HEALTH AND STRESS

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WHAT WILL MEDICINE BE LIKE IN TWENTY YEARS?

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Predicting progress in medicine is risky. It seems that several times a week we hear of some startling breakthrough with the potential to cure everything from cancer and AIDS to the common cold and getting bald. Many of these reports are based on laboratory studies that have had a spin put on them by writers who want to make their stories "sexy". In other instances, the extravagant extrapolation of results in animals to the treatment of human diseases is engineered by manufacturers who manipulate material fed to the media to raise funding and/or the price of their stock.

Experience shows that few of these promises are fulfilled and long term predictions are particularly hazardous. **Who could have forecast in 1900 or 1950 what medicine would be like fifty years later?** Most of these attempts have been miserable failures.

Despite this, the public's appetite for such prognostications seems to be insatiable. It's also very tempting for physicians and medical writers to dabble in this. Everyone has their own personal preferences and suspicions, although these are more often based on hope and media hype rather than any first hand experience with a drug, device or procedure.

I have no crystal ball or qualifications to suggest I might fare better than anyone else in predicting what the future will hold. However, decades of following medical news releases have helped me to distinguish between those that are apt to be deceptive and others with more promising potential. Although medicine has been changing at a more rapid rate than ever before, it may be possible to identify advances and trends in certain areas that are likely to persist.

I think it is safe to say that **existing technologies will become less expensive and therefore more widespread**, such as cochlear implants that bypass defective ear structures and send messages directly to the brain to correct this cause of deafness. Senior citizens, particularly those over 80, are the fastest growing segment of the population, and also consume a greater percentage of health care costs. As indicated by what follows, a major goal for 21st

Century medicine will be adding life to their years, rather than simply years to their lives.

Sensational Sensors & Reliable Robotics

Sensors are one example of how technological industrial advances will find medical applications. Japanese engineers have already designed a toilet that weighs whoever sits on it, tests the urine for bacteria and sugar levels and transmits the results directly to the doctor. Diabetics can also look forward to an under the skin sensor that regularly monitors blood sugar levels or a wristwatch device that does this by producing tiny electric shocks to open pores enough to extract fluid, replacing the frequent finger-prick blood tests currently required. Implanted insulin reservoirs responding to this information will automatically release the right amount of insulin when necessary, eliminating or reducing the need for daily injections.

Gut sensors will allow sufferers from irritable bowel syndrome to detect imminent diarrhea and prevent it by pressing a drug-filled pouch under the skin. Many procedures performed in laboratories will be done automatically by sensors either implanted in or worn by patients. Operating room tables and hospital beds will be replaced by multipurpose units equipped with sensors that can provide suction and ventilation during surgery, monitor vital signs and control post operative delivery of intravenous fluids and pain medications.

This should lessen the need to put patients in recovery rooms and intensive care units and reduce the associated risk of spreading infections. In addition, ceiling vents installed in hospital lobbies will monitor the air to detect and report any visitors who might also spread airborne infections to patients. Spectacular sensors strategically placed in electric-powered wheelchairs will let users balance on two wheels, drive through sand and gravel, climb curbs and even steep stairs.

Robotic surgery will allow operating with greater precision through smaller incisions, even by a surgeon thousands of miles away. The most effective way to learn any new procedure is directly from someone skilled in the technique. That's not always practical due to travel expenses and scheduling problems. Teleconferencing is another option but current systems often fail to transmit a clear or steady non-pixelated image for remote viewers. A new computer motion system called SOCRATES seems to have solved these problems.

The computer motion system was pioneered at Johns Hopkins around five years ago with the AESOP program that demonstrated the feasibility of telerobotic surgery in multicenter and transcontinental clinical trials. Canadian surgeons recently reported performing a series of telecollaborative surgeries including an appendectomy, lung biopsy, lung resection, mitral valve repair and two coronary artery bypass procedures. In all instances, the mentor actively participated in a "hands-on" manner from a remote location. This promises to facilitate the expansion of new minimally invasive operations to sites around the world where they are not available because of lack of trained personnel or financial constraints.

The FDA has cleared a surgical robot that uses the HERMES control center to voice control a network of "smart" medical devices. While not yet available here, the ZEUS system is approved in Europe, where it is used for new minimally invasive endoscopic and microsurgical procedures. These include the ability to perform coronary bypass on a beating heart, thus minimizing the mental complications that can result from conventional cardiac surgery.

Vaccines For Cancer And Heart Disease

Because some fatal skin cancers disappear spontaneously, researchers have suspected that the immune system might hold a key to a cure. Recent trials of vaccines designed to stimulate the body's immune response to malignant melanoma have been particularly encouraging and suggest that it may significantly reduce the more than nine thousand annual deaths in the U.S. from this deadly disease.

