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Can we engineer our way to good health?

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Abstract

Engineering technologies contribute to our health. Purification of drinking water has been of great benefit to public health. Large-scale production of penicillin is another engineering triumph that improved our health.

Medical imaging technology has come a long way since the X-ray. Ultrasound and MRIs are now commonplace. Can imaging technologies be used in new ways in our search for better health? Computer simulations promise greater understanding of physiologic processes in disease and health. Simulations require quantitative mathematical models of physiology.

Digital wireless communications can be used to build a national medical database. The benefits of such a database are great. What challenges must be overcome to make this a reality? The current identity-theft problem indicates that security and privacy are significant hurdles.

Chemistry is now being miniaturized, much like electronics were 50 years ago. EMTs could use "lab-on-a-chip" devices to get an "instantaneous diagnosis" from a drop of blood. Understanding of fluid behavior and chemical reaction on the micro-scale is required to develop a working "lab-on-a-chip."

The April 1999 issue of Scientific American *gave a glimpse of how "tissue engineering" might help health care. "Apligraf," a tissue engineered skin product, is a shining success. Other efforts have been less successful. After more than 30 years, the search for a small-bore vascular prosthesis continues.*

Unfortunately, the more technology we introduce into health care, the more expensive it becomes. Can we make these technologies affordable?

Engineering has a long history of improving public health. One hundred years ago, chlorination of drinking water started in the United States at Jersey City, N.J. In the beginning of the past century, local transportation was still by horses, even in the cities. As a result, animal waste was a major disposal problem and water-borne diseases such as cholera, typhoid, dysentery, and hepatitis A were killing about 25 out of 100,000 people in the U.S. at the time. Today, these diseases are virtually eliminated in America, and this is largely due to the purification and distribution of clean drinking water. The use of filtration and chlorine to halt the spread of water-borne diseases is often considered the most significant public health advance in history. Chlorination works because chlorine is a strong oxidizing agent, which "breaks" down the cell walls of the bacteria in the water. Chlorine activity continues while the water is in storage tanks and pipes so that the bacteria cannot repopulate. Clean drinking water continues to be a great need in many parts of the developing world and the design and construction of purification and distribution systems presents a major undertaking. Even in "developed" countries, continued vigilance on water purification is required. There was a five-year epidemic of cholera in Latin America starting in 1991 largely because of reduced disinfection of drinking water. This relaxed attitude toward drinking water chlorination was partly due to U.S. reports about disinfection by-products in treated water. Research in water purification today includes the use of ozone and ultraviolet radiation.[1]

Alexander Fleming discovered the antibiotic properties of *penicillium notatum* by accident in 1928. A stray spore of *penicillium n.* accidentally landed in a Petri dish that was prepared for a culture of *Staphylococcus*. After incubation, he noticed the presence of mold colonies surrounded by a zone of growth inhibited staph. To further explore the properties of this mold, he grew *penicillium n* in a surface culture on a liquid medium. After a week, the liquid under the growing mold colony, which Fleming called penicillin, was harvested. The introduction of penicillin as a therapeutic drug for medical care on a large scale did not occur until the middle 1940s. Fleming's penicillin was extremely dilute, impure, and chemically unstable. In response to fire bombings in England during World War II, a group of Oxford University researchers improved the surface-culture method to make enough penicillin for clinical trials. The dramatic effects of penicillin on wound healing convinced the Allies that the large-scale production of penicillin would save the lives of thousands of servicemen. Chemical engineers, microbiologists, chemists, and biologists from universities, government, and industry set out to mass produce penicillin. They searched for new strains of the mold and created mutant strains with ultraviolet light. They discovered better culture media. They invented a new purification processes. Even freeze drying was explored as a means to stabilize the antibiotic. Perhaps the most important development was the shift from surface culture of the mold to submerged fermentation in huge tanks. Problems in heat and mass transfer and careful control of the environment inside the tanks needed to be solved. By 1944, 100,000 unit vials of penicillin were coming off the end of the line at the Pfizer plant faster than they could be counted. The American Institute of Chemical Engineers considered the large-scale production of penicillin to be one of the greatest chemical engineering achievements of the century. The development and production of therapeutic chemicals is important in chemical engineering today as bioengineering represents a growth area.[2]

Imaging technology has come a long way from the X-ray. The ability to "see" what is happening inside the body can guide the diagnosis and effect the treatment of illness. Signal processing and the graphical representation of information in a visual format have led to novel ways of producing medically useful images. Computed tomography (CT scans) take a series of X-ray images and computationally reconstructs a 3D image. When my first child was born three decades ago, ultrasound imaging was fairly new. Now it is quite common. In my own family, ultrasound imaging has been used for prenatal care in pregnancy, amniocentesis, and echocardiograms. Magnetic resonance imaging provides greater contrast between "soft" tissues than X-rays and has found widespread use in medicine exploring brain, heart muscle, and cancer tissues. Infrared signals might be useful to detect breast cancer at a very early stage based on differences in the amount heat generated in cancer cells as opposed to normal tissue.[3] Image signal processing and "machine vision" might be useful for examining light microscope slides for detecting differences between normal and diseased cells. Can image processing and computer simulations be used to create "medical simulators" like those used in the training of airplane pilots?

