Science and Technology for Inclusive Innovation- Role of Women

Abstracts
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WHY DO WE NOT HAVE A VACCINE AGAINST HIV OR TB?

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Nobel Laureate

The Spectrum of biological research comprises extreme points of view: One is, everything is possible and therefore all results are correct, if correctly measured. The other one is, that it is more important to always ask and ask again what matches evolution, is frequent and enhances survival versus what is rare or an exception. With this in mind, I will evaluate the key parameters of immunity and the question of why we have efficient vaccines against small pox, measles, polio, tetanus and meningococci, but not against HIV or TB.

Using infectious diseases and immune protection against such infections, I shall explain, basic immunological mechanisms and confront the insights with current immunological dogma. Various concepts, including so called tolerance, i.e. absence of an immune response against self- or foreign antigens, the idea of immunological memory or the concept of immunological specificy are reviewed. These well accepted concepts will be confronted with experimental findings that question the biological and medical relevance of many theoretical immunological concepts and demonstrate alternative possibilities that may be exploited medically e.g. for vaccine strategies.

While it is well accepted that cell-destroying virus infections must be dealt with efficiently by adaptive immune responses, this is less clear for infections with non-cytopathic or persisting virus infections. Some infections (e.g. by papilloma viruses causing warts) stay outside of the reach of immunity by avoiding antigen transport to, or infection of, the draining lymph node or the spleen. Others get transferred from a virus-carrier mother to the offspring at or shortly after birth, when the infant has no mature immune system yet. Such infections are non-cytopathic and therefore cause no rapid and direct harm to the host. The pathology that may develop is via T cell mediated immune responses causing immunopathology and takes often years to develop (e.g. AIDS or aggressive hepatitis). If an infection persists at sufficiently high levels, then chronically activated immunity may cause immunopathology; such processes may be responsible for many so called autoimmune or chronic, degenerative or other unexplained chronic and slowly developing diseases. Persistently circulating antigen or virus can cause specific T cell and partially also B

cell elimination called immunological tolerance.

The fact that children once infected with measles virus will be immune to measles challenge infections for the rest of their life has led to the idea of so called immunological memory. i.e. a primed hosts will make a quicker and better response to a second antigen encounter. The question is, does this definition always correlate with protection? While for most acute cytopathic classical childhood infections, tetanus, diphtheria, measles, polio or small pox, our usual in vitro assays ELISA, ?-IFN producing T cells or T cell proliferation correlate reasonably well with the above definition of immunological memory. It does not however always correlate with protection, e.g. HIV-1 infections induce quick and very good ELISA positive responses, although there is obviously no protection against this virus. In contrast, neutralizing antibody responses are induced very late by HIV in humans (or by LCMV in mice). This common feature applies to several human persisting viral infections, including HBV, HCV, HIV (and many parasitic infections). If a neutralizing antibody arises and viraemia re-emerges, then often neutralizing antibody escape mutant viruses get selected. This indicates that only a multi-specific type of vaccine may eventually control such infections. Since this may include up to 10'000 or 100'000 variations for HIV (or 1'000 for influenza virus), such a vaccine will be very difficult to develop. In addition, there is good evidence that only persisting and re-encountered antigen maintains the specific neutralizing antibody, but also response of the host. This antigen-dependence of protection is a far cry from the usual definition of immunological memory and its relationship to vaccine mediated protection to become plasma cells. Therefore impact of antigen dependent protection via activation of B cells or effector T cells impinges on our understanding of protective vaccines, particularly against chronic persistent types of infections. Evidence accumulated so far indicates that vaccine strains that tend to persist, such as BCG., loose protective capacity once the vaccine strain has been eliminated by the host. On the other hand attenuated vaccine strains may regain virulence under certain circumstances (e.g. HIV-1 or SHIV) suggesting that development of sufficiently attenuated but not too much attenuated vaccine strains may be either extremely difficult or impossible. In this context the parallels between successful vaccines against acutely cytopathic and potentially lethal virus infections versus the absence of such vaccines against chronic persistent types of infections (including the ones mentioned above, but also Herpes viruses) reveals a very delicate balance between epidemiology and maternal immunity, that is handed down via antibodies to the offspring. Attenuation in the offspring during early childhood of epidemiologically important

infections and the consequences of this almost Lamarckian-type of handing down of acquired immunological experience across generations opens up interesting perspectives. Could for example juvenile diabetes or some forms of rheumatoid arthritis correlate with certain childhood infections dependent on the passively acquired maternal antibody coverage? And what are the relationships between the timing of first infections and many immunopathological diseases?

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Zurich, July 22, 2011

BASIC RESEARCH AND HUMAN DAILY LIFE

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Many seminal results from basic research during the 20th Century add greatly to the quality of present daily life, and in most instances we enjoy these benefits without remembering their roots. Illustrations from my own research areas of nuclear magnetic resonance (NMR), structural biology and structural genomics will be presented, including the use of magnetic resonance imaging (MRI) in human medical diagnosis, structure-based rational drug discovery and drug design, and applications in agricultural science.

ACADEMIC OPPORTUNITIES FOR SHAPING A BETTER FUTURE

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The lecture emphasizes the importance that academics and academic institutions carry in shaping a beneficial global future for all. They are the educators and motivators of the future leading heads in politics, business, and academia. A new spirit shall be developed and spread within the academic community and society that is based on cooperation, foresight, and compassion in order to counterbalance our deadly money-mindedness and our egomaniac cravings for materialistic goods that lead us into the present global disarrays. The best advice that can be given at present is contained in the Imperative of Responsibility by the philosopher Hans Jonas: *"Act so that the consequences of your action are compatible with the permanence of genuine human life on Earth." Or: "Act so that the consequences of your actions are not destructive for the future possibilities of human life."* This is the basis of ultimate sustainability. It is our task to educate future generations of leaders who, hopefully, commit fewer errors than our present generation.

We all know that researching and exploring nature is a fundamental human driving force. All human beings are researchers by nature, and without this gift, mankind would not be where we are today, with all our opportunities and threatening problems. Today, research is indispensable for understanding nature, on the one hand, and for stimulating industry, on the other. Research is indispensable for solving the great pending problems: sustainable development, saving resources, such as energy and water, improving health worldwide, and reducing the gap between the rich and poor by providing employment for all.

Seen from the point of view of an academic scientist, our world seems to be split into a scientific world that enjoys discovery and a world at large that is suffering. Our time is characterized by a never ending row of catastrophes, wars, environmental damage, selfishness, greed, corruption, crime, and poverty. If we would not maintain our inborn believe in the benevolence of human beings, we could despair. We should remember the words of the Sufi teacher Nawab Jan-Fishan Khan: *"The candle is not there to illuminate itself."* This refers also to academic responsibility outside of our ivory tower. We are called up to build bridges based on tolerance and responsibility, bridges between science and the public, between the rich and the poor, between developed countries and developing countries, and between religions.

We seem to experience today a loss of values; cultural and ethical values are gone down the drain. What remains is money-mindedness with all its consequences of egoism, exploiting the innocents, lust for power, racism, and violence. Indeed, we are caught in a deep identity crisis, in a crisis of objectives. Competition is today of greater significance than cooperation, also in science, as can be read in Nature Vol. 438/24 November 2005: *"Tales of brilliant scientists and their heroic discoveries can overshadow the true nature of scientific communities, which are often dominated by battles for power and success."* We are in great need of novel, comprehensive, and lasting approaches! But who will keep our boat afloat? Politics, economy, or the academic community? Surely, we all have to collaborate. But certainly, academics also have to contribute their share in terms of honesty and foresight.

Three academic responsibilities come to our mind: Educating future leaders, research for solving the great problems of our time; and planning of a beneficial future. Indeed, the development of leadership qualities among our students might be even more important than the training of specialists. This requires the provision of skills, knowledge, understanding (wisdom), ethics and responsibility.

Research and teaching are not our only academic obligations. Equally important are foresight and the planning of our future! If we want to change the world, we have at first to change ourselves, following the advice by Mahatma Gandhi who said: *"We must be the change we want to see."*

We researchers should learn to operate on two levels. The basic research level, of course,

is indispensable where we dig as deep as possible in the foundations of science and nature to understand our world. On the other hand, it is equally important to be able to operate on an upper societal and global level where we acquire knowledge and understanding of the world at large and can appreciate the long term needs of future generations.

I envision our world as a two-wheel vehicle, with society being the passengers, kept in a good mood by the politicians so that nobody jumps from the vehicle. Industry is represented by an enormously strong power wheel that drives the vehicle forward at maximum speed, irrespective of the direction, and the long-term destiny is irrelevant, even if the vehicle is driving to hell. What counts are the momentary profits! Finally, the guiding wheel represents the academic community that has indeed a steering function, its main activity being the education of responsible leaders of tomorrow who possess the proper spirit.

Finally, let us remember the words by François Rabelais (1494-1553): "Science sans conscience n'est que ruine de l'âme.*" Science without conscience ruins the soul.* The formation of responsible and innovative leaders with long-term vision, willing to serve society will remain a main obligation of universities. Let us become pathfinders of society! And finally, we should never forget the strong and positive words that the philosopher Karl Popper said in Berlin, 1993: *"Optimism is our duty. We all are jointly responsible for what will come."*

mHEALTH: HEALTH CARE FOR ANYONE, ANYTIME ANYWHERE

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India is indeed a paradox. Considered a third world, developing country, we fall far short of the minimum health standards, recommended by WHO. It is unlikely that the 750 million Indians living in suburban and rural India, will have easy direct physical access to India's medical specialists, as 80% of them, reside in urban India, catering to only 20% of the population. At the same time, we have 900 million mobile subscribers. Rural teledensity even in Northeastern India is now 55%. According to TRAI projections Kerala with a 100% penetrance will be the first state with no urban rural divide in mobile telephony. In 2014 broad band penetration is expected to be only 60 million, while sales of smart phones could exceed PC's, as would wireless access to the internet. mHealth therefore is more relevant in India than conventional eHealth. The fierce price war in the Indian telecom space, in the past couple of months, has seen rates for voice calls plunge to an all time low. To recover the crores of rupees invested in 3G, Indian telecom companies have to necessarily offer Value Added Services and we can now count upon proactive measures from them, to make mHealth reach that critical mass, so essential for a successful take off. It is therefore not surprising that mBanking, mCommerce, mEntertainment and mGovernance have already started making inroads into the Indian diaspora. Today 35 banks with 70 million customers offer mBanking. 35 TV channels can be accessed on the mobile. Several government initiatives in mGovernance clearly indicate that this will be a major thrust area. **mHealth however is conspicuous by its absence** .

In August 2007 in collaboration with Ericcson, the author carried out the first clinical trial in South Asia, on wireless medicine, using a 3G spectrum specially obtained for the study. Clinical evaluation of 240 patients was done through a webcam , including BP evaluation, tele auscultation

and transmission of 12 lead ECG's. Subsequently a mini master health check up was carried out in a village, for 75 patients, using EDGE technology . Xrays and ultrasound images including video streaming of ECHO cardiograms were transmitted thro wireless from a Hospital on Wheels to Apollo hospitals at Madurai. Electronic house visits have since been carried out using a commercially available wireless modems.. A 24/7 Medical Response Center is now operational in Chennai and Hyderabad since March 2011. Accessible to mobile phone users, these cost effective resource centers, are manned by trained personnel, who use customized, evaluated algorithms/triage protocols to provide authenticated health information for just Rs 35. This presentation will review the several pilot projects being carried out in mHealth followed by some crystal ball gazing. As a guestimate, there are probably about 25 active mHealth pilot projects being carried out in India. They include use of mobile games to enhance HIV/AIDS awareness. Handheld devices have been used to collect raw health data, which are transmitted in real time to a Health Information System Database. Disease and Epidemic Outbreaks have been tracked and daily health alerts sent to subscribers. The multifarious ways in which the mobile can be used to deliver health care to anyone, anytime anywhere will be reviewed. . The mobile can bridge the urban rural health divide, truly transforming the delivery of health care. Simple SMS reminders could promote adherence and compliance for medications, self care, self management, wellness activities and assist in management of chronic diseases like diabetes. Support can be provided for giving up smoking, in antenatal care and women's health besides providing daily health tips. As better health, implies reduced claims for insurance companies they could be called upon, to financially support these ventures. SMS can be used to inform, motivate and assist patients besides informing doctors about admissions, laboratory results etc Other applications of mHealth include educating patients, creating awareness, remote data collection, communication and training for healthcare workers, disease and epidemic outbreak tracking, diagnostic and treatment support and even remote physical monitoring, Access to technology, end user and health care provider acceptance, lack of regulatory issues, challenges in logistics and non availability of appropriate, need-based, customized solutions are some of the key issues. Eventually the mobile could become a hand held hospital,. Refractive errors can be checked, diagnostic images can be manipulated, ECG;s reviewed and heart sounds heard. It can even be used as a microscope, store personal health records and be a storehouse of information

to understand safety of drugs prescribed, particularly when they are multiple.

Challenges in deploying mHealth are many. They include changing the mind set of all the stakeholders, convincing them with success stories, providing education and training , providing solar units for charging the phone in rural areas and making available appropriate, cost

effective, need based, Value Added Services. Critical success factors to scale mHealth include creating the right "fit" between mHealth applications and health care needs ; mHealth should be need driven not technology driven delivered not in isolation but in combination with other mServices Proof of concept projects deploying mHealth are insufficient. Evidence based impact studies are necessary to convince the authorities , to accept mHealth as a thrust area. Health Care is more than diagnosis and treatment. From hospitals and doctor's offices, health care is moving to homes. Health is not curing illnesses, but promoting wellness. Knowledge is power and the mobile is the simplest tool to provide health information to everyone.. mHealth can go a long way in providing equitable, sustainable health care bridging the health divide and indeed help touch billions of lives. This illustrated presentation will provide enough data that mHealth is a doable practical sustainable scalable solution which can be incorporated into the core of the health care delivery system in India. "Health Care Without Borders-The Tele-Medicine Way" could very well be replaced with the words " the mHealth way" for this would be the simplest, fastest, quickest cost effective method of reaching the unreached. Wireless, mobility and universal availability will be the buzz words in healthcare of the future. The mobile phone is already proving to be the moist disruptive innovation of the 21st century.

SPACE TECHNOLOGY AND ITS INNOVATIVE APPLICATIONS BY ISRO- THE HARBINGER OF TELEMEDICINE PROGRAM IN INDIA.

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With a proven track record in developing, launching and operating a host of satellites for earth observation, communication and meteorology, Indian Space Research Organisation (ISRO) is also a pioneer in their applications for societal benefits. India started integrating the developments in Space Technology and advances in the field of Information and Communication Technologies (ICT) along with medical sciences to bring their benefits to the Healthcare delivery at grassroot level a decade back. Faced with rural urban divide in health care India took to the technology based INFOstructure route to supplement the traditional route of INFRASTRUCTURE to address the need and problems.

While Indian Space Research Organisation (ISRO) spearheaded the Indian Telemedicine Programme it was well supplemented by other Government and Private agencies that made strides towards technology based health care delivery system, popularly known as Telemedicine/ e-health. Starting with the thrust areas focused on providing Technology and Connectivity for Tele-consultation, ISRO has enabled reducing the distance between remote hospitals and the speciality hospitals; gave a fillip to the Continuing Medical Education (CME) and also heralded advanced Mobile Tele-health facilities and Disaster Management Support.

In tandem with the technology demonstration and awareness campaigns, ISRO focused on technology upgradation and cost reduction efforts resulting in a higher pace of expansion across the length and breadth of the country.

ISRO's efforts were recognized and appreciated by all the stake holders- Stage Governments, Private Hospitals, Doctors, Industry and Health Administrators in addition international recognition for the application of space technology to the benefit of the man at the grass-root level. If the first decade belonged to diligently marshaling the diverse groups of stake holders for

a common cause kindling awareness and motivation among them, the next decade is set for taking it to the next level.

On one hand ISRO is gearing up not only to revive but expand Telemedicine network with the availability of transponder capacity from the recently launched GAST-12 satellite, on the other, the central health ministry responsible for the healthcare in the country has recognized the benefits of the technology in supplementing the traditional mechanisms to reach-out the needy. Also the industry is gearing itself to play a major role in this important endeavor.

The presentation covers the initiatives and discusses the sustained efforts of ISRO, and all other players in India to take the programme to the next level of operationalisation and also discusses the future plans of ISRO. The need for taking to a revenue model for long-term sustenance and the efforts of different stake holders will also be discussed.

TELE-ULTRASOUND FOR REMOTE MONITORING OF HIGH RISK PREGNANCY

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One area of women's health care where telemedicine has offered some of the greatest opportunities is in pregnancy and prenatal care. A high-risk pregnancy generally involves at least one of the following: the mother or baby is more likely to become ill or die than usual or complications before or after delivery are more likely to occur than usual. Identification and early management of such pregnant women will help not only in reducing feto-maternal morbidity but also reduce mortality. Ultrasound has played a significant role in identifying, monitoring and managing such women. Numerous studies from several continents have confirmed the efficacy of tele-ultrasound for women in remote areas. Tele-ultrasound is used in identifying maternal and fetal conditions like multiple gestation, pre-term labour, intrauterine growth restriction, fetal anemia, oligo/poly hydramnios and fetus at risk of chromosomal abnormality etc. Monitoring for preterm labour is now considered routine in high-risk obstetrical patients in many centres, other programmes have moved on to remote active monitoring of the fetus itself in these high-risk patients.

Fetal ultrasound continues to be a useful application of telemedicine and undoubtedly will become increasingly common in the future. In 1997 Malone et al published a comparison of real-time evaluation of fetal ultrasounds with interpretation via recorded videotapes and concluded that there was a significant improvement in results with the use of telemedicine. Other studies have since documented the feasibility of even more advanced fetal ultrasound capabilities such as a virtual fetal cardiological examination via telemedicine. Apart from detection of structural fetal malformation, tele-ultrasound can be used in guiding invasive pre-natal diagnostic and therapeutic procedures, the expertise of which is limited to few centres in India.

The cost of telemedicine services will be readily justified by the resultant antenatal and neonatal cost reductions, if they are used in these cases. Tele-ultrasound can give an opportunity to those living in rural areas for access to tertiary centre experts and thus to improve the access to a specialist care.

APPLICATION OF TELEMEDICINE IN SURGICAL EDUCATION AND POST-OPERATIVE CARE

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In a developing nation like India there is lack of adequate number of tertiary care specialized Surgery centers, capable of imparting high- standard education to the medical students and state of art clinical care to the patients. Though, there is no dearth of talent in our country, this is limited to a few specialized centers in big cities. Telemedicine technology can bridge the gap between the teachers and students; and patients and care providers.

Telemedicine has a huge potential in uplifting the standards of surgical education as well as clinical care of the patients. Various applications of telemedicine in surgical practice can be classified into following categories.

1. Telesurgery
   - ☞ Telepresence Surgery
   - ☞ Telerobotics
   - ☞Telementoring / Teleproctoring
2. Tele healthcare for surgical patients
   - ☞ Teleconsultation
   - ☞ Treatment planning
   - ☞ Tele-follow up
3. Remote surgical education and training
   - ☞ Interactive virtual class room
   - ☞ Web casting
   - ☞ Surgical education portals
   - ☞Teleconferencing of surgical conferences, CMEs and Workshops

So far as telemedicine technology is concerned only "Telesurgery" needs to be separately understood from the rest of the applications of the technology. "Telesurgery" has been defined as: 'Surgery, procedure or technique performed on an inanimate trainer, animate model, or patient in which the surgeon is not at the immediate site of the model or patient being operated on. Visualization and manipulation of the tissues and equipment is performed using electronic devices'1. "Telesurgery" is an umbrella term covering educational and professional assessment techniques, surgical discussion among remote participants, and surgery using telemanipulation (the expansion of a person's movements to a remote location) and telepresence (telemanipulation with added sensory information to make the operator feel that they are physically present at the remote site)2. Rest of the applications of the telemedicine technology e.g.: teleconsultation, distance education, tele follow up, telementoring/ teleproctoring and teleconference are same as utilized in any discipline of the medicine. However, each of this application needs to be customized according to the sub-specialty of the surgery and while the concept could easily be amalgamated to some surgical disciplines in other only specific aspect of surgical education and patient care could be addressed via telemedicine technology.

Apart from education, one of the potential still unutilized applications of telemedicine is follow-up post-operative care of the patients. Patients have to travel a huge distance in order to get surgery done and subsequently for follow-up. Frequent post-operative visits to hospital apart from being inconvenient in the immediate post-operative period results in substantial financial and work- hour loss to the patients and escorts. Tele follow up facility could be utilized in cutting the number of post-operative visits. Wound inspection, histology (biopsy) report discussion, certain drug dosages modification, further treatment planning can be done using telemedicine technology, which has been shown to be feasible, safe and economic for certain surgical conditions.

At our department we have tried to incorporate the telemedicine technology in surgical education and patient care and our initial experiments with both the aspects have been successful 3,4. We have shown that the concept of training a group of motivated general surgeons to practice safe sub-specialty surgery (endocrine surgery) at a remote center, via telemedicine-aided reinforcement of training is feasible which might be applicable to development of other sub-specialty of medicine in a developing country. Similarly we found that tele follow up is a feasible option for continuity of care following thyroid and parathyroid surgery for benign thyroid and

parathyroid disorders and a subset of patients with thyroid cancers. The technology seems cost-effective and ensures satisfactory postoperative follow-up.

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TELE-HEALTH SYSTEMS AND PRACTICE, WHERE DOES INDIA STAND NOW IN GLOBAL CONTEXT

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Tele-health systems and practice in India has gone through metamorphic change in terms of applications at different tiers of health care system. While the Telemedicine/Tele-health started in bits and pieces during the 1990's the Tele-health revolution got initiated in a broad manner during the year 2001 when simultaneous initiatives were brought on board by the leading government organizations like Indian Space Research Organization (ISRO), Department of Information Technology (DIT), State Government and some of the leading health care providers and institutions like SGPGI, Luknow; Apollo Hospitals, Chennai; Narayan Hrudayalaya, Bangalore; SRMC Chennai; Shankara Netralaya, Chennai; Aravind Eye Hospital, Mudhurai and host of other institutions joining movement subsequently.

Key growth drivers of Tele-health in India

- Wide reach of connectivity over satellite, fiber optic, wireless bandwidth
- Lack of disease management framework
- Lack of healthcare facilities in far-off regions
- Reduced technology cost and availability of qualified technical personnel
- Shortage of qualified medical professionals
- Increased governmental focus on healthcare for all
- Urban-Rural divide causing disparity in medical faculties
- Dedicated satellite for communications from ISRO

- Growth of Information and Communications Technology (ICT) as a sector
- National Telemedicine Grid concept to connect practitioners and institutions
- PPP model for development of healthcare infrastructure

The major effort in the arena of Tele-health was the visionary effort by the ISRO which provided the technology and connectivity free of charge and funded the whole effort in establishing Telemedicine System both at the remote rural district hospitals and the participating specialty hospitals located in major cities, training of personal for appropriate usage and creating over all awareness. That is virtually marshalling different stake holders for a common cause for providing health to the rural population of India. The DIT established the standards and guidelines for practice of Telemedicine/Tele-health which has been approved by the union Ministry of Health.Some other State Governments participated effectively in setting up the state Tele-health network in association with ISRO, DIT and other agencies/ hospitals.

Based on this efforts Ministry Health Government of India constituted a National Task Force in the year 2005 for effectively administering the procedure and methodology of adopting Tele-health systems and a phased plan of implementing Tele-health practice and the Tele-health network in different parts of country. This was envisaged to usher in this technology based health care services in to the main stream of health care delivery system.

Indian Tele-medicine program also got recognition by the International agencies like International Society of Telemedicine and e-Health (ISFTeH), American Telemedicine Society (ATA), World Health Organization (WHO) and other entities. Telemedicine society of India (TSI) which was formed in 2001 was formalized in 2005 and till now Seven International Conference of TSI has been conducted in different parts of the country. State Chapters of TSI has also started with the initiation of the Orissa State Telemedicine Society at Bhubaneswar.

In these ten years the Tele-health initiative have brought in sufficient awareness among various strake holders like the Doctors, Health Administrators, Health Providers, Rural District Hospitals, Specialty Hospitals, Industry and above all the General Public who are the recipients of this service. It is to be noted that every due diligence is completed today for establishing Tele-health practice in India like:

- Technology-Hardware, Software, Video Conferencing System and Data base
- Connectivity - Terrestrial, Wireless, Satellite etc
- Standards for Hardware, Software and connectivity
- Procedure for Medical consultation between the remote/ patient end and the specialist doctors end
- Training of Doctors and Paramedics for usage of Tele-health system
- Technical and Social evaluation of Tele-health system and services

In the Global Scenario India stands out among various countries in the implementation of Tele-health. Because of lack of proper Business and Revenue Model due to of the predominant government healthcare system run by state government in the rural areas, lack organized penetration by Private/Corporate Health Care agencies, and lack of Medico Legal Framework for Tele-health. As it happened in developed countries the Tele-health service in the healthcare system has long gestation period before it takes of in to regular service. Hence, India is not falling behind in this effort.

The establishment of regular Telemedicine practice both at the Government and the Private Health Care delivery is not a distant dream since the fruits of above effort will get percolated to the mains stream of health care delivery system integrating the Tele-health service along a suitable Medical Insurance System. A proper Business model and Revenue model for the practice of Tele-health is to be effectively evolved in the near future, though there have been some efforts in this direction in bits and pieces.

However, the recent International conference of TSI held in Mumbai in November - 2011 has clearly recommended that initiatives in terms of Public Private Partnership (PPP), Private Partnership Enterprises (PPE) and NGO Partnership Enterprises (NPE) needs to be considered. This will usher in the Tele-health Care Service along with the Insurance agencies for an effective delivery of Health care to the semi-rural, semi-urban/ urban/ population initially and to be followed by the approaches for effectively reaching the grass rootlevel rural population in the country through the Primary Health Care

Telemedicine: Regulations in India

Does this imply only "Doctors" and "Hospitals" can offer Telemedicine as a "service"?

What are the liabilities of offering a telemedicine service?

Is there scope for creating a "Telemedicine Service Provider"?

Telemedicine in India: Motivating Factors

- Access to medical expertise

  - Largely underserved population (1 doctor to 1722 people, as of 2005)

  - Mismatch in supply and demand

- Doctors: 75% Urban + 23% Semi-Urban

- Patients: 70% in Rural areas

- "Corporate Social Responsibility" of Hospitals

  - Sometimes helps in increasing "bed occupancy"

Key growth drivers of Telemedicine in India

- Low cost and wide reach over satellite or fibre optic bandwidth
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- Reduced technology cost and availability of qualified technical personnel
- Shortage of qualified medical professionals
- Increased governmental focus on healthcare for all
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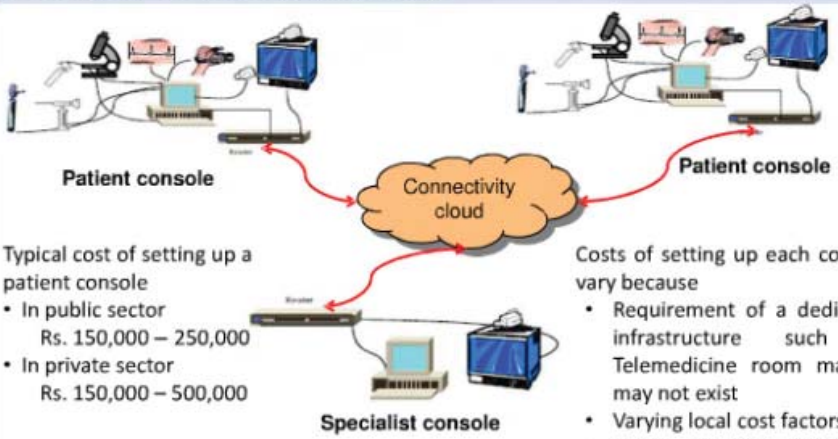
- Dedicated satellite for health communications from ISRO
- Growth of Information and Communications Technology (ICT) as a sector
- National Telemedicine Grid to connect practitioners and institutions
- PPP model for development of healthcare infrastructure

A Typical Telemedicine Setup



Typical cost of setting up a patient console
- In public sector
  Rs. 150,000 – 250,000
- In private sector
  Rs. 150,000 – 500,000

Costs of setting up each console vary because
- Requirement of a dedicated infrastructure such as Telemedicine room may or may not exist
- Varying local cost factors
- Ability of public bodies to subsidize the input cost
- As a policy ISRO provides free satellite bandwidth for Telemedicine

Telemedicine setup adapted from "Telemedicine in India: Initiatives and Perspective" I.S.Bedi, Senior Director, Department of IT)

The Opportunity and Trends

- To achieve 2 bed, 1 doctor and 2.3 nurse per 1000 of population by 2025 the healthcare infrastructure in India needs huge investment - $86bn
- With CAGR of 19% from 2005, global market opportunity for Telemedicine by 2015 stands at - $18bn
- The Indian Telemedicine market potential in 2007 - $500mn
- Revenue from Indian Telemedicine market in 2007 - $50mn
- Telemedicine provides multiplier effect on ancillary industries creating new opportunities for
  - Medical consumables
  - Medical equipments
  - Drugs
  - Medical technology

With the thrust behind improvement in healthcare delivery, the opportunity presented by Telemedicine is too significant to ignore

Status check on Telemedicine implementation

- ISRO's Telemedicine network has touched more than 300,000 people
- Various state governments under National Rural Health Mission (NRHM) have begun implementing Telemedicine network
  - States such as Andhra Pradesh, Karnataka, Chattisgarh, Rajasthan and Kerala have all district covered under Telemedicine network
  - States such as Haryana, Madhya Pradesh, J&K, Punjab including North East states have taken to Telemedicine in big way.
- Under NRHM, government has allocated a budget of Rs. 10 million per annum for each state to increase Telemedicine nodes at district level.
- Telemedicine network under the eHealth initiatives has been put to use to provide Continual Medical Education (CME) for doctors and nurses
- Large companies such as ONGC have adopted Telemedicine for their remote operations.

Telemedicine is a process, not an event. The opportunity lies in being an early mover and erecting entry barriers to gain competitive advantage

# of Telemed Remote Sites	50
Min Patient Visits Per Site Per Day	10
Charges Per Visit	INR 50.00
% of visits needing referral	5.00%
Avg. referral fee commission	INR 250.00
% of visits needing consumables/medicines	80.00%
Avg. commission on consumables/medicines	INR 10.00
% of visits needing consumables/medicines	80.00%

CAPEX (one time)	Expert Center Setup	INR 1,000,000.00
	Expert Center VideoConf	INR 50,000.00
	Remote Sites Setup (Unit)	INR 500,000.00
	Remote Sites VideoConf (Unit)	INR 15,000.00
	Total Remote Sites Cost	INR 25,750,000.00
	NoC Setup	INR 500,000.00
	Total CAPEX	INR 27,300,000.00
OPEX (Recurring per yr)	Internet Charges (Expert Center)	INR 500,000.00
	Internet Charges (Remote Site) (Unit)	INR 60,000.00
	Internet Charges Total Remotes	INR 3,000,000.00
	Internet Charges (NoC)	INR 500,000.00
	Manpower Training Costs	INR 500,000.00
	Overheads/Maintenance	INR 1,000,000.00
	Total OPEX	INR 5,500,000.00

Yr	1	2
Revenues	INR 7,210,250.00	INR 7,210,250.00
Expenditure	INR 32,800,000.00	INR 5,500,000.00

FIRST DECADE OF INDIAN TELEMEDICINE PROGRAM AND ITS IMPACT

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Introduction:

In a developing country like India, there is huge inequality in health-care distribution. People of rural India have poor access to modern medicine. Similarly education in medical colleges of India is yet to meet the desired goal due to shortage of competent teachers and study material in many teaching institutions. Telemedicine technology is being used for last 10years to eliminate such deficiencies. It is time for a critical appraisal of its utility.

Material & Methods:

Several Government & Private agencies have adopted information & communication enabled health technology to bridge the health care divide existing between rural & urban India. Similarly Ministry of Health & Family Welfare, Govt. of India is in the process of bridging the knowledge divide existing in the field of health education. Efforts are on to bring all Govt. Medical Colleges of this country under one umbrella through a high speed fiber-optic network,

The major implementing agencies working towards telemedicine application in India are Ministry of Health & Family Welfare, Govt. of India; ISRO/ Dept. of Space, Govt. of India

Department of IT/Ministry of Communications & IT, Govt. of India and Ministry of External Affairs, Govt. of India.

ISRO in collaboration with state Governments has established around 439 telemedicine nodes in this country. Mobile vans equipped with VSAT units and other medical equipments are being used by a number of leading hospitals in this country to reach rural population. Recent successful launch of GSAT 12 Satellite by ISRO is expected to boost the existing telemedicine network.

Integrated Disease Surveillance Project (IDSP), National Rural Telemedicine Project, Onconet-India and upcoming National Medical College Network Project are some of the major initiatives being undertaken by various Ministries of central Govt. PAN Africa e-Network established by Ministry of External Affairs, Govt.of India connects 53 countries of African union to 7 universities and 12 super-specialty hospitals of India for extending tele- education and telemedicine services to those countries.

A school of Telemedicine & Biomedical Informatics housing the national telemedicine resource centre has been established at SGPGIMS, Lucknow with support of Dept. of IT/Govt. of India & UP Govt. Similarly state-level telemedicine resource centers are coming up in places like Cuttack, Orissa. These centers are designed to work towards research and development along with capacity building in the field of telemedicine through structured telemedicine course curricula.

There are good numbers of industries in India now to provide hardware and software to meet the growing need.

Result:

Kerala oncology network has been providing services for cancer detection, treatment, pain relief and patient follow-up by connecting regional cancer center, Thiruvananthapuram. to some peripheral hospitals of the state. Similar activities are also being undertaken by Tata Memorial Hospital,Mumbai; UP Tele-Radiotherapy Network; RCC,Adyar,Chennai. Webel, kolkata using wide area network has played a significant role in diagnosis & monitoring of tropical diseases.Tele-ophthalmology mobile vans are used by Sankara Nethralaya,Chennai;

Aravind Eye Hospital , Madurai & few other hospitals to provide ophthalmic care at the doorsteps. Tripura Tele-Ophthalmology Project has shown remarkable achievement.

SGPGIMS,Lucknow; AIIMS, New Delhi & PGIMER, Chandigarh are connected to a number of Medical Colleges of India to offer distant medical education Apollo Telemedicine Network Foundation, Chennai; Narayan Hrudayalaya, Bengaluru; Amrita Institute of Medical Sciences, Kochi; SRMC, Chennai & many other corporate hospitals are using telemedicine technology for benefit of their patients residing in remote locations.

District Networks of many states have enabled strengthening of medical care thus cutting down the number of referrals.

Unpublished data available from most telemedicine centers and analysis of feedback reports reaching the above mentioned funding agencies appear encouraging in terms of technology utilization.

Conclusion:

Telemedicine Technology has received widespread acceptance in India. Most state Govts. have made regular budgetary provisions to meet the maintenance cost of state telemedicine projects

Broadband Connectivity is widely available & the cost is coming down. Recently launched GSAT 12 Satellite by ISRO is expected the increase the utilization of the new medical Technology by making available enough bandwidth to meet desired need, Medical Council of India is eager to use the technology for bringing uniformity of medical education & examination in the country,

The first decade of telemedicine application in India has undoubtedly laid a strong foundation for a bright future. The rapid integration of e-health & e-education modalities with conventional health and educational practices is expected to reshape India to meet the need of 21st century..

FOOD AND NUTRITION SECURITY THROUGH FOOD SAFETY - ISSUES RELATING TO CLIMATE CHANGE AND ALSO TRACEABILITY

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The issue of Food and Nutrition security embedded with Food Safety is a triangle which has a tremendous impact on the population. In many of the emerging economies nearly 50% of the expenditure is on Food from an average household income. The role of Climate change, plant breeding and health and wellness appears to be directly or indirectly related and has an issue of Safe Food to the consumer. On top of it sits the Traceability issue. To correct the same such that it is well mitigated and adopted for future learning Process by incidents is very important for any Country as a matter of fact . The importance of Risk Analysis of many protocols and products should not be undermined for not only Local Foods of the Country but also the Transcontinental and Global Trade of Food. The aspects of intricate issues of Food Safety in the Food Chain will be highlighted during the talk using case studies and examples.

VITAMIN D IN MATERNAL AND CHILD HEALTH CARE

Devendra K. Agrawal

Vitamin D is a potent micronutrient that plays a significant role in the immunomodulation of human diseases. In recent years, Vitamin D has become one of the key nutrients of modern times. The importance of this micronutrient began with elucidating the role of vitamin D in the maintenance of musculoskeletal health by regulating calcium homeostasis, and thus bones formation and resorption. Only recently the role of vitamin D in extraskeletal tissues has been recognized. This has significant impact on the maternal and child health care.

Vitamin D is a potent regulator of both innate and adaptive immunity as it relates to host defense from infections as well as auto-immunity in which the immune cells turn against self-antigens. There is a fine balance between a protective and pathogenic immune response in a healthy human host. If this balance is altered it can lead to disease induction. Vitamin D Receptor (VDR) and CYP27B1 (25-hydroxyvitamin D-1-?-hydroxylase) enzyme is expressed in most of immune cells and investigations are ongoing to elucidate the exact role and mechanism of action of the VDR as it relates to the function of a particular cell and also in regards to its interaction with the surrounding tissues. Anti-microbial peptides (AMPs), such as cathelicidin and defensins that are released in response to vitamin D, have many complex actions of their own, over and above their usual antimicrobial role. Vitamin D also plays a crucial role in the initial activation and polarization of dendritic cells and T-lymphocytes.

Deficiency/Insufficiency of Vitamin D

There is a significant prevalence of vitamin D deficiency and insufficiency not only in the North American population, but across the globe. Vitamin D deficiency and insufficiency could be linked to several different diseases, especially those that involve innate and acquired immune response. Serum 25(OH)D levels have been used as a surrogate measure of an individual's Vitamin D status as it reflects both Vitamin D intake from the diet and the intake from skin synthesis of Vitamin D. In 1997, a report of the Institute of Medicine specified that serum 25(OH)D concentrations >12 ng/mL are an indicator of vitamin D adequacy for adults. Since this report of the I OM in 1997, others have suggested different cut-off point values as determinants of Vitamin D 'deficiency' or 'insufficiency'. These include serum 25(OH)D concentrations ranging

from <20 ng/mL to values above 50 ng/mL. These cut-off points have not been derived from a systematic, evidence-based consensus development process. Individuals with levels of serum 25(OH)D above 20 ng/mL may have been diagnosed as vitamin D- deficient and treated with high-doses of supplemental vitamin D containing many times the required levels of intake. Use of higher cut-off points for serum 25(OH)D levels would be expected to artificially increase the estimates of the prevalence of vitamin D deficiency. However, in a recent report of 2011 by the Institute of Medicine (IOM), it is stated that "…a considerable over-estimation of the levels of vitamin D deficiency in the North American population now exists due to the use by some of cut-points for serum 25(OH)D levels that greatly exceed the levels identified in this report as consistent with the available data…". Thus, the current lack of evidence-based consensus guidelines is a problem and is of concern because there is a controversy over the cut-off-point values as determinants of 'deficiency' or 'insufficiency'. None-the-less, vitamin D is a key regulator of inflammatory and pathophysiological processes in several human diseases. It is critical to evaluate the relationship between vitamin D deficiency/insufficiency with the pathophysiology and severity of the disease and determine whether supplementation with oral vitamin D would alleviate these problems, especially in pregnant women, the fetus and the child.

Vitamin D and Maternal Health during Pregnancy

It is now very clear that vitamin D sufficiency during pregnancy and lactation is necessary to ensure the demand of calcium by the fetus and the suckling neonate. Indeed, the calcium absorption increases during pregnancy with near doubling in the serum concentration of 1,25 (OH)2D (calcitriol, the active form of vitamin D) during second and third trimester. The increase in the calcitriol levels surpasses the increase in vitamin D binding proteins, resulting into net increase in free 1,25 (OH)2D levels.

Vitamin D deficiency during pregnancy may increase the risk of preeclamsia and gestational diabetes, and are more likely to have a cesarean delivery than the women with sufficient serum 25 (OH)D levels. In addition, the prevalence of bacterial vaginosis positively correlated with vitamin D deficiency during pregnancy.

Vitamin D status during Pregnancy and Childhood outcomes

There are several reports on the outcomes in children born to mothers with vitamin D deficiency/insufficiency during pregnancy. There is significant increase in rickets in infants and children born to mothers with severe vitamin D deficiency during gestation and early life. Increased incidence of pneumonia and other acute lower respiratory infections have also been reported in infants born to vitamin D-deficient mothers. In a recent study, at ages 5 and 9.5 years children born to vitamin D deficient (defined as serum 25OHD levels <50 nmol/L or <20 ng/ml) mothers, had smaller arm-muscle area, lower weight, fat mass, lean mass, whole body and lumbar spine and mineral content and higher insulin resistance than in children born to mothers with vitamin D-sufficiency. In another study, high maternal vitamin D intake from food and supplements during pregnancy was protective for the development of wheezing outcomes. In a prospective study involving 884 HIV+ pregnant women, a low maternal serum 25(OH)D (<32 ng/ml) was associated with 50% higher risk of mother-to-child transmission of HIV at 6 weeks, 2 times higher risk of mother-to-child transmission of HIV during breast feeding and 46% overall risk of mother-to-child transmission of HIV. These studies demonstrate deficiencies in current literature and the need to carry out more prospective studies and clinical trials to determine the effect of vitamin D on infection and immunity.

Thus, there is a widespread global prevalence of vitamin D deficiency/insufficiency during pregnancy, which has significant adverse effects on maternal pregnancy and fetal and postnatal growth and development, and thus affecting the health of present and future generations. This warrants immediate attention on evidence-based consensus guidelines on the intake of supplemental vitamin D during pregnancy to maintain an optimal circulating 25(OH)D levels throughout pregnancy.

THE PANDA PROJECT: FACILITATING BEHAVIOUR CHANGE IN TYPE 2 DIABETES TREATMENT

Catherine B. Chan

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The prevalence of type 2 diabetes is increasingly steadily around the world. In Canada it is estimated that the number of people with diabetes will increase from 2.7 to 3.5 million between 2010 and 2020. Once almost unheard of in India, there are now more than 50 million people afflicted with the majority living in the wealthiest provinces. The prescription for type 2 diabetes is a combination of lifestyle modification and drug treatment. However, only about 30% of people with diabetes routinely adhere to recommendations to modify their lifestyle. This is not surprising, considering that in Canada there are 11 recommendations for nutrition and 2 recommendations for physical activity. Therefore, the purpose of our research is to develop simple, practical behavioural interventions to enhance the ability of people with type 2 diabetes to change their lifestyles.

The approach of our research team is to consider intervention development within the context of a 4-A Framework. The first A stands for *adequate* and means that the intervention is consistent with the recommendations for nutrition and physical activity. The second A stands for *acceptable,* to ensure that interventions are culturally relevant. The third and fourth As stand for accessible (financially) and available (physically). Ensuring that the elements of an intervention meet these 4-As is hypothesized to lower barriers associated with adherence to behaviour change. Therefore, in our research we have first assessed the health behaviours of people with T2D in the context of the 4-A Framework.

We assessed dietary intake patterns (3 day food record) versus demographic variables and the elements of the 4-A Framework. We also measured food purchases using grocery and dining receipts in a sample of 50 people with diabetes. The mean age was 61 years, BMI 32.6 kg/m2, duration of T2D 8.5 years, hemoglobin A1c 7.3%.

Over 3 days, on average, participants met the nutrition guidelines of the Canadian Diabetes Association with respect to protein % total energy (18 3%TE), carbohydrate (52 8 %TE) and total fat (31 7 %TE) as well as fibre (28 10 g/day). Thus, overall average diets were nutritionally adequate. However, saturated fat intake exceeded the guideline of <7 %TE (10 3 %TE). However, when the number of recommendations met each day was computed for each participant, no one scored higher than 8 (maximum of 11). The median score was 5. This suggests that adherence fluctuates from day to day and shows that only 33% of respondents meets half (6) of the guidelines each day. Intake of fat (r=0.414), MUFA (r=0.298) and sodium (r=0.425) was positively correlated with waist circumference. High intakes of fat (r=.332, p=.021), saturated fat (r=.352, p=.014) and sodium (r=.294, p=.043) were associated with higher A1C values.

Diet acceptability was assessed by a questionnaire. The majority of participants reported regularly buying and consuming recommended foods. Higher intakes of carbohydrate (r=.367, p<.05), fibre (r=.407, p<.005) and sugar (r=.359, p<.05) were reported by participants who chose more frequently to buy foods that were part of their recommended diet. Similarly higher intakes of calories, protein, carbohydrate, fibre and sugar were observed when participants reported that they enjoyed eating the recommended foods most days of the week. Increased consumption of calories (r.301, p<.05), fat (r=.402, p<.005), saturated fat (r=.300, p<.05), MUFA (r=.326, p<.05) and PUFA (r=.326, p<.05) correlated with increased frequency of choosing non recommended foods. However 42% of respondents indicated that dining away from home was less enjoyable after their diagnosis of T2D, while overall enjoyment of eating the recommended foods was the same or increased for 85%. Of the 29 people who reported eating "ethnic" foods, 38% said they had changed their consumption of such foods since their diagnosis. Protein intake was positively associated (r=.298, p<0.05) with frequency of consumption of foods from the participants' ethnic heritage whereas saturated fat intake (r=.298, p<0.05) correlated with consumption of foods not part of the participants' ethnic heritage. These results suggest that acceptability of their diet was not a barrier to adherence when eating at home but that dining out was more difficult. The results also suggest that people should continue to eat foods that are part of their ethnic heritage.

Availability and accessibility to the foods recommended in the diet was also assessed by a questionnaire. Most people in our sample did not have difficulty finding the recommended foods in their local shops. However, we found that people who shopped 2 or more times per

week and those who spent more than 90 minutes in shopping-related activity had better blood sugar control and/or lower body mass index. Interestingly, we found that blood glucose control was best in people with an intermediate income, whereas people with either low or high income had less optimal control.

These findings provide valuable information regarding the development of future nutrition interventions for people with type 2 diabetes. For example, nutrition education should spend more time on fat and sodium reduction. Programs that promote retention of ethnically relevant foods should be encouraged. On the other hand, societal changes that would benefit people with T2D include healthier options for dining out and mechanisms to simplify shopping trips for busy people who don't have time to make multiple trips or spend hours looking for the best food choices. The 4-A Framework can be used as a guide for assessing local barriers and challenges to adhering to guidelines for treatment of T2D.

MATERNAL MALNUTRITION REDUCES THE DISTANCE BETWEEN WOMB AND TOMB OF THE PROGENY

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Double Burden of Diseases

India - a country in developmental transition faces the double burden of pre-transition diseases like communicable diseases and under- nutrition and growing incidence of non-communicable diseases like obesity, diabetes, blood pressure, heart diseases, and cancer. Under-nutrition increases the susceptibility to communicable as well as non-communicable diseases. Malnutrition-infection is a vicious cycle. Malnutrition reduces immunity and increases susceptibility to infections. Infections reduce appetite, and also deplete the tissues through metabolic loss of nutrients from the body.

India has among the highest incidence of malnutrition in the world. Almost 50% of Indian children and 30% adults suffer from protein energy malnutrition as judged by anthropometric deficits- height and weight. Almost 50-70% women (particularly pregnant women), adolescent girls and children suffer from iron-deficiency anaemia. Deficiencies of other micronutrients like iodine, zinc, vitamins A, B2 (riboflavin), folic acid are rampant. More recent studies reveal deficiency of even vitamin D (despite tropical sunshine) and vitamin B12. Almost a third of Indian infants are born with low birth weight (LBW, less than 2.5Kg), suggesting maternal malnutrition and neglect of maternal health. The adverse consequences of LBW are: 1. High morbidity and mortality. Malnutrition contributes to almost 50% of all childhood deaths, 2. Adverse outcome of future pregnancy in daughters-a multi generational effect. 3. Slower growth rate -stunting, 4. Impaired physical and mental performance, 5. Increased susceptibility to adult on-set diseases. Early intervention (within one year), can reduce the disadvantage.

Foetal origins of adult diseases

According to Barker's hypothesis, individuals born with low birth weight due to intrauterine malnutrition (IUGR) are more susceptible to life- style- associated diseases like type II diabetes,

hyper-lipidaemia, hypertension and CVD (the metabolic syndrome), in later life, particularly if there are lifestyle changes. Due to epigenetic effects, their bodies have higher fat/muscle ratio than well nourished babies, which leads to abdominal obesity in later life.

Thus the distance between the womb and the tomb is greatly determined by how well your mother nourished you in womb. Female health and nutrition throughout the life cycle is of prime importance if the nation has to be healthy and productive. Social engineering is needed to remove gender bias against females, typical of India.

Nutrition security goes beyond food security

For nutrition security there has to be "Physical, economic and social access to an age-and physiological status -appropriate balanced diet, safe drinking water, environmental sanitation, and primary health care for all and awareness to utilise these". Thus Malnutrition has a complex aetiology- diet being an important one.