A vaccine to prevent cervical cancer is now in the works. About nine of ten women with cervical cancer also show evidence of infection with the human papilloma virus (HPV), which is thought to be responsible for this common malignancy. This link is so strong that women with pap smears showing

atypical cells that could be cancer precursors but whose blood tests show no evidence of HPV infection, can be reassured with 95 percent certainty that they do not have cervical cancer. Researchers hope to begin testing a vaccine against HPV to be administered to 5 - 7 year-old girls that will prevent the subsequent development of cervical cancer.

Heart attacks and strokes are due to deposits of atherosclerotic plaque that interferes with and eventually blocks blood flow. There is increasing evidence that in many cases, these inflammatory lesions result from the body's response to chronic low grade infections due to common organisms like chlamydia that cause few if any symptoms. Heart attack and stroke victims show significantly higher antibody titers to chlamydia compared to hospital patients admitted for other conditions. Atherosclerosis also progresses more rapidly in patients with high antibodies and the organism has been cultured from atherosclerotic lesions obtained at surgery or autopsy. Some preliminary studies suggest that antibiotic prophylaxis may reduce the incidence of future heart attacks and stroke. However, **a vaccine to prevent chlamydia and other infections that contribute to plaque formation would seem to be a more effective and less costly prophylactic approach**. Such a vaccine has proven effective in animals and will soon undergo clinical trials using a single oral dose.

Cystic Fibrosis, Diabetes And AIDS

The ability to manipulate genes appears to offer great potential for constructing and administering vaccines by novel methods. Researchers recently combined parts of the deadly Ebola and AIDS viruses to produce a hybrid bug they hope can cure cystic fibrosis when sprayed into the lungs. The new virus is designed to take advantage of Ebola's unusual ability to bind to lung cells and the AIDS virus's talent for persisting in the body. Copies of the gene that is deficient in cystic fibrosis patients will also be introduced to complete the concoction. The scientists are confident that their creation will be safe since it contains none of the key components that are required to cause these dreaded diseases.

Insulin dependent Type I diabetes is due to an immune system T cell response that destroys the insulin producing cells in the pancreas. Canadian researchers have identified a gene that causes these cells to manufacture a protein that T cells attack as if it were a foreign substance and destroys these cells as well. In mice bred to develop Type I diabetes, they were able to inactivate the gene so that the animals remained free of the disease. They expect to **develop a vaccine that will make the immune system ignore the gene and prevent diabetes in young children at risk or who have recently developed the disorder**. The DiavaX synthetic peptide vaccine produces antibodies that suppress these destructive T cell responses, and is being tested in Sweden.

Several AIDS vaccines are also in the pipeline. One uses the hybrid approach described above for cystic fibrosis. Another is based on the finding that AIDS is a major cause of death in the slums of Nairobi. Prostitution is the only way many Kenyan women can support their children and almost all are infected and eventually succumb to AIDS. However, several dozen who have been followed for over a decade seem to be immune. Most are related and all have large numbers of cytotoxic T cells that quickly detect the virus and kill it. Scientists have made a vaccine, which includes their DNA fragments, they believe will stimulate the development of AIDS protection for others.

Stem Cells For Strokes And Parkinson's

Many authorities believe that stem cells will be used routinely within the next decade to replace tissues that are diseased or damaged. These are very primitive cells that can be nudged or manipulated to develop into almost any kind of tissue, including parts of the brain injured by strokes, Alzheimer's and Parkinson's disease. The major source of stem cells is from aborted fetuses or embryos discarded by fertility clinics but this has become a controversial and contentious issue. It is vigorously opposed by anti-abortion groups and some members of Congress because the practice requires the death of a fetus.

Federally funded scientists are presently banned from research that involves the use of an embryo or fetus. New NIH guidelines do permit federal funding but only if the cells are extracted from embryos in labs not receiving government grants. Some researchers have sought NIH support under this provision but no grants have been issued.

Harvard Medical School as well as NIH researchers report they have been able to "cure" Parkinson's disease in mice and rats using stem cells from animal embryos. In both instances, fetal cells were carefully processed and then grafted into animal brains to replace cells damaged by Parkinson's disease. Both groups of researchers are anxious to begin human trials using stem cells but are unable to do so because of regulations and political pressures. The new secretary of Health and Human Services said he is now reviewing current policies dealing with this issue. In the interim, clinical trials may be undertaken in Britain, France, or the Netherlands, since these countries are adopting policies to encourage human embryonic cell research.

