LESSON 13

SIR ALEXANDER FLEMING

Patrick Pringle

Pasteur discovered germs, and Lister killed them. These two men together revolutionized the theory and practice of medicine.

Louis Pasteur, a French chemist, discovered that disease was caused by living organisms so small that they could not be seen with the naked eye – micro-organisms, or microbes, or bacteria, or germs; the words all mean the same thing. Joseph Lister, an English surgeon – later Lord Lister, the first medical peer – applied Pasteur's discovery to surgery.

Since germs are alive, germs can be killed. They can be destroyed by heat or poisoned by certain chemicals, called antiseptics; carbolic acid is one, and that was the germ-killer Lister used. Previously surgeons had, without knowing it, infected their patients on the operating-table with germs, chiefly from their surgical instruments. Lister sterilized his instruments with carbolic acid, and used carbolic acid to kill the germs on his hands, on the patient's skin, and even in the air in the operating-theatre. Then he could cut his patients open without fear of infecting them with the germs of disease.

Lister's aim was the prevention of disease. The object of his antiseptic method, as it was called, was to stop germs from getting into the body. The cure of disease was a more difficult problem, for here the germs were already inside the body. Certainly they could be killed by the same antiseptic method: but it was soon found that a chemical that destroyed germs also destroyed the cells of the body. Injecting carbolic acid into the blood was tried, and quickly abandoned for it did more harm than good. To kill all the germs the dose would have had to be strong enough to kill the patient, too.

It was a bacteriologist named Metchnikoff, a pupil of Pasteur, who revealed the true nature of the problem. He discovered the body's natural armour against disease — the leucocytes, or white cells of the blood. He showed that when germs enter the body they are immediately attacked by hosts of white cells from the whole neighbourhood, which rush to join battle with the invader like soldiers answering a bugle-call. He showed that disease was, in fact, a fight between the leucocytes and the germs — and a fight to the death, for it ended only with the death of the germs or the death of the patient.

Carbolic acid and all the other known antiseptics did more damage to the leucocytes than to the germs. The problem was to find something that would attack only the germs, and to help, not destroy, the fighting leucocytes.

The problem was still unsolved in 1906, when Alexander Fleming passed the finals of his medical examination and joined the staff of the Inoculation Department of St. Mary's Hospital, Paddington.

Alexander Fleming was born on a farm near Darvel, in Ayrshire, on August 6, 1881. He was the youngest of a family of eight. His father died when he was seven years old, and his eldest brother, Hugh, took over the management of the farm. Alexander was then still going to the village school. At ten he went to Darvel School, and stayed till he was twelve. That was the age-limit. The question was then discussed whether he should continue his education or go back to the land. It was decided to keep him at school, and he went to Kilmarnock Academy. At fourteen he went to London, and for the next two years he studied at the Regent Street Polytechnic.

Three of his brothers were already in London when he arrived. One of them, Thomas, had studied medicine at Glasgow University, and was a qualified oculist. Two others became opticians. And back in Scotland one of his sisters married a Darvel doctor, and another a veterinary surgeon. The Flemings, born on the land, were becoming a medical family. But when Alexander left the Polytechnic, at sixteen, he was to take a job as a clerk in a shipping firm in Leaden-hall Street. There was not enough money for him to study for a profession or trade.

Fleming worked in Leaden-hall Street for four years. Then, at twenty, he received a share in a legacy. It was not large, but enough for him to train for a career with better prospects. His brother Thomas was then in Harley Street; and according to Fleming himself, "My brother Thomas pushed me into medicine."

There were twelve medical schools in London, and Fleming knew nothing about any of them. He chose St. Mary's for no better reason than that he had played water-polo against the Hospital team.

For eight years Fleming worked in Wright's laboratory; for eight years he sought to find a means to aid the leucocytes in their fight against invading bacteria. Then, in 1914, he joined the R.A.M.C., and came face to face with one of the main medical problems of the First World War: the treatment of infected wounds.

