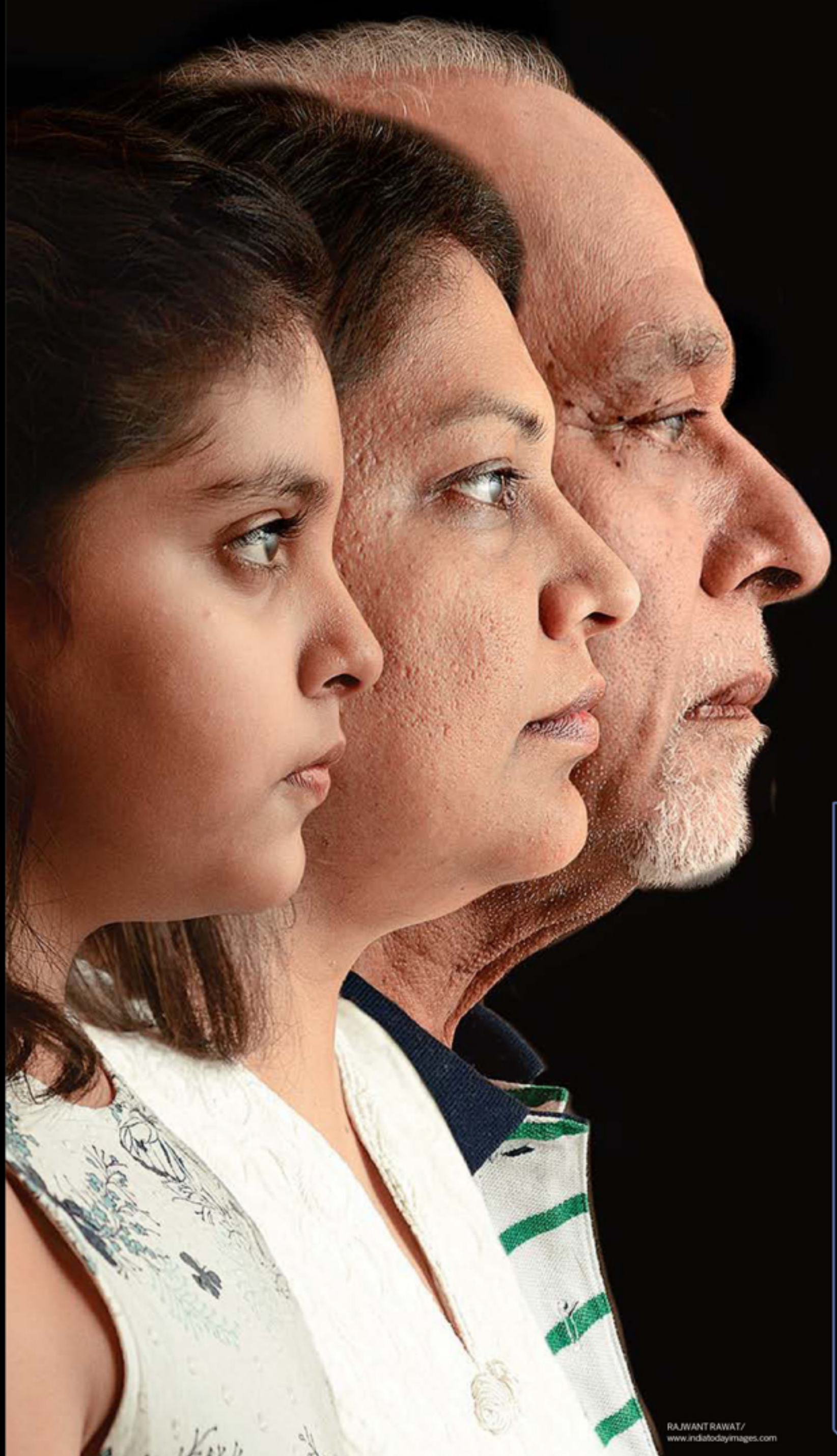

RAJWANT RAWAT/
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In Cancer's Shadow

Lovina got the faulty gene from her father Satinder Gujral. Her daughter Rhea is at risk. There's cancer on Rhea's father's side, too. Can doctors protect Rhea? There's hope now for the Gurgaon family...

