History

It is widely believed that the story of vaccination began with Edward Jenner, but it had, in fact, started nearly a millennium earlier when people in India, China and Africa deliberately exposed themselves to milder strains of a disease in order to protect themselves against the more virulent forms of the disease.

The Jenner story has many forms but essentially he noticed that milkmaids who had contracted cowpox, a mild disease, did not suffer from smallpox. In 1796 he purposely infected a young local farm boy by putting the pus from a cowpox sore into two small cuts he had made on the boy’s left arm. When the boy recovered from the cowpox he was then deliberately infected with smallpox and fortunately he did not contract the disease. The immunisation did not always work and many people were afraid and tried to make a fool of Jenner and immunisation using cartoons showing people growing parts of cows. Luckily immunisation did work often enough for the idea to eventually catch on.

Vaccination is derived from the Latin “vaccinus” meaning “of or from cows”. In the late 1800’s Louis Pasteur built on this foundation and produced vaccines against chicken pox, cholera, anthrax and then rabies. Although he knew vaccination worked he did not know how. The process of administering the vaccine is called inoculation.

How do Vaccines Work?

Vaccination works by activating the body’s natural defence systems to produce immunity — that is, the ability resist a particular disease when exposed to it, or at least limit it to a mild form. The majority of vaccinations are for viral diseases but some are used to treat and prevent cancers, to treat snake bites, and are even being developed to help treat addictions.

The pathogen (disease causing organism) is called the antigen and the body produces a specific protein called the antibody that attacks the antigen. Initially the production of the antibody is slow, and it is a race between the antibody production and the reproductive rate of the pathogen that determines the outcome. If the pathogen wins, death is often the result in serious diseases.

However, if the antibody production wins the disease is overcome. At the same time as antibodies are produced other cells called memory cells are produced and continue to circulate in the blood and lymph for long periods of time. In any subsequent exposure to the pathogen these cells very rapidly produce large amounts of antibodies, and the pathogen is destroyed before any symptoms of the disease occur. This is called active immunity and is long lasting.

A second type of immunity called passive immunity involves the supply of antibodies produced either in breast milk (natural), or by another organism (artificial). In artificial passive immunity the antigen can be produced either by an animal (e.g. horse) or by genetically engineered microorganisms and it is normally given by injection e.g. anti–tetanus to prevent lockjaw. This type of immunity is generally short lived lasting between five and ten years.

Vaccine Types

First Generation

Killed: Previously virulent microorganisms destroyed by heat, chemicals or radioactivity e.g. cholera and bubonic plague.

Attenuated (live but weakened): These microorganisms have been cultivated under conditions that disable their virulent properties, or are closely related, but less pathogenic, organisms. They generally produce a stronger immune response and are at present the preferred type of vaccine for healthy organisms e.g. MMR and yellow fever. The BCG vaccine (named after its developers’ initials) is made from a non-contagious, virulently modified strain. With this type of first generation vaccine there is always a chance (very slight) that the organism may revert to a dangerous form.
Second Generation

Here the pathogen is not directly involved so there is no danger of reversion to the dangerous form.

Toxoid: This is made from the inactivated toxic products of the microorganisms. The immunity conferred is generally short lived (from 5 to 15 years) e.g. anti-tetanus and diphtheria and this results in a need to get booster inoculations to maintain full immunity. Not all vaccinations are against diseases; there is a toxoid vaccine against rattlesnake bites for dogs.

Fragments of Organisms:

Subunit: The immune system does not normally recognise the whole virus, but rather one or more proteins that occur on its surface. These proteins are antigenic but can still prime the immune system to attack the whole virus.

Genetic engineering can produce antigens without having to grow the pathogens. If the genes for the production of these proteins can be found, isolated, and inserted into bacteria or yeasts then huge quantities of the protein can be produced leading to a safe and relatively cheap vaccine e.g. hepatitis B which is now produced by recombination of the viral genes into yeast.

Conjugate: certain bacteria have polysaccharide outer coats that only produce a weak immune response. If these are linked to proteins (e.g. toxins) a strong immune response can be triggered. e.g. Haemophilus influenza type B and Neisseria meningitidis vaccines.

