OCCASIONAL PUBLICATION 102

IIC

Friends, Heroes, Scientists, Women

by

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Friends, Heroes, Scientists, Women*

Introduction

Where are we today with regard to the role of women in science, technology, engineering, medicine (among other fields), women in leadership roles, and what are the challenges that lie ahead of us? In that context, it is very interesting to address both biology and sociology, and the reason we need to address the former is that explanations for why societies manifest in certain ways, or not, often hinge on our recourse to biology in various ways. As far as biology goes, humans are the consequence of hundreds of million years of evolution, from unicellular organisms to multiple kinds of multicellular organisms. There are a great number of animals with behaviour and nervous systems, and functions and physiology, which have many similarities with humans. Many animals run, many walk, many taste and smell in ways we do, and so on. Some animals fly, we do not.

That brings us to sociology, and how our societies grew. Humans are distinct from other animals, in that, over evolutionary time, we chanced upon ways by which we could throw objects, and therefore make tools and engineer nature. We could speak and therefore communicate with each other and develop language.

This combination of engineering and language then dramatically transformed us and our ways of communication over distances. Because of the way we cooked food, our brains grew disproportionate to our body and, therefore, we could have overdesigned computers in our brains, which could deal with

* Inaugural lecture by Gagandeep Kang in the Women in Science and Technology Series delivered on 1 August 2019 at the India International Centre. The introduction was by K. Vijayaraghavan.

abstractions in a way no other animal can. This combination resulted in us breaking our biological bonds and learning how to fly, for example, or go to outer space. Yet, ironically, when we deal with our societies, we often talk about 'biological limitations' when we have already overthrown so many biological limitations.

One common argument for why we do not find women in leadership roles, or women and employment in sectors in a manner in which we find men, is biological. However, that argument is untenable, incorrect. For all the reasons enumerated earlier, men and women are no longer constrained by their biological limitations because our societies, our languages, our technologies, have the ability to limit, if not completely overcome, whatever those limitations might or might not be.

So why then do we find such disproportionate under-representation of women in public life? The answer must therefore lie not in biology, but in sociology, in economics, and in the way society is structured. And our societies are structured in a very simple manner. When the man goes to work and spends 24x7 thinking about his job, he has a workforce behind him, which gets him ready for that purpose. And this workforce involves the woman, family members and a support system. That economic vestige of early economic growth in our societies remains in a completely changing world. But it is time it is overthrown. Unless that changes fundamentally—and it is eminently overthrowable—we are going to be trapped in a system where we provide biological excuses to problems which do not have any such basis.

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Science and technology, and our institutions,

have an extraordinary opportunity too, because these structures are flexible and do not require a person to come and leave at a particular time. There are all sorts of other flexibilities about where one works, when one works, how one works. And, therefore, in terms of setting examples, there is an incredible opportunity which we have started to grasp, but now need to grasp a lot more and address.

Gagandeep Kang

I come from a section of society where we have had every opportunity to do all the things we have desired and in every field. Women in this class of society are not restricted in terms of education; we get support in many shapes and forms. When I look around me, I see women achievers everywhere in India, including in the fields of science. So when I analysed my own journey in science, I thought I was simply doing what everybody else was, until I started to look at the numbers. This was an exercise that was, to some extent, forced on me by the National Institute of Health which asked me to measure the number of women at every level of academia in my institution.

At the Christian Medical College (CMC), Vellore, an institution started by a woman, where at least 40 per cent of every incoming class consists of women, I found that at the assistant professor level, the ratio was 50:50. But as one scaled the ladder, the percentage of women decreased. I began to ask myself, if it could happen in a place like CMC, what did this mean for the rest of the country? When I joined the Translational Health Science and Technology Institute, it was interesting to note that there was only one other woman on the faculty—we become the exceptions when we come up to this level. I will first reflect on my work and then about how I reached where I am today.

Let me begin by asking you to picture this: if you lift the skin on a child's abdomen, it takes more than two seconds to become flat. This is a pinch test, done when a child has diarrhoea to assess dehydration. Longer than two seconds indicates that the child is dehydrated and requires rehydration. If we think of the average person, let us say he or she is about 60 kilos—the average baby at about six/seven months of age is about six kilos. But in terms of surface area, the baby has about a quarter of the surface area of an adult at a tenth the weight. This means when diarrhoea strikes, dehydration happens much faster in children.

This is critically important because dehydration can kill. I work on a rather pretty virus—the rotavirus—a very simple one with 12 proteins. One of those proteins, which is a non-structural protein, affects cells in the gut. Through a mechanism of calcium signalling, it leads to a great deal of chloride secretion into the gut. When chloride is secreted into the gut, water follows. And if the colon cannot absorb the amount of water that is entering the gut, it results in diarrhoea. This loss of fluid from diarrhoea can lead to dehydration.

