Lysozyme

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SIR · ALEXANDER · FLEMING
CHANCE FAVORS THE PREPARED MIND
1881 — 1955
ABRAM BELSKIE SCULPTOR


· INSTITUTE OF CANCER RESEARCH ·
1922
LYSOZYME
1972
COLUMBIA UNIVERSITY
OCT 29-31 1972
· COLLEGE OF PHYSICIANS & SURGEONS ·

The Fleming–Lysozyme Medal

This medal was created to commemorate the fiftieth anniversary of the discovery of lysozyme by Sir Alexander Fleming and to mark the occasion of the Lysozyme Conference held at Arden House, Harriman, New York, October 29–31, 1972, under the auspices of the Institute of Cancer Research of the College of Physicians and Surgeons of Columbia University. This medal was presented at the meeting to Lady Amalia Fleming, Honorary Chairman of the conference.

The portrait on the obverse side of the medal shows Sir Alexander at approximately the time (1922) of the lysozyme discovery. Under the microscope to the right of the portrait are two preparations of *M. lysodeikticus*. The upper field shows the untreated bacteria, and the lower shows the organisms after exposure to lysozyme, markedly swollen and with distorted cell walls. This representation of the morphologic effect of lysozyme was taken from an illustration in Fleming's original report of the lysozyme discovery (*Proc. Roy. Soc. London* **B93:** 306, 1922).

To the left of the portrait is the well-known dictum of Pasteur, "Chance favors the prepared mind." This was frequently cited by Sir Alexander, and assuredly applied to his own life and contributions.

On the reverse side of the medal, lower center, is another illustration adapted from Fleming's original article showing a culture plate with a heavy growth of *M. lysodeikticus*. In the middle of this bacterial growth, a small well has been cut in the agar and filled with tears. After a period of several hours a zone of clearing due to bacterial lysis was evident around the tear sample. The labeling of *"M. lysodeikticus"* and "lysozyme (tears)" is in Fleming's own hand.

A part of the three-demensional molecular model of hen egg-white lysozyme, representing the present state of knowledge of the enzyme, surrounds Fleming's initial culture plate. The portion shown is the active site of the molecule as defined by the X-ray crystallographic studies of David Phillips and his associates. The four circles represent the oxygens of the aspartic 52 and glutamic 35 residues which specifically accomplish the

hydrolytic cleavage of the lysozyme substrate. This molecular model is representative of the wealth of information concerning Fleming's lysozyme which has been assembled through the efforts of a great many investigators in the fifty years since Fleming's discovery.

The medal was created by the distinguished sculptor Abram Belskie, renowned for his many works relating to landmarks of medicine and science and their discoverers. Born in London, Mr. Belskie spent several years in Scotland apprenticed to William Petrie. Thus, he felt a particular kindred to Scottish-born Sir Alexander Fleming. After coming to the United States in 1939, Mr. Belskie worked extensively with the brilliant sculptor, John Gregory.

Mr. Belskie is the recipient of many prizes and honors, including the Sir John Edward Burnett prize, the Lindsay Morris prize, and the Golden Anniversary prize of the Allied Artists of America. He is a fellow of the National Academy of Arts and the National Sculpture Society.

Mr. Belskie resides and has his studio in Closter, New Jersey.

ELLIOTT F. OSSERMAN

Personal Recollections of Lysozyme and Fleming

It is well known that Fleming is famous for his discovery of penicillin and indeed for its value in the treatment of diseases and for starting the era of the antibiotics. Fleming's first paper on penicillin is already extremely important and "a milestone in the history of medical progress," as the Editor of the *British Medical Journal* has called it (1). However, seen from a purely scientific point of view, the discovery of the substance to which Fleming gave the Greek name "lysozyme" is quite possibly greater. At the time of his lysozyme studies, Fleming himself, the introvert, was unable to hide his excitement. His rich imagination and the dreams which he kept so cautiously to himself overpowered him, and he expounded a stream of wonderful hypotheses. The six papers (2–7) which he wrote about lysozyme show perhaps more than any of his other work the brilliance of his mind.

Fleming had two great reasons to cherish lysozyme. It was the first antiseptic he had studied during long years of hard work and search which fulfilled what he required from a bactericidal substance: that it be *selectively more lethal to bacteria than to the host cells.* And what was more and dearer to Fleming's heart, lysozyme was a constituent of human cells and part of the whole body's natural resistance mechanism. As a pupil of Almroth Wright, Fleming had high respect for natural defense mechanisms, and he kept this respect to the end in spite of the miraculous achievements of his penicillin and all the other antibiotics.

