVF for healing chronic non-healing diabetic ulcers and limb salvage- our 5 year experience

Dr Deepali Tiwari, MS(Ophthal), Dr Sandeep Sharma, MS, M.Ch(Plastic Surg.)
Baroda

The prevalence of Diabetes has reached epidemic portions, especially in INDIA. There are 40 million diabetics in India. 15% of all diabetics have a Diabetic Foot(6 million). 5% of these will end up with amputation, making it more than 50 thousand amputations each year. All this also punches a big hole into the health budget of the individual and the nation.

Over the last 5 years, we have observed significantly improved outcomes in patients with these difficult to treat lower limb ulcers. Based on these successful results, in our series of 57 cases, we have now moved from only treating the intractable non-healing ulcers to even the early complex ulcers. The hypothesis for our early intervention and successful approach is that in addition to achieving quick and complete healing, the quality of healed tissue and the neurovascular recovery are unparralled. Furthemore, the safety and advantages of using allogenic SVF has further reduced the treatment associated morbidity and opened a limb saving option in patients with significant morbidity and advanced disease.

The safety issues of allogenic mesenchymal stem cells have been addressed by several clinical trials done in cardiology, hepatology, etc. The ease of retrieval of large numbers of healthy MSC's from donors lipo-aspiration procedures provides an exciting and rewarding answer to the challenge of producing adequate number of MSC's to treat a variety of conditions. Our experience in using allogenic SVF in successfully treating cases of intractable non-healing diabetic ulcers and ischaemic limbs is drawing us to the conclusion that this is the future as we document the amazing outcomes, to further realize their potential.

Role of stem cells in female infertility

Dr. Varsha Baste
Nashik

Adult stem cells are rare undifferentiated cells that have been identified by their functional properties in most adult tissues and organs in the body. Their role is to maintain tissue homeostasis, providing replacement cells lost through cellular turnover and following tissue damage. Recently rare populations of epithelial progenitor cells and mesenchymal stem / stromal cells (MSC) were identified in human endometrium and are likely responsible for regenerating the functional layer of the endometrium following menstruation and parturition.

HLA- and gender-mismatched transplant studies in human and mouse suggest that stem cells may incorporate into the endometrium in a setting of ongoing tissue damage and inflammation. This opens up a new vista for the treatment of endometrium related disorders. This talk will review the use of stem cells in the area of endometrium repair and health.

Role of Autologous Bone Marrow Stem Cells In Alcoholic Liver Cirrhosis.

Dr. Deepak Verma, MBBS, MS (Ortho)
Orthopedic, Trauma & Joint Replacement Specialist,
Gurunanak Hospital & Research centre, Ranchi
Fellow joint replacement Surgery, Sancheti Hospital, Pune
Regenerative Orthopedic Specialist, Reelabs Pvt. Ltd., Mumbai.

The liver is critical for sustaining life. It metabolizes nutrients, removes waste products, filters toxic substances and drugs, maintains the levels of blood sugar, fat and hormones, and participates in immune responses.

The short life span of hepatocytes (150 days) requires the liver to constantly regenerate itself to remain healthy.

Cirrhosis is a serious condition where liver tissue is replaced by scar tissue, compromising its synthetic and metabolic function. It has multi factorial etiology.
Currently the only curative option for end stage liver disease is liver transplantation.

Stem cells treatment is the most state of the art treatment means for cirrhosis.
The mechanism may be:

- The induced pluripotent cells that hold the promise of unlimited production of hepatocyte like cells can be used in ex-vivo liver assist devices (liver dialysis machines or bio-artificial liver BAL)
- Replace directly the affected liver cells
- Rebuild the hardened blood vessel network and increase the blood supply to affected areas, creating a good environment for liver cells.
- Stem cells produce nutrient substances which revitalize the impaired and still alive cells.
- Promote the growth of new liver cells and relieve liver dysfunction caused by non-viable or non-apoptotic cells.

Stem cells sources for liver disease therapy

1. Liver derived stem cells - Both adult liver stem cells, called Oval cells &Fetal liver stem cells, called Hepatoblasts are bipotent and can differentiate into hepatocytes or bile duct cells.
2. Bone marrow derived stem cells - Both hematopoietic and mesenchymal stem cells. MSCs have a higher potential for liver regeneration. In addition their strong paracrine & immunomodulatory properties help.
3. Annex stem cells - From placental tissue, umbilical cord and cord blood and amniotic fluid are pluripotent and have higher differentiation and proliferation potential.
4. Embryonic stem cells - Are totipotent.
5. Induced pluripotent stem cells -

The master stem cell is the embryonic stem cell because it can make an entire human being. Scientists have turned back the clock on adult somatic cells and reprogrammed them to act like ESCs.