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The rotavirus also has another trick up its sleeve—it causes vomiting. As is commonly known, during diarrhoea, when all that is required is to administer fluids, it becomes difficult to give fluids orally when the patient has both vomiting and diarrhoea. That is why children who cannot get care quickly enough die. Essentially, for the last 25 years I have studied diarrhoea in both the community and in hospital, and made estimates for how much death is caused by diarrhoea.

Statistics show that of the 27 million children that are born in India every year, one in two children will have diarrhoea, one in eight will require an OPD visit for diarrhoea, one in 30 will be hospitalised, and one in 350 will die. We know this because we conducted community studies all over India, and in hospitals. For the deaths, we recorded the diarrhoeal deaths in our community and hospital populations. But we were just a few sites, so we also looked at government estimates of how many children were dying of diarrhoea in different states of India, and also what this meant for households. If you have a child admitted with diarrhoea and you work in the kinds of places where we were doing the surveillance, a rotavirus hospitalisation costs five per cent of the mean annual household income. So, with a rotavirus infection, not only do you have a child who is sick enough to be in hospital, you are also taking a significant economic hit because of this virus.

This led us to studies in the community to try to understand how we could protect against this virus. The first studies were rather disappointing. There were studies done in other parts of the world which showed that, essentially, if your child has had two rotavirus infections—natural infections—he/she would be 100 per cent protected from diarrhoea. But for children in Indian slums, two infections conferred only approximately 57 per cent protection, and three infections only 80 per cent protection. That information was plugged into a model which calculated that a vaccine would provide about 45 to 50 per cent protection. However, that protection was unlikely to last beyond a year or two. In rich countries, where children get much better protection, that protective shield would be good and last for a long time. But that would not be the case when the vaccines were brought to India.

Nonetheless, given the fact that we have so many diarrhoeal infections, we also estimated that if we had a vaccine that was even 50 per cent effective, as

predicted, this would save 30,000 lives every year. We worked with a very large consortium, and that resulted in a rotavirus vaccine that was supported through its development by the Department of Biotechnology for over 20 years. It was finally made by an Indian company—Bharat Biotech—and was introduced into the national immunisation programme in 2016. Now, in order to see whether the vaccine was really working very well or not, we did a study with 34 hospitals, assessing children who were admitted with diarrhoea, then looking backwards to see whether or not they had been given the vaccine.

Usually, a trial testing of vaccines takes very healthy babies, gives them the vaccine, and then follows them up to see if they are protected from disease. In the trials that we did towards licensure, those babies had protection—about 55 per cent protection in the vaccine trial—as predicted by our model. But we wanted to see if that would be the case in the real world. The data that are just emerging are unpublished, but show us that vaccine protection is as much as we saw in the efficacy studies in the first year of life. But, this is the real world, and all children are not healthy. Now, chronically malnourished children are usually stunted, i.e., they are short for their age. Stunting is a sign of chronic malnutrition. The data from our effectiveness studies show that in the first year of life, stunted children are reasonably well protected, but they have no protection in the second year of life, while normally nourished children maintain that protection. So the prediction in our model, which was built on stunted children, is holding up.

Now, why is this important?

Children who live in abject poverty take multiple hits. Let us take the example of a little girl born with low birth weight. The first child of a minimally educated mother, she had very little breastfeeding as she was

weaned early. Her growth chart showed that she was well below the average. For instance, as against a height for age Z score of minus two, her's is well below that score. So this child can be considered chronically malnourished.

Because stunted children look healthy, stunting is a hidden burden of malnutrition that we do not see. One of the things that I have tried to understand in my studies on nutrition and immune responses to infection and vaccines, is the gut environment.

Because stunted children look healthy, stunting is a hidden burden of malnutrition that we do not see. One of the things that I have tried to understand in my studies on nutrition and immune responses to infection and vaccines, is the gut environment. To do that, I decided to induct children from well-off families. At the Christian Medical College (CMC), where staff live on campus, families are not rich but are definitely better off than those who live in slums. We measured two things: one, the number of potentially dangerous bugs in these children's guts. In the slums, each child who looked healthy, and did not have diarrhoea, had four bugs. Doctors' children at CMC had one bug each. Therefore, four times greater pathogens were being carried in the intestinal tracts of slum children. Second, inflammatory markers examined for both sets of children found the levels in doctors' children to be almost nil, while children in the slums showed very high levels—roughly 1,600. Consider this—the diagnosis for inflammatory bowel disease is a level above 200; these slum children have eight times greater inflammation in their guts than an adult with a diagnosis of inflammatory bowel disease. Consequently, there is no question that their guts are damaged.

