

SHORT COMMUNICATION**A DOCTOR'S DILEMMA
(DNA TESTS—A DOCTOR'S DILEMMA)**

D. Balasubramanian*

Royalty in Europe married within itself—a policy steeped both in the idea of keeping the money and the power within a small number of hands. But it did have its downside too, one of which was the frequency of the disease haemophilia. The Royal Barber had to shave His Royal Highness gingerly and with great care, lest he cuts the skin and draws blood. If he did, the consequences would be disastrous not only for the barber but for His Royal Highness as well. Haemophilia is a disease in which the mechanism by which blood clots goes awry. We now know it to be associated with an error in DNA. The Royal Physicians who knew no DNA, knew however that the condition runs in families and is hereditary. Consequently, they advised the Royal matchmakers to choose the alliances carefully enough so as to avoid haemophilia.

Hereditary diseases do not belong to palaces alone. The neurological condition called Huntington's chorea is a gene-related disorder that affects thousands of people all over the world. First discovered and described in some detail in America, it was established that this disease had descended from two brothers with Huntington's chorea, who migrated to the US from England. Patients afflicted with this disease

show signs of brain malfunction that includes restlessness, dance-like gestures (hence the name "chorea" from the Greek word for dance) to severe grimacings and grotesque motions. It also leads to progressive intellectual impairment and paranoid delusion. The patients need to be contained in hospitals and psychiatric clinics. Unfortunately, unlike its earlier cousin, Sydenham's chorea, also called the St. Vitus dance, Huntington's disease has no cure. Sydenham's chorea appears to arise from autosuggestion and is manifested as a kind of frenzy. Rampant in 11th and 12th centuries Europe, it involved dozens of people dancing in a frenzied fashion in churches, for periods lasting from minutes to days. They were considered possessed and the cure was thought to be through the blessings of St Vitus. Alas, Huntington's disease is not only more severe and incurable, but also one that involves a genetic disorder. The gene for Huntington's disease has been identified and is found to have a large number of "spelling errors", namely repeats of the base-sequence CAG. Close to 30,000 families in America are estimated to harbour this condition. We do not have any reliable statistics about its incidence and prevalence in India.

Or take what is now called Alzheimer's disease. First discovered by the German physician Alois Alzheimer in 1907, this condition manifests

*L.V. Prasad Eye Institute, Road No., Banjara Hills, Hyderabad-500034. E-mail:dbala@luplyestph.net. Article published earlier in the Hindu. Reproduced with permission.

itself in later middle life as a neurological disorder involving loss of memory, impaired thought processes and abnormal behaviour. The disease usually starting before the age of 65 is commonly referred to as Alzheimer's, and if it occurs after the age of 65 it is called senile dementia. It is estimated that as many as 5% of the American population over 65 years of age suffer from this condition and also that it is somewhat more prevalent among women than men. It runs its course anywhere from three to eight years and the hapless sufferer dies with no cure.

Modern genetics has thrown light on the molecular basis of these and a few other diseases. Just as Huntington's disease is associated with a stuttering of the gene with the CAG signal, Myotonic dystrophy another severe neuromuscular condition, is associated with a similar triplet stutter in another gene, this time involving CTG as the repeat. Such mistakes in spelling, phrase or syntax that occur in the genetic message are called mutations. Mutations can range from being occasionally helpful (new, improved message) to benign and often deadly. Mutations in what is called the *ApoE* gene seem associated with Alzheimer's disease. Every year, with increasing frequency, the litany of mutations and genetic disease in man rises. Many a cancer, whether it is ovarian or breast cancer in women or colon and prostate cancer in men, appear associated with mutations in one or more genes in our body.

SHOULD WE TEST ?

As these discoveries are made, there is an increasing tendency to move them from the

research table to the pathology laboratory. The urge to do genetic testing increases. A family might wish to know whether any debilitating condition like Huntington's or Alzheimer's, runs in the family and whether a child may carry the lethal gene.

In some instances, prior knowledge about a condition may be helpful. A woman who tests positive to breast cancer, might decide to go for mastectomy or surgical removal of the tissue, as a preventive measure. Or a person who discovers that he is a potential diabetic may change his habits and diet right away so as to lessen or annul the effects of the debilitating condition. Thus, there are tangible benefits to testing. On the flip side is the question of whether such a genetic testing is always desirable, especially in cases where there is no cure. If one is tested for such a mutation and the answer is negative, the result is an enormous relief and one can lead an ordinary life. But what if one tests positive? That would then turn out to be today's equivalent of the sword of Damocles. As is to be expected in a situation like this, there are extreme and divided views and stands taken. The Government of India, for example, banned prenatal testing for determining the sex of the yet-to-be-born baby in order to legally curb female infanticide, one of the worst ills of our society. Should there also be a ban on genetic testing for Alzheimer's, Huntington's and similar incurable diseases?