SATINDER GUJRAL 70
Rx Male type breast cancer
Gene BRCA
Carrier Mother's side; three sisters with breast cancer
Undergone Surgery, chemotherapy, radiation

LOVINA GUJRAL 42
Rx Breast cancer
Gene BRCA
Carrier Father's side; father and three aunts
Undergone Surgery, chemotherapy, radiation

RHEA GUJRAL 9
Rx **At risk** of cancers diagnosed in family members
Gene BRCA likely
Carrier Both parents; mother, two grandfathers, three grandaunts
Options Gene counselling, gene testing, lifestyle change, chemo-prevention, preventive surgery

It's in Your Genes

New breakthrough in genetics now helps families with a history of cancer predict and prevent the world's most dreaded disease

By Damayanti Datta

Dr Nirmala Vaze's family tree is not just a patchwork of long-forgotten names and dates. There's a secret that flows through its branches: Cancer. It shows up like clockwork with every new generation. Breast, ovarian, uterine, blood, throat, prostate—you name it and it's here. It has ravaged 15 lives in the last three generations, the 67-year-old Nagpur gynaecologist being one of three in her generation of 10 to have defied death, if not cancer. It has also spilled on to generation next, with the age of onset falling from 40s to 20s: Vaze's architect daughter, Sampada Peshwe, 39, was diagnosed with breast cancer at just 26. If this is a family saga of heartbreak, it's also one of hope. The war on cancer has turned a new corner. And radical new genetic management of the disease, even before cancer strikes, is catching on. The Tata Memorial Centre (TMC) in Mumbai, where Peshwe was a patient, has put 35 members of Vaze's family through genetic tests: To predict their cancer risk and prevent it on time.

Vaze and her relatives were not surprised when Hollywood star Angelina Jolie vaulted into global headlines in May with her double mastectomy. Jolie may have stunned the world, but it's a story quietly being repeated all over the country, and the world. Hereditary cancers are in the news. Breathtaking changes in genetic research have given doctors new tools and tests to sort out the abnormal genes that lead to cancer. Going by statistics, just 10 per cent of all cancers are inherited. But by absolute

numbers, it's no less than 50,000 lives each year in India, says Dr Rajiv Sarin, who set up one of India's first cancer genetics units at TMC with support from the Indian Council of Medical Research. As the geography of investigation shifts from organs, tissues and cells to the DNA, it becomes increasingly possible for families with a history of cancer to buy their way out of destiny.

"In fact, Angelina Jolie has put us in a fix," says Dr Harit Chaturvedi, director of surgical oncology at Max Healthcare in Delhi. "We are now flooded with patients asking for the same type of treatments she went through." Preventive surgeries, where the surgeon removes tissue that does not yet contain cancer cells but may become cancerous, have been steadily rising in India in the last three years. Dr Chaturvedi has been doing at least one such surgery every two months. But his chamber is filling up with anxious men and women keen to follow in Jolie's footsteps. "Surgery is not the only preventive option," he says. Cancer genetics has opened up a whole new world: Genetic counselling, testing, screening, chemoprevention, surgery and, of course, aggressive lifestyle modifications. "What started with breast cancer has spread to ovarian, thyroid, uterine, colon and some rare gastric and kidney cancers. We can help more patients now," he says.

Ruchi V., 25, of Chennai is one such patient. Her mother has just been diagnosed with cancer, the dreaded word that unites her blood family. The disease has snuffed out five precious lives in the last three generations. Ruchi had always considered the deaths and the diseases unrelated. It is only now that she has started giving more than a fleeting thought to the idea that so many cancers in one family might not be normal. At a different time, she would have waited silently, in fear and faith, for the disease to strike. Today, thanks to the new treatment options, she can walk up to an oncologist and ask: "Can you tell me what I can do to save myself from cancer?"

TRACKING THE DEADLY GENE

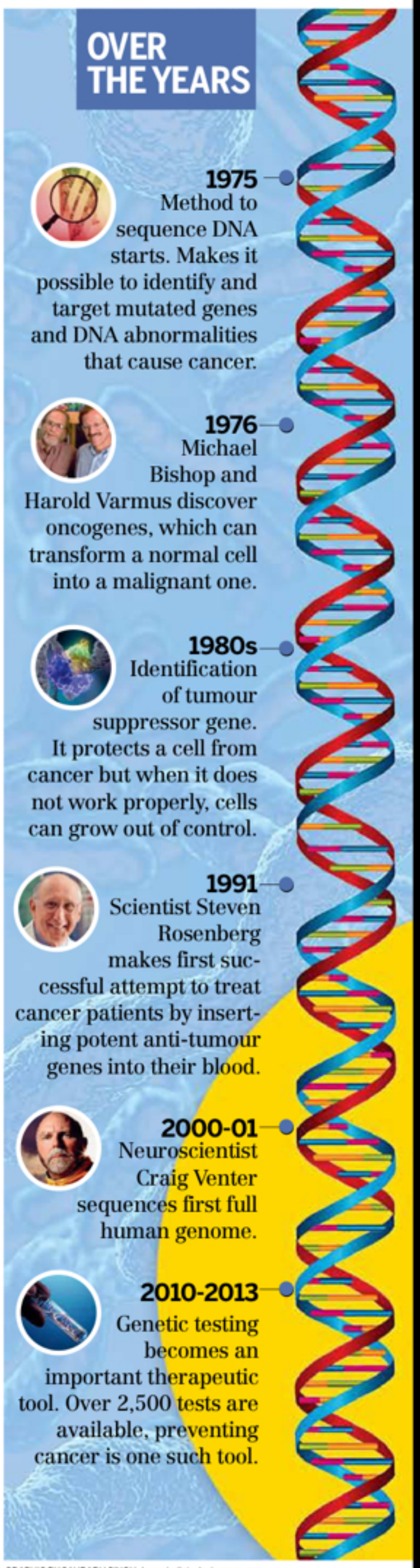
It's a typical question Dr Amit Verma, who runs the Familial Cancer Clinic at Max Healthcare, tries to answer. On any given day, his clinic fills up with men and women asking anxious questions: "My mother had cancer. Will I get it, too?", "Will I pass it on to my children?" Like a super sleuth, the cancer geneticist asks plenty of questions, fills his notebooks with sketches of family trees—circles for female, squares for male—sifts for clues in gene pools, simulates genetic models on his computer, does the algorithm to figure out