Indian diets: Country- wide diet surveys done by the National Nutrition Monitoring Bureau (ICMR), NIN, show : 1) qualitative deficiency of vitamins and minerals in Indian diets due to inadequate intake of pulses, vegetables, fruits and animal products, and neglect of nutritious millets (Sorghum, pearl millet, finger millet, minor millets). 2) Within a family, diet of infants and children is more deficient than that of adults.

Strategies for Combating Malnutrition- the three A approach

For combating malnutrition there has to be Awareness, and Access at Affordable Cost to: 1. Balanced diet and correct feeding practices for infants and children, 2. Safe drinking water and clean environment to ensure absorption and assimilation of nutrients, and 3. Primary health care outreach.

Awareness : Nutrition literacy should be there at all levels- policy makers (politicians), administrators, all categories of professionals (medical, agriculture, teachers, media etc.), besides the community. Awareness creates demand, which should be accesable at affordable cost. Female literacy has been shown to have a good impact on child nutrition. One IFPRI study showed that among factors that could contribute to reduction in child malnutrition by 15%, increase in women's

education accounted for 43 percent of the total reduction; by far the largest contribution.

Access to food: Agriculture should be nutritionally oriented and not just focus on income and export. Micronutrient -rich foods such as fruits and vegetables, millets, pulses and animal products should be promoted from production to consumption. Homestead production can help. Wastage of farm produce, (almost 40%) should be reduced through proper storage and value addition. Government feeding programmes (ICDS, MDM), and micronutrient supplementation programmes (anaemia prophylaxis, massive dose vitamin A), need better targeting and efficiency. Food-based approach through dietary diversification, can be strengthened through bio-fortification to enrich germ plasm of plant foods with micronutrients. Chemical fortification also has a place to increase access to micronutrients. Iodised salt has helped to reduce the incidence of iodine deficiency goitre. Now salt double fortified with iron and iodine developed by the NIN, Hyderabad, (iron fortified iodised salt) is available and it should replace iodised salt to tackle the dual problem of anaemia and goitre.

Affordability: Government programmes like Public distribution system (PDS) should become more efficient, and universal. The basket of foods supplied should include pulses, millets, oil etc. Most importantly, community, particularly women should be empowered towards gainful employment through, appropriate education and skill development. Till then programmes like the employment guarantee scheme should continue, and be used to generate useful assets and skill development.

The bottom line is:

1. leadership at all levels and governance to ensure convergence between the efforts of different departments/programmes. 2. Make nutrition an important input and output parameter for all govt. programmes that can directly or indirectly impact nutrition. 3. Targeting and monitoring. 4. Focus on women's health, nutrition and empowerment through education and skill development. 5. Nutrition should be the focus of development, and not trickle down beneficiary of economic growth.

MATERNAL MICRONUTRIENTS (FOLIC ACID, VITAMIN B^{12}) AND OMEGA 3 FATTY ACIDS AND RISK FOR ADULT NON COMMUNICABLE DISEASES

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Nutrition security in pregnant women

Mother and Child Health is a major health issue globally, especially in developing countries like India where inadequacies of micronutrient such as folic acid, vitamin B12 and DHA are common and associated with significantly high pregnancy complications. Each of these complications has a prevalence of approximately 5 to 10% is steadily increasing and has multifactorial aetiologies in a general obstetric population. Understanding of mechanisms of aetiologies can help early detection and prevention of these pregnancy complications. But such studies are limited and hindered by variety of difficulties. Therefore, there is a pressing need to better understand the mechanisms of these diseases, with the ultimate goal of preventing these economically and socially devastating disorders. In developing countries like India, inadequate prenatal care results in complications like preeclampsia and preterm labor which are associated with maternal mortality and low birth weight.

Inadequate maternal nutrition: A leading cause of increasing incidence of non communicable diseases in adult life

Low birth weight (LBW) is a major public health problem in India and is attributed mainly to maternal malnutrition. India is facing a rapidly rising epidemic of diabetes, cardiovascular disorders and neurodevelopmental disorders. The prevalence of the metabolic syndrome has recently been shown to be 3 to 5 fold increased in those with a history of pregnancy complications like preeclampsia during pregnancy. This prevalence may increase in near future very rapidly

with globally increasing child bearing age, obesity, dietary (reduced antioxidants and omega-3 fatty acids) patterns and stressful life style. Epidemiological studies have shown that poor intrauterine growth is associated with non communicable diseases in later life. Evidence is increasing to indicate that adverse conditions during early life can result in the resetting of physiological systems, thereby predisposing the individual to chronic disease later in life. It has been suggested that a growing fetus faced with adverse conditions, responds with endocrine, metabolic and vascular or other structural adaptations. These adjustments during developmental periods are 'imprinted', affecting the response of the system in future life ('programming') resulting in a number of diseases like diabetes, coronary heart disease and psychiatric disorders in adult life.

Role of micronutrients in pregnancy complications

Studies at IRSHA have been addressing the issue of nutritional security during pregnancy and their risk for adult non communicable diseases by carrying out both animal and human studies. Clinicians, biochemists, nutritionists and molecular biologists at ISRHA work together on a single platform and are attempting to provide nutritional solutions along with conventional treatment to prevent complex health problems pervading the society. Human studies are carried out in an urban hospital at the Dept of Obstetrics and Gynaecology, Bharati Medical College Hospital, Pune wherein pregnant women, enrolled for delivery are recruited in the study to examine the association of maternal micronutrient status with birth outcome. Micronutrients like vitamin B12, folate and omega-3 essential long-chain fatty acids (docosahexaenoic acid, DHA) are key constituents of one carbon metabolism that influence DNA and chromatin methylation patterns which may be the key common mechanism in programming the fetus for neurodevelopmental and metabolic disorders in adult life.

A series of our studies have shown altered maternal micronutrients, increased oxidative stress and reduced DHA levels in pregnancy complications. We have also reported that reduced DHA levels are associated with increased homocysteine and may also result in diversion of methyl groups towards DNA in the one carbon metabolic pathway leading to altered placental global DNA methylation patterns. These changes may reflect an increase in methylation of regulatory regions of numerous genes resulting altered expression of vital developmental genes

like growth factors and angiogenic factors. Influences of maternal nutrition on epigenetic programming are most important during prenatal and early postnatal development, when epigenetic mechanisms undergo establishment and maturation. Disruption of normal gene-specific methylation patterns by perturbations in maternal nutrition may affect pregnancy outcome having long term implications in the offspring.

Our studies for the first time have shown an association of long chain polyunsaturated fatty acids (LCPUFA) and micronutrients like folic acid and vitamin B12 with pregnancy outcome. Simultaneous, animal studies are carried out to help delineate the mechanisms that will provide the important therapeutic clues for the prevention and/or amelioration of pregnancy complications. **These early findings support our major hypothesis that micronutrients (folic acid and B12) and omega-3 fatty acid imbalance can alter the one carbon metabolic cycle that lead to increased homocysteine and oxidative stress, and further lead to epigenetic "imprinting" of vital genes involved in metabolic and neurodevelopmental syndromes in adult life.**

These studies are can be vital in predicting the risk of developing non communicable diseases in adult life. Based on these findings large scale therapeutic intervention studies can be undertaken for prevention or at least substantial amelioration to reduce the risk to the health of mother and her baby. Thus the mother and child program at IRSHA as a whole aims to guide public health policy for ameliorating risk for behavioural and metabolic disorders like diabetes and cardiovascular diseases in adult life in India.

Conclusion

In conclusion, maternal and child care with specific reference to micronutrients is an extremely vital issue since it has far reaching effects in adult life. Clinical, biochemical, epigenetic and animal studies at IRSHA have clearly shown how micronutrients and omega 3 fatty acids play an important role in maternal nutrition and protects the fetus from diseases later in life.

WHY WE NEED A UNIVERSAL RIGHT TO FOOD

Madhura Swaminathan

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Ensuring food security and eliminating mass malnutrition is perhaps India's biggest and most serious development problem and challenge for policy makers. Food is the first among many basic human needs, and it is for this reason that "the human right to food is recognised in several instruments under international law (UN 1999)." Specifically, Article 11 of the International Covenant on Economic, Social and Cultural Rights recognises "the fundamental right to freedom from hunger and malnutrition (ibid.)."

The scale of the problem is established by national and international data on the incidence of malnutrition in India. According to the 2007 Progress for Children Statistical Review by the United Nations Children's Fund, the proportion of underweight children below the age of five- an indication of malnutrition-was 28 per cent in sub-Saharan Africa and 42 per cent in South Asia (43 per cent in India). The Report on State of Food Insecurity in the World 2006, by the Food and Agriculture Organization of the United Nations, confirms that no country comes close to India in terms of the sheer number of people living in chronic hunger.

According to findings from the National Family Health Survey of 2005-06, 45.9 per cent of children below the age of three were underweight or malnourished in terms of the standard weight-for-age criterion. The corresponding proportion in 1998-99 (NFHS-2) was 46.7 per cent. Over seven years, change in this key indicator of child malnutrition has been negligible. The rate of decline in the absolute number of malnourished persons has been very slow, slower than the rate agreed upon at the 1996 World Food Summit in Rome. India has fallen short of meeting the Millennium Development Goals targets it set for itself in the Millennium Development Goals.

In this context, it would appear that there would be a strong movement for establishing a universal right to food. On the contrary, an emphasis on fiscal costs and the supposed large burden of the food subsidy bill led to the introduction of the targeted PDS in 1996. A decade afterwards, it is clear that the TPDS has not been effective in addressing the problem of mass

food insecurity. The TPDS has segregated the population in to below-poverty-line (BPL) and above-poverty-line (APL) categories, and resulted in large errors of wrong exclusion. Targeting Errors can be classified into errors of wrong inclusion (E mistakes) and errors of wrong exclusion (F mistakes). While a universal PDS has a higher risk of wrong inclusion, a targeted PDS has a higher risk of wrong exclusion. Given the trade-off between the two types of errors, I argue that priority should be given to elimination of F mistakes since F mistakes have welfare consequences (malnutrition) while E mistakes result only in additional expenditure to the government.

A recent evaluation of the PDS by the Planning Commission (GoI 2005) states that only about 57 per cent of BPL households are covered by the targeted PDS. There are large errors of both exclusion and inclusion. In fact, according to the Report, "transition from universal PDS to TPDS has neither led to a reduction of budgetary food subsidies, nor has it been able to benefit the large majority of the food insecure households in the desired manner" (GoI, 2005, p. xi). The scale of error has now been established with data from the 61st round of the National Sample Survey (GOI 2007). These data show that targeting has led, in rural India, to high rates of exclusion of needy households from the system and a clear deterioration of coverage in States like Kerala where the universal PDS was most effective (Swaminathan 2008). Moreover, the excluded households belong to vulnerable groups such as agricultural labour households, Scheduled Caste and Scheduled Tribe households.

More recently, there are suggestions for a shift from the PDS to food stamps, food coupons or even direct cash transfers (Virmani and Rajeev 2001, World Bank 2011, Ganesh-Kumar et al). For cash transfers to work better than kind transfers, the very minimal assumptions are that there are no supply side problems, and that only a small target population has to be reached on account of relatively high levels of attainment in the indicator of concern. These minimal conditions are not met in many developing countries, including India, and introducing cash transfers in such situations can be harmful.

At the same time, the Government of India has introduced the National Food Security Bill 2011, and I shall critically discuss the key provisions of this bill. Most importantly, I argue that the opportunity to eliminate chronic hunger and malnutrition and ensure food security to all has been lost by restricting the Act to certain sections of the population.

MEETING THE CHALLENGES OF SEA LEVEL RISE

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Key words: *Mangroves, integrated mangrove fishery farming system, seawater farming, halophytes*

The livelihood security of the coastal communities and ecological security of the coastal zones of India is already under stress due to various reasons, which made more than 100 million people, who depend on coastal natural resources for their livelihood, vulnerable. The predicted sea level rise will aggravate this problem. It has been projected that along the Indian coast sea level would rise by 15 to 38 cm by 2050 and 46 to 59 cm by 2100 (NATCOM). The NATCOM also indicated that sea level rise will have a variety of impacts such as land loss and population displacement, increased flooding in low-lying coastal areas, salinization of land and water, etc. The most vulnerable areas along the Indian coastline are Kutch region of Gujarat, deltaic regions of Ganges, Cauvery Nadu, Krishna and Godavari and Lakshadweep islands. A recent estimate indicates that sea level rise would lead to inundation of sea water in about 5700 km2 of land along the coastal states and nearly seven million coastal families would be directly affected. India already has more than three million ha of coastal saline lands and addition of another half million ha would seriously affect ecological livelihood security in coastal area.

Increasing adaptive capacity of vulnerable coastal communities to cope up with increased salinization of land and water resources due to sea level rise is an important step to meet the challenges of sea level rise and for this purpose three strategies are proposed.

Strategy 1: Restoration and conservation of existing mangroves and creation of new mangroves wetlands in suitable areas

Strategy 2: Development seawater water based agro-aqua farming system that integrates growing of salt-tolerant plants and fish, prawn and crab.

Strategy 3: Identification of new of commercial crops from salt-loving halophytes and developing biosaline agriculture methods to grow them in saline affected areas

Strategy 1 Mangrove wetlands: Mangroves are dominant features of tropical and subtropical coastal line and Intergovernmental Panel on Climate Change (IPCC) considers mangroves as first line of defence against sea level rise. A recent research indicates that platform of coastal wetlands such as mangroves rises annually due to accumulation litter from vegetation and also due to capacity of mangroves to trap sediments. It has been estimated that annual increase in the height of mangrove platform (forest floor) is more or less equal to the rate at which sea level rises. Such a kind of equal increase in coastal landform and sea level effectively prevents entry of seawater inland. The study also indicates that it is possible only if the plant communities of the mangroves are well conserved and continuous supply of sediment is ensured. Hence, restoration and conservation of mangrove wetlands is one of the critical steps in meeting the challenges of the sea level rise. MSSRF in partnership with local community and state Forest Department and Ministry of Environment and Forests, Government of India introduced Joint Mangrove Management programme in all the major mangrove wetlands located along the east coast of India resulting in restoration of hundreds of hectares of degraded mangroves and conservation of large areas of pristine mangroves.

Strategy 2 Integrated Mangrove Fishery Farming System: Capacity of coastal community to sea level can be enhanced by changing the land use pattern in saline areas by introducing new sustainable production systems. One such system envisaged and demonstrated with the participation of community and other stakeholder is Integrate Mangrove Fishery Farming System, wherein raising of mangrove trees is integrated with fish culture. It is a new kind of farming system wherein conventional earthen aquaculture ponds are modified in such a way to provide about 30% of the space for raising mangrove plantation and 70% water spread area for fish cultivation. Space for growing mangroves and other vegetation is created by constructing linear bunds or mounds inside the pond. To construct these inner bunds and mounds mud is removed from the bottom of the pond, which made the bed of the pond lower than the low tidal level. As a result water is exchanged between the pond and nearby creeks by tides through gravitation and thus, pumping water in and out of the ponds to maintain water quality is not avoided. Secondly, daily exchange of water brought in a lot of fresh food in the form of planktons to the pond. This

avoided using artificial feed. Zero use of energy and artificial feed greatly reduces input cost and also avoid environmental pollution and thus, make Integrated Mangrove Fishery Farming system sustainable and remunerative. Above all, presence of dense mangrove trees would mitigate the impact of sea lever rise.

Strategy 3 Biosaline agriculture and halophyte cultivation: Halophytes are salt-loving plants and they occur over a wide range of salinity. A study conducted in 1989 indicates the presence of about 1560 species of halophytes globally. Halophytes are considered as rare plants and they evolved independently from unrelated families. Because of this multiple origin they differ widely in salinity tolerance. The cut-off level for salinity tolerance of halophytes at the low end is 0.5 grams of salinity per one litre of water and the upper limit is around 100 grams of salt per litre. It is considered that many of the high saline tolerant halophytes can be grown in the farms irrigated with seawater as a) cash crops to produce edible oil, vegetables, medicinal plants and flowers, b) fodder for cattle, sheep, goats and feed for fish and wildlife, c) raw materials to produce various fine chemicals and new products, d) producer of lumber and building materials, e) producer of biofuels and d) planting materials for rehabilitation of degraded coastal areas.. MSSRF in collaboration with other research institutions is developing biosaline agriculture method to cultivate these halophytes in saline affected areas, which will also enhance capacity of coastal communities to meet challenges of sea level rise.

EARTH SYSTEM SCIENCE IN INDIA: A PERSPECTIVE

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The Earth behaves as a single inter-linked system. The energy and material transfer within and across different sub-systems, viz., atmosphere, ocean, cryosphere, geosphere, and biosphere are complex. The understanding of such interactions can lead to improved prediction of weather, climate and hazards for societal, economic and environmental benefits. The net economic benefit of services can be of order of 0.4 to 1.2 per cent of GDP.

Weather and Climate prediction over India is focused on the monsoons and has a history of well over a century. The short-term weather forecast has improved considerably and being used to generate advisories for farmers. As climate change issues take center stage, the need for a deeper understanding of the components of earth systems is recognized as critical for learning how the earth is changing. The long-term measurements, both in situ and satellite are crucial for improved predictive capability to forecast weather, climate and hazards. The atmospheric and ocean observations are being augmented by deploying automatic weather stations, automatic rain gauges, doppler weather radars, argo floats, HF radars, moored buoys, current meters, etc. Capacity building in climate change research is also paramount for responsible stewardship of the Earth as an integrated and it is an investment that will pay dividends for generations to come. A number of programs focused on monsoons to earthquakes to energy and ecosystems are being planned to tackle these important issues. The success of these programs depends not only on technology and infrastructure but on people, an education system that produces the scientists and managers needed for implementing such an approach. We need to build effective communication with various stake-holders including policy makers.

SIMULATION OF EXTREME WEATHER EVENTS OVER INDIAN REGION WITH HIGH RESOLUTION DATA ASSIMILATION AND MESOSCALE MODELING SYSTEM

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The coastal region of India is one of the most disaster-prone areas in the world due to the experience of different types of extreme convective weather events through out year. The genesis and development of weather events involve complex interaction mechanism of mesoscale convective organization embedded in large-scale circulation. The ability to anticipate the formation, intensity, and movement of organized convective storms remains a major challenge for numerical prediction models as well as for human forecasters. The study is undertaken to improve the forecast skill of the mesoscale model (WRF) for high impact weather extremes through assimilation of different high resolution/quality observations. Study results provide a positive proof of concept that the assimilation of the different data sets within WRF can help improve the simulation of intense convective systems influencing the large-scale flow.

Keywords: mesoscale model, data assimilation, extreme weather events

1. Introduction

The coastal region of India is one of the most disaster-prone areas in the world. Increasing dramatic weather catastrophes over the region are due to an increase in the number of severe events and an increase in population densities, which increase the number of people affected and damage caused by an event. Severe weather systems such as severe thunderstorms (STSs), tropical cyclones (TCs), heavy rainfall events (HRE), western disturbances and monsoon depressions (MDs) etc can cause severe damage to lives and economy. The extreme weather events evolve

from different scales of processes. The genesis and development of these weather events involve complex interaction mechanism of mesoscale convective systems/organization embedded in large-scale circulation. The ability to anticipate the formation, intensity, and movement of organized convective storms remains a major challenge for numerical prediction models as well as for human forecasters.

With the advancement of high resolution non-hydrostatic mesoscale models have shown increased skill in producing not only the realistic rainfall intensity and location but also timing of evolution of the convective systems. Much of the success is due to the developments in numerical techniques, improved understanding of physical processes, improvements in observing systems and advanced data assimilation techniques. The forecast performance of the mesoscale models critically depends on the quality of initial conditions. Therefore, assimilation approaches that ingest local observations are important to develop improved analyses. The prime objective of the study is to asses the impact of different observational data sets using Weather Research and Forecasting (WRF, dynamical core ARW)-three dimensional variational (3DVAR) data assimilation modeling system for simulation of extreme weather events occurred over Indian region.

2. Impact of assimilation of remote sensing data (DWR and Satellite)

Here, an attempt is made to assess the impact of high resolution remote sensing observation data sets viz. reflectivity and radial velocity from Doppler Weather Radar (DWR) as well as satellite derived winds for prediction of different extreme weather events (two STSs, four TCs, two MDs and one HRE) using WRF-3DVAR system. For this purpose, a set of three numerical experiments were conducted in a single domain with horizontal resolution 3 km (for STSs), 9 km (for TCs and MDs). The first experiment, namely the control simulation (CNTL) was carried out with FNL analyses ($1^\circ \times 1^\circ$ resolution) as initial and boundary conditions without any data assimilation. The second experiment (GTS) was carried out by inserting all conventional and non-conventional observational data and the third experiment known as DWR was carried out by inserting DWR data along with GTS data into model (FNL) initial conditions.

In case of thunderstorm, the initial wind strength at 925 and 850 hPa is found relatively stronger by about 5 knots in the DWR data assimilation experiment compared to other simulations.

These strong winds have pumped in more moisture and have modified the atmosphere enough to become more unstable, leading to thunderstorm activities. The assimilation of DWR data mainly reflectivity has brought about a change in the initial moisture field in the lower levels. Further, the DWR simulated reflectivity has also been analyzed and it had been found that the development and intensification of the echoes is consistent with that of the simulated rainfall. The DWR experiment well simulated the thermodynamic parameters evolved during the thunderstorm activities as compared to the other simulations.

The results show that even though MDs are large synoptic systems, assimilation of DWR data has a positive impact on the prediction of the location, propagation and development of rain bands associated with the MDs. All aspects of the MD simulations such as mean-sea-level pressure, winds, vertical structure and the track are significantly improved due to the DWR assimilation. The averaged 24 hrs (48 hrs) forecast of track errors of the MDs are 102 (93) km in DWR simulation, while for GTS and CNTL the errors are 223 (209) and 274 (309) kms respectively. With the improved movement, the rainfall prediction improved and consequently resulted with high spatial correlation and less RMSE in rainfall quantitative predictions.

Based on 97 cases of real-time prediction of TCs using WRF modeling system over the north Indian Ocean (NIO), it is noticed that the initial vortex position error is about 80 and the 72 hr forecast error is about 350 km which is quite high. The best method to reduce this error is to assimilate the high resolution non-conventional data such as from satellites or DWRs over the data sparse oceanic region. Based on the DWR data impact study, the DWR data reveals its positive impact in the best fit of background field with the observations. At lower levels, RMSE is less for DWR analysis compared to GTS analysis, particularly in case of wind and humidity. Also, the short-term (6 hour) forecast of structure of hydrometeors is improved with DWR data compared to that of GTS and CNTL. Therefore, DWR experiment shows better intensity evolution in the first 24 hours forecast. The improved structure of initial fields helps in better prediction of track in DWR experiments with large gain in skill, particularly at longer forecast intervals. Study results provide a positive proof of concept that the assimilation of the Indian DWR data within WRF can help improve the simulation of intense convective systems influencing the large-scale flow.

The sea surface satellite derived winds from QSCAT and SSMI also had a significant impact in improving the track of the cyclones. Based on 24 case studies, a mean improvement of 34% in the initial vortex position with the satellite data assimilation over the FNL analyses is noticed. The landfall prediction is significantly improved in 17 cases out of 24 cases by about 38%. Kinematic and thermodynamic structures of TCs are also better explained, as it could simulate heat and momentum exchange between sea surface and upper air.

The unprecedented localized intense rainfall 90-100 cm during 26-27 July 2005 was recorded over northeast parts of Mumbai city, however, southern parts received only 10 cm. Model simulation with data assimilation experiment is reasonably well predicted the rainfall intensity (80 cm) in 24 hr and with accurate location over Mumbai agreed with observation. Divergence, vorticity, vertical velocity and moisture parameters are evaluated during the various stage of the event. It is noticed that maximum convergence and vorticity during the mature stage at the same time the vertical velocity also follows the similar trend during the period in the assimilation experiment. Vorticity budget terms over location of heavy rainfall revealed, the contribution of positive tilting term produced positive vorticity which triggered the convection and negative contribution to vorticity from tilting term to precede the dissipation of the system.

3. Impact of improved land surface conditions through LDAS:

It is also investigated that the impact of updated soil moisture and soil temperature on the prediction of STSs through Land Data Assimilation System (LDAS). Three STS cases occurred on 16, 21 and 26 May 2007 are considered. Similar to above, two experiments without and with the assimilation of soil moisture and temperature into the FNL initial analyses are conducted with a single domain of 2 km resolution using WRF modeling system.

The CNTL experiment overestimates the land and 2m air temperature and underestimates the soil moisture particularly, over the eastern parts of India (Odisha, Gangetic West Bengal, Bihar etc) where the thunderstorm was occurred. The land was wet during these cases because of *priori* rainfall due to thunderstorms. These local variations in the soil moisture could not reproduce in CNTL experiment from the climatological values of USGS. Considering the LDAS experiment, the hetrogeneity of soil moisture is well represented close to reality. Hence, the latent heat flux is significantly high in LDAS experiment compared to CNTL. Due to accurate representation of

land conditions, the lower atmospheric variables such as 2m temperature, surface relative humidity and 10m wind etc are well represented in LDAS experiment. The Time-longitude section of vorticity also reveals that, the time and strength of convection is significantly improved in LDAS experiment. The instability parameters such as CAPE and CIN were also well captured by the LDAS experiment and are attributed to improved soil moisture which influences the lower atmospheric moisture. The reflectivity is well simulated in LDAS experiment and is in agreement with the rainfall patterns. The 6-hr accumulated rainfall amount and location (±3 hours of thunderstorm time) is also well captured in LDAS experiment, at the same time many rainfall patches are missed out in the CNTL experiment.

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RECENT ADVANCES IN REMOTE SENSING FOR ATMOSPHERIC STUDIES - INDIAN SCENARIO

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The Earth's atmosphere is a complex system with many interactions with hydrosphere, lithosphere and biosphere. To understand these linkages repeated observations of the Earth's atmosphere over spatial scales ranging from regional to global and temporal scales ranging from minutes to decades are essential. Remote sensing technology provides such observations. Remote sensing is a science of observing, identifying and monitoring the object of interest without coming into direct contact with it. Remote sensing of the atmosphere can be done from various observational platforms, i.e., ground, air and space. There are two types of remote sensing instruments - passive and active. Passive instruments sense only radiation emitted by the object being viewed or reflected by the object from a source other than the instrument. Active instruments transmit electromagnetic radiation to illuminate the object or scene they observe and then receive the radiation that is reflected or backscattered from that object. The field of remote sensing has evolved over the years from the humble beginning of taking aerial photographs from aero planes to the monitoring of weather patterns using the first satellite (TIROS) in 1960 and to the effective utilization of microwave radars for digital land mapping and rainfall estimation. In addition, remote sensing technology has found important applications in mapping land-use and cover, agriculture, soil mapping, forecasting potential fishing zones, city planning, disaster monitoring, military observation, monitoring of trace gases, aerosols, estimation of precipitation, profiling of atmospheric temperature and humidity, etc.

India has made giant strides in the field of remote sensing (in both ground-based and space-borne) in the recent past. Although the modern remote sensing technology started little

late in India, but the growth is rapid in the last four decades, which contributed significantly to the development of the country. With a constellation of 10 INSAT (Indian National SATellite) and 11 IRS (Indian Remote Sensing) satellites in orbit, India today has become one of the few nations having such a constellation of satellites. The recent successful launch of Megha-Tropiques, an Indo-French satellite, aimed to study the water cycle and energy exchanges in the tropics is one of the land marks in the Indian remote sensing satellite endeavours. Because it is not only the first dedicated Indian satellite for studying the water cycle, but also the first in the constellation of 8 satellites planned for Global Precipitation Mission (GPM). It also contains another interesting payload "ROSA" (Radio Occultation Sensor for Vertical Profiling of Temperature and Humidity), which uses occultation of radio wave from GPS (Global Positing System) satellite to obtain profiles of atmospheric temperature and humidity. The forthcoming INSAT-3D is also an advanced meteorological satellite having a 19-channel sounder and a 6-channel imager to provide an operational, environmental and storm warning system. The data from these dedicated remote sensing satellites are going to be vital for operational people for monitoring severe weather systems and also for atmospheric scientists to address basic scientific problems. Along with space-borne technology, the ground-based remote sensing technology also advanced to a great extent in India. In the last 20 years, several Doppler radars and lidars were developed indigenously to monitor atmospheric parameters and weather patterns and also for better understanding of processes occurring in the atmosphere.

Although remote sensing technology is being employed in several fields of research, the focus of this article is on the remote sensing of the atmosphere, in general, the troposphere, in particular, in which most of the weather phenomena occur and climate change issues are of major concern. Therefore, the presentation confines to the introduction of different types of advanced remote sensing techniques (both space-borne and ground-based) and how effectively the data are being used to address fundamental questions related to the Earth's atmosphere. Special emphasis is put on Indian efforts of Atmospheric Remote Sensing Technology and Applications.

BIOLOGY OF NEURONAL CYTOSKELETON REGULATION NEURODEGENERATION AND DEMENTIA; A NOVEL APPROACH TO RESCUE THE PHENOTYPES OF DEGENERATION AND DEMENTIA, IN ALZHEIMER DISEASE MODEL

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Among many other neurodegenerative diseases Alzheimer's disease (AD) is the most common cause of dementia among older people, but it is not a normal part of aging. Dementia refers to a decline in cognitive function that interferes with daily life and activities. AD starts in a region of the brain that affects recent memory, then gradually spreads to other parts of the brain. Although treatment and life style can slow the progression of AD and help manage its symptoms in some people, currently there is no cure for this devastating disease. The number of people with AD doubles for every 5-year interval beyond age 65.

AD is named after Dr. Alois Alzheimer, a German doctor. In 1906, Dr. Alzheimer described changes in the brain tissue of a woman who had died of an unusual mental illness. He found abnormal clumps (now called amyloid plaques) and tangled bundles of fibers (now called neurofibrillary tangles). Today, these plaques and tangles in the brain are considered hallmarks of AD. The third main feature of AD is the gradual loss of connections between nerve cells (neurons) in the brain. This loss leads to diminished cell function and cell death. We don't know what starts the AD process, but we do know that damage to the brain begins as many as 10 to 20 years before any obvious signs of forgetfulness appear. As nerve cells die throughout the brain, affected regions begin to shrink. By the final stage of AD, damage is widespread, and brain tissue has shrunk significantly. In the years to come, AD is expected to pose physical and emotional challenges for more and more families and other caregivers, in addition to those with the disease. The growing number of people with AD and the costs associated with the disease also will put a heavy economic burden on society.

The Biology of Neurodegeneration and dementia program evolved in my laboratory studying the basic biology of neuronal cytoskeletal protein phosphorylation regulation during development and normal function in the adult. To understand the molecular basis of neurodegeneration our major focus has been to study the regulation of compartment-specific patterns of cytoskeletal protein phosphorylation in neuronal perikarya and axons. We have demonstrated that phosphorylation of the numerous acceptor sites on such proteins as Tau and neurofilaments was tightly regulated topographically and generally confined to the axonal compartment. It was recognized that in neurodegenerative disorders such as Alzheimer's disease (AD) and Amyotrophic lateral sclerosis (ALS), the pathology was characterized by an accumulation of aberrantly and hyper- phosphorylated cytoskeletal proteins in cell bodies, suggesting that topographic regulation had been compromised. This led inevitably into studies of neurodegeneration in cell culture and model mice with emphasis on a specific neuronal protein kinases, e.g. cyclin dependent kinase5 (cdk5), MAPKs that targets numerous neuronal proteins including cytoskeletal proteins, which when deregulated, may be responsible for the pathology seen in neurodegeneration. In cell systems, neuronal stress leads to deregulated kinases, for example, cdk5, accompanied by abnormal cytoskeletal protein phosphorylation and cell death characteristic of neurodegeneration. Recently we have developed peptides derived from, p35, a neuron specific activator of cdk5, for deregulated cdk5 activity which rescue cells in vitro from this stress induced pathology. The questions currently being investigated are (1) How is cytoskeletal protein phosphorylation topographically regulated in neurons? (2) What factors are responsible for the deregulation of cdk5 in neurons? (3) Can mouse models of AD and ALS be treated therapeutically with peptides that specifically inhibit deregulated but not the regulated cdk5 activity which is essential for nervous system development, function and survival?

SELECTIVE INHIBITION OF P25/CDK5 DEREGULATION THROUGH THE OVEREXPRESSION OF CDK5 INHIBITORY PEPTIDE (CIP) - THERAPEUTIC AVENUES FOR NEURODEGENERATION.

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Cyclin dependent protein kinase (Cdk5) is a proline-directed protein kinase that phosphorylates serine and threonine residues. Cdk5 and its regulatory subunit p35 are integral players in the proper development of mammalian central nervous system. Proteolytic cleavage of p35 generates p25 leading to aberrant Cdk5 hyperactivation and it has been shown to be responsible for the development of pathological hallmarks found in a number of neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Amyotrophic Lateral Sclerosis. Two of these hallmarks are the hyperphosphorylation of the microtubule associated protein tau and the improper processing of the amyloid precursor protein (APP) leading to amyloid beta accumulation. Previous studies showed the identification of a specific fragment of p35, Cdk5 Inhibitory Peptide (CIP), had potent inhibitory action on p25/Cdk5 activity in vitro as well as in cellular models. This was especially significant since the inhibition was specific to p25/Cdk5 hyperactivation, without affecting 'normal' p35/Cdk5 activity. Our study aims to investigate the selective inhibition of aberrant p25/Cdk5 hyperactivation through the overexpression of CIP, in vivo, in mice. We developed a transgenic mouse that overexpressed CIP constitutively and specifically in the forebrain under the direction of the CamK2a promoter. Initial characterization of the CIP mice did not show any alterations in cortical patterning as well as any observable phenotypes and the mice were normal in all aspects. We then crossed this line with that of the p25 transgenic (p25Tg) mice obtained from Jax which allows for induction of p25 expression in vivo through the control of the tetracycline promoter to get the tetra transgenic mice (tetraTg mice) that co-express CIP and p25. The tetraTg mice were then investigated and compared to the

p25Tg mice which showed tau hyperphosphorylation by 4-8 weeks and accumulations of intra-neuronal amyloid-beta from 8-12 weeks. Our results show that CIP, when co-overexpressed with p25 was able to reduce the hyperphosphorylation of tau compared to p25Tg mice. Additionally, an intra-neuronal accumulation of amyloid was completely abolished in the tetraTg mice. To determine whether this reduction has any significance on cognitive function, the tetraTg and p25Tg mice were subjected to radial mazes and it was found that tetraTg mice showed improved cognitive performance compared to p25Tg mice. We also performed MRI imaging to show gross morphological changes in vivo and found p25Tg mice exhibited loss of white matter and shrinkage in brain volume, all of which was rescued by the co-expression of CIP in vivo. The results reported here present a substantial breakthrough in targeting aberrant Cdk5 hyperactivation and with further work will provide exciting advances in a field of study which has stagnated due to the non selective approaches in targeting Cdk5 hyperactivity.

'UNDERSTANDING THE MECHANISTIC BASIS OF TDP-43 NEUROTOXICITY IN AMYOTROPHIC LATERAL SCLEROSIS'

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Amyotrophic Lateral Sclerosis (ALS) is an adult-onset neurodegenerative disease that targets motor neurons of the brain and spinal cord, causing progressive paralysis and death, usually within 3-5 years from diagnosis. There is no known cure or effective treatment. Approximately 5-10% of ALS cases are familial (fALS), the remaining 90-95% of cases are sporadic (sALS), with no known cause.

A confirmed diagnosis of ALS is obtained at autopsy, with the presence of various types of intraneuronal ubiquitinated inclusions a characteristic feature of the disease. In 2006, a major component of these inclusions was identified as the TAR DNA binding protein-43 (TDP-43). TDP-43 is a nuclear DNA/RNA binding protein involved in regulating numerous functions, including transcriptional regulation and alternative splicing.

In ALS, TDP-43 is mislocalized from the nucleus to the cytoplasm of diseased motor neurons, where it forms abnormally phosphorylated and ubiquitinated inclusions. Interestingly, TDP-43 pathology is also a major feature of some forms of frontotemporal dementia (FTD), in which there is a clinicopathological overlap with ALS. Indeed, over 50% of ALS patients exhibit signs of cognitive decline, many cases of which are consistent with a diagnosis of full blown FTD.

Over 30 different mutations have now been identified in the TDP-43 gene in both familial and sporadic forms of the disease, most of which are localized to exon 6, correlating to the unstructured and phosphorylated region of the protein. This region is involved in protein binding and it may be that the mutations in TDP-43 act by interfering with protein-protein interactions.

Since, in ALS, TDP-43 is depleted from the nucleus of affected motor neurons forming inclusions in the cytoplasm, toxicity could be elicited via a loss of nuclear function, a gain of cytoplasmic

function, or some combination of both. As TDP-43 is involved in RNA processing events in the nucleus, it is likely that abnormalities of TDP-43 would be reflected by changes in regulation of RNA expression and alternative splicing. To this end we used the technique of UV crosslinking and immunoprecipitation (UV-CLIP) of human neuroblastoma cells, SHSY5Y, to identify RNA targets of TDP-43. Using conventional cloning techniques we identified 127 different RNA targets of TDP-43 representing numerous biochemical pathways, such as cytoskeleton organization and biogenesis, and metal binding We have shown that some of these targets are abnormally alternatively spliced in ALS, indicating that RNA targets of TDP-43 are abnormally processed in ALS, and that dysregulation of these genes may contribute to the neurodegenerative cascade.

In addition to the full-length protein of 43 kDa, pathological TDP-43 is characterized by the presence of lower molecular weight species observed on immunoblots of diseased tissues, typically brain tissue from cases of FTD, which is easier to access. The most predominant species are of 35 kDa (TDP-35) and 25 kDa (TDP-25), although in our hands, in ALS lumbar spinal cord, the most predominant species is TDP-35, with TDP-25 present at a lower level.
TDP-35 and TDP-25 have been considered caspase-3 (C-3) degradation products since cleavage at the C-3 consensus sequences DETD89A and DVMD219V can generate species of 35 kDa and 25 kDa in vitro, respectively. However, there is no direct proof that these species are generated by C-3 cleavage in disease.

Since TDP-43 is a splicing regulator and is itself alternatively spliced, we explored the possibility that the lower molecular weight species of TDP-43 found in diseased tissues may not be C-3 degradation products, but instead, alternatively spliced (AS) variants of TDP-43. Genome bioinformatics databases were mined for AS transcripts of TDP-43. We identified an AS variant of TDP-43 with 91 bp skipped in exon 2 that was upregulated in ALS spinal cord compared to controls. The 91bp deletion caused a frameshift and to use of a downstream alternate translation initiation codon, ATG^{Met85}. Expression of this transcript in cells generated a species of 35 kDa, named AS-TDP-35 (for alternatively spliced generated TDP-35), that formed cytoplasmic aggregates both in SHSY5Y cells and primary neurons, causing neurotoxicity.

We have shown using neoepitope antibodies made to the different N-terminal sequences, that the pathological TDP-35 species observed in ALS is generated by expression from Met^{85} and not by C-3 cleavage at DEVD89A. Specifically, we have found that the pathological TDP-35 species observed on immunoblots of ALS lumbar spinal cord tissues is labeled with antibody specific to AS-TDP-35, but not C3-TDP-35 antibody. Moreover, AS-TDP-35 antibody labeled ALS disease pathology, whereas C3-TDP-35 antibody labeling was negative.

These results show that the lower molecular weight TDP-43 species of 35kDa present in ALS spinal cord tissues is generated by expression from Met^{85}. We propose that this occurs through expression of an AS variant of TDP-43, in which there is a 91 bp deletion in exon 2, causing a frameshift and alternate translation initiation.

In more recent studies we have generated transgenic expressing AS-TDP-35 under control of the hamster prion promoter. These mice show a progressive decline in motor performance and exhibit deficits in cognition at 10 months of age. These behavioural changes correlate with the formation of abnormally phosphorylated and ubiquitinated inclusions containing AS-TDP-35 in the cytoplasm of affected neurons. This collective evidence shows that a combination of alternative splicing and alternate translation initiation leads to the generation of pathological TDP-35 in ALS, and expression of this species in transgenic mice recapitulates features of both ALS and FTD, identifying AS-TDP-35 as a potential therapeutic target.

HISTONE METHYLATION-DEPENDENT TRANSCRIPTIONAL REGULATION OF COCAINE-INDUCED BEHAVIORAL AND STRUCTURAL PLASTICITY

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Cocaine-induced alterations in gene expression cause changes in neuronal morphology and behavior that may underlie cocaine addiction. We have identified an essential role for histone 3 lysine 9 dimethylation (H3K9me2) and the lysine dimethyltransferase G9a in cocaine-induced structural and behavioral plasticity. Repeated cocaine administration reduces global levels of H3K9me2 in nucleus accumbens (NAc). This reduction is mediated through repression of G9a expression in this brain region, which is regulated by the cocaine-induced transcription factor ?FosB. Using conditional mutagenesis and viral-mediated gene transfer, we found that G9a downregulation increases dendritic spine plasticity of NAc neurons and enhances preference for cocaine. Due to high incidences of co-morbidity between substance abuse and stress-related illnesses, administration of drugs, such as cocaine, causes neural adaptations that may promote vulnerability to later stress experiences. We have identified histone methylation in NAc as a candidate mechanism linking drug exposure to enhancement of stress vulnerability. Repeated cocaine administration, prior to sub-chronic social defeat stress, potentiates depressive behaviors in mice through decreased H3K9me2 expression in NAc. Cre-mediated reduction of G9a promotes increased susceptibility to social stress, similar to that observed with repeated cocaine, whereas overexpression of G9a after repeated cocaine protects mice from the ensuing consequences of social stress. This form of resiliency is mediated, in part, through repression of Ras, a member of the BDNF-TrkB signaling cascade, which is induced after both repeated cocaine and chronic stress. Identifying such common regulatory mechanisms may aid in the development of therapeutics aimed at alleviating severe cases of addiction and depression.

NEUROPROTECTIVE STRATEGIES IN THE TREATMENT OF GLAUCOMA.

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Glaucoma is a neurodegenerative disease that affects more than 70 million people worldwide and while approved drug treatments have been able to slow the progression of the disease they do not provide protection against neuronal cell death that appears to continue over time. Neuroprotective strategies have been slow in coming due to the long evaluation process and end points that must be assessed, particularly as any therapy is proposed for use in humans. Many of the studies conducted on neuroprotection strategies have been accomplished using animal studies. In these studies either intraocular pressure is elevated using several different approaches, or there are animals, like the DBA/2J mouse that develops glaucoma pathology or in the spontaneous glaucoma that develops in the dog in three breeds (American cocker spaniel, basset hound and beagle). In subhuman primates typically intraocular pressure is elevated by some technique in order to develop glaucoma pathology. Some investigators use a more acute approach and produce optic nerve crush to induce death of retinal ganglion cells in order to study this process and possible ways to mitigate cell death. Our laboratory is also interested in neuroprotective strategies, and has approached this by first looking at isolating primary retinal ganglion cells to test certain agents and cell manipulations to determine potential strategies for providing neuroprotection in vivo. We are also identifying those cellular pathways that lead to cell death in retinal ganglion cells and potential sites for developing neuroprotective strategies. One such pathway we have identified is the neuroprotective actions of activation of sigma-1 receptors. In particular, we have been investigating the effects of sigma receptors and their role in providing protection against cell deathas it relates to calcium cell over load and in providing protection during pathological insults like hypoxia or ischemia. We have found that sigma 1 receptors appear to act to decrease calcium entry by interaction with the L-type voltage gated calcium channels and decrease apoptosis in isolated primary retinal ganglion cells. Moreover, we are able to use sigma-

1 agonists to activate this system and to demonstrate protection against cell death following pathological challenges and demonstrate that antagonists can potentiate calcium signaling through voltage-gated calcium channels. Sigma-1 receptor's ability to bind and associate with L-type voltage gated calcium channels, regulate neuronal intracellular calcium concentrations when exposed to pathological conditions, and to prevent glutamate excitotoxicity of RGCs when exposed to sigma-1 agonists are some of the key mechanisms underlying sigma-1's neuroprotective actions. Activation of sigma-1 receptors could be a strategy that may be useful in providing neuroprotection from elevation in IOP. Preliminary data suggests that during elevation of intraocular pressure in a rat model of glaucoma there is some decrease in sigma-1 expression consistent with sigma-1 receptors role in providing protection against further neurodegeneration. Similarly is our finding that over expression of the sigma-1 receptor can also protect primary retinal ganglion cells from calcium over load and decrease cell's apoptotic mechanisms. Perhaps if we can increase sigma-1 expression in vivo we can prevent further neurodegeneration. We are in the process of testing this approach. There are also a number of other pathways that can be activated to provide neuroprotectionand we are investigating these as well.

NEUROTROPHIN, NEUROENDOCRINE AND NEUROIMMUNE FUNCTION IN DEPRESSION AND SUICIDE PATHOPHYSIOLOGY

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Depression and suicide are major public health concern worldwide. About 30,000 people die by suicide in the USA alone. It is therefore important to examine the causes for suicide and suicidal behavior and its prevention by appropriate treatment. Mental disorders are major risk factors for suicide, and depression appears to be an even bigger risk factor. The other risk factors that have been studied recently are the abnormal neurobiological factors. We have been studying the neurobiology of depression and suicide using postmortem brain samples obtained from control subjects and suicide victims, and have observed an abnormality in serotonin function in suicide. There is a strong interaction between the serotonin, neurotrophins, neuroendocrine and immune systems, and hence it was logical to examine if abnormalities in neurotrophins, neuroendocrine and immune functions are associated with suicide and/or with depression.

Brain-derived neurotrophic factor (BDNF) is an important member of the neurotrophin family and is involved in the proliferation, migration and survival of neurons and thus maintains the structural integrity of the brain. Its abnormalities have been implicated in depression and suicide. We have therefore studied the role of BDNF in depression and suicide using peripheral cells and postmortem brain for these studies.

Abnormalities of hypothalamic-pituitary-adrenal (HPA) axis in depression and suicide are among the most consistent findings in biological psychiatry. However, the specific molecular mechanisms associated with HPA axis abnormalities in the brain of depressed and suicidal subjects are unclear. We have studied the mechanism of this dysregulation of the HPA axis in suicide, and have determined the protein and mRNA expression of the various components of HPA axis in suicide brain.

Several studies also suggest an association of an abnormal immune function in suicidal behavior. The abnormality in the immune function is caused by abnormal levels of

proinflammatory cytokines, which are also known as the mediators of the immune function. To address this issue, we have determined the protein and mRNA levels of proinflammatory cytokines in plasma and brain.

The postmortem brain samples were obtained from the Maryland Brain Collection at the Maryland Psychiatric Research Center, Baltimore, MD, USA. Psychological autopsy was performed and the subjects were diagnosed according to the Schedule for Clinical Interviews for DSM-IV (SCID). The brain samples were stored at -80°C till assayed. Protein expression was determined using Western blot or enzyme-linked immunosorbent assay (ELISA) techniques. Gene expression (mRNA) was determined using real-time RT-polymerase chain reaction (qPCR). Platelets and lymphocytes for BDNF studies were obtained from patients with mood disorders and normal controls.

We observed that protein and gene expression of BDNF and its receptor TrkB is significantly decreased in the prefrontal cortex (PFC) and hippocampus of depressed suicide victims and in the platelets and lymphocytes of patients with mood disorders.

In the study of HPA axis components, we found that the protein and gene expression of glucocorticoid receptors (GR) is significantly decreased in the PFC and amygdala, but not in the hippocampus of teenage suicide victims compared with normal control subjects.

However, there were no significant differences in the protein or gene expression of MR in any of brain area studied. The protein and gene expression of corticotropin releasing factor (CRF) was significantly increased in the PFC and amygdala, but not in the hippocampus of teenage suicide victims. The levels of CRF-R1, but not CRF-R2, were significantly increased in the PFC and amygdala of suicide victims.

The studies of proinflammatory cytokines indicated that the protein and gene expression of the proinflammatory cytokines interleukin (IL)-1?, IL-6 and tumor necrosis factor (TNF)-? was significantly increased in the Brodmann area 10 (BA-10) of suicide subjects compared with normal control subjects. There was a significant increase in plasma levels of IL-1? and TNF-? in patients with mood disorders.

Conclusion

Studies of HPA axis components suggested that increased levels of circulating cortisol in depressed and suicidal subjects and the abnormal HPA axis function, as evidenced by abnormal DST are related to a decrease in GR levels in the brain, thus causing an increase in the levels of CRF in the brain. Our studies also indicate an abnormal immune function in suicide due to an increase in levels of the proinflammatory cytokines, especially IL-1?, IL-6 and TNF-? in plasma and brain of depressed and suicidal subjects. The abnormalities in BDNF levels, HPA axis function and in proinflammatory cytokines may eventually cause brain atrophy observed in depressed and suicidal patients. These results also suggest that neurotrophins, HPA axis components and cytokines may be possible targets for developing newer and more appropriate therapeutic agents for the treatment of depression and suicidal behavior, and that BDNF and proinflammatory cytokines may be useful biomarkers and therapeutic targets. Based on these findings a biological framework for depression and suicide will be presented and discussed.

