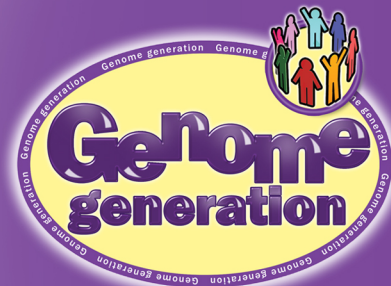


Genome generation

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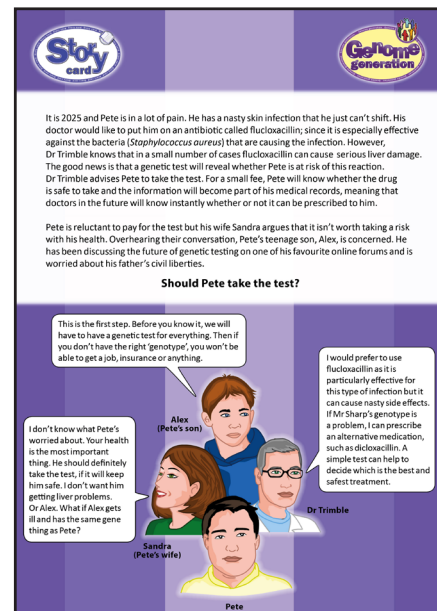
Pete's potential adverse drug reaction

This scenario is set in the future. A test for the genes linked to this drug reaction does currently exist, but is not currently widely available to patients.

Summary: This scenario is centred on Pete whose doctor would like to prescribe the antibiotic flucloxacillin, since it is particularly effective for his type of infection. However, in rare cases flucloxacillin can cause a serious liver injury, and Pete is offered a test to determine whether he has a particular genotype associated with this severe reaction. Pete is concerned about the cost but his wife is keen for him to take the safe option. His teenage son is concerned about misuse of the data if it becomes part of his medical records. The group has to decide whether Pete should take the test.

Initial question: Should Pete take the test?

Key issues: Access to data and data storage issues; Impacts on families; Issue of who should pay



Complexity, sensitive issues & guidance on providing support

This scenario may be more suited to A-level students.

The scenario introduces the idea of personalised medicines – using knowledge of our genes to determine the effectiveness and safety of using particular medicines.

Some groups may need to be reminded that there are economic factors in this scenario. They may assume that the NHS should pay for all healthcare. Remind them that the NHS budget is not endless. The budget to cover one area may mean the budget for another area of medicine is reduced.

Some groups may question why a different antibiotic could not be prescribed. In some cases this is not always possible and some medications are more effective than others. For example flucloxacillin may be the better option as it is effective against penicillin-resistant bacteria.

Some of the issues or questions that may be explored during discussions

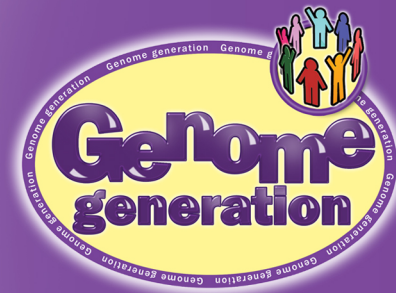
What are the implications of taking the test?

If a patient takes a test and discovers they are not at risk, their medical records can reflect this and they will be given the most appropriate medication quickly.

If a patient takes the test and finds that they are at risk of a reaction, should they be refused the treatment, or be allowed to opt to take the risk?

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Who should pay for the test?

Should the health service pay for these tests? If not, is it fair that only those who can afford the test are able to safeguard against a severe drug reaction?

Is personalised medicine the right way forward?

Medicines do not all have the same effect on everybody. Some treatments are not as effective on some people as they are on others; others require different dosage levels; and some people suffer from severe side effects. If we develop personalised medicines, we can ensure safety, get the correct dosage right away and give people the treatment most likely to be successful for them.

Are personalised medicines feasible?

There are so many different genotypes that it would take a great deal of time and money to develop treatments that are perfect for everybody. What if we do invest in personalised medicines? What will happen to those people whose genotypes are not suitable for particular treatments? Should they be allowed to take a treatment that may not be effective, or is that a waste of resources?

Should our genetic information be made available to researchers?

Should people's medical records be made available to researchers, to enable them to learn more about the genetic links to disease? If so, should they also be made available to pharmaceutical companies? Should people with a certain genotype be targeted by companies marketing drugs and treatments for their specific genes?

Further information – what they might need to know

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 remove harmful substances including drugs from the blood. Some chemical compounds such as antibiotics and other prescription drugs are not efficiently cleared by the liver. As a result it can become damaged, or in severe cases, stop working. 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 duodenum – the first part of the small intestine). It can even lead to chronic 'vanishing bile duct syndrome', a condition where the bile ducts are progressively destroyed and ultimately disappear.

Genes and flucloxacillin

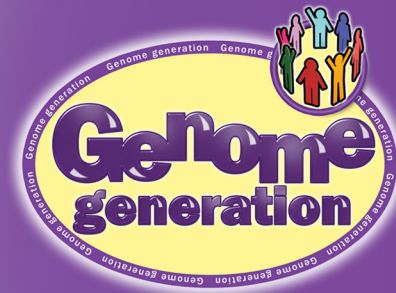
Genome studies of people who suffered flucloxacillin-related DILI have identified a specific gene variant, associated with an increased risk of liver damage as a result of using the drug. However, despite being at substantially higher risk than non-carriers, only a small proportion of people with this gene variant actually develop liver problems after receiving the antibiotic. Further research will be needed to determine whether a test could predict susceptibility to flucloxacillin-related DILI.

Genetic testing and insurance

There is currently an agreement between the Association of British Insurers (ABI) and the UK government

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that ensures that the results of *predictive* genetic tests do not affect a person's ability to take out life insurance under £500,000. Above this amount, insurers can only ask for results of predictive tests specifically approved by the Government. (Currently only the test for Huntington's Disease is approved in this way). Insurers can use clinical information and a family history (including *diagnostic* genetic tests). This agreement is currently in place until 2017 and will be reviewed in 2014 to decide whether it should be extended. The US has prohibited the use of genetic information in health insurance and employment through the Genetic Information Nondiscrimination Act (GINA) of 2008. Healthy individuals with a genetic predisposition to a particular disease cannot be prevented from getting health insurance or charged higher premiums simply because of their genetics.

Further reading

The following news story and website can be used in addition to the information cards to provide extra background information to help students understand the major issues raised in this scenario.

Genetic testing for drug intolerance

<http://www.guardian.co.uk/lifeandstyle/2012/apr/15/genetic-testing-for-drug-intolerance?newsfeed=true>

Pharmacogenomics and pharmacogenetics

<http://www.yourgenome.org/sis/pharm/>

Further information for students

Students can find out more information about flucloxacillin and drug-induced liver injury from the following websites:

NHS Choices

NHS Choices is produced by the National Health Service (NHS) and provides information on a range of different health issues. The page below provides information on flucloxacillin.

<http://www.nhs.uk/medicine-guides/pages/MedicineOverview.aspx?condition=Bacterial%20infections&medicine=flucloxacillin%20sodium&preparation=>

Follow up activity

Ask the students to write an essay on the pros and cons of the use of personalised medicines based on a person's genotype. Make sure their essay considers the economic impact of this new way of prescribing drugs. The *Pharmacogenomics* section of www.yourgenome.org can be used for background information.