What can you expect?

- No ill effect from the treatment.
- without albumin and other blood products injection, the Ascites improves.
- Jaundice and pruritus improve.
- Anorexia, abdominal distension improves.
- Increase in stamina, energy and sense of wellbeing.
- Improved biochemical markers like SGOT, SGPT, Albumin.
- Improved Child Pugh and MELD scores.
- Stoppage of progression of disease.

Alcoholic cirrhosis has a better and more apparent improvement than viral cirrhosis.

MUSE-AT Stem cells through Water jet Liposuction

Dr. Narinder Pal
MD, FRCP (Glasgow), FRCP (Edin), FRCP (Ire)
Consultant Physician

Water jet assisted liposuction has revolutionized the procedure of fat removal as it offers body contouring, fat grafting and retrieval of stem cells in the most aseptic manner.

Liposuction has evolved over time, from manually operated to motorized cannulas, Laser and Vaser (ultrasonic) machines. Water jet liposuction by "Body Jet" from Germany is the latest technique which is FDA approved. After injecting small volume of tumescent fluid, it uses a pressurized stream of saline to dislodge sheets of fat cells along with interspersed stem cells and allows their collection in a lipo-collector in an aseptic manner. There is an added advantage of less bruising, swelling, pain, which shortens the recovery time. Hence, it can be performed under local anesthesia.

Multilineage differentiating Stress enduring- Adipose tissue (MUSE-AT) stem cells were introduced to the scientific community in 2010. They are present in abundance in adipose tissue, which is easily accessible and non invasively extracted from human body. Thus, they can be harvested for autologous stem cell banking.

MUSE-AT pluripotent cells have an advantage over embryonic stem cells and induced pluripotent stem cells (IPS), as they do not form teratomas. They are inherently resistant to cellular stress and genetically resilient to DNA damage.

Because of their differentiation capacity, MUSE cells may be utilized to regenerate any type of tissue. The potential application of MUSE-AT stem cells in regenerative stem cell therapies is both innovative and promising.

Stem Cell Applications in Cardiac Disease

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Stem cells appear to be a promising modality for management of rising burden of Heart failure patients worldwide especially in developing countries like India where heart transplant, ventricular assist devices and artificial heart are far beyond the reach of most of the patients . Ischemic heart failure following acute coronary syndromes and chronic myocardial ischemia are the most common indications apart from other cardiomyopathies. The results of myocardial revascularisation in ischemic heart failure are limited by the proportion of already infarcted myocardium .Several clinical trials have revealed the potential of Stem cells in improving the myocardial function and in the last decade results of injecting stem cells originating from skeletal muscle , adipose tissue , autologous bone marrow and induced pleuripotent cardiomyocytes have been explored however, it is still not clear which type of stem cells in what quantity and what route of injection would provide the best results.

Multivariate analyses of all these randomised trials has revealed that although stem cells can improve the left ventricular ejection fraction in significant proportion but there is no proven survival benefit so far. Most of the benefits of stem cell applications may be because if the paracrine effects as 80 % of the cells die within 48 hours of injection .Although several routes of injection have been tried which include intravascular, intracoronary, intra coronary sinus, endo ventricular and direct intramyocardial injection, it is not yet clear how much improvement can be actually attributed to the effects of myocardial revascularisation in improving hibernating myocardium and whether there is actually a significant additional benefit of Stem cells . Several modalities of Regenerative therapy in which techniques of cell culture , scaffolding and gene therapy are currently being studied to evolve an ideal form of therapy that could not only regenerate adequate cardiomyocytes and produce enough neovasculogenesis that could result in clinical benefit and also improve long term survival.

Therefore, there is a need for several well designed randomized clinical trials to explore the potential of stem cell applications in Cardiac diseases and to further substantiate the ideal form of therapy.

1st Annual Conference of Stem Cell Society (India) held at Renaissance Convention Centre, Powai, Mumbai on from 27 Feb-1st Mar, 2014

2nd Annual Conference of Stem Cell Society (India) held in Delhi on 31st May 2015-1 June 2015