"I had cancer at 22. It's typical in cancer families." Shachi Marathe, 30 Mumbai

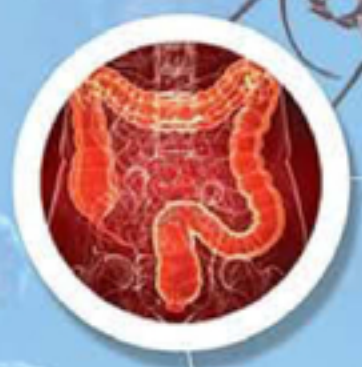
Her world came crashing down when she was diagnosed with breast cancer at just 22. There was a history of cancer in the family; her mother had also died of ovarian cancer. But Marathe had too many dreams and she fought back, with her childhood sweetheart by her side, through the rounds of surgery, chemotherapy and radiation.

She went through genetic counselling and testing after that, to prevent future incidents. Happily married and on routine check-up now, she, however, could not convince her relatives to follow suit. "They prefer to deal with cancer only after they get it," she says.

SHIVANGI KULKARNI



GRAPHIC BY SAURABH SINGH /www.indiatodayimages.com



COLON

Have a routine colonoscopy every 1 or 2 years, beginning at puberty; otherwise screen with endoscopy.

Relatives of people testing positive should consider genetic counselling and testing.

Large doses of aspirin over a long period of time may reduce risk. But beware of side effects.

Doctors may recommend removal of entire colon and rectum in case of rare, inherited syndromes.

GENE APC mutation

UTERINE

Medical examination of uterus and ovaries every year if at high risk.

Endometrial biopsy (tissue sample taken from lining of uterus) based on symptoms or examination every year, starting at age 30-35.

Utrasound based on symptoms or examination.

Hysterectomy (removal of uterus).

