UK CLINICAL RESEARCH COLLABORATION

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Centre of the Cell

New Vaccines Workshop

Introduction

These activities introduce the concept of vaccination and why it only protects the population if most people are vaccinated. They show how early vaccination was tested and discuss the role of informed consent in Clinical Research. Pupils learn about the process of developing a new vaccine.

What is a vaccine?

The immune system "remembers" its reaction to pathogens and is able to replicate this response. Vaccines work by triggering a controlled immune response, so that a person's immune system is able to recognize and destroy pathogens before that person becomes ill.

Curriculum Links

KS3 Science
KS3 Citizenship
KS3 History
KS4 Science
KS4 Citizenship
AS/A2 Level Chemistry
AS/A2 Level Biology
SQA (5-14): Environmental Studies
SQA Access, Intermediate and Higher: Biology, Biotechnology

Keywords

Vaccination
herd immunity
informed consent
clinical trials
history of vaccination
research ethics
patients' rights
the Declaration of Helsinki
Lady Wortley Montagu
Edward Jenner

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Activities

Activity 1: Creating Herd Immunity

Background Information

Vaccination is a good strategy for containing the spread of disease. For a vaccination programme to be successful, it depends on **herd immunity**. If the majority of a population is vaccinated, not only are those people kept safe, but viruses cannot spread between immunised people. The immunised people provide a barrier that stops the infection from spreading to others in the group.

If only a few people are vaccinated, this will help *them* avoid infection, but it will not protect the group. The following activity demonstrates how much better a population is protected from disease when a vaccination programme achieves herd immunity.

Teacher-led Activity (whole class)

Materials Needed

Three large mixing bowls or other bins
One piece of paper in each bowl for each pupil (for example, if there are 30 pupils in the class, each bowl will contain 30 papers)

- The first bowl should contain 3 papers marked “vaccine”, 3 papers marked “virus” and the rest blank.
- The second bowl should contain 3 papers marked “virus”, half the remaining papers marked “vaccine” and the rest blank.
- The third bowl should contain 3 papers marked “virus”, 3 papers blank, and the remaining papers marked “vaccine”.
- All the papers in the bowls should be folded so that no one can read them.
- The teacher should pass around the first bowl. Each pupil takes a piece of paper. The teacher explains that three will receive the virus, three will receive the vaccine, and the rest of the pupils will receive neither.
- When all the pupils have a piece of paper, they unfold and read them. Then each pupil shakes hands with the students seated adjacent to them, in all directions.
- Now ask the pupils who had the cards marked “virus” to raise their hands,
- Anyone who shook hands with a person who had the virus card now has the virus. Count how many people the “virus” has spread to. Anyone who has a vaccine card is protected.
- Repeat this exercise, with the pupils who received the “virus” in the first round able to spread it in the second round. Count how many people the virus has spread to now. Repeat this exercise a third time, if desired.
- Now repeat the demonstration with the cards in the second bowl. Explain that this time; half the class has been vaccinated. Count how many people the virus has spread to at the end of each round.
- Finally, repeat the demonstration with the cards in the third bowl. Explain that now; all but six members of the class (three who have blank cards and three who have virus cards) have been vaccinated. Again, count how many people the virus has spread to at the end of each round.
- For an additional activity, the numbers of people who are infected at the end of each round can be tallied on a whiteboard and made into graphs to compare the benefits of vaccination for a few or for an entire population.

Follow-up Questions

- In the second round of the game, half the class was vaccinated. How effective was this at blocking the spread of the virus?
- In the final round of the game, there were still three people who did not have the virus or the vaccine at the start of the round. Was the vaccine still effective at blocking the virus?
- Should the government require that all citizens are vaccinated against some diseases, such as measles, smallpox, or polio, to encourage herd immunity? Why or why not?
- Ask pupils to play the Flu Epidemic game (available on the Centre of the Cell website: **http://www.centreofthecell.org/interactives/flu/index.php**) to see if they can control the spread of infection.