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PLATELETS AND LYMPHOCYTES AS NEURONAL MODEL FOR SELECTED CNS DISORDERS

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Due to several similarities with neurons, platelets have been widely used as model for neuropsychiatric disorders. Earlier we showed presence of dopamine (DA)-D2 and serotonin (5-HT)-2A receptors in platelets and nitric oxide in PMNs with pharmacological responsiveness similar to brain. Attempt was now made to identify peripheral markers for Parkinson's disease, migraine, depression and schizophrenia. In agreement with the studies on brain by others, a significant increase in the activity of platelet MAO-B was observed in Parkinson's cases. Further studies showed that polymorphism in the genes and coding proteins involved in toxication and detoxication and dopamine pathways such as CYP2D6, CYP2E1, GSTs, MAO-B, DRD2, and DAT can modify the risk to Parkinson Disease. Nitrite content was significantly enhanced in PMNs without any change in platelets and plasma. A decrease in the affinity of 3H-Ketanserin binding to platelet membrane with no change in the number of receptor binding sites (Bmax) was observed in cases of migraine in comparison to controls. Further, equilibrium dissociation constant (Kd) in patients with migraine (1.71 _ 0.19 nM) was found to be significantly lower ($P < 0.001$) as compared with controls (3.14 _ 0.33 nM) without any significant change in the maximal number of binding sites (Bmax) in patients. Though no relationship of Kd with type of migraine, presence of vomiting, family history, frequency of attack, duration of illness and menstrual migraine was observed, the results suggest involvement of the dopaminergic system in migraine and also patients exhibited no change in nitrite content in PMNs, platelets and plasma as compared to controls. In cases of depression, a significant increase in the Bmax of platelet 5-HT2A receptors was observed in comparison to healthy controls and first degree relatives of patients. Interestingly, cases of depressives with suicide intent had significantly higher Bmax than those with non-suicidal intent. These cases also exhibited an increase in platelet intracellular

calcium and a decrease in membrane fluidity. A significant decrease in PMNs nitrite content was observed in cases of depression compared to controls and the change was more marked in cases with positive family history of depression. A significant increase in platelet 5-HT2A receptors and no change in intracellular calcium levels and membrane fluidity in platelets was observed in cases of schizophrenia. Nitrite content in PMNs in cases of schizophrenia was decreased but no such change in nitrite content was observed in platelets. An increase in malonaldialdehyde levels in PMNs observed in cases of schizophrenia suggest enhanced oxidative stress in the pathogenesis of the disease though no change in the superoxide dismutase, catalase and glutathione peroxidase activity was observed. The study suggests that alterations in DA-D2 receptors in Parkinson's disease and 5-HT2A receptors in depression in platelets are selective. Further, changes in PMNs nitrite content exhibits specificity in diseases like Parkinson's disease, depression, migraine and schizophrenia and strengthen the usefulness of platelets and PMNs as surrogate models for CNS disorders.

NBC THREAT PERCEPTION AND COUNTERMEASURES

S Kumar

NBC threat has increased manifold around the world as a result of proliferation of NBC weapons, otherwise known as Weapons of Mass Destruction (WMD). Non state actors either independently or in collusion with state actors are seeing to possess NBC weapons with the capacity to inflict catastrophic damage (physical, economic, psychological) on developing Nations. The use of NBC material is seen by such non state actors as a low cost, high impact option since even in a crude form with an efficient dissemination mechanism the economic and psychological effects of such incidents can be significant.

The divesting effects of nuclear, biological and chemical warfare agents are well known and the methodology for their preparation is available in literature and on internet. The knowledge of sources for acquiring these agents illegally at various parts of the world is available in public domain. With this, there exists a possibility for non state actors to obtain such material from various countries.

In case if such device is used by any terrorist group, the effect will be tremendous on public and to restore normalcy is a really great challenge to all developed and developing countries.

India is facing threat from terrorists for last two decades mostly from neighbour sponsored and home grown terrorist groups. It is well documented that some of the incident of illicit trafficking of nuclear materials came to the notice of security forces. Therefore, the possibility of use of such devices by any terrorist group in any part of the country cannot be ruled out.

To counter the types of NBC threat, certain guidelines are required. These guidelines/SOP are based on the approach and technology available within country. These technologies are broadly classified into four categories. These are basically Detection, Protection, Decontamination and Medical Management. Over the years DRDO has developed large number of the products/systems based on different types of technologies and productionized through the trade. The features of the DRDO technologies are at par with internationally available technologies around the world. Prominent among them are sensors for detection of Nuclear, Chemical warfare agents, antigen

based Biological Kit, Surveillance Systems, Individual Protection Kits, Collective Protection Shelters, Mobile Decontamination Systems and Antidotes for Medical Management etc. Besides DRDO has also provided support to paramilitary forces. All these systems, the details of these and various approaches to cater NBC threat will be discussed in detail.

RESPIRATORY MANAGEMENT IN NBC ENCOUNTER

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Modern scenario of combat envisages the use of cheap but very effective Chemical Warfare (CW) and Biological Warfare (BW) agents as weapons. Once considered unconventional, CW and BW weapons are now a routine part of the Armed Forces World over. The physical and physiological stress implicated by chemical or biological weapon is very difficult to cope with unless we are fully geared up to meet the threats. The CW and BW agents are effected through the mode of inhalation or percutaneous entry causing soldier casualties. Thus protection is the foremost aspect of concern in the NBC warfare.

Respiratory protection is the most important aspect in NBC protection. Normal humans require around 450 liters of air at STP per hour for the normal physiological function. Armed Forces personnel require certainly more than 450 liters per hour due to their additional functions. The rate of entry through percutaneous route is always very less compared to the respiratory route. Even miniscule amount of CW agents dispersed in the atmosphere is very dangerous. Thus respiratory protection and management in the contaminated area has taken precedence over percutaneous protection.

In NBC scenario, Respiratory protection is achieved by the respiratory protective equipment. There are four types of respirators commonly used, namely Disposable Dust Respirator, Half Mask Respirator, Full Face Mask Respirator and Powered Respirator. Depending on the requirements, the type of mask is selected. In an NBC warfare scenario, both Full Face Mask respirator and Powered Respirator are commonly used.

In spite of using respirators, there are cases reporting entry of CW and BW agents due to accident or improper fitment or malfunctioning of the mask. In such scenarios, Resuscitators are commonly employed to restore the respiration. Provision is made to even evacuate the victims through Evacuation Bag.

DEBEL is one of the premier DRDO laboratories working on protective equipment for respiration management. NBC Respiratory Mask, Integrated Hood Mask, Manual Resuscitator are already used by Army, Navy, Air Force, BSF, CISF, ITBSF, Low Intensity Conflict (LIC) and Police Department of various States. Our laboratory has developed a system for respiration protection of Air Crew of Transport Aircraft and Helicopter based on powered breathing which is under evaluation. For crew of Fighter Aircraft, special respiratory protection devices called Aircrew Ensemble are under development. Development of Automated Resuscitators is already completed. DEBEL is also working on NBC protective devices which can work in conjunction with On-board Oxygen Generation System (OBOGS) with foreign collaboration. DEBEL has already initiated work on the development of CATOX-based system for the purification of air entering the cockpit of fighter aircraft.

To meet the challenges of respiratory management in NBC environment, DRDO has taken up many initiatives which include CCS program on NBC defence technologies. Under this programme, DRDO is working on various aspects of detection, protection, decontamination, medical management etc. in collaboration with various leading academic institutes and industries in India. DRDO also encourages international collaborations with Countries having advanced technologies. At present, India has the capability to face any NBC threat, be it internal or external in nature, and is expanding its capabilities to the state-of-the-art in technology as a measure of continuous improvement in technology for protection against NBC warfare agents.

MEDICAL PROTECTION FOR CHEMICAL AND BIOLOGICAL WARFARE AGENTS AS FIRST AID

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Toxic chemicals and pathogenic organisms can be used as chemical and biological warfare agents respectively. Some toxic chemicals act in very small quantities and very rapidly, and death may occur in minutes. In comparison to the chemical warfare agents, the biological warfare agents may not be lethal to the individuals immediately, due to their incubation time for the development of the disease. Exposure to chemical and biological agents may occur as a surprise and before detection and physical protection individual may be exposed considerably. Hence, protection has to be taken immediately in terms of physical as well as medical protection. Medical protection has to be given in the form of first aid, either by self or by the companion. A first aid kit has been developed by Defence Research and Development Organisation, for chemical and biological warfare agents (FAKCBW) with the objective of, easy detection, personal decontamination, antidotes for nerve agents, antidotes for sulphur mustard and phosgene, antidote for cyanide, antidote for radiation exposure, antidote for bacterial agents, antidote for pain, fever and inflammation, and an user handbook with a simple Standard Operating Procedure. In addition the kit is rugged to withstand normal jerks and vibration, and is water-proof.

DETECTION TECHNOLOGIES FOR BIOLOGICAL EMERGENCIES

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Biological weapons are as old as humanity itself and have been used with regularity throughout history. Recent bioterrorist events have emphasized the need to immediately detect and identify biothreat agents. Rapid, accurate identification of such agents is important not only to confirm that a bioterrorism event has occurred, but also to determine whether suitable measures should be implemented to protect public health. The era of biological weapons was significantly advanced in the 20th century by modern microbiology and multiple international wars. The biological and chemical horrors inflicted during World War I resulted in the drafting of the 1925 Geneva Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases and of Bacteriological Methods of Warfare. However, many countries that signed the document did so with contingencies in the event of attack by a nonratifying entity and with the stipulation that the protocol did not prevent investigative research.

There have been significant advances in the field of biotechnology. The major advances have occurred in the fields of genetic modification, genomics, proteomics, bioremediation, biocontrol agents, vaccine development and bioinformatics. While offering obvious benefits to mankind by providing mechanisms for enhancing protection and prophylaxis against pathogens, advances in these technologies can be used to produce new substances or modify old ones and lead to novel and significant toxins and biological or biochemical weapon threats. Nation should remain cognizant of and carefully monitor for potential abuse of these evolving technologies.

The ability to rapidly identify the introduction of a bioterrorist agent into the civilian population, animal herds and field crops will require highly sensitive, specific, inexpensive, and easy-to-use diagnostic tools readily available with primary care centers for immediate deployment. The prospect of biological terrorism presents many challenges for detection platforms. Some challenges are unique to bioterrorism and others are common for all testing situations. Ideally, detection platforms should be capable of rapidly detecting and confirming biothreat agents, including modified or previously uncharacterized agents, directly from complex matrix samples,

with no false results. Furthermore, the instrument should be portable, user-friendly, and capable of testing for multiple agents simultaneously.

Detection platforms that have been developed specifically for the identification of bio-threat agents are predominantly nucleic acid or antibody based systems. Nucleic acid-based detection systems are more sensitive than antibody-based detection systems. The PCR assay can detect 10 or fewer microorganisms in a short period of time. However, PCR requires a clean sample and is unable to detect protein toxins and other non-nucleic acid containing analytes such as prions. Furthermore, cultures of the target organism are not available for archiving and additional tests after PCR analysis. **Quantitative real-time PCR (Q-PCR)** combines PCR amplification with simultaneous detection of amplified products based on changes in reporter fluorescence proportional to the increase in product. Most of these systems are sophisticated molecular-based platforms that perform best in a laboratory setting such as hospitals, monitoring offices, and research laboratories. **Loop-mediated isothermal amplification** is a method of isothermally amplifying DNA using a novel strand displacement approach. The technique uses DNA polymerase and four specially designed primers that are specific for sequences on the sense and antisense strands of the target DNA. Loop mediated isothermal amplification-based assays have been used to detect several viruses and bacteria and fungus.

Immunological detection has been successfully employed for detection of biothreat agents such as bacterial cells, spores, viruses, and toxins based on the concept that any compound capable of triggering an immune response can be targeted as an antigen. Most of the detection platforms are similar to, or derived from, the classic sandwich assay based on the enzyme-linked immunosorbent assay (ELISA) design. Immunoassays can be performed with a variety of substrates and labels (fluorescent, chemiluminescent, and electrochemiluminescent), as well as on multiple platform types (biosensors, flow cytometry, microarray, and lateral flow diffusion devices). However, there are two main categories of immunoassays used with a few adaptations, mainly variations of (i) solid-support models (a) **Luminex xMAP-** technology uses the basic "sandwich" assay format, but the capture antibody is coated onto the surface of a polystyrene bead rather than in a microwell plate. These beads are processed through the assay and separated for analysis via flow cytometry, (b) **BV technology-** uses electrochemiluminescence to detect reporter molecules used in the sandwich assay. BV assays use paramagnetic beads as the support

structure for the capture antibodies, (c) **Bio-Detector- uses** ELISA principles on a tape format in a portable rugged housing, (d) **DELFIA-** (dissociation-enhanced lanthanide fluorescence immunoassay) system is one example of a format based on time-resolved fluorescence and (ii) lateral flow diffusion apparatuses, also known as "smart ticket" technology or hand-held assay devices.

The success of immuno detection methods is dependent on the specificity and affinity of the antibodies that are deployed in them. Synthesis of chimeric genes encompassing immunodominant regions of biothreat agents by a novel tandem alignment process of multiple DNA sequences employing a two step PCR, directional cloning of these chimeric genes with PCR-preformed cohesive ends results in generation of recombinant proteins for generation of specific monoclonal antibodies The hybridoma technology established in DFRL, Mysore in the has helped to rapidly generate specific high affinity MoAbs resulting in development of totally novel, low-cost, reliable, use-friendly and rapid immunobased BW agents and food safety concern toxin and organism detection kits and systems. Innovative dot ELISA kit for simultaneous detection of Salmonella genus, Shigella genus, members of E.coli and Proteus group, Western blot and dot ELIS based system for detection of SEB and Tsst of S. aureus Sandwich ELISA and Immuno-PCR based detection of B.anthracis and Ochratoxin A.

Biochip array based methods for pathogen detection are under investigation. One approach uses dielectrophoresis to concentrate target agents for identification and then detects them using an electric-field-driven immunoassay or by DNA amplification using strand displacement amplification and analysis using an on-chip electric-field driven hybridization assay. A second method uses a sensor array constructed on a complementary metal oxide semiconductor integrated circuit to detect targets on a microarray. The optical detector can interrogate all spots on the array simultaneously or individually.

Bio-sensor technologies for bioterrorism defense can be divided into a few broad groups according to the way they recognize and respond to a biological threat agent. These groups are defined as biochemical, immunological, nucleic acid, cell/tissue, and chemical/physical technologies. Each of these recognition systems must be paired with a transducer that can transform the response into an analyzable signal. **Surface plasmon resonance-based biosensors** directly

detect target analytes by measuring the refractive index changes that occur when a target binds to the surface of a metal-coated (generally gold or silver) surface. **Evanescent-wave biosensors** involve Evanescent-wave excitation of fluorophore-labeled antibodies attached to targets captured on a waveguide surface. **Cantilever and acoustic wave** technology uses changes in mass to detect target agents trapped on the device surface. Target specificity is achieved by adsorbing or attaching some type of capture molecule to the surface substrate. As target is captured, the added mass results in a frequency shift from the normal oscillation of the cantilever. An additional shift in resonance frequency is observed upon capture of the target.

Bioluminescence has been used widely in clinical, food, and environmental settings for monitoring incidences of bacterial contamination. The Profile-1 hand-held system (New Horizon Diagnostics Inc., Columbia, MD) uses a microluminometer to read sample bioluminescence and a Filtravette (New Horizon Diagnostics Inc.) sample processing unit to remove nonbacterial ATP

sources. This combined system has been used to examine contamination on meat carcasses, test biological aerosols and detect Bacillus species spores in powders.

Quantum dots and upconverting phosphors are inorganic fluorescent nanocrystals that are color-tunable by varying the size and composition of the crystal core. They have a wide absorption spectrum and a narrow emission peak, which makes them ideal for multiplexing.

Although many different detection technologies have been introduced, few of these technologies have been extensively evaluated or reviewed under field conditions. Many challenges, including processing of complex sample matrices and detection of multiple types of agents and modified or previously uncharacterized agents in a sample, remain to be resolved.

Protection and decontamination is the immediate effort of utmost importance once the BW agents are detected. Protection efforts involve personal protection and collective protection: Personal protection involves protective masks, personal protective equipments (positive pressure suits, PPEs (Personal Protection Equipments) like Hazmat suits, Helmets, protective goggles, state-of-art B-masks and B-suites) and vaccines for first responders. Vaccine research has historically been focused on the use of formalin-inactivated toxins or toxoid vaccines. While

toxoid vaccines have proven to be capable of stimulating protective immunity in animal models, they are unlikely to be approved for human use because of safety concerns. Current vaccine research is now turning to the development of non-toxic recombinant or subunit vaccines, combined vaccines and fusion protein vaccines and DNA vaccines. Collective protection involves provision of shelters (preferably underground) with protected air supply equipped with Multi-Cell Radial Flow (MCRF) filter unit.

ENERGY, CARBON EMISSIONS AND BUILDINGS.

K.S.Jagadish

The issue of energy in Buildings has been engaging the attention of engineers and scientists since the first oil crisis in 1973.However, other issues related to the environment, have arisen with reference to Buildings.The concept of ' Green Buildings ' encompasses the whole gamut of environmental issues like energy,carbon emissions, water quality, waste management and indoor air pollution. Energy and Carbon emissions represent global problems due to local practices by individuals and Institutions. The other problems are more local in character. This paper emphasizes the energy and carbon emissions due to Buildings and examines ways to mitigate the related problems.

Two aspects of energy in Buildings need to be considered namely: (a) Embodied energy in a Building at the time of its construction and (b) The operational energy spent during the lifetime of the building. The embodied energy consists mainly of energy in the production and transportation of building materials and the energy spent during the construction of the building. The common elements like bricks, cement and steel need considerable energy for their production. For instance, a brick needs about 3.75 to 4.5 MJ of energy for its production. Alternative materials like Stabilized Mud Block and Hollow Concrete Block require about 25% of brick energy and hence represent Green building materials. In some locations cut stone(sand stone/lime stone) are even more energy efficient.

Selection of appropriate construction technology can further lead to greater energy and carbon emissions reduction. It is now common to use reinforced concrete framed construction when the number of storeys are more than two. Since such structures make extensive use of steel and concrete, they entail significant energy expenditure and concomitant carbon emissions. However, using load bearing masonry of high strength Hollow Concrete Blocks, even High Rise Buildings can be built of Masonry. In order to mitigate earthquake problem, one can use vertical and horizontal reinforcement. Such buildings lead to nearly half the energy consumption and 60% carbon emissions of framed structure. Europe and United States often use load bearing masonry going up to 16 storeys. Sometimes two storeyed buildings with Stabilized Mud Blocks or Hollow Concrete Blocks for intermediate floors can lead even lower energy expenditure.

The issue of operational energy becomes important since this energy outstrips the embodied energy in a few years time. An upper middle class home in Bangalore will need about 35Kwh/m2/year for the operational energy covering all domestic electrical gadgets(except AC).However, a Platinum rated building in Gurgaon consumes 191 Kwh/m2/year after reducing energy by 40%.The so called Platinum rating is a misnomer in the Indian Context.I feel they have to reduce the energy needs to about 50 Kwh/m2/ year by using Solar Passive Cooling to be called a green building.

A number of examples of Alternative Buildings, the World Over, show how embodied energy can be saved.16 storeyed buildings of Europe and the US and 6 storeyed buildings of Mumbai may be mentioned in this context. A number of Alternative Buildings around Bangalore use Stabilised Mud Blocks, Prefab Roofing's etc. to save embodied energy. While these examples are pertinent and show the way, there is inadequate efforts at Governance level and the Industrial Sector to push in this direction more vigorously.

CONSTRUCTION MATERIALS AND SUSTAINABILITY - AN OVERVIEW

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Indian construction sector contributes more than 10% to nations GDP. It is the biggest in terms of volume of materials produced and consumed, and employment generated. Also, it responsible for 30% of green house gas (GHG) emissions. Construction sector greatly depends upon the processed and manufactured materials. Use of materials in their native state is nearly absent. Varieties of construction materials are used. Production of construction materials needs two major resources, viz. raw materials and energy. Except for biomass based products the raw materials needed for the production of construction materials are mined from the earth. Sustainability of any activity dependent on mined resources is questionable. This paper attempts to analyse some facts about Indian construction sector particularly with reference to sustainability of mined resources and the path ahead to keep the growth of construction sector without jeopardising the prospects of future generations.

Sustainable Society is the one which manages its economic growth in such a way as to do no irreparable damage to its environment, and it satisfies the needs of its people without jeopardizing the prospects of future generations (Kumarappa 1930). Sustainability is associated with

1. Earth's capacity to sustain a large human population (~7 billion & still rising)
2. Pollution causing climate change (GHG emissions & global warming)
3. Managing the material resources in a sustainable fashion
4. Development with minimum or no damage to environment

Construction sector encompasses varieties of structures for infrastructure (roads, bridges, stadiums/sports facilities, etc.), buildings (for residential spaces, commercial and industrial spaces, public buildings and offices, educational institutions, etc.), dams, irrigation structures, etc.

Materials consumed in bulk quantities are listed below. Annual consumption of construction materials amounts to 1.25 billion tonnes which translates to per capita annual consumption of 1.1 tonnes as against per capita food grains consumption of only 0.20 tonnes.

Type of material	Annual consumption
1.	Burnt clay bricks 150 x 10^9 Nos.
2.	Cement 240 x 10^6 t
3.	Steel 50 x 10^6 t
4.	Coarse aggregates 300 x 10^6 m^3
5.	Fine Aggregates 350 x 10^6 m^3

Life cycle analysis of these materials shows that it is difficult to get back the raw materials even after the end of life of the material. For example clayey soil is needed for the brick manufacture and it is not possible to get back clay minerals from the burnt clay bricks. Mining of river beds for sand is prohibited in many places, leading to crushing of rocks for the manufacture of sand, which again is an environmental concern. Thus it is clear that the Indian construction industry is surviving on mined resources. Hence, sustainability of construction sector is a big question mark?

One side of the construction sector is gobbling up of natural material resources and the other side is pollution caused due to energy expenditure to manufacture the materials and maintaining the indoor environment quality in the modern buildings. For example built environment consumes apart from land and water 30% of material resources and 40% of energy resources, at the same time responsible for 40% CO2 emissions generating 50% pollution load. Addressing the issues pertaining to energy, related pollution, and waste and water management (as majority of the rating systems attempt to address), does not lead to the construction sector becoming sustainable. Also, green buildings need not be sustainable constructions. Apart from the energy and pollution issues one has to take serious note of the consumption of mined raw material resources in order to address the sustainability issues.

Augmenting the material resources for the construction sector and conservation of natural resources necessitates considering actions on the following points.

(i) Considering the end of life of a manufactured materials i.e. effectively recycling and re-use of construction and demolition (C&D) wastes.

(ii) Effect minimum changes to natural materials during production processes. Discarded materials should go back to their native state with minimum environmental costs.

(iii) Recycling non-organic solid wastes (from industries, mines, C&D, agro-wastes, etc) into construction materials and products.

(iv) Developing building products from renewable materials such as biomass, bamboo, timber, agro residues, etc. which are truly renewable

(v) Use of structurally and functionally efficient building envelopes and construction systems

Industrial and mining activities produce more than 300 million tonnes of non-organic wastes annually. Fly ash, bottom ash, coal mine waste, mine tailings (several types of mines), slag, marble/granite dust, red mud, phospho-gypsum, slag, C&D wastes etc. represent some of the non-organic wastes. In addition, there is enormous amount of accumulated non-organic wastes unutilized over a period of several decades. For example there are 2 - 3 billion tonnes of accumulated wastes like coal mine waste and fly ash/bottom ash. In Karnataka state there is 200 million tonnes of iron ore tailings and 30 million tonnes of gold mine tailings. R&D work on these two materials revealed that 50% of fine aggregates can be substituted with these tailings in cement and structural concrete. Karnataka state consumes 20 millions tonnes of fine aggregates annually and facing serious problems of sand mining. Iron ore tailings can meet several decades of sand requirement in Karnataka state.

Use of natural materials without much modification to the native state is another option to address the sustainability of construction sector. Earth based materials like stabilized soil products (stabilized soil blocks, rammed earth, adobe, poured earth, etc.), bamboo composite products (e.g. glu-bam composites), straw-bale construction, natural fibre composites, fly ash products, etc. represent the potential construction materials addressing the issues of energy, emissions and mined resources.

The era of unrestricted use of construction materials is over. Now, there is a need for taking stock of raw material resources and finding alternative materials. The challenge before us is, apart from addressing GHG emission reductions we should learn the new game of managing raw materials for sustainable construction practices.

TRADITIONAL BUILDINGS AND THEIR RESPONSE TO CLIMATE

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ABSTRACT:

Bulk of the traditional buildings in a nation with mature culture draws its formative essence from its own culture. And the local climate refines the evolving building form to its temporal perfection. The traditional buildings everywhere were also found in intimate dialogue with the climatic variables in its informal mode to bring about necessary changes in plan and in detailing.

But with the advent of modernism, professionals with their institutional training have taken over the job of design and construction of building. In this process of creating contemporary built environment, local culture is losing its traditional linkages with buildings. The result may or may not be a humen, culturally and climatically satisfying built environment. Professionals and architects today enjoy dealing with an alien and adventurous built-form and solve the emerging climatic problems with modern technologies. In this process, the growths of imported/new technology become related to novelty and architectural adventurism. But unfortunately our dependence or inclination towards new technological solutions made us a consumer of techniques or gadgets developed in a different cultural and climatic context.

Indigenous development or a sensible local adaptation of building technologies and process of design need a critical appraisal in this context. These issues in architecture were identified well by various architects in different parts of the world, particularly in developing nations and nations with live cultural heritage. Hassan Fathy from Egypt was one such dedicated soul. Drawing inspiration from them, a selected group in India initiated a series of investigations on Traditional Buildings, its materials, technologies and their response to local natural resources and climate.

Author was initiated in one such group in early eighties and continued exploration in this area actively with the students of architecture later. This presentation will be a selective extracts of some such investigation of Traditional building and their response to climate.

Early works of Vinod Gupta on traditional Building in north Indian context need a special mention here. Studies of thermal performance of traditional buildings in Northern (hot-dry), Coastal (warm-humid) and interior (moderate) Karnataka will be discussed here with field measurements and observations. A few inspiring examples of modern buildings too will be discussed about their response to climate.

Rural settlements in river plains and coastal areas of eastern India has been facing the climatic extremes like cyclone and flooding periodically. In this context, historic response of Indus valley civilization settlement planning on built-up earth mound or citadel should be considered as a viable option for present rehabilitation program.

Traditional built-form, materials used, its elements and details in India are still alive in our vernacular architecture and potent enough to inspire our contemporary architectural mind. To create a meaningful exposure of the same to trigger an evolutionary development in building with local tradition as its base is the attempt here.

BUILDING CLIMATE-RESPONSIVENESS AND THERMAL COMFORT - SALIENT ISSUES FOR INDIAN CONDITIONS

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Buildings have evolved to provide habitable indoor thermal comfort by regulating the thermal influences of external climatic conditions. This regulation of building climate-responsiveness iswell-exhibited in traditional solar-passive (vernacular) architecture. Solar passive designs havenot only provided habitable and productive indoor living environments in extreme climaticregions, but have also nurtured the physiological ability of its habitants to adapt and remaincomfortable over wider thermal ranges (between summer and winter). The thermal comfortrange was lower in winter and higher in summer.

With the advent of modern power-intensive air-conditioning prowess, modern building designsworry little about its own ability to passively regulate indoor thermal comfort. In addition, conventionally adopted ASHRAE thermal comfort concepts prescribe a narrow thermal comfort range to be maintained indoors independent of external climatic conditions. While the understanding and rig our involved in arriving at ASHRAE thermal comfort standards is commendable, it mush however be noted that most studies were conducted in artificially controlled environments for European subjects. Evidence also indicates that controlled indoor thermal environments inhibit the physiological ability of its inhabitants to adapt to even small climatic variations leading to mental distress and physical intolerance.

India is gifted with a bounty of vernacular designs adopting a variety of local buildings materials with climates varying from composite to hot-humid and cold-cloudy. Most inhabitants, particularly rural, still exhibit much wider thermal-comfort adaptability ranges that defy conventional prescribed standards. The objective here is to discuss salient issues pertaining to thermal comfort standards applicable for Indian conditions.

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NANOMEDICINE IN MENTAL HEALTH AND NEUROLOGICAL DISORDERS. CURRENT STATUS AND FUTURE PERSPECTIVES*

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Nanomedicine is a developing subject that primarily deals with therapeutic advancement of drugs using nanotechnology [1]. Thus, drug delivery to the target organs, e.g., brain that posses a blood-brain barrier (BBB) restricts entry of most of the foreign substance that are not lipid soluble [2]. As a result, many drugs could not gain access into the brain to have good therapeutic effects [1,2]. Nanomedicine is aimed to deliver druse tagged with nanoparticles in such a way that the "nano-drug complex" could bypass this BBB easily to gain access into the brain tissues for selective and enhanced therapeutic effects within the localized brain areas [3,4]. This is especially needed to treat brain tumors, localized brain infarcts, Alzheimer's disease, Parkinson's disease or selective brain injury with severe edema where dead or injured tissues are not responding to any treatments [6]. For advance drug delivery, nanoparticles either composed of lipid molecules known as liposomes (soft nanoparticles), or nanowires made from silica, silver, platinum or titanium, as well as other nanomaterials viz., carbon nanotubes, gold, silver, iron or aluminum are used [1,2,6]. Selected drugs could be tagged with nanowires or encapsulated within the nanoparticles that are delivered either systemically or through local application for enhanced drug-delivery to the brain [7]. In some cases magnetic nanoparticles are used to enhance drug delivery to the target organ through a peripheral guided magnetic probe [8]. Also specific antibody-tagged nanoparticles containing drugs are also sued for selective brain delivery or for specific diagnostic purposes [1,7]. Using nanobiotechnology, the drug could enter into the CNS tissue faster and deeper and thus could have widespread effects on cells and tissues [6]. Thus, nanodrug delivery could potentiate the therapeutic effect of the parent compounds within the CNS. Another advantage of nanodrug delivery is a sustained and prolonged action of the drug that is achieved by a slow release of the compound from the nanoparticles or nanowires as well is the nanoboud drug is also protected form rapid catabolism by endogenous enzymes [9-11].

These observations suggest that nano-drug delivery results in superior effects of the parent compounds than the conventional drugs.

However, the effects of nanoparticles per se in inducing neurotoxicology, if any is still being largely ignored [11,12]. Thus, it is still unknown what will happen once the nanoparticles once entered into the CNS compartments in relation to its potential safety, toxicity or other immunologic or metabolic effects on the cells or tissues within vascular or neuronal compartments [8,12,13]. Additional questions about how long the nanoparticles could stay in cells or within the interstitial fluids or other biological compartments and how they are excreted or metabolized require further investigation.

Interestingly, nanoscale materials and their possible effects on the biological system especially on the CNS in vivo satiation are still not well explored [14,15]. Nanoscale materials comprising "microfine particles" that are normally present in the environment, or "engineered nanomaterials from metals" emanating from some industrial sources at certain work places could affect our central nervous system (CNS) function [1,2]. On the other hand, several nanoformulation of drugs are used to enhance brain drug delivery to achieve better therapeutic successes [4,11]. Thus, the need of the hour is to focus on research related to nanoparticles on the CNS toxicity in vivo situations. It appears that our brain function is severely compromised following exposure to these microfine particles [8]. We need to find out whether presence of carbon nanoparticles in the environment due to motor vehicle exhausts, or silica dust in desert environment could influence our reactions to stress or CNS injuries [1,8-10]. Furthermore, whether the effects of neuroprotective drugs are also altered in CNS injuries during nanoparticles intoxication [16,17]. However, the potential neurotoxic effects caused by nano-drug delivery should be examined first in great details.

There are evidences that nanoparticles derived from metals, e.g., silver, copper or aluminum could induce profound neurotoxicity probably by inducing breakdown of the blood-brain barrier (BBB) [15-18]. Furthermore, chronic nanoparticles treatment could exacerbate the adverse effects of hyperthermia induced heat stress, emotional stress or CNS trauma leading to greater brain pathologies [19,20]. This indicates that our military and personals if they are exposed to desert environment breathing silica dust or exposed to areas with high environmental pollution

comprising motor vehicle exhaust emitting carbon nanoparticles or other microfine particles they could be more vulnerable to additional stress or trauma, e.g. in the battle field or combat operation [8,18-20]. If these personals are exposed to high environmental heat or get injuries caused by blast or gun shot, their brain pathological reactions will be munch more exacerbated than other healthy personals that are not exposed to nanoparticles.

We tested this hypothesis in model experiments in rodents. Experimental observations in our laboratory clearly show that nanoparticles from silica, copper, silver or aluminum intoxication in rats or mice alters the physiological response of hyperthermia, hypertension, diabetes, CNS injury or stress [14-16,18-20]. Thus, nanoparticles intoxicated animals when subjected to heat stress at 38° C for 4 h, immobilization stress or sleep deprivation, or brain or spinal cord injury brain damage in these animals was 2- to 5-fold exacerbated than normal healthy animals. Likewise, diabetic or hypertensive animals exhibited greater brain pathologies after nanoparticles intoxication than saline treated groups. This suggests that nanoparticles intoxication could alter the cellular and molecular mechanisms of CNS function and making them more vulnerable to additional stress or trauma.

Interestingly, Ag, Cu or SiO2 nanoparticles induced higher brain damage than Mn or Al. Nanoparticles with smaller sizes (20-30 nm) produced more brain damage than the larger sizes of the same nanoparticles, e.g., 50-60 nm or 89-90 nm. Thus, the effects of nanoparticles are dependent on their inherent properties and sizes [21,22].

Furthermore, in nanoparticles intoxicated animals also altered the dose response of neuroprotective agents. Thus, normal dose of the several neuroprotective drugs, e.g., cerebrolysin, growth factors, growth hormone and other agents are unable to induce brain protection in nanoparticles intoxicated animals [23]. When their doses are enhanced from 2-to 4-fold some neuroprotection is seen in these animals. Interestingly, nanodrug delivery using nanowires or nanoparticles also failed in inducing good neuroprotection. Instead, the nanoparticles used for drug delivery induced moderate neurotoxicity in these animals. These observations suggest that on one hand nanoparticles induced drug delivery could enhance neuroprotection in normal animals on the other hand in nanoparticle intoxicated animals nano drug delivery could do more harm than benefit. Thus, new investigations are needed to further expand our knowledge in the field of

Nanoneurosciences, nanoneuropharmacology, nanoneuroprotection and nanoneurotoxicity. The effects of nanoparticles on our health system can't be ignored now.

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THE NANOMECHANICAL SIGNATURE OF CELLS AND TISSUES – NORMAL VERSUS PATHOLOGICAL

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*present address: nCATS, School of Engineering Sciences, University of Southampton, UK We have established atomic force microscopy (AFM) as a powerful tool for imaging, measuring and manipulating soft biological matter at all relevant scales of cell and tissue architecture [cf. Stolz *et al.* (2003) *BioWorld* **4**: 2-5; Reichlin *et al.* (2005) *J. Struct. Biol.* **152**: 52-63; Stolz *et al.* (2007) *Nanomedicine* **3**: 53-62]. Recently, we have documented that indentation-type AFM (IT-AFM) performed at the nanometer scale is superior over conventional/larger scale tissue analyses. For example, NanoIT-AFM detects early pathological changes of the articular cartilage (AC) in a collagen IX-deficient mouse model for osteoarthritis (OA) and allows to measure early OA using AC biopsies from patients [cf. Stolz *et al.* (2009) *Nature Nanotechn.* **4**: 186-92]. Most significant, all morphological and biomechanical changes at the onset of the disease could solely be depicted at the nanometer scale [cf. Stolz *et al.* (2004) *Biophys. J.* **86**: 3269-83; Loparic *et al.* (2010) *Biophys. J.* **98**: 2731-40]. Hence, IT-AFM harbors a big analytical potential to design and optimize engineered cartilage that exhibits long-term mechanical stability, functionality and biocompatibility for use in OA joint arthroplasty. Moreover, it holds a great promise for direct *in situ* detection of the early stages of OA. To this end, we are developing an arthroscopic AFM for direct, quantitative *in situ* inspection of AC morphology and biomechanical properties at the nanometer scale [cf. Imer *et al.* (2006) *Japan. J. Applied Phys.* **45**: 2319-23; Staufer *et al.* (2007) *Microelectronic Engineering* **84**: 1681-4; Imer *et al.* (2007) *J. Phys. Conf. Series* **61**: 467-71]. To probe the nanomechanical properties of cells and tissues in relation to changes in cytoarchitecture and microenvironmental conditions, we have been employing AFM complemented by light microscopy. To this end, we have manipulated the vimentin filament network of Rat2 fibroblasts, i.e. by transient transfection with mutant desmin variants, in order to examine the contribution of the intermediate filament (IF) cytoskeleton to cell stiffness [cf.

Plodinec *et al.* (2011) *J. Struct. Biol.* **174**: 476-84]. In contrast to the stiffness changes that accompanied interference with the IF system, expression of a mutant actin variant that renders Rat2 cells tumorigenic, did not alter the stiffness of cells cultured on solid substrates. To exclude impacts of substrate attachment on the organization of the cytoskeleton, we probed the stiffness of normal and tumorigenic Rat2 cells grown as 3D spheroids. On day 3, tumor spheroids exhibited a gradual softening from the periphery to the core accompanied by hypoxia. Low oxygen differentially affected the mechanical properties of tumor versus normal spheroids. Similarly, we have used punch biopsies from human solid breast tumors for nanoITAFM. Subsequent histopathological examination of the same specimens allowed us to directly correlate high-resolution stiffness maps with the spatial distribution of specific morphological variants within the tumor tissue. NanoIT-AFM performed on more than 35 human breast tissue biopsies revealed malignant lesions to be characterized by a distinct radial stiffness gradient that strongly correlated with the malignant phenotype. AFM stiffness maps also revealed the stromal tumor tissue at the periphery to be stiffer than the underlying tumor. In contrast, benign lesions typically showed a uniform stiffness, consistent with their fairly homogenous tissue morphology. Most significant, comparison of stiffness distribution to the histopathological diagnosis suggests a high ratio of soft versus stiff areas to be an indication of a more aggressive phenotype. Therefore, AFM stiffness testing might prove a valuable prognostic marker for tumor progression with significant implications for treatment [cf. Plodinec and Schoenenberger (2010) *Breast Cancer Res.* **12**(4): 308 Epub 2010 Aug 23].

NANOSTRUCTURED MATERIALS IN TISSUE ENGINEERING, THERAPEUTICS AND DIAGNOSTICS SYSTEMS FOR BIOMEDICAL APPLICATIONS

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The nanotechnology is considered to have great potential for the development of new innovative materials with an environmental advantage, the so-called 'eco-innovation' materials. However, it is necessary to have in-depth understanding in this area, in order to facilitate and not at least to accelerate implementation of nanocoatings or nanomaterials in different end products. Nanostructured materials (in particular Inorg-polymer, org-polymer, hybrid coatings) are expected to create radical changes in diverse fields. Potential applications for micro and nanostructured materials include pharmaceuticals, cosmetics, medical diagnostics, catalysts and supports, membranes and filters, batteries and fuel cells, hydrogen storage systems, electronic, magnetic and optical devices, flat panel displays, biomaterials, drug delivery systems, structural materials and protective coatings and defense related applications. To meet the requirements, the sol-gel process represents a flexible chemical route to synthesize various high performance nanostructured ceramic materials with controlled internal morphology and chemistry. Sol-gel technology can alone bring all the nanomaterials (nanostructured thin films, nanostructurted coatings, nanocomposites, inorg-polymer hybrid coatings, nanostructured conducting polymers, aerogels, hydrogels, xerogels, nanoparticles, nanofibers, nanospheres) to apply to various industrial applications that include energy, transport, health, food, life sciences. The process is also assisted by microwave technique, electrospinning techniques to create various nanostructures applicable to various fields (demonstrated products) such as, antivirus, wound healing, chemical warfare agents decontamination, hydrophobic, photocatalytic, gas sensors and nanofibers applicable to energy (H2 storage) and defense, chemical (liquid and air filters, biogas detection) and biotechnology (algae treatment, antibacterial, toxic materials degradation etc.,) industries.

In biological and medical applications, controlling interactions at the level of natural building

blocks, from proteins to cells, facilitates the novel exploration, manipulation, and application of living systems and biological phenomena. Nanoengineered tissue scaffolds and nanostructured biomaterials and coatings for implants and prostheses are leading to better solutions in tissue design, reconstruction, and reparative medicine. Synthetic nanopores of tailored dimensions are probing, characterizing, and sequencing biological macromolecules. Application of these techniques to create novel materials and devices for tissue engineering, diagnostics, and therapeutics will profoundly impact the practice of medicine. In medical diagnostics, the speed and precision with which a condition is detected determines patient prognosis. With the development of lab-on-a-chip and other miniature point-of-care (POC) devices, the speed and precision with which health care is administered can be radically enhanced. In addition, novel analysis techniques allowing for acquisition of previously unattainable information and, consequently, leading to improved diagnosis have been enabled by micro- and nanoscale technologies. Nanotechnologies developed at Nano RAM Technologies company will be presented.

Keywords: Sol-gel process, nanostructures, thin films, nanoparticles, nanospheres, nanofibers, antibacterial, hydro-oleophobic, photocatalytic, anticorrosion, gas sensors, chemical warfare agents, diagnostic systems

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NANOTECHNOLOGY AT THE CROSSROADS:

WITH A SPECIAL EMPHASIS ON DENDRIMER NANODEVICE

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Nanotechnology can be broadly defined as science at nanometer range. More precisely, nanotechnology is the art of managing structures, devices and systems by controlling shape and size at the nanometer scale. Till now research was mostly focused on either atomic level or macroscopic level. Behavior of small discreet entity or assembled structure changes according to its size/length scale. At different size scale materials can behave differently and can confer novel chemical, physical or biological properties.

Nanotechnology is said to be the next big thing, which may change the face of the world. It is going to affect every aspect of life and expected to exceed the impact of industrial, textile, automobile, railroad, electricity, biotechnology, and computer revolutions. As of now, USA is the leader in nanotechnology sector and Japan, Germany, and South Korea are fast emerging as big players. India has missed many opportunities of technological revolution in the last three centuries. Just by exploiting a part of computer revolution in its fag end, India gained respectability in the world arena. Recent world economy churning has produced a new world dynamics and India emerged as an important player. This is a crucial time to make big leaps and nanotechnology can be a tool for India to move towards becoming a superpower and more importantly solving many of the pressing domestic problems.

Although nanotechnology has an immense potential, its transformation from bench to the bed side or mass usage is still a difficult journey. The commercialization of nanotechnology for mass usage has both technical and business roadblocks. Critical issues are- effect and interaction of nanomaterials on living and environmental factors, stability of nanomaterials, manufacturing at large scale, ignorance and misconception about nanotechnology with researchers, public and

media, lack of confidence from business investors due to uncertain outcomes, and the decreasing investments in research.

Important synthetic nanomaterials are carbon nanotubes and fullerenes, dendrimers, ceramic nanoparticles, metal nanoparticles, nanoporous materials, nanostructured metals, nanostructured surfaces, nanowires, quantum dots and nanoclays. With the advent of new nanomaterials, there are efforts to prepare nano-periodic table to find the patterns and rules pertaining to the nanomaterials.

Quest to control the structure of nanoscale objects with respect to size, shape, surface chemistry, and flexibility led to invention of dendrimers. Dendrimers are one of the important components of the growing field of nanotechnology. Dendrimers are core-shell nanostructures with precise architecture and low polydispersity, which are synthesized in a generation-by-generation fashion around a core unit, resulting in high level of control over size, branching points and surface functionality. Dendritic polymers (or dendrimers) are now officially fourth class of polymers. Due to its unique structure and architecture dendrimers have been used for various new applications in virtually all fields such as energy, food and agriculture, water remediation, pharmaceutical and medical diagnostics, veterinary, biotechnology, forestry, environment, personal, household, chemicals and manufacturing. Dendrimers have shown potential in pharmaceuticals mainly for solubility enhancement and drug delivery. The ability to tailor dendrimer properties to the needs of a drug makes them ideal carriers for drug encapsulation. Release of drug can be controlled be physical and chemical laws. Moreover, targeting of dendrimer based nanodevice was achieved by diffusion based passive targeting and ligand/antibody mediated active targeting. Dendrimer provides a platform to engineer a nanodevice for advanced therapeutic applications.

New generations of nanomaterials will evolve, and with them new and possibly unforeseen issues may arise. It is important to balance the approaches to harness the benefits and foresee toxicological concerns regarding existing and evolving nanomaterial technology. Nanotechnology is in nascent stage of evolutionary development. Though many breakthroughs have been achieved in this field, understanding of nanotechnology is still incomplete. Before we start celebrating great success of nanotechnology, it is very important to understand the negative impacts of this technology.

There is a need for multi-pronged approach towards nanotechnology development in India. i) propagate nanotechnology education, ii) encourage nanotechnology research in academia iii) establish industry-academia partnership, iv) facilitate capital investment in new nanotechnology ideas for start-up companies.

Nanotechnology needs positive approach with caution. It is almost like riding a tiger: we cannot afford to come down and we have to be careful while riding. At the end it is a matter of better understanding and smart management- *Nano-thinking*.

ADVANCES IN GENETIC MYSTERY OF PSYCHOSOMATIC DISORDERS BY EPIGENESIS AND UTILISATION OF NANOSCIENCE AND NANOTECHNOLOGY

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Nanoscience and nanotechnology have produced remarkable advances in diagnosis, treatment monitoring and control of biological systems and these are now referred to as nanomedicine.

Nobel Prize winner R.P. Feynman in 1959 suggested the idea of studying things at the atomic level and nanoscience was thus evolved. Nanoscience is thus the science behind the abilities to employ nanotechnology which again is defined as the manipulation of matter at nanoscale. The capabilities in nanoscience to study the phenomena and manipulation of atomic, molecular and macromolecular scales make it a novel research tool to diagnose and treat the genome or genetic disorders in human beings and also in medicine at large.

In 1974, Norio Taniguchi of the University of Tokyo coined the word "nanotechnology" and it refers to the ability to produce materials at the nanometer level.

The application of nanotechnologies in medicine is multiple for example, improving diagnosis of diseases, improving drug delivery, improving therapeutic efficacy, correcting defective DNA and genomic disorders, developing technologies for nanosurgery, diagnosis and cancer management. Because of nanotechnologies being used in many areas of medicine, NIH coined the word "nanomedicine".

Vast areas of nanomedicine include the nanoparticles which act as biological mimetics, nanofibers, biomaterials, sensors and diagnostic agents.

The future hope for nanomedicine is to utilize nanoscience and nanotechnologies for getting early detection of diseases quickly. Genomic sequencing, genomic disorders, gene therapy and general cellular processes including signaling pathways could be done cheaply.

Our research work in epigenesis in psychosomatic disorders including signaling pathways is one example where nanomedicine and nanotechnologies can be utilized for confirming the diagnosis and etiological factors of psychosomatic disorders.

Most psychiatric and psychosomatic disorders involve mutation in molecular disturbances entailing multiple genes and signals that control their expression.

Epigenesis or epigenetics, derived from the Greek word, was coined by Waddington in 1942, refers to interaction of genetic and environmental factors. Changes by this genetic mechanism are developed due to outside influence rather than genetically determined and one that is outside conventional genetics. These changes may remain through cell divisions for the remainder of the cells life or may also last for multiple generations.

In psychosomatic disorders the influences of outside factors on genetic material from the very beginning to whole life are observed thus showing the involvement of the ongoing epigenesis process.

The underlying mechanism of epigenesis thus involves non-interpreted genes induced by environmentally modified gene expression without altering DNA sequences. When responses are mismatched, the risk of psychosomatic disorders increases.

Phenotype established between genes and environmental factor using the process of developmental plasticity procedures the match for example if inserting phenotype is matched best suited to environment the illness will not be present but mismatch reduces the individual capacity to respond to environment and risk of illness increases.

Molecular basis of epigenesis is a complex and multiple inherited system and may play a role in forming cell memory. The important disease related effect in humans is produced by genomic imprinting and related disorders and also by transgeneration observation.

Epigenetic gene regulation in neurons producing complex behaviour has been implicated

in many psychosomatic disorders including depression, anxiety, and drug addiction.

Recently the regulation of gene expression has been suggested as one molecular mechanism of adaptation and maladaptation in the brain thereby causing alteration in behaviour in human beings. MRNA changes have been seen in specific regions of the human and animal brain for altered behaviour by the above mechanism. Epigenetic processes which exert lasting control over gene expression without altering the genetic code or DNA may be responsible or stable changes in human illness.

The present paper thus will discuss the exciting areas of future research not only in diagnosis of psychosomatic disorders but also in etiology and finally in treatment where the utilization of nanotechnology and nanomedicine is very essential.

A NOVEL ALLOSTERIC MODULATOR OF THE DOPAMINE D2 RECEPTOR: IMPLICATION FOR TREATMENT FOR SCHIZOPHRENIA USING NANOPARTICLE FORMULATIONS:

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Current APDs bind directly to the DA D2R orthosteric site in order to elicit the desired physiological or pharmacological effect. In contrast, allosteric modulators bind their target receptor at a site other than the orthosteric site, known as the allosteric binding site. Many pharmaceutical companies are now turning their attention to the development of allosteric drugs.