Computer simulations require quantitative mathematical models of physiological processes. My own experimental research has focused on peculiarities of blood flow in small vessels that are incorporated into computer simulations of blood flow in microvascular networks. These types of simulations are used to answer questions about hypertension, vessel remodeling, and drug delivery among others. The use of mathematics to describe physiological phenomena has the potential to quickly advance our understanding of both normal and pathological physiology.[4]

When faced with an unusual or interesting clinical case, sharing information with other physicians can be invaluable to a doctor. In teaching hospitals, Grand Rounds is a formal meeting where doctors discuss current or interesting cases. Patients then receive input from several experienced medical personnel. This also increases the experience base of the doctors. Modern communications technology makes the sharing of information between doctors much easier. Today heart patients with an implanted cardio defibrillator can transmit information from the implant over the telephone to their doctor. This is a step in providing real-time medical monitoring of the patient to the health professional.[5] Suppose EMTs could have access to information about prescription, allergies, etc. for victims when responding to emergencies. This could be done with a national medical database. What are the challenges of such an enterprise? Who is responsible for input of data? Who can have access to it? Who maintains the database once it is functioning? Can we protect patients' privacy? Technologically, it appears feasible, but several social questions need answers.

Imagine instantaneous diagnosis from a drop of blood when the EMT arrives in response to a 911 call. This is known as point-of-care testing and is one of the dreams driving the development of a "lab-on-a-chip." This is a Micro Mechanical Electric Systems, MEMS, device into which a drop of blood flows through a series of small channels, tens of microns in diameter, and chemical reactions are monitored to diagnose the condition of the patient. Such a device requires the understanding of micro-nano– manufacturing, fluid flow in very small channels (microfluidics), and chemical reaction at the micro scale. Although applications are limited today, great potential exists for the contribution of MEMS to health care delivery.[6]

Tissue engineering concerns the use of living cells to improve health. Can we engineer replacement tissues for humans? The possibility is suggested by the discovery of stem cells and growth factors and the idea of cell differentiation. One of the first growth factors, BMP (bone morphogenetic protein), spontaneously induced the growth of new bony tissue when placed in animals. Not surprisingly, bone and cartilage are two of the first applications of tissue engineering with therapeutic value. The most successful tissue engineered product is human skin equivalent by Organogenesis. This is a product made from two layers of cells in collagen. This product promotes healing for persistent wounds and promoted the migration of host skin cells into the wound to replace the transplanted cells. Other attempts at tissue engineering have not been as successful. After more than thirty years of effort, the search continues for a small bore artificial blood vessel, as well as for cellular-based therapies for liver, pancreas, and heart disease.[8]

The technical possibilities of engineering our way to good health are fascinating. There are many problems to overcome and the journey should be exciting. A final question, however, does need to be considered. Can engineering technology make health care more affordable? In many endeavors, the introduction of more and more technology has made things more affordable. The tremendous research efforts in agriculture have resulted in very affordable food crops in the U.S. Communications, transportation, and housing are more affordable because of the use of technology. Is the same true for health care? The inclusion of innovative technologies into health care delivery has been cited as a major driver of the increase in the cost of health care. Certainly, health care costs have risen with the inclusion of more innovation, but availability of services has also grown.[9] Finally, can we engineer our way to good health in a manner that we can afford?

Notes:

1. The faculty involved with the Water Treatment Technology Center are very active in projects to maintain our access to healthy drinking water. Professors Ballestero, Collins, Jacobs, Kinner, and Malley of the Civil Engineering Department are very active in this research. One of the Environmental Engineering courses (ENE 740) is entitled Public Health Engineering.

2. For a fascinating history of the development of penicillin in the 1940s see *Chemical Engineering Progress Symposium Series* Vol 66 No. 100 (Eng TP 1.A62 No.100). PT Vasudevan, chair of the Chemical Engineering Department, teaches a Biochemical Engineering course at UNH (ChE 761) and many of our graduates work in the biopharmaceutical industry. Professor Vasudevan does important research in the area of enzyme kinetics and has developed a rapid assay for total blood cholesterol measurement.

3. Processing and interpretation of signals interacting with biological systems is taught in Biomedical Instrumentation ECE 784. CT scanners were invented at EMI (Electric and Music Industries Ltd) in England. It is often said that the funding for this project came from the success of their music recording business (Beatles, Beach Boys, etc.). Richard Messner of the Electrical and Computer Engineering Department is an expert on video image signal process and pattern recognition and has made attempts to automate the visual screening of malignant cells from Alzheimer's patients. F. William Hersman, Physics Department, polarizes Xenon to enhance MRI images of the lung.

4. See, for example, *Annals of Biomedical Engineering vol. 33* pp 764-771, 2005. Greg Chini, Mechanical Engineering Department, has done recent work on particle deposition and impingement on thin liquid films in the lung.

5. Real-time monitoring of health parameters (vital signs) provides a measure of both wellness (normal state) and the onset of illness. The following video segment on the Internet may be interesting. http://spie.org/documents/newsroom/videos/HaroldSzu.mov

6. Nivedita Gupta, Chemical Engineering Department, has started a new course on Microfluidics ChE 722. The Material Science Program and the Chemistry Department participate in the Center for High-rate Nano-manufacturing, which is involved with MEMS devices.

7. *Scientific American* April 1999 issue starting on page 59. An interesting note: Gary Bowlin, graduate of the Chemical Engineering Department, is very active in tissue engineering research at the Biomedical Engineering Department of Virginia Commonwealth University. http://www.egr.vcu.edu/FacultyDetail.aspx?facid=5

8. An interesting view of the price of penicillin is included in the Chemical Engineering Progress Symposium Series vol. 66 No. 100 pp 20-21 mentioned earlier. Also see *Annals of Internal Medicine 142*:932-937, 2005 "High and Rising Health Care Costs. Part 2: Technological Innovation" for a recent analysis of technology-related health care costs.