Medical histories

4000–200 BC

In India, the concepts of Ayurvedic medicine are first laid out in sacred texts known as the Vedas. The goal of the medicine is to maintain balance between body, mind and spirit. Treatments are tailored to each person's *prakriti*, or constitution.

1865

"The true sanctuary of medical science is in a laboratory," writes French physiologist Claude Bernard in his *Introduction to the Study of Experimental Medicine*. Aided by a new understanding of bacteriology, and emerging technologies such as the blood-pressure cuff and X-rays, scientists start to develop better treatments. Doctors focus on assessing symptoms, taking shorter medical histories, and quickly categorizing patients according to their diagnosis.

FROM PEAS TO PEOPLE

1900

Three European botanists — Hugo DeVries, Carl Correns and Erich von Tschermak — work out the laws of genetic inheritance, by using flowering plants, maize (corn) and peas. They realize that Gregor Mendel reported the same laws in 1865, although his publication had largely been ignored. This time, the scientific community takes notice.

1902

London physician Archibald Garrod studies alkaptonuria, which causes dark urine. It arises in siblings, and he links it to Mendel's laws of heredity, the cause being genetic variation in metabolism: "Just as no two individuals of a species are absolutely identical in bodily structure neither are their chemical processes carried out on exactly the same lines" (A. E. Garrod *Lancet* **2,** 1616–1620; 1902).

RISE OF PHARMACOGENETICS

1932

Arthur Fox of DuPont Laboratories allows phenylthiocarbamide (PTC) powder to drift around his lab. A colleague complains of a bitter taste, which Fox cannot detect (A. L. Fox *Proc. Natl Acad. Sci. USA* **18,** 115–120; 1932). Geneticist Laurence Snyder finds that PTC "taste blindness" is recessively inherited, indicating a genetic origin for responses to chemicals (L. H. Snyder *Ohio J. Sci.* **32,** 436–440; 1932).

400 BC GREEK HUMOUR

Hippocrates establishes the scientific practice of medicine in Greece. He believes everyone has four humours — blood, phlegm, and black and yellow bile — and treats people as individuals of unique age and health status.

1763 CLARIFY AND CLASSIFY

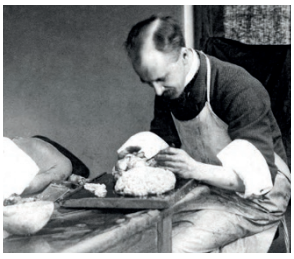
The 'father of taxonomy', Carl Linnaeus, catalogues diseases based on symptoms into groups such as 'feverish' or 'painful'. This does not always lead to better treatments.

1878 FOUL SOLUTION

US physicians use arsenic, in Fowler's solution, to improve white-blood-cell counts in a subset of leukaemia patients. It does not help most patients, and can have side effects such as liver disease, but becomes the standard treatment.

1892 WORK OF ART

In his influential textbook *The Principles and Practice of Medicine*, Canadian physician and pathologist William Osler (**pictured**) writes: "If it were not for the great variability among individuals medicine might as well be a science and not an art."



1907 BLOOD BROTHERS

Reuben Ottenberg of Mount Sinai Hospital in New York becomes the first to record testing a patient and donor for matching blood type before a transfusion. The practice makes transfusions safer, although it will be decades until this becomes common practice.

CLOCKWISE FROM TOP LEFT: FREDERIC SOLTAN/GETTY; SSPL/GETTY; NATL LIB. MED./SPL

The first medical interventions were often individualized but ineffective, because doctors lacked an understanding of disease biology. As medicine became more scientific, physicians started grouping patients by disease. Now, genetic insights let doctors consider their patients' unique make-up when prescribing treatments. **By Amber Dance.**

1957

US geneticist Arno Motulsky proposes that inherited traits explain why people react differently to medications. As the use of medicines grows in the 1950s, adverse reactions are more common. Variation in the enzyme glucose-6-phosphate dehydrogenase explains sensitivity to the antimalarial primaquine, for example, and a prolonged response to succinylcholine, used in anaesthesia, results from pseudocholinesterase deficiency. Later, Friedrich Vogel coins the term 'pharmacogenetics'.