Allosteric modulators of GPCRs are emerging as a new class of effective small molecules that may offer a competitive advantage over conventional therapeutic agents. This potential stems from their key pharmacological features. Allosteric modulators are highly selective for their target and generally act only in the presence of natural or artificial ligand. PAOPA, as one of these allosteric modulators, can potentially be developed into a more advantageous treatment for SZ because of its self-limiting activity, as the ceiling to its effect is set by levels of endogenous ligand. The study of PAOPA will advance our understanding of the molecular basis of SZ and other mental illnesses.

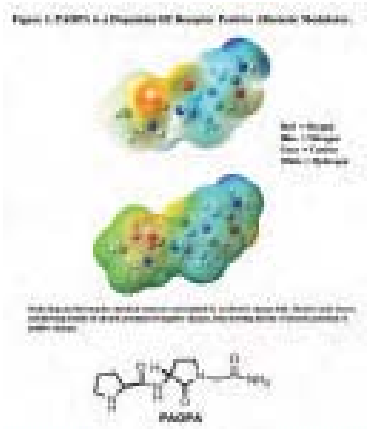
Currently, there are few known allosteric modulators of the DA D2R, including Zn2+ and homocysteine. However, these agents are non-specific for the DA D2R as they modulate other GPCRs such as adrenergic, serotonergic, and melatonin receptors. Pharmaceutical companies are currently developing allosteric modulators to treat SZ by targeting metabotropic glutamate receptors (mGluRs). For example, ADX63365 (Addex Pharmaceuticals) targets the mGluR5 subtype. In addition, LY487379 (Eli-Lily) targets the mGluR2 subtype, whereas LY2140023 targets the mGluR3. These compounds are in the early stages of development and not in the clinic yet. These are all positive allosteric modulators of mGluRs, and have no direct effect on the DA D2R. However, the DA D2R is a more effective target as the clinical efficacy of all APDs is directly correlated to their occupancy at the DA D2R. Despite its importance in the etiology of

SZ, currently no current therapeutic strategy exists that is able to modulate the DA D2R in an allosteric manner.

We have, in collaboration with Dr. Johnson at University of Minnesota, synthesized and evaluated over 185 analogues of endogenous brain tripeptide L-prolyl-L-leucyl-glycinamide (PLG). Our studies have shown that some of these compounds act as allosteric modulators specific for the dopamine D2S and D2L receptors, without affecting ligand binding to other neurotransmitter receptors such as adrenergic, serotonergic, GABAergic, and glutamatergic receptors. Among the various analogues synthesized and evaluated, we found PAOPA to be the most potent allosteric modulator of the dopamine D2 receptor. Detailed pharmacological experiments revealed the following results: PAOPA acts as a positive allosteric modulator by specifically increasing agonist binding to dopamine D2 receptors, without affecting antagonist binding.

This compound readily crosses the blood-brain barrier and does not induce any extrapyradmidal or metabolic adverse effects; PAOPA does not induce abnormal behavioural or toxicological effects. For example, there were no obvious neurological abnormalities in rats at various doses of PAOPA. There were no extrapyradmidal side effects, as commonly observed by typical antipsychotic drug (e.g. haloperidol) treatment in rats and humans. Furthermore, there were no adverse metabolic effects of PAOPA as commonly seen by atypical antipsychotic drug (e.g. olanzapine) treatment in rats and humans. Clinical laboratory tests revealed no changes in liver and kidney enzymes as a result of PAOPA treatment. Furthermore, blood parameters (hemoglobin, red blood and white blood cells, platelets) remained normal. There were no observed organ pathologies. Taken together, these data suggest that PAOPA can potentially be developed as an effective drug once its validity is established in human subjects; PAOPA displays an inverted "U" shape pharmacological dose response curve, indicating that this compound has a ceiling to its pharmacological effect; In preliminary experiments, PAOPA has been shown to prevent and reverse schizophrenia-like behavioural abnormalities in an amphetamine sensitization rat model of schizophrenia. Briefly, the behavioural abnormalities, namely deficits in prepulse inhibition, deficits in social interaction, and hyper locomotor activity were prevented and reversed by PAOPA. Additionally, amphetamine-induced reductions in striatal dopamine levels were prevented by the co-administration of PAOPA; In order to address the molecular mechanisms involved for the

therapeutic effects of PAOPA on behavioural abnormalities, experiments on dopamine D2 receptor internalization were performed. The results of these experiments revealed that PAOPA causes increased D2 receptor internalization and subsequent down regulation in the presence of D2 receptor agonist.



Collectively, these data indicate that PAOPA is a promising therapeutic agent for the development of a new class of drugs to treat schizophrenia. Considering the compound's novelty as an allosteric modulator for the dopamine D2 receptor and these remarkable findings, it is necessary and appropriate to generate nanoparticle formulations of this compound. Using the technology available in this faculty of engineering a McMaster University, nanoparticle formulation suitable for intranasal drug delivery system is currently been exploited. Such preparations will enhance the rate and extent of drug absorption for compounds demonstrating limited solubility.

THE WONDERFUL WORLD OF ONE-DIMENSIONAL NANOWIRES

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Semiconductor nanowires offer a unique approach for the bottom up assembly of electronic and photonic devices with the potential of integrating different technologies on a common platform. The one-dimensional geometry allows efficient transport of charged carriers, photons and phonons in a highly directed manner. In addition, the anisotropic geometry and mesoscopic lengthscales of nanowires also makes them very interesting systems to study a variety of size-dependent phenomenon and configure new devices. We will discuss the intriguing size-dependent properties of one-dimensional semiconductor nanowires at the 20-200 nm lengthscales. At these length-scales not only finite-size effects become important, but also other length-scales such as visible optical wavelengths, strain fields, interfacial, and polarization scales become comparable to the size of the nanostructures. Proper understanding of these phenomena and the effect of different lengthscales on nanowire properties becomes important, which is also required to rationally design functional devices with tunable and precisely controlled responses.

We will discuss different examples: size-dependent interaction of light within nanowire optical cavities and their very unique waveguiding and slow-light propagation properties; nanowires integrated with plasmonic nanocavities allows precise control over their excited state lifetimes, which can be shortened by more than three orders of magnitude to sub-picoseconds due to strong confinement of the optical fields based on the surface plasmon effect; size-dependent electrical properties that lead to structural phase change phenomena, which are very important for new types on nonvolatile memory devices. None of these phenomena exists in bulk systems or in extremely small systems with sub-10 nm sizes. The unique aspects of each size-dependent phenomenon in nanowires will be discussed and explained with the help of simple models. The implications of these findings for assembling novel and reconfigurable electronic and photonic devices will be discussed.

ADVANCES IN ELECTRONICS FOR MEDICAL DIAGNOSTICS

Dr. Srinagesh Satyanarayana

CEO/ Co-Founder

Nano Science Diagnostics Inc.

A significant amount of electronics is used in medical diagnostics. In the last decade electronic techniques have advanced significantly. These advancements have made it possible to make medical diagnostic more efficient. In parallel, advances in molecular biology and nanotechnology have opened new doors for diagnostics. New electronic techniques to enable and leverage these advances in molecular biology and nanotechnology have further helped in advancing medical diagnostics.

In this talk I will outline the advances in electronics for medical diagnostics. I will also discuss new trends in diagnostics as a result of these advances. They include

1. Transformation from centralized lab testing to point of care testing.
2. Lab-on chips is a new format to run the tests
3. Transformation of some diagnostics from the lab to the patient

ADVANCES IN MEDICAL DIAGNOSTICS USING NANOTECHNOLOGY

Dr. Sulatha Dwarakanath

CTO/ Co-Founder , Nano Science, Diagnostics Inc., Austin, TX, USA

Time and sensitivity are very critical in diagnosing certain diseases especially infectious diseases such as viral (Eg. H1N1, HIV, Dengue) and bacterial (Eg. TB, MRSA). Advancements in nanotechnology has made it possible to achieve these goals. Nanotechnology combined with advancements in electronics have made it medical diagnostics more efficient and affordable.

In this talk I will outline the advances in nantechnology and its applications in food and medical diagnostics. I will also discuss:

1. How some of the advances over the last decade has made the transformation of centralized lab testing to point of care testing.
2. How nanotechnology has made it possible to have very highly sensitive test.
3. How nanotechnology combined with electronics have made the diagnostics test very affordable.

MULTIFUNCTIONAL NANOPARTICLES FOR DETECTION AND THERAPY OF CANCER

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Among the potent anti-cancer agents, curcumin has been found to be very efficacious against various cancer cells. Despite multiple medicinal benefits of curcumin, poor water solubility, poor physiochemical properties and low bioavailability continue to pose major challenges in developing a formulation for clinical efficacy. Lower serum and tissue levels of curcumin are observed irrespective of the route of administration due to extensive intestinal and hepatic metabolism and rapid elimination, thus limiting the bioavailability of curcumin. To improve its potential application in the clinical area, we formulated poly lactic-co-glycolic acid (PLGA) nanoparticles. The PLGA nanoparticles were formulated using solid-oil/water emulsion solvent evaporation method and then characterized for percent yield, encapsulation efficiency, surface morphology, particle size, drug distribution within nanoparticles and drug polymer interaction. Our studies showed the successful formation of smooth and spherical curcumin loaded PLGA nanoparticles with a high percent yield of about 92.01±0.13% and an encapsulation efficiency of 90.88±0.14%. The mean particle size of the nanoparticles was found to be 145nm. The in vitro drug release profile showed 55-60% drug release from the nanoparticles over a period of 24 hours with continued sustained release over a period of 8 days. Exposure to curcumin loaded nanoparticles resulted in reduced cell viability of cancer cells compared to normal cells.

Targeting anticancer drugs to their specific molecular targets is a major challenge in cancer therapy. However, advances in biomedical and protein engineering have led to novel nanoparticle targeting approaches. In our present study, we used a novel non-covalent insertion of a homo-bifunctional spacer for targeted delivery of curcumin to various cancer cells. Functionalized

nanoparticles for antibody/targeting agent conjugation was prepared using a cross-linking ligand, bis(sulfosuccinimidyl) suberate (BS3), which has reactive carboxyl group to conjugate efficiently to the primary amino groups of the targeting agents. In our studies, we demonstrated successful conjugation of antibodies, Annexin A2 or prostate specific membrane antigen (PSMA), to curcumin loaded PLGA nanoparticles for targeting to prostate and breast cancer cells. The percent antibody attachment to PLGA nanoparticles was found to be 92.8%. Efficient intra-cellular uptake of the targeted nanoparticles was observed in the cancer cells.

Bone is a major site of metastasis in several type of cancer including breast, prostate, lung cancer and multiple myeloma. Metastasis of cancer to the bone could results in both osteolytic and osteoblastic lesions. The current standard therapeutic interventions such as radiation, surgery, chemotherapy and bone marrow replacement are limited by toxic side effects, drug resistance and lack of efficacy. Our multifunctional biodegradable nanoparticle technology is an innovative tool to deliver chemotherapeutic drugs such as curcumin and bortezomib to the bone. This will substantially increase the drug payload and prevent the growth and progression of bone-residing metastatic nodules. Our results indicate efficient encapsulation of curcumin and bortezomib within PLGA nanoparticles. We found that combination of these agents have synergistic effects in preventing the cell growth; however, does not have synergistic effect in inhibition of osteoclastogenesis and bone resorption. Interestingly, curcumin alone is sufficient to inhibit the osteoclastogenesis at given concentration. Using non-invasive optical imaging system, we validated that a bis-phosphonate, alendronate,-coated nanoparticles preferentially localized to bone marrow as compared to untargeted nanoparticles. Moreover, upon histopathology of the mice bones, we found an abundance of fluorescent nanoparticles in the bone marrow. This was further confirmed by prussian blue staining and transmission electron microscopy (TEM) of decalcified mouse bones treated with of iron oxide encapsulating PLGA nanoparticles decorated with alendronate for bone targeting.

For the transition of these curcumin loaded nanoparticles to the clinical phase, our aim is to successfully optimize, scale-up and characterize our curcumin nanoparticles in the laboratory to the pilot level. To this end, we determined the effect of formulation variables such as amount of PLGA, concentration of stabilizer and the volume of organic phase and their influence on the

physiochemical properties of the nanoparticles. The responses evaluated were particle size, polydispersity, encapsulation efficiency and percentage drug loading. We applied the Reponse Surface Methodology (RSM) using Central Composite Design (CCD) model for optimizing our formulation. An analysis of variance was performed to determine response surfaces. Furthermore, the desirability function approach was applied to obtain the best optimized solution among the multiple responses. The optimal conditions for the formulation were found to be 85mg PLGA, 1% PVA (w/v) and 4.5ml volume of ethyl acetate. The optimized particle size was in the 150nm range and polydispersity was found to be 0.13. In vivo testing of these nanocurcumin particles show promising results in terms of pharmacokinetics, pharmacodynamics and biodistribution in mouse model system. Further, in vivo testing and toxicity studies in dogs have shown that there is no heamolysis detected with the administration of curcumin loaded PLGA nanoparticles and therefore demonstrate clinical efficacy of these nanocurcumin particles.

These results have emphasized the potential of our multifunctional curcumin nanoparticles to improve the clinical efficacy of curcumin therapy in patients with cancer.

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ALTERNATIVES TO ANIMALS IN EDUCATION, RESEARCH AND TESTING

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Animal experimentation remains a matter of debate and controversy. On one side there is opinion that animal use in education, research and testing raises concerns relating to ethical treatment of animals, the source from which animals are brought, ill-designed experiments, relevance/inferences of the testing outcomes, safety issues, biodiversity issues, environmental concern, etc. On the other side there is also opinion that the benefits that have come from animal testing research such as organ transplants, open-heart surgery techniques, life saving drugs, effective insulin and cancer treatments, and animal and human vaccines, would not have been realized if not for animal experiments. One cannot deny the contribution made by animals for the betterment of human and animal health but it is also important to recognize that animal testing is not the gold-standard, given the hundreds of drugs that have been retracted from the market due to their ill-effects in the consumers but were before launching declared safe after having passed a gamut of animal tests required by the Regulatory Authorities. As scientists it is important to make our choices with a scientific rationale and as teachers we need to incorporate a sense of compassion and ethics to the use animals and look to the need / possibility to use better, humane and more precise tools in life science education. It is, thus, time to STOP and THINK: Does education, research and testing really require this many animals? Can animals be used in a way that they do not feel distress or pain? Can animals be replaced with alternative methods?

Historically, these three questions led to the 3R's principle of Replacement, Reduction and Refinement in the use of animals in experimentation, otherwise known as the concept of ALTERNATIVES. Once a matter of imagination, today science has evolved such that drugs,

cosmetics and agrochemicals can be tested adopting scientifically validated non-animal methods, saving / protecting the lives of human beings and yet saving the lives of several million animals from pain / distress and / or death. Alternatives, undisputedly, have paved the way for better, precise and more credible scientific research. Besides the aspect of animal welfare, the alternatives offer advantages such as cost-saving and higher throughput.

Today, the science of alternatives has gained recognition from both ethical and scientific points of view. The breaks through in ICT, cell culture techniques, in vitro toxicology, molecular tools, functional genomics, tissue engineering, systems biology, etc., have made it possible to take the concept of alternatives from a myth to reality. The discovery of E-cell is expected to revolutionize prediction of toxicity. The Limulus Amoebocyte Lysate assay, is in as alternative to the rabbit pyrogen test, reaching an annual turnover of $200 million and saving one million rabbits annually! The human whole blood pyrogen test has been developed to replace both these progen tests. Engineered skin/epithelial models have come to replace the animals in the skin/eye sensitization/irritation/corrosion testing of cosmetics. Mathematical models such as Quantitative Structure Activity Relationships (QSARs) have come to be in application to predict biological (toxic / pharmacological) activity associated with chemical structure. EbTrack and ToxCast, and newer in *silico* analytical tools are on the way.

Europe and USA are the fore-runners and strong propagandists of alternatives concept. The *EU Directive 86/609/EEC* on "the protection of animals used for experimental and other scientific purposes" was amended in 2010 and is being replaced by the *Directive 2010/63/EU* which requires in *Article 4:* "Member States shall ensure that, wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure"; and in *Article 47:* "The Commission and the Member States shall contribute to the development and validation of alternative approaches which could provide the same or higher levels of information as those obtained in procedures using animals, but which do not involve the use of animals or use fewer animals or which entail less painful procedures, and they shall take such other steps as they consider appropriate to encourage research in this field."

ZEBET, established in Germany in 1989, aims to bring about the replacement, particularly of legally prescribed animal experiments with alternative test methods, to reduce the number of

test animals to the absolutely necessary level and to alleviate the pain and suffering of animals used in experiments..ECVAM, established in Europe in1992, and ICCVAM, established in USA in 1997, have as main mandate to coordinate and promote the development and use of alternatives in basic and applied research and regulatory testing. ECVAM and ICCVAM helps promoting a dialogue between legislators, regulators, and all relevant stake-holders, in particular industry, biomedical scientists, consumer organizations and animal-welfare groups, with a view to the development, validation, regulatory acceptance, international recognition, and application of alternative approaches. More than 55 alternative methods have been validated and have reached the market, and more are in the pipeline. JacVAM and KoreaVAM are recent additions along this line. OECD, on its part, is playing critical role in reducing use of animals in experiments.

Some of the best known validated alternatives in regulatory testing for drugs and agrochemicals are : the replacement of the classical acute toxicity test or LD50 with Acute toxic class method / Fixed dose procedure / Up-and-down procedure where in the animals have been reduced from 45 to 8 per test chemical; the absolute replacement of the Eye corrosion test done on the rabbit eye with the Bovine corneal opacity permeability (BCOP) test and / or Isolated chicken eye (ICE) test; the Murine local lymph node assay for skin sensitization; CORROSITEX® / EPISKIN™/ EpiDerm™ / TER assay / SkinEthic™ in vitro human skin model for skin corrosivity; Limulus amebocyte lysate (LAL) assay / Human whole blood assay for rabbit pyrogenecity test; etc.

In the realm of cosmetics the Seventh Amendment to the *EU Directive 76/768/EEC (the Cosmetics Directive)* has come to be one of the most appreciated directions in favor of alternatives, which states that as of 11th March 2009, Member States shall prohibit the marketing of cosmetic products containing ingredients or combinations of ingredients which, in order to meet the requirements of this Directive, have been the subject of animal testing using a method other than an alternative method, with some exceptions.

The Center for Alternatives to Animal Testing (CAAT), Johns Hopkins University Bloomberg School of Public Health, aims at promoting humane science by supporting the creation, development, validation, and use of alternatives to animals in research, product safety testing, and education. CAAT seeks to effect change by working with scientists in industry, government,

and academia to find new ways to replace animals with non-animal methods, reduce the numbers of animals necessary, or refine methods to make them less painful or stressful to the animals involved. The Center for Alternatives to Animal Testing - Europe (CAAT-EU) has been founded based on collaboration between the Johns Hopkins Bloomberg School of Public Health and the University of Konstanz. CAAT-EU will coordinate transatlantic activities to promote humane science in research and education, and participate, as partner or coordinator, in publicly and privately funded European projects.

There has been a landmark publication by the National Academy of Science (NAS) in June 2007, under the auspices of National Research Council (NRC), *Toxicity Testing and Assessment in the Twenty-first Century: A Vision and a Strategy.* This report advocates sweeping and transformative changes in regulatory toxicity testing, and is a reflection of CAAT's ideas, as it envisages a shift from current whole-animal based systems to testing founded primarily on *in vitro* methods, human cells in culture, in silico biokinetic modeling, and mechanisms of toxicity as understood through systems biology. On February 14, 2008, the Environmental Protection Agency (EPA), the National Toxicity Program (NTP), and the National Institutes of Health (NIH) signed a memorandum of understanding (MOU) to develop and implement new high-throughput in vitro methods for testing chemicals and drugs. Based on the recommendations of the NAS report, this MOU will allow the collection of data requested in the NAS report. This significant step toward US development of alternative methodologies reflects both the best science and the most humane science. To help implement the recommendations of the NAS report as quickly as possible, the Doerenkamp-Zbinden Foundation (DZF) and CAAT collaborated to establish the *Transatlantic Think Tank of Toxicology,* the t4.

The 3Rs have steadily become better and more widely known, although much still has to be done to ensure their wider implementation. The discussion of issues such as unnecessary use or reasonable alternatives and their interpretation according to the law is essential for a critical, workable and consensual approach to the 3Rs principle. At the same time, pertinent and well-designed alternatives experiments, political support, financial assistance and technical acumen are to be brought in for the development and advancement of alternatives dogma. More important is for those countries which lag behind to catch up and realize that alternatives are just not humane science but better science. Wake up India, and catch up with the international trend!

NEED FOR ANIMAL ALTERNATIVES IN EDUCATION AND THE ALTERNATIVE RESOURCES

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The practice of animal dissection in the laboratories was first introduced in schools in the 1920s. Dissection is the act or the art of cutting an animal into pieces in order to ascertain the structure of its parts. Dissect means to cut into parts for the purpose of minute examination. Dissection is the exploration of dead animals in the classroom to see what their internal parts look like and how they work. Vivisection is animal experimentation- cutting, burning, shocking, drugging, starving, irradiating, blinding and killing animals. Every year, millions of animals are dissected or vivisected in schools and universities. Approximately 170 species of animals are used for dissection and vivisection. Cats, frogs, fetal pigs, grasshoppers, mink, earthworms, rats, mice, dogs, pigeons, turtles, etc., are used. According to the Humane Society of the United States (HSUS), most animals used in dissection include amphibians, birds, snakes, turtles, fish and invertebrates which are captured from the wild, even though many have been declining in population. It is reported that millions of frogs are captured form the wild every year. Although habitat loss, pollution and climate changes are the primary causes, demand for dissection specimens increases pressure on threatened species. The use of animals in education has a fair share in the killing of animals all in the name of imparting knowledge about animal anatomy. It is ironical that Zoologists, on the one hand, emphasize the role of every living organism in the delicate balance of nature, while on the other hundreds of animals are killed and dissected in the laboratories to study the anatomy. The zoology teachers teach importance of biodiversity/wildlife

and conservation in the class rooms and the same teachers kill animals and let the students dissect them in the laboratories ignoring the concept of biodiversity conservation. As zoologists every one of us should contemplate whether animal dissection is a process of learning or skill development? Most of the zoology teachers accept that from the skill development point of view also, dissection is no more relevant. A single supplier catches 3000 frogs per month. We can imagine the extent of biodiversity loss.

India has one of the most comprehensive animal protection laws in the world. Detailed codes of conduct govern our use and treatment of animals, both domestic and 'wild'. In fact, India is unique in this respect. Unlike other countries, our Nation recognizes animals in our constitution, and every citizen is required to show compassion to all living beings. The animal protection laws viz., The Wildlife (Protection) Act, 1972, Prevention of Cruelty to Animals Act, 1960, and The Constitution of India, Section 51A (g) directly or indirectly guide the educators to use alternatives in the place of animals. Ignorance of these legal provisions is not an excuse for those who kill animals, especially sharks, frogs, lizards, rats, mice, guinea pigs and rabbits. Computer-aided services have started coming up and students can be trained in animal anatomy using computers, and even on line. The zoology teachers are, by and large, bogged down with the faith that dissections are the only method of acquiring knowledge of animal anatomy. As zoology teachers and biodiversity conservationists, why not we change our attitude towards better and humane science? As a positive development in this direction, The University Grants Commission (UGC) has constituted an Expert Committee to look into the possibility of reducing / dispensing with dissection of animals in colleges and universities.

The teachers have the right and academic freedom to change the zoology laboratory curriculum to replace the dissections. Alternatives, in the present context, are defined as educational aids or teaching approaches that replace harmful animal use or complement humane education. The different types of non-invasive animal alternative resources such as models, mannequins, videos, multimedia computer simulators, interactive software and online simulations, microlabs, ethically sourced animal cadavers and in vitro models that are now available should be used in the place of animals.

Today we in an ICT world and it require that teachers are both digitally literate and liberally

sensitive. Teachers must be multi-skilled in order to manage the multi-skill demands of a curriculum. The time has come to change the practical curriculum and to make use the available digitalized (CD ROMS), the other animal alternatives and web resources. The teachers must be aware of the fact that these animal alternatives are cost-effective and affordable when compared to the cost of animals. The added advantages of these alternatives are saving in the cost, conservation of animals and balanced ecosystems. The teachers and students can make use of one CD-ROM repeatedly. On the other hand, the dissection requires multiple animals to be purchased. Added to this, the time spent in dissecting animals can be spent to advantage by taking the students to learning of live zoology- learning about animals in their natural habitat and their diversity, observing their behavior, understanding their role in the ecosystem, etc., through field visits.

"You must do today's job with today's tools

If you do today's job with yesterday's tools

Tomorrow you will be out of business"

MOLECULAR AND BIOACOUSTICS TOOLS ALONG WITH HIGH RESOLUTION DIGITAL IMAGING CAN OBVIATE ANIMAL KILLING IN BIOSYSTEMATICS STUDIES

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A large number of animals are used in teaching and research all over the world. In zoology laboratories dissection or vivisection has been a common practice to to understand the internal organization of an animal. In physiological and biochemical tests also often animals are used. Such practices have resulted in severe loss of biodiversity because greedy animal catchers often totally sweep large number of animals from their natural habitats. Most animals used in the laboratory exercises are generally wild-caught. Some species are even listed under Schedule I *(Scoliodon laticaudus)* II (A) and Schedule IV *(Hoplobatrachus tigrinus)* of the Wild Life (Protection Act) 1972 of India. Over-exploitation of these and other species in vivisection and dissection have resulted in their almost complete removal from nature. The best example of such a loss which I report from Rajasthan is Sara hardwickii *(Uromastix hardwickii).* This lizard used to be a common reptilian model for dissection tray in many institutions until 1980's when it was realized that it disappeared almost completely from most parts of India.

In realization of this loss, the University Grants Commission, many non-Government organizations, etc., started putting serious thought in to the matter. Universities have now realized to change the curriculum of zoology so as to replace many exercises in which animals are used in large numbers. School-governing authorities have also made several restrictions on dissections. Many new approaches and alternatives have come into picture to replace animal dissection / vivisection. Teachers, scientists and curriculum-planners are now paying serious attention to the principle of 3R's, i.e., Replacement, Reduction and Refinement of animals in teaching and research

as suggested by W. M. S. Russell and R. L. Burch (1959).

After animal dissection the next important aspect in zoology study in which large number of animals is collected by the animal suppliers is in making museum specimens. Study of classification, taxonomy and phylogeny (Biosystematics) is generally conducted using formalin-fixed or resin-embedded animals. A large number of animals are regularly collected from nature, irrespective of their IUCN status, for this purpose. A zoology museum keeps thousands of animals in formalin-filled glass jars. Their maintenance is so bad that after some time it is difficult to identify the animal. In as much as many digital alternatives have come up for the replacement of animals in vivisection, dissection and physiology and biochemistry exercises, very little effort is put to search for alternatives in biosystematics.

. We have found that high resolution photographs of an animal with close-ups of some key features, with biometric database and their digitization, associated with bioacoustics and molecular characteristics can convincingly replace animal killing in biosystematics studies.

Bio-acuostic Tools in Biosystematics

The call characteristics of sound-producing animals are species-specific. Therefore, it is possible to identify a species on the basis of their characteristic sound spectrum. This way one can identify a frog, bird or a mammal simply by hearing their calls and analysis of the spectral characteristics. Detailed analysis of spectral pattern can help in developing a supporting taxonomy, Sono-taxonomy, along with the conventional taxonomy. After detailed digital imaging of an individual of a species followed by call analysis, one can convincingly identify a species without killing, and such a technique can save lot of lives.

The call analysis system includes (i) sound sampling, (ii) storage and conversion in a proper format, (iii) generation of spectrogram, and (iv) analysis of spectral pattern. Most graphical display devices present sound as time domain feature. Time domain display of sound waves has limitations in analysis. Frequency domain representatives of spectrum are improved displays which are achieved by Fourier transformation that provides better opportunities for sound analysis. Many hardware and software are available for this purpose.

Further, microanalysis of a spectrogram could be achieved by slicing the spectrogram. A

spectrogram slice view is a plot of relative intensity versus frequency at a particular point in time within a signal. A spectrogram slice represents a section through a spectrogram at a single time, but rotated 90° so that the frequency axis is horizontal. A spectrogram is built of a series of spectrogram slices stacked side by side (with their frequency axis running vertically). A spectrogram view shows a series of slices at successive points in time, and represents power at each frequency. There are several advantages in sound-based identification.

Molecular Tools in Biosystematics

Every species is characterized by its specific genomic organization. Recent developments in the field of genomics have suggested many marker tools not only for the identification but also to establish phylogenetic relationship among the organisms. All the organisms have conserved sequences in their nuclear as well as mitochondrial DNA. About 26 marker genes have been identified which are not only species-specific but also show excellent phylogenetic trends e.g., Cytochrome-b; Cytochrome Oxidase I; 12 s rDNA; 16 s rDNA; ND4; Rag, etc.

The technique for identification of these marker genes is based on isolation and characterization of DNA from a few cells, without killing the animals. The cells obtained from the surface of the body or from a drop of blood provide sufficient quantities of DNA copies of marker genes on application of PCR techniques. Partial or full gene sequences can be carried out using auto-sequencer. We have sequenced 12s rDNA, 16s rDNA and Histone H4 of herpetofaunal species of Thar Desert and Central Aravalli Foothills of Western parts of India without killing and disturbing the individuals. About 100 sequence of herpetofaunal species have been released by the Gene Bank (NCBI). Results of phylogenic study based on sequence analysis are often more convincing than the conventional methods which involve collection, fixation and preservation of large number of individuals. DNA bar code development for biosystematics study is also in progress.

INVERTEBRATE ALTERNATIVES FOR TOXICITY TESTING:

HYDRA STAKES ITS CLAIM

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An ever expanding range of chemicals used in every day life accumulate in the environment and pose potential threat to the quality of life, health and survival of various life forms including humans. These include pharmaceutical products and their metabolites, industrial effluents, farm run-offs, house-hold products and genetically modified biological products. Toxicity assessment measures the adverse effects of toxicants on living organisms quantitatively and qualitatively. These effects can be acute, noticeable within a short period of time, or chronic, with cumulative effects that manifest over longer periods. When these effects result in the death of the organism they are called lethal and when they only affect the normal activity or structures of the organism without killing, they are called sub-lethal. The extent of toxicity depends on many factors like the concentration of the toxicant, properties of the toxicant, exposure time and environmental conditions, and susceptibility of the model organism to the toxicant. Measuring the extent of toxicity can be done in *vivo or in vitro.*

Toxicity of chemicals needs to be tested for their safe use in humans as well as in animals as also for their potential to pollute the environment and cause health hazards. Toxicity testing includes evaluation and interpretation of the harmful effects of a substance by using model organisms and extrapolating the results to determine the dose that will produce similar effects in humans or other animals. A model organism is a living, non-human animal used for toxicity testing without causing harm to human beings during the process. Inexpensive, rapid and reproducible methods are preferred for toxicity testing. These often involve studies of whole animals, typically mammals like monkeys, rats, mice, dogs, rabbits, although other species, including humans, can be used.

The use of vertebrates to predict possible adverse effects to humans arising from chemical exposures is often challenged for scientific, ethical, and philosophic reasons. The ultimate goal of any animal welfare measure is the elimination of all experiments on animals that are likely to

cause pain or distress. As a step towards this goal, strategies are being developed to eliminate or at least reduce the number animals as much as possible. This, however, needs to be combined with maintenance of good standards of science. It involves reducing the number of animals used to obtain information of a given quality, refining the steps to decrease the severity of distress to test animals, and replacing the higher vertebrate models with non-sentient invertebrates as well as isolated cells and tissues.

Based on these principles, steps are designed to avoid unnecessary repetition of animal experiments, by using databases and bioinformatics tools including in *silico* simulation studies, cell lines, stem cells, organs and tissues. An alternative strategy is the use of evolutionarily simpler organisms with limited sentience. These include invertebrates like hydra, *Daphnia, Caenorhabditis elegens elegans* and *Drosophila.* Selection of a model organism for a particular study depends on similarity of its physiology to that of higher vertebrates, its sensitivity and tolerance towards the test chemicals, cost of maintenance, ease of handling, rate of reproduction, reproducibility of results, availability of test protocols and depth of information available.

Lower invertebrates are valuable models for environmental pollution studies. They are among the most widely distributed living organisms on earth. They have a relatively short life span, reproduce quickly at higher rates and are sensitive to pollutants. Invertebrate-based tests are cost-effective, reasonably quick and easy to perform with reproducible standard protocols. Many of these organisms can reproduce asexually producing a large number of clones. Wild specimens generally adapt quickly to laboratory conditions, making standardization easy.

Hydra, a Cnidarian, is a simple freshwater invertebrate with a cosmopolitan distribution. It usually resides in unpolluted fresh water. It has a simple cylindrical body with radial symmetry. It has a conical hypostome with mouth surrounded by a whorl of tentacles at the oral end and a basal disc at the aboral end which anchors the body to the substratum. Both body column and tentacles are highly contractile. Cnidarians are among the simplest animals to possess an organized nervous system, albeit as a simple nerve net. Body column is made up of just two layers of cells, outer ectoderm and inner gastroderm or endoderm, separated by an acellular mesoglea. This allows all its cells to be in constant contact with the aqueous environment, making it a sensitive environmental indicator. It has a tremendous ability of regeneration. Its simple body plan and transparent body, allows one to monitor changes in response to exposure to xenobiotics like pesticides, heavy metals and antibiotics.

Hydra is useful for establishing lethal and sub-lethal doses and effects of toxicants. It is widely used in small scale bioassays designed to study sub-lethal effects of test chemical which result in characteristic changes on the morphology of the animal. These include alteration in tentacle morphology, loss of tentacles, alteration of body length, irreversible contraction of body column, altered rate of budding, reduction or loss of regenerative capacity, induction/ inhibition of gonad formation under standardized condition, ability to attach to the substratum, in addition to mortality indicated by disintegration. Further, behavioural changes in hydra can be a sensitive test parameter and more predictive of toxicity level than more conventional lethality test. Feeding rates, i.e., the number of ingested prey per unit time are particularly important in regulating hydra population densities. The steps between capture of the prey and ingestion are called feeding reaction or response. Effects of toxicants on the feeding rates, contractility of the body, latent time between stimulation and contraction etc. can indicate their hazard potential.

Remarkable regenerative capacity of hydra is due to the presence of mitotically active multipotent stem cells in its gastric region in the ectodermal layer. These cells contribute to regenerate a new organism or lost body part. Presence of toxicants in the medium can affect or inhibit this process. Drugs and pharmaceuticals targeted at mammalian receptors have also been shown to adversely affect hydra, making it a good model to assess the potential toxicological effect of pharmaceuticals. Recently the whole genome sequence has become available in the public domain which will enlarge the scope of testing tremendously making this system more versatile.

While there is no doubt about the flexibility and adaptability of invertebrates as models for toxicity testing, one can not overlook the limitations of these models. Structural and functional simplicity of these organisms, while being their strength, also acts as their limitation. The complex metabolic and enzymatic processes and the delicate balance between different pathways in vertebrates cannot be matched or fully studied in these organisms since crucial steps in the vertebrate metabolic pathways are absent in these models. Experiments designed using these animals have to be necessarily simpler, which sometimes may have to be considered as simplistic. Therefore, while these models are very convenient and are very good alternatives in answering some questions regarding the toxicity of a range of chemicals, they cannot completely replace vertebrate models.

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TESTING TIMES IN TOXICOLOGY- IN VITRO VS. IN VIVO TESTING

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Scientists across the world have embarked on a pioneering and novel project, in the lines of the 'Human Genome Project', called the "Human Toxome" project with the idea of mapping the 'Pathways of Toxicity' (PoT) in man. PoT include pathways of endocrine disruption, perturbations of the hormonal system or other physiological disruptions which manifest themselves as adverse health effects, tumors, birth defects, developmental disorders, etc. The project "Human Toxome" will use integrated testing strategies that combine transcriptomics and metabolomics data with computational models with a view to create a public database of PoT, enabling full access to researchers around the world.

Global initiatives to move from our current reliance on high-dose animal toxicity studies to a wide range of new tools like functional genomics, proteomics, metabolomics, high data content screening, pharmacokinetic modeling and systems biology, to study the effects of chemicals on cells, tissues and organisms in a rapid and cost-efficient manner, is the sweeping change we observe in toxicology testing today. High-dose animal toxicity studies and the application of extrapolation procedures, with focus on signs of gross toxicity alone, renders a uncertainty when used in human health risk assessment, as observed by tragedies associated with new drugs / therapeutics and that hundreds of drugs that have been forced to be revoked from the market during the last few decades due to their adverse side effects in humans but were not manifested or predicted by animal studies.

Advances in molecular biology, biotechnology and other fields are also paving the way for major improvements that help scientists evaluate the health risks posed by potentially toxic chemicals found at low levels in the environment. This convergence of factors, coupled with the need to evaluate the safety of an increasingly large number of chemicals and their mixtures, has prompted a call for a fundamental and paradigm shift in toxicology testing. AXLR8 and SEN-

SI-TIV in the European Union, TOX21 and TOX-CAST initiatives by EPA, etc., are global initiatives that are looking to move to quick, robust and reliable non-animal methods in toxicology testing and prediction.

In this scenario we are seeing a sure and fast transition of toxicology testing from the 50 year old animal tests to *in vitro* methods, virtual tissues, robotic automation and beyond, where in mathematical modeling, structure activity relationships of chemical molecules and computational toxicology are being used to predict with precision and high throughput, animal tests used in toxicity testing are being pushed to a fading pale past. Time-consuming, expensive and, often, faulted to provide results of limited predictive value for human health, be it for industrial chemicals, pesticides, drugs or cosmetics, and reliance on animal testing has led to a backlog of more than 80,000 chemicals for which potential toxicity remains largely unknown.

The scientific understanding of how genes, proteins, and small molecules interact to form molecular pathways that maintain cell function has evolved rapidly, thanks to advances in molecular and computational tools. This knowledge gives non-animals methods an edge over *in vivo* testing, taking away that adjunct of variations that comes in animal testing due to the pain and distress that laboratory animals suffer during an experiment. This un-assessed and un-quantified variable of stress which interferes with physiological processes and disrupts critical pathway, interferes with the experimental design, results and observations and, thereby, the ultimate inference of the level of toxicity, underplaying or exaggerating the same. The absence of this variable in non-animal testing makes them more robust, adding high throughput, high precision and a better prediction potential. Reconstructed human tissues, 'neurons on microchips', 'organs- on-a-chip' and 'brains-in-a-test tube', and further moving on to computational toxicology and '-omics', have taken toxicology testing to greater heights in human risk assessment giving scientists the possibility to work with real-world human exposure levels.

Today in knowledge and convinced with evidence that alternatives to animal testing far excel in precision and prediction, brings us back to history and the eternal philosophy which says that the ultimate search for truth culminates in 'Non- violence'. At this juncture, as Indians we cannot but honor the Great Mahatma who said more than half a century ago, ***"I abhor vivisection with my whole soul. All the scientific discoveries stained with innocent blood I***

count as of no consequence". Every sage, saint and philosopher ha spoken about 'ahimsa' as the ultimate truth that goes beyond being not just a way of life but it has a bearing on every aspect of our lives, be it societal, environmental, educational or scientific research, a truth that goes beyond scientific reason and mathematical algorithms. The science of alternatives is to know that humane science is better science giving a three-fold advantage of being precise, predictive and pain-free. To quote the world-famous scientists William Russel and Rex Burch, ***'If we are to use a criterion for choosing experiments to perform, the criterion of humanity is the best we could possibly invent. The greatest scientific achievements have always been the most humane and the most aesthetically attractive, conveying that sense of beauty and elegance which is the essence of science at its most successful.'***

The paper discusses scientific and humane reasons to move on non-animal alternatives in toxicology testing and will elaborate on practical and state-of-the-art options in non- animal methods used in toxicology in basic biomedical science and regulatory testing.

Instead of focusing on signs of gross toxicity at high doses in living animals, an alternative '21st century' approach advocated by leading scientific and regulatory authorities is to work towards a mechanistic understanding of how chemicals interact with cellular response pathways in the human body at environmentally relevant exposure levels. As critical pathways are identified, human cell-based tests can be developed to study chemical interactions at key cellular and molecular targets within a pathway. Through robotic automation, cell-based *in vitro* methods can enable the high throughput testing of thousands of substances in a single day. Data from toxicity pathway assays could then be integrated and interpreted with the aid of systems biology tools controlling pathway function and be combined with pharmacokinetic modeling to relate *in vitro* conditions to real-world human exposure levels.

REDUCTION AND REFINEMENT ALTERNATIVES : WHERE, WHEN AND HOW

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Safety evaluation studies are regulatory requirements to fulfill risk assessment mandate. All most all new chemical, pharmaceutical and biotech products entering the market should be assessed for intrinsic toxicity by a battery of *in vivo* animal studies covering acute to chronic and special studies such as reproduction, neurotoxicity and others. Although extrapolation of animal data to man is not always possible and easy, these animal data could be used to avoid introduction of a potential toxic product. Over the past 20 years, a number of validated *in vitro* methods have been developed as potential replacement to *in vivo* regulatory toxicity studies. The in vitro genotoxicity studies - micronucleus, chromosomal aberration and mouse lymphoma (gene mutation) studies, coupled with the classical Ames bacterial assay, are the most well-established battery of mutation studies the results of which are widely used to draw conclusions on mutagenicity of a chemical/drug/impurity. New methods have totally avoided/replaced the painful and unethical *in vivo* studies in new chemical and drug development. The introduction of *in vitro* skin (OECD 431) and *in vitro* eye (OECD 438) do not require the use of rabbits in new product risk assessment for skin and eye. Reduction of animals has been successfully achieved for LD50 studies from the classical multiple treatments dose studies to up and down / limit dose investigations, in which only one sex animals of as low as 3 numbers are experimented. Further, the allergy skin sensitization study, which is based on evaluations in guinea pig, is now replaced with mouse lymph node assay (OECD 229).

The introduction of all these alternatives has reduced the use of animals by many folds in the drug and chemical development. In August 2011, OECD has officially accepted the extended one generation reproduction study protocol (OECD TG 443) in place of the existing 2 generation reproduction study design. This new one generation method will use only 1400 rats per study as compared to 2600 rats used in the existing 2 generation guidelines. OECD Expert Group concluded that with such reduction of animals, meaningful conclusions can still be drawn on the risk of

reproductive toxicity of the compound under investigation.

Although the exact *in vitro* alternatives for many *in vivo* animal studies may not be possible at this time, some of the replacements, alternatives and refinements discussed above must be continued in search of reduction of number of animals in other regulatory studies.

Indian regulators still demand in vivo skin irritation, eye irritation and guinea pig based allergy studies and 2 generation reproductive toxicity study reports on products as dossier. It is time that we abolish these studies and shift to the alternatives that are available and globally accepted. At least in case of me too registrants, repetition of such studies involving whole animal should be discouraged, and risk assessment should be made with the already available *in vivo* data. Mere repletion of some of these *in vivo* studies must be avoided or discouraged and a more logical approach must be taken. Registration guidelines must be modified to accommodate these practices. Now that India is a member of OECD GLP system (www.indianglp.nic.in), it is required that Indian regulators align their test guidelines to OECD guidelines and methods.

Some regulators do not accept test reports which are not GLP (Good Laboratory Practices) compliant. Therefore, they ask for repetition of studies which are not GLP. So, if all regulatory *in vivo* tox studies required are generated under GLP compliance, such test findings will be accepted across the world and thus avoid repetition of studies and hence reduce animal use. Since GLP ensures maintenance and experimentation of animals under humane and ethical environment, only GLP-based studies must be encouraged.

The Committee for the Purpose of Control and Supervision of Experimental Animals (CPCSEA) is a body operating under the Ministry of Environment and Forests of GOI and is responsible for the welfare of animals under experimentations in India. CPCSEA has been actively promoting the concept of 4 Rs and playing a critical role in the reduction of animals and promotion of *in vitro* methods in education, academia and regulatory testing in our country.

Recently, EPA has launched a program to evaluate 10,000 chemicals for potential toxicity by a program called ToxCast. Its goal is to reduce expensive animal studies and use novel technologies to predict toxicity by using stem cells and others.

Thus, research must be encouraged to help scientists to search more such alternatives with a goal to reduce the number of animals in regulatory studies and still make predictions of toxicity close to reality.

INTEGRATED DISCRETE MULTIPLE ORGAN CO-CULTURE (IDMOC) SYSTEM FOR THE EVALUATION OF XENOBIOTIC PROPERTIES IN VITRO

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A major advancement in the application of in vitro experimentation system is the development of primary cells or stem cell-derived cultures that retain differentiation properties representative of the major organs or origin. These systems can be applied readily to evaluate the effects of xenobiotics on specific organs. One major challenge, however, is the lack of multiple organ interactions which may be critical to the properties of a xenobiotic in the intact organism. Multiple organ or multiple cell type interactions include the following: 1. Metabolism: a xenobiotic and its metabolites may be metabolized by multiple organs and may have multiple organ effects. 2. Endocrine signaling: a xenobiotic may cause adverse effects due to its effects on an endocrine organ, leading to perturbation of the functions of the distal target organs of the endocrine signals. 3. Paracrine signaling: perturbation by a xenobiotic of paracrine signaling between two or more cell types. The IdMOC system is developed as an experimental model to allow evaluation of multiple cell-type/multiple organ interactions. The IdMOC (in 6-, 24- and 96-well formats) is based on a "wells-in a well concept", with multiple small wells inside a larger, containing well. It, therefore, allows co-culturing of multiple cell types as physically separated cells in the inner wells, followed by interconnection of the inner wells by an overlying medium, modeling an intact organism with multiple organs connected by the systemic circulation. IdMOC can be used to evaluate multiple organ xenobiotic effects including distribution, metabolism and toxicity as well as a basic research tool to study paracrine and endocrine signaling. Via the co-culturing of normal and cancer cells, IdMOC can be used as an in vitro "tumor-bearing man" for the discovery and development of anticancer agents.

Results from our laboratory have demonstrated the proof-of-concept of IdMOC. Evaluation of organ-specific toxicity with IdMOC is shown with multiple hepatotoxicants. For instance,

aflatoxin B1, a known hepatotoxicant and hepatocarcinogen, has been shown to be specifically cytotoxic to hepatocytes, and less cytotoxic to renal proximal tubule cells and pulmonary epithelial cells in IdMOC with the three cell types. Tamoxifen, an anti-breast cancer drug, is found to have selective cytotoxicity towards MCF-7 breast cancer cells and less cytotoxic towards co-cultured hepatocytes, renal proximal tubule cells, pulmonary cells, vascular endothelial cells and neuronal cells. IdMOC co-cultured with hepatocytes and renal proximal cells can metabolize P450 substrates (hepatic metabolism) and gamma-glutamyl transpeptidase substrates (renal metabolism). Additional applications of IdMOC to evaluate inflammation-induced multiple organ effects and pharmacological effects on multiple cell types will also be shown.

As a conclusion, IdMOC represents a new generation of in vitro experimental systems pushing forward the frontier of using in vitro systems to replace the use of whole animals in research. Via the use of human cells, IdMOC will allow the development of data to advance the understanding of the properties of xenobiotics in humans which may not be readily obtained from laboratory animals due to species differences in xenobiotic metabolism, pharmacological pathways, and mechanism for the manifestation of toxicity. Application of IdMOC to evaluate endocrine and paracrine signaling allows in vitro experimentations for investigations that are routinely performed in animals.

FROM ALTERNATIVE METHODS TO A NEW REGULATORY TOXICOLOGY

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The 3R concept to replace, reduce and refine animal experiments celebrated recently its 50th anniversary. In the meantime, a mechanistic toxicology has evolved which is effectively relying to a large extent on methodologies which substitute or complement traditional animal tests. The biotechnology and informatics revolution of the last decades has made such technologies broadly available and useful.

Regulatory toxicology has only slowly begun to embrace these new approaches. Major validation efforts, however, have delivered the evidence that new approaches do not lower safety standards and can be integrated into regulatory safety assessments.

Political pressures, especially in the EU, such as the REACH legislation and the 7th amendment to the cosmetic legislation, further prompt the need of new approaches. In the US, especially the NAS vision report for a toxicology in the 21st century and its most recent adaptation by EPA for their toxicity testing strategy have initiated a debate how to create a novel approach based on human cell cultures, lower species, high-throughput testing and modeling. A systematic mapping of the entirety of pathways of toxicity, the Human Toxome, has been started.

The lecture summarizes the lessons learned from the development, validation and acceptance of alternative methods for the creation of a new approach for regulatory toxicology. Beside the technical development of new approaches, a case is made that we need both conceptual steering and an objective assessment of current practices by evidence-based toxicology. It is suggested to apply an approach modeled on Evidence-Based Medicine (EBM), which over the last two decades has demonstrated that rigorous systematic reviews of current practices and meta-analyses of studies provide powerful tools to provide health care professionals and patients with the current best scientific evidence for diagnostic and treatment options. Similarly, a portal for high-quality reviews of toxicological approaches and tools for the quantitative meta-analyses of data promise to serve as door opener for a new regulatory toxicology. The Evidence-based Toxicology

Collaboration has been created in the US in 2011 and a European equivalent is in preparation.