By 1914 Lister's antiseptic method of surgery had been largely replaced by what was called the aseptic method. Instead of chemicals heat was used to sterilize instruments, clothing and other operating-theatre equipment. The purpose was the same, to prevent germs from getting into the wound. In peace-time this was adequate for most surgical cases; but in the treatment of war wounds prevention was not enough. In nearly every case the wound was infected before treatment could be begun. Thus the surgeon's problem was the same as that of a physician treating disease: he had to try to kill the germs without damaging the leucocytes that were already fighting against them.

There was no solution — and the problem was tremendous. For the first time in warfare high explosives were used extensively, and wounds that were not infected were rare indeed. The surgeons were unprepared. Thanks to the antiseptic and aseptic methods, infection in surgical cases had become the exception instead of the rule; now it was the other way abo**t again. "We have in this war gone back to all the septic infections of the Middle Ages", said the Director General of the Army Medical Service.

Medical officers treated infected wounds by the only method they knew, with chemical antiseptics. They applied carbolic acid, iodine, and other chemicals to open wounds in an attempt to destroy as many germs as possible. They could not destroy all the germs, but thought that if only some were killed it would be better than none.

Meanwhile Fleming, a medical officer himself, was still working with his old chief. Sir Almroth Wright had been made a Colonel in the Army Medical Service, and had set up a research laboratory at Boulogne. There, with the help of Fleming, he set to work to tackle the problem of *wound infection*.

Wright and Fleming discovered that the treatment being used was doing more harm than good. Each of the chemical antiseptics was more harmful to the leucocytes than to the germs: and in some cases the antiseptic actually helped the germs to grow and multiply. And Wright and Fleming both insisted that the method was basically wrong – that the surgeon's aim should be not so much to kill the germs with an outside agent as to help the leucocytes do their natural germ-killing work.

Experiments were made with different chemicals, and one after another became fashionable and then gave way to the next. And at the end of the War, which had killed about seven million men, the problem was still unsolved.

Fleming, now thirty-seven, went back to St. Mary's and continued research. And in 1922 he discovered an antiseptic — not a chemical like carbolic acid, but a natural antiseptic manufactured by the body.

He made the discovery by what he modestly called an accident. He was suffering from catarrh, and began to examine his own nasal secretions. In these secretions he discovered a substance that destroyed microbes on the culture plate. He called it lysozyme.

Lysozyme proved to be of little practical use in the treatment of disease, but the discovery was of considerable importance: for it was the forerunner of penicillin.

Lysozyme was not a chemical but a natural antiseptic; and unlike chemical antiseptics, it destroyed germs and yet had no harmful effect on the leucocytes. It was, in fact, the first antiseptic discovered that was harmless to the cells of the body.

Penicillin was the second.

The discovery of lysozyme did not bring Fleming popular fame, but it raised his position in the world of science. The medical profession began to pay more attention to what he said: and at this time he had quite a lot to say on the subject that had occupied his mind ever since the First World War. Chemical antiseptics were fashionable again, and Fleming once more reminded doctors of the greater importance of the natural defences of the body.

In 1928 Fleming was appointed Professor of Bacteriology in the University of

London and in the same year he "hit on" penicillin. The phrase in his own. "The very first stage in the discovery," he says, "was due to a stroke of good fortune." But only the first stage.

In his laboratory at St. Mary's he was carrying out a series of experiments on the common germ called staphylococcus. He was growing colonies of the germs on plates spread with agar. The plates were kept covered, but to examine them under a micro-scope he had to take the covers off. "As soon as you open a culture plate," he said afterwards, "you are asking for trouble. Things drop from the air. One of those bits of trouble happened to be penicillin. A mould spore, coming from I don't know where, dropped on the plate."

Presumably the spore of the mould, or fungus, was blown in through the window. It may have come from the larder of a forgetful Paddington housewife — for this particular mould commonly breeds on damp bread, cheese, and preserves. It grows best when the conditions are cool and damp and the summer of 1928 was very cool and damp.

