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## Indian Council of Medical Research: then and now

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*'O, what a fall was there, my countrymen!'*  
—*The tragedy of Julius Caesar*,  
by William Shakespeare (Act 3, Scene 2)

Successor to the Indian Research Fund Association (IRFA), the Indian Council of Medical Research (ICMR) had Dr CG Pandit as its first director. He set high standards of probity and economy and was scrupulous in all his activities. He ensured ethical conduct in all activities of the council.

The contrast between the reputation of the council in its early days and that today is striking. I have chosen two heads of the council—Dr CG Pandit and Dr NK Ganguly—and have used illustrative examples from their tenures. I have also used an example from 1996, before Dr Ganguly was appointed director-general, to highlight the impotence of the council today when faced with a catastrophic breach of medical ethics.

A noticeable decline from Dr Pandit's standards was noted over the decades following his departure and reached a nadir when Dr NK Ganguly publicly praised Dr P Venugopal for his use of stem cells in the treatment of cardiac disease (1). The recent scandal in which Dr Ganguly has been implicated (2) adds nothing to his stature or that of the council.

### Spartan values

Dr CG Pandit remains the gold standard against whom all succeeding heads of the council must be measured. His life and work have been recorded in his own words (3). I strongly recommend this work to all those having the best interests of medical research in India at heart.

Dr Pandit has described in this book the foundation and functions of IRFA and his appointment to IRFA as secretary in 1948 by Dr Jivraj Mehta. When IRFA was replaced by ICMR in 1950, Dr Pandit was appointed as its first director.

Let me provide some examples of his philosophy concerning the council.

A head clerk at the council told me in the 1970s that he had been with the ICMR since its beginning: "I remember the day when Dr Pandit moved into his room. It was spartan in its simplicity. It had a cupboard for his files and books, a table and two simple chairs—one for himself and the other for a visitor. A fan whirred overhead during the summer. . . Now there is wall-to-wall carpeting, air-conditioning, fancy lighting, a number of telephones, an array of other machines and an annexe where the personal assistant awaits summons from the director-general."

As an afterthought, he added: "And there are fancy flowerpots and other decorations."

The clerk also narrated a conversation with Dr Pandit's driver. "As director he was entitled to the use of an Ambassador car. On one occasion he had to attend a meeting with the minister and his secretary in the afternoon. As it progressed he realised that the meeting would go on beyond 5 pm. Excusing himself briefly from the meeting, he came to the driver and told him to return to the ICMR, as he would be delayed. 'What will you do about returning home?' asked the driver. 'Oh, I will manage. I cannot keep you and the car waiting beyond office hours,' he replied as he returned to the meeting."

On page 332 of Dr Pandit's book we learn that while he was at the helm, the yearly expenditure on the headquarters office of the council always remained around 7% of the total grant received by the council. About 4% of the grant was spent on laboratory animals, scientific reports, publications, library and stores, and other such activities; 89% of funds were spent on research and development activities including grants, pay and running expenses of scientific workers.

### Critical self-analysis

When Dr Pandit neared the end of his stint at the ICMR, Dr S Sriramachari, additional director-general, suggested that he analyse the activities of the council from 1948 to 1965.

Dr Pandit in turn asked him to do the study impartially, documenting failures and achievements.

Dr Pandit was quick to point out that this was not the first time that such an assessment was made. "No organisation can continue to function effectively unless a periodic assessment is made of its working," he wrote (3: p 331–2).

The report by Dr Sriramachari, a document of over 150 pages, was produced and presented to the governing body. Dr Pandit joked that it was his last will and testament as far as the ICMR was concerned. It is difficult to recall a parallel situation in India, when a retiring chief, on the eve of his laying down office, placed an impartially drawn up balance sheet of the organisation on the table.

### **Need for another 'Sriramachari Report'**

We await a similar analytical report as the council has completed 100 years. This is especially important as the budget allocated for the ICMR during the 12th Five-Year Plan is Rs 8,500 crore (4: p 315).

This report should also embody a cost–benefit analysis of the council, its several institutes scattered throughout the country and the research projects carried out from Delhi and at each of the institutes. The analysis of the council and of each of its institutes could be along the lines of the report by Dr Sriramachari referred to above.