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Biosketch

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In 1991 Dr. Hartung received a PhD in Biochemical Pharmacology from the University of Konstanz, Germany, and an MD in Toxicology in 1992 from the University of Tubingen. He completed his medical internship at the University of Freiburg in surgery at the hospital of Singen, Germany.

Dr. Hartung joined the faculty at University of Konstanz in 1994, where he served as an Assistant Professor of Biochemical Pharmacology until 1999, and then as an Associate Professor until 2002. He has been an honorary full professor of Pharmacology at Konstanz since 2003. From 1996 to 2002, Dr. Hartung also served as the CEO of the Steinbeis Technology Transfer Center for In Vitro Pharmacology and Toxicology (InPuT).

In 2002, Dr. Hartung became the Head of the European Centre for Alternative Methods (ECVAM) at the European Commission Joint Research Centre in Italy. He has authored more than 350 publications.

VALIDATION OF REPLACEMENT ALTERNATIVES: WHY AND HOW?

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Validation is a normal procedure in all fields of science, once a test is developed. It is intended to provide confidence into the results, to define where the test may or may not be applied and to give account of test characteristics such as precision, accuracy, specificity, sensitivity, robustness and transferability.

In the field of alternative methods, there has been a lot of focus on one particular aspect of validation: the comparison to animal data. In this sense, validation and the wordings "valid methods" and "validated methods" have been used in legal texts, such as the European chemical regulation REACH, the seventh amendment of the European cosmetics directive, and the new directive on the use and protection of experimental animals (2010/63EU). One of the consequences was the creation of a European validation agency in the field of toxicology, the European Center for Validation of Alternative Methods (ECVAM) in Ispra (Italy). Comprehensive validation is a prerequisite for the adoption of a new method into a legal frame work, such as the OECD test guidelines, or the European pharmacopoeia.

The field of cosmetics is a good example: replacement methods for some toxicological domains have been validated. These include phototoxicity, skin corrosion, skin irritation, eye corrosion, and eye irritation. Refinement/reduction methods are also available for acute oral toxicity (altered variants of the LD50 test) and skin sensitization (local lymph node assay). Many of these tests have been accepted by the OECD, and some have substituted the corresponding animal experiments to a large extent.

In 2013, animal testing has to stop in further toxicological domains according to current legislation. These domains include toxicokinetics, skin sensitization, repeated dose toxicity, carcinogenicity and reproductive toxicity. A recent report commissioned by the European Union

stated that sufficiently validated methods are not available in these domains yet. This opinion was confirmed by a large expert panel assembled by the centre for alternatives to animals in Europe (CAAT-Europe). Thus, test development and validation is ongoing with high pressure in these domains.

The validation process itself has evolved over time to allow higher throughput, flexibility and efficiency. For this, it is important to recall the main elements of an alternative method. Evidently, a test system is involved. This needs to be coupled with analysis endpoints and a data analysis procedure. Sometimes the third component is neglected: the prediction model relating the results of the method to predictions for human safety. A modular approach has been useful accelerate the validation procedure. First, the reliability of the test system needs to be validated. This includes testing of the descriptive assay parameters, at increasing levels of complexity, i.e., within a laboratory (different operators) and between different laboratories (transferability). In parallel, the mechanistic validity and scientific relevance can be evaluated. In a third line of validation, the predictive capacity is evaluated. Up to now, this has been done by correlation of the test results with the results of animal experiments. This process may yield information on applicability domains, e.g., only certain types of chemicals, but not others.

In particular, the last point has been criticised a lot. One of the arguments is that animal experiments may not be suitable as a gold standard, as they do not correlate good enough with human data. Another argument is that such a correlative process is not possible, when test batteries are used, that do not model a defined animal experiment. Therefore, new ideas have been voiced to overcome this problem. The most extreme approaches suggest to neglect the correlation aspects initially, and to focus instead much more on the first two domains of validation: high quality of the test system and high scientific relevance may provide by themselves a good predictivity for human safety. Such concepts are at present being tested and further developed with high speed.

Developmental neurotoxicity is an area that requires such new validation concepts, as not enough animal data are available. A recent review revealed that just over 100 compounds have been tested in studies using the OECD 426 draft guideline on developmental neurotoxicity. Most of these compounds were pesticides (66%) and only 8 industrial chemicals were included. Another review identified about 174 compounds for which neuro-behavioural risk assessment

had been performed, in many cases also on the offspring of the exposed animals (F1 generation). Only 1% of these compounds were industrial chemicals. Thus, the available data regarding the developmental neurotoxicity of industrial chemicals is rather limited. For some compounds developmental neurotoxicity is the most sensitive of all toxicity endpoints evaluated in a broad safety evaluation battery. Thus, although developmental neurotoxicity appears to be an important domain of safety evaluation, test capacity is limited and test costs are extremely high. This puts pressure on the development of faster and cheaper *in vitro* systems that can predict developmental neurotoxicity, give information comparable to behavioural readouts, and facilitate screening or at least prioritization of relevant drugs and chemicals for further testing. We envision that future *in vitro* test systems for developmental neurotoxicity will combine the above approaches with exposure information, and we suggest a strategy for test system development and cell-based risk assessment

We propose that the emerging knowledge from molecular and cellular neuroscience and mechanistic neurotoxicology can be exploited to design *in vitro* tests that read out cellular and molecular endpoints that are predictive of behavioural signs of neurotoxic exposures in humans. For acute or more chronic neurotoxic effects the onset of these effects is temporally associated with the onset of the chemical exposure and usually follows a dose-response relationship. However, the discipline of developmental/ neurodevelopmental toxicology faces an additional problem. It is difficult to provide evidence for cause-effect relationships for processes with a long lag time, and to identify suitable test systems for delayed effects. Research in this particular area is also motivated by increasing incidence of neurodevelopmental disorders such as autism, ADHD and schizophrenia and the growing awareness that environmental factors influence susceptibility and/or severity of these diseases.

Health risk of nanotechnology- Expanding the horizon of toxicity testing and need for more *in vitro* models

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The increasing interest in Nanotechnology has stimulated the researchers to scrutinize biological elements and learn from nature. However, little is known about the potential risks of the nanoscale, especially with nanoparticles, and the control of adverse effects is a high political priority in the world. The ability to generate three-dimensional (3D) *in vitro* living organs that can mimic organ and tissue structure and function is of benefit for a variety of biological applications from basic biology to drug discovery, and will have great impact on the future of science to use human organs and tissues not only as new therapeutic approaches but also as intelligent biological tools for many applications such as early detection of newly formed diseases, next generation of diagnostic tools, and an alternative energy source called "bio-energy" devices. Many 3D models currently in practice, however, require expensive equipment, large sample volumes, long incubation times and/or extensive expertise, and the most disadvantages of them is that they are too far from the nature of human organs. Because of the above problems, research and development on drug discovery, regenerative medicine, biotech and pharmaceutical Industries are very costly and takes several years to bring a single drug/product to the marketing. The goal of this research is to merge biomaterials science, nanotechnology, and biological principles to generate 3D *in vitro* living organs to mimic organ/tissues in order to partially reduce the amount of *in vitro* and *in vivo* animal testing, clinical trials, and to solve the above problems. We propose to do all above costly and timely tests in a rapid and cheap way. At the nanoscale, we play with the chemistry and materials to fabricate novel type of hydrogels that are similar to human organs, infusing the cell-laden hydrogels with extracellular matrix (ECM) molecules and gradients of signaling molecules to influence cell development and aggregation. At microscales, we employ fabrication technologies borrowed from the semiconductor industry, such as photolithography, to mass-produce identical building blocks in a variety of shapes and sizes. These products will have to mimic the physical, chemical, and biological properties of natural organ and tissues at

different scales, from molecules to cells to building blocks to organized clusters. Microscale technologies are potentially powerful tools for addressing some of the challenges in 3D *in vitro* models. MicroElectroMechanical Systems (MEMS), which are an extension of techniques used in the semiconductor and microelectronics industries, can be used to control features at length scales <1 μm to > 1 cm^3. In the past few years, microfabrication has been increasingly used in biomedical and biological applications. This is partially due to the emergence of techniques such as soft lithography to fabricate microscale devices without the use of expensive 'clean rooms' and photolithographic equipment. These techniques are compatible with cells and are now being integrated with biomaterials to facilitate fabrication of cell-material composites that can be used for biomedical engineering [1]. In addition, microscale technologies allow for an unprecedented ability to control the cellular microenvironment in culture and miniaturize assays for high-throughput applications. Initial experiments used micromachining technologies on silicon surfaces to generate vascularized systems. Subsequent work on the replica molding of biocompatible polymers such as poly(dimethylsiloxane) (PDMS) from patterned silicon wafers has resulted in the fabrication of biocompatible scaffolds. More recently, microfabricated capillary networks have been fabricated out of biodegradable elastomers such as poly($_{DL}$-lactide-*co*---glycolide) (PLGA), polyurethane, and poly(glycerol sebacate) (PGS). However, there are potential disadvantages with the use of these polymers which include its rigid mechanical properties and bulk degradation kinetics. Alternative methods of fabricating scaffolds with micro- and nanoscale resolution include 3D printing, microsyringe deposition, tissue spin casting and electrospinning of nanofibers. However, these approaches are difficult to perform and scale-up for fabrication of large 3D organs. A potentially powerful approach to engineering the microvasculature is to use cell-laden hydrogels. Recently it has been demonstrated that biomaterials made from hydrogels can be molded to fabricate microchannels. Although this technology has not yet been used for 3D living models, the ability of this approach to mimic organ and tissues is useful in engineering complex, vascularized organs. One of the main features of the proposed approach is that it will use microengineered cell-laden hydrogels for 3D *in vitro* living organs. These hydrogels mimic the natural tissues in that they provide a 3D environment for cells. To use hydrogels in various biological applications, it is desirable to control their mechanical properties which affect cell attachment, differentiation, viability, and proliferation. Therefore there is a need for generating hydrogels that can mimic the mechanical, biological and physical properties of native tissues.

However, despite significant progress many current approaches to fabricate hydrogels do not result in the synthesis of constructs with desired mechanical and chemical properties. Limitations with generating robust hydrogels that can withstand the *in vivo* environment include the need for low overall concentration of material, the requirement for degradation and the need for cytocompatibility. Our research aims to use Interpenetrating networks (IPNs) as a powerful method of modifying hydrogel properties. Furthermore, we will be able to tailor the mechanical, physical, chemical and biological properties of these hydrogels. Over the years much has been attempted in generating tissue engineered products. One strategy for engineering 3D engineered tissues is to cultivate cells within biodegradable scaffolds made from either natural or synthetic materials. A major challenge in 3D tissue engineering is that cells quickly lose their differentiated function. This is in contrast to the behaviors of cells in the body which have the capability to regenerate. Thus, it is desirable to formulate alternative approaches to more precisely control the organization of cells and vascularization of engineered tissues. Traditional 3D scaffolding approaches are not suitable for generating such complex structures due to lack of control of the tissue architecture and cell-cell interactions. In particular, cells in 2D culture as well as within traditional 3D scaffolds simply do not organize as they do in normal tissue; their metabolic properties are therefore unsuitable for tissue engineering applications. Our research plan aims to make an advance in 3D models by developing the basis for fabricating tissues made from cell-laden hydrogels with engineered microvasculature. Although engineering microscale features into tissue engineering scaffolds has been attempted before, in this proposal we will use a cell-laden hydrogel, which will eliminate the difficulties associated with other microfabricated tissue engineering scaffolds such as uniform cell-seeding. In the present seminar, I'll present our new technology on the fabrication new devices for clinical and biological application.

HOW TO OVERCOME THE BARRIERS OF MAINSTREAMING BIO ENERGY IN INDIA & OTHER RENEWABLE

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In our country, whenever we speak of Energy it is equated with Electricity. When we speak of Electricity it is understood as grid based electricity. Unfortunately, there is very little understanding of what Energy is all about and how we can meet our various Energy needs through various sources. A typical case in example would be, almost 40% of electrical energy being used for heating application. All our programs whether solar photo voltaic or solar thermal think of electricity generation and it would be criminal to use this electricity for heating applications with such low conversion efficiencies.

While a lot of estimates have been made on Bio mass potential, we have hardly made any attempt to critically look at various Bio mass harnessing technologies that have been developed and what barriers needs to be crossed for effective mainstreaming of Bio Energy. An integrated approach to Bio Energy planning is totally missing. The IPCC report suggests that the world has the potential to meet more than 70% of its total Energy needs from Bio mass by 2050 and even in the worst case it could be around 15%. If we have to get anywhere near the optimistic scenario of achieving the Energy mix of 70% coming from Bio mass, we need to urgently put our act together.

Current Bio mass estimates suggest that it can only meet very small percentage of our Energy needs today. Increasing Bio mass production means more pressure on land. A cursory look at our arable land and land use pattern, we see a whole lot of land that has been left barren or underutilized. Arguably, we have around 120 million Hectare of land classified as waste or marginal lands which in reality are wasted lands. Out of the nearly 160 million Hectare of agricultural land roughly about 25% have been brought under irrigation. The rest of the agricultural land is rain fed and only one crop in monsoon is raised. The land is left barren for at least 6-8 months in a year. A systematic identification of such land available across the nation, and a

massive program of planting perennial Energy crops on waste and marginal lands are to be taken up. Varieties of short gestation crops which can be grown in dry months with little or no external input, specific to different geo climatic zones of the country need to be promoted.

We have First generation technology quite well developed within the country for bio mass conversion into liquid fuels such as Ethanol and Bio Diesel. Several initiatives are in place to evolve second generation fuels through lingo cellulosic conversion of agricultural residues and forest bio mass as well as micro and macro algae for bio diesel. There is National policy in place and the use of bio fuels is mandated. We are fully aware of the multiple value addition possibilities in the entire biofuel value chain. We have excellent technologies working quite efficiently for Bio methanation and gasification processes. We seem to have miserably failed in large scale deployment of these technologies as our approach is totally faulted. A typical centralized corporate approach to Bio Energy has failed us completely. Renewable Energy in general and Bio Energy in particular is highly decentralised. We need to assess the type of Bio mass available or can be produced in a specific region and adopt appropriate conversion technology most suited for that bio mass and meet the local energy needs.

It is also very important that the Bio Energy program for its success has to be driven with the total involvement of the rural communities. The rural communities have to be recognized as an important stake holder and empowered. They should be totally involved in production of the bio mass, Bio mass conversion into Energy and his energy needs must be addressed first. A holistic approach to solving our energy needs through Bio mass will go a long way in greening our land mass, employment and income generation in rural areas which will considerably control the migration of masses from rural areas to urban areas.

Other renewable options such as cogeneration, wind, solar, mini and micro hydels etc needs to be given the due importance. We continue to lay emphasis on fossil fuel which are exhaustible and nuclear power which is highly uneconomical and fraught with danger. With little or no support the renewable energy in this country has started making significant contribution. Lot more needs to be done with regard conservation and increasing efficiency in generation, transmission, distribution and user applications.

All these and more can be achieved only if we are able to create a robust policy frame work, funding mechanism and put in place an effective and result oriented institutional mechanism. The present institutions such as MNRE and various state level renewable Energy development corporations despite their best efforts have failed to deliver.

Solar Thermal Energy for Industrial Process Heat: Status and Challenges

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Abstract

Solar energy is available widely and freely without any pollution. However, devices to catch it and convert it to usable form are costly. Further, conversion of solar energy to electricity involves loss of 70 to 85% of energy due to low efficiencies. On the other hand, solar energy can be utilized in the form of heat for domestic or industrial process heat application. Low temperature solar flat plate collectors delivering thermal energy or heat are commercially produced and are being widely used in India. They have made a small but encouraging impact on the Indian energy scene. These flat plate collectors normally can supply heat (in the form of hot water or air) up to a temperature less than 100°C. This limits their application in industrial thermal processes, where the temperatures required are often above 100°C. Though rigorous data are not available, a conservative estimate based on the analysis of industrial process data suggests that about 90% of the total industrial thermal process energy is being utilized at temperatures above 100^0C, and about 35% is in the range of 100°C and 300°C.

Concentrating solar collector systems, which can deliver 50 to 200 kWth power at temperatures above 120^0C, can potentially replace up to 20 to 35% of the liquid fossil fuels like diesel, LDO or furnace oil or electrical power being used in the industry. This is about 5 to 10% of the total industrial thermal process energy is being utilized in India. Further, the energy pay-back period is typically 15 to 18 months and economic pay-back period is 40 to 50 months.

Four generic types of concentrating solar collector systems can be used for thermal applications at medium or high temperatures.

1. Line focusing parabolic systems, also called as parabolic trough collector (PTC) systems
2. Line focusing Linear Fresnel Reflector (LFR) systems
3. Central receiver systems with heliostats, and

4. Point focus paraboloid systems

These solar concentrating collector technologies can be compared on the basis of their efficiencies at different operating temperatures. The efficiency of paraboloid dish collector with point focus is 20 to 25% higher than that of line focus systems at absorber temperature of around 200 to 300^0C.

Internationally, work on solar concentrators is mainly focused on the application for solar thermal power generation. Extensive work is carried out on Parabolic Troughs, Paraboloid dish, LFR and CLFR along with a variety of designs. However the efforts are grossly lacking in the IPH sector. No serious mention is cited in the literature regarding field installation, testing and operation of Solar IPH except some efforts in southern Europe recently. Of course, for completeness, the effort of Dept of Energy, US of installing and testing solar collectors for 50 industrial applications in 1980's need mention. However, it is disheartening that the effort was cautiously aborted for the want of long term goals. Presently a few European and US companies are trying to enter Solar IPH sector in India with well designed concentrators. However, they face entry barriers in term of integration challenges and reliable long term operational support.

Work on commercially available comparatively large solar concentrators started in India in around 1997 when Mr. Wolfgang Scheffler started work in development of flexible reflector paraboloid dish of 7 sq.m reflector area with two axes of freedom and one axis automatic tracking with fixed focus on ground. This was a land-mark effort in India and was taken ahead commercially by Mr. Deepak Gadhia to a long way in community cooking. At the same time, in April 1997, Dr. Shireesh Kedare, with support from his team of ex-IITian friends, started work on Fresnel paraboloid reflector. A 10 sq.m reflector area was successfully built and tested in May 1998. The effort of developing the solar concentrator by Dr. Kedare was taken ahead by Clique Devlopments Ltd., an engineering (EPC) company, from year 2000.

The focus on solar industrial process heat (SIPH) came in the last decade in India. ARUN160, a Fresnel paraboloid concentrator having 169 sq.m aperture area with cavity receiver at its focus was designed, installed, commissioned and field tested in years 2004-2007 by Clique Developments Ltd at Mahanand Dairy, Latur with support from Ministry of New and Renewable Energy, Government of India in collaboration with IIT Bombay. Industrial quality thermal

integration system was also installed with energy efficient thermal storage for delivery to the stringent process heat requirement for milk pasteurization within ±0.5 °C temperature band in add-on mode with existing furnace–oil fired boiler. the performance of the concentrating dish was tested and characterized in field based on the optical and thermal performance testing procedure developed by at IIT Bombay.

Instigated by the issues of integration exposed during this project, a work on optimization of integration components, mainly solar collector area and storage volume for different load conditions has been developed at Department of Energy Science and Engineering, IIT Bombay. A Design-Space approach for system optimization has been applied to the problem of solar thermal integration with IPH and has been validated at two sites.

Further to this, Clique has carried out IBR certification to qualify ARUN160 as first IBR-approved industrial solar boiler. The Scheffler community cooker being manufactured by 5 to 7 different agencies in India has been taken to industrial process heat applications, but without any major landmark installation. Efforts by Prof. Ajay Chandak, Dhule and Prof. Milind Rane of Mech Engg Dept, IIT Bombay have helped the developments in this area. The entry of Thermax Ltd. in the field of SIPH using Scheffler system gave a boost and brought in the competitive spirit in the sector. Dr. Srinivas Reddy, faculty in Mechanical Engineering dept of IIT Madras also started work on concentrators.

However, the efforts seem to be subcritical as yet and need organized technical professionalism in design and execution, more so in thermal integration of solar concentrators for industrial process heat. Optimization need for the concentrator design within the specific technologies and across the technologies for minimum cost to energy performance is not yet addressed. The more challenging is the work on thermal integration and its optimization for variety of IPH applications. Finally, there is a need to create awareness about technical feasibility and economic viability of using solar energy for medium temperature industrial process heating and cooling. It is as far the best way for utilizing solar energy and saving liquid fossil fuels, which is the most important target today.

BIOGAS ENERGY MADE ACCESSIBLE AND EMPOWERING

Keystone Technology Approach

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Biogas technology, although over a hundred years old in India, has yet eluded reaching all homes in India, especially rural India where the required feedstock and need for them exist. Much of the earlier biogas plants have focused on animal wastes as the only source and as a result only a few designs and certain focused niches have been reached. India generates about 50, 200 and 500 million tons of mixed urban solid wastes (USW), cattle dung and usable rural residues (URR, dry basis), respectively, having a tremendous potential for biogas generation and providing clean biogas energy to everyone in rural /peri-urban India. Only, cattle dung plants have been disseminated in a big way and the other two feedstocks have remained poorly addressed. Developing anaerobic digesters and valorization technologies for urban and rural residues that are appropriate and acceptable to the Indian context has been difficult because these residues are difficult to ferment in modified animal dung digester designs unless they are well segregated, pulverized and rendered into a flowable aqueous slurry and used in typical animal waste digesters (with few exceptions). On the one side the rapidly dwindling biomass resources in rural areas has put in immense pressure to develop alternatives to the inefficient an unhealthy traditional woodstoves in rural areas. Also there has been a gradually reducing use of cattle in agriculture and a consequent reducing access to cattle dung. There has been an urgent need to examine non-dung based biogas plants. Second, the traditional biogas plants, although more relevant now than in the past, has constantly been considered to be uneconomic and less attractive in a non-level playing field inundated by fossil fuels. The challenge is thus to develop new generation multi-feed biogas plants, overcoming conventional understanding of cost benefit and also to make it economically and commercially viable. Critical is to evolve new fermentation processes that suit typical fermentation and physical properties of agro-residues and weed biomass. At a second level of complexity is enabling such fermenters to be capable of accepting a wide variety and rapid fluctuations between dry and green feedstocks as found season-wise in the field. Only a few of the new fermentation processes have addressed this issue of unfavourable physico-

chemical and fermentation properties and even fewer have addressed how to make the digesters become more attractive and viable to rural users, economically speaking. For a long time, because of the subsidized costing of fossil fuels especially LPG, biogas plants were 'considered' expensive and could never become economic in its lifetime. However, as LPG prices are being rationalized, biogas is fast becoming, in cost-benefit terms, economic. However, at this stage, the expectations of sustainable technology practitioners have also increased. Effort is underway to improve the stake in biogas technology to make it not merely a clean fuel but ***available, accessible, acceptable*** and finally ***attractive.*** The cost-economics of the biogas plant has always been considered merely as a mechanism wherein the investment is paid back in an acceptable period of time. It is time to look beyond this to make biogas plant use not merely economic but also positively attractive and ensuring that they lead to attractive rural livelihoods.

It is clear that meeting everyone's primary energy needs through biogas, especially development needs that include clean cooking fuel and for energy services such as home illumination and drinking water supply for all rural homes requires that we use all the animal dung in the country as well as alternative feedstocks - rural biomass residues such as non-woody soft biomass from crop residues and agricultural weeds. Conventional biogas plant technologists attempt to generate two key products namely digested residue and biogas. Biomass fed biogas plants can produce three outputs namely biogas, digested solid residue and surplus digester liquid. When these outputs, after meeting the primary need of cooking and compost, the surpluses can be converted to over 15 value added products. These increase daily cash returns from the biogas plant making the plant only to pay back investment but also become a means for daily livelihoods. Once technologies for a battery of these byproducts are evolved and field demonstrated, it is expected that it will be a matter of time before such plants not merely extend a clean energy technology, it would become available, accessible, acceptable and most importantly attractive (and sustainable) to rural users.

A case study of using a 3-zone plug flow fermenter that converts 60-98% rural residues to gas and multiple byproducts is discussed. When run as decentralized units, they have low-C footprint, recycle or reuse a large extent of secondary residues and can create many local enterprises. The anaerobically digested residue of herbaceous biomass feedstock has high moisture holding capacity, is usable by secondary colonizers that could use either the bacterial carcass or

residual lignocellulose, filtered digester liquid could be used for its high nutrient content or for exploiting unusual properties of the organics in the digester liquid. The gas in addition to its use for cooking could be converted to pico-level power for household uses, for disinfestation of stored agro-produce, a low cost source of CO2 or automotive gaseous fuel substituting CNG. When, fibrous materials such as banana (plantparts), linseed, pine apple leaves, etc. are fermented individually, the fermentation process can be tweaked to yield, in addition to biogas and compost valuable fiber that could be the basis of a chain of livelihoods starting from fabric, paper, upholstery and biofilms. In this paper the conversion of biogas outputs to a variety of byproducts (pico-power, mushroom, vermicompost, fiber, pest repellant, disinfestant, inoculant carrier, methanogenic biofilms etc.) are discussed. Household level production of such byproducts leads to potential micro-enterprises that firstly strengthen grassroot development and make them environmentally, socially and economically sustainable. Such plants can not only provide clean energy but also a variety of livelihood generating products. A veritable keystone technology - that anchors over 15 livelihood products, micro-enterprises taking biomass biogas plants beyond merely clean energy that is available but to higher levels of being accessible, acceptability and attractive to users.

RENEWABLE ENERGY FOR ENERGY AVAILABILITY AND AFFORDABILITY

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Role of science

One of the key roles of science is to improve peoples' lives and help mitigate problems arising in the path of development. In the energy sector this role is becoming critical. Past developments, based on fossil fuels have lead to three major problems that need urgent solution. First, a large section of world population lack access to clean and affordable energy sources. This population, usually comprising of the poorest of sections, end up paying heavily for the basic energy services. Second, the energy resources fuelling economic growth are dwindling rapidly. Predictions of global oil production soon reaching a peak and then decreasing, are gathering increasing momentum. Even the coal resources, that are more abundant than oil, are getting more difficult to mine, partly responsible for increasing coal prices. The only silver lining on this front is the recent finds of potentially large quantity of shale gas across different countries, thought the environmental impacts of their exploitation are yet to be known. If impacts are low, it can act as a transition fuel. As discussed later, the resource limitation is acute for India. Third, problem relates to climate change primarily caused by burning of fossil fuels. It has reached such a proportion that unless major course correction is done in the coming decade, human activity may threaten the very stability of earth's climate - which is foundation of all life. Another problem relating to environmental effects of energy use; is the local air, water and soil pollution and competition for limited water and land resources.

Context of Indian Energy system

Extreme inequity in the access to affordable and clean energy sources in India needs more attention than given. If Indian population without electricity access was to form a separate nation, it would be the third most populated nation in the world. Over 70% of Indian households (~160 Million) have to rely on highly polluting and inefficient biomass cook stoves, causing serious indoor pollution. (Venkatraman et al, 2010) estimates that 5.7 lakh Indians (mainly women) die prematurely of cooking related pollution every single year. The problem of limited fossil resources

is already acute in India. We import about 80% of oil and now about 15% of coal requirement. It is estimated that for continuing a GDP growth of 8% or more, by 2032 our energy demand would increase by 300% or more. The energy import dependence is slated to increase steeply due to limited domestic resources and social and local environmental problems associated with mining of resources. India has limited responsibility for the third problem, that of climate change. It has contributed only 2.5% in the historical (1850-2007) build up of CO2 emissions, despite supporting over 15% of the global population. But the limited remaining C-space would require India to limit its fossil fuel use.

The conventional energy resources that produce low or no GHG emissions include nuclear and large hydro power, both of which would play a limited role in the coming decades. Hydro, due to it limited potential and large socio-environmental impacts, and nuclear due to its high cost, risks and excessive time for construction. Even with determined support by the government, the share of nuclear electricity capacity is destined to remain about 2% even by 2020. An important resource that needs to be aggressively tapped is of improved efficiency of energy use. In most cases, the energy use can be reduced by 40 or even 50% for doing a specified activity. In the coming decade, the efficiency gain in electricity can yield a benefit larger than the expected combined benefit from hydro-power, nuclear and natural gas. Even the much reduced energy demand is unlikely to be met fully by conventional fossil fuels.

Role of Renewable Energy and Role of Policy

The science and technology, supported by appropriate Policy, should help solve these energy problems. The role of renewable energy is large on this back-drop.

The costs of renewable energy from wind, solar and biomass are steadily dropping and reliability of equipment improving. The wind power costs are now comparable to gas power; bio-ethanol (from land rich countries like Brazil) is cheaper than oil. Even thought solar power is yet expensive with a cost of about four times the coal based power, it is economical for niche applications. Within next five to seven years, solar technology is expected to improve substantially and costs to drop. The Photo Voltaic panels on urban building are expected to deliver power at a price lower than the electricity supplied by the electricity companies to commercial /industrial consumers. Once this happens, we will potentially see an effortless expansion of solar power.

But today, even in the niche applications, where renewable energy is already economical; its adoption is slow. This needs to be remedied by policy, and doing so will help improve the energy access to the full population. For example, cost of renewable energy systems is less than the cost of providing grid power for lighting in the remote villages where grid has not reached, or has reached but does not supply power at the evening peak time, when it is most needed. This gap is primarily due to failure of market and problems created by policy. Extension of Grid as well as power supply is subsidized for the rural consumers, by large pool of all consumers connected to the grid, but not so for the distributed renewable energy sources. The existing subsidies are only from government budget and are aimed to compensating the high installation cost of renewable energy systems. The lack of incentive for maintaining the services from these systems - while the benefits are expected to accrue over several years in future is creating a mismatch. This is limiting the adoption of RE systems mainly to cases where the direct beneficiaries (usually the very poor consumers) can pay the full cost of system without a major dependence on subsidy. Here the policy should find ways for spreading the cost to all consumers, and link financial support for the operators of renewable energy systems to maintaining delivery of promised service in the future years. This requires cutting down the multitude of non-transparent capacity based subsidies and moving towards performance based incentives while linking incentive delivery to a system for monitoring of benefits. Fortunately, technology has now made this possible. Even for small systems of five to ten KW, it is possible to collect real-time data and make on-line payment of subsidy. The concept of performance based subsidy should also be attempted for improved cook stoves or solar heating systems. Such policy will encourage small entrepreneurs to install and run renewable energy systems in rural areas and small industries.

As a supporting policy, renewable energy entrepreneurs and consumers wanting to install such systems should get easy access to low interest loans. Usually the poor consumers and small entrepreneurs end-up having to pay excessive interest rates. Cutting down transaction costs will result in immediate acceleration of deployment of small RE systems.

This brings us to third component of required policy. We are heading towards a hybrid energy system which will contain a mix of (a) fossil fuel and renewable energy and (b) centralised and de-centralised supply. The system design should encourage cordial coexistence and complementarity between these components having fundamentally different nature and strengths.

For example, the distributed micro-grids supported by renewable energy should seamlessly interact with the main electric grid - either to export or draw power as per the gap between its generation and local demand. This applies to all small systems - biomass based power or roof-top PV systems. Designing technical specifications and incentives appropriately will help us leap-frog into the renewable based future.

The fourth and the major requirement for increased energy self reliance is the technology. The envisaged shift to increased renewable energy can limit fuel imports. But if we continue to import the renewable energy equipment we will not achieve energy security. Last three years have been a water-shed, as the global investments in renewable energy exceeded the investments in expanding fossil energy systems [Global Trends in Renewable Energy Investment 2011, UNEP]. The balance is fast tilting towards renewable energy. In the coming years, we should explore the potential for exporting renewable equipment and in thus target to leap-frog. To achieve this, we need to boost renewable energy R&D aimed at cost reduction, increased reliability, and usability of renewable energy systems. Special technology hubs, increased academia-business linkages, and financial support for R&D are essential components for this. Cost reduction of simple devices such as solar water heaters, solar dish heaters can have immediate benefits of reduced oil use in industries and morning peak of power systems. Where as, innovations in the field of PV materials, battery and bio-fuel technology will have a mid-term but far reaching impacts.

The future will also require a lot of soft research. Working out ways to integrate wind, distributed solar with existing coal, gas and hydro power and using smart meters, smart appliances to balance loads with generation. Developing and main-streaming the low or zero energy building to ensure that there are no incentives for constructing or buying inefficient premises. Early evaluation of desirable urban layout with public transport system, combination of electric cars with renewable based power system can help us optimise our systems as we are building them.

Creating employment is a major policy priority for India; we should explore how to convert it into our asset. Using the employment guarantee scheme to promote biomass based energy systems can help promote renewable energy at an affordable price while offering meaningful and continued work. If we can promote biomass based construction materials as replacement for steel and cement, we can convert biomass into high value materials, and then pay higher prices

for biomass. Such an approach will have multiple benefits - employment, value addition in rural economy, and reduced energy intensity.

The last aspect I want to highlight relates to apportioning of costs of shift to renewable future. While the cost of RE is high, we need to carefully analyse who is expected to pay for this. Equity and fairness in this will enhance public acceptance and accelerate the shift. For example, realising that the limited availability / usability of low cost fossil fuels is the fundamental concern, fairness demands that there be a fair allocation of this limited resource. This can then be translated into several policy options. The inefficient malls, office building or factories, consuming more energy than can be justified based on efficient norms can be mandated to install renewable energy for the incremental consumption that is over and above the norm. To avoid high up-front investment of solar panels, all new commercial complexes will be well-designed, avoiding a massive waste of energy. Similarly, farmers and poor household consumers should not pay for cost of promoting renewable energy. This can be achieved by linking renewable energy target for to expected tariff impacts on consumers. Another route to achieve this is to introduce a uniform cess on all affording consumers in the country. Such policies can bypass the geographical constraint of renewable resource while achieving a fair distribution of the extra costs.

In summary, appropriate policy and regulatory interventions that take into consideration the national objectives and the Indian reality can enable rapid scale up of implementation. Small scale distributed RE can go a long way in providing immediate access to electricity and large scale RE can help mitigate emissions and add to energy security in the medium term.

THE NEED FOR AND, THE POTENTIAL OF BIOFUELS FOR SUSTAINABLE RURAL DEVELOPMENT IN INDIA.

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1. Motivation: The need for biofuels.

Energy is the most sought after commodity today as everything, including food production and transportation depends entirely on the availability of this resource. With the alarming decrease in fossil fuel sources and the ever increasing demand, several alternatives have been suggested. We look at why biofuels are the most promising candidates for India!

2. Problem statement: Roadblocks to achieve sustainable rural development.

India has about two thirds of her population in the rural areas. For most, agriculture is the main stay. According to estimates by Professor M S Swaminathan, about 100 million families are involved in agriculture. Most of these families practice subsistence agriculture; i.e. grow one monsoon crop and wait for the next monsoon to come. A survey in a small cluster of villages in a semi arid area indicates that the monsoon crop absorbs about 16% of the potentially available wage days. In other words about 200 million able-bodied wage workers are practically unemployed for most of the year. Agriculture however, seems to already produce enough food, for them to survive, in most of the years. No country can ever hope to progress with such a large number of idle workers. On the other hand it is not a simple matter to add 200 million jobs in the rural areas considering that education levels are pitiful and savings, and the related capital formation levels, have been even worse in all the decades after independence. No country in the world is up to the task and certainly none of them have the requisite capital resources.

3. Approach: Looking for a way out of the difficulties.

Nevertheless India should develop; develop she must, to ensure a reasonable, productive life to all her citizens. Conventional economic and development theories depend on capital, raw

materials, value-addition and products for consumption. Since such a route is unthinkable because of the enormity of the numbers involved, India should think differently. Looking at non-monetary capital, and the ways and means by which the rural workers can use it, could be a possible alternative. Is there enough of such capital that can be used in the villages? Interestingly, we have it in India in the form of land resources.

India has one of the largest parcels of arable land amongst all the countries in the world. While most of it is currently used for subsistence agriculture during the monsoons, only a small part of it is irrigated so that more than one crop is possible. Besides this, a comparable area of marginally-used and waste land is also available. There is no dearth of water as the overall precipitation, averaged over the entire sub-continent, is about 1000 mm. If properly managed with already known technologies, the water availability can support year round photosynthesis over the entire land area and therefore crop production. In exact contrast to this unique opportunity, unique because nowhere else in the world is there as large a piece of land blessed with adequate precipitation and year round sunshine, the crop intensity factor in India is about 1.1 i.e. in only about 10% of the land, more than one crop grown. Why is there such a reluctance to use the land year round?

The hesitation to further increase farm output comes from the current levels of demand. The practice of mostly single cropping already produces nearly 250 million tons of food grains, 150 million tons of fruits and vegetables and 350 million tons of sugarcane annually. Even in farm based secondary production, India is the largest producer of milk and, with respect to meat or poultry products etc, either the largest producer or at least one of the large producers. Thus the requirements of the Indian population are already met in some sense and she has one sixth the population of the whole world! Many of these farm products cannot be easily exported to other countries because of the policies many of them follow, supposedly based on their food security issues.

Thus the Indian farmer has no option to increase the farm output without further jeopardizing the already fragile economics of production. Many alternatives have been attempted in the past like growing medicinal herbs and plants, growing of timber, bamboo, fuel wood and pulpwood species etc. but collectively all of them could never absorb the excessive potential that exists to any significant level. Under the circumstances, there appears to be a desperate need for a candidate

crop, more if possible, which can be grown in most places in the country and whose produce can be consumed in quantities comparable to food grains.

4. Results: Bio fuel could be the savior.

Pervading discussions on peak oil, global warming and the impending energy crises also suggest that growing of oil seed crops, seasonals, annuals and tree based perennials, could be an answer both for mopping up the excess capacity in arable lands and to take advantage of marginal, unused and barren waste lands. The currently used 130 million tons of crude and 350 million tons of coal can generate demands for comparable quantities of oilseeds, quantities that can easily be produced in farm lands. It is well known that vegetable oils are good substitutes for petro diesels and could also be processed into other fuels to meet the requirements for petro derived fuels for transport. Residues and byproducts from production, seed cake, plant residues etc are also good calorie sources and could be alternatives to coal.

India has, within the country, more than 400 oil seed bearing species and there is therefore no need for propagating monoculture. The attendant carbon sequestration and spread of green cover reduce effects of global warming. Growing of oil seed crops and plantations will absorb the existing skills and presently available potential wage days in the rural areas increasing labor utilization to significant levels. Critical dependence on import of petro fuels can be minimized improving energy security issues. Since most of the infrastructure for processing and use of petro fuels and coal already exists along with the additional capacity to grow in farm lands, the capital required, to create new infrastructure, is neither phenomenal nor is it beyond the capacity of the exchequer

5. Conclusions: The most promising renewable alternative energy.

Thus there exists an opportunity to gain advantage from the unutilized labor in the rural areas at nearly their current skill levels and grow oil seed crops using the excess capacity of the farm lands,existing marginal lands and waste lands. More than contributing towards mitigating global warming and alleviating energy security issues, the main benefit will be to gainfully employ people in the rural areas. It will not be news if along with energy self-sufficiency, the rural income more than doubles and India gets catapulted to a higher GDP bracket!

BIO-ETHANOL FROM AGRI-RESIDUES/WASTES - A VIABLE OPTION

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Ethanol has been in use as a substitute to petrol (gasoline) in some countries for over four decades now thanks to some bold initiatives taken by Brazil in 1970`s. Brazil produces most of its ethanol by direct fermentation of sugarcane juice followed by distillation. With kind of resources enjoyed by Brazil in terms of land area and water, this seemed to be a perfect solution to the demands of the transportation sector there. However, if we consider things on global perspective, this kind of utilization of land and water will result in "food versus fuel" debate sooner than later.

India has been one of the few countries producing potable alcohol from molasses for several decades. Last ten years has seen some of these distilleries producing ethanol for transportation purposes. However, there is a limit to the quantity of alcohol one can produce in the country from the molasses route for two reasons. One is that availability of molasses is rather limited, being a by-product of sugar industry. In addition, several other industries such as cattle-feed industry, IMFL industry and some chemical industries require molasses as raw materials. Other disadvantages of ethanol from molasses are that sugarcane as a crop and distillation as a process are highly water-intensive; distillation is also a heavy polluter of soil & ground water.

Therefore there seems to be considerable merit in looking at biomass as a raw material for ethanol production especially by the enzymatic route. Some of the obvious advantages of this way of producing bio-ethanol are:

- Agri-residues/wastes which are normally left in the fields to decay and have no other traditional use except for burning can be usefully utilized for production of a transport fuel
- Being mostly enzymatic processes, they are more environmental friendly and energy efficient
- Till recently such methods were perceived to be expensive (unfortunately most costing methods do not take the environmental costs of existing processes); but this is now changing because of extensive research that have been carried out all over the world

The process of manufacturing ethanol consists of pre-treatment of agri-mass, enzymatic or

chemical degradation into sugars, microbial fermentation into alcohol and finally distillation into power ethanol. For reasons of environment & energy, the enzymatic degradation of agri-bio-mass is preferred over chemical processes. This also implies that for each raw material, processes have to be standardized before commercialization. This poses major challenges before R&D community.

The agri-wastes/residues could comprise sugars & starches that are generally not considered edible (a recent study by the author in coastal districts of Karnataka indicated abundant availability of cashew apples, colocasia tubers, jackfruit seeds and coffee pulp etc) which can be ground, subjected to amylase treatment to reduce to sugars & lower saccharides and then fermented using yeast cultures. Another class of raw materials are celluloses, hemi-celluloses and lignocelluloses whose pretreatment & reduction into lower saccharides is somewhat more complicated. Some of the examples of this are crop residues of major cereal crops like paddy, wheat etc.; coconut husk, shells & leaf fronds; arecanut shells & leaf fronds; bagasse & sugarcane shoots; jackfruit skin & other residues. It is obvious that in a country like India, there will be several such promising raw materials that can be tapped.

While India with its own set of concerns would be better off with trying to utilize agri-wastes/residues, developed nations that do not have pressures of food availability are looking at commercial production of raw materials by trying out several agri & marine based raw materials in addition to utilization of agri-residues. They also have the advantage of large and organized farm sector where collection of raw materials can be managed much better and more economically.

There have been persistent R&D efforts in India to improve the efficiencies of enzymatic degradation of starchy & cellulosic raw materials and to improve fermentation efficiencies. As a result, some researchers are already claiming that their cost of production of ethanol from cellulosic sources (on a lab-scale) is now comparable to costs of production from molasses. There are now academia-industry collaborations that are trying out such processes & their economies at a pilot/ industrial scale.

There are similar efforts in several parts of the globe in academic circles. More importantly, the industry in the west seems convinced of the promise of this technology. Several MNC`s lead by companies like Novozymes have been investing heavily in this process development. In fact,

some of the claims made by Novozymes suggest that their processes are already cost-effective in several parts of the world.

In other words, bioethanol from agri-mass holds promise of a major contribution to the efforts to solve the global energy crisis in an environmental-friendly way. In the main presentation, some important statistics regarding present role being played by ethanol in the transportation sector, global ethanol production, raw material availability for production of cellulosic ethanol etc will be presented. Socio-economic impact of this concept on developing nations heavily dependent upon agriculture will also be discussed. Some of the costings presented by researchers/ companies in recent months will also be made known to give an overall perspective of this important process.

NOTCH SIGNALING AND CANCER STEM CELLS

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Cancer stem cells have the ability to give rise to various cell types within a tumor. They are highly tumorigenic and cause relapse and metastasis. The Notch signaling pathway is dysregulated in many cancers, and is believed to control stem cell proliferation. The notch receptor is a unique transmembrane receptor protein. It is composed of a extracellular domain that associates with a smaller piece of the notch protein composed of a short extracellular region, a single transmembrane domain, and a small intracellular domain. When a ligand such as Jagged or Delta that present on a neighboring cell interacts with the Notch receptor, two sequential proteolytic cleavage events occur. The first occurs at the cell surface catalyzed by an ADAM-family metalloprotease called TACE (Tumor Necrosis Factor Alpha Converting Enzyme). Then, a second enzyme complex, ?-secretase cleaves the notch protein just inside the cell membrane releasing the intracellular domain (NICD). The ?-secretase complex is composed at least four individual proteins: presenilin (catalytic subunit), nicastrin, APH-1 (anterior pharynx-defective 1), and PEN-2 (presenilin enhancer 2). Upon release from the membrane, NICD moves to the nucleus, where it can regulate gene expression by activating the transcription factor CSL. Our group is focused on identifying natural and synthetic small molecule inhibitors of Notch signaling pathway. My talk will include studies with honokiol and its effects on colon cancer stem cells. Honokiol is a biphenolic compound present in the cones, bark, and leaves of Magnolia grandifloris. We tested the combination of honokiol with radiation. Treatment with resulted in a dose dependent reduction in colon cancer cell proliferation and colony formation. Furthermore, it inhibited Notch activation, resulting in the reduction of downstream target genes Hes-1 and Hey-1. There was also a reduction in the expression of Notch ligand Jagged-1 and the ?-secretase complex proteins Presenilin-1 and Nicastrin. Moreover, there was a significant reduction in stem cells. Taken together, these data suggest that the combination of honokiol and radiation is a potent inhibitor of colon cancer stem cells by suppressing the Notch-1 signaling pathway.

THERAPEUTIC OPTIONS FOR BLADDER CANCER:

APOTENTIAL ROLE FOR CANCER STEM CELLS

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Urinary bladder cancer is the seventh most common malignancy and the second most common genitourinary cancer in men throughout the world with a distinct difference in type and mortality rates between developed and developing countries. In developed countries including North America, Europe, and Australia bladder cancer is highly prevalent being the fourth most prevalent cancer in males and the ninth most prevalent cancer in females **(1).**While transitional cell carcinomais the most commonly diagnosed histological form of bladder cancer in western countries, in parts of the developing and under-developed countries squamous cell carcinoma is the most commonly diagnosed form. Bladder cancer incidence increases with age, presumably reflecting cumulative exposure to carcinogens and increasing life expectancy.The uroepithelium is physiologically distinct from other tissues; composed of at least three layers; a basal cell layer attached to the basement membrane, an intermediate layer and a superficial layer composed of hexagonal cells connected by tight junctions that ensure reduced permeability of the cells to small molecules **(2-7).** Basal cells of the urothelium are thought to the precursors of other cell types with one of the slowest turnover rates of any mammalian cell **(4).** The initiation of urothelial proliferation is believed to involve up-regulated growth factors such as fibroblast growth factor (FGF) and nerve growth factor (NGF) **(8-9).** Loss of heterozygosity at chromosome 9, deletions of 8p, 11p and gains of 1q and 17q are considered to be the most common early events in bladder carcinogenesis and correspond clinically to non-invasive bladder cancer **(10-11).** On the other hand progression of non-invasive tumors to muscle invasive disease is associated with a wide spectrum of genetic alterations including the inactivation of p53 and Rb1 **(12-13)**.

Approximately 75 percent of bladder cancer patients have non-invasive tumors at clinical

presentation with about 80 percent of these tumors having recurred within twenty years. Thus patients require frequent and repeated surveillance cystoscopy and often multiple resections for disease management. The need to monitor and treat bladder cancer patients on a long-term basis has made bladder cancer the costliest (on the basis of per person) cancer to treat. It is estimated that clinical management of bladder cancer has a price tag of approximately $4 billion in the US **(14).** Up to 45% of non-invasive bladder cancer ultimately progresses to invasive disease and this is accompanied with striking decrease in survival. Recent analyses of SEER data shows that the relative five-year survival rate decreases from 88% in stage I to about 15% in stage IV disease **(15).** Metastatic bladder cancer has a five-year survival rate of 6% for which combination chemotherapy is the primary treatment modality. Current diagnosis and treatment modalities for bladder cancer are extremely limited and although newer compounds have reduced toxicity, median survival time still remains at twelve to twenty months.

Intravesical immunotherapy, using an attenuated Bacillus Calmette-Guerin (BCG) strains and intravesical chemotherapy are the modalities most commonly used to decrease disease recurrence rates. Although these agents significantly reduce relapse rates, multiple repeated instillations are needed and application is limited in many patients due to local side effects. Furthermore, even with complete treatment, disease recurrence remains high and patients still require long-term intense surveillance with bladder cystoscopy. These facts point to the need for additional therapeutic options for this disease.Standard treatment regimens for muscle-invasive bladder cancer that has penetrated through the muscle wall and metastasized into other organs include radiation and or chemotherapy followed by radical cystectomy all of which have debilitating effects in addition to toxicity. Indeed quality of life is immensely affected for those patients who progress to muscle-invasive bladder cancer and require surgical removal of their bladder. Therefore there has been a great need for other agents that can provide the therapeutic benefit with minimal toxicity and impact on quality of life.