Gut damage includes an inability to absorb nutrients and points to chronic malnutrition. In this setting, we found that these children have about 30 per cent stunting. We decided to try to analyse the physical and mental consequences of stunting in our children. It is to see what happens to their

physical development because children can be skinny and short, assessing mental development is harder. After tracking these children for nearly 20 years, with multiple assessments, we find that the median IQ in slums is 89. That is low-normal; 90 to 110 is normal. So if this is our median IQ, there is a distribution around it. Going deeper into the distribution and the factors that determine it, we found that children who have been persistently stunted—stunted for long periods of time—had IQs significantly lower than children who have never been stunted. The resultant outcome—in terms of society, in terms of economy—has been measured by overseas researchers and economists. It has been estimated that for every five points lost in IQ, about 10 per cent is lost in terminal income.

This is a problem for India, because between three and four of 10 children in India are chronically stunted in more than 200 districts. There is no district in India with less than 10 per cent stunting. The distribution is such that it is worse in the north and the centre of the country, less in the south. Our data are from the south, and show the enormity of our burden; we have no measurements of this kind from the north.

How did I get involved with this kind of work? My father was in the Railways—that meant we moved a lot. Unlike in the army where you get furniture when you move, in the Railways you have to move your entire household, every last bit of it. In addition to being an outstanding teacher who worked her whole life, my mother was an expert in logistics, and she could pack and unpack a house in three days flat. We moved during our holidays, from school to school; I studied in 10 different schools. That taught me a lot about flexibility. My father and mother were responsible for me playing catch-up every time I went to a new school because, in those days, every school had a different system of education. Therefore, you had to decipher what had been going on in classes before you got there, and

then try and make your way up to competence in class.

Then I went to medical school in Vellore. This was the first time that I had actually stayed in one place for five years, and I have stayed in Vellore pretty much ever since. I think what medical school taught me was that there are a lot of unexpected things that are thrown at you. You have classes—I spent a lot of time not attending classes; I spent a lot of time with friends, and making new friends. Vellore had this wonderful system of foster families where you were taken into households, and sometimes you clicked and sometimes you did not. You desperately—as all students do—studied for exams. But I think what mattered to me most was that we spent a great deal of time doing things that had nothing to do with medicine.

The highlight of my career was being the person who did props for *Evita*. And I made a lot of friends who have stayed friends ever since. After I completed my MBBS, I had to think about what I really wanted to do. And it had to be an MD. I did not think I was cut out to be a surgeon. I thought about Ophthalmology, I thought about Psychiatry, and then I finally went into Microbiology. At the end of it, the only thing I could think of was: I do not really want to do this day in and day out. After much thought and discussions with many friends, I decided that I would go into a field that was more about research.

Why did I choose diarrhoea? Because diarrhoea is complicated. When studying infectious diseases, most other sites in the body deal with sterile environments. When you find a bug, it is almost inevitably causing a disease. With diarrhoea, the gut environment is very much more complicated, because it is not sterile. So each time you have to decipher what is going on, is there an association with disease or not? The gut has complicated

functions. Immunity is obviously important, but, as mentioned earlier, with the rotavirus vaccine, our children do not respond as well as in other places. Nutrition is also an important function of the gut. That is determined both by the damage that is done to the cells in the gut, as well as the composition of the flora that is within the gut. These are the issues on which we are now working.

It is well known that in an environment concerning medicine and research, the one thing that is almost never done in India is to tell people at a junior level that they are doing a good job. I had the opportunity to go on a fellowship to the United Kingdom and then to the United States, and I found that, for the first time, people were telling me, yes, you are capable and you can do this. They believed in me, and they thought I could get things done.

Nevertheless, in addition to the verbal validation, some level of street credibility is required. So I took the Royal College of Pathology membership exams and went to work in the United States with an outstanding woman, Mary Estes. She introduced me to the rotavirus, and has been a support ever since. When you are doing well in the United Kingdom and the United States, you are inevitably faced with the obvious question: Why not stay here? It is such a comfortable environment, and you can do so much research.

But the one thing I realised during my stints abroad was that if I stayed back, I would be one of a thousand or a hundred thousand people who could do what I could do. However, if I returned to India and brought back with me all of the new tools that I had acquired, I would be one among very few who were able to do the kind of research I was considering, and perhaps I could use these tools to solve problems. Now, that was aspirational—that

was really wonderful. You feel idealistic and think you are going to save the world. Then you find that things are a lot harder than you had anticipated. And, for me, they were even harder because many of those who were supposed to work with me had been promoted to other positions. So I had to handle many different things by myself, and that is when I had to call on all kinds of support systems.