It would be right to say that lysozyme made the discovery of penicillin easier, although my own feeling is that it might have been better if penicillin had come first. Ironically, the reading before a learned audience of colleagues of both these extremely important papers was received with the same icy silence and indifference. Both substances have very much in common. They were discovered in almost an identical way. To study penicillin, Fleming used the methods he had devised to study lysozyme. And what is particularly important, and perhaps more so to me, both discoveries show the two great qualities of Fleming's mind. The first characteristic was that he would immediately understand the implications of a chance phenomenon

and go straight to the right conclusion. Other scientists before Fleming had noticed the bactericidal power of egg white (8), and much work had been done on that of leucocytes. It is probable that these scientists were investigating the actions of lysozyme but, as Fleming said in his Presidential Address to the Royal Society in 1932, "All these authors considered that the antibacterial phenomena they observed were peculiar to the substance with which they were working—leucocytes or egg white—and none of them apparently had any inkling that the lytic element was widely distributed throughout the animal and vegetable Kingdom" (9).

A drop from the nose of Fleming who had a cold fell onto an agar plate where large yellow colonies of a contaminant had grown, and lysozyme was discovered. He made this important discovery because when he saw that the colonies of the contaminants were fading, his mind went straight to the right cause of the phenomenon he was observing: that the drop from his nose contained a lytic substance. And, also immediately, he thought that this substance might be present in many secretions and tissues of the body. And, he found that this was so—the substance was in tears, saliva, leucocytes, skin, fingernails, mothers' milk—thus, very widely distributed in animals and also in plants.

The circumstances of the discovery of penicillin were very similar. Other scientists, and I believe his friend the Belgian Professor Gzatia was among them, had seen colonies of bacteria fading around a chance mould contaminant, but they did not realize the possible significance of what they were seeing—and they did not discover penicillin.

This great ability which Fleming possessed to understand immediately the meaning and cause of things often impressed me. If I had a problem which to me seemed difficult and confused and I felt like I was helplessly searching my way in a thick wood, he used to find the solution immediately, giving me the impression that he was looking at this inscrutable forest from above and could easily and clearly see the tortuous little path out, and how and where it led.

Fleming's second important characteristic was that his mind was not cluttered or closed to new findings and developments by the beliefs his previous experiments had led him to. And this is proved by the way he threw overboard all these beliefs when he discovered lysozyme and after it penicillin. Hundreds of his neat, conclusive experiments had shown that all antibacterial substances in use at the time, and in the way they were used, did more harm than good. All were killing the bacteria only in concentrations which destroyed the leucocytes. By contrast, lysozyme was harmless to leucocytes and killed some bacteria. Its bactericidal action on the pathogenic bacteria was very weak, which also was natural because otherwise the bacteria would not have been able to establish themselves in

the body and be pathogenic; they would have been killed by the lysozyme. Fleming thought that the definition of a pathogenic germ was just that—that it was resistant to lysozyme, at least to its usual concentration in the body. Having found that in egg white the concentration of the lytic element was much greater, a hundred times higher than that in the tears—which he had found to be the richest in lysozyme in the human body—he tested the toxicity of this higher concentration with his usual comparative tests on leucocytes and bacteria. With delight he found that in this higher concentration, lysozyme was still absolutely harmless to the leucocytes while it had a marked effect on some pathogenic bacteria. Fleming then injected egg-white solution intravenously in a rabbit and found that it did not upset the rabbit, while it markedly enhanced the bactericidal power of its blood. He tried to obtain the lytic element in pure form to inject it into the blood stream. But neither he nor anyone else in Almroth Wright's team was a chemist. Almroth Wright despised chemists and would not have one in his laboratory! And so, having nothing better to use in the blood stream, Fleming tried diluted egg white and wrote his conclusion: "It is possible that in cases of generalized infection with a microbe susceptible to the bacteriolytic action of egg white . . . the intravenous injection of a solution of egg white might be beneficial . . ." (5). Yet, earlier, in his 1919 Hunterian Lecture, he had dismissed the possibility of benefit from any of the antibacterial substances then known. "It seems a pity," he had said, "that the surgeon should wish to share his glory with a chemical antiseptic of more than doubtful utility . . ." (10).

Exactly the same thing happened with the biological testing of penicillin. Fleming tested the broth culture of the mould for toxicity in his usual way and found that the antibacterial substance it contained, although very powerful on pathogenic bacteria, did not interfere with the action of leucocytes. He then gave intravenous injections of the broth culture filtrate to rabbits and found that it did not upset the animals more than pure broth (11). Fleming once again dismissed his previous convictions regarding the "doubtful utility" of "chemical antiseptics." Actually, earlier in the *same year* that he discovered penicillin, while studying a mercury compound which seemed to have some possibilities, he had written, "There is little chance of finding any general antiseptic capable of killing bacteria in the blood stream, though there is some hope that chemicals may be produced with special affinities for special bacteria which may be able to destroy these in the blood, although they may be quite without action on other, and it may be, closely allied bacteria" (12).