Activity 2: Smallpox Vaccination and Informed Consent

Background Information (Smallpox)

Smallpox used to be one of the deadliest of infectious diseases. It was caused by a virus that was spread by airbourne mucous particles (sneezing) from an infected person. People who came in contact with an infected person could also become infected through close contact (within six feet) with an infected person or objects contaminated by an infected person's bodily fluids. This caused pustules to rise on the skin and eyes, eventually covering the body. The pustules were accompanied by extremely high fever. Between 20 and 60 percent of all people infected, and up to 80 percent of all children infected, died of smallpox. Those who survived were often disfigured or blind.

Teacher-led Activity (whole class)

Materials Needed

Case Studies (pages 8 - 9)

- Give your pupils a copy of each of the two case studies. Alternatively, read the case studies out loud or project them onto a whiteboard.

Case Study 1: Lady Wortley Montagu

- Ask the class what she should have done:
  A. Not done anything
  B. Given them the inoculation, even with the risks
  C. Waited until they were adults, then let them decide

- Answer:
  B. Lady Worley Montagu did have both of her sons inoculated, at ages 4 and 5. They both survived the inoculation, and did not become ill with smallpox later.

Case Study 2: Edward Jenner

- Ask the class what he should have done to test his vaccine:
  A. Not done anything
  B. Tested the vaccine on himself
  C. Asked an adult to test the vaccine
  D. Tested the vaccine on a local boy

- Answer:
  D. Edward Jenner did not test his vaccine on himself, but on 8-year-old James Phipps, a local boy. Jenner later tested his vaccine on several other children, including his own 11-month old son. His patients all survived the inoculation and did not get ill with smallpox.

Background Information (Informed Consent)

Edward Jenner and Lady Wortley Montagu would not have been allowed to do what they did today. They both made choices which could have caused harm to the health of people who were too young to consent. Today, vaccines must be tested on animals before they are tested in humans, to ensure their safety.

Even though the children concerned did survive, and did not get smallpox, this was not guaranteed. Today, smallpox has been eradicated, thanks to a world vaccination programme.
More information on the immune system, vaccinations and their development can be found here: **http://www.abpischools.org.uk/res/coResourceImport/resources04/immune/index-2.cfm**

It is unethical to use patients in research without first gaining their informed consent. This means that the patient is aware of the potential risks, as well as the potential benefits, of a treatment, and accepts them.

One of the most important documents guiding research today is the Declaration of Helsinki. This is a document that was drafted in Helsinki, Finland, by the World Medical Association in 1964, updated several times since, and it sets out rules for ethical medical conduct. It states that, “In medical research on human subjects, considerations related to the well being of the human subject should take precedence over the interests of science and society.”

Adherence to the guidelines in the Declaration of Helsinki is necessary for any research to be published in reputable scientific journals.

The Declaration of Helsinki can be found here: **http://www.wma.net/e/policy/b3.htm**

Teacher-led Quiz: The declaration of Helsinki Rules (True/False)

- Ask pupils to make a list of ethical rules that they think a declaration of medical ethics, like the Declaration of Helsinki, should contain. Briefly discuss the pupils’ reasons for choosing their rules, and write ten or so suggestions on the board.
- Now read the statements below about the Declaration of Helsinki, and ask the pupils to vote whether they think the statements are true or false.
- At the end of the quiz, reveal the answers and the reasons why.

1. **Scientists, working for a government, can force people in prison, or in the military, to volunteer for tests of a new vaccine.**

   Answer: False

   Researchers cannot coerce volunteers to participate in medical research. This violates the principle of informed consent, as prisoners or soldiers are compelled to follow orders, so cannot consent.

   Article 8 of the Declaration of Helsinki says that “Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognised. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.”

2. **Volunteers can remove their consent at any time during a study.**

   Answer: True

   Volunteers are free to remove their consent at will, and this should be explained to them at the start of a study. Article 22 states that, "In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed."

3. **If a disease is spreading quickly, researchers do not have to test a treatment for it in cells or on animals first—they can test it in human volunteers to save time.**

   Answer: False

   Statement 11 of the declaration states that, "Medical research involving human subjects must conform to generally accepted scientific principles, be based on thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation."

   Testing an experimental treatment on humans without previous experimentation in the laboratory and on animals would expose human volunteers to an unnecessary risk.