THE GENETIC AGE

1990 GENETIC INTERVENTION

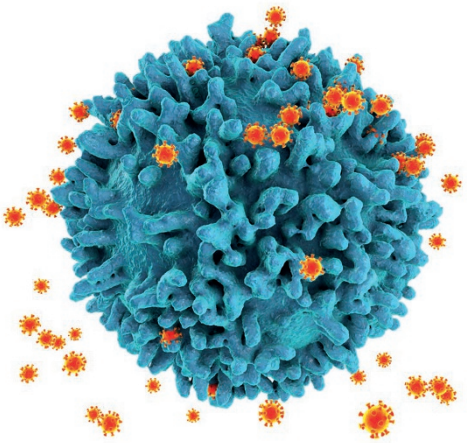
US researchers initiate a gene-therapy trial in two girls with severe combined immunodeficiency (SCID) by inserting a functional adenosine deaminase gene into their blood cells. Both girls develop stronger immune systems.

1998 MEDICINE FOR HER

The US Food and Drug Administration (FDA) approves the first matched drug and diagnostic test: trastuzumab for breast-cancer patients whose tumours overexpress the HER2 protein. This is the first major application of precision medicine to fight a type of cancer.

2002

Scientists discover why 1 in 20 patients with HIV (**pictured**) are sensitive to the reverse transcriptase inhibitor abacavir. Certain HLA types — the protein markers that allow the immune system to distinguish self cells from foreign invaders, and that are used to match organ transplants — predict who will respond badly (S. Mallal *et al. Lancet* **359,** 727–732; 2002, and S. Hetherington *et al. Lancet* **359,** 1121–1122; 2002). A large clinical trial shows that genotyping patients eliminates hypersensitivity reactions (S. Mallal *et al. N. Engl. J. Med.* **358,** 568–579; 2008).



2003 HUMAN GENOME 1.0

After 13 years of effort, and at a cost of around US$3 billion, scientists collaborating across 6 nations complete the Human Genome Project, producing a sequence of human chromosomes encompassing more than 20,000 genes from the DNA of several volunteers.

2004

Roche Diagnostics' AmpliChip CYP450 test — a microarray that classifies patients according to their cytochrome P450 (CYP) enzymes — is approved in both the United States and Europe. These enzymes are known to partly determine how a person metabolizes and reacts to medications. The test can help doctors to select the right drug and dosage for medications such as antipsychotics and cancer treatments. However, the high cost — frequently upwards of $1,000 — means it is not widely used.

2007

The FDA approves a genetic test to improve the prescription of warfarin, a blood-thinning drug that 2 million US people start taking every year. Responses to the drug vary widely, and taking the wrong dose risks blood clots or excessive bleeding. The test checks two gene variants that encode CYP2C9 and VKORC1, the latter of which is the enzyme targeted by the drug that affects blood clotting. The FDA updates the labels on warfarin, explaining that genetics partly determines an individual's response to the drug.

2009 TUMOUR TESTING

Massachusetts General Hospital says it will be the first clinic to profile tumour genes for all cancer patients. It will check 13 genes for 110 mutations that predict which drugs will be most effective. The cost is about $2,000, and if insurers won't pay, the hospital or its patients may have to.

2012

UK Prime Minister David Cameron launches the 100,000 Genomes Project to read the DNA of people with cancer or rare diseases and their families. Other large-scale sequencing projects also try to advance precision medicine into the clinic. In 2015, US President Barack Obama outlines the Precision Medicine Initiative, a $215-million project to study the genomes and health status of 1 million volunteers and develop the required databases and privacy standards. In early 2016, China reveals plans to sequence genomes and connect them with clinical data.

2014 CHEAPER BY THE DOZEN

US biotech company Illumina announces a system capable of sequencing a genome for only $1,000. However, the $10-million initial cost of the ten-instrument arrangement effectively limits its use to institutions that do high-volume sequencing.

L: JAMES KING-HOLMES/SPL; R: KATERYNA KON; SPL