I suggest the following points for inclusion in this analysis as regards each of the major, expensive projects:

1. Names, affiliations of principal researchers
2. Title of project
3. Time taken from submission of project proposal to decision on the proposal by the ICMR and actual start of work on the project
4. Summary of aims and objectives of the project
5. How many of these aims and objectives were achieved
6. Reasons why the rest were not achieved
7. Whether the research resulted in one or more patents
8. If patents were obtained, what was the subsequent fallout in terms of:
  - a. Income to ICMR
  - b. Income to researchers
  - c. Commercial exploitation of the product in India thus far (give details)
  - d. Commercial exploitation of the product abroad (give details)
9. Publications on the project with bibliographic references
10. Time frame under which the project was to be completed according to the initial project proposal
11. Time frame under which the project was actually completed
12. Reasons for overshooting time if delays had occurred

13. Cost of the project according to the initial project proposal
14. Actual cost of the completed project
15. Reasons for extra expenditure, if any
16. Feedback from the researchers on:
  - a. Whether they encountered any difficulties in getting their project proposal approved
  - b. Whether they encountered any difficulties in getting their funds each year at the start of the financial year
  - c. Whether their communications to ICMR were promptly and efficiently dealt with
  - d. Whether they encountered any difficulties in patenting
  - e. Whether they encountered any difficulties in getting their patented product into commercial production through a third party on payment of royalties
  - f. Whether they are satisfied with the returns from such commercial exploitation
  - g. Any other observations they might like to make

In 2011, the IRFA/ICMR published a compendium of papers to celebrate its centenary (5). This is a step in the right direction but we also need a detailed analysis as outlined above.

### **The ICMR today**

#### ***Naming the ICMR building***

In 2002, when it was decided to name the building designed and set up by Dr Pandit, he was ignored in favour of Dr Ramalingaswami. While the latter scientist's claim to fame cannot be disputed, it is difficult to accept that his contributions to the development of the ICMR were greater than those of Dr Pandit. Dr NK Ganguly, director-general of ICMR, who should have known better, was a prominent participant in the dedication ceremony of this "historic event" (6).

#### ***No action against unethical research***

The ICMR's responsibilities include ensuring that research in this country is conducted ethically, and "the Central Ethical Committee of ICMR on Human Research constituted under the Chairmanship of Hon'ble Justice (Retired) MN Venkatachaliah held its first meeting on September 10, 1996. Several subcommittees have been constituted to address specific topics, viz., epidemiological research; clinical evaluation of products to be used on humans; organ transplantation; human genetics, etc." (7).

In December 1997, Dhani Ram Baruah transplanted a pig's heart into Purna Saikia, an Assamese farmer (8), without preclinical studies, and without developing a means to overcome the certain rejection of the xenotransplant. Predictably, Saikia died soon after the operation.

I have failed to find a scientific paper published by Baruah on this operation, the studies that went into its planning and its sequel.

As late as February 2012, an editorial by Manji et al in the *Indian Journal of Medical Research*, published by ICMR, noted that even the limited use of heart valves of porcine origin, preserved in glutaraldehyde, should ideally be from “genetically-engineered” pigs (9). It is unlikely that any thought in this direction troubled Baruah six years earlier.

I have also been unable to lay my hands on any document published by the ICMR describing an inquiry undertaken by it into Baruah’s unethical and fatal operation.

Far from being punished after due process of law, Baruah appears to be flourishing going by his several claims on his website, including the use of pig blood transfusions into humans and the “first successful clinical transplantation using pig as donor” (10).

ICMR and other national bodies created to further medical and scientific research appear to be indifferent to the operation in 1996 and the many other activities proudly referred to on Baruah’s website.

### **Dr NK Ganguly**

Graduating in medicine from Calcutta, he obtained his MD in microbiology from the Postgraduate Institute of Medical Education and Research, Chandigarh. He served as director-general ICMR from 1998 to 2007.

As with my account on Dr Pandit, I include some incidents which have struck me as important. The first dates to his term in the ICMR.

### **The use of stem cells in cardiology at AIIMS**

The ICMR has as its mandate the promotion of medical research of the highest standards throughout the country. To ensure this it must maintain an unfailing vigil for unethical practices anywhere and nip them in the bud, disciplining those guilty of such practices. Like charity, such vigil must begin at home and its environs. The All India Institute of Medical Sciences (AIIMS), a nationally reputed undergraduate and postgraduate institute, is the next-door neighbour of ICMR. The many links between ICMR and AIIMS should make it easy for ICMR to detect and correct unethical practices at the AIIMS.