Work from our laboratory has led to the identification of capsaicin as a potential anti-bladder cancer agent. Capsaicin is the active compound derived from chili peppers of the genus Capsicum. Data from our laboratory and those of others show that capsaicin induces apoptosis through the disruption of mechanisms that operate through the mitochondria **(16-18).** We have

also found that capsaicin deregulates expression of several miRNAs including miR138 which leads to inhibition of telomerase activity in bladder cancer cells. Given the recurrent nature of transitional cell carcinoma of the bladder, the involvement of cancer stem cells in this cancer type cannot be ignored. Urothelial cancer stem cells have been found in advanced bladder cancer specimens and appear to have many properties of normal urothelial stem cells **(19-20).** It has become evident that therapeutic efficacy may be reliant on the effect of the drug on cancer stem cells. In this regard weare examining the effect of capsaicin on urothelial cancer stem cells. Intravesical instillation of capsaicin has been utilized in the treatment of hypersensitive bladder disorders and for patients with bladder pain or detrusor hyperreflexia. Results from these studies indicate that intravesical capsaicin may be safe and tolerated at doses up to 1-2mmol/L **(21-22).** Therefore capsaicin holds great promise as an agent for treatment of bladder cancer.

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INHIBITING WNT/NOTCH SIGNALING IN BREAST CANCER: EFFECT ON CANCER STEM CELL PROLIFERATION, METASTASIS AND ANGIOGENESIS

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INTRODUCTION:

Activation of Hedgehog (Hh), Wnt and Notch, often results in induction of epithelial-to-mesenchymal transition (EMT) in cancer stem cells (CSCs) which leads to cells with a mobile, invasive phenotype. CSCs and the EMT process are currently being investigated for the role they play in driving metastatic tumor formation in breast cancer. Data accumulated in recent years have shown that oncogenic deregulation of canonical (Wnt/?-catenin), non-canonical (?-catenin-independent) Wnt pathway and Notch signaling leads to tumorigenesis and promotes invasiveness and metastasis in cancer stem cells. The major effectors of Wnt signaling includes the genes and transcription factors involved in cell proliferation, survival, angiogenesis and most importantly regulators of epithelial mesenchymal transition (EMT). In our study, we have intended to explore the effect of psoralidin, a bioactive compound derived from herbal plant, *Psoralea corylifolia* on canonical Wnt signaling and its phenotypic effects in breast cancer cells.

METHODS: To determine the effect of Psorlaidin on BCa cells, estrogen-receptor positive (ER+)-MCF-7 and estrogen-receptor negative (ER-)-MDA 231 cells were treated with psoralidin and the cell viability, apoptotic, cell cycle, Western blot and Promoter assays were performed. To determine cytotoxicity of psoralidin on normal breast epithelial cells, we used MCF-10A cells. To test the in vivo efficacy, female athymic mice inoculated with MDA-MB-231 xenograft were treated with 50 mg Psoralidin/kg body weight by orally and tumor inhibition studies were performed.

RESULTS: Our results revealed significant decrease in the expression of Wnt-3a at protein level in MCF-7/MDA-231 breast cancer cells treated with psoralidin. In addition to this, we found that psoralidin inhibits the expression of β-catenin and angiogenic proteins, although increase in the E-cadherin expression levels was observed, suggesting that psoralidin regulates

Wnt mediated EMT in breast cancer cells. Further, we have checked the effect of psoralidin on Notch-1 signaling and interestingly, the results revealed significant decrease in the expression levels of Notch-1 in MDA-231/MCF-7 breast cancer cells. Confirming these results, cell migration assays showed inhibition of cell migration and metastasis in psoralidin treated MDA-231 cells. Augmenting these results, treating MDA-231/MCF-7 breast cancer cells with psoralidin also resulted in growth inhibition, without significant cytotoxicity to the normal breast epithelial cells (MCF-10A). Presently, we are analyzing breast cancer stem cell markers CD44, DCLK1 and CD133 and determine their role in Pso-mediated anticancer effect in breast cancer cells. we are extending these studies in xenograft breast cancer models to check the *in vivo* efficacy of this herbal compound in animal models.

CONCLUSIONS: Pertinent to the fact that, Wnt and Notch-1 signaling is involved in proliferation of breast cancer stem cell activation and tumorigenesis, crippling these pathways using the multi-targeting effect of psoralidin based treatment modalities with least side effects will be of immense importance in paving way towards prevention and cure of breast cancer.

CANCER STEM CELLS: NOVEL TARGET FOR PANCREATIC CANCER

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Pancreatic cancer is the fourth leading cause of mortality in the United States and no significant treatment is currently available. Although an increasing number of therapeutic options exist for patients with advanced disease, their efficacy is time limited and non-curative. Presently approximately close to 60% of cancer patients in the United States are believed to utilize therapies derived from plants, herbs, flowers, or nutrients either exclusively or concurrently with traditional chemotherapy or radiation therapy. A growing body of evidence suggests that cancer stem cells (CSCs) within a solid tumor including in pancreatic cancers, initiate and sustain tumor growth. Furthermore, they are quiescent and are therefore not responsive to therapeutic intervention by common anti-cancer drugs. Targeting signaling pathways that regulate pancreatic CSCs could lead to novel targets for drug intervention. Expressions of putative markers in pancreatic CSCs such as CD44, CD24, Doublecortin Calmodulin like kinases-1 (DCLK-1), epithelial cell adhesion molecule (EpCAM) and aldehyde dehydrogenase (ALDH-1) demonstrated highly tumorigenic potential and possessed ability to both self-renew and to produce differential prodigy that reflected the heterogeneity of patients primary tumor.

Recent studies showed that hedgehog (Hh) is a secreted protein involved in regulating self-renewal of normal and malignant stem cells by utilizing both in vitro and mouse model systems. Hedgehog-Gli signaling has also been shown to control the self-renewal behavior of CSCs and tumorigenicity. Hedgehog signals through binding to its transmembrane receptor Patched (Ptch). In the absence of hedgehog ligands (Sonic Hedgehog, Desert Hedgehog and Indian Hedgehog), Ptch associates with Smoothened (Smo) and blocks Smo function. When hedgehog binds to Ptch, Smo is released, triggering dissociation of transcription factors, Gli1, Gli2 and Gli3 from Fused (Fu) and suppressor of Fused (SuFu), leading to transcription of an array of genes, such as cyclin D, cyclin E, Myc and elements of EGF pathway. Dietary compounds have been shown to interfere in cancer stem cell related to hedgehog pathways and therefore offer a promising approach for prevention of pancreatic cancer.

The role of the cancer stem cell marker, CD166, in maintaining the stem cell niche

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The existence of intestinal stem cells residing in an interactive niche has been well-accepted as the source of continual self-renewal of the intestinal epithelium in both the small intestine and colon1,2. The intestinal stem cell was first described through label-retaining studies, suggesting that it resides at the +4 position in the crypt1. It was subsequently shown that the stem cell gives rise to multiple epithelial lineages (enterocytes, goblet, enteroendocrine and Paneth cells)3,4. The exact number of active stem cells populating each crypt is disputed, but originally speculated to be around 4-61,5. To define this stem cell population, efforts were made by laser capture microdissection to isolate crypt-based cells and profile their genome6. From this study one interesting marker, Doublecortin and CaM

Interestingly, CD166 or Activated Leukocyte Cell Adhesion Molecule (ALCAM) expression is pathologically correlated with aggressive disease in a variety of cancers including melanoma, prostate, breast, ovarian, esophageal, and bladder cancers kinase-like-1 (Dcamkl1), displayed an intriguing stem cell expression pattern7. Further, two independent studies, one surveying all Wnt target genes within the intestinal crypt8, and the other examining an important gene in neural, hematopoietic and leukemic cells9, identified two additional molecules with intriguing stem cell-like patterns, Lgr5 (Leucine-rich repeat-containing G-protein coupled receptor-5)10 and B lymphoma Mo-MLV insertion region 1 (Bmi1)9. Interestingly, when both of these loci were examined in a promoter-reporter context, the reporter gene was expressed in all intestinal epithelial lineages, lending support that these cells represented the intestinal stem cell populations. However, most intriguingly, Lgr5- and Bmi1-expressing crypt cells do not have overlapping expression domains: Lgr5-expressing cells are nestled in the base of the crypt between Paneth cells and are Wnt signaling pathway responsive, while Bmi1-expressing cells reside at position +4 within the crypt, and endogenously, at least seem to function in a Wnt independent function. Intriguingly, we have identified novel and discrete expression of a cell adhesion molecule, CD166 within the base of the intestinal crypt.

11-17. In human colorectal cancer, aberrant cell surface CD166 expression is strongly correlated with a 15 month shortened survival18. Further, isolation of CD166/CD44 or CD166/ESA double-positive cells from human colorectal cancer cells can recapitulate tumorigenesis when xenografted at low numbers into immune-deficient mice19, a hallmark of a cancer initiating population. Although these findings suggest that CD166 may have a role in the progression of colorectal cancer, little is known about its endogenous function and cellular localization within the intestine.

In other organ systems, CD166 has a myriad of functions. This conserved cell adhesion protein participates in physiologic processes including leukocyte intravasation across the blood brain barrier, monocyte migration across endothelial junctions, angiogenesis, capillary formation, protection against apoptosis in breast cancer cells, and T-cell activation by both antigen presenting and tumor cells20-26. Further, CD166 has been described as a ligand that binds to CD6 on thymic epithelium27-29, acting in homophilic adhesion complexes between epithelial cells30, and as a cell surface marker for both a subset of hematopoietic progenitor cells31,32 and multipotent mesenchymal stem cells 33,34. Based upon the intriguing CD166 expression pattern in multiple stem cell populations, this molecule has a potential role in maintaining stem cells in both normal and disease states.

Correlation of the CD166 expression pattern with aggressive disease has led to efforts for targeting this molecule as a cancer therapeutic. Treatment of cancer cells with a CD166-internalizing antibody conjugated to chemotherapy filled lipid vesicles was shown to effectively target and kill CD166-expressing ovarian cancer cells and prostate cancer cells in vitro35,36. While early results from these types of targeted cancer therapies appear promising, it necessitates an even more careful understanding of the endogenous expression pattern and function of CD166. We have recently analyzed CD166 expression in normal human and mouse intestine and identified enriched cell surface CD166 expression in the colon and small intestine crypt-base. Interestingly in the small intestine, CD166 is expressed on the cell surface of the differentiated Paneth cell population and the intervening crypt-based columnar cells. Notably, normal CD166 expression patterns were conserved in mice, highlighting the value of using a mouse model for studying CD166 function within the stem cell niche. Further, we show that a subset of CD166-ex-

pressing cells residing in the stem cell niche co-express other putative stem cell markers, including Musashi-1 (Msi-1), Dcamkl-1 and Lgr510, 37-38. We propose that CD166 defines the normal intestinal stem cell niche and encompasses both differentiated Paneth cells as well as stem cell and progenitor populations. A possible function for CD166 may be to maintain the epithelial microenvironment of the stem cell niche. Therefore, targeting this cell surface antigen in cancer therapy requires careful consideration of potential effects on normal tissues.

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SKIN CANCER PREVENTION BY α -SANTALOL

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In United States, skin cancers are most frequently diagnosed in Caucasians accounting for over 1.3 million cases each year. The major causative factor for skin cancer is UV radiations from sunlight. It has been proposed that the use of sunscreens alone are not sufficient to prevent skin cancer, thus there is a need for more effective waysX to prevent this malignancy. In this approach, chemoprevention of skin cancer by natural compounds has gained importance in recent years. More than 1000 phytochemicals have shown chemopreventive effects against various cancers. Effects of sandalwood oil and its major constituent ?-santalol were investigated for the chemoprevention of skin cancer.

α

Emulsion, paste, or essential oil of sandalwood (Santalum Album Linn) has been used for centuries in India for the treatment of inflammatory and eruptive skin diseases. The essential oil of sandalwood is distilled from the small chips and billets cut out of the heart wood of sandalwood. The oil is extremely viscid, of a light yellow color and possesses a characteristic pleasant odor. The major constituent of oil is - santalol. Sandalwood oil treatment significantly ($P<0.05$) decreased papilloma incidence and multiplicity in dimethylbenzanthracene (DMBA)-initiated and tetradecanoylphorbol acetate (TPA)-promoted skin cancer development in CD-1 mice. Sandalwood oil treatment also significantly ($P<0.05$) decreased TPA-induced ornithine decarboxylase (ODC) activity. Our laboratory has isolated ?-santalol from sandalwood oil and characterized it by NMR and GC-MS. ?-Santalol topical treatment during promotion phase significantly ($P < 0.05$) decreased the papilloma incidence and multiplicity in DMBA-initiated and TPA promoted skin cancer development in both CD-1 and SENCAR strains of mice.

-Santalol treatment also resulted in a significant ($P < 0.05$) inhibition in TPA-induced

ODC activity and incorporation of 3H-thymidine in DNA in the epidermis of both strains of mice.

Pre-treatment with ?-santalol one hour prior to UVB exposure significantly ($P < 0.05$) reduced tumor incidence and multiplicity, and resulted in a significant ($P < 0.05$) increase in apoptotic proteins, caspase-3 and -8 levels and tumor suppressor protein p53. These results suggest that -santalol prevented skin cancer development by inducing proapoptotic proteins via an extrinsic pathway and increasing p53.

Treatment of human epidermoid carcinoma A431 cells with -santalol resulted in a concentration- and a time- dependent cell growth inhibition and cell death. FACS analysis of Annexin V/PI stained cells revealed that -santalol induced a strong apoptosis as early as three hours post-treatment, which increased further in a concentration- and a time-dependent manner up to 12 hours. Mechanistic studies showed an involvement of caspase-3 activation and PARP cleavage through activation of upstream caspase-8 and -9. - Santalol resulted inhibition of cell growth via induction of G2/M phase arrest in both A431 cells and melanoma UACC-62 cells by altering multiple cell cycle regulatory proteins and complexes. Taken together, this study demonstrated that the induction of apoptosis and arrest of cell cycle by -santalol may be the mechanism of its overall cancer preventive efficacy in mouse skin cancer models. Sandalwood oil and -santalol has pleasant fragrance and a great potential for the skin cancer prevention.

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Tissue Banking in Regenerative Medicine

Raj Manda

Abstract

Regenerative medicine has made rapid strides in the last three to four decades both in terms of procedures and products. Disease and trauma often result in extensive tissue damage that the innate regenerative mechanisms cannot adequately restore. The options available to the surgeons include autograft – patient's own tissue excised from a healthy part of the body and transplanted at the site of deficiency, allograft – donated human cadaveric tissue processed and distributed by tissue banks, xenograft – tissue of a different species, synthetic tissue substitutes, and metal products. All these options have their own unique advantages and disadvantages. Autograft has long been considered the gold standard because it does not carry the risk of disease transmission; however, the second surgical site morbidity can be significant. Allografts are easily available in required quantity and get incorporated into the recipient's tissues. The perception of the risk of disease transmission is the main limiting factor in allografts gaining universal acceptance. Synthetic tissue substitutes and metal products have zero risk of disease transmission, but do not get integrated into the host tissue.

United States is the global leader in the tissue banking industry, with some of the European countries making up a very distant second tier. Tissue banking has evolved in the recent years into a multibillion dollar industry in the United States. Much of this growth can be attributed to the advances in tissue cleansing, processing, and preservation technology and increasing oversight of the industry by regulatory agencies such as American Association of Tissue Banks and Food Drug Administration both of which make the tissue grafts safe, as well as to the increasing understanding at molecular level of the tissue regeneration science. Currently, there are more than 100 AATB accredited tissue banks in the United States.

Tissues recovered from a consenting donor include bone, skin, tendons, heart valves, blood vessels, fascia, cartilage, pericardium, peripheral nerves etc. Bone constitutes close to 70% of the processed tissue and is used in the surgical specialties of spine, orthopedics, trauma,

implant dentistry etc. The evolutionary stages in Bone regeneration using allograft in the past 50 years include using whole bone, demineralized bone, pure recombinant bone morphogenetic proteins and stem cells. Applications of the different types of allografts in the different surgical specialties, current trends involving recombinant growth factors and stem cells and issues associated with these trends will be discussed.

ECOLOGICAL SUSTAINABILITY FOR A GREEN FUTURE

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Ecological sustainability has been defined in many ways, but the most frequently quoted definition is from Our Common Future, also known as the Brundtland Report: "Sustainable development is development that meets the needs of the present without compromising the ability of future generations to meet their own needs".

In order to realize this definition, we need to think that our human community is an element of the Earth, not the other way around. All human endeavors are situated within the dynamics of the biosphere. If we wish to have sustainable institutions and enterprises, they must fit well with the processes of the Earth. Unfortunately, the ideology of industrialism, in both capitalist and communist countries, insisted that modern society lives on top of nature and could rightly use and despoil the rest of the natural world as we desire. This is because that we thought any loss of the ecosystems is merely an "externality" in economic perspective and because any problem can be addressed later by a technological fix. The result is that we are now living through the painful consequences of this arrogant and ignorant perspective. Many of our children are suffering from accumulations of mercury and other toxins in their neurological systems; environmentally related cancer is on the rise; and our air and water are increasingly polluted. Meanwhile, we are trying to compromise our ecosystems by the increasing presence of genetically engineered organisms.

In this talk, we will take look into the Ecologically Sustainable development, which requires that we see the world as a system - a system that connects space; and a system that connects time. When you think of the world as a system over space, you grow to understand that air pollution from North America affects air quality in Asia, and that pesticides sprayed in Argentina could harm fish stocks off the coast of Australia. And when we think of the world as a system over time, we start to realize that the decisions our grandparents made about how to farm the land

continue to affect agricultural practice even today; and the economic policies we endorse today will have an impact on urban poverty when our children become adults. We also understand that quality of life is a system, too. It's good to be physically healthy, but what if someone is poor and don't have access to education? It's good to have a secure income, but what if the air in some parts of the world is unclean? And it's good to have freedom of religious expression, but what if one can't feed his own family? The concept of sustainable development is rooted in this sort of systems' thinking. It helps us understand ourselves and our very own world. The problems we face are complex and serious, and obviously we can't address them in the same way we created them. But we can definitely address them if we start thinking and begin practicing in some other way.

We will discuss how the Ecologically Sustainable development is trying to explore the alternatives that now exist and that could be encouraged. It is focused in extending the greening of waste management by encouraging the spread of such practices as reduce, return, reuse, and recycle. The health of the life-support systems - the ecosystems on our continent - is of paramount importance. Inherent in the efficient dynamics of those ecosystems is a vital profusion of biodiversity. We will see that the sustainability demands that we humans have a moral responsibility to all of our biologically diverse relations, many of which are facing extinction because we carelessly and permanently halt their long evolutionary journey. It also supports the spread of organic agriculture and the careful tending of our nation's precious remaining topsoil. Limitations of greenhouse emissions, conservation of energy, increase in the use of clean renewable energy (e.g. solar / hydro / wind), reduction of nuclear wastage are some of the most important aspects of this ecologically sustainable development. Finally we will take an in-depth look into two case-studies regarding ecological sustainability of two major modern industries (1) Auto Mobile Industry (2) Electronics Industry.

GREEN COMMUNICATIONS: ISSUES AND RESEARCH DIRECTIONS

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The steady rise of energy cost and the need to reduce global CO2 emission to protect our environment are today's major economical and ecological drivers behind the objective of energy optimization. The European Union has acted as a leader in energy saving across the world and targeted a 20 percent greenhouse gas reduction. China's government has also promised to reduce the energy per unit of gross domestic product (GDP) by 20 percent and major pollution by 10 percent by 2020. Like all other scientific fields, investigation and studies in IT, communications and computer science are also gradually focusing on this emerging research area. Triggered by network operators, experiencing energy cost as a significant new factor of their calculation, researchers have started to investigate approaches for reducing power consumption. Naturally, manufacturers have also started offering energy-efficient network components. Standards bodies, such as the IEEE, are already ratifying standards for these energy-efficient protocols. However, research and development in these areas are still at an early stage and the space of potential solutions is far from being explored.

The prime objective of this presentation (talk) is to bring together the academic and industrial leaders for discussing energy-efficient communications. We can notice particular potential for reducing energy consumption in mobile and wireless access networks, broadband access networks, and home networks. For example, broadband to the home is introducing the additional issue of power consumption in the home. The European Commission is estimating that by 2012 the energy consumption in the home for broadband fruition will reach 50 TWh, from basically 0 TWh in the year 2000. Of the 10% (electricity consumption) globally spent for ICT, already today 70% are spent in homes / offices and only 30% in the network / server farms. This means that energy consumed by the homes will be twice as large as the one consumed by networks to bring broadband into the homes. The operators may contribute to stem the increase of power

consumption in the home by an intelligent control of residential energy from the network.

Data rates in wired and wireless networks are driven by "Moore's Law" and are thus rising by a factor of roughly 10 every 5 years. The price paid for this enormous growth is a doubling of the power consumption in cellular networks infrastructure (i.e. base stations and core network) every 4-5 years. This has already reached to 60 TWh (billion kWh) in 2007. The radio access network accounts for 80% of this energy consumption. In developing countries, like India, operators now spent more than half of their Operating Expenditure (OPEX) only for the diesel required to keep base station generators up and running. Increasing the energy efficiency of base stations has thus become a key challenge of mobile networks operators of India and other countries of the world. Hence, it becomes urgent for mobile operators to maintain sustainable (environment friendly) growth and, at the same time, limit its own electric bill. For instance, Vodafone Group has announced to reduce its CO2 emissions by 50% from its 2006-2007 baselines of 1.23 milliontons by 2020.

This talk will also highlight different dynamic energy management mechanisms, green radios and trade offs for cellular networks to understand quantitatively the scope for potential energy savings, and also the technical challenges that arise in implementing these mechanisms, particularly to ensure that energy efficiency does not come at the expense of reduced quality of service for mobile customers.

Self-coexistence Issues in Cognitive Radio Networks: A Game Theoretic Approach

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With the recent proliferation of spectrum-dependent operations such as cellular communication,public safety, military tactical networks, wireless LANs etc., the wireless industry isexperiencing a fast paradigm shift from static spectrum allocation to opportunistic dynamic spectrum access (DSA) and cognitive radio (CR) network based on DSA has become one of the prime foci in wireless networking.

While other aspects of cognitive radio networks have received significant attention in the recent time, the issues of self-coexistence in the cognitive radio networks is still in its nascence.

The opportunistic and network-aware real-time DSA nature of the system introduces entirely new classes of threats and challenges in this paradigm. As networks do not have information about which bands other DSA networks will choose, the self-coexistence game is played under incomplete information and becomes even more challenging. Therefore, efficient dynamic channel access among these networks is of utmost importance and must be energy-aware so that the interference among DSA networks can be minimized; else the throughput, quality of service (QoS) and system longevity will be compromised.

To make the matter worse, presence of malicious agents can make the cognitive radio network and DSA process highly vulnerable to various *denial-of-service (DoS) threats* in the hostile network environment. Unfortunately, due to the unique DSA-based communication paradigm, the traditional techniques fail to incorporate the emerging self-coexistence issues in the CR networks.

In this research, we borrow techniques from game theory to capture the conflict of interest among CR networks. We identify the key vulnerabilities in CR networks along with potential mitigation approaches. We explain how situations of this kind can be modeled by making use of game theory and present a game-theoretic framework that can be used to guide the self-coexistence process of cognitive radio networks in the presence of unintentional and intentional disruptions.

CO_2 SEQUESTRATION, CARBON TRADING AND WOMEN EMPOWERMENT FOR SUSTAINABLE ENERGY FUTURE

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'Climate mitigation and adaptation strategies must be developed with women,

not for them, and women must be involved alongside men in every stage

of climate and development policy-making.'

--Mary Robinson Foundation in 2010

Global warming and climate change are providing new threats to our energy security and sustainability. The above quote may be true for the women in developed countries, but those in developing countries are still grappling to think about it. Energy security is of prime concern of every citizen of the globe, man or women. It is determined by energy availability for meeting the basic needs in transportation, building, industrial and agriculture activities. Fossil fuels continue to dominate the world energy scene and are currently meeting 82% of the global energy needs. They are also the reason for increasing CO2 and other greenhouse gas pollution. The average atmospheric concentration of CO2 present in the atmosphere as a trace gas in preindustrial era was 280 ppmv. In 1958 the observed concentration was 315 ppmv, which suggested an increase of about 0.5 ppmv per year in the initial half of the 20th century. In 2005 the measured concentration of CO2 was 374 ppmv, suggesting an increase of about 1 ppmv per year in the latter part of the 20th century. As the greenhouse gas emissions are increasing, their concentrations in the atmosphere are rising, resulting in global warming. According to IPCC 2007 mean rise in global temperature has been recorded as 0.74oC from 1905 to 2006.

India has a unique energy portfolio of primary energy supply and consumption pattern. Current energy situation in India is dominated by the use of coal in power generation as well as in industrial production. The total electricity installed capacity has reached approximately 170

giga watts (GW) in 2010. Fossil fuels continue to dominate and the projected growth in the use of fossil fuels in 2031-32 (the installed capacity approaching 800 GW - Integrated Energy Policy of India 2006) indicated coal dependence could be almost 50 per cent of it. For energy sustainability, the CO2 sequestration (carbon capture and storage - CCS) is an emerging technology option for capturing excess CO2 from air and fixing it permanently away from the atmosphere. The CO2 sequestration is having a technology focus, currently in research & development phase. A few demonstration projects have been launched internationally.

At the same time, new market based international collaborations are appearing on the scene through Carbon Trading as a tool for reducing global carbon emissions. An outcome of Kyoto Protocol (put forward in 3rd Conference of Parties) under United Nations Framework Convention on Climate Change (UNFCCC), carbon trading is relevant to both developed and developing countries. The schemes like emission trading (ET) and clean development mechanism (CDM) have become operational as mandated and voluntary mechanisms. New carbon trading mechanisms are being suggested. The 9th meeting of Conference of Parties adapted land use and land use change and forestry (LULUCF) as loss of forests may contribute up to 20 per cent of the total emissions. Another carbon trading mechanism is Reducing Emissions from Deforestation and Degradation (REDD) proposed in the Bali meeting of 13th COP in 2007 as a means of CO2 sequestration through 'avoided deforestation'. The REDD is seen as an instrument for women empowerment and making them responsible for developing strategies for adaptation and mitigation of climate change.

In this paper we start with global warming as an effect of accumulation of greenhouse gases in the atmosphere. Limiting the carbon dioxide (CO2) emissions from energy sector has become one of the most daunting global challenges of 21st Century. India's current energy status and government's policy initiatives under national action plan on climate change are described. We then give a brief account of CO2 sequestration technologies and strategies for sustainable development. The usefulness of CO2 sequestration approaches for sustaining coal based energy generation is also discussed. With more than 60 per cent of the Indian population depending on agriculture or forests, the significance of carbon trading mechanisms in these sectors is deliberated. Inclusion of new methodologies within REDD framework, role of women and future directions in mitigation options for a sustainable energy future are presented.

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'ENHANCED RURAL LIVELIHOOD THROUGH LIVESTOCK HEALTH MANAGEMENT'

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India is endowed with huge and diverse livestock breeds that significantly contribute to 23% of the national agricultural GDP. Livestock sector receives only about 2.5% of the public expenditure, which is much less than the contributions made by small ruminants alone to the total value of output of the livestock sector. This sector will play a significant role in the coming decade in impacting the livelihoods security and as an insurance cover to cope with crop failures particularly for rural landless, small and marginal farmers.

Livestock sector is a major provider of animal proteins for human consumption in India. Per capita consumption of meat presently is only 5.4 kg/year compared to 33kg/year in the developed countries. Current availability of animal proteins (10.8gms/day/capita) is just half of the daily requirement of (20 gm/day /capita - targeted to achieve by the year 2020.

The rural poor communities prefer rearing sheep, goats, pigs and backyard poultry over dairy cattle and buffaloe keeping because of low investments, easy to raise and manage funds, low feed requirement (compared to cattle) , ability to thrive on different feed and fodder, high disease resistance, and superior market and profit potential.

Some of the limitations and challenges in marginal farmer livestock production system are inadequate/limited availability of animal health services and poor infrastructural facilities leads to heavy economic losses due to high mortality. If organized efforts are undertaken to improve the preventive and curative livestock health services by timely vaccinations for diseases like Peste de Petits Ruminants (PPR), bluetongue enterotoxaemia and sheep/goat pox in small

ruminants, classical swine fever in pigs and Newcastle disease in poultry can enormously improve economic gains to farmers.

Studies show that during the period 1991- 2005 sheep and goat mortality due to PPR, sheep and goat pox, enterotoxaemia and contagious caprine pleuropneumonia was 74% and economic loss in goats alone was Rs. 264.8 lakh ($5.8 lakh), with PPR contributing 37%.

Eradication of Rinderpest from India and the world (first animal disease to be globally-free and the second after human smallpox) has provided huge impetus for major livestock diseases control initiatives - which are bound to immensely benefit the rural poor.

The national control / preventive programmes for these diseases by Govt of India will be presented. Issues related policy matters, vaccine requirements, and preventive health support, delivery system, cold chain management and disease reporting will be discussed briefly.

SCOPE OF BIOTECHNOLOGY IN DEVELOPMENT OF VACCINES FOR INFECTIOUS DISEASES.

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Basic strategy of isolation, inactivation and injection of the pathogen has guided the development of vaccines against many diseases during 20th century. However in several disease models it was not possible to prepare potent vaccines using conventional approach. The failure to develop effective vaccines against many diseases has led the researchers to probe into the molecular biology of disease process, immune response and host pathogen interaction. A wealth of knowledge has accumulated during the 70 year period of research which is now guiding the rational approach to vaccine development. Added to the basic knowledge, availability of tools in molecular biology and biotechnology make the process of vaccine development a rapid and meaningful scientific approach. The advancements in present modern Biotechnology made one to realize that it is easy to produce any candidate vaccine in vitro with no environmental concern.

The recombinant DNA approach to produce any protein in heterologous host system is a big breakthrough in Biotechnology. Immunogenic surface proteins have been successfully used as vaccine in the case of Hepatitis caused by Hepatitis -B virus (HBV). This approach is more relevant in viral diseases where the antigenic moieties are limited and can be selected easily. The technology is very much cost effective as there is no requirement of sophisticated infrastructure for vaccine production. In the case of HBV the surface glycoprotein itself forms virus like structure which can mimic live virus in terms of host immunological responses and elicits good immune response. However, in most cases the protein sub-units attain undesirable conformational structure or does nit carry post translational modification. Such molecules fail to elicit strong immune response when used as vaccine. However these could be overcome by the use of suitable host systems. Sometimes expression of complete array of antigenic moieties help in the

development of potent vaccine. Empty capsids of viral pathogens produced through recombinant technology is being tried extensively for development of vaccines.

Though the biosynthetic antigens can elicit humoral response, mere antibody response is not sufficient for protective immunity, as cellular responses play major role in clearing the pathogen. Also strong cell mediated immune response is essential for curing the carrier animals, as in the case of highly contagious diseases like FMD, persistent infection is a major problem to control this disease in endemic countries like India. Thus the vaccine should elicit both cellular and humoral responses.

Genetic vaccines have been found to elicit good cellular response, while inducing low levels of humoral response. Strong humoral response in addition to cellular response is needed for effective control of FMD. Alpha virus replicase based DNA vaccine vectors which act like self replicating gene vaccines are ideal in achieving both humoral and cell mediated immune responses. Biotechnology has necessary tools to develop suitable vectors which can be used for the delivery of multiple antigens in the host so that protection can be achieved against two are more diseases. Attenuated non pathogenic viruses like pox viruses have been used as vectors to develop potent vaccines for successful control of zoonotically important deadly disease like rabies in wild animals.

It has been shown in the case of small pox, rinder pest, polio and other diseases, that vaccination using attenuated viruses is the best approach for successful control. However naturally-selected attenuated viruses carry the risk of reversion to virulent forms. Thus genetically modified viruses are the best candidates. To achieve this, the sequences necessary for virulence can be modified and the candidate vaccine strain after thorough study may be used for vaccination. With discovery of reverse transcriptase it has become possible to develop vectors carrying replicon of highly mutable RNA viruses like FMD using reverse genetics approach. These vectors can be used for rapid selection of field strains without compromising environmental safety. Moreover such constructs are helpful in developing tailor made vaccines which include marker vaccines to differentiate infected and vaccinated animals.

Most of the vaccines available today can only be used as prophylactic vaccines, and they have limited use at the phase of outbreak. Control of carrier status and persistent infection is as

important as prevention since, the replication of virus in subclinical state results in generation of antigenically variant pathogenic strains. Thus therapeutic vaccines are needed for using at the phase of outbreak. The recent understanding on RNA interference has helped to develop Sh-RNA candidates which can be used as therapeutic vaccines.Similarly mucosal vaccination using edible vaccines developed through plant expression system has the potentiality to emerge as future therapeutic vaccines.

Present day strategy in vaccine development is to include marker facility that helps in distinguishing antibody response due to vaccination vis-à-vis infection in vaccinated animals. Such information becomes relevant for effective disease control programmes especially when using inactivated virus vaccines against highly contagious like FMD. The antibodies generated in the animals, only through vaccination, is the measure of vaccine efficacy and safety. The quality of the vaccine depends on the efficacy in generating protective antibody response with broad antigenic coverage. Since, only antibodies against capsid proteins are expected to be generated in vaccinated animals which cannot be distinguished from that of infected animals, one needs to assay the antibody response against non structural proteins(NSPs). Therefore the vaccine must be free of contaminated NSPs. In endemic countries one can expect the presence of antibodies against NSPs as the animals are exposed constantly to the virus circulated in the air. Hence use of negative marker vaccine may be of little help. Alternatively one may develop a positive marker vaccine by including a foreign protein or epitope which is not expected to be present in the vaccine and the antibodies generated against which helps in detecting the vaccine related response. This presentation deals with these developments using biotechnology tools in the case of foot and mouth disease. These approaches may be used in dealing with other viral diseases of economical importance.

ROLE OF PORCINE REPRODUCTIVE AND RESPIRATORY SYNDROME VIRUS PROTEINS IN INFECTION AND IMMUNITY

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Porcine reproductive and respiratory syndrome (PRRS) is considered to be globally the most significant infectious disease of swine. PRRS was first detected in North America in 1987 and in Europe in 1990 and has since then been recorded in all pig-producing countries throughout the world (except Australia and New Zealand). The causative agent of the disease is the PRRS virus (PRRSV), which has now been found to be endemic in most pork-producing countries. An economic study in 2011 revealed that the cost of PRRSV to swine producers in the USA alone was estimated to be over US$660 million. The economic impact of PRRSV, the sudden emergence of new PRRSV strains of unprecedented virulence in China and S.E. Asia, and the current inability to effectively control the disease emphasize the importance of this disease to the international animal agriculture. Effective vaccines or therapeutics to combat the virus are not available at the present time due in part to the lack of comprehensive knowledge of the biology and immunopathogenic mechanisms of the virus. Although more than 20 years have elapsed since the discovery of PRRSV, much remain unknown about the immunology of this virus. Development of adaptive immune responses after infection of naive pigs with PRRSV is known to be anomalous. Pigs infected with PRRSV do not elicit strong neutralizing antibody response. While the mechanisms of protective immunity against PRRSV may not have been fully appreciated, studies clearly indicate that neutralizing antibodies are important contributors to PRRSV protective immunity. Further complicating the immune protection against PRRSV is the pronounced diversity of this virus. PRRSV exists as two major genotypes, European (Type 1) and North American (Type 2). There is only limited immunologic cross-protection between the isolates within these genotypes. Moreover, considerable variation exists between field isolates of each of these genotypes indicating continuing divergence of viral genomic sequences. To generate an efficacious and safe vaccine against PRRSV, three major technical challenges or knowledge gaps need to be addressed: (i) to identify structural components of PRRSV and host mechanisms involved in

PRRSV protective immunity, (ii) to understand the mechanisms involved in PRRSV attenuation in order to reduce virulence and/or increase immune responses of the vaccine strains, and (iii) to improve the meager protective efficacy of current vaccines against heterologous PRRSV strains, mainly by ascertaining what defines a heterologous strain in terms of protective immunity. The presentation will address each of these aspects by outlining studies from our laboratory. The focus will be placed on examining the role of specific viral structural and nonstructural proteins that contribute to our understanding of biology and immunopathogenesis of the virus.

YEAST MICROBIAL CELL FACTORIES FOR BULK PRODUCTION OF RECOMBINANT PROTEIN OF PROPHYLACTIC AND DIAGNOSTIC IMPORTANCE- AN EXAMPLE OF INFLUENZA A HEMAGGLUTININ RECOMBINANT PROTEIN.

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New findings in scientific research related to Biotechnology have broad applications to variety of sectors like livestock, agriculture and human health. They are also expected to make considerable contributions towards the development of new therapeutics, vaccines and diagnostic methods. Yeasts have been used over last thirty years for the large scale production of intracellular and extracellular proteins of animal, human and plant origin. Among various heterologous expression platforms available to date, Yeast, especially Pichia pastoris stands unique and offers several advantages over other conventional expression platforms. The following are the important factors that contributes for this system's popularity: firstly, the use of the alcohol oxidase I (AOX1) promoter, one of the strongest, most regulated promoters known; secondly, the ability to stably integrate expression plasmids at specific sites in the P. pastoris genome in either single or multi copy; thirdly, the ability to culture strains in high density fermenters; and finally, its ready availability as a kit from Invitrogen Corporation (USA).

The Influenza A virus Hemagglutinin (HA) protein is a glycoprotein that comprises virus

neutralizing epitopes on its surface. Majority of the antibodies in case of Influenza infection will be targeted against HA protein of the virus. Hence HA is the ideal target either for developing subunit based candidate vaccine or a suitable diagnostic platform. Considering some of the practical disadvantages associated with the bacterial system in terms of protein purification, refolding, inability to carry post translational modifications, one has to look for an alternative heterologous system for rapid, easy and economical production of Hemagglutinin protein in its glycosylated form. In light of these drawbacks and also considering the safety, reliability and economic potential of yeast expression system, we have successfully employed Pichia pastoris expression system for recombinant expression of Hemagglutinin (HA) protein of Influenza A virus. The HA gene of novel H1N1 A/California/04/2009 was engineered for expression in Pichia pastoris as a soluble secreted protein. The full length HA- synthetic gene having ?-secretory tag was integrated into P. pastoris genome through homologous recombination. The resultant Pichia clones having multiple copy integrants of the transgene expressed full length HA protein in the culture supernatant. The production of this recombinant protein was further scaled up via fed batch fermentation and downstream processing parameters were optimized to recover the target recombinant HA protein from the Pichia culture supernatant in its native trimeric form. The recombinant yeast derived H1N1 HA protein elicited neutralizing antibody response in mice and rabbits. The sera from immunized animals also exhibited Hemagglutination Inhibition (HI) activity.

Polyclonal antibodies were developed against yeast derived recombinant HA protein in rabbits (IgG) and chicken egg yolk (IgY). These purified polyclonal antibodies detected the native Influenza virus and also the recombinant protein recognized the virus specific antibodies through Enzyme linked Immunosorbent assay (ELISA). These findings have suggested the feasibility of using yeast expression platform as an economical alternative for large-scale production of recombinant influenza HA protein and its subsequent use as candidate vaccine and also as a diagnostic reagent. This technology can be easily extended for rapid production of recombinant proteins of several other influenza virus subtypes or any other viral diseases that affects animals, humans or even both. Thus, yeasts have become theatrical stages where complex molecular phenomena of eukaryotes can be recreated and reengineered.

THE ROLE OF WOMEN IN TAKING SCIENCE TO THE COMMUNITY: EXAMPLES FROM THE FIELD AND CHALLENGES AHEAD

Mrs. Sunita Nadamuni

CEO, Arghyam, Bangalore

An oft-neglected challenge in science in India is that of popularizing science among the general public and increasing scientific literacy at large. In this plenary, we will view that through the lens of the water sector, which is a critical sector for India. There are areas in the water sector where the elected representatives and the general public will be called upon to understand complex scientific matters in order to make good decisions. It will be the responsibility of the scientific community to present the essence of the relevant science in a manner ("as simple as possible but no simpler") that is accessible and usable by non-scientists.

In keeping with the theme of this Science Congress, we will particularly focus on the various roles of women in this task of taking science to the people. In the vast majority of households in our country women are primarily responsible for water and sanitation in the household. Therefore making them aware of the scientific facts around water and sanitation is crucial and popular communication must be tailored for them. Elsewhere, in interventions such as watershed development, time and again the value of having women as full participants in the processes has been seen on the ground. With reforms in Panchayati Raj, women are in positions of decision-making at the Panchayat level. Women are also in leadership positions as heads of NGOs and civil society organizations. We will hear from women in these roles and the particular challenges they face and their successes in negotiating science and technology matters in their work.

A few examples of areas in the water sector where science and technology communication to the common man have a particularly key role to play at this point in time:

Water quality - As fluoride, arsenic and other threats to water quality spread in India, the common public will be called upon to understand the nature of these public health risks, the methods to test for them and to make decisions between different treatment technologies and approaches. Local communities and their representatives and bureaucrats will need to work

through all the facts and make good decisions. Households will need to understand the importance of toilets, handwashing and proper household level treatment of water, and the science behind these facts will need to be well-communicated.

Groundwater - Groundwater is now a critical resource in India, both for domestic and agricultural use. We are however using it up unsustainably and polluting precious groundwater sources. One of the factors contributing to this is the lack of popular understanding of groundwater. The science of groundwater is difficult ; it is compounded by the fact that we cannot see what is going on, all the action happens in the soil beneath our feet and out of our view. The challenge of a widespread understanding groundwater to enable its wise management is a big one for citizen science. Possibly, we will need a cadre of citizens who understand it enough to operationally manage it wisely, without having to be professionally qualified ("barefoot hydrogeologists"). Their training and scientific literacy will be the challenge.

Watershed Management - Rainfed areas of the country critically depend on watershed management to improve the water availability and increase crop productivity and secure livelihoods. While significant progress has happened so far in watershed management programmes, much more work lies ahead to cover all the areas that remain uncovered. Watershed programmes need to involve citizens in the planning, design and implementation of watershed interventions. As more and more areas implement these interventions, we will need to find ways to train large numbers of people in the science and engineering of watersheds.

This plenary will bring in views from experts working in these areas to address the issues raised and the special relevance to women in their various roles.

BRIDGING THE BENCH TO BEDSIDE GAP WITH PHYSICIAN - SCIENTIST COLLABORATION.

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In the arena of bench to bedside research (sometimes termed "translational research" in the United States of America), the spectrum of potential investigators ranges from basic scientists to physicians/clinicians. Less common are the physician-scientists (MD-PhDs), who have received formal training in both the research laboratory and the clinical setting. As the sheer amount of medical knowledge grows, the expectation that a single investigator (or even a single collaborative team) can actually bridge the gap between basic research knowledge to bedside application becomes a more and more unrealistic goal. Moreover, our investigation suggests that MD-PhD programs are declining in popularity and therefore in admission. This downward enrollment trend is not because of the intellectual or professional challenges of such dual training, but rather because the extra years of training (typically 2 years) are increasingly viewed as unfavorable especially by female trainees, a growing contingent of the medical practitioner field. Additionally, those who do complete the MD-PhD program frequently find that the demands of clinical work in our current system, leave them no "protected time" to pursue their research. The information explosion is no more evident than in the clinical field, where it is estimated that knowledge doubles every 18 months to 2 years. This, coupled with the fact that researchers trained in both basic science and clinical medicine appear to be diminishing in number, leads to an unsustainable situation that does not well serve our society. We believe that the emphasis must necessarily shift to expanding translational research to bridge between basic science producing medically relevant information and the application of that knowledge in clinical and other care-giving settings by increasing the occurrence of direct and structured collaboration between basic scientists and clinicians.

Major expansion of the pipeline for translational research, however, will require a change of both culture and approach. We can no longer simply wait for basic scientists to publish their findings in appropriate journals, and then wait for the busy clinician to read about those findings (if they even have time to venture into the basic science literature). Moreover, the flow of

information should not just be "up" from the bench to the bedside. Rather, basic scientists need to hear about the insight from findings of clinical trials as they occur, not when (or if!) they are published. While we can leave this two-way communication to occur by chance, we can also move forward to weave the importance of such communication into our trainees at all levels. This will require the real world approach of creating cross-, multi-, and interdisciplinary teams consisting of proponents of the "bench-to-bedside" approach, and showing our trainees first-hand the true power of this form of collaboration. It may also mean choosing animal models that particularly lend themselves to translational research. For example, the zebrafish, an animal model that is gaining popularity in basic research, shares huge components of its genome, its molecular and cellular biology and its physiology with humans. At our university we have explored collaborations that involve screening trials with zebrafish, leading directly to large animal trials with ungulates, that in turn lead to approved trials in humans. Key to this collaboration, however, is that a finding that emerges on Friday in the operating room may very well be back in the hands of the basic scientist by Monday, enabling researchers to modify their basic studies and screening. It is the cycling of information that is truly translational about this approach. Additionally, building the bench to bedside transfer into the project from the very inception ensures that the models and goals remain relevant at all points of the research.

Collaboration as a core value is not a given in most of our current training regimes, however. We have a value and reward system that primarily emphasizes individual rather than team success. Trainees start by getting individual grades, they are admitted to doctoral programs or medical school as individuals, and as individuals they subsequently receive job offers and promotions. While many may see the advantage of collaboration, they also must be exposed, through both examples and inculcation, to understand collaboration among basic scientists and clinicians from the perspective of ethics, credit (and credit sharing) and measurements of success. While many institutions world-wide have begun implementing the changes we suggest, they remain the unusual rather than the usual.

The effort required to rethink our training programs and their embracement of collaborative approaches along the full spectrum of basic science to clinics will be more than outweighed by the ability to quickly move discoveries up the chain from animal models to humans and then equally quickly generate immediate feedback from the clinical investigators about how to subsequently shape the basic science thrusts in the collaboration team. Rethinking our training approaches will additionally create a new generation of trainees better equipped to deal with the near-overwhelming information expansion in both the basic and medical sciences.

DEVELOPING AND SUSTAINING A PHYSICIAN SCIENTIST PROGRAM: THE AMERICAN EXPERIENCE.

Anand Kumar, M.D.

Lizzie Gilman Professor, Head, Department of Psychiatry, University of Illinois, Chicago.

With rapid developments in all areas of biomedicine, there is a need to develop a small cadre of individuals, trained in both clinical medicine and biomedical research, with the ability to integrate and translate between the preclinical and clinical domains. Developing Physician-Scientist training programs requires a clear vision, commitment and years of effort. It also requires close collaboration between the medical and scientific establishments, a shared vision and a commitment to work together towards a common goal. The United States has nurtured and developed physician scientist training programs, in all major medical schools nationally, for over half a century. This presentation will provide a summary of the American experience with developing and sustaining physician-scientist programs, with special emphasis on the MD, PhD program. The emphasis will be on developing a clear, promising career path for individuals who show an interest in science and medicine early in their professional development. The structure of the program together with the incentives needed to sutain it and outcome measures will be presented and discussed. The American experience may provide the basis for a pilot study limited initially to a few medical schools with the interest in providing leadership and supporting this initiative.

BENEFITS OF TRAINING PHYSICIAN SCIENTISTS IN INDIA: AN AMERICAN LESSON

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Scientists are those who perform intensive research to advance knowledge in any branch of Science. In order to conduct research, a PhD, the highest degree of scientific training, is usually required. However, as with any rule, exceptions do exist. Take, for example, Srinivasa Ramanujam and Sir CV Raman, both of whom, without PhD degrees, made extraordinary contributions to science. In the United States, the degree required to practice in the clinical field is an MD, a post-graduate degree. Some individuals, after receiving their MD training, decide to pursue academic and scientific careers. These MDs are self-made pupils of academia and several have attained the highest distinctions in their field, such as receiving the Nobel Prizes in Physiology and Medicine. Since several clinical fields require research, and MDs are appropriately suited for this, it follows that a program to train these individuals to pursue research-based careers should be a necessity. This fact has been recognized in the U.S. and programs such as MD-PhD as well as other programs in which MDs can pursue research have already been introduced. These MDs are typically relieved of clinical burdens and their time can be spent performing research. Furthermore, they are also encouraged to obtain grant funding from public sources like NIH.

Indian medical education differs in how it trains physicians in that an MBBS degree, a baccalaureate degree, is sufficient to begin clinical practice. While some individuals with an MBBS degree perform research, most medical schools in India are not research intensive and are programmed to be pure teaching schools. The exceptions to this generalization are some of the top medical schools in India, such as AIIMS and CMC. Furthermore, the training in basic sciences is limited in Indian medical system. For example, a medical student in the USA finishes an initial 12 years of schooling, a four year BS degree, and an additional four years of curricular training to obtain an MD. Thus, a total of 20 years of education, not including years spent in

residency, are needed to obtain an MD. In contrast, only 16.5 years of curricular training are needed to obtain an MBBS degree in India, without considering the internship. Thus, there are at least 4 fewer years of exposure to science in the MBBS degree compared to the MD degree. Curiously, although British and Indian medical school systems require the same number of years to obtain an MBBS degree (since the Indian education system is inherited from the British), British medical schools are performing class one research. This discrepancy is probably due to differences in interactions between University scientists and academicians in the medical school and/or there is a greater research focus in British medical schools. Thus, more interactions between physicians and scientists or more research programs in medical schools are needed to enhance research in the Indian medical system.

