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It is 2025 and Pete is in a lot of pain. He has a nasty skin infection that he just can't shift. His doctor would like to put him on an antibiotic called flucloxacillin; since it is especially effective against the bacteria (*Staphylococcus aureus*) that are causing the infection. However, Dr Trimble knows that in a small number of cases flucloxacillin can cause serious liver damage. The good news is that a genetic test will reveal whether Pete is at risk of this reaction. Dr Trimble advises Pete to take the test. For a small fee, Pete will know whether the drug is safe to take and the information will become part of his medical records, meaning that doctors in the future will know instantly whether or not it can be prescribed to him.

Pete is reluctant to pay for the test but his wife Sandra argues that it isn't worth taking a risk with his health. Overhearing their conversation, Pete's teenage son, Alex, is concerned. He has been discussing the future of genetic testing on one of his favourite online forums and is worried about his father's civil liberties.

Should Pete take the test?

This is the first step. Before you know it, we will have to have a genetic test for everything. Then if you don't have the right 'genotype', you won't be able to get a job, insurance or anything.

Alex
(Pete's son)

I don't know what Pete's worried about. Your health is the most important thing. He should definitely take the test, if it will keep him safe. I don't want him getting liver problems. Or Alex. What if Alex gets ill and has the same gene thing as Pete?

Sandra
(Pete's wife)

I would prefer to use flucloxacillin as it is particularly effective for this type of infection but it can cause nasty side effects. If Mr Sharp's genotype is a problem, I can prescribe an alternative medication, such as dicloxacillin. A simple test can help to decide which is the best and safest treatment.

Dr Trimble



Pete



What impact will Pete's decision have on the rest of the family?

Who should pay for the test? Is it fair for patients to have to pay or should the cost be shouldered by the health service?



What if seriously ill, hospitalised patients cannot be prescribed the drug unless they have taken the test?

If Pete opts for the test and discovers that he does have an increased genetic risk of suffering a reaction, should his son Alex also be tested for future medical purposes?





What might the consequences be if decisions about medical treatment are based on our genotypes – should we have personalised medicines?

Who should have access to the results of the test?
Pete's family? His doctor? Insurance agencies?
Researchers? Pharmaceutical companies?
Potential employers?



Flucloxacillin v other antibiotics

Flucloxacillin is especially useful for treating bacterial infections which are penicillin-resistant.

Bacteria sometimes produce an enzyme called *penicillinase* which breaks down some penicillins and stops them from killing the bacteria. This enzyme does not affect flucloxacillin.



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What is flucloxacillin?

Flucloxacillin is an effective medicine in the group of antibiotics called penicillins. It is used to treat infections caused by bacteria, e.g. bacterial meningitis, blood infections, infections of the lining of the heart and bacterial infections of the lungs, skin, ear, nose, throat and sinuses. It is also used to prevent bacterial infections during major surgery, e.g. heart surgery.



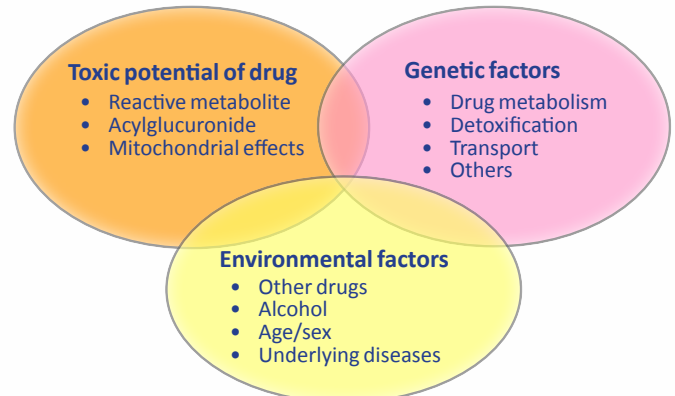
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Drug-induced liver injury (DILI)

Antibiotics are the largest single class of agents that cause drug-induced liver injury (DILI). One of the main purposes of the liver is to detoxify the blood of harmful substances but it often fails to recognise certain chemical compounds, such as antibiotics and other prescription drugs. As a result it can become damaged, or in severe cases, stop working.

Risk factors for susceptibility to drug-induced hepatotoxicity



Source: Kaplowitz N. *Clinical Infectious Diseases* 2004; 38: S44-S48



Flucloxacillin and liver injury

The liver injury associated with flucloxacillin would consist of prolonged jaundice and often involves cholestasis (a condition where bile cannot flow from the liver to the small intestine). It can even lead to 'vanishing bile duct syndrome', a condition where the bile ducts are progressively destroyed and ultimately disappear. Studies have shown that people with a certain genotype are at significant risk of developing flucloxacillin DILI.

It is estimated that 8.5 in every 100,000 patients treated for the first time with flucloxacillin are affected by DILI.



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Pharmacogenomics and personalised medicines

In some cases there are genetic factors associated with how we respond to medicines, which means that a test can show how well a drug will work for a given individual. Pharmacogenomic research could mean that we have personalised medicines which are most effective for people with particular genetic markers. A test will show whether an individual has the genetic marker associated with certain side effects or response rates to particular medicines.



Drug safety and adverse drug reactions

The expression 'adverse drug reaction' (ADR) describes harmful effects caused by taking medication at normal doses. ADRs have serious consequences and they can even be fatal. Managing them has been estimated to cost the NHS around £2 billion each year. Pharmacogenomics could address up to 40% of ADRs.

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Testing is not 100% accurate

There are several genetic factors involved in a person's response to a drug. It is very rare for one gene to cause one effect. A person's genetic makeup may increase the likelihood of a particular reaction but does not guarantee it. Testing might exclude people who could have been treated successfully. Conversely, people without that particular genotype may also suffer a reaction.



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Genetic testing and insurance

There is currently a voluntary moratorium between the government and the insurance industry in the UK. It limits the access insurers have to genetic test results, with the exception of tests relating to Huntington's disease. It is unclear what will happen when the moratorium ends in 2017.



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Genetic testing and employment

The 'Equality Act 2010' restricts the use of genetic tests by employers. Employers may only ask for information that is directly relevant to an applicant's ability to carry out the work.



Our DNA

Our bodies are made up of around 50 trillion cells. Most of these cells contain a person's genetic information within a long molecule called DNA (deoxyribonucleic acid). This DNA contains the genetic information that we inherit from our parents.

DNA is made up of specific sequences of letters or bases that encode instructions on how to make proteins. These bases [Adenine (A), Guanine (G), Cytosine (C) and, Thymine (T)] are lined up along two strands of DNA. The DNA is coiled into a double helix structure that resembles a twisted ladder.



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Gene mutations

A mutation is a permanent change in the DNA sequence. Mutations come in a number of different forms and can change the functioning of our genes. Some mutations may lead to a difference in the amount, or structure, of a protein produced by specific genes. Some mutations may switch genes on at the wrong time, preventing a protein from doing its job, or changing the way it does its job.



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Our genes

Most of the DNA in human cells is packaged into 46 chromosomes, arranged in 23 pairs. Our genes are arranged along these chromosomes and carry the instructions to make molecules, such as proteins. To function properly, each cell depends on thousands of proteins doing the right job, in the right place, at the right time. Our complete set of DNA, containing all the instructions required to make us, is called a genome.