SERENDIPITY AND SCIENTIFIC DISCOVERY

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ABSTRACT

Serendipity has played a crucial role in science. The majority of the most important and revolutionary discoveries in biology and medicine have a serendipitous element in them (Beveridge, 1957, 1980). A few examples are the discovery of penicillin, heparin, Dramamine, X-rays, the Gram staining technique, the pancreas's role in diabetes, and the anesthetic effects of ether and nitrous oxide. In other areas of science, the discovery of pulsars, electric current, the connection between electricity and magnetism, and the detection of cosmic microwave radiation background, all involved serendipitous events.

INTRODUCTION

Serendipity has played a crucial role in science. The majority of the most important and revolutionary discoveries in biology and medicine have a serendipitous element in them (Beveridge, 1957, 1980). A few examples are the discovery of penicillin, heparin, Dramamine, X-rays, the Gram staining technique, the pancreas's role in diabetes, and the anesthetic effects of ether and nitrous oxide In other areas of science, the discovery of pulsars, electric current, the connection between electricity and magnetism, and the detection of cosmic microwave radiation background, all involved serendipitous events.

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THE PRINCES OF SERENDIP: CHANCE AND THE PREPARED MIND

The word serendipity was coined by Horace Walpole, an eccentric English writer, in a letter to Sir Horace Mann in 1754. "This discovery is almost of that kind which I call serendipity, a very expressive word. . . . I once read a silly fairy tale called The Three Princes of Serendip: as their highnesses traveled they were always making discoveries, by accidents and sagacity, of things which they were not in quest of . . ."

Almost all recent popular dictionaries have changed Walpole's definition of serendipity although they still credit him with the origin of the word. Examples of recent definitions include "the faculty of making providential discoveries by accident" (Noah Webster's), "the faculty of finding valuable things not sought for" (Meriam Webster's), and "an aptitude for making desirable discoveries by accident" (Random House). The key word sagacity has been omitted. Sagacity, defined as penetrating intelligence, keen perception and sound judgment, is a key element of serendipity.

In the original story, sagacity permeates the lives of The Three Princes of Serendip. Although they've been incorrectly portrayed as bimbos who keep accidentally bumping into good fortune, their actual abilities are more akin to those of Sherlock Holmes.

The three princes received the best formal education possible. The king correctly realized when his sons had reached the peak of their book knowledge and decided their further education best come from the experience of traveling in other lands.

In Persia, the three princes encountered a camel driver searching for his animal. Through astute observation, the princes were able to determine that the camel was blind in one eye, missing a tooth, and lame. They also concluded that the animal was carrying a load of butter on one side, honey on the other, and a pregnant woman. Convinced that only thieves could know such details, the camel driver had the princes arrested. When the missing camel was subsequently found, the princes were asked how they were able to determine so many details. The answer, of course, relies more on sagacity than on chance.

The brothers, in turn, confessed the following . . .

> I thought he must have been blind in the right eye, because only the grass along the lef side of the trail was eaten even though it was not as thick as that over the right side.
>
> I guessed that the camel lacked a tooth because the way the grass cuds were chewed indicated that a tooth was missing.
>
> I guessed that the camel was lame because only three footprints were clearly indicated, whereas the fourth print was dragged.

They continued:

I guessed that the camel had a load of butter on one side because there were many ants on one side of the trail, and I thought he carried honey on the other side because many flies gathered along the other side of the trail.

I guessed that the camel must have carried a woman because I noted a footprint and found some female urine near where the camel had knelt.

And the third prince concluded:

I guessed that the woman was pregnant because the hand prints nearby showed that she had helped herself up with her hands after urinating.

(Summary by Austin (1978) of the tale in Remer (1965), which is authenticated by Cammann (1967).)

This excerpt was selected to illustrate the princes' keen perception and intelligence, although it fails to display their good judgment. Throughout the rest of the story, their highly developed mental powers enable them to take advantage of the chance opportunities they encounter.

The Princes of Serendip have their parallels in the scientific world. Perhaps the most famous example of serendipity is the discovery of penicillin, a story which essentially captures the powerful interaction of chance with the prepared mind.

FLEMMING AND PENICILLIN

When Alexander Flemming noticed a mold had grown in one of his culture dishes and the staphylococcal colonies around the mold were dead, he decided to explore this promising lead. At least 28 scientists believed Flemming reported a mold killing one or more colonies of bacteria during an experiment, but all chose to view it as an unfortunate error rather than an opportunity for discovery (Selye, 1975). For example, Scott noticed the inhibition of a staphylococcal colony by a mold; he viewed it as a nuisance. He later emphasized that Flemming's discovery was mainly attributable to tenacity in seizing an opportunity others had let pass rather than due to just pure chance (Scott, 1947).

What caused Flemming to pursue the promising lead that was ignored by so many scientists before him? There is no single answer. As Austin (1977) observes, "the most novel, if not the greatest discoveries occur when several levels of chance coincide."

Nine years before his discovery of penicillin, Flemming observed that the bacteria in one of his dishes died after being contaminated with his nasal drippings (Maurois, 1959). This serendipitous occurrence led to his discovering the bacterial enzyme, lysozyme, which is found in nasal mucus. Although lysozyme proved inappropriate for medical use, the experiments reinforced his professional interest in bacterial inhibitors, furthered his career, and made him more receptive to the potential implications of the penicillin mold he would eventually encounter.

