The Scientific Method in Vaccine History

The scientific method is a disciplined, systematic way of asking and answering questions about the physical world. Though it can be useful to think of the scientific method as a simple series of steps, in fact, there is no single model of the scientific method that can be applied in all situations. Rather, different scientific investigations require different scientific methods. Certain qualities, however, must apply to all applications of the scientific method. One important quality of a scientific investigation is that it must attempt to answer a question. In other words, an investigation should not attempt to “prove” a point, but should be an attempt to gain knowledge. Another quality is that careful, controlled observations must form the basis of information gathering. Finally, the results of a scientific investigation must be reproducible: other investigators, using the same process, must be able to observe the same results. If a result is not reproducible, the original conclusions must be questioned. What we think of today as the “steps” of science have developed over time, and they may differ according to the type of investigation being conducted.

Observation

Scientific investigations usually begin with an observation that points to an interesting question. One famous example of an observation that led to further investigation was made by Scottish biologist Alexander Fleming in the 1920s. After an absence from his lab, he returned and began to clean some glass plates on which he had been growing a certain kind of bacteria. He noticed an odd thing: one of the plates had become contaminated by mold. Curiously, the area around the mold looked free of bacterial growth. His observation indicated that a causal relationship might exist: the mold or a substance produced by the mold might prevent bacterial growth. Fleming's observation led to a series of scientific tests that resulted in new knowledge: Penicillin could be used to treat bacterial infections.

Hypothesis

A hypothesis is a proposal or possible solution generated by observation. In Alexander Fleming's investigation of antibiotic properties of mold, his hypothesis might have been something like, “If filtrates from a certain type of mold are introduced to bacteria, the bacteria will die.”

Good hypotheses share several qualities. First, they usually begin with existing knowledge. That is, they don’t propose ideas that are wildly at odds with our general knowledge about how the world works. Additionally, good hypotheses are simple, involving a single problem and possible solution. Finally, good hypothesis are testable and “falsifiable.” That is, the proposed solution in the hypothesis can be subjected to an observable test, and through the test, it is possible for the investigator to prove the hypothesis false. The hypothesis above relating to Fleming’s studies of mold is falsifiable, because a test in which bacteria grew in the presence of a filtrate of the mold would have disproven the hypothesis, if it hadn't been true.

Testing

Many modern scientific studies involve experimentation -- a test with a control group and an experimental group. Other kinds of studies can be done with modeling or with research and data analysis.

The investigator conducts the experiment on the control group just as with the experimental group. The only difference is that the investigator does not subject the control group to the single factor or intervention being tested. This single factor being tested is known as the variable. The control group exists to provide a valid comparison to the experimental group.

For instance, in an experiment testing Fleming's hypothesis, a scientist could introduce filtrates of mold to cultures of bacteria on glass plates. This would be the experimental group. A control group would contain similar cultures of bacteria, but with no addition of mold filtrates. Both groups would be subject to exactly the same conditions otherwise. Any difference between the two groups would result from the variable, or the single difference between them: the introduction of mold filtrate to the bacterial cultures.

Careful observations and recording of data are crucial during the testing phase of the scientific method.

Conclusion

A final step in the scientific methods involves analysis and interpretation of the data gathered during the testing phase. This allows the researcher to form a conclusion based on the data. A good conclusion takes into account all the data gathered and will reflect on the hypothesis, whether it supports the hypothesis or not.
**SCIENTIFIC METHOD IN ACTION – Edward Jenner: The Importance of Observation**

- Edward Jenner, born in England in 1749, is one of the most famous physicians in medical history. Jenner tested the hypothesis that infection with cowpox could protect a person from smallpox infection. All vaccines developed since Jenner’s time stem from his work.
- Cowpox is an uncommon illness in cattle, usually mild, that can be spread from a cow to a human via sores on the cow’s udder. Smallpox, in contrast, was a deadly disease of humans. It killed about 30% of those it infected. Survivors often bore deep, pitted scars on their faces and other parts of the body affected by the blistering illness. Smallpox was a leading cause of blindness.
- Jenner is said to have been interested in the observation of a dairymaid. She told him, “I shall never have smallpox, for I have had cowpox. I shall never have an ugly pockmarked face.” And many other dairy workers commonly believed that infection with cowpox protected them from smallpox.
- Given that the protective effect of cowpox infection was common local knowledge, why was Jenner’s involvement important? Jenner decided to systematically test the observation, which then would form the basis of a practical application of the benefit of cowpox infection.
- Jenner scratched some material from a cowpox sore on the hand of a milkmaid into the arm of eight-year-old James Phipps, the son of Jenner’s gardener. Young Phipps felt poorly for several days, but made a full recovery.
- A short time later, Jenner scratched some matter from a fresh human smallpox sore into Phipps’s arm in an attempt to make him ill with smallpox. Phipps, however, did not contract smallpox. Jenner went on to test his idea on other humans and published a report of his findings.
- We know now that the virus that causes cowpox belongs to the Orthopox family of viruses. Orthopox viruses also include variola viruses, the ones that cause smallpox.
- Jenner’s method of vaccination against smallpox grew in popularity and eventually spread around the globe. About 150 years after Jenner’s death in 1823, smallpox would be making its last gasps. The World Health Organization eventually declared smallpox to be eradicated from the planet in 1980 after a massive surveillance and vaccination program.