More than a million Americans suffer from Parkinson's, which is due to the death of brain cells that produce dopamine. It can be treated with L-dopa, a drug that increases brain dopamine, but improvement is only temporary. Limited experiments using brain cells from aborted fetuses have allegedly stabilized some patients for up to 12 years, presumably because the transplanted cells start to produce dopamine.

These claims have been questioned because of the lack of any control group for comparison. In an effort to evaluate the risk/ benefit ratio of this approach, a double blind, placebo controlled study was performed in 40 patients. Half received the transplanted fetal brain cells and half underwent a placebo surgical procedure during which nothing was injected. The results, which were reported in the New England Journal of Medicine in March, showed that 85 percent of patients who received the implants showed growth of the new brain cells, and although most showed improvement in their symptoms after a year, some had long-term complications. About 15 percent later experienced excessive, abnormal movements suggesting that the transplants were producing more dopamine than optimal for those individuals and this disturbing complication far outweighed the initial benefits.

A recent report suggests that cells from umbilical cord blood may work just as well with respect to speeding recovery from strokes in animal experiments. Researchers obtained stem cells from umbilical cord blood and treated them with retinoic acid and growth hormone to transform them into primitive nerve cells. In a study of 60 rats suffering from the same type of experimental stroke, half received an intravenous injection of 3 million of these nerve cell precursors. One month later, almost 80 percent of this group had recovered from their stroke compared to only 20 percent of untreated littermates.

Around four million babies are born in the United States each year and their umbilical cords are discarded. One or two cords could probably provide enough stem cells to treat one human stroke victim and these cells could also be frozen for future use without diminishing their effectiveness. Plans are underway to conduct clinical trials in the next year or two in human stroke patients after safety standards are satisfied and a proper protocol has been established. Umbilical cords might well be an excellent source of stem cells for other neurological disorders such as Parkinson's and Alzheimer's that would avoid the ethical concerns associated with the use of fetal tissues.

Farming Fat Cells To Build Bone

Cartilage is classified as a type of connective tissue that serves to provide a protective inner lining for joints. Unlike most kinds of connective tissue, cartilage has a very poor blood supply and is composed of cells that have limited metabolic activities. As a result, cartilage heals slowly following injury and rarely regenerates completely, especially as we grow older. Researchers have tried to get around this by transplanting bone marrow

stem cells at sites of damage where they are eventually transformed into cartilage cells. Tiny holes are also drilled into adjacent bony structures to improve local blood flow in an effort to speed up the healing process. However, this can be a painful procedure and the availability of satisfactory replacement tissue is limited.

Scientists have now found a way to use fat, which is plentiful, to serve as a substitute for bone marrow. Fat removed during liposuction was dissected to separate out the stromal supportive connective tissue that covers and lies between fat layers. This tissue is composed of precursor cells that under normal circumstances become fat cells, but can be manipulated to turn into other types of tissue.

In one report, these primitive cells were coaxed into becoming chondrocytes or cartilage cells by exposing them to a biochemical cocktail of steroids and growth factors. **Two ounces of fatty connective tissue treated in this fashion were able to produce 1 billion cells that behaved just like normal chondrocytes.** Using computer and genetic modeling, the cells were grown in a three dimensional matrix that produced a coin-sized product in two weeks. It is hoped that implanting this into a damaged joint would serve as a sort of surgical paste to promote healing. While human trials may not take place for a year or two, one of the most promising applications would appear to be in young trauma victims.

As will be seen, Pulsed Signal Therapy has already been shown to stimulate chondrocyte production, relieve pain and restore mobility following joint damage. It achieves its reparative rewards by reduplicating the natural electrical signal responsible for bone growth.

Turning Skin Cells Into Heart Tissue

Heart and brain cells do not divide and therefore cannot repair themselves following injury. Other cells accomplish this by entering into a cycle in which their DNA is duplicated and a new cell is born. Skin and blood cells go through such cycles regularly and some muscle cells can be stimulated to shift from normal function into cell replication if needed to repair damage. Myocardial cells remain in an adult state permanently to perform their functions. Attempts to stimulate them into entering a reparative cell cycle like other muscle cells have not been successful.

Last October, the company responsible for cloning the sheep called Dolly was awarded a $1.9 million grant from the Department of Agriculture to determine whether certain livestock cells could be coaxed into a more primitive stem cell state that could subsequently be trained to develop into other cell types. The company recently announced that it had been successful in using skin cells (fibroblasts) as the source for basic bovine stem cells that were then transformed into myocytes, or heart muscle cells. It is believed that this same approach could be used to train these cells to develop into nerve and brain tissue as well as blood, rather than using embryos as a source.

