

# Discover Generics

Cost-Effective CT & MRI Contrast Agents





## **Perspectives**

M. Castillo

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#### **PERSPECTIVES**



Dip the apple in the brew, let the sleeping death seep through.

The Evil Queen in Snow White and the Seven Dwarfs

Why Steve Jobs chose an apple as the symbol for his cool company is not certain: Was it working at an apple farm when he was young or admiring the Beatles, Isaac Newton, and Alan Turing? The apple he chose to represent his line of computers was a Macintosh. No doubt apples are attractive: wide shoulders leading to feminine rounded sides ending in a wide stem bowl, superiorly and inferiorly in a narrow calyx, all wrapped in a colorful skin freckled with lenticels, and they are also good for you—2 (or 3) apples a day keep the neurologist away. Animal studies prove that antioxidants, acetylcholine and quercetin, occurring in apples are good for the aging brain and may even help prevent Alzheimer disease. Apple juice is said to improve the mood of patients with Alzheimer disease, and some compounds in apples may help fight the disease.<sup>2</sup> Apples also help the circulatory system by decreasing serum low-attenuation lipoproteins (bad cholesterol). Hence, there must be some truth to the old adage "An apple a day keeps the doctor away," which comes from the even older English version, "An apple before going to bed keeps the doctor from winning his bread."3 However, apples are also associated with evil behavior and forbidden love.

On June 7, 1954, Alan Turing was 42 years of age, fat and flabby with enlarged breasts, when he carefully injected cyanide into an apple—a red one, his favorite—and started eating it. The next day he was found dead with half of that apple beside him. Before his suicide, he was working on mathematic representations of biologic processes now considered the forebearers of the Chaos Theory and the Singularity Event. His purpose was to discover how computers might merge with human processes. That same year he had imagined a computer that could play chess. For nearly all of the previous decade he had been designing the Automatic Computing Engine while working at the National Physical Laboratory in London.<sup>5</sup> His article "Computing Machinery and Intelligence" published in 1950 is said to be the most quoted paper in modern philosophic literature. During this time, he established a homosexual relationship, and one of his partner's friends broke into his house at night to steal. Turing reported this incident to the police, confessed his homosexuality, and was charged with gross indecency. Punishment: chemical castration (which explains his physical condition and psyche at the time of his death).

Chemical castration induces depression, anxiety, and decreased cognitive abilities and verbal memory. Androgen blockade also leads to increased levels of cerebral  $\beta$ -amyloid, which is associated with Alzheimer disease. Conversely, estrogen administration to postmenopausal women leads to lower levels of  $\beta$ -amyloid and improved cognition. Although depression is a major risk factor for suicide, suicidal individuals have other more pronounced brain chemical abnormalities than those who are "only" depressed. Among those who com-

mit suicide, levels of corticotropin-releasing hormone in the red nuclei and several parts of the frontal lobes are increased. Other hormones are also affected: vasopressin is high in some brain regions and low in others. Less well-known hormones such as gastric-releasing peptide are high, and neuromedin B is low. Depression may also exert epigenetic influences by increasing the methylation of a gene that regulates the expression of DNA methyltransferase, leading to abnormal function of the frontopolar cortex. Thus, although suicidal tendencies are probably not genetic, environmental factors can drive genetic changes that lead to them.

When he was 18 years of age, Turing fell in love with a fellow student who later died of tuberculosis acquired from drinking unpasteurized milk. This death shattered all his religious convictions and strengthened his interest in mathematics. As a teenager, he was sent to study in Dorset. He was said to have been disorganized, disheveled, and perhaps not too clean. He had a strange voice, high-pitched and halting, that did not change with adolescence and separated him from other boys. As a young boy, one of his favorite stories was Snow White, particularly the part when the evil queen cooks the poisoned apples. The queen tricks Snow White into eating one by making her believe that it is a magic wishing apple.