In 2005, Dr P Venugopal, professor of cardiac surgery, AIIMS, and his colleagues published two papers on the injection of autologous stem cells into the coronary arteries in patients with cardiomyopathy and in those with ischemic heart disease (11, 12). Each paper occupied just one page and concluded that the pilot study indicated the safety of the use of bone marrow cells and showed clinical and echocardiographic improvements. It did not refer to any experimental studies on the use of stem cells in cardiac disease by this group or preclinical trials. We are not informed whether informed consent was obtained from these patients especially since we have no references to similar use of stem cells anywhere in medical journals and since marrow was obtained from iliac crests, coronary angiography and endomyocardial biopsies were carried out. There is no

note to show that the research projects were approved by the ethics committee of the institute. There are no details that can help the reader to judge whether there was any significant improvement. We are expected to take statements made in the paper at face value.

Other authors from AIIMS proposed the use of stem cells as a therapeutic modality in the treatment of motor neurone disease and other neurodegenerative diseases (13) and in static encephalopathy including cerebral palsy (14) in the same supplement of the journal. In all cases there are no references to similar usage elsewhere in the world or of their own experimental studies.

In the same year, Devendra Gupta and Shilpa Sharma of AIIMS published a review paper (15). I quote a paragraph from their paper:

*The All India Institute of Medical Sciences (AIIMS), New Delhi has taken the global lead in using the autologous stem cells obtained from bone marrow (sternum, tibia) and using them for various disorders (cardiomyopathies, diabetes, bony disorders, biliary atresia and choledochal cyst (cirrhotic livers), spina bifida, cerebral palsy and muscular dystrophy). This has been possible following an extensive background research that has gone for more than 2 years before using the stem cells on the human beings. At AIIMS, stem cells have been used in more than 150 patients, including neonates and infants for various disorders.*

While this paper does refer to ethical issues, these pertain to the storage of umbilical cord/blood and not to informed consent or sanction by the institute’s ethics committee. We are provided no references to the “*extensive background research that has gone for more than 2 years before using the stem cells on the human beings*” although they list 31 other references.

My own search for references to the experimental work on stem cell work at the AIIMS leading to these papers has proved unrewarding. If, indeed, there be no preclinical study, phase I and phase II studies on the effects of the introduction of stem cells into human beings to cure disease, the scientific foundation of the claims made by Venugopal and others at the AIIMS lack validity and the experiments are patently unethical.

A study of pronouncements made by Venugopal to the press, in 2005, lead to greater consternation. A news item (16) claimed: “All India Institute of Medical Sciences is on the threshold of a medical breakthrough. The country’s premier medical institute is preparing proof of efficacy of its stem cell therapy for the global medical fraternity. The institute has conducted tests on 33 heart patients over the last 18 months using the therapy and ‘all of them are showing positive results,’ says Dr P Venugopal, director, AIIMS.”

Despite my efforts, I have been unable to secure a copy of the document offering ethics clearance for these tests. I have also failed to obtain papers detailing the techniques used in the treatment or objective assessments of the patients used in

these trials by impartial experts before and after treatment. If one takes the news item at its face value, the AIIMS team was “preparing proof of efficacy of its stem cell therapy.” If this was true, would it not have been proper to await scientific publication of the claims in a reputed, indexed medical journal after peer review before making the news public? It would be of interest to learn how many more stem cell transplants have been carried out at AIIMS from 2005 to date on the basis of claims and suggestions made in the papers published in 2005 and the improvements that followed in these patients.

As regards the statement that “no ethical issues are involved in the stem cell research using adult cells,” there are considerable grounds for disagreement. Sharma (17) has pointed out:

*A lot more basic information about stem cells and their behaviour are [sic] required before they can be used for treatment. Extensive basic research is required for standardization of methods for the isolation of embryonic and adult stem cells from various sources. Future prospects for embryonic stem cell research include the following: generation of therapeutic grade cell lines; identification of human embryonic stem cells (hESC) growth factors; controlled differentiation, i.e. generation of specific cell population; study of fundamental changes in cell cycle control that occurs during embryonic stem cells differentiation; maintenance of stem cell in undifferentiated stage; regulation of differentiation of ESC; pluripotency and differentiation of established cell lines; standardization of animal free defined culture conditions; developmental potential of human versus mouse ESC; standardization in use of specific stem cells to specific organ systems, etc. In addition, ESC could also be used for toxicology tests and may be valuable tools for traditional drug discovery...*

Venugopal and his colleagues should have complied with the need for such studies before embarking on their clinical usages. I have failed to find evidence that they did.