GENE HNPCC, BRCA mutation

BREAST

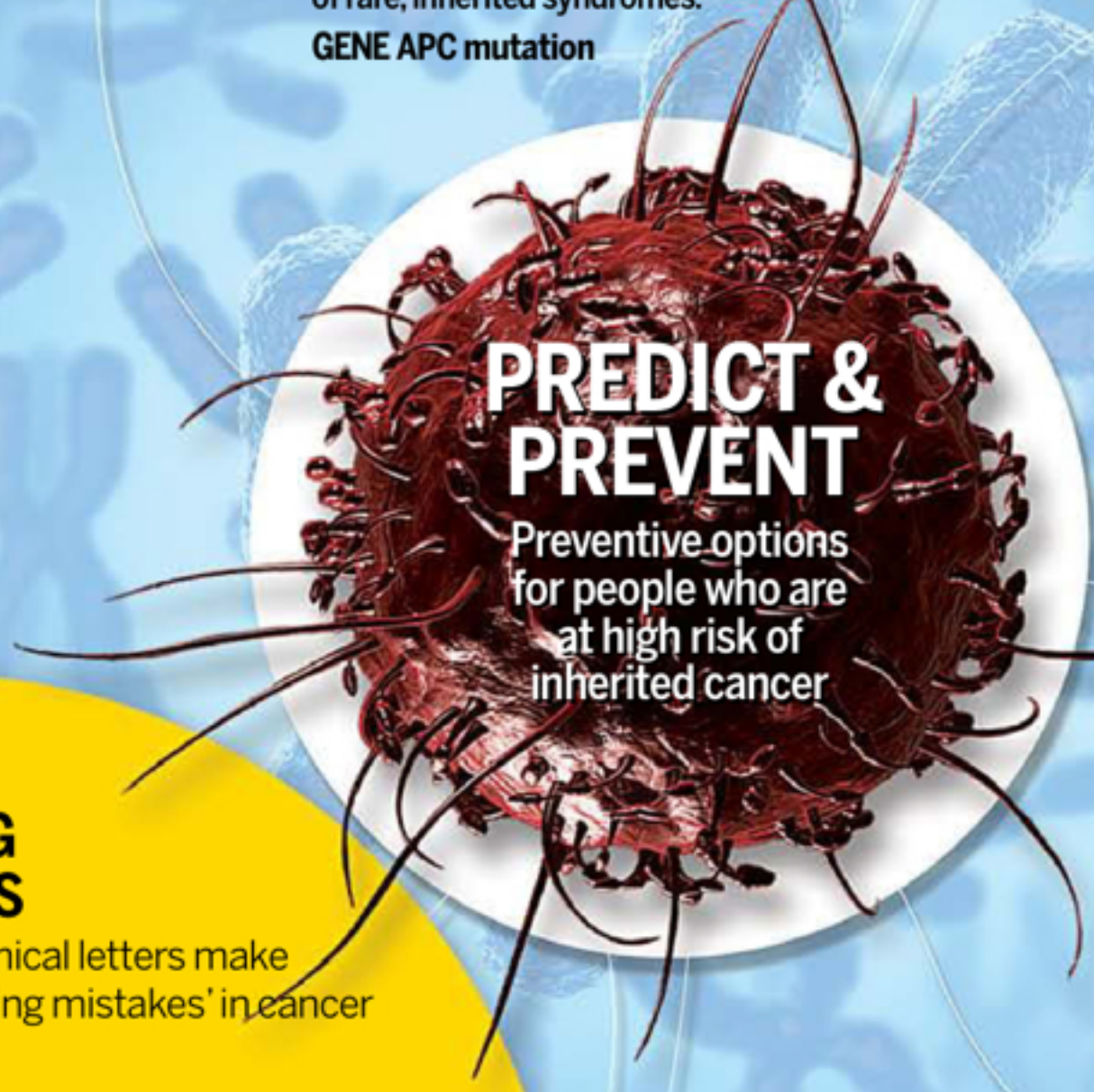
Genetic counselling or analysis of family, personal history.

Screening tests from breast self-examination, clinical examination to lab test of tissue.

Genetic tests that look for certain gene mutations.

Risk-reduction strategies like chemoprevention and prophylactic mastectomy.

GENE BRCA1, BRCA2 mutation



PREDICT & PREVENT

Preventive options for people who are at high risk of inherited cancer

OVARY

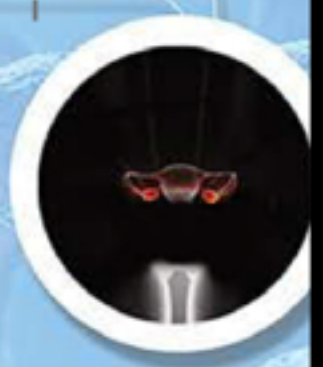
Pelvic examination every 1-2 years; every year from age 30.

Pelvic ultrasound per symptoms from age 30 or sooner, going by family history.

Oral contraceptives can reduce ovarian cancer by 50%.

Oophorectomy (ovary removal) on abnormal examination.

GENE BRCA, HER2, HNPCC mutation

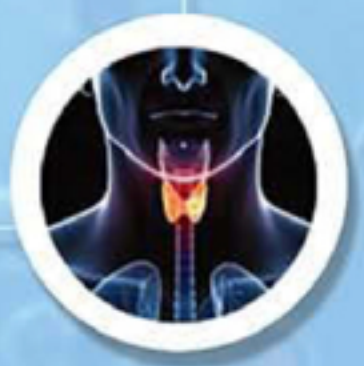


THYROID

Surgical removal of thyroid gland eliminates the risk of certain types of thyroid cancer.

A healthy diet, with five servings of fruits and vegetables daily. Antioxidants protect cells from damage. Unsaturated fats (Omega-3 fatty acids) may also help protect against cancer.

GENE RET mutation



SPELLING MISTAKES

DNA's 4 chemical letters make genetic 'spelling mistakes' in cancer

—MUTATION
When a change in a genetic letter takes place, like A changing into C.

—DELETION
When part of the DNA sequence goes missing.

—INVERSION
When a portion of the DNA sequence is reversed.