Third Generation

Third generation vaccines are still very much at the experimental stage of development, but do hold considerable promise. Here are a few examples:

DNA Vaccines

These involve the injection of plasmids (small circular pieces of bacterial DNA) without the use of a vector. To produce a vaccine for West Nile virus two characteristic genes are removed and then inserted into a plasmid. The plasmids are multiplied, purified by column chromatography and injected into the cells of the host. The inserted DNA is read by the host’s cells which then produce these two foreign proteins. These proteins are recognised by the body as foreign and an immune response is triggered.

Dendritic Cell Therapy

This is used to treat and prevent certain cancers. Dendritic cells are relatively rare, naturally occurring defence cells that recognise and present antigens to T cells. The therapy involves harvesting these cells from the patient and producing large numbers of them in the laboratory before injecting them into the body to produce a massive response. This can be used to treat HPV (human papillomavirus) one of engineered to express a surface antigen of foot-and-mouth disease virus. One leaf of an infected pea plant can contain enough antigen to produce hundreds of doses. Also, a highly antigenic part of the cholera toxin has been expressed in Alfalfa plants, and mice treated with this have shown an immune response to the disease. The use of other plants such as tomatoes and lettuce are also being investigated.

Adjuvants

These are ingredients (e.g. aluminium salts) that stimulate the immune response to a vaccine or they can be liposomes (lipid bi-layers) which can be used to improve the delivery of the vaccine and thus increase its potency. They can make existing vaccines more effective and continued work on them may make vaccines that are impossible today the reality of tomorrow.
Pfizer is one of Ireland’s leading employers and the largest pharmaceutical sector investor and employer. One of the first pharmaceutical companies to locate in Ireland (1969), Pfizer has a rich heritage of innovation and expansion over a forty year period. Pfizer employs over 4,000 colleagues across ten locations in Cork, Dublin, Kildare and Limerick.

Pfizer Ireland Pharmaceuticals’ Grange Castle manufacturing plant is situated on a 90-acre site at the Grange Castle Business Park in Clondalkin, South County Dublin. Grange Castle’s state-of-the-art technology, cutting edge thinking and production expertise result in the production of quality-driven products that improve people’s lives around the world. The focus on the site is Biopharmaceuticals and Vaccines. The site manufactures a number of products for the prevention or treatment of serious illnesses such including rheumatoid arthritis and pneumococcal disease in young children. Over 1,200 full-time employees work at Grange Castle.

You can find this and other lessons on www.sta.ie.

You can find out more about Pfizer at www.pfizer.ie.
Teaching Notes

Syllabus References

1.3.6 Structural Role of Biomolecules
- Carbohydrate, e.g. cellulose as a component of cell walls.
- Protein, e.g. fibrous proteins – as keratin in hair and skin, myosin in muscles.
- Lipid, e.g. component of cell membranes.

3.5.3 Responses in the Human
- The defence system in humans: general defence system to include the skin and mucous membrane lining of the breathing, reproductive and digestive tracts.
- Phagocytic white blood cells.
- Specific defence system (immune system): antigen antibody response.
- Definition of “induced immunity”.

Vaccination and immunisation.

3.5.4 Viruses
- Viruses: identify the problem of definition.
- Economic and medical importance of viruses: two harmful examples, one beneficial example.

H.3.5.7 Human Immune System (Extended Study)
- Role of lymphocytes: B and T cell types. Role of B cells in antibody production.
- Role of T cells as helpers, killers, suppressors, and memory T cells.

3.1.3 Monera, e.g. Bacteria
- Bacterial cells: basic structure (including plasmid DNA), three main types.
- Understanding of the term “pathogenic”.
- Definition and role of “antibiotics”.
- Economic importance of bacteria: examples of any two beneficial and any two harmful bacteria.
- Potential abuse of antibiotics in medicine.

Learning Outcomes

On completion of the lesson the student should be able to:
- Understand what is meant by vaccination.
- Outline how the immune system operates and how vaccination brings about immunity to a particular disease.
- To distinguish between active and passive immunity.
- Describe the main kinds of vaccine.
- Describe in outline how DNA vaccines are produced.