4. **If a parent gives their permission for a minor child (a child under the age of 18) to participate in research, the research can go ahead, even if the child does not want to participate.**

   Answer: Almost Always False

   According to the declaration, a parent or guardian (or "responsible adult") is able to consent on behalf of a child or otherwise legally incompetent person.

   If a child is old enough to understand the research then their views must be taken into account. They will generally only get treatment against their wishes in extreme cases – perhaps to save their lives. This would only rarely involve research.

5. **If you are testing a vaccine for a disease (such as HIV) in healthy volunteers, and there are known methods that allow people to prevent infection, people in the trial for the vaccine should be made aware of these methods.**

   Answer: True

   Article 18 says, "Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subjects. This is especially important when the human subjects are healthy volunteers."

   In the case of an HIV vaccine, it would be considered unethical to not inform volunteers about ways to minimise their risk of contracting the virus, such as the use of condoms or abstaining from sexual intercourse.

Follow-up questions

- Ask the class if any of these answers surprised them. Why or why not?
- Distribute copies of the Declaration of Helsinki. Ask the class what Edward Jenner and Lady Wortley Montagu might have done that would have violated the Declaration of Helsinki. Were they right to do what they did? Why or why not?
- Ask the class to research the history of the Declaration of Helsinki and the reasons for the changes that have been made to it over the years.
- The Declaration of Helsinki is not the only document that medical researchers apply to their research to ensure that it is ethically sound. The Good Clinical Practice guidelines, set down by the International Conference on Harmonisation, and laws of the country where trials take place also warrant consideration. Ask pupils to research some of these other guidelines and write a report comparing them to the Declaration of Helsinki.

Activity 3: Developing a New Vaccine

Background Information

How do scientists develop vaccines today? To make sure that their vaccines are safe and effective, they must go through several stages of testing. In the following activity, ask your pupils to put the steps for creating a vaccine for an imaginary disease, ICV, into the correct order.

All materials are to be found at the Materials section at the end of this document.

Materials Needed

Anti-ICV cards (page 11 - 12)
News Flash cards (page 10)

- Pupils should work in groups of 4-5.
- Give each group a News Flash Card. This tells them the aim about the activity and includes instructions.
- Give each group a set of Anti-ICV cards. These describe the steps of developing a new vaccine.
- Tell the pupils to work together to put the cards in the correct order.
- When the class has finished, check and discuss their work. The cards should be in the following order:

1. *PharmaCell scientists study ICV and the people infected with ICV.*
2. *The scientists create a new vaccine, 'Anti-ICV', by using a live but weak ICV virus.*
3. *Scientists test 'Anti-ICV' samples.*
4. *'Anti-ICV' is tested on animals.*
5. *Anti-ICV is tested on up to 30 healthy volunteers. Half of the volunteers receive a placebo (an inactive substance, given in the same form as the active vaccine) whilst the others receive Anti-ICV.*
6. *Anti-ICV is tested on hundreds of healthy volunteers.*
7. *Anti-ICV is tested on thousands of healthy volunteers.*
8. *PharmaCell are awarded a license to mass-produce the Anti-ICV vaccine.*

Materials

Activity 2: Smallpox Vaccination and Informed Consent

Case Studies

Case Study 1: Lady Wortley Montagu

In 1717, Lady Mary Wortley Montagu travelled to Turkey (then the Ottoman Empire) with her husband, the British ambassador, and their children. She lived there from 1716-1718, and wrote many letters recording her observations of life in Istanbul. She learned about *inoculation* (also called *engrafting* or *variolation*): the Ottoman technique for prevention of smallpox, and introduced it to the West. This technique exposed people to a small, controlled amount of smallpox that their bodies could more easily combat. This technique was first developed in China, where people would snort the ground-up scabs of people who had previously had smallpox, or make a cut and put the ground-up scabs in the wound.

Here's Lady Wortley Montagu's description of inoculation:

> "…the old woman comes with a nut-shell full of the matter of the best sort of small-pox, and asks what vein you please to have opened. She immediately rips open that you offer to her, with a large needle (which gives you no more pain than a common scratch) and puts into the vein as much matter as can lie upon the head of her needle, and after that, binds up the little wound with a hollow bit of shell, and in this manner opens four or five veins… The children or young patients play together all the rest of the day, and are in perfect health to the eighth. Then the fever begins to seize them, and they keep their beds two days, very seldom three. They have very rarely above twenty or thirty in their faces, which never mark, and in eight days time they are as well as before their illness."