This presentation will discuss various programs in the USA that enhance physician scientist training as well as the interactions between scientists and academicians. Furthermore, I will share with you the interactions I have had with Indian medical fellows trained in my laboratory and how well these individuals have performed in the fundamental research of my laboratory on hemostasis and thrombosis, as well as how my research has provided fertile grounds for training these Indian medical graduates. I will also share my experiences in NIH study sections in which I was a reviewer and evaluated the Physician Scientists training grant applications. These avenues, when implemented in India and further enhanced in other countries including the USA, may lead to the production of increasingly excellent physician scientists, a necessity if we wish to improve upon medical research conducted for the betterment of our community.

BIODIVERSITY CONVENTION: PUTTING THE TREATY FIRMLY ON AN IMPLEMENTATION COURSE

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The Convention on Biological Diversity (CBD) set a doctrinally new international regal regime in conservation by equally placing conservation, sustainable use and equitable benefit sharing in biodiversity management. The Convention has created massive political awareness about biodiversity, catalyzed the publication of a large body of literature on the subject and National Biodiversity Strategy and Action Plan has been formed in 173 countries. However, the enforcement of the treaty over the past two decades leaves much to be desired. The 2010 target of significantly reducing biodiversity is acknowledged to be missed, biopiracy from the bio-rich countries of the global south continues to unabated, indigenous communities in many countries remain alienated from the biodiversity of which they were the historical custodians, and biosafety remains precarious in spite of a dedicated protocol. Although the treaty was negotiated and came into force in line with the provisions of the Vienna Convention on the Law of Treaties, the legally binding nature of the treaty has been undermined in the years since it has come into force. In order to realize the tremendous potential of the treaty, the forthcoming meetings of the Conference of Parties (CoP) at Hyderabad as well as the future ones- need to review the state of implementation of the different articles of the treaty and seriously consider issues of infractions. The talk will address this issue and highlight the need to reform the national biodiversity management system by incorporating the triple objectives of CBD (conservation, sustainable use and benefit sharing) as an essential means to reverse the trend of biodiversity loss.

TRANSITION TO TRANSLATION:

PHYSICIAN-SCIENTIST AS ONE OR THE OTHER

Dr. Srinivas Pentyala

Director of Translational Research Centre, Stony Brook Medical School

Any individual who has the passion to help others and commit themselves for the betterment of society, often limit themselves to perform their designated duties and dwell in the satisfaction that their best is good enough. However, this sort of contribution is the nexus for advancement of science. Particularly the field of biomedical sciences is an area where intense bench research is being done to understand the mechanisms that regulate life, suffering and death. Innovation can propel a simple finding in basic science to a concept that can be of immense value to society. While applying these novel innovations that came out by studying the basic mechanisms, an offshoot of applied branch has transitioned. This field which is now widely referred to as "Translational Research" utilizes basic science findings and propels these discoveries into innovative concepts for the benefit of mankind. This branch of science has evolved into a multidisciplinary juggernaut encompassing all known fields of science, even including fields as varied as law, economics, sociology, etc. With the ever increasing interest in this branch, and the dreams and aspirations that this field can bring, innovators are now taking a bold step into this new realm, merging different fields of knowledge to come up with novel inventions. This approach needs discipline and a step-by-step systemic approach. The most important question that still needs to be answered is whether one individual can fulfill the role of being a healer and a discoverer or different individuals should perform their designated duties and effectively interact with each other. Taking a few simple basic science discoveries related to diseases and symptoms from our research laboratory and few clinical observations from our hospital as examples, the whole concept of thinking outside the box and taking the next step from basic science to applied and translational sciences for improving the quality of life will be presented. Development of a successful Physician-Scientist model involving the following concepts will be presented.

1. Highlighting the importance of translational research.
2. Educating the basic scientist as well as clinicians in the concept of translational research.
3. Encourage the concept of doing translational research at an early stage.
4 Brainstorming - bringing minds together and discuss research/clinical observation/problem and evaluate its potential to be a translational/applied project.
5. Tools and mechanisms for free discussions.
6. Bridging the gap (between basic and clinical science, prospective and retrospective studies, sparking ideas and inventions).
7. Encouragement to proactive curious/inventive person to find time/space to execute the project.
8. Defining partnerships and responsibilities.
9. Identifying and aligning pairs or groups based on the need/expertise.
10. Discovery management- Goal oriented advancement.
11. Technical and logistical support (Idea is not enough).
12. Mechanism of support.
13. Public-Private Partnership : Interaction with Pharma/Biotech.
14. Innovation leading ultimately to an application.
15. Outcomes and rewards.

ICT: A TOOL FOR ACHIEVING VISION 2020

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Information and Communication technologies have had a salient impact on India's economic growth rate over the last two decades. Because of intensive competition and a potential large market, Communication technologies like mobile phones have transformed the landscape, bringing information and efficiencies across all strata of Indian society. Today, we can boast of the lowest mobile call rates in the world and a mobile market of 625 million subscribers that continues to grow at a breakneck pace.

Information Technology, on the other hand, has led an impact till now only in pockets of the country but the IT industry has made a strong impact in other ways: During the current financial year, direct IT industry employment is expected to reach nearly 2.5 million, an annual addition of 240,000 employees, while indirect job creation in the IT eco-system is estimated at 8.3 million. As a proportion of national GDP, the IT sector's revenues have grown from 1.2 per cent in FY1998 to an estimated 6.4 per cent in FY 2011. And its share of total Indian exports (merchandise plus services) increased from less than 4 per cent in FY1998 to 26 per cent in FY2011. The industry is nearing the $100 billion milestone and Nasscom estimates that it can generate revenues of $139 billion by 2015 from $88 billion at present.

As 3G and broadband networks become all pervasive over the next few years, given the government's initiatives to connect universities and gram panchayats to the information grid, it is crystal clear that ICT will become an even more powerful tool to spur economic growth and help India achieve its Vision 2020.

Growth after all is the source of our energy. It fuels investment and expenditure but more importantly, it allows every Indian to dream of better things and then go out and realise them. It is estimated that the compounded effect of achieving the targeted annual GDP growth rate of 8.5

to 9 per cent over the next 20 years would result in a quadrupling of the real per capita income and almost eliminating the percentage of Indians living below the poverty line. This will mean, India will move from a low income country to an upper middle income country by 2020-2025.

Job Creation: An Opportunity cloaked in Challenge

The Vision 2020 document released by the Planning Commission in 2002 highlights the many priorities we must tackle to achieve development and growth. But one factor stands out as the key challenge: employment generation.

To fulfill its promise of delivering a higher standard of living for its 1.2 billion population, India faces the key challenge of generating 200 million new employment opportunities over the next decade. The Planning commission report calls for raising employment generation to the top of the nation's development agenda and marshalling all available resources to create employment opportunities for all job-seekers.

The challenge is made more enormous by the fact that we are already starting from a negative or job deficit situation. More than 34 million people are presently unemployed and merely making them productive will and gainfully employed will itself require major changes in our talent and skilling policy both at the central as well as state and local levels. The private sector will need to be even more involved in working closely with the government to create opportunities.

But if one steps back for a moment and takes a global perspective, the challenges give way to a once-in-a-century opportunity. The United Nations estimates that India will account for almost 26% of the increase in global working-age population over the next 10 years. The UN estimates that by 2020, India will contribute an additional 136 million people to the global labor pool or 17 per cent of the additional global workforce.

This is in stark comparison to other regions of the world. In the same period, China and the US will only contribute an addition of 23 million and 11 million workers to the global workforce respectively while on the other hand, Japan's and Europe's working populations are estimated to decline by 8 million and 21 million by 2020.

Indeed, given the global impact of demographic trends, this is a big challenge for India but also a global opportunity on a grand scale. This deficit in working age populations will create

many policy disruptions for the western economies. For example in Europe, to compensate for or counter current ageing trends, the continent will need to increase migration by 30 times the current levels and sustain it for 20-25 years. Clearly this may be more difficult to achieve given the cultural and other sensitivities surrounding large-scale immigration.

Therefore the large increase in India's working population over the last decade, in my opinion, will force other economies and nations to recognise the role of Indian talent to ensure their own future global competitiveness and output dynamics. New business and delivery models will emerge as India's talent becomes a global resource base not just a national one.

The role of ICT has to be seen in the global context , the scope for impact using the latest information and communication technologies is greater than ever imagined before.

Maximum impact

While acknowledging that ICT will have a positive impact on all the priorities defined to speed up economic growth and achieve our vision 2020, my address today will focus on three key areas where Information and Communication Technologies can have the maximum impact to help India achieve its vision 2020. These I believe, will have the maximum impact on employment creation and growth.

1. Use ICT to create a framework of Good Governance and Total Transparency enveloping major aspects economy and society

2. Use ICT to help encash India's demographic dividend by creating Employment, Education, Training, Skilling using technology-based business and delivery models. Encouraging the growth of technology and other knowledge-based employment opportunities in a globalizing world

3. Use ICT to spur Inclusion and bring the far-flung, unconnected communities into the mainstream of society so that they are able to enjoy Financial, Education, Health services, many of us in urban areas take for granted

A holistic enabling environment for all these aspects could truly help tackle the number one priority of employment generation and unleash the innovative and entrepreneurial spirit of the Indian people, not only to India's advantage but also for the benefit of the world.

BIOLOGY OF NEURONAL CYTOSKELETON REGULATION NEURODEGENERATION AND DEMENTIA; A NOVEL APPROACH TO RESCUE THE PHENOTYPES OF DEGENERATION AND DEMENTIA, IN ALZHEIMER DISEASE MODEL

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Among many other neurodegenerative diseases Alzheimer's disease (AD) is the most common cause of dementia among older people, but it is not a normal part of aging. Dementia refers to a decline in cognitive function that interferes with daily life and activities. AD starts in a region of the brain that affects recent memory, then gradually spreads to other parts of the brain. Although treatment and life style can slow the progression of AD and help manage its symptoms in some people, currently there is no cure for this devastating disease. The number of people with AD doubles for every 5-year interval beyond age 65.

AD is named after Dr. Alois Alzheimer, a German doctor. In 1906, Dr. Alzheimer described changes in the brain tissue of a woman who had died of an unusual mental illness. He found abnormal clumps (now called amyloid plaques) and tangled bundles of fibers (now called neurofibrillary tangles). Today, these plaques and tangles in the brain are considered hallmarks of AD. The third main feature of AD is the gradual loss of connections between nerve cells (neurons) in the brain. This loss leads to diminished cell function and cell death. We don't know what starts the AD process, but we do know that damage to the brain begins as many as 10 to 20 years before any obvious signs of forgetfulness appear. As nerve cells die throughout the brain, affected regions begin to shrink. By the final stage of AD, damage is widespread, and brain tissue has shrunk significantly. In the years to come, AD is expected to pose physical and emotional challenges for more and more families and other caregivers, in addition to those with the disease. The growing number of people with AD and the costs associated with the disease also will put a heavy economic burden on society.

The Biology of Neurodegeneration and dementia program evolved in my laboratory studying the basic biology of neuronal cytoskeletal protein phosphorylation regulation during development and normal function in the adult. To understand the molecular basis of neurodegeneration our major focus has been to study the regulation of compartment-specific patterns of cytoskeletal protein phosphorylation in neuronal perikarya and axons. We have demonstrated that phosphorylation of the numerous acceptor sites on such proteins as Tau and neurofilaments was tightly regulated topographically and generally confined to the axonal compartment. It was recognized that in neurodegenerative disorders such as Alzheimer's disease (AD) and Amyotrophic lateral sclerosis (ALS), the pathology was characterized by an accumulation of aberrantly and hyper- phosphorylated cytoskeletal proteins in cell bodies, suggesting that topographic regulation had been compromised. This led inevitably into studies of neurodegeneration in cell culture and model mice with emphasis on a specific neuronal protein kinases, e.g. cyclin dependent kinase5 (cdk5), MAPKs that targets numerous neuronal proteins including cytoskeletal proteins, which when deregulated, may be responsible for the pathology seen in neurodegeneration. In cell systems, neuronal stress leads to deregulated kinases, for example, cdk5, accompanied by abnormal cytoskeletal protein phosphorylation and cell death characteristic of neurodegeneration. Recently we have developed peptides derived from, p35, a neuron specific activator of cdk5, for deregulated cdk5 activity which rescue cells in vitro from this stress induced pathology. The questions currently being investigated are (1) How is cytoskeletal protein phosphorylation topographically regulated in neurons? (2) What factors are responsible for the deregulation of cdk5 in neurons? (3) Can mouse models of AD and ALS be treated therapeutically with peptides that specifically inhibit deregulated but not the regulated cdk5 activity which is essential for nervous system development, function and survival?

RESEARCH & INNOVATION : MANY DIMENSIONS

R. Chidambaram

Research involves generation of new knowledge and innovation requires adding economic value, societal benefit or strategic value to knowledge. India is changing fast and its technology needs range from nuclear to rural. India's science and technology programme must balance basic and applied research with innovation, commercialisation and societal reach.

Innovation in high-technology enterprises requires strong R&D inputs and academia-industry interactions. Indian policy must encourage early introduction of new advanced technologies. Proven technology is also, of course, important but proven technology is often a synonym for obsolete technology! Indian potential for manufacturing competitiveness is seen globally as driven by talent-driven innovation.

In the chain ' research - development - delivery', while the weakness in the context of industrial development is 'development', in the context of rural development, the weakness is in 'delivery'. Inclusive growth would demand that we enhance academia-industry interactions for industrial development and improve systems for technology delivery for rural development. For the latter, there is also need for what I call 're-innovation', i.e. repetitive suo-moto innovation, starting from the same core concept.

India needs to support strongly research in all its dimensions : self-directed basic research - we must encourage the highest intellects to work on fundamental problems of their choice - , backed by what I call 'directed' basic research; pre-competitive applied research as well as applied research for proprietary product and process development. Again innovation must cover all its dimensions - product, process and design and a mix of them as appropriate.

The e-science infrastructure is improving rapidly in India. The National Knowledge Network under establishment will link the country's knowledge institutions at speeds scalable up to tens of gigabits per second. This will help both research and innovation, including national and international collaboration in both. We must learn to leverage international collaboration to strengthen our own initiatives.

In the ultimate analysis, science is done by scientists. The most important issue, therefore, is to attract talented young people to careers in science and technology, particularly in those areas important for the country's development.

PRESENTATION TOPIC: TREATMENT OF INDIVIDUALS WITH MENTAL ILLNESS AND DRUG USE DISORDERS: AN OVERVIEW

Vinay Nagaraj, MD

Length: 45 minutes + 15 minute Qs & As session

Mental illness can be extremely debilitating for both individuals who suffer from it and their families. There are many forms of mental illness, including disorders of mood (depression and bipolar spectrum illness), anxiety (generalized anxiety, panic disorder, social anxiety, obsessive compulsive disorder, post traumatic disorder), psychosis (schizophrenia spectrum disorder). Each of these disorders has very different clinical presentations, progression, and response to treatment. There are a multitude of challenges to effectively treating these individuals, including-but not limited to-the diminished insight of affected individuals to remain in treatment, inability to access treatment for a variety of reasons, limited knowledge of the individual and their caregivers as well as societal stigma.

In addition, individuals with mental illness commonly suffer from drug use disorders (D-addiction). There are many types of substances that can affect individuals, including alcohol, cocaine, marijuana, heroin, club drugs, prescription pain and sedative-hypnotic medications. The most effective treatment includes behavioral modification techniques in addition to limited pharmacologic options. The challenges of treating individuals with D-addiction mimic the challenges of treatment of those with mental illness.

During the first part of this presentation, we will discuss the different types of mental illness as well as the mainstay of treatment for each disorder. The second part of the presentation will take a look at the types of drug use disorders and current treatment strategies. Special emphasis will be placed on the obstacles to effective treatment for this needy subset of the population.

BIODIVERSITY AND SUSTAINABLE DEVELOPMENT

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Sustainable Development is a most quoted word since several years upon witnessing abnormalities with basic natural resources. Sustainable Development concept came into being after the UNCED Conference in 1992 where in, the development was spelt in harmony with nature without stressing its resources beyond its regenerative capacity. It is particularly relating to the status of natural resources and its relationship with the livelihood status of humankind. Scientific communities all over the world are designing and developing new strategies to sustain production systems in alliance with the ecosystem. Scientists and development agents have been looking for different options/strategies/approaches towards tackling various issues relating to the basic natural resources of the terrestrial and aquatic ecosystems. Evolution of Participatory Approaches "one of the modern social techniques" entangled with biological methods of conservation paved way for sustainable development in different parts of the world. It is of utmost importance that "Biodiversity" is central for sustainable development. Biodiversity will be critical for achieving the goal of sustainability, and its loss at the three levels- genetic diversity, species diversity and ecosystem diversity will be one of the greatest disasters ever the world would have witnessed. World Wide Fund for Nature (WWF) indicates that, one third of the natural biological wealth has already been depleted by human action in the last 30 years. The benefits of biodiversity are well known as it is a platform and a base for economic growth and development. Loss of biodiversity puts aspects of our economy and quality of life at risk, and reduces socio-economic options for future generations. It is thus felt that scientific approaches have to be given greater significance to conserve biodiversity at the national and international level. The present paper deals with certain aspects of biodiversity and sustainable development that promotes life and life management systems of human beings.

Agriculture is one of the major areas of food production. Although agricultural production

is encouraging, there is widespread poverty in many developing countries. It is necessary that agricultural production should meet adequate food supply and generate income and employment for sustainable living. Considering the expanding human population worldwide especially in the developing world, it is paramount that agricultural production has to be increased. It has been reported that assuring a population growth of 2%, world food production has to be doubled in the next fifty years. The point that has to be borne in mind that instead of using the same rice varieties repeatedly there is an imperative need to explore more genetic diversity that would enhance food production for sustainable living. Further, the factors responsible for declining agriculture biodiversity have to be identified and efforts have to be taken to mitigate it. The major factors responsible for decline of biodiversity include soil erosion, landslides, drought and desertification, lack of proper watershed etc. For agriculture to sustain certain aspects such as stress biology, use of biofertlizer, biopesticides and vermicomposting have to be given importance.

Besides agriculture, forest and forest cover is an another significant resource for livelihood. Forests sustain life of millions of rural people in diverse ways. It serves as food, fodder fuel, medicine, shelter etc. The forest cover in the developing countries in the Asia and Pacific region has the largest share with 79 percent. The remainder is distributed between Latin America and Caribbean countries (13%) and African countries (8%). According to the latest report from WWI, forest cover has declined significantly in both area and quality in the last fifty years. Almost half of the forest cover of about 3 billion hectares has disappeared. Records give a picture that nearly 200 million hectares of tropical and temperate forests have been moved out between 1980 and 1995 alone. Forest and trees contribute livelihood of the poor in five major ways; by satisfying subsistence needs for forest products and service; by playing a role gap filler or safety net in times of food shortage; by generating income through forest harvesting, marketing or processing; by providing inputs to farming and animal husbandry and by empowering people through the community ownership of this most important resources. For sustaining forests for improving life status, it is necessary that the factors that affect forest biodiversity have to be properly identified and appropriate measures have to be initiated to overcome such problems.

The fish are the most species -rich vertebrate group with an estimated 32,500 species. Among this 43% of species are found in freshwater habitats, such as lakes and rivers. Changes in

biodiversity due to human activity were more rapid in the past 50 years than at any time in human history. From the available reports it is seen that the average decline of species abundance was about 40% between 1970 and 2000.

Fisheries and aquaculture is gaining exceptional significance all over the world, and the production potential reported through improved / new technologies is highly encouraging. Aquaculture has been developed as alternate methods to capture fisheries and the production potential emerged out of aquaculture technologies is highly significant. Fisheries provide ample livelihoods and employment with quality protein in order to achieve food security and poverty reduction. Current global economic crisis, food price volatility and increase in weather events constitute global challenges to fisheries and aquaculture sector. Fisheries and aquaculture support the livelihoods of about 540 million people. Substantial declines in inland fishery resources have been caused by irresponsible practices, habitat degradation, over exploitation, pollution, reclamation.

Though this sector is contributing significantly for food production, alleviating poverty and malnutrition, generating income and employment, yet this sector has not well developed in many developing countries. Aquaculture thus has to play a significant role for imroproving the nutritional scenario in developing countries. For this the biodiversity potential of fish species of such countries have to be spotted out and action to be initiated to bring these fish biodiversity under the grove of aquaculture for enhancing the productivity besides sustaining the life of poor fish farmers. In order to sustain fish biodiversity, it is mandatory that improved awareness and appropriate action are required to conserve aquatic ecosystems and safeguard the resources that form the basis for fish food production.

Based on the above background this paper is presented to provide a general outlook on the link between biodiversity and sustainable development with case studies from different parts of the world. However, certain cases from Ethiopia are highlighted as Ethiopia is one of the hot spots of biodiversity.

MAGNETORECEPTION IN BIRDS

By Fleissner, Ge.*, Fleissner, Gue.*, Bali, G. °, and Falkenberg, G.+

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It is long known that birds are capable of sensing the Earth's magnetic field and use this sense for example, for navigation during their yearly north-south-north migration in spring and fall, and for preparing their metabolisms for a long lasting period of food deprivation during their migratory route. The receptor system responsible for this function has, however, long been enigmatic. For birds, two hypotheses have been worked out in the last years: one mechanism, a magnetic compass, based on a conformational change of Cryptochrome, is proposed to be located in the avian retina, a second mechanism, a magnetometer, based on magnetic crystals in sensory dendrites, has been identified in the avian upper beak by our team.

Our contribution will deal with the second mechanism, the iron-based magnetoreceptor. The data are compiled in an interdisciplinary project by neurobiologists, cell biologists, nuclear and theoretical physicists. Histology on the light and electron microscopic level, combined with micro-X-ray analyses in synchrotron institutions revealed a - so far - unique structural candidate for an avian magnetic field receptor in various bird species. Within certain sensory dendrites of the Ramus ophthalmicus medialis (ROM) of the trigeminal nerve magnetic iron crystals, maghemite and magnetite, are localised in subcellular compartments: (1) bullets (diameter 1 μm) consisting of 6 nm thick nanomagnets adhere to the cell membrane; (2) several short chains of monocrystalline platelets (1x1x0.1 μm) are aligned along the terminal dendrites; (3) a vesicle surrounded by an iron crust lies in the middle of the terminal dendrite. Based on these data and nanomagnetic considerations we suggest a functional model on the transduction of the magnetic field into receptor potentials, in which each dendrite can sense the magnetic field in one direction only. As the dendrites occur in 2 bilateral sets of three separate fields, each with a different

spatial orientation, the entire system allows for the complete measurement of the 3-dimensional magnetic field. In the central nervous system this peripheral information is evaluated as the local magnetic field vector, independent of the bird's head position or movement, it may be used as a biological GPS system. Manifold behavioural experiments and mathematical simulations have corroborated our magneto receptor model.

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FUNCTIONAL FOODS IN HEALTH AND DISEASE

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Rodents are widely used to understand human physiology and pathology. Our first aim was to develop a rat model of diet-induced metabolic, cardiovascular and liver changes that mimicked the human metabolic syndrome. Male Wistar rats were fed a high carbohydrate/high fat diet containing condensed milk (39.5%), beef tallow (20%), fructose (17.5%), rat food (15%) and minerals (1%) supplemented with fructose (25%) in the drinking water, for 16 weeks; condensed milk, beef tallow and fructose were replaced by corn starch in control rats. The high carbohydrate/high fat diet increased body fat mass, systolic blood pressure, heart weights, abdominal circumference, visceral fat pad deposition, glucose tolerance after oral glucose loading, infiltration of inflammatory cells in left ventricle and liver, cardiac collagen deposition, left ventricular diastolic stiffness, liver collagen deposition and plasma liver enzyme markers. This diet then mimics most of the symptoms of the human metabolic syndrome, including hypertension, abdominal obesity, glucose/insulin intolerance, fatty liver and inflammation.

Nutraceuticals and functional foods have been used for thousands of years to treat human disease, including the symptoms of the metabolic syndrome such as obesity, diabetes, hypertension and liver dysfunction. Our second aim was to determine whether these diet-induced symptoms could be reversed by supplementation with purple carrots, curcumin, rutin, piperine, chia seeds or olive leaf extract containing oleuropein and hydroxytyrosol as additions to the diet for 8 weeks starting 8 weeks after the diet was initiated. Treatment prevented or attenuated these cardiovascular, metabolic and liver changes, although curcumin and olive leaf extract did not lower blood pressure significantly. The interventions prevented inflammatory cell infiltration into the heart, liver and fat pads, and decreased plasma inflammatory biomarkers. These results strongly suggest that functional foods reverse the chronic low-grade inflammatory state that induces the cardiovascular, metabolic and liver signs in this rat model of diet-induced metabolic syndrome.

'ENHANCED RURAL LIVELIHOOD THROUGH LIVESTOCK HEALTH MANAGEMENT'

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India is endowed with huge and diverse livestock breeds that significantly contribute to 23% of the national agricultural GDP. Livestock sector receives only about 2.5% of the public expenditure, which is much less than the contributions made by small ruminants alone to the total value of output of the livestock sector. This sector will play a significant role in the coming decade in impacting the livelihoods security and as an insurance cover to cope with crop failures particularly for rural landless, small and marginal farmers.

Livestock sector is a major provider of animal proteins for human consumption in India. Per capita consumption of meat presently is only 5.4 kg/year compared to 33kg/year in the developed countries. Current availability of animal proteins (10.8gms/day/capita) is just half of the daily requirement of (20 gm/day /capita - targeted to achieve by the year 2020.

The rural poor communities prefer rearing sheep, goats, pigs and backyard poultry over dairy cattle and buffaloe keeping because of low investments, easy to raise and manage funds, low feed requirement (compared to cattle) , ability to thrive on different feed and fodder, high disease resistance, and superior market and profit potential.

Some of the limitations and challenges in marginal farmer livestock production system are inadequate/limited availability of animal health services and poor infrastructural facilities leads to heavy economic losses due to high mortality. If organized efforts are undertaken to improve the preventive and curative livestock health services by timely vaccinations for diseases like Peste de Petits Ruminants (PPR), bluetongue enterotoxaemia and sheep/goat pox in small

ruminants, classical swine fever in pigs and Newcastle disease in poultry can enormously improve economic gains to farmers.

Studies show that during the period 1991- 2005 sheep and goat mortality due to PPR, sheep and goat pox, enterotoxaemia and contagious caprine pleuropneumonia was 74% and economic loss in goats alone was Rs. 264.8 lakh ($5.8 lakh), with PPR contributing 37%.

Eradication of Rinderpest from India and the world (first animal disease to be globally-free and the second after human smallpox) has provided huge impetus for major livestock diseases control initiatives - which are bound to immensely benefit the rural poor.

The national control / preventive programmes for these diseases by Govt of India will be presented. Issues related policy matters, vaccine requirements, and preventive health support, delivery system, cold chain management and disease reporting will be discussed briefly.

SCIENCE & TECHNOLOGY FOR WATER SECURITY IN INDIAN CONTEXT

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The world is not facing a water crisis because of actual physical scarcities of water but there may be a water crisis in the future because of widespread and continuous mismanagement of water. Even for the very arid regions of the world, there should be no water crisis, provided the available water resources are managed prudently and efficiently. Likewise, present water crisis in India is mainly not because of physical scarcity of water but because of inadequate or inappropriate water governance (& management practices), institutional arrangements and socio-political conditions. Growing demand across competitive sectors, increasing droughts and floods, declining water quality (particularly of groundwater), and inter-state river disputes, inadequate institutional reforms and enforcement are some of the crucial problems faced by the country's water sector. Emerging challenges include concurrent management of existing infrastructure and of the demand and supply scenario of the water resource itself, especially in view of the climate variability.

Application of technology in solving water shortage problem in a region can serve three purposes- assessment (exploration) of the resource, monitoring of changes in quantity and quality in space and time, and for specific interventions (e.g. water purification, desalination, wastewater treatment, water harvesting, groundwater recharging, efficient irrigation, soil moisture conservation, evaporation control). Effective solution to the water shortage problem in India lies

in tackling both the supply and demand side, and should start with identification of users' actual needs at different locations and proceed with the identification and mapping of appropriate technologies and associated systems to provide the desired solution. While planning for a water supply system, status of existing supply as well as potential of future utilization from different sources should be taken into consideration. To solve his water shortage problem, the user needs a total solution, which is appropriate, affordable and sustainable. Selection of appropriate technology for such applications assumes great importance. Besides providing immediate solution to the emergent problems in identified locations, the country would also need some long-term technology interventions to facilitate mitigation and solution of water scarcity problems on sustainable basis.

A sound technology-based solution to the water shortage problem in the country lies in tackling the issue using a holistic approach. A competent team of specialists covering various disciplines and local communities would be required to implement the solution in a time bound manner. The paper presents the issues of water shortage in the Indian context and outlines the potential of science & technology in achieving the water security.

TECHNOLOGICAL ADVANCEMENTS! PAST EXPERIENCES FUTURE CHALLENGES FOR HEALTH AND ENVIRONMENT

Qamar Rahman

Visiting Professor Rostock University, Germany

Science and technology are the main components for, economic, and social development and globalization.

Technological development on one hand is responsible for the improvement in the quality of life, but on the other hand, if proper safety evaluations are not applied before their use, they may have serious adverse health impact not only on the health of exposed population, but also on the related environment.

During various technological revolutions as agricultural, industrial and biotechnological, and the most recent nanotechnological, fibers/particles/nanoparticles have become a part of these revolutions. They were emitted knowingly or unknowingly from various sources.

Among fibers come asbestos, technical use was introduced in 1878. Commercially it was used in thousands of products and industrial applications all over the world. Because of its fire resistance, high tensile, strength and durability, asbestos was used in the construction industry and its breakdown products created a major health hazard even in public schools. Several diseases including the malignant mesothelioma of the pleura and peritoneum, pulmonary fibrosis and cancer of the lung are caused by asbestos exposure. However, these diseases caused by asbestos were identified only after a long latency period[1].

The novel and rapidly growing field of nanotechnology, using engineered and artificially synthesized nanoparticles (NPs), currently expands to another cardinal source of man-made NP exposure. It is the science of extremely small particles (app 1-100 nm range), revolutionized the field of engineering, electronics, medicine, information technology etc., mainly because of their extreme surface area and the resulting high activity. Present studies suggest threats to human health and environment[2].

The great speed at which new engineered NPs are being manufactured far exceeds the potential avenues, abilities and resources available for their parallel scrutiny of physicochemical

analysis and investigation of their possible toxic health effects. Among the several types of engineered nanoparticles, Carbon Nanotubes (CNT) has become one of the most promising nanomaterials in many industrial and biomedical applications. Due to their unique physicochemical properties, interest is growing in the manufacture of CNT-based products and their subsequent marketing. Assessment of risks to human health and adoption of appropriate exposure controls is critical for the safe and successful introduction of CNT-based products. The growth and use of this material without prior human health evaluations challenge society with the possibility that CNT could become the "asbestos of the 21st century".

Multiwalled Carbon Nanotubes (MWCNT) with several similar properties to that of asbestos such as durability and high tensile strength resulting in multitude of applications in industry and medicine. Several in-vitro / in-vivo studies have already demonstrated that exposure to MWCNT causes acute inflammation, oxidative stress, and a rampant granulomatous fibrotic response associated with molecular changes[3]. It was also reported that MWCNT are biopersistent in the lung and are translocated to sub-pleural areas and induce mesothalioma.

In my presentation, I will discuss the problems faced by asbestos, toxicity and future challenges of nanoparticles especially carbon nanotubes, along with my own findings.

The presentation will also discuss the issues of evidence based safety policies on nanotechnologies.

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ABSTRACT FOR INDIAN SCIENCE CONGRESS

Dr Chitra Rajagopal

Sc 'G' and Associate Director, CFEES, DRDO, Delhi

Family and Educational Background From the earliest years that I can remember, Science was a living breathing entity in my family. Discussions at the dinner table would invariable revolve around some aspect or other of Science. So it was a given, that I, would opt for some branch of Science/ Technology. After completing my Bachelors at the Deptt of Chemical Engg and Technology, Panjab University, Chandigarh, I joined for PhD in Chemical Engg Deptt, IIT Delhi. The years spent in the two institutions were invaluable, and laid the foundation for my future career as a Chemical Engineer. I owe my interest and motivation in my work to some of the finest and dedicated teachers there.

Doctoral Research : My doctoral work on Heat Pipes was appreciated in the scientific circles with an acceptance of my paper as the opening paper of the First International Heat Pipe Conf in Grenoble, France, invitations to present a paper in 2nd International Heat Pipe Conference in Minsk, Russia and for Thermal Science openings in Wright State University, Dayton, Ohio.

Professional : A Chemical Engineer by profession, and with a doctorate in Heat Transfer from IIT Delhi, I joined the DRDO in 1988 as Scientist 'C', after a brief stint as a Technical Consultant in the Bureau of Industrial Costs and Prices.

Contributions in R&D :

i. Design of combustors / Heat transfer equipment for MoD applications: In the first few years at DRDO, with my background in Heat Transfer and Fluid Flow, and using the analytical and computational skills gained during my doctoral work, and starting with rate equations and chemical kinetics, I carried out simulation & modeling of Combustors for use in Gas Dynamic Lasers, which resulted in their optimal design and also provided inputs for up-scaling of the system. Laser mirror cooling using flat heat pipe design and Raman based Blue Green Lasers were other successfully completed projects where my expertise in the area of Heat Pipes added value.

ii. Evolution of Lab Charter : As one of the founding members of the Centre for Environment and Explosive safety (CEES), I had the opportunity of working with distinguished scientists to evolve the charter of duties of the Centre, as well as planning the experimental and

infrastructural facilities for environmental and explosive safety; interacting with the Ministry of Environment and Forests to get CEES nominated as the nodal agency for implementation of environmental rules & regulations in MoD establishments; recognition of the lab as a Centre for Environmental Analysis as per GoI notification and personal recognition as a certified analyst, and, providing DRDO inputs in the formulation and amendment of the MSIHC Rules under the EPA act.

iii. Infrastructure planning: Planning and Setting up of the following facilities Environmental Monitoring and Hazard Evaluation Labs, Simulation and Modeling facility, Pilot plant facilities, Test and calibration facilities for instrumentation

iv. Development of Eco-friendly technologies for MoD: To address the explosive safety/ waste management / environment safety problems faced by DRDO / Ordnance Factories/ Services, a number of eco-friendly materials/ processes/ technologies were developed and innovative designs/ operational schemes/ software/ safety management techniques, were generated. My young and motivated team of scientists has come out with creative solutions to problems specific to Defence sector. Keeping in view the requirement for energy security in Defence and the need for sustainable carbon neutral energy technologies, work on generation of hydrogen from bio-fuel in compact, on-board reformers has been taken up.

v. Addressing the Ammunition Storage Needs of the MoD Stakeholders: A number of innovative technologies (LRC Igloos, Unit Risk principle based explosive store houses, Underground Storages) and management initiatives (Quantitative Risk Assessment), have been undertaken to address the following emergent needs of the MoD Users.Comprehensive storage solutions have been provided to Army and Air Force based on site visits and assessments. Full scale instrumented blast trials have been conducted to validate the CFEES designs of explosive storehouses and to refine the non-linear dynamic models predicting blast effects on structures.

vi. Transfer of Technologies to Civil Sector: The technologies developed could be patented and resulted in spin-offs to the Civil sector, thus enthusing the team further. Some of the technologies have been selected / transferred under the DRDO-FICCI-ATEC programme for global commercialization.

vii. Application of Risk Assessment techniques to HAZCHEMs in Defence: A quantitative approach to probabilistic analysis has been evolved, resulting in Risk values which could be compared with Internationally acceptable standards, and a Sensitivity analysis which

helped provide inputs for decision making in prioritising safety measures and Emergency planning.

viii. R&D activities/ consultancies provided in the areas of Risk and Hazard Analysis & Disaster Management (disasters involving Fires, Explosions and Toxic Releases), Hazchem & Hazwaste management, Environment Impact Assessment and Safety Audit, occupational Safety, Hazard classification of ammunition & explosives, safe disposal of obsolete/ rejected ammunition, accident investigation

ix.Application of Learnings from Training Programmes and Visits : I was introduced to the concept of working in cross-functional groups and learning to build teams and work in a multi-disciplinary and multi-cultural milieu to arrive at solutions to environmental problems at the local, regional and global levels. The application of principles and lessons I learnt during these International and National level training programmes, specifically the Leadership modules, team development and project management modules, effected the formation and deployment of highly effective project and functional groups and teams.

x. Contributions to meeting national obligations under International conventions:

My contributions to meeting the national obligations under various International conventions including the Chemical Weapons Convention, UN Committee on Transportation for Hazardous Goods, and meeting DRDO obligations under National acts and regulations including the MSIHC Rules, PLI Act, Crisis Management Rules, included conduct of EIA/ RHA studies, evolution of Environment Management Plans and Safety Plans, compliance monitoring, participation and contribution in design reviews, assessment of competing technologies, training of International and National inspectors, presentation of DRDO/ India's contribution in International and national for a. Sensitisation of DRDO labs and other MoD establishments (Ordnance Factories, Services) through training / lectures / technical literature and advice rendered on specific issues to meet their obligations under the various Acts and rules.

xi. Regulatory : The group I head is also entrusted with both explosive and environmental safety regulatory activities and compliance monitoring in MoD, (Army, Navy, Air Force, Ordnance factories, DRDO labs, Defence public sector undertakings, quality assurance estts)

xii Capacity building : Planning and setting up of facilities and creation of expertise and skills in the areas of preparation and characterization of special polymers, reforming catalysts design, Composite materials, fabrication and testing against blast loads; blast instrumentation;

modeling and simulation of non-linear dynamic phenomena; EIA/ RHA tools; Experimental hazard evaluation of hazardous materials..

xiii. Human Resource development : To meet the aspirations of young scientists of the team, continuous efforts have been made to get them enrolled for PhD/ acquire higher qualifications in reputed academic institutions. This has resulted in a number of PhDs granted from reputed academic Institutions in the past years. Creativity/ innovation, paper publications/ patents are encouraged, resulting in a record number of innovations, publications from the group in high impact factor journals and the filing of patents.

xiv.Knowledge dissemination : A number of initiatives have been introduced for effective and speedy dissemination of the knowledge created and compiled, which have been well appreciated. These include Preparation of User friendly documents, Conversion of explosive safety regulations codified in 25 pamphlets, to an electronic format, Formation of Study groups with MoD User, to address their specific issues, Organisation of Lectures/ training programmes for sensitizing MoD establishments on relevant safety issues.

xv. Academic Contributions : Over the years, expertise has been sought by International and national bodies and I am an expert member of various National and MoD/ DRDO Committees. I have also been associated with the recruitment and assessment process in DRDO, over the past 12 years. I have been nominated for the last five consecutive years by Marquis Who's Who in Science and Engineering, and for Tech Museum awards for use of technology to benefit humanity in the field of Environment. I was awarded the DRDO Scientist of the Year award for 2010. I have been invited to talk in various International and national fora and am a recognized Guide and examiner for PhD/ MTech in a number of academic institutions. I have also had occasion to organize National level and Organisational level training programmes and workshops.

The last 24 years at DRDO have been eventful and have offered rich opportunities for research in areas having direct application for MoD. In order to meet Services requirements, my team and I have visited Depots and establishments located in all remote corners of the country. The management of large scale field trials enabled the interaction and co-ordination with multiple agencies.

In all these efforts, I have been guided by certain luminaries both within and outside the organization, who served as inspirational role models

LONG RANGE MISSILE SYSTEMS - TECHNOLOGY BREAKTHROUGH

Tessy Thomas

Scientist 'G' & Project Director, Agni

Advanced Systems Laboratory, Defence R&D Organisation, Hyderabad

Missile Systems can be broadly classified into Strategic and Tactical Systems. Missile Programme of DRDO has a wide reach ranging from a few kilometer 'Nag' missile to Thousands of kilometer 'Agni' missile systems. Strategic Systems play a vital role in the country's defence and to provide a minimum deterrence against external threats. Basic design drivers for a Strategic missile system are many, the primary being the range capability, accuracy, survivability, mobility and anti-ballistic defence capability, which forms the design specifications.

The primary component of this system is Propulsion stages. The stages of rocket motor are propelled either by solid or liquid propulsion systems, which have their own merits and limitations. A new guidance scheme was designed and evolved for Agni solid propelled system, which gave a technology breakthrough in establishing long range explicit guidance system with high accuracy. This guidance scheme is used in all the Agni series.

Mission Design of a strategic missile is the most challenging field which includes the mission sequencing. The main features of mission sequencing are event based decision making, backup time for critical events and software interlocks between events. Design of strategic missions is a confluence of scientific and mathematical formulations, statistical techniques, engineering concepts, numerical simulations and threat analysis, involving a tremendous effort of multi-disciplinary optimization at all phases of design. Mission design culminates from many design conciliations by careful optimizations of configuration design, to achieve a final system that meets the overall system requirements.

On ground the performance prediction is essentially done before flight in six Degree of freedom trajectory simulation. The real time simulation is performed in OBC-In-Loop simulation and hardware in Loop simulation (HILS). Missile trajectory is simulated in a 6-DOF environment

and performance of the system such as flight loads, aerodynamic and wind dispersions are evaluated for design of flight control systems. This simulation is also used to interpret the flight data and reconstruct the flight events by plugging in the flight data. Hence 6 DoF Simulation is an efficient mathematical tool which is used right from a system design, validation of Control & Guidance algorithms to realization of a mission and also after flight for post flight analysis.

DEVELOPMENT OF HIGH TEMPERATURE COMPOSITES FOR STRATEGIC APPLICATIONS

Smt. G. Rohini Devi, Sc 'H'

Design and development of Aerospace Systems operating in hypersonic environment pose extraordinary challenges to material Scientists and Technologists towards developing high temperature and ultra high temperature materials. The rapid change in temperature of the vehicle during flight environment induces severe thermal stresses with surface temperatures reaching upto 3000 degrees Celsius. Materials and structures are the key elements in determining the reliability and performance of such systems. Material erosion due to high aerodynamic shear has to be minimized with suitable material architecture.

A family of high temperature composite products with carbon and ceramic matrix have been designed and developed to meet the thermal, thermo-structural and other functional requirements of end products. Key technologies developed include multi-directionally reinforced fibre architectures, perform densification technologies and product design, development and testing. Challenges associated in developing highly process intensive technologies and facilities are addressed.

HARNESSING REMOTE SENSING TECHNOLOGY FOR NATIONAL NEEDS - AN EXPERIENCE

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The planet Earth could be viewed in its totality only after the launch of Satellites into Space. Over a span of four decades, the space borne remote sensing capabilities have grown to such an extent that space based observations have become the prime source of information on earth's resources and it's environments, enabling a host of applications related to the protection of our planet Earth. Space has become an attractive arena for remote sensing due to its unique features. It enables synoptic observations of large areas on a repetitive basis with unparalleled speed; over even remote inaccessible areas. In view of several beneficial applications, ISRO put considerable emphasis on realizing an operational remote sensing programme, with strong accent on societal needs. Significant progress has since been made in reaching the benefits of this technology to the grass root level, thus making the Indian remote sensing programme, one of the widely acclaimed efforts, world over.

THE BEGINNING:

During 1980 ISRO embarked on the first operational Indian Remote Sensing (IRS) programme IRS-1A. On the ground segment there was a need to work out the detailed specification

requirements for the design and development of the front end hardware, a very critical unit for Frame Synchronization and De-commutation of serial data from the satellite in real-time. The Quick Look System (QLS) facilitated the visualization of the raw data on the display systems in real-time during the satellite pass, which was realized using a microprocessor based hardware. The major challenges were realization and qualification of the systems with simulated data leading to a fully operational system, validated with actual data after launch in 1988. This was followed by the launch of the IRS-1B in 1991, later second generation satellites IRS-1C, IRS-1D with enhanced resolutions were launched as follow-on to these satellites, and thereafter application specific satellites such as Oceansat, Resourcesat etc., gained prominence.

Enabling Data Exploitation:

Commensurate with the developments in satellite technology, there was a need to plan infrastructure for effective utilization of the satellite data. In order to optimally utilize the data from various Indian Remote Sensing satellites for various applications, a National Natural Resources Management System (NNRMS) was setup in which several user Ministries/ Departments of Government participated in planning the use of space based remote sensing in their respective fields. Visual interpretation techniques were then predominantly used for identification of objects and classification from photographic prints based on the image characteristics. With the advent of computers, the digital processing and analysis techniques gained momentum in view of its inherent advantages which facilitated using various advanced techniques for enhancing the interpretability for mapping purposes.

Considering the need for enabling users to use the digital techniques for resource mapping, under the aegis of the NNRMS, five Regional Remote Sensing Services Centers (RRSSCs) geographically distributed to cater to the different regions, were established. In addition, four associate centers were also operationalized. As the leader of the team for establishing these centers, the challenges faced were multifold. It involved planning of the infrastructure, finalization of system configuration and sizing of the systems based on the throughput requirements, evaluating the various image analysis software packages, finalize and operationalize the same. The total qualification procedures had to be formulated and audit of the procedure and results finalized. A number of application specific software packages were developed and installed at these centres.

The digital analysis methodologies were developed for various national applications projects such as the generation of normalized differential vegetation index imagery for the whole country on a regular basis (fortnight) basis for various software packages such as the Drought Mission, land use/land cover mapping, crop acreage and production estimation, forest change detection, command area monitoring etc. All the nine centers were fully operationalized during 1985-87 linked with the launch of IRS-1A in1988.

While remote sensing data was operationally being utilized for mapping various resources, the need was integrating these resource maps with other socio-economic data for generating action plans. Availability of an indigenously developed GIS package was of utmost importance. Spearheaded the development of a raster-based GEOSPACE package and planned its usage at various user agencies. This culminated in organizing the National Resources Information system (NRIS) across 34 districts, spanning 17 states in the country. The challenge was to evolve a standard for the classification schemes for the database layers in close co-ordination with the user community.

Concerted efforts were put to conduct training programmes for the user departments both at district and state levels. Creation and validation of the GIS databases, integration of the software models and generation of action plans on the click of a button for the decision makers was an uphill task which was successfully achieved.

Turnkey Solutions:

The efforts on usage of remote sensing technology for Natural resources survey opened up a new frontier for strategic applications. This paved the way to provide end-to-end solutions from data reception to processing and analysis. Most importantly the entire processing had to be time critical. This resulted in a new paradigm shift in the data processing approach. While conventionally the processing systems were satellite specific, now it called for an integrated multi-mission approach. The technological advances in computers and communication facilitated exploitation of high performance computing techniques which enabled the data readiness in less than two hours. Emphasis was predominantly on automation for change detection, time series analysis floods inundation estimation for relief operations, early warning systems to plan precautionary measures to reduce the risks and damages, etc, all in near real time. Creation of

seamless large databases to meet the National needs warranted quick turn around time for data products. The state of the art Grid computing methods were effectively exploited for this purpose and successfully utilized.

The next leap during the last couple of years was harnessing of the GP/GPU technology. The challenges were enormous as it called for re-engineering the programming approach to optimally utilize all the cores with a major thrust on parallelizing. The results were very encouraging. This in conjunction with 3G network provided a breakthrough in dissemination of the data in real time on to a PDA / iPAD, which could be with a field personnel in remote areas to meet emergent needs was a major stride forward. This is the first of its kind realized in the country for multi-mission real time processing and dissemination.

Future Direction:

While great milestones have been achieved in the areas of application of satellite based remote sensing technology to meet the day-to-day needs of the Nation, the continuous advances in satellite technology and increasing satellite constellations pose a major challenge to the exploitation approaches. The volume of data that needs to be handled would call for better performance systems both on-board and ground systems, newer techniques in data analysis, and higher bandwidths for data dissemination.

FUNCTIONS OF VIRAL ENCODED INTRINSICALLY DISORDERED DOMAINS / PROTEINS

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Intrinsically disordered proteins / domains lack a well defined tertiary structure, although they may contain residual secondary structural elements. Such domains often attain folded conformations upon interaction with specific target proteins or ligands. Higher structural flexibility of these domains allows interaction with a large milieu of targets and thereby permits regulation of a number of biochemical processes. Viruses, which have very small genomes, have adopted the strategy of coding for intrinsically disordered domains to regulate the function of their own proteins as well as those of the susceptible host. Such disordered domains tend to be rich in charged amino acid residues and contain relatively lower content of hydrophobic residues. They have characteristic CD spectra and exhibit abnormal behaviour when examined by size exclusion chromatography.

Several viral genomes have a covalently linked protein domain (VPg) at their 5' end. The VPg domains of both Sesbania mosaic virus (SeMV) and Pepper vein banding virus (PVBV) are interesting examples of intrinsically disordered domains. These polypeptides interact with a repertoire of proteins and regulate multiple processes vital to virus propagation and multiplication. The VPg domain is covalently linked to the C- and N-terminus of the respective protease domains in SeMV and PVBV. We have carried out extensive investigations on how the interactions of the VPg with the protease domain influence the structural and functional characteristics of the two domains. The protease and VPg domains of these viruses, as well as the fusion polypeptides SeMV protease-VPg and PVBV VPg-NIa and their mutants have been over expressed and purified. Functional analysis of these recombinant proteins clearly demonstrates the importance of interaction between the intrinsically disordered VPg and the folded protease in modulating the function of both of these domains.