I presume Dr Ganguly was privy to data not available to the rest of us for on April 5, 2005, *The Hindu* reported: “ICMR okays stem cell research by AIIMS” (1). The opening sentence of the report said: “Giving a thumbs-up sign to stem cell research work at the All-India Institute of Medical Sciences (AIIMS), the director-general of the Indian Council of Medical Research (ICMR), Dr NK Ganguly, today said he stood by the ‘authenticity of the work by the Institute.’ Dr Ganguly continued: “We have no plan to legislate the guidelines that are in place for carrying out stem cell research.”

This rapid assessment by the head of ICMR of work that was just being reported is surprising, to say the least. One would have expected a careful study of the preclinical work, phase I and phase II clinical trials and observation of the results of treatment over years to identify ill-effects and confirmation of clinical improvement by impartial observers before making any comments.

Equally puzzling was the statement by Dr Vasantha Muthuswamy, deputy director-general, ICMR, and in charge of developing ethical guidelines for stem cell research and treatment: “We are only a block away from AIIMS and we did not know this (stem cell work) was happening there. If the nation’s premier medical institute did not ask our permission for such therapy, how can we blame private clinics for what they do?” (18) Was the enthusiasm of Dr Ganguly for the claims of AIIMS based on non-scientific reasons?

I am also struck by the fact that despite the “research” in India, experts abroad are proceeding cautiously. Martin-Rendon and colleagues (19) concluded their systematic review of randomised controlled trials in the use of stem cells in acute myocardial infarction (AMI) thus: “Stem cell treatment for AMI still holds promise. Clinically, these data suggest that improvement over conventional therapy can be achieved. Further, adequately powered trials using optimal dosing, longer term outcome assessments, more reliable, and more patient-centred outcomes are required.” Note that they recommend further, adequately powered trials and not unrestricted usage.

As noted above, despite the existence of guidelines for carrying out stem cell research, Dr Ganguly did not find it necessary to proceed to legislating them. Dr Dorairajan Balasubramanian, research director at the LV Prasad Eye Institute in Hyderabad, himself involved in the use of stem cell to treat eye diseases, had pointed out the need for legislation so that rogue researchers can be punished. “Guidelines are only guidelines. Any violations cannot be punished.” (20). As I write this, the guidelines for stem cell research prepared by the ICMR and the Department of Biotechnology remain in draft form (21). The failure of ICMR and other national agencies to get the legislature to act on these guidelines have laid us open to international ridicule. Salter et al (22) referred to “a 2005 survey by ICMR [that] showed that in the absence of any powers of enforcement only a minority choose to do so... As stem cell science moves from the laboratory to the clinic and the experimental treatment of patients, it does so in a governance vacuum. As a result, scientists like Dr Geeta Shroff can publicise her treatment of 100 clinical cases of spinal injuries, paralysis, tuberculosis, neuro-muscular dystrophy and multiples sclerosis conducted without ICMR approval and receive simultaneous praise from the Indian health secretary and condemnation from Western stem cell scientists...”

### ***Dr Ganguly and others implicated in ICMR land scandal***

*The arrests of several high-profile current and former officials of the Indian Council of Medical Research (ICMR) on corruption charges have sent shockwaves through the Indian medical establishment.*

*The government-funded ICMR, headquartered in New Delhi, coordinates and promotes biomedical research in India and runs 28 research institutes across the country.*

*Those arrested by the Special Fast Track Court of the Central Bureau of Investigation include Bela Shah, head of*

the ICMR's division of non-communicable diseases; Ashok Kumar Srivastava, its executive engineer; and Bhawani Thyagarajan, a retired joint secretary in the Ministry of Health, among several others. Following their arrests, Shah and Srivastava have been suspended by the ICMR while the investigation takes place.

The case follows a comprehensive investigation run by the government's audit body, the Comptroller and Auditor General of India, which found that land procurement and irregular transfer for proposed building works by the ICMR between 2002 and 2008 were subject to large-scale irregularities, wasteful expenditure, cost overruns and inadequate oversight...

Specific to recent arrests, the auditor found that land owned by the ICMR-affiliated Institute of Cytology and Preventive Oncology (ICPO) was illegally transferred to a private housing society of employees by the ICMR executive council at a fraction of its market price, causing massive losses to the government exchequer...

Nirmal Kumar Ganguly, a former director-general of the ICMR and a leading Indian scientist, is also accused of the charges. He has an arrest warrant against him but has so far not presented himself in court. Ganguly is also chairman of the governing body of the Jawaharlal Institute of Postgraduate Medical Education and Research in Puducherry, and heads a medical ethics committee for the Medical Council of India... (2)

The final 11 words emphasise the tragic state of affairs in Indian medicine.

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