How much would such a knowledge add to the quality of life of the person who tests positive? Can he ever lead a stress-free life thereafter? Then, there are other implications and overtones. For example, insurance companies can refuse to insure people who are

prone to such conditions. Would it be right for insurance companies, therefore, to demand the genetic testing of prospective clients? Or is the individual better off not knowing anything about such a condition lurking in his genes?

The practice of every doctor before he starts his career is to solemnly swear by the oath of Hippocrates. The great Greek physician of the 5th Century BC wrote the following oath to be taken by every physician :

I will look upon him who taught me this art as one of my parents. I will share my substance with him and I will supply his necessities, if he be in need.... The regimen I adopt shall be for the benefit of my patients according to my ability and judgement and not for their hurt or any wrong....

Then should the doctor, in his wisdom, hide the information from his patient, in the best interest of the latter's physical and mental health? The basic advice a doctor ought to follow is : "First do no harm".

Despite this risk of psychological devastation, Dr. Richard Meyers, of the Boston University School of Medicine, has offered tests for the Huntington gene. He concedes that the benefits of such testing are not always clear, but he says he offers the test because he believes a person has an inalienable right to his or her genetic destiny. Dr. Meyers' assertion is a take-off in the spirit of the American constitution which offers its citizens the inalienable right to life, liberty and the pursuit of happiness. One needs to ask whether knowing that you have the Huntington's gene gives you the right to life and the pursuit of happiness?

ARE TESTS INFALLIBLE ?

On a completely different footing are the objections to this raised by other scientists. Dr. Francis Collins, who heads the National Centre for Human Genome Research, USA and also chairs the US National Advisory Council for Human Genome Research (NACHGR), has recommended against testing for some mutations which are thought to be associated with some form of colon cancer. The reason for their doing so is the inherent inaccuracies that creep into any such gene testing.

Collins argues that we do not yet understand what type of "false positives" and "false negatives" will occur in such testing. For example, in looking for a given gene you might find some abnormality in a given patient. There may be one or two bases that are altered in his gene when compared to the normal gene. Are these mutations and are they necessarily deadly? The difference between a dangerous mutation and a polymorphism—just a harmless genetic variant—is not easily interpreted. Polymorphism will thus appear as a false positive in the genetic testing. The "polymorphous" patient who came in for the testing might thus be unnecessarily worried—and the doctor too, for that matter. As of today there is no foolproof and general way to tell apart a potentially harmful change in the gene from a benign one.

Then there is the "false negative". Finding no abnormality in one gene does not guarantee that the testee is safe. There could be alterations or mutations in regions of the chromosome other than the candidate gene tested. Several instances are reported where not one but two or

three genes act in tandem to produce an effect.

That there is a demand and a market for genetic testing, at least in the US, is clear. An informal poll on 500 Americans found half of them opting for gene testing. It is certain that similar sentiments exist around the world. The feeling among the experts is that as of the moment, the worries regarding gene testing are more substantial than the benefits. The latter, though they may be much larger one day, are

small for one who test positive. The field of gene identification is still evolving. Scientists need to arrive at a consensus on how many genes, which genes and what sequences need to be tested. The methods need to be worked out made more rigorous and definitive. All this requires more work in the research laboratories before foolproof protocols and guidelines can be suggested to the pathologists. The bottom line is that it is too early to offer these services.

S & T ACROSS THE WORLD

EU—INDIA WIND ENERGY NETWORK

With over 2600 MW of installed wind power capacity, a robust growth rate and supporting government policies, wind energy seems to be blowing in the right direction in India. Further, the recently approved “EU—India Wind Energy Network (EIWEN)” project will help it gather speed. The network, co-funded by the European Commission, has been established under the EU-India Economic Cross Cultural Programme and is being implemented by a consortium comprising CII, ECN (Netherlands) EWEA (Belgium), Rise National Laboratory (Denmark), India Wind Turbines Manufacturers Association and Centre for Wind Energy Technology in India. The main object of the 36-month project is to facilitate entrepreneurial partnerships among wind energy actors in India and Europe. The project offers exciting opportunities to promote durable collaboration between the Indian wind industry and European counterparts. A help desk is proposed to be created in CII to ensure smooth and efficient dissemination of data/information gathered through the project to the industry, financial institutions and technical/research centres.

