The Story of Dactinomycin

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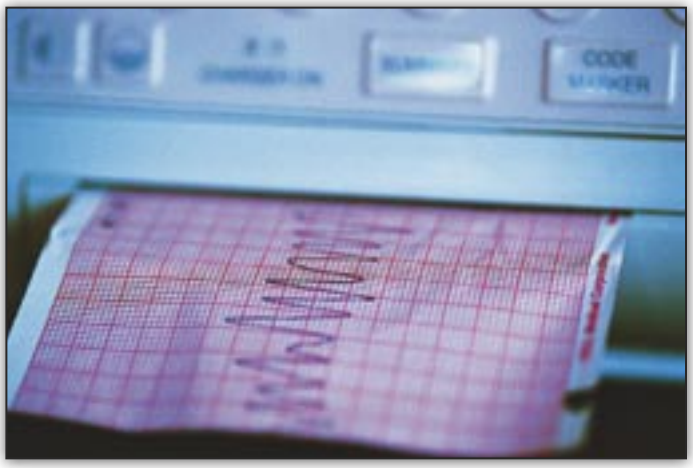

Many of the major advances in science have been made serendipitously. What this means is that efforts directed towards one objective accidentally found something quite wonderful on the way. Columbus's discovery of America is an example. This can happen in science as well; for instance, the discovery of x-rays by W. Roentgen. While doing experiments in a darkened room, he noticed that a bit of paper covered with a certain substance glowed when he turned on his apparatus, and stopped glowing when it was turned off. This was a completely surprising phenomenon; and he reasoned that there were penetrating rays coming from the apparatus he was using. He did not know their nature and therefore called them "x-rays" meaning an unknown kind of ray.

Now about dactinomycin. In 1940, Selman Waksman, a professor at Rutgers University was trying to isolate antibacterial substances from melon molds that he was growing in his laboratory. This was an outgrowth of the serendipitous discovery of penicillin which also came from a mold.

Working with H. Boyd Woodruff of the Merck and Co. laboratories, Professor Waksman isolated a series of compounds that he called the "actinomycins" named after the type of mold he was growing. He found that these substances were extremely toxic to the mice in which they were tested. He noted his observations and closed the file because he believed the actinomycins to be too toxic for use in humans. In 1952, an investigator in Germany named Hackmann looked through the Waksman and Woodruff files, and noted that the experimental mice reported by them had small thymus glands and spleens. These organs are packed with lymphocytes, one of the components of the white blood series. Hackmann reasoned this was because the actinomycin compounds destroyed the lymphocytes. He further reasoned that if the chemicals killed normal white blood cells (lymphocytes), they might do the same for malignant white blood cells; namely leukemia.

The substance was included in the animal screening tests then being run in Washington at the National Cancer Institute. It was found not to be effective against the types of cancer used in the animal models that were included in those screens, those cancers being the kind that grow in adults. Childhood cancers are different, so actinomycin D, one of the series, was sent to Dr. Sydney Farber of the Boston Children's Hospital in 1955. It was immediately found to produce remissions in children with Wilms tumor! This was the birth of effective chemotherapy for the "solid tumors" of childhood like Wilms tumor; that is, the malignant diseases not originating from blood elements, such as leukemia. It was soon tested in children with various malignant diseases, and the first responses in other childhood "solid tumors" such as rhabdomyosarcoma, a muscle tumor, were soon recorded.

Also serendipitous was the observation that dactinomycin (as it has since been named) acted with radiation to produce reactions in normal tissues at much lower doses than when x-radiation was used alone. Studies showed that this combined effect was true not only in normal cells but also within cancer cells.

Thus, starting with a mold grown in a biology laboratory in the hope of finding a substance that would fight infections, there resulted one of the most useful chemotherapeutic agents in pediatric oncology. It was discovered through a series of chance observations. The important point is that an alert eye and a prepared mind used the information obtained serendipitously and directed that information to the fight against cancer.