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Serotonin

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Vittorio Erspamer was an Italian pharmacologist and chemist, noted for the identification, synthesis, and pharmacological research of more than sixty novel chemical compounds. Erspamer was born in 1909 in the little village of Val di Non in northern Italy, which was then part of Austria-Hungary. He attended school in the Roman Catholic Archdiocese of Trento before moving to Pavia to study medicine and surgery at Ghislieri College, from which he graduated in 1935. He then became an assistant professor of anatomy and physiology at the University of Pavia, one of Europe's oldest universities. In 1936, he was awarded a scholarship to attend the University of Berlin's Institute of Pharmacology. He returned to Italy in 1939 and settled in Rome, where he became a professor in pharmacology.

The story begins in the early 1930s, when Vittorio Erspamer worked at the Institute of Comparative Anatomy and Physiology at the University of Pavia in Italy. In the 1930s, Dr. Erspamer became interested in the smooth muscle constricting or contracting capabilities of numerous amine compounds found in the skins and intestinal tracts of many species, including rabbits, molluscs, and frogs. One chemical that interested him was found in enterochromaffin cells of the intestines. An acetone isolate of the cells produced smooth muscle contractions, particularly in the rat uterus. He concluded that the drug was not epinephrine and, based on colour testing, was most likely an indole. Erspamer wondered if this chemical was epinephrine, a hormone identified a few decades ago that causes muscular contractions. But the compound was not epinephrine, but something new. He termed the substance enteramine and continued his research on smooth muscle for several years. He also investigated the mollusc heart and enteramine levels in salivary glands of octopus.

In the late 1940s, doctors of Cleveland Clinic investigating hypertension, or high blood pressure, were perplexed by a strange chemical. Physiologist Irvine Page, the first Director of Cleveland Clinic's Division of Research, felt that hypertension was induced by substances in the blood that constrict blood vessels. Page had already identified angiotensin, a hormone that regulates blood pressure, and so he intended to find other similar chemicals. As a contaminant kept interfering, Page recruited two scientists, biochemist Arda Green and organic chemist Maurice Rapport, to help isolate the supposed clotting compound.

To analyze this contaminant, Rapport needed lots of blood, which he acquired from a nearby slaughterhouse. They provided 45 litres of clotted cow blood. He hauled buckets of coagulating blood back to his lab and strained it through a huge cheesecloth. Rapport chemically separated the unknown substance from the serum. Then, Green prepared an assay to test whether the compound constricted blood vessels. It ultimately took Green and Rapport huge amount of cow's blood, but the scientists finally produced a very small amount of the mysterious compound. In 1948, Maurice M. Rapport, Arda Green, and Irvine Page of the Cleveland Clinic discovered a vasoconstrictor chemical in blood serum, which they termed as serotonin because it was a serum agent that affected vascular tone. In 1952 it was found that enteramine was the same substance as serotonin. Serotonin was established as 5-hydroxytryptamine.

Around the same time, Betty Twarog, a PhD candidate at Harvard University, was researching the signalling chemicals that trigger muscular contraction in molluscs. Molluscs may cling to surfaces for extended periods of time because their muscles, unlike those of many other animals, remain constricted. Twarog hypothesized that serotonin was signalling the muscles. Serotonin sent important messages across the mollusc's nervous system, directing muscles to relax and release. This revealed that serotonin was more than just a molecule in the circulatory system; it was also a neurotransmitter, which permits the neurological system to connect.

During the 1950s, research demonstrated that serotonin was present in the brain and nervous system



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and could function as a chemical messenger between neurons. This transformed the understanding of serotonin from simply a vasoconstrictor into an important neurotransmitter.

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Vittorio Erspamer at work in his laboratory at the University of Rome

Picture Courtesy: Whitaker-Azmitia, P. The Discovery of Serotonin and its Role in Neuroscience. *Neuropsychopharmacol* [https://doi.org/10.1016/S0893-133X\(99\)00031-7](https://doi.org/10.1016/S0893-133X(99)00031-7) 21 (Suppl 1), 2–8 (1999).



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