From *Lady Mary Wortley Montagu, Letters of the Right Honourable Lady M--y W--y M--e: Written During her Travels in Europe, Asia and Africa. . . , vol. 1 (Aix: Anthony Henricy, 1796), pp. 167-69; letter 36, to Mrs. S. C. from Adrianople, n.d.*

Lady Wortley Montagu knew the dangers of smallpox from experience: her brother had died of the disease. She had survived it a few years earlier, and still had the pockmarks scarring her skin to show for it.

Inoculation used a less virulent strain of smallpox, which made it safer than catching smallpox during an outbreak. However, inoculation still involved being infected with a virus that caused smallpox. The risk was much smaller than the risk of death from catching smallpox, but people inoculated this way could still die. Approximately 0.5 to 2 percent of all people inoculated this way died of smallpox.

Lady Wortley Montagu had two young sons whom she wanted to inoculate.

Case Study 2: Edward Jenner

Edward Jenner was a medical doctor living in Gloucestershire in the late eighteenth century. Folklore of the countryside told that milkmaids, who were exposed to the cowpox virus from the cows they milked, were immune to smallpox. In 1796, Jenner decided to test this idea by squeezing some pus from a cowpox-infected cow, and using it as an experimental vaccine. (The word *vaccine* comes from the Latin *vacca*, for cow.)

Because Jenner believed that cowpox was similar to smallpox, he thought that a person who was exposed to cowpox would develop an immunity to it as well as an immunity to smallpox. He also believed that inoculating people with cowpox would be safer than inoculation with smallpox, which created immunity to smallpox but also carried a small risk of death.

Activity 3: Developing a New Vaccine
News Flash and ICV Cards

BREAKING NEWS

New Virus Alert

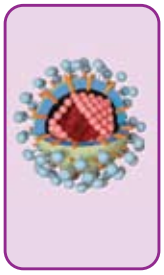
There's a new virus called 'Infectious Cell Virus (ICV)'.

ICV spreads very quickly and can kill people before medicines have the chance to work.

PharmaCell is a pharmaceutical company trying to develop a new vaccine against ICV, called 'Anti-ICV'. A new vaccine would give people the ability to fight the virus themselves (known as 'immunity').

Help PharmaCell to find a new vaccine to immunise people against ICV by putting the stages in the correct order.

PharmaCell scientists study ICV and the people infected with ICV.



Understanding the virus and how it infects people will help them to design a new vaccine.

The scientists create a new vaccine, 'Anti-ICV', by using a live but weak ICV virus.

When the weak ICV virus is given to people they develop the ability to fight the virus without developing the disease (known as an immune response). Their body remembers how to fight the virus if they become infected in the future. This is known as immunity.

Scientists test 'Anti-ICV' samples in cells.

Live vaccines are tested in cell culture to ensure they:

- Are not toxic
- Do not cause the disease
- Create a specific cell response

'Anti-ICV' is tested on animals.

The immune system involves many types of cells. Animals such as mice and rats have very similar immune systems to people, and are better models than cultured cells. Testing Anti-ICV on animals helps to ensure that the vaccine produces a desired immune response.

Anti-ICV is tested on up to 30 healthy volunteers. Half of the volunteers receive a placebo whilst the others receive Anti-ICV.

It's important to find out:

- if the new vaccine creates the desired immune response
- the dose of vaccine to use
- if the new vaccine is safe
- how the volunteers' bodies cope with the vaccine

Anti-ICV is tested on hundreds of healthy volunteers.

It's important to find out:

- if the new vaccine creates the desired immune response
- if the vaccine dose is correct
- if the new vaccine is safe

Anti-ICV is tested on thousands of healthy volunteers.

It's important to find out:

- if the new vaccine creates the desired immune response
- if the vaccine dose is correct
- if the new vaccine is safe

PharmaCell are awarded a license to mass-produce the Anti-ICV vaccine.

There are enough data to show that the vaccine protects people from ICV and is safe to use. Anti-ICV is produced and sent to hospitals, health centres, travel clinics and doctors' surgeries around the world.