(CII Communique, July 2004)

OBSERVATION OF EARTH FROM SPACE

Indian Space Research Organisation (ISRO) and the US National Oceanic and Atmospheric Administration (NOAA) announced recently that India and United States intend to work together

on the National Polar-Orbiting Operational Environmental Satellite System (NPOESS) which is engaged in remote sensing from a polar orbit. Expected launch of NPOESS is in the year 2009. NPOESS will provide rapid distribution of global and regional environmental imagery, meteorological, climatic, terrestrial, oceanic and solar-geophysical data for use by the international community. Data from this system is expected to help in the timely prediction of cyclones, support disaster management efforts and benefit the development and management of agriculture, fisheries, maritime industries and other sectors.

(Chemical Weekly, June 29, 2004)

ISRO'S TELEMEDICINE NETWORK

Launch of the operational phase of Karnataka Telemedicine Project and the recent inauguration of Telemedicine projects in West Bengal and the North East gives further fillip to ISRO's telemedicine network. Telemedicine helps to connect remote real hospitals/health centres to super specialty hospitals located in the cities and helps patients in remote and rural areas to avail timely consultation from specialist doctors without the ordeal of travelling. The system consists of customized medical software integrated with computer hardware along with medical diagnostic instruments connected to VSAT (very small aperture terminal) at each location. In the past three years, ISRO's network has expanded to connect 45 remote and rural hospitals and 15 super specialty hospitals. The remote/rural nodes include the offshore islands of Andaman & Nicobar and Lakshadweep, the mountainous and hilly regions of Jammu & Kashmir including Kargil & Leh, Medical

College hospitals and some of the rural/district hospitals in Orissa and some in the mainland states. In West Bengal, besides earlier connectivity between the district hospitals and Bankura and Siliguri with Asia Heart Formation, Kolkata and Naryana Hrudayalaya, Bangalore, other recent connections are district hospitals at Krishna Nagar, Malda and Balurghat with super specialty hospitals Sri Ramakrishna Seva Prasthan Hospital and SSKM hospital in Kolkata besides others North Eastern States.

(Space India, Jan-Mar., 2004)

NANO SILICON

The tiny science on nanotechnology could give a big boost to cancer patients undergoing tumor treatment. BrachySil by biotech firm pSivida, is a silicon-based nanoscale system that takes drugs direct to the tumour site. Silicon structure carries and electrical current, is porous and adaptable to managing release of right amount of drug when needed. Biosilicon material is said to be cheap to make, biodegradable and safe to administer. Silican can also be very porous at that tiny scale. The pores are typically about 10 atoms across and can be loaded with drugs, peptides, genes, proteins, radionuclides and other therapeutics or vaccines. BrachySil is made by concentrating phosphorus in the silicon and putting it in a reactor. This creates the radioactive isotope phosphorus-32, which has a long half-life of 14 days, much longer than other radionuclides currently used, which often break down after just 60 hours. So far, lab tests have

been very successful, and the next phase of human testing in Singapore on primary liver tumour patients is expected to yield results by September or October, 2004. Singapore has one of the highest rates of liver cancer in the world.

(BBC News, June 18, 2004)

BUILDINGS AT RISK

Even though historic buildings and monuments may have stood for a couple of thousand years, they could be badly affected by a change in patterns of wind, rainfall and solar radiation, as observed by Britain's University of East Anglia. Italian researcher Cristine Sabbioni opines that sand storms caused by desertification could lead to the erosion of stones used to build the ancient temples and historic places of southern Italy. In view of the above, European experts are putting together a "Noah's Ark" list of famous and historic buildings that could be at risk from climate change. The three-year scheme backed by 1.2 million euros in funds from the European Commission, is being coordinated by the Institute for Sciences of the Atmosphere and Climate at the National Research Council in Bologna, Italy. Researchers from ten countries will set up a number of test sites to assess the risk of climate change on culture heritage. They will subsequently draw up a "Vulnerability Atlas" to indicate the areas which could be at threat, for necessary possible remedial measures.

(PTI Science Services, July 16-31, 2004)