Other contributing factors include his being an artist with acute powers of observation, his frugal Scottish background which encouraged his tendency not to discard any laboratory dish until learning all he possibly could from it (Austin, 1977), and his damp and readily contaminated laboratory in St. Mary's Hospital in London. (Interestingly, he chose St. Mary's because of its swimming pool where he could play water polo, rather than because of its scientific facilities.) Although most reports say the penicillin mold came into the laboratory through the window, possibly with the London Fox, Hare (1970) suggests that the mold came from Dr. La Touche's laboratory one floor below. Hare supports his hypothesis by noting that when American pharmaceutical companies studied hundreds of strains of penicillin in the late 1940s, they found only two which produced a better yield than Flemming's original strain. It is now also known that had the London summer temperatures been at their normal level during those crucial days in 1928, the higher temperatures would have prevented penicillin from having any effect on the staphylococcal colonies (Ellis-Pegler, 1985).

Flemming's excitement at the time of the discovery was not shared by his colleagues. The antiseptics they had used in field hospitals during World War I killed white blood cells, which protect the body against germs, more efficiently than they killed the germs themselves. Flemming was able to show that penicillin did not impair white cells, but he was unable to develop it as an effective antiseptic. For some reason, perhaps the lack of resources and encouragement at St. Mary's or the many other promising areas of research Flemming was pursuing, the development of penicillin stopped for ten years (Sheehan, 1982).

During the 1930s, the discovery and successful use of sulfa drugs finally convinced the medical community that safe and effective antiseptics were possible (Shapiro, 1986). Florey and Chain restarted the research on penicillin and miraculously cured mice infected with deadly pneumonia (Chain et al., 1940). Flemming might have been able to do that experiment, but he had never attempted it.

Comroe (1977a) notes that chance favored Chain and Florey when they used mice rather than guinea pigs; Penicillin is non-toxic to mice but quite toxic to guinea pigs. Although they thought their extract was relatively pure penicillin, in actuality it was only 1% penicillin and 99% impurities. Had the impurities been toxic, penicillin would have appeared dangerous, delaying further development (Taton, 1957).

Even with this fortunate ending, 17 years elapsed between the initial discovery of penicillin and the awarding of the 1945 Nobel Prize in medicine to Flemming, Florey and Chain. Serendipity does not provide an instant solution. Systematic scientific work always follows the initial fortuitous observation, with the eventual application evolving from rigorous experimentation and extensive knowledge of the field.

THE SCIENTIFIC METHOD AND THE UNEXPECTED EVENT

As Pasteur observed in the mid 1800s, "chance favors only the prepared mind." Several years earlier Joseph Henry, the first director of the Smithsonian, said: "The seeds of great discoveries are constantly floating around us, but they only take root in minds well-prepared to receive them." Winston Churchill made a similar point: "Men occasionally stumble across the truth but most of them pick themselves up and hurry off as if nothing had happened." Serendipity can indeed play a key role in uncovering the truth, but because traditional scientific training and thinking favor logic and predictability over chance, that role is often overlooked in the scientific literature.

Comroe (1977b), after reviewing 33 major discoveries in biochemical science in which serendipity played a crucial role and questioning other researchers, concluded that when it comes to "chance" factors, few scientists "tell it like it was" in their writings. Even if they did, journal editors would probably delete, as unscientific, the "chance" aspects in the paper. When interviewers used tape recorders and asked certain structured questions about the work environment (Amabile & Gryskiewicz, 1987), scientists tended to overlook or not mention the significance of chance occurrences. Not surprisingly, older scientists who have achieved high honors are more willing to acknowledge their indebtedness to chance (Comroe, 1977b).

In a two-year research project at the prestigious Salk Institute, Latour (1979) studied the scientists around him while working as a laboratory assistant. He found that unpredictable events which critically influenced the research were usually omitted in the final publication. Instead, rational processes and a pseudo-sense of underlying logic were superimposed on the experiments. Often this distortion was not deliberate. Gordon and Pose (1981, 1987) emphasize that people are usually unaware of the exact thinking processes preceding a discovery and therefore are unable to provide a completely accurate account of what transpired.

Real life science is quite different from the neat logical process conveyed in journal articles. Parkes (1958) states that most discoveries in biology could not have been arrived at through reason alone. "To perceive the unexpected result or to discern the promising clue from among the multitude of irrelevant odd things that happen almost every day in an active laboratory is perhaps the very essence of the art of research."

Successful researchers watch closely and are willing to view the data from several different perspectives. They have questioning minds which challenge existing assumptions when they are incongruent with empirical observations. These scientists, realizing that serendipitous events can generate important research ideas, recognize and appreciate the unexpected and encourage laboratory assistants to observe and discuss unusual happenings.

Serendipity can be enhanced in appropriate group settings. What's needed is a "critical mass" of scientists from diverse disciplines working together in an environment conducive to frequent and open communication. In such an environment, researchers are more likely to consult with colleagues when developing and evaluating research ideas, with the results illustrating the old adage that "the whole is greater than the sum of the parts." An unusual observation that doesn't fit in with a scientist's work or interests can be shared with a colleague who may be able to find an application for the new information.

Even scientists who recognize and appreciate the significance of the unexpected may find their time and resources totally committed to existing projects. For example, most grant proposals require clearly defined research, leaving little room for discovering anything truly new. Although hypotheses can be explored and checked out, possible outcomes are already explicit in the grant application. Humphrey (1984) states that an ideal application would read "these are the lines along which I expect to begin my experiments, but I really hope an unforeseen observation will prompt an unexpected idea," but he realizes only an unusually enlightened committee would award such a grant. Yet this is how breakthrough discoveries are usually made. As Koestler (1964) said, "The history of discovery is full of arrivals at unexpected destinations, and arrivals at the right destination by the wrong boat."

Scientists have the analytical training and the keen intelligence necessary for their exploratory voyages. By realizing that discovery involves a dynamic interplay between conventional scientific methods and chance in all of its forms, and by cultivating an aptitude for serendipity, scientists can greatly enhance their investigative powers.

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