With penicillin he had this chemical, he had this antibacterial substance; a mould was producing it. Again he tried to extract the active element pure from the culture but, as with lysozyme, he failed again. And so did

all the chemists he asked to try to do it. As he obviously could not inject a broth culture into the blood stream of humans, he tried giving to patients who were dying from septicemia (because only then would the physicians allow him to do so), a *milk* culture of the mould to eat. It looked like Stilton cheese, although certainly not tasting as good. This therapeutic effort sometimes brought slight, short-lasting, unreliable beneficial results. To be used, penicillin and lysozyme would have to wait until they were purified.

With the discovery of lysozyme, Fleming's mind gave birth to wonderful hypotheses, and most of them he proved. Lysozyme, he thought, was the natural defence of the organism, the defence Nature had provided to all living organisms: human, animal, and vegetable. Perhaps at some primeval time no germ could establish itself and cause a disease: they were all sensitive to lysozyme. He thought that pathogenic germs, as we know them, were in fact pathogenic because they had become resistant to the action of lysozyme; that is, they are probably the descendants of resistant mutants of sensitive bacteria. Fleming himself produced such resistant mutants *in vitro,* and using them he proved that the intracellular digestion of bacteria was related to the action of lysozyme in these cells (7). He thought that the different pathogenicity of bacteria to different animals might be due to strain differences in the quantity and quality of lysozyme. He thought that lysozyme *should be* in greater concentration in these parts of the body more exposed to infections or lacking other forms of natural protection. And he proved that this was so.

Years earlier, during World War I, Fleming had struggled to find an efficient antiseptic which would help prevent and cure the wound infections. At that time he had dreamt that Nature (this Nature he believed in so much) *must* have provided every living thing with an effective defence mechanism which would protect it *in all its parts*. With the discovery of lysozyme, Fleming believed that he had found this primeval general natural defence mechanism. He had also found something much greater: he had found *Hope*. Lysozyme proved that a substance did exist which had selective bactericidal action while being harmless to human cells. So this, which up to that time had been considered impossible, *was* possible. Fleming thought that if nothing else could be found, lysozyme, purified and many times more potent, might be an answer—might be a help.

Fleming believed in lysozyme. He believed that it was bound to have a great future; he had discovered it and had done marvelous work on it. Other scientists would follow the path he had opened. Others would purify it, advance it. With absolute confidence he used to say, "We shall hear more about lysozyme."

Your work has made Fleming's prophecy come true.

LADY AMALIA FLEMING
Cheyne Walk, London

BIBLIOGRAPHY

1. Fleming, A. The discovery of penicillin. *Brit. Med. J.* **1:** 711, 1955.
2. Fleming, A. On a remarkable bacteriolytic element found in tissues and secretions. *Proc. Roy. Soc. London* **B93:** 306, 1922.
3. Fleming, A., and Allison, V. D. Further observations on a bacteriolytic element found in tissues and secretions. *Proc. Roy. Soc. London* **B94:** 142, 1922.
4. Fleming, A., and Allison, V. D. Observations on a bacteriolytic substance—lysozyme—found in secretions and tissues. *Brit. J. Exp. Path.* **3:** 252, 1922.
5. Fleming, A., and Allison, V. D. On the antibacterial power of egg white. *Lancet* **1:** 1303, 1924.
6. Fleming, A., and Allison, V. D. On the specificity of the protein of human tears. *Brit. J. Exp. Path.* **6:** 87, 1925.
7. Fleming, A., and Allison, V. D. On the development of strains of bacteria resistant to lysozyme action and the relation of lysozyme action to intracellular digestion. *Brit. J. Exp. Path.* **8:** 214, 1927.
8. Rettger, L. F., and Sperry, J. A. The antiseptic and bactericidal properties of egg white. *J. Med. Res.* **26:** 55, 1912.
9. Fleming, A. Lysozyme. *Proc. Roy. Soc.* **B26:** 1, 1932.
10. Fleming, A. The action of chemical and physiological antiseptics in a septic wound (1919 Hunterian Lecture). *Brit. J. Surg.* **7:** 99, 1919.
11. Fleming, A. On the antibacterial action of cultures of penicillium with special reference to their use in the isolation of *B. influenza*. *Brit. J. Exp. Path.* **10:** 226, 1929.
12. Fleming, A. The bactericidal power of human blood and some methods of altering it. *Proc. Roy. Soc. Med.* **21:** 839, 1928.

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