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THE WELLNESS SUTRA
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IT'S ALL IN THE GENES

Do you need to know if your DNA is imbedded with disease-causing mutations?

The answer is, it depends.

In May, actor Angelina Jolie announced in an article in *The New York Times* that she had a double mastectomy, or the surgical removal of both her breasts. She wrote that she chose this path because of a heightened risk of breast cancer given her family history and because her DNA carries breast cancer-related mutations in the BRCA1 and BRCA2 genes.

It is no surprise then that mutations in these genes—basically errors in their blueprint—predispose us to cancer. Mutations in these genes prevent damaged DNA from being repaired and this DNA damage over successive replications can result in the cell growing uncontrollably and the tissue becoming cancerous.

All cancers are caused, in part, by mutations to the DNA, but only 5-10% of all cancers are caused by mutations inherited from our parents. As we age we tend to accumulate mutations as a natural part of ageing and these mutations can result in cancer. But these mutations are not inheritable, which is why in most people cancer appears later in the lives.

Vijay Haribhakti, consultant surgical oncologist, Jaslok Hospital and Research Centre, Mumbai, worries about Jolie's decision and the impact it can have. "Some women in India may choose to undergo a preventive double mastectomy when they do not need to," he says. According to him, 80% of his efforts in surgery are on breast conservation and his advice is that a double mastectomy followed by reconstructive surgery is not something to take lightly. "It is a major surgery with risks of complications at several junctures. Also, latest research shows that compared with a double mastectomy, a double mastectomy combined with an oophorectomy, or the removal of the ovaries, is even better at risk reduction if that is the end-point being considered," he adds. However, an oophorectomy has its own side-effects of accelerated ageing and accelerated osteoporosis.

"Knowing that you carry a cancer-causing mutation can be a source of unwarranted stress but getting tested isn't cheap; it costs ₹50,000 per BRCA gene," explains S.J. Patil, consultant, clinical genetics, Narayana Hrudayalaya, Bangalore, in an email interview. Eventually, such a procedure costs around ₹1 lakh.

Like BRCA1 and BRCA2, there are other genes that have been linked to cancer syndromes. Colon and prostate cancer are cancers for which gene mutations have been identified that can be passed on within a family. And genetic testing is advised if there are immediate members in the family with cancer or if the cancer appears early in a family member.

"Family history of rectal cancer combined with colon cancer in a person who is in his 30s or 40s strikes our curiosity and we recommend genetic testing in such a person," says Niby J. Elackatt, senior genetic counsellor, department of molecular genetics, Manipal Hospital, Bangalore.

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Cancer may require genetic testing depending on the circumstances but one disease in India necessitates it, and that is Beta-Thalassemia (B-Thalassemia) major. According to a paper by Dr Sarita Agarwal and colleagues from the department of genetics, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, published in January in the *Mediterranean Journal of Hematology and Infectious Diseases*, there are an estimated 45 million carriers of B-Thalassemia gene and about 12,000-15,000 infants are born with B-Thalassemia major every year in India. B-Thalassemia major is a disease where normal haemoglobin production is suppressed so that the patient needs regular blood transfusion and iron chelation therapy, both of which are very expensive. Iron chelation therapy is the removal of excess iron from the body with special drugs. While bone marrow transplantation is a cure, it is possible in only 30-40% of cases, write Dr Agarwal and colleagues.

"It should be tested for in every pregnancy and we routinely perform the blood test on all our patients," says Dr Gandhali Deorukhkar, consultant, obstetrics and gynaecology, Gynaecworld, Mumbai. If the blood test confirms that the mother is a carrier then the husband is tested as well and if they are both carriers then the chance that the child will be a carrier is 25%. "Many gynecologists require their pregnant patients to undergo a blood test and NT scan to check for Down's syndrome in the baby but don't require that they undergo the thalassemia test which can just as easily be tested for as well," says Elackatt. So expectant mothers should go through the test.

B-Thalassemia major is a monogenic disease, or one caused by a mutation in a single gene. More commonly occurring diseases like heart disease, diabetes and hypertension have multiple genes involved in their pathology. In the US, the cluster of genes that play a role in these diseases has been characterized by large population-based studies, which strengthen the link between the disease and the gene so that genetic testing for these diseases by studying the whole genome of a patient becomes a viable disease-prevention strategy and an emerging area of medicine. But applying the same technology in India right now doesn't make sense, says Anoop Misra, director and head, department of diabetes and metabolic diseases, Fortis Hospitals, Vasant Kunj, New Delhi.

"Whether the genes that play a role in say cardiovascular heart disease in Western patients will also play a role in Indians is not clear at all," he says. "If the risk is calculated based on Indian studies, then these are so few in number and of such small size that the risk calculated isn't accurate."

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A stitch in time: *Angelina Jolie (right) underwent double mastectomy due to a heightened risk of breast cancer.*