**Robert Koch: Steps to Identify the Cause of a Disease**

- Robert Koch (1843-1910) was a German physician who helped establish bacteriology as a science. Koch made important discoveries in identifying the bacteria that cause anthrax, cholera, and tuberculosis, at a time when understanding of microbes was just emerging.
- Koch and his colleague Friedrich Loeffler developed a method to identify a disease-causing agent. Scientists today follow these basic principles, which we now call Koch’s postulates, when trying to identify the cause of an infectious disease. Koch’s postulates are based on careful observations and reproducibility.
  1. The microbe is present in each case of the disease.
  2. The microbe can be taken from the host and grown independently.
  3. The disease can be produced by introducing a pure culture of the microbe into a healthy experimental host.*
  4. The microbe can be isolated and identified from the host infected in Step 3.

*One exception to Step 3 is that some individuals may be infected with a disease-causing microbe and not show signs of the disease. These are known as asymptomatic carriers.

**Pearl Kendrick: Using Careful Controls**

- During the 1930s, Pearl Kendrick at the Michigan Department of Health developed a whooping cough (pertussis) vaccine that she hoped would be more effective than previous vaccines. An important part of showing the effectiveness of the vaccine involved a control group of children who did not receive the vaccine. This was something of an innovation at the time, but Kendrick knew that having a control group would add weight to her findings if the vaccine proved to be effective. The rate of pertussis disease in the control group would allow Kendrick to easily demonstrate whether or not her vaccine could reduce the rate of disease in the experimental group.
• Kendrick assigned children to her pertussis experimental group if they came to a clinic seeking pertussis vaccination. For the control group, she found children at random from a list kept by a city health department of unimmunized children. One fault that we would see today in Kendrick’s experiment design was the lack of randomization in the assignment of children to either the experimental group or the control group. Randomization is a method of using chance alone to assign subjects to a control or experimental group. Researchers use randomization because it helps to ensure that differences between the two groups will not influence the outcome of the experiment. If Kendrick had randomized assignments, she would have minimized differences between the vaccinated group and the group she merely observed.

• In spite of this shortcoming, Kendrick’s trial helped establish norms and expectations for future vaccine trials, and it clearly showed the efficacy of her vaccine.

**Jonas Salk: A Double-Blind Randomized Trial**

• The 1954 field trial of Jonas Salk’s inactivated poliovirus vaccine (IPV) was another important milestone in the use of the scientific method to test a vaccine. This trial enrolled a huge number of subjects—1.3 million children in all—in what is the largest medical field trial ever conducted.

• The Salk trial was a carefully designed double-blind randomized experiment. This meant, first, that children were randomly assigned to either the control or the experimental group. “Double-blind” meant that no one—not the child, the parent, the person who gave the injection, nor the person who assessed the child’s health—knew whether an individual child received the polio vaccine or a placebo injection. (A placebo is an inactive substance. In this case, the placebo was a saltwater solution.) The information about whether the child received the vaccine or the placebo was encoded in numbers on vials from which the injected material was taken, and it was linked to the child’s record. Only after the observation period was over and the result recorded—did the child develop polio during the observation period or not?—was the child’s experimental or control status revealed.

• Authorities did not achieve the double-blind, randomized standard across the entire polio vaccine trial. In some communities, officials objected to the use of a placebo injection, so the children in the control group were merely observed for signs of polio. These groups were known as observed controls. Some designers of the study worried that differences between the observed control and experimental groups might influence the outcome. For instance, the observed control group included children whose parents would not consent to their receiving the vaccine. Were there important differences, such as income or housing or parental age, between children whose parents would not consent and those who would? And might those differences affect whether children had already been exposed to and become immune to polio?

• The Salk vaccine trial successfully showed that the vaccine helped prevent paralytic polio, and licensure of the vaccine quickly followed. The disease that once paralyzed thousands of children has now been eliminated in the Western Hemisphere.
Scientific Method in Vaccine History QUESTIONS:
1. Why is there no single method of the scientific method?

2. Do scientists try to prove their ideas by using the scientific method? Explain.

3. What are the qualities of a good hypothesis?

4. What are the three types of scientific studies?

5. What is the difference between the experimental group and the control group in an investigation?

6. How did Edward Jenner test the observation of a milkmaid that had cowpox?

7. What was Robert Koch’s method of identifying the cause of a disease?

8. What was Pearl Kendrick’s contribution to the development of a scientific method for testing vaccines?

9. How did Jonas Salk’s method of testing his polio vaccine improve the way new vaccines are tested?