I am lucky to have phenomenal friends. My roommate, my classmates, all rallied round whenever I needed them. When I had to write my PhD thesis, my friend stayed up with me because I had two children by then. I had to look after them during the day, but she would sit up with me at night and we would type together, which was very helpful.

Anna Jacob is my husband's great aunt. She passed away two years ago. She became a nurse in 1932 and was Nursing Superintendent of CMC for 28 years. She flew for the first time in 1947, and sailed across the Atlantic to go to college at McGill (Canada). I met her when I got married. She became a role model for me, someone who was always cheerful, who had lots of stories to tell, and had done incredible things in her life at a time that was much more difficult than the time that I was facing problems. She always had a smile on her face and the ability to calm one down, which is really important when one is getting stressed by multiple problems.

Sasirekha Ramani was my first PhD student, and she is now an assistant professor at Baylor College of Medicine. When you start out with your first student, you do not know how to handle things. So it is a learning experience for both of you. I think we did a reasonable job, because I am really proud of the fact that now she is well ahead of me when we talk about science.

So which are friends, heroes, which are scientists? I think all of them are my friends, my heroes and scientists.

When I first started my cohort, there were many learning experiences along the way. It encouraged us to think about how to keep women in the cohort, particularly if you wanted to do so for really long periods of time. And one of the ideas I came up with is to invite them to the clinic on their children's birthdays and photograph them. That photograph would be framed and given to them as a gift. Obviously, this was in the days before the smartphone. These children are now adolescents and are still part of our studies, and this relationship really matters to me.

I believe that working in the community reminds you why you are doing the work that you are doing. The kinds of problems that these women have had—whether it is domestic violence; or the husband getting into debt, and the wives then needing to go out and work; when their children have had serious illnesses—and the manner in which they tackled their problems has taught me a lot.

This is what I have learnt in 30 years of being in science: a strong foundation, having a strong family and friends, are valuable. I believe what has distinguished me from others is that I am quite willing to desperately cry for help when I need it. And help has always come. I think being curious, asking questions and looking for answers is the way forward for women in science—in fact, it is the way forward for everybody working in science. We will either solve problems, or we will conclude that they cannot be done quite that way. I believe that not staying with problems, giving up too easily, or going into too many different areas is the problem. If

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you stay with one question long enough, you will discover the answer. The most important thing to remember is finding out, from talking to my peers, to my students, that I am making a difference and how much of a difference.

Now it is time for me to become even more ambitious. Next, I plan to start working on pregnancy risk stratification in a border district of Assam, with a wonderful group of people who have established a hospital there.

Some districts in Assam have the highest maternal and infant mortality in the country and that is why I want to work there to ensure that we can create pathways to care for women and children. This is the work that I want to do in the community. There is also work that I want to do in the laboratory and hospital, and for that I plan to work on human infection studies. This involves asking volunteers to infect themselves with pathogens that cause diseases in our populations. Why did I consider this? For instance, the typhoid conjugate vaccine, which is made in India, had to be taken to Oxford to test its efficacy on Oxford undergraduates, which may not reflect exactly what we will see in India. Unfortunately, we do not do these kinds of studies here. I would like to establish these studies because I believe that in India we should be thinking about innovation for ourselves. If these systems help us to get answers, if we can really investigate responses to vaccines and drugs on our own populations, our chances of getting them out to people are that much higher, and are going to be faster.

To conclude, the most important thing I have learnt is that my environment shaped me. I am what I am because of all the influences on me, because of all the support systems that I have had. When we think about women in science, I believe the most important thing is to remember, particularly for people who do not come from a place of privilege like us, is that you cannot be what you cannot see.

About the Author

Professor Gagandeep Kang is the Executive Director, Translational Health Science and Technology Institute (THSTI), Department of Biotechnology. Previously, she was Professor and Head of the Wellcome Trust Research Laboratory, and the Division of Gastrointestinal Sciences at the Christian Medical College in Vellore. Professor Kang's research is on enteric infection and its consequences in children. With comprehensive studies on rotavirus, she is internationally recognised for her contributions to vaccine development and vaccine policy. She has established a strong training programme in clinical translational medicine, aiming to build a cadre of clinical researchers studying relevant problems in India. Her work has been recognised through several awards, most notably the Infosys Prize in Life Sciences, the first awarded to a physician. In 2019, she was elected a Fellow of the Royal Society.

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