Having settled on the culture plate, the mould began to grow. And almost at once the microbes round it began to disappear.

Fleming put aside the work he was doing and began to investigate. He made a pure culture of the mould, and tried its effect on other bacteria. Some grew right up to it; others, like the staphylococci, stopped short, inhibited by its antibacterial action.

The next step was to produce the anti-bacterial substance free of the mould. Fleming did this by plating the mould on a meat broth. It grew on the surface as a felt-like mass, and turned the broth yellow. After a week's growth the fluid was strained through a fine filter and tested for its anti-bacterial properties, The results were as favourable as before, and Fleming knew that he had discovered another natural antiseptic with far greater possibilities than lysozyme. He called it penicillin.

Further experiments showed that, in its effects on germs like staphylococci, penicillin was about three times as strong as carbolic acid and all the other chemical antiseptics, it had no toxic effect at all on leucocytes. Theoretically it looked like an ideal germ-killer – the antiseptic that had been sought ever since Pasteur discovered germs. In practice there was one big obstacle: in its crude form penicillin was unstable, and it could not be used in the treatment of disease until a means was found of concentrating it.

That was a chemist's job, and Fleming was a bacteriologist. He tried to concentrate the drug, but failed. He lacked both the training and the equipment needed for the job. He published his findings, and continued to proclaim his faith in penicillin; and he kept his original culture of the mould. It can be seen today, dried up but still recognizable, in a place of honour in the Museum of the Medical School of St. Mary's Hospital.

So it seemed that penicillin was, like lysozyme, just another laboratory success. And regretfully Fleming turned to other things.

Meanwhile a fresh attempt had been begun to solve the problem of concentrating penicillin. It was made at Oxford by a team headed by Professor (now Sir) Howard Florey and Dr. E. B. Chain.

The Oxford team included trained chemists as well as bacteriologists, and had all the equipment that Fleming had lacked; yet it was a long, hard struggle before they succeeded in producing a practical concentration of penicillin. The first human cases were treated in 1941, and the problem then became a matter of production. One of the Oxford team went to America, where new methods of manufacture were discovered, and in 1943 penicillin reached the Eighth Army in Egypt. In the words of Viscount Montgomery of Alamein, "The healing of war wounds was revolutionized." Penicillin arrived just in time to save countless lives. It was easily the strongest weapon yet forged in the fight against disease.

While penicillin was being hailed as a wonder drug, the name of its discoverer was hardly known outside the medical profession. Then Sir Almroth Wright wrote a letter to, 'The Times' telling the world who had made the discovery. And Fleming became famous.

He was knighted in 1944, and awarded the Nobel Prize for Medicine in 1945. Government and universities all over the world showered him with honours. He had to travel widely, attend functions, make speeches, received thanks — often personal expressions of gratitude from people who owed their lives to his discovery. In Italy once, at a medical gathering, an unknown man in short-sleeves pushed himself and his three children forward to reach Fleming. "If these children are alive," He said, "they owe it to you." Then, pointing to Fleming, he told his children, "Never forget to ask God in your prayer to bless this man."

But Fleming protested that such gratitude was not due to him. "Everywhere I go people thank me for saving their lives," he said, "I don't know why they do it. I didn't do anything; Nature makes penicillin. I just found it." It was not just modesty that made him say this. It was a restatement of his belief in the healing power of Nature. He protested vigorously against the idea that penicillin was a man-made invention. 'I have been accused of inventing penicillin, but no man could have done that. Nature, in the form of a lowly vegetable, has been making it for thousands of years. I only discovered it." And always he insisted that he discovered it by chance.

"Happy is he who already belonged to history in his own life-time," said Lord Moran, referring to Fleming, but Fleming was not happy in the limelight. "I am a simple bacteriologist," he said; and as soon as he could slip away he went back to his laboratory at St. Mary's and got back to work.