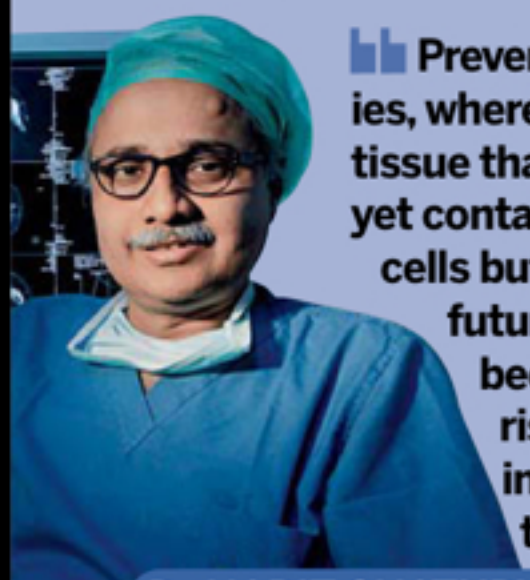
—INSERTION
When extra genetic alphabets are added to the sequence.

Source: Cancer Genetics Clinic, Tata Memorial Hospital and ACTREC, Mumbai; Dept. of Molecular Oncology, Adyar Cancer Institute, Chennai; Familial Cancer Clinic, Max Superspeciality Hospital, Delhi

Dr RAJIV SARIN

RADIATION ONCOLOGIST AND CANCER GENETICIST

In the last two years, the trickle of patients with inherited cancer has turned into a tide, with one or two coming to us every day now.



Preventive surgeries, where we remove tissue that does not yet contain cancer cells but may in future, have been steadily rising in India in the last three years.

Dr HARIT CHATURVEDI

SURGICAL ONCOLOGIST

Indians tend to marry within a given caste and sometimes within the family. This leads to the potential for relative inbreeding and possible segregation of genes.

Dr T. RAJKUMAR

MOLECULAR ONCOLOGIST

I have seen patients with strong family history of mutations but never expressing cancer, even at age 70, because of good lifestyle.

Dr AMIT VERMA

MOLECULAR ONCOLOGIST AND CANCER GENETICIST

percentage risk of cancer in one's genes and suggests the best battle plans to ward off cancer. And often his diagnosis is the discovery of a lifetime, the lifetime of his patients, for better or for worse. "Cancer is a disease of old age, but most family cancers strike at an unusually young age, even in teens and often before age 40," he says. "And all those who carry mutated genes have a 60-100 per cent lifetime risk of cancer."

At the root of it is God's own jigsaw puzzle: The human genome, or the entire set of inheritable traits in our cells that make us who we are. With scientists mapping more genes in the human body, cancer genetics is now one of the fastest expanding medical specialities. And it is altering clinical practice, with oncologists and geneticists targeting genes that are 'faulty' (*see box*). Hereditary cancers arise from altered genes passing down generations. "The probability of an inherited cancer goes up if you have a number of close relatives with cancer," says Dr Sarin. There are other pointers, too: Cancer at a young age and if the types of cancers in a family are similar. "For instance, all breast cancers are linked to ovarian or prostate cancers," he says.

A BOMB WAITING TO EXPLODE

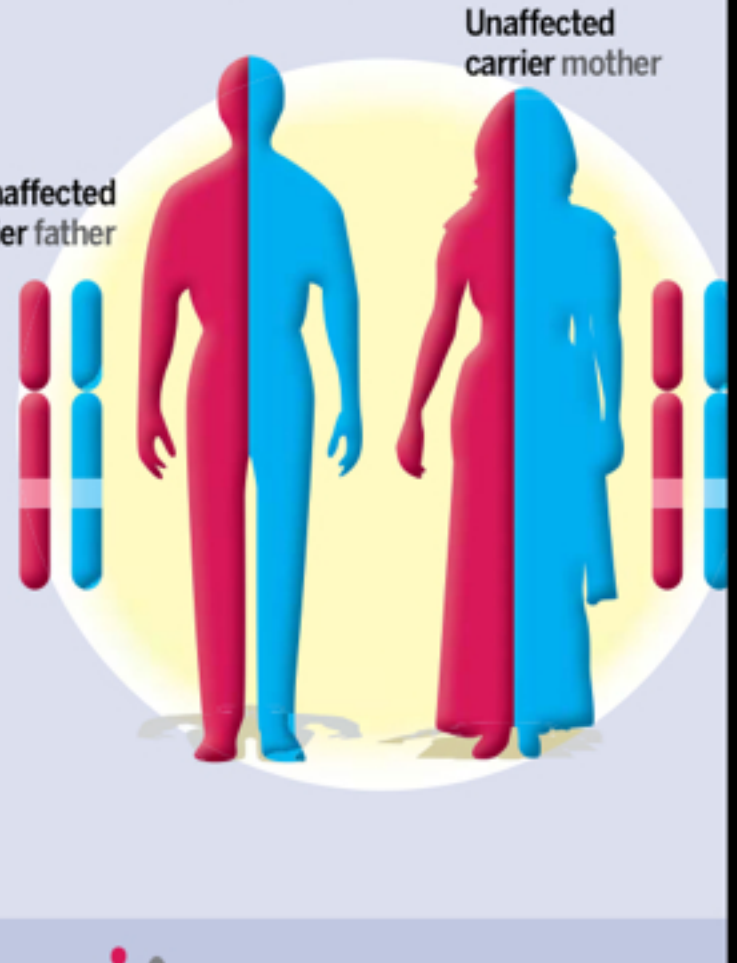
Age is a time bomb for inherited cancer. Vaze was 41 and a mother of two when she found a lump on her breast. She was not aware that some cancers could run in families, although her elder sister had been diagnosed with breast cancer. "Are you going to die like aunty?" her children asked. "I am sure I will come out of it," she told them. That was the pattern, even when she got cancer in her other breast 17 years later. "None of us sat and cried." But it broke her heart when her daughter was diagnosed with breast cancer at 26, just a month after her wedding. "What have I passed on to you," she had said. "Your cancer, yes, but also your fighting spirit," her daughter replied.