Homosexual men show brain differences compared with others. The volume of their anterior commissure is larger than that of heterosexual males and females. The suprachiasmatic nuclei are also larger in gay men.<sup>9</sup> No one knows when these differences are established. A prenatal surge in luteinizing hormone and a decrease in testosterone are thought to influence sexual orientation. 10 The volumes of the cerebral hemispheres are nearly identical in homosexual men and heterosexual women but different from those of heterosexual men and lesbians. Functional connections as inferred from PET studies follow these same characteristics. 11 Different types of auditory and masticatory patterns and increased left-handedness are found in gay men. Today, in our Western world, punishing someone for his or her sexual preference sounds extreme, but it is to be remembered that homosexuality is still punishable by death in 7 countries and illegal in nearly 40% of all

Most of Turing's fame came from his work as a cryptographer during World War II. Initially he was able to solve the "indicator system" used in cypher texting, which showed the initial position of the rotors in a coding machine before messages were transmitted. On the same day that he solved the indicator issue, he also conceived of a technique that would break the secrecy of the Nazis' famed Enigma code (used to transmit instructions to U-boats). Because the Enigma was capable of  $4\times 10^{26}$  combinations, just having the chutzpah to imagine a method to break its codes is mind-blowing. <sup>12</sup> These techniques led to the creation of the first programmable computers (the Heath Robinson and the Colossus), though he was not directly involved in building these.

Before working for Naval intelligence, he spent 2 years in the United States at the Institute for Advanced Study at Princeton, where he obtained his PhD. The topics of his dissertation were ordinal logic and relative computing, which helped "Turing machines" solve problems not hitherto possible. Turing machines, also known as "universal machines," were intended to solve anything that is computable.<sup>13</sup> These machines were

capable of manipulating symbols found on a strip of paper (or other materials) separated by other symbols (colons, semicolons) or cells and were the ancestors of modern central processing units. On a strip of paper, a black square may have signified zero, while a white one meant 1. Thus, the binary code was put to practical use, and Turing used numbers to represent other numbers, creating modern computing. Because computers can compute forever without knowing when to stop, Turing solved this issue by creating an algorithm called the "halting problem," which represents the first decision-making program.

In the late 1940s, Turing began tinkering with artificial intelligence (AI) (he is now called "the father of AI"). During this time, he developed the "Turing test," intended to determine a machine's ability to exhibit intelligent and humanlike behavior. For this, he asked a human judge to engage in conversation with another human and a machine, not knowing which one was which. If the judge was unable to differentiate between these, the machine passed the test and was considered intelligent. It was not until 1966 that a computer program passed this test. The reverse of this test type is called CAPTCHA, and it ensures that a response is human. All of us are familiar with this test because it is commonly found when registering for on-line services as a series of letters and/or numerals that are distorted and crowded, making segmentation difficult. These must be retyped correctly by a human user:



The apple has much more to do with modern neuroradiology than just Turing and his machines. Electrical and Musical Instruments (EMI) is a British consortium that developed radar and stereo sound recording.<sup>15</sup> Perhaps, the best known division of EMI is Abbey Road Studios, which opened in 1931, the year EMI was formed. Before Sir George Martin brought the Beatles to the studios, classical luminaries such as Elgar, Toscanini, and Klemperer recorded there. In 1967, the Beatles started Apple Corps (comprising a group of companies) and issued their first Apple recording, "Magical Mystery Tour." Although EMI considered itself a "serious company" and viewed Abbey Road Studios as its black sheep, there is no denying that together with Apple Records, they brought it tremendous wealth. It is with this income that 4 years after Turing's death, Sir Godfrey Hounsfield built the first fully transistorized computer (EMIDEC 1100) by using many of the concepts invented by Turing. The EMIDEC 1100 manipulated information encoded in punched cards or tapes similar to the Turing machine. In 1967, after EMI gave Hounsfield "time to think about some research which may be fruitful," he started exploring the idea of pattern recognition with computers.<sup>16</sup> One year later, EMI patented Hounsfield's idea for body scanning by using x-rays, and in 1971, the first brain CT study was done at the Atkinson Morley Hospital in London. It is said that thanks to the sales of 200 million vinyl Beatles singles, EMI was able to fund the 4 years that it took Hounsfield to realize his idea.<sup>17</sup>

Nowadays, Apples (computers, not fruit) are said to be addictive. In 2011, the British Broadcasting Company screened a documentary, and in it, a devotee of Apple computers underwent an fMRI study that showed that the brand stimulated the same brain areas as religious faith does. Applephilia can become a disease, and some individuals claim to think about Apple 24 hours a day.

In 1966, the first Turing Award was given and is now considered the Nobel Prize of computing. The award comes with US \$250,000 and is sponsored by Intel and Google. No person related to the field of medical imaging has received it.

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   M. Castillo

Editor-in-Chief

N.B. For a wonderful fictional history of Turing, I recommend *A Madman Dreams of Turing Machines* (New York: Anchor Books, 2006) by Janna Levin, a Professor of Physics and Astronomy at Columbia University. Also see The office of Janna Levin at http://www.jannalevin.com.

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