General Learning Points

The following information can be used to revise the lesson’s main learning points and inform discussion.
- Vaccination has been used for over two hundred years. Edward Jenner is generally regarded as the father of vaccination.
- Vaccines stimulate antibody production and memory cell production.
- Vaccines can be dead or attenuated pathogens or closely related non-pathogenic organisms.
- Vaccines can be parts of an organism or substances produced by the organism.
- Active immunity is conferred when the body produces its own antibodies.
- Passive immunity is conferred when the body gets its antibodies from outside.
- DNA vaccines use plasmids to produce parts of the pathogen.
- Plants can be engineered to produce antigens and these can be used to induce immunity.
**Student Exercises**

**Student Activities**

- Find and make a list under the headings virus diseases and bacterial diseases for which vaccinations are available.
- Find as many animal vaccines as you can and how common their use is in Ireland.
- Have you a pet? Has it been vaccinated and if so against what?
- Find out about the MMR/autism debate.

**True/False Questions**

(1) Smallpox does not exist as a disease any longer.
(2) Only humans can be given vaccinations.
(3) Vaccination is always successful.
(4) Vaccines can prevent certain cancers.
(5) The BCG vaccine is used to treat a bacterial disease.
(6) Tetanus injection will protect you for life.
(7) The process of administering a vaccine is called inoculation.
(8) The presence of adjuvants make vaccines less efficient.
(9) Antigens are produced by the body in response to the presence of a foreign organism.
(10) A pathogen is a disease causing organism.

*Check your answers to these questions on www.sta.ie.*

**Examination Questions**

**Leaving Certificate Biology (HL) 2007 Q. 14 (c)**

What is meant by the term immunity?

Outline briefly the role of B lymphocytes in the human immune system.

Distinguish between active and passive immunity.

“Vaccination gives rise to active immunity”. Explain this statement.

In certain situations a person is given a specific antibody rather than being vaccinated.

Is this an example of active or passive immunity?

Under what circumstances might an antibody, rather than a vaccination, be given?

Comment on the duration of immunity that follows the administration of an antibody.

**Leaving Certificate Biology (HL) 2005 Q. 15 (a)**

Comment briefly on the difficulty in classifying viruses as living organisms.

Name two diseases of humans caused by viruses.

Name two types of lymphocyte and state a role of each when viruses or other micro-organisms enter the blood.

“Immunity that results from vaccination is effectively the same as the immunity that develops following an infection”. Do you agree with this statement? Explain your answer.

**Leaving Certificate Biology (HL) 2004, Q. 15 b**

What is meant by the term immunity? Distinguish between active and passive immunity.

Describe two ways in which the skin helps to defend the body against pathogenic micro-organisms.

Lymphocytes play a vital role in the body’s immune system. To which group of blood cells do lymphocytes belong? Name two types of lymphocyte and state a role of each.

What is the purpose of vaccination?

**Did You Know?**

Smallpox has been eradicated since the 1960’s and only exists (as far as we are aware) in two laboratories where it is kept for research purposes, in case it is used in bioterrorism.

Polio is the next target for eradication. It is now endemic in only four countries, Afghanistan, India, Nigeria and Pakistan.

Eradication is only possible where the disease has no wild hosts of the disease.

**Biographical Notes**

**Bacillus Calmette-Guérin (BCG)**

Jean-Marie Camille Guérin (1872-1961), a French veterinarian, bacteriologist and immunologist, in collaboration with Albert Calmette, (1863 – 1933) developed the Bacillus Calmette-Guérin (BCG), a vaccine against tuberculosis. They reduced the
virulence of the tuberculosis bacillus by repeatedly culturing it in different nutrient media. The first BCG vaccine were administered in 1921.

Public acceptance was greatly damaged in 1930 by the deaths from tuberculosis of 72 infants out of a total of 240 who were vaccinated. It was later discovered that the vaccine had been contaminated with a virulent strain of the bacterium. Despite such serious accidents the BCG vaccine has become the most widely used vaccine in the world and has saved the lives of countless millions.

Maurice R. Hilleman (1919–2005)
Maurice R. Hilleman, an American microbiologist, is credited with developing more than 36 vaccines including those for chickenpox, hepatitis A and B, measles, meningitis, mumps and pneumonia.

He developed more vaccines than any other scientist and is thus credited with saving more lives than any other scientist in the 20th century. He developed the mumps vaccine from material that he collected from his daughter when she contracted mumps.

Revise the Terms
Can you recall the meaning of the following terms? Reviewing terminology is a powerful aid to recall and retention.

antibody, antigen, attenuated, B lymphocyte, immunity, inoculation, lymphocyte, memory cell, pathogenic, polysaccharide, protein, T-cell, vaccination, vaccine, virulent.

Check the Glossary of Terms for this lesson on www.sta.ie.