Shachi Marathe, 30, lost her mother to ovarian cancer by the time her breast cancer was spotted. The Mumbai girl was just 22. Her childhood sweetheart was by her side through the rounds of surgery, chemo and radiation. "We got married three years ago," she says. With a very strong family history of cancers on her mother's side, doctors at TMC offered genetic counselling and testing for her blood family. This would allow geneticists to study how the mutated gene behaves in her family and help those at high risk avoid cancer. And if a family member did get cancer, they would know exactly which genes to look for. "Unfortunately, many in my family did not agree to such tests," says Marathe. "They prefer to deal with cancer only after they get it."

That's exactly what doctors are warning against. "Cancer does not happen overnight. It's a process that takes time and then manifests one day," says Dr Verma. One's stress level, physique, weight, diet—all these come into the picture. "I have seen patients with strong

How cancer genes

Parents may carry hidden cancer



Two or more members, on the same side of the family, have similar types of cancer.

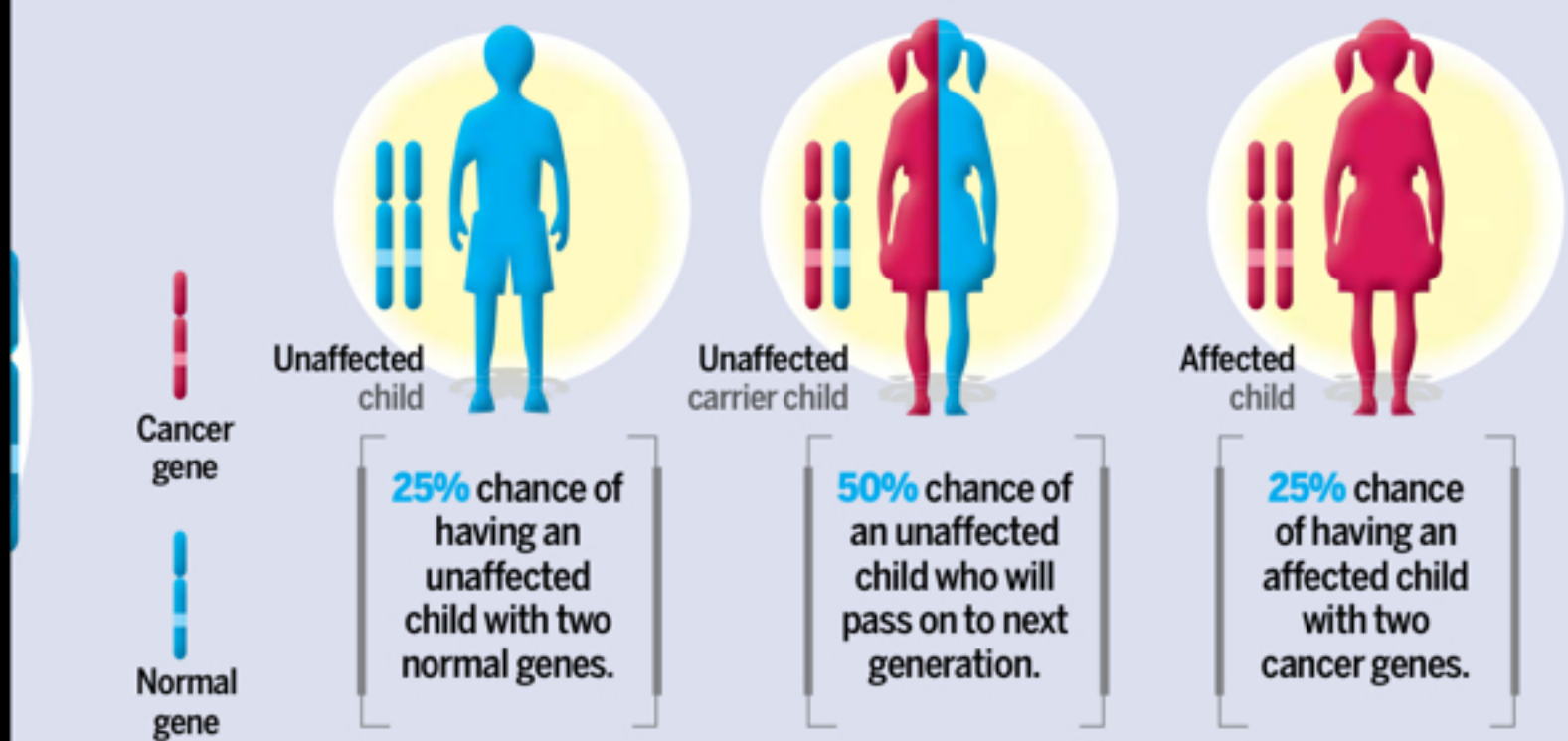
Cancer in two or more generations.

