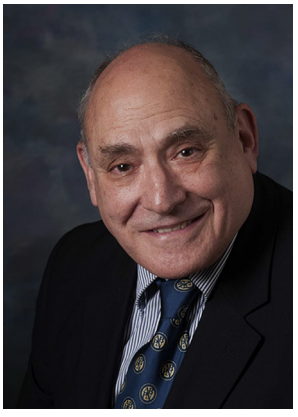
Editor-in-Chief's Note

Some Thoughts About Artificial Intelligence



Richard I. Shader, MD

I majored in physical sciences as an undergraduate. In 1953, my summer job was to plot the trajectories of surface-to-surface missiles fired from Cape Canaveral's Patrick Air Force Base in Florida. I assessed the altitudes and angles of flight of missiles by using multiple photographs taken along their flight paths from launch to landing in the Atlantic Ocean somewhere east of Nassau and the Bahamas. We used the word *azimuth*[1] to describe what I was calculating, a term I have never used or heard since then. Hours were spent punching data onto cards that were fed into an early digital electronic computer called FLAC (Florida Automatic Computer).[2] FLAC was gigantic; it used vacuum tubes, weighed approximately a half ton, and was built at the cost of about one-half billion US dollars. I was employed by RCA (Radio Corporation of America), a contractor to the US Air Force's Long Range Proving Ground Division. A decade later, while I was at the National Institutes of Health in Bethesda, Maryland, we were taught and used Fortran (derived from FORmula TRANslation),[3] a general-purpose, compiled imperative programming language. About two decades later, I purchased my first personal computer—a Compaq Portable. Each subsequent laptop has become faster, smaller, and lighter, and none requires any of my earlier, tediously learned skills.

It was around this time that I had the good fortune to meet the late Joseph Weizenbaum, who at that time was a professor at MIT (Massachusetts Institute of Technology). We often discussed his natural language processing program ELIZA.[4] At that time, some felt ELIZA was a suitable substitute for a Rogerian, person-centered psychotherapist.[5] ELIZA was an early practical demonstration of what is now called artificial intelligence (AI). As the years passed, Weizenbaum became disenchanted with computers and AI, feeling that they had a dehumanizing downside. I wrote down a few statements he said about this which I thought were quite profound: "No other organism, and certainly no computer, can be made to confront genuine human problems in human terms"; "Our indiscriminate adoption of computers is like taking in a slow-acting poison"; and "Human thought is not reducible to logical formalism." I saw Joe only twice after he moved to Germany; he died there in 2008 at the age of 85 years. Germany was also his birth country. Over the course of about 50 years, he moved from being an iconic hero of AI to being one of its most vocal skeptics.

After writing my Editor-in-Chief's Note about IBM Watson and big data,[6] I was given the opportunity to pose three questions to Watson. One question involved the fitting of unknown molecules into a known pharmacophore. A second question involved predicting drug interactions from molecular structures. The third involved genetic factors and clozapine-associated hematologic changes, including agranulocytosis. I was told that my questions could not be answered because insufficient data resided within Watson's existing database. In my opinion, much of what we would like to think that AI can do for us is still a dream. Questions can only be answered once sufficient amounts of relevant data have already been inputted. Only then can we benefit from AI's power, speed, and learning and synthesizing capabilities.

I recently heard about a computerized reading of a lung scan in which a ground-glass lesion[7] was identified and surgery was recommended as part of the program's algorithm. The patient was known to have been exposed to many years of second-hand smoking. The responsible radiologist concurred with the computer's interpretation and recommendation. However, the patient's cardiologist advised that surgery was too risky and the patient declined surgery. Over the next 5 years, the lesion did not change in shape or size. When the patient died of unrelated causes

after one additional year, his autopsy revealed a benign lesion. The computer was no smarter than the trained clinician, and, in this case, both were wrong.

My feeling is that we are not yet close to the time when computers can solve complex or confusing clinical problems. Computers cannot read human emotions nor can they reliably pick up revealing gestures or behaviors or nuanced responses. I also have some discomfort about having so much personal information available in electronic formats. I have heard some experts say that up to a 5% error rate is not uncommon when inputting large data sets. I found one reference consistent with this claim: "The error rate for more complex logic errors is about 5%...."[8] Touch typists who average 58 words per minute have an error rate of about 4%,[9] and materials from typists and clerks contain nonsense words at a rate of about 7%.[10] However, most sources indicate that the "…average benchmark for data entry error rate is generally acknowledged to be 1%."[11] In my opinion, any amount of error at the individual patient level is a bit scary, although when data sets are large enough, even error rates of 5% should be mitigated by randomization.

What about electronic data security? I was very amused to read that President Donald Trump's GHIN (Golf Handicap and Information Network) golfing handicap scores were falsely posted because the database holding them had been hacked.[12] That is the funny news. The bad news is that hacking into electronic health information databases is quite common.[13,14] A white paper produced by Verizon suggests that ransomware and laptop thefts from providers' cars are common ways data are stolen.[14] One concerning finding was that over half of these breaches were inside jobs; employees are most often the bad actors. Breaches can be used for profit; they can also result in data loss.

I recently saw a specialist at a major medical center. While we were discussing my status, he was busy typing his observations and the results of his physical examination into my electronic health record (EHR). I asked that his findings be transmitted to my primary care physician who is based at another hospital. This proved to be impossible, because the two EHR systems cannot "talk" to each other. I am also aware that EHRs developed for certain subgroups may not be able to communicate even within the same hospital (eg, ophthalmology with cardiology, pediatrics with adult medicine, podiatry with adult medicine). Some would say it would be anti-American to require a single system to be used by all health care providers. Such difficulties limit the use of clinical information for big data analyses.

Although AI has been around for over 50 years, much progress is still needed for it to be effectively used in drugs and biologics development. Our Update topic this month is titled Artificial Intelligence and Patient-centric Approaches to Advance Pharmaceutical Innovation.[15–18] It was assembled by our Topic Editor for Drugs and Biologics Development, Dr. Kenneth I. Kaitin.

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This month's Drugs and Biologics Update is a special feature which is available as FREE ACCESS content on the journal's website. One of the previous Drugs and Biologics Updates, entitled "Regenerative Medicine at the Forefront of Innovation: Update from Japan" was published in Volume 40, No. 11 of Clinical Therapeutics. To view the previous Update, see the articles below:

Milne C-P, Kaitin KI. Regenerative Medicine at the Forefront of Innovation: Update From Japan

Sawada M, Sugiyama D, Nii T, et al. A Japanese Bioventure Company's Application of Stem Cell Technology in Regenerative Medicine

Tsuruya N, Kawashima T, Shiozuka M, et al. Academia–industry Cooperation in the Medical Field: Matching Opportunities in Japan

Shigeto J, Ichiki T, Nii T, et al. Preclinical Toxicity Studies for Regenerative Medicine in Japan

Asano S, Nakanishi Y, Sugiyama D. Intellectual Property in the Field of Regenerative Medicine in Japan