In SeMV, the inactive protease is activated by the covalently linked VPg domain. The crystal structure of the protease shows a well-formed active site and an oxyanion hole as in

chymotrypsin like proteases and yet the protease requires VPg as a C-terminal fusion domain to be catalytically active. Interestingly, addition of purified VPg *in trans* to the protease does not activate the latter. Our results suggest that aromatic stacking interaction between Trp43 of VPg with Trp271 and His275 of the protease is responsible for this activation. In contrast to these findings, the same VPg domain, when present at the N-terminus of RNA dependent RNA polymerase (RdRp) renders it less active.

PVBV protease domain is active as an isolated protein. However, its activity is enhanced by the presence of VPg *in cis* as well as *in trans.* VPg interacts *in vitro* NIa-Pro that results in the quenching of the intrinsic tryptophan fluorescence of the NIa -Pro. Analysis of the structure of protease obtained by homology modelling reveals that Trp143 is the only surface-exposed aromatic residue present in the protease domain. It occurs on the W-C loop which also contains the active site residue Cys151. This loop has been earlier shown to be crucial for interaction with the incoming substrate and products. Additionally, we have shown that Trp143 is hydrogen bonded to Ser129 of NIa-Pro. Ser129 gets phosphorylated by host cell kinases and thereby abrogates catalysis. Interaction of VPg with NIa-Pro prevents phosphorylation of Ser129, as the residue is in the close proximity of Trp143. Molecular dynamics simulations of the wild type and S129D NIa-Pro, the phosphorylation-mimic mutant of the protease, have shown that the W-C loop undergoes gross structural changes when compared to the wild type protease, with the result that Cys151 in the mutant is flipped away from the active site accounting for the loss of protease activity. Trp143 might also influence the orientation of Cys151 by its interaction via His142 and His167. These residues undergo concerted movements during the simulations. Therefore, conformational changes that take place at the surface (Trp143) in the presence of VPg can be relayed through main-chain interactions along the W-C loop or via His142 and His167 to the active site pocket (Cys151). This in turn could influence catalytic activity of the protease.

Interestingly, PVBV VPg acquires a new function upon interaction with the protease domain. The cleavage site mutant of PVBV VPg-Pro, E191A VPg-Pro is capable of hydrolyzing ATP whereas the individual VPg and Pro domains cannot. This is the first example of disordered domain assuming an altered /ordered structure upon interaction with a globular domain that makes it an ATPase. Infact, addition of NIa-pro in trans also results in a functionally active ATPase. Analysis of the amino acid sequence of PVBV VPg revealed the presence of Walker A

and B motifs, commonly found in nucleotide binding proteins and ATPases. Mutation of Lys47 of walker motif A and Asp88:Glu89 of walker motif B to alanine resulted in the loss of almost all ATPase activity in E191A VPg-Pro confirming that the ATPase function is inherent to the VPg domain and is induced only by its interaction with the protease domain. Further, the structural characteristics of VPg were altered upon interaction with the protease domain. The presence of the folded globular NIa-Pro domain at the C-terminus stabilizes the PVBV VPg structure which manifests as an ATPase. This could have important implications in several crucial steps in the viral life cycle. Until recently it was believed that disordered proteins act as hubs and provide platforms for interaction with proteins from multiple convergent pathways while ordered proteins are crucial for enzymatic activities. Our results show that disorder-to-order transitions of VPg could lead to a catalytically active ATPase. Thus, the disordered segments of viral encoded proteins play crucial structural and functional roles and regulate the functions of neighbouring folded domains.

THE ENIGMA OF HUMAN LEPROSY

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Leprosy is an ancient disease which mainly affects the skin and nerves of man. It is the only bacterial infection that affects the peripheral nerves thereby leading to loss of sensation and causes ulcers in the limbs. It is caused by *Mycobacterium leprae* a close kin to the tuberculosis causing organism and is not cultivable in the laboratory. Both these bacteria hide within macrophages thereby escaping attack by antibodies of the host. Of interest to immunologists has been the fact that the disease presents in 5 different forms by symptoms, signs and histological features even though all forms are caused by infection of same organism. This clinic-pathological spectrum consists at one end of localized skin patches with nil or few bacteria called tuberculoid leprosy and at the other end by generalized disease called lepromatous leprosy affecting most of the skin and other organs and characterized by a high load of detectable bacteria. In between these polar types which are stable are also 3 forms of leprosy which are unstable and called borderline leprosy. In addition, leprosy patients develop episodes of fever, joint and nerve pains which are clinically serious and need immediate intervention by the doctor. These are of 2 types, type 1 or reversal and type 2 or erythema nodosum leprosum reactions. These various forms of leprosy are thought to be due to the immune response of the host and not due to differences in the pathogen. Since the bacilli are not cultivable, it has not been possible to understand the organism till the genome of the organism was published and the armadillo was shown to be a large reservoir of bacilli after infection with the human strains. Recent evidence from Mexico suggests that the organism causing severe reactions has DNA sequence differences which may put it in another category to the classical organism.

Of interest is the fact that whereas the patients with localized disease have low antibodies and high cellular immunity by T cells, those with generalized disease shows the opposite. Intriguingly, such patients can recognise other organisms and mount an immune response but are unable to *recognise M.leprae* even after treatment. This T cell decifit which is exquisitely

antigen specific would be the focus of my talk. In addition, it has been shown by our group that such patients can recognise the organism when they develop reactions. This recognition wanes off after the episode is controlled by drugs. In order to address the question of whether we can stimulate the immune response in the lepromatous group we also looked at cytokine therapy with interferon gamma one of the cytokines which we and others had shown earlier to be lowered in lepromatous patients and which is required for killing intracellular bacteria. As suspected this cytokine was able to kill bacteria in the patients faster than the muti drug therapy currently used. Thus it is possible to combine cytokines with drugs to treat patients in a shorter time. Due to its cost this cytokine is considered not to be useful on a large scale.

The conventional model for studying drug resistance and therapy efficacy was the mouse foot pad model which used to take 9 months and required air conditioned facilities with constant electricity, features which are not always available in countries which have the disease. Taking a clue from GPTalwar's initial report our group developed an in vitro model which maintained organisms from patient's skin biopsies in human or mouse macrophage cultures and studies their viability using radio-labelled markers.This assay took 2-3 weeks and was amenable to studying drugs and viability of organisms. To understand the organism of leprosy better we developed strategies to study the *M.leprae* lambda gt 11 expression library. Using patients sera we identified Lsr 2 gene which mimicked the native bacillus in immune responses and were able to identify the amino acid sequences that were identified by antibodies and T cells of the patients. Moreover we were able to show the type of cytokines that were important for the immune response against the organism. This also provided clues for predictors of reactions.

Since the peripheral nerve was a target of the bacillus and it was involved in reactions we wished to find ways to predict reactions or find therapy efficacy in a non invasive manner. Using color Doppler high resolution sonography Suman Jain showed thatthis methodology was useful in patients for both diagnosis and for monitoring treatment. Thus using a muti pronged approach of immunology, molecular biology, tissue culture and ultrasonograpghy our group has been trying to understand the basic immune-biology of this disease as well as provide possible tools for the clinician.

ABSTRACT FOR INDIAN SCIENCE CONGRESS

Nabanita Radhakrishnan

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A Scientist's Journey in DRDO

Science & Technology plays a pivotal role in determining the trajectory and projected course of a nation. Part of the S & T requirements of India is met by DRDO-One of modern India's largest R & D organisation. DRDO's mission is to design & develop state-of-art defence systems and technologies and to provide technological solutions to the Services while developing infrastructure and committed quality manpower. For its over 25,000 personnel DRDO offers a multitude of scientific,technologicaland techno-managerial challenges which are a feast for the fertile minds of its enthusiastic workforce.

This presentation describes the journey of one such scientist who has travelled up the ladder.

As a young scientist inducted into DRDO in the early eighties she had the good fortune of working for two of DRDO's biggest programs - the Main Battle Tank (MBTArjun) and the Light Combat Aircraft (LCA Tejas). In the MBT Program, she worked for the evaluation of all major subsystems of the MBT- the engine, suspension and transmission. This was the first exposure to a massive combat platform with every sub-system bigger than life, which necessitated development of a continuous learning curve, working with newer and cross technology domain- a confluence of hydraulic, mechanical, electronics, and control system knowledge. This resulted in the setting up test and evaluation centres and carrying out assessment of the operational capability of imported and indigenous sub-systems. The next major activity was challenging task of development and qualification of the Aircraft Mounted accessory Gear box for LCA- India's indigenously developed combat aircraft.She was instrumental in assessing the system requirement and developing state-of-the-art Test facilities for the qualification of AMAGB and the indigenously developed Power Take off shaft.As Project Manager, she oversaw the completion of over 1000 hrs of testing and the critical airworthiness certification process of AMAGB- and its installation as the single largest, dynamically operating, indigenously developed LRU in LCA.

A major change in hercareer came when after 20 years in the lab, she moved to the Corporate Hrqrs to assist in techno-management analysis and decision making process for policy development. Here her focus for the next 4years was in the science & technology global developments- assessing its impact, comparative technology status in the country and providing decision aids for development priorities.

Based on her experience of project system development and backed by her Corporate experience, she was given the responsibility of heading the newly created Directorate of Management Systems & Technology with the opportunity to work in the field of Information Technology and take DRDO as an organisation into the next generation IT enabled processes.The focus was in the reorganization and upgradation of the PAN-India intranet of DRDO called DRONA- DRDO's Rapid Online Network access. The intranet is the backbone of the communication mechanism of DRDO and facilitates information sharing and everyday communication amongst the various laboratories of DRDO. It is also imperative to maintain the security of the intranet and protect it from threats and unauthorized access and hence a 3 tier security system was put in place for each of the physical, network and application layers.

With the accelerated pace of technology development both in IT and Networking domains, there was requirement of simultaneous voice, video, data transaction in addition to bandwidth intensive applications across domains and labs. Hence was established a DRDO wide Video Conference system for online reviews and deliberations. A wide range of ICT applications, systems and services have been progressively hosted on DRDO's Intranet in the areas of Corporate and technical functioning including Project Management, Mailing services and Open & Closed Interest Groups. A web-based project reporting and analysis system (PTS) has been created for Tracking of projects by DRDO's top management.

The above have been challenging tasks cutting across technology streams,which have aided in broadening one's horizons while working in such a technologically diverse organisation like DRDO.

ABSTRACT FOR INDIAN SCIENCE CONGRESS

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The Indian soldiers require scientific interventions for sustaining themselves in the most difficult to inhabit terrains. I have worked substantially for contributing towards improvement in the quality of life of the soldiers deployed at high altitudes. After completing my M.Sc. and Ph.D. in Physiology from All India Institute of Medical Sciences, New Delhi, I joined DRDO in 1990. I have had the privilege of being the lady Director in DRDO to have served in immensely difficult terrain like Leh? Ladakh. My innovative approach ensured health & food security even at frontier posts of the Indian Army and has resulted in close interaction between the troops and natives providing insulation from security threats to this region.

The troops deployed at high altitude complain of anorexia, loss of appetite which leads to decrease in body weight. Another common complaint is the impairment in cognitive functions of the troops posted at high altitude which are unique to Indian army as our soldiers are posted at extreme high altitude. I have worked in the field of high altitude physiology and pioneered the development of nutraceuticals and prophylactics for several high altitude maladies that include hypophagia and cognitive impairment. The studies have led to elucidation of some of the basic mechanisms involved in hypophagia at high altitude in terms of taste receptor sensitivity changes. We developed a method for ameliorating hypophagia by taking ginger based appetizers before meal.

Results from our study showed that impairment in memory function is mainly due to the oxidative stress leading to neuro?degeneration in brain structures (hippocampus, cortex and striatum) involved in learning and memory. We have contributed in the development of supplementation with antioxidant and cholinomimetic drugs to improve high altitude induced impairment in cognitive functions. In pursuit for developing therapeutic strategies for amelioration of hypoxia induced neurodegeneration, we investigated the therapeutic efficacy of several antioxidants like N?acetyl?cystein, Acetyl?L?Carnatine and elaborately elucidated their mode

of action. We formulated a composite herbal formulation to combat

hypoxia induced cognitive deficits in the soldiers guarding the frontiers of the nation.

Our findings on changes in evoked potentials and altered hedonic matrix in soldiers deployed at high altitude conditions have lead to formulation of herbal interventions for amelioration of hypobaria induced sleep disturbances and hypophagia in troops. Following preliminary studies on the alterations in P3 brain waves and occurrence of cognitive dysfunctions on exposure to high altitude, she pioneered the research on identification of suitable therapeutic targets for amelioration of hypoxia induced cognitive impairment. Our studies revealed novel therapeutic targets for hypoxia induced neuronal damage that include p75NTR receptors, Sp family of transcription factors and they ARE regulating Nrf?2.

We participated in the Indo -Krygyz project entitled "Study of Physiological mechanisms of human adaptation at high altitude in population to evaluate and increase acclimatization to HA" which led us to the understanding of differential physiological responses of Indian and Kyrgyz soldiers posted at high altitude. Acute induction to HA at 3200m affected the cardio respiratory, hematological and endocrinal system to the similar extent in Indian and Kyrgyz volunteers. Indian subjects exhibited improved ? adrenoreceptor desensitization compared to Kyrgyz subjects.

I have taken initiatives for permafrost based germplasm conservation, climate change mitigation and development of herbal interventions for improving performance at high altitude.

In DIHAR, my endeavors have resulted in augmentation of fresh food productivity through introduction of new varieties, establishment of greater infrastructure and intensification of lab to land programme. I have implemented technologies like vermi?composting for organic farming and non?conventional methods of storage of fresh produce. Development of broiler sheep for MOH and installation of world's highest biogas plant. During my tenure as Director DIHAR, National Mission on Seabuckthorn was launched. Appointment of DIHAR as Technical Agency for "Seabuckthorn Cluster Development in Ladakh" for promoting small scale industries, program initiated by Khadi and Village Industries Commission.

The establishment of permafrost based germplasm storage facility at 5360m, biogas plant

at DIHAR and establishment of Biotechnology lab at Chandigarh are other achievements. Establishment of Physiology Workstation and establishment of National Germplasm Storage Facility at Changla Top (Only second of its kind in the world after Norway) were other achievements during my tenure.

During my tenure at Leh, DIHAR was registered in Limca Book of Records 2009 for the World Record of having highest agro?animal technology Institute in the world. It also holds a National Record for producing some of the largest agricultural crops in the country and for growing 78 different types of vegetables in one season.

INVOLVING WOMEN IN SCIENCE & TECHNOLOGY: AN EMPOWERING TOOL

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The gender dimension of science and technology has become one of the most important and debated issues worldwide. Over the past 30 years, the United Nations General Assembly and UN Economic and Social Commission (ECOSOC) have emphasized issues related to inequalities, insufficiencies and disparities in the access of women to education, training and the labor market. Various major international initiatives on the subject have been undertaken, including the United Nations Decades on Women and Development, and special attention has been directed towards the role of women in science and technology. Gender equality is one of the eight United Nations Millennium Development Goals, which clearly call for action related to science, technology and gender. (UNESCO Report on Science, Technology & Gender, 2007)

Women are identified as seriously under-represented in science, mathematics and engineering fields. They are an under-utilized pool of talent and resource that could contribute immensely towards the social and economic development of societies through participating in science and technology programs. Women comprise more than half of the population of any society.

The challenge is to find ways of changing the situation such that women can be used as a resource for science and technology. There is no doubt that countries the world over need to open up opportunities to bring more women to science and technology, thereby producing a critical mass of scientifically skilled women. It is important for ordinary women to appreciate and access the findings of science and technology so as to improve the living conditions of families and that women scientists take up this agenda and develop projects to address the under-representation of women.

There is need to remove structural obstacles and barriers that continue to exclude girl children and women from the study of science and technology. There is urgent need for the development and mobilization of all segments of populations across cultures to contribute to the eradication of poverty, fighting diseases, stemming environmental degradation and improving global economic competitiveness through the application and development of science and technology.

Science and Technology have been an integral part of Indian civilization and culture. Over the years Indian women have overcome the traditional mindsets and have excelled in professions like teaching, medicine and pure sciences. Women have made important contributions in all walks of life and made inroads into new fields like engineering, information technology, biotechnology, nuclear science, space and many such specialized fields in the domain of science and technology.

While these developments have been highly satisfying, constraints in the form of socio-cultural factors, discrimination, lack of self-confidence and disparity between the sexes continue to affect Indian women and their choices of career.

In an Indian National Science Academy (INSA) study in 2006 on "Gendered Science: Trends and Analysis of Contributions of Indian Women Scientists", taken up with a view to focusing on achievements and recognition of Indian Women scientists, it has been pointed out that women reaching to higher positions in the cadre in their science careers are few and far between. Many women have done exceedingly well in their scientific and academic pursuits, however not many are seen being awarded and rewarded. Some of the contributing factors mentioned in the INSA study were: family, motherhood, inadequate support systems, societal/ cultural issues that could be due to fixed mind set, restriction on movement, nepotism and sexism.

The study revealed dissatisfaction of most respondents regarding professional growth and career advancement. Reasons cited were lack of time; household responsibilities; lack of encouragement from the organization and ill health. Respondents who were denied promotion attributed it to gender bias and lack of connections. The parameters focus on strong flavor of gendered science. The study suggests that remedial measures to improve women's participation in science need to be implemented at the earliest.

It has pointed out that in India, as in many other countries, women have had to fight to be accepted as capable of being equal partners with men in science and technology. (http://www.indiatogether.org/2004/jun/ksh-science.htm) Within science, there are areas considered suitable for women and others considered outside their realm of capability. Thus it has taken a struggle, for instance, for women to become engineers. Rather than looking at the reason why more women do not pursue careers in a particular branch of science and technology, it is generally concluded that women have no aptitude for that stream. Each time a woman becomes an aeronautical engineer, or a nuclear physicist, or excels in some area previously considered a male preserve, she is applauded and celebrated, but strictly as an exception.

Even before they reach the point of choosing a career in science, women have to make difficult choices. Every year, girls do far better than boys, in science and arts, in the Class X and Class XII examinations. In some institutions, the majority of the toppers are girls. What happens to them after that? Do they drop out? Are they forced by their families to make choices which are not their own? Do they fail to get through the competitive entrance examinations? Are they forced to make pragmatic choices about the future because they are conditioned to believe that marriage and family come first? Is there no way for them to balance their commitments to family with their desire to follow a career? There are great concerns now being shown in India about careers for women in science and consideration is being given to nurturing their talent by facilitating and providing various options.

The declining number of girls who follow through on their apparent aptitude for science at the school level is evident in the few women scientists at the top of the academic pyramid. Those women who do manage to pursue a career in science, often have to strategise how to survive and to move ahead.

In the education sector, information and communication technologies (ICTs) hold great potential. Distance education can enable women who don't have physical access to schools to participate through online, radio or other ICTs in education classes and programs. E-learning, which can involve a wide variety of technologies such as DVD, CD-ROM, or internet, offers students access to a vast amount of information and resources that are not possible in a single instructional setting. Online teaching support programs for teachers who have minimal teaching

background can assist with lesson planning, curriculum design and other learning tools. Training of women in the use of ICTs, media management and content development can enable them to participate in decision-making processes at government, private sector and civil society levels. Moreover, teaching methods and tools must be gender sensitive and responsive to women's and girls' unique need and learning styles.

Education, training and skill development are critical to ICT interventions. These areas represent an entry point for encouraging women to become more involved in ICT applications development, shaping ICT solutions and framing ICT policies according to female-specific needs and experiences.

Scholars argue that women suffer from an unequal attainment in other scientific fields too - from engineering and biology to nuclear science - and the inequality is observed along some important dimensions: recognition, awards, productivity, consulting, and inventions (scientific entrepreneurship). Some recent evidence gives cause for optimism showing that, especially in the field of biological sciences, the gender gap has narrowed. This evidence pertains only to the most-developed societies of Western countries and it does not necessarily represent the situation in a wide range of countries.

A recent survey of ten women achievers in life sciences industry reveals the following:

- Successful women leaders in this stream believe that women entrepreneurs face the same challenge as men
- Entrepreneurship is not gender based
- Follow gender-blind hiring process
- Practice meritocracy in performance management
- Offer reasonable flexibility to both women and men to balance their professional and personal commitments
- It also revealed that the number of women in the life sciences industry is quite significant.
- In US more women are pursuing science and higher studies than men are.

- More women are opting for engineering and medicine; the challenge is to pull women from small towns;
- For women to reach senior level management right amount of training and business exposure should be given
- Challenge is to fight stereotype views that society had about the role that women play in the world. The best way to overcome this is to stay committed and focused to one's objectives, and persistently try to achieve & excel.
- Organizations must make sure that equal opportunities exist for women, not only in letter but also in spirit.
- Implementing small but effective changes like flexible office timings for women can bring promising results.
- Few common traits for successful women entrepreneurs-passion & perseverance to succeed, flexibility to adapt, perceptiveness in identifying and seizing opportunities.
- Family support is important.
- Women in life sciences industry are armed with "can do attitude" and look for feedback frequently.
- Most women are better at multi-tasking and have the ability to stay focused on work along with nurturing and caring for their families.
- There are several jobs in life sciences sector that require staff to be present at night and after hours.These are by nature difficult for women.
- About 60 % of women take up science at the college level, and not all start a career in their field after college. This is why few women reach leadership roles. (Biospectrum Volume 8 Issue 11 November 2010)

The gender gap persists in a majority of developed and developing countries. The diverse underlying causes of gender disparity in science could be summarized as pertaining to the overall

level of societal development determining the level of economic opportunities open to women for employment and education; to the existing political system promoting or inhibiting policies of gender equality; and to gender stereotypes depicting women as incapable of achieving in technical and scientific fields.

The gender gap in academic science, in technology and engineering is not only a topic of ongoing policy changes and scholarly debates, but also is of interest to policy makers and governments engaged in initiatives to narrow the gap between women and men in these fields.

Much progress has been made toward the empowerment of women through science and technology interventions, but much more needs to be done before women and men can be said to enjoy equal status.

I would now like to share some of the initiatives that I have taken for empowering women in the domain of science & technology :

One had organized a Round Table Discussion on "Sharing Best Practices for Increased Participation of Women in Science & Technology Education & Career" (February 10, 2007) with the following objectives :

- To explore the challenges encountered in participation of women in science and technology education and career.
- To brain storm on low enrollment of girls in science & technology education & to explore solutions for overcoming the same.
- To help academicians and professionals develop innovative strategies, policies and actions for enhancing their participation in Science and Technology education, research and career.
- To discuss technological interventions for empowerment of rural women.

Deliberations of one-day Round Table Discussion:

1. Good Institutions must have systems in place which not only show but actually incorporate the following :

- practice good quality education
- have conducive environment for girls
- good job opportunities for females & males
- make efforts for enhancing skills of both-female & male students by improving their communication skills, leadership role, opportunity for creativity.

2. Women employees should be provided alternative work arrangements; flexible hours; flexible locations; child care in the work place, care of elderly parents in specific cases; maternity and paternity leave.

3. With regard to correcting gender imbalance, there is a need to build a culture to allow full participation of women.

4. Accessibility; affordability; acceptability and mentoring in relation to science stream need to be realized.

5. Infrastructure at rural areas; streamlining quality education and provision of e-learning distance coaching for competitive examinations and also e-learning for distance education in rural areas should be made.

6. There should be motivational exercises for women scientists. There is a need to speak about role models and mentors. Awards and fellowships should be introduced. There is also a need to encourage Industry to take CSR initiatives to introduce scholarships for women scientists for higher studies.

7. India has more female doctors as compared to other countries. These strengths should be harnessed.

8. There is a need to realize the gaps which are existing at the Plus Two level, e.g. investment in girls for higher education; discrimination at that level could be addressed at the societal level, but at the same time scholarships for bright girls from Institutions/Industry should be provided.

9. Very few women innovators are reflected in relation to Intellectual Property Rights, this issue needs to be addressed.

10. Rural schools should be provided with the facilities of laboratories for practicals; provision of mobile laboratories.

11. Increased appreciation of science and technology should be on the agenda of the local governments and also proper allocation of funding should be utilized realistically for providing the infrastructure; quality teachers etc.

12. Counseling at the Plus Two level is needed on importance of science streams especially for girls.

13. Primary concern being livelihood, girls tend to select lower career streams.

14. There is a need to publish and analysis data in relation to girl students not opting for science streams.

15. Suggestion to premiere institutes to bring out the best practices

16. There is a need for more Science & Technology Universities for women.

17. Women representation should be made mandatory in recruitment procedures.

18. Mid-career continuing education for women is needed

19. Learning exchange programs globally should be encouraged and processes streamlined.

20. Need to give priority to home science and other related streams for addressing development issues.

21. There is a need to explore the possibility of finding excellent talents in various Institutions for scholarships and designing projects/programs. Need to decentralize the process.

22. Sibling differential is an issue to be understood.

23. Reasons for de-streaming girls from S&T career need to be understood not only at the familial level and at the plus two level, but with the view of global market that is inequitable.

24. Various studies have shown that as the brand value of the Institutions decreases, the ratio of girls entering into various streams of S&T increases.

25. With commercialization of education, coaching for entrance examination has also become commercialized. There is a need to raise voice against it. Advertisement of Brilliant Tutorials is made only for male students

26. Refresher courses for teachers for ten plus two classes should be done so that the coaching pressure is reduced after ten plus two as most parents especially from small towns do not want to send their girl child for coaching due to security and economic reasons.

27. Need is to understand the issues and perceptions for not pursuing career in science and technology and to start women centered educational programs.

28. Gender is a cross-cutting issue which takes the center-point to develop linkages with other development issues like poverty, health, education and environment.

29. Millennium Development Goal indicators highlight one of the important indicators such as gender parity in education, equal access to wage employment and participation in governance. These are to be seen from the critique point of view but at the same time three important issues are to be addressed e.g. compatibilities, opportunities and the environment.

30. Gender is not only a woman's issue, but it relates to the shared power, recognizing the capabilities of men and women and how they could be leveraged together.

31. The power of knowledge is to be provided to women to access the choices; providing timely information; strengthening support system and enabling them to select the higher streams like Science, Technology and Information Technology.

32. Women must decide for themselves what they would like to do.

33. Women's access to resources is very important, which should be taken care of.

34. Young children internalize their potential and make up their minds to select the streams for higher education.

35. Teachers should also be motivated to pursue research studies at the university level.

36. In relation to the rural women, need is to enhance their knowledge, skills and capabilities.

37. Right information at the right time for right girls and women need to be provided at the village level.

38. Need is to bring the IT revolution in rural India.

39. Need is to collect success stories and innovative experiences at one place.

40. On-line knowledge-based information on women and entrepreneurship and the role of ICTs need to be collated and shared

41. There should be online information/knowledge at one website on "Women and S&T". Like-minded institutions can join hands to establish a cell to provide online information.

✡ **Study on 'Gender Related Issues Regarding Admissions to Higher Professional Educational Institutions' (2008-09)**

We undertook a study on above mentioned topic with the objective of finding out reasons for low enrollment of girls in engineering and management institutions. (% of girls fell drastically at BITS,Pilani once competitive examination replaced admission based on 10+2 marks).

Closed ended questionnaire was designed highlighting gender dimensions in admission to higher professional Institutions. Two sets of questionnaire were prepared and posted along with stamped self addressed envelopes to 70 professional educational Institutes in India during September, 2007. One set of questionnaire was prepared for the Registrar of the Institute and another was designed for students of IITs, IIMs, NITs, BITS-Pilani and various professional Institutes across the country. 10 sets of questionnaires were mailed to Presidents of Student Union of the Institutes to be filled by 5 female and 5 male students. 429 filled in questionnaires were received.

The key finding was that almost 70% of the respondents were influenced by their parents in choosing the particular stream in professional educational Institutions. Since enrolment of boys is more than girls in educational Institutes undertaken for the study, it may be inferred that

parents motivate boys more than girls to seek admission in professional educational Institutions. Gender sensitization of the society at large would help in this direction.

ICT Interventions for Empowerment of Rural Women (2006-7)

A project on "Socio economic up-liftment of Rural Women through Technology Intervention: Realizing Millennium Development Goals through ICTs" was launched during February, 2006 by Centre for Women Studies in collaboration with One World South Asia, New Delhi.

Goal

Empowering communities on health, social and development issues through Mass Media and promoting various ICT tools

Objectives

Address Millennium Development Goals directly related to health such as :

reduce Infant Mortality

reduce Child Mortality

improve maternal health

Efforts towards prevention from

communicable and sexually-transmitted diseases.

To address other related issues like literacy, sanitation and hygiene, employment having direct or indirect relation to improving health & livelihood indicators

Strategies :

Promotion of Mass Media and various ICT tools in connecting communities and empowering people

Advocacy Centers

Two village knowledge centers (called Advocacy Centers) which empower rural women and the village communities with knowledge on social awakening, health and environment relevant to local needs were established near Pilani in Rajasthan - the first one at Jherli Village near Pilani and the second one at Dhandhar Village Panchayat during February, 2006 respectively.

After the establishment of Advocacy Centers in early 2006, CD players and CDs with pre-recorded audio programs were distributed to selected volunteers.

These programs addressed issues on gender, health, education, superstitious beliefs, poverty, unemployment and green environment.

The information dissemination was done through listeners' clubs. Series of capacity building workshops were organized by CWS in collaboration with One World South Asia, New Delhi at Advocacy Centre, Jherli near Pilani for village volunteers during 2007.

The village volunteers were trained to collect local knowledge, add global knowledge provided by Centre for Women Studies and One World South Asia and address the issues related to MDGs. Capacity building on Hindi typing was imparted to the volunteers for sharing of knowledge-based content.

Volunteers were also trained to write and upload local stories on Ek Duniya website (www.ekduniyagyansagar.net) in order to connect communities and empower them through sharing local knowledge. They were also trained on designing of local newsletter.

Outcome

Increased awareness on gender sensitization.

Techno-savvy and computer literate.

Some of the volunteers involved in the project are now working at BPO, Pilani.

Training Program in Computer Literacy for rural women and girls (2005-10)

Objective : To train rural girls and women in computer literacy and library management

Strategies : A three and a half months training program in computer literacy and cataloguing

of books and journals for rural based girls and women has been imparted every semester since October 2005. Evaluation scheme comprises of three tests and a home assignment. After completion of the Training program, Certificates are given to the participants.

Outcome: After completion of the training, some of the trainees from previous batches have got employment in government, private schools and at computer training Institute. A trainee of the second batch, now runs a Computer Centre .

Training on Paper Recycling (2007-10)

Objective : To help rural women in entrepreneurial activity

Strategies : Everyday lot of paper waste gets collected. An activity on recycling of paper was initiated by setting up the Mini Paper Recycling Unit purchased from "Technology and Action for Rural Advancement" (TARA) during September, 2007. Ten rural women were trained by me & the team on recycling of waste paper. Out of these, four were selected for making paper sheets. This skill is helping them create a mode of economic livelihood. A calendaring machine has been installed at paper recycling unit during July 2008. The trained women are using the recycled paper sheets for making letter pads and visiting cards.

Outcome

Rural women/girls have been trained in skills for paper recycling, Income generating activity

Awareness & Training Program on Effective Use of Domestic Electrical Appliances for on-campus Women' (2009)

Objectives :

To promote awareness regarding basic understanding about electricity, maintenance and repair of domestic electrical & electronic appliances

To promote awareness about saving energy

To build confidence and reduce the fear of handling electrical equipment

Strategies: The training was conducted in collaboration with Instrumentation Unit of the Institute

on Sept 20, 2009. 20 females participated in this Workshop. "Learning by doing" was the approach. The first lecture covered history of electricity, various means of generating electrical energy, scientists who are the founders of electrical engineering, terms & units used in electrical circuits, basic circuit components, their characteristics, governing equations, safety precautions in handling electricity, tips for saving energy. Lectures were followed by hands-on-experience in understanding working of tube light, testing various components of tube light, connections of PCs. Lectures were also delivered on optimal use of energy, use of instruments to monitor the performance and safe operation, working of home appliances like iron, grinder, geyser. The hands on experience on seeing waveforms on CRO, soldering, fixing three pin plug, setting up circuits to read voltage, current and power consumed by bulbs, tube light, iron were performed.

Outcome : The female participants were very happy with the learning experience and have requested for continuation of such sessions with combination of theory and practical knowledge.

WOMEN'S CRITICAL ROLE IN INNOVATION & ENTREPRENEURSHIP IN LIFE SCIENCES

Nandini Tandon

Abstract:

- It is imperative to make the benefits of science and technology accessible to the masses and women can play a very critical role in doing so as entrepreneurs.
- Biotechnology and medical technology industries are prime examples of how new thinking has allowed for novel life extending and lifesaving products,; this is in contrast to the giant pharmaceutical companies which are cash rich but innovation poor.
- Research is about taking risks and entering unchartered waters and so too is entrepreneurship about taking risks and charting a new course.
- Women in life sciences can play a critical role by not only looking at medical problems from the scientist's eyes but also trying to provide cost effective solutions as an entrepreneur so the base of the pyramid can be better served.
- Both public and private sector scaffolding and support will be needed to help women to become entrepreneurs, but the returns the society may reap from the mentoring of women in this area can be invaluable
- Case study of several successful entrepreneurial stories will be provided by Dr. Nandini Tandon, a veteran Life sciences venture capitalist in Silicon Valley, who has invested and helped build more than a dozen new technology companies in Life Sciences.
- These companies span across a wide spectrum from Alzheimer, breast cancer imaging, cell death, cardiovascular to vaccines etc..
- Women, indeed can play a pivotal role in looking at age old problems from an entrepreneur's new vision, thus contributing to both science and community!

BIOTECHNOLOGICAL TOOLS TO MEET FUTURE FOOD CHALLENGES

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Climate change will have far reaching consequences in agriculture that will disproportionately effect poor and marginalized groups who depend on agriculture for their livelihoods and have lower capacity to adapt. Climate related crop failures and fishery collapses and livestock deaths are already causing severe economic causes thus undermining food security. These are likely to be more severe as global warming continuous. Agriculture and related activities also contribute to global warming by generation GHG emissions and altering the land surface. Presently agriculture is estimated to account for about 15% of global GHG emissions and for about 26% if the emissions due to deforestation in developing countries is included.

Sustainable food security for the world growing population and changing diets is the major challenge which is further complicated due to climate change. The relationship among climate change agriculture and food security are complex and dynamic. The challenge is how to integrate new biotechnological tools so as to develop crop varieties which address biotic and abiotic stresses introduced by the changing climate, whether it is raising temperature or uneven precipitation.

It calls for revisiting the available germplasm for using genetic and species diversity so as to enhance adaptation resilence. Genebanks set up by individual nations as well as CGIAR systems and even private companies have huge germplasm collections. Most of these germplasm has been retained with some passport data in terms of region from where it was collected and important traits. Making use of recent advances in molecular technology specially the chip technology, perhaps one can evaluate the existing germplasm on molecular basis for selected traits and use it either for mining of genes for unique traits or for breeding thus making combinations of desirable traits. In last few decades our entire focus of agriculture researchers was on improving yields resulting in some compromise in terms of susceptibility to diseases and

even nutritional quality. Revisiting germplasm for these traits will be extremely important for future food and nutritional security issues.

The progress in molecular analysis and gene mining for traits such as drought, salinity, tolerance to temperature fluctuation etc. have already been isolated largely by multinational corporations. All these has been possible through huge investments of MNCs. This will also get translated into high license fee specially for the crops of international importance. One must acknowledge the contribution of private seed companies in bringing science to the next level and that for continuation of future research, they do require funds. However, these companies are expected to share the technologies including genes on humanitarian grounds for resource poor farmer and for crops which are of no interest to them. Unfortunately, in the prevailing environment of liability resting with the developer of the technology, it is not taking off. The current legislations puts the entire liability whether it is in terms of allergenicity or adventious presence recorded elsewhere on the developer of the technology, this is proving to be a major hindrance in developing public private partnerships.

The role of public sector and development of public goods is becoming extremely important in developing part of the world so that the technology is scale neutral is accessible to resource poor farmer with limited resources. Also for maintaining biodiversity it is important that open pollinated varieties of wide range of species are improved. This can be made possible through development of international public goods; working out appropriate licensing arrangements and negotiate internationally issues related to stewardship and liability. To ensure that new technologies are accessible to the developing world one also as to create capacities to respect intellectual property rights. The researcher and farmers must understand that in the long run new technologies are going to help them with improved quality and quantity of food through access to latest technologies. It is also essential to empower farmer with capacities to absorb new technologies and have enabling tools such as crop insurance in place so that he can take risk of adapting technologies that are resource incentive.

MITOCHONDRIAL ATP-DEPENDENT POTASSIUM CHANNELS AS NOVEL TARGET FOR DRUG DEVELOPMENT IN THE TREATMENT OF SEPSIS AND RELATED CARDIOVASCULAR DISORDERS

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Introduction

Despite advances in critical care medicine research, death due to sepsis and associated pathologies has increased by alarming proportions in the last two decades. It is well recognized that severe sepsis is associated with cardiac failure and high mortality rates ranging from 30-60%. Alterations in sepsis, septic shock and related pathologies involving mitochondrial ultrastructural changes and oxidative mechanisms have received major attention in the last few years. In a model of endotoxemia, Crouser et al. demonstrated that endotoxin-induced mitochondrial damage was related to an imbalance in mitochondrial respiration. The severity of sepsis has been shown to correlate with mitochondrial damage and bioenergetic dysfunction in both human and experimental models. In another model of bacterial challenge, the oxidation of myocardial mitochondrial protein and lipid was observed at 4 and 24 hr, suggesting outer mitochondria membrane (OMM) damage.

For several years, our laboratory has produced evidence of molecular apoptotic mechanisms in sepsis-induced myocardial and ARVM dysfunction. Our data also demonstrated the role of mitochondrial-mediated intrinsic apoptosis cascade and stress-mediated mitogen-activated protein kinases in the regulation of sepsis-induced adult rat ventricular myocyte (ARVM) dysfunction. In experimental endotoxemia, mitochondrial dysfunction has been characterized by mitochondrial membrane potential collapse and transitional changes in mitochondrial membrane permeability, along with the release of cytochrome C. Earlier, we reported that a progressive decline in myocardial performance at 3 and 7 days in a hyperdynamic model of sepsis is associated with increased levels of proapoptotic caspase-3, increased B-cell leukemia (Bcl2)-associated protein x (Bax)/Bcl2 ratio and release of cytochrome C [8]. Mitochondrial outer membrane permeabilization (MOMP) is controlled by the translocation of Bax on OMM. Disturbance of

OMM leads to MOMP and release of a large number of intramitochondrial proteins, including cytochrome C, via the formation of permeabilization pores primarily composed of Voltage Dependent Anion Channels (VDACs). Besides VDACs, including VDAC1, which are present on OMM, the inner mitochondrial membrane (IMM) bilayer also possesses mitochondrial KATP (mitoKATP) channels. The Kir subunits of mitoKATP channels are closely associated with sulphonylurea protein SUR2A, which is a regulatory protein for the passage of pharmacological agents through these channels. Several researchers have shown that mitoKATP channels are directly activated by diazoxide and blocked by 5-hydroxydecanoate (5HD). Even though both diazoxide and 5HD have been shown to be only partially specific to the mitoKATP channels, 5HD apparently remains the most selective antagonist of the mitoKATP channels available.

NE is a positive inotrope used in the current therapy of sepsis to maintain hemodynamic support for the ICU patients but has been shown to produce cardiodynamic dysfunction in septic animals. Our previous findings have demonstrated that NE produces blunted contractile response to ARVMs along with up regulation of mitochondrial-driven apoptotic cascade.

In the present study we speculated that OMM damage during sepsis could be accompanied by the opening of mitoKATP channels that play a critical role in the transport of ATP across mitochondrial membranes. We hypothesized that 5HD, a putative mitoKATP channel blocker, will ameliorate sepsis-induced cardiodynamic and ARVM contractile dysfunction, restore mitochondrial membrane permeability alterations and improve the survival rate. Therefore, we determined the effect of mitoKATP inhibition on sepsis-induced mortality, myocardial and ARVM contractile dysfunction by using 5HD. The effect of 5HD was examined in presence and absence of NE on ARVM contractility and release of cytochrome C, and levels of Bax and VDAC1. In addition, we determined whether modulation of the mitoKATP channels affected the IMM events leading to the release of cytochrome C in the myocardium in a severe septic rat model

Methodology/Principal Findings:

Male Sprague-Dawley rats (350-400 g) were made septic using 400 mg/kg cecal inoculum, ip. Sham animals received 5% dextrose water, ip. The Voltage Dependent Anion Channels (VDAC1), Bax and cytochrome C levels were determined in isolated single ARVMs obtained from sham and septic rat heart. Mitochondria and cytosolic fractions were isolated from ARVMs

treated with norepinephrine (NE, 10 ?moles) in the presence/absence of 5HD (100 ?moles). A continuous infusion of 5HD using an Alzet pump reversed sepsis-induced mortality when administered at the time of induction of sepsis (-40%) and at 6 hr post-sepsis (-20%). Electrocardiography revealed that 5HD reversed sepsis-induced decrease in the average ejection fraction, Simpsons + m Mode (53.5 ± 2.5 in sepsis and 69.2±1.2 at 24 hr in sepsis + 5HD vs. 79.9 ± 1.5 basal group) and cardiac output (63.3 ± 1.2 mL/min sepsis and 79.3 ± 3.9 mL/min at 24 hr in sepsis + 5HD vs. 85.8 ± 1.5 mL/min basal group). The treatment of ARVMs with 5HD also reversed sepsis-induced depressed contractility in both the vehicle and NE-treated groups. Sepsis produced a significant downregulation of VDAC1, and upregulation of Bax levels, along with mitochondrial membrane potential collapse in ARVMs. Pretreatment of septic ARVMs with 5HD blocked a NE-induced decrease in the VDAC1 and release of cytochrome C.

Conclusion:

This study provides evidence for the first time of the protective nature of 5HD due to the stabilizing effect on the OMM and the decreased release of cytochrome C on myocardial morbidity and mortality in a polymicrobial septic rat model. The 5HD when administered at the time of induction of sepsis reversed sepsis induced mortality suggest that 5HD infusion has potential to be part of therapy in septic patients. We concluded that mitoKATP channel inhibitors (such as 5HD) can be a novel class of agents with the potential to delay sepsis-induced morbidity and mortality. The data suggest that Bax activation is an upstream event that may precede the opening of the mitoKATP channels in sepsis. We concluded that mitoKATP channel inhibition via decreased mitochondrial membrane potential and reduced release of cytochrome C provided protection against sepsis-induced ARVM and myocardial contractile dysfunction.

ON SCIENCE EDUCATION AND WOMEN EMPOWERMENT

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It is a fact that science education brings growth and well being to people and it is not only the empowerment of women through science but also the enrichment of Science & Technology through women participation. Study of science does not ensure further opportunities and smooth career path for women - thanks to the notorious "Glass Ceiling"; there is a tremendous sexual nepotism and women who seek science career have to face triple burden of professional work, domestic work and fighting male chauvinism. Recognition received by women scientists and their total R&D work force reveals gender discrimination relative presence of women is our own national establishments like CSIR, ICAR, DOD, DAE, I.I. Sc. and all Central Universities is less than 10% and much less as the promotional ladder goes up. My own involvement in research reveals that even the epidemiological survey of industrial toxicity being caused to women has not been carried out. I had to struggle over the last 30 years to establish that men work in mines (specially in Coal Mines) and their wives suffer from still births, premature deaths of infants, genetic deformation etc., Similarly, women exposed to tobacco dust in beedi women works suffer from increased incidence of Cancers, Still- births and genetic deformations etc. in their off springs. Our male dominated national research establishments are doing research for their own satisfaction to gain International recognition and to have publications in high impact parameter Journals rather than solving our own national industrial and technical development.

Empowering women in science will certainly have the much needed national outlook towards our National goals of R&D activities. Recent trends based on market survey, driven by Globalization of economy, have been widening the gap between men and women for better opportunities making them to join software oriented jobs at the cost of getting into science stream of education.

Girls are often taken away from secondary school level as soon as they reach puberty especially in impoverished communities in India. In our country the first worry in getting the daughter married. Denial of school education blocks the stream that would feed to higher

education. These challenges can be overcome by promoting fellowship facilities and making the teaching of science more female oriented. Activities like, Science and Mathematics teaching camps at school levels, carrying out Science & Technology quizzes, regularly for girls and encouraging them to take up science based courses. Government should establish workable and properly implementable policy to empower women in innovative scientific activities integrated with Science & Technology policy. Further, special efforts to develop appropriate technologies suited to women's needs as well as to reduce their drudgery have to be given a special focus.

My lecture will also will include statistical data on various aspects to high light the need for empowering women through science education and related R&D activates. "Where a man is educated an individual is educated, when a women is educated a family and a country are educated" - M K Gandhi - Father of the Nation.

LOW COST SUSTAINABLE TECHNOLOGIES FOR COLD ARID DESERT

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The Indian soldiers require scientific interventions for sustaining themselves in the most difficult to inhabit terrains. I have worked substantially for contributing towards improvement in the quality of life of the soldiers deployed at high altitudes. After completing my M.Sc. and Ph.D. in Physiology from All India Institute of Medical Sciences, New Delhi, I joined DRDO in 1990. I have had the privilege of being the lady Director in DRDO to have served in immensely difficult terrain like Leh- Ladakh. My innovative approach ensured health & food security even at frontier posts of the Indian Army and has resulted in close interaction between the troops and natives providing insulation from security threats to this region.

The troops deployed at high altitude complain of anorexia, loss of appetite which leads to decrease in body weight. Another common complaint is the impairment in cognitive functions of the troops posted at high altitude which are unique to Indian army as our soldiers are posted at extreme high altitude. I have worked in the field of high altitude physiology and pioneered the development of nutraceuticals and prophylactics for several high altitude maladies that include hypophagia and cognitive impairment. The studies have led to elucidation of some of the basic mechanisms involved in hypophagia at high altitude in terms of taste receptor sensitivity changes. We developed a method for ameliorating hypophagia by taking ginger based appetizers before meal.

Results from our study showed that impairment in memory function is mainly due to the oxidative stress leading to neuro-degeneration in brain structures (hippocampus, cortex and striatum) involved in learning and memory. We have contributed in the development of supplementation with antioxidant and cholinomimetic drugs to improve high altitude induced impairment in cognitive functions. In pursuit for developing therapeutic strategies for amelioration of hypoxia induced neurodegeneration, we investigated the therapeutic efficacy of several antioxidants like N-acetyl-cystein, Acetyl-L-Carnatine and elaborately elucidated their mode of

action. We formulated a composite herbal formulation to combat hypoxia induced cognitive deficits in the soldiers guarding the frontiers of the nation.

Our findings on changes in evoked potentials and altered hedonic matrix in soldiers deployed at high altitude conditions have lead to formulation of herbal interventions for amelioration of hypobaria induced sleep disturbances and hypophagia in troops. Following preliminary studies on the alterations in P3 brain waves and occurrence of cognitive dysfunctions on exposure to high altitude, pioneered the research on identification of suitable therapeutic targets for amelioration of hypoxia induced cognitive impairment. Our studies revealed novel therapeutic targets for hypoxia induced neuronal damage that include p75NTR receptors, Sp family of transcription factors and they ARE regulating Nrf-2.

We participated in the Indo -Krygyz project entitled "Study of Physiological mechanisms of human adaptation at high altitude in population to evaluate and increase acclimatization to HA" which led us to the understanding of differential physiological responses of Indian and Kyrgyz soldiers posted at high altitude. Acute induction to HA at 3200m affected the cardio respiratory, hematological and endocrinal system to the similar extent in Indian and Kyrgyz volunteers. Indian subjects exhibited improved β adrenoreceptor desensitization compared to Kyrgyz subjects.

I have taken initiatives for permafrost based germplasm conservation, climate change mitigation and development of herbal interventions for improving performance at high altitude.

In DIHAR, my endeavors have resulted in augmentation of fresh food productivity through introduction of new varieties, establishment of greater infrastructure and intensification of lab to land programme. I have implemented technologies like vermi-composting for organic farming and non-conventional methods of storage of fresh produce. Development of broiler sheep for MOH and installation of world's highest biogas plant. During my tenure as Director DIHAR, National Mission on Seabuckthorn was launched. Appointment of DIHAR as Technical Agency for "Seabuckthorn Cluster Development in Ladakh" for promoting small scale industries, program initiated by Khadi and Village Industries Commission.

The establishment of permafrost based germplasm storage facility at 5360 m, biogas plant

at DIHAR and establishment of Biotechnology lab at Chandigarh are other achievements. Establishment of Physiology Workstation and establishment of National Germplasm Storage Facility at Changla Top (Only second of its kind in the world after Norway) were other achievements during my tenure.

During my tenure at Leh, DIHAR was registered in Limca Book of Records 2009 for the World Record of having highest agro-animal technology Institute in the world. It also holds a National Record for producing some of the largest agricultural crops in the country and for growing 78 different types of vegetables in one season.

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