Cancer at an unusually young age, like colon cancer in a 20-year-old.

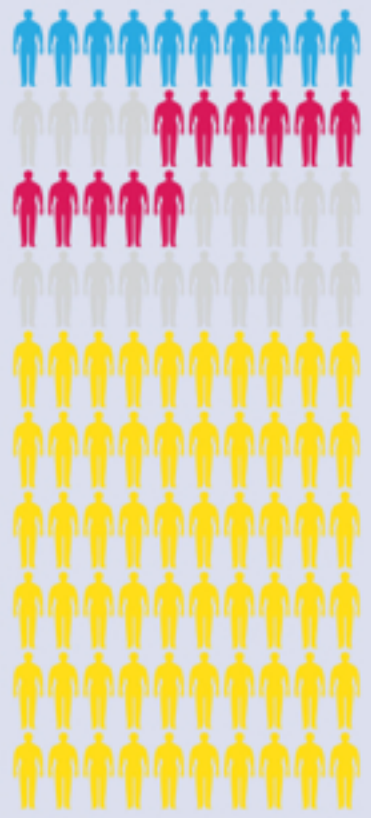
GRAPHIC BY RAHUL AWASTHI /www.indiatodayimages.com

are carried in a family

gene. This is how it is passed on.



FAMILY SHARE



5-10% are hereditary cancers with gene mutation

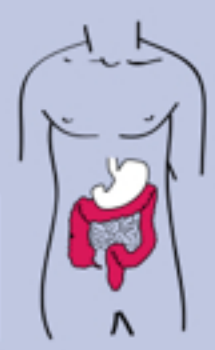
15-25% are familial cancers with no gene mutation but genetic and environmental factors.

60-100% life-time risk of developing cancer for those with inherited genes.

DO YOU RUN THE RISK OF CANCER IN YOUR FAMILY?

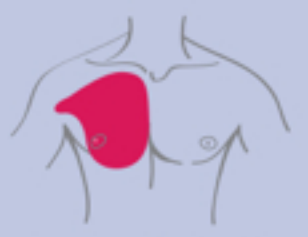
Yes, if one or several of these feature in your family

Cancer in paired organs (for instance, both breasts, both eyes).



A single person has more than one type of cancer (like both colon and uterine cancer, or both breast and ovarian cancer).

More than one cancer in a set of siblings.



The presence of a very rare cancer (like male breast cancer).

One is a member of a population, including Ashkenazi Jews, Dutch or Icelanders, known to carry the mutation.

Source: Cancer Genetics Clinic, Tata Memorial Hospital and ACTREC, Mumbai; Dept. of Molecular Oncology, Adyar Cancer Institute, Chennai; Familial Cancer Clinic, Max Superspeciality Hospital, Delhi

SHEKHAR SONI

"The Jewish gene makes us more prone to cancer."

Nirmala Vaze, 67, with daughter Sampada Peshwe, 40 Nagpur

Folklore says the Konkanastha Brahmins migrated to India from the frontier lands of Europe. When Vaze went for genetic testing at the Royal Marsden Cancer Hospital in London, it revealed a sub-type of an inherited genetic mutation found in the cancer-prone Ashkenazi Jews of Eastern European descent.