The Americans visited the laboratory and were amazed. One said it was "like the backroom of an old-fashioned drug store." He found it hard to believe that penicillin could have been discovered there. Fleming laughed, and in Detroit, where he was shown over the last word in research laboratories — a gleaming, dustless, air-conditioned, sterilized sanctum — he shocked his hosts by saying, "Wonderful, but penicillin could never have been discovered in a lab like this." When they saw the point they could not deny it. Their culture plates were never contaminated, for the air was too pure: there was no way in for spores of a common mould.

Fleming's achievement was not only the discovery of penicillin. As the Surgeon-General of the United States Forces said, "Fleming, like Pasteur, has opened up a whole new world of science." He founded the antibiotic — that is, growth inhibiting treatment of disease. He provoked others to seek new antibiotics, and all research-workers to be on the lookout for them, particularly in moulds and fungi; and out of these researches, which but for Fleming would not have been started came new drugs, made by nature and at last discovered by man, of which the best known at present is streptomycin. Fleming himself regarded this as the most important result of his work. Even before penicillin was in general use, he said, "The greatest benefit penicillin has conferred is not to the drug itself but the fact that its discovery has stimulated new research to find something better."

Sir Alexander Fleming died in 1955 at the age of seventy-three. His work will never die.

NOTES

Words Explained:

revolutionize : make complete change in something

theory : reasoned view of what may be the cause of relation between facts or events

peer : in British society, a man of high inherited rank (duke, earl, baron, etc.)

infection : giving of disease through atmosphere or water

sterilize : make free from living bacteria

abandon : give up

reveal : give knowledge

armour : metal cover for body

hosts : great number of

invade : go into a country or body to make attack

polytechnic : school teaching a number of different trades

oculist : a specialist in treating eye disorders

optician : maker or trader in optical instruments

profession : way of making living specially in law, army, medicine and teaching

legacy :	money etc. given by owner at his death
prospects :	expectations, hopes
research :	work done with a view to discovering of new facts
vaccine :	poison produced in body by the disease of cows like smallpox
therapy :	medical treatment
tremendous :	very great
explosives :	substances with tendency to go off with great noise
exception :	thing that does not follow the rule
middle ages :	about the years 1000 – 1400
tackle :	grapple with
multiply :	increase rapidly
modesty :	not over-valuing oneself, not putting oneself forward
catarrh :	diseased condition of throat or back of nose as in cold
forerunner :	one coming before another in history, making the way ready for
colonies :	groups of animals living together
mould :	wool-like growth of fungi formed on wet things
spore :	living unit by which plant without flower is produced
larder :	store-room, cupboard for food
preserves :	substances kept from going bad, specially food
broth :	thin meat soup
crude :	substances in natural condition, un-worked
concentrate :	increase strength of liquids by reducing volume
regret :	sad feelings caused by having done or not done something
lack :	not having enough of, be without
hail :	salute or greet
protest :	make statement pointing out what is wrong
limelight :	very bright light; in the limelight; getting public attention
last word :	the latest or best example, the best view about
air-conditioned :	room or the building having the air in it brought to a standard temperature
sanctum :	holy place, a person's private room or study
contaminate :	make unclean or diseased
provoke :	make angry
stimulate :	rouse to activity or excite to action

ANSWER THESE QUESTIONS

1. What are antiseptics and what is the antiseptic method?
2. What was the chief defect of antiseptic method?
3. What part is played by the white cells in the blood of a human body?
4. Give an account of the early life of Fleming.
5. Describe how Fleming discovered penicillin.
6. In what respect is penicillin better than the chemical antiseptics?
7. What do you know of the Oxford team?
8. How did they make penicillin more effective?
9. Write a note on penicillin as a wonder drug.
10. Was Fleming proud of his discovery?
11. Why couldn't penicillin have been discovered in the research laboratories of America?
12. Fleming's achievement paved the way for other discoveries in the medical field. What are they?