The 'faulty' gene that led Angelina Jolie to decide on a preventive double mastectomy is also an 'Ashkenazi Jewish mutation'. For Vaze, it was a moment of deep connect with her family's ancient legacy: The genetic root that explained why cancer had ravaged 15 lives in the last three generations. Vaze was 41when she found the first lump on her breast. It broke her heart when her daughter Sampada was diagnosed with breast cancer at 26. "What have I passed on to you," she had said. "Your cancer, yes, but also your fighting spirit," her daughter had replied.

family history of cancer and harbouring such mutations, but never suffer from cancer. Maybe their healthy lifestyle is protecting them," he says.

Shalini Shenoi, 69, of Bangalore, has avoided cancer. The social worker, who heads a health and family welfare NGO, Mahila Dakshata Samiti, is a firm believer in the power of prevention. She has lost 16 people in her family to cancer, including her mother. She has been screening herself regularly since 1989. "My father heard that the first mammogram machine arrived in Delhi and I got myself tested." Years later, genetic tests revealed abnormal mutations of the gene responsible for ovarian and breast cancer. "I carried on with my work, healthy lifestyle and managed to ward off the disease. Although I've had several false alarms and some lumps were taken out of my breasts, I never got cancer," she says.

"I had genetic mutation but no cancer."

Shalini Shenoi, 69 Bangalore

She escaped cancer by the skin of her teeth. Despite several false alarms and some surgeries, she has never actually had cancer. Born to a family where 16 people died of cancer, she has inherited the faulty family gene. But she was proactive about getting herself screened regularly since 1989, and living a healthy lifestyle.

Then genetic tests arrived on the scene. They revealed abnormal mutations of the BRCA gene, responsible for ovarian and breast cancers, but fortunately, no cancer.

NILOTPAL BARUAH/www.indiatodayimages.com

The nation's cancer treatment landscape is changing. New types of clinics are mushrooming, to assess susceptibility toward cancer running in families. New genetic testing labs are coming up, investigating blood, saliva and other tissue samples for cancer-causing changes in DNA. Star hospitals are expanding their cancer-care packages to include genetic options. "It's the new way to tackle the disease that has been too smart, too complex, too hostile and too quick at outsmarting therapies," says biotechnologist Anubhav Anusha, who started Nutragene, one of the first commercial genetic testing companies in the country in 2011. But genetic tests are expensive and can exceed Rs 80,000.

It's not just the economics; what gets in the way of prevention is attitude, feels Harmala Gupta, a cancer survivor who set up cancer support group CanSupport in Delhi. "Cancer has a huge stigma attached to it," she says. "Especially cancers that run in the family. Most Indian marriages are arranged and there's a fear that girls from such families will not get married." That stops people from seeking help. There is little awareness about familial cancers, she explains. "Not all cancers running in families follow the laws of inheritance." Some are caused by a combination of genetic, lifestyle and environmental factors; others are purely hereditary. "But how many families bother to find out what afflicts them?" she says.

"I carry a 'faulty' gene, BRCA1, which sharply increases my risk of developing breast cancer and ovarian cancer," wrote Angelina Jolie, defending her decision to remove her breasts. Her mother died of breast cancer at 56. Her aunt died of it on May 28. The surgery reportedly brought down her risk from 87 to 5 per cent. "I can tell my children they don't need to fear that they will lose me to breast cancer."

NOT ONE SIZE FITS ALL

Jolie's surgery spurred intense debate worldwide: Is it a cool extreme trend or a pointless risk? Ask Dr T. Rajkumar, professor and head of molecular oncology at Adyar Cancer Institute in Chennai. "If the risk of developing cancer is very, very high then surgical intervention is right," he says. Consider Familial Adenomatous Polyposis (FAP). It is an inherited disorder with cancer in the large intestine, or colon, and rectum. "People with the classic type of FAP begin to develop hundreds and thousands of benign polyps in the colon even in their teens. Unless the colon is removed, these turn malignant," he says.

Cancer is no longer a one-size-fits-all field. Treatment is not just tailored to unique genetics of an individual or the tumour now, it is also based on probabilities and permutations of risk. But in India, where one in 26 women develop breast cancer, with over 50 per cent patients visiting a doctor at stage 3 and 4, would such treatments be viable? Also, even if one's genes show an 80 per cent risk of cancer, can any doctor confirm that the patient will get cancer? How many Indians can afford such expensive treatments? Will the Jolie hype create unnecessary fear of cancer and needless amputations?

Doctors are too excited to care about the realities of the world beyond human life. "The more we understand the genetic basis of cancer, the more patients we can help," says Dr Chaturvedi. Cancer staging and prognosis in India is still based primarily on shape and size of tumours, he says. "Greater understanding of cancer biology, how genes grow out of control, the role they play in making normal cells malignant can only lead to better outcome." Genetics is the next stage in cancer research, he believes: "Let's first map the genes and save some lives." ■