One potential drawback is that stem cells from adults do not appear to have the flexibility of those derived from fetal tissues and their end products may not last as long. **Dolly could be susceptible to premature aging disorders because her genes were copied from a 6-year old sheep.** All chromosomes are capped with tips known as telomeres that prevent a cell's genetic code from fraying. When the telomere finally wears down after repeated cell division, it signals the cell to self-destruct as part of the aging process. Although Dolly acts like a healthy four year-old and has given birth to several normal lambs, researchers report that her telomeres are shorter than normal. Only time will tell whether this approach is a viable alternative to fetal stem cells and whether there may be other unknown long term hazards. Until this is clarified, it is doubtful that attempts will be made to conduct clinical trials.

The Potential For Genetic Profiling

The completion of the human genome project promises to offer the following by 2020:

- **More Effective And Safer Pharmaceuticals**

It is estimated that by 2020 at least 3000 new drugs will have been identified

and tested. All will be manufactured by recombinant DNA technology so that they will be pure and safe, just as human insulin and growth hormone have become. Medical records will include your complete genome information, making it possible to accurately predict your responses to certain drugs and environmental influences. This will also permit predicting susceptibility to specific diseases so that you can make lifestyle changes or be treated with appropriate drugs to delay the onset of disease.

A significant number of patients fail to respond to drugs used to treat depression, hypertension, or certain infections and it is impossible to identify these individuals in advance. **Twenty years from now, medications will be more effective because doctors will be able to match a patient's genetic profile against a panel of drugs available for a specific condition and select the treatment with the greatest potential benefit.** Over 100,000 people die each year from adverse reactions to medications and millions suffer from dangerous or disabling side effects, such as heart valve damage from diet drugs and neurologic disturbances with antidepressants. As genetic traits and specific DNA sequences that influence drug responses are increasingly identified and categorized, severe toxic reactions and most side effects should drop dramatically.

- **Societal Implications**

Society will have to deal with disturbing confidentiality consequences if your medical records are made available to life and health insurance companies. There might be higher premiums or enrollment fees. Your genetic profile might be requested by an employer interested in learning about your risk of developing certain conditions to avoid hiring you or to restrict the kind of work you could do. A request for DNA testing to detect a tendency for carpal tunnel syndrome was recently rejected and is being appealed.

- **Gene Therapies**

In 1990, an 11 year-old girl with severe immune system deficiency underwent the first successful gene therapy treatment. Since then, gene therapy has been used to treat patients with cancer and hemophilia and has been able to grow new blood vessels in heart patients. Gene therapy for single-gene diseases will probably be routinely available in 20 years. Over 200 diseases could be cured by replacing the aberrant genes that cause them with normally functioning versions, and neonatal genetic testing for these conditions will be standard procedure. We should also know the timing of expression of different genes and how to direct their differentiation, so that a desired cell type, simple structure, or even parts of more complex organs can be grown for transplantation.

- **Understanding Life And Evolution**

An inevitable consequence of the genome project will be a much greater understanding of basic biology. Darwin's theory is supported by the observation that the biologic differences between man and lower forms of life are not nearly as great as we thought. Some three dozen organisms have already been completely sequenced, including the fruit fly, which is being used to model the essential features of human disorders such as Parkinson's disease. This genetic approach may provide powerful insights into the development of Alzheimer's and other degenerative disorders and lead to developing more effective treatments.

- **A Two-Edged Sword?**

Using DNA sequencing will become less expensive and will be used routinely and reliably in criminal cases, paternity problems and to identify missing persons. We have already seen numerous examples of how DNA tests have freed prisoners jailed for years for crimes they did not commit. However, attempts to ascribe behavioral tendencies to a person's genes could cause problems, especially when someone's behavior and actions conflict with laws. Should courts interpret behavior as a consequence of free will or as influenced by genetic constitution? **"Not guilty because of genetic abnormality?"** At what point does society mitigate responsibility or punishment?

The Genie Is Now Out Of The Bottle

To parody the 50 year-old popular song from *The Fantasticks*, "Quick Send In The Clones - Don't Bother They're Here." Dolly jump-started a flood of interest in

cloning that has turned into a tidal wave. Since then, pigs, goats and rodents have been cloned and companies have made a business of cloning cows for farmers who want to copy the genes of their most productive animals to boost milk and meat output. Several hundred cloned cows have already been produced in the US alone and cows have been used to give birth to a bison and a guar, a species close to extinction. The huia bird, moa, and the woolly mammoth, which has not been around for over 10,000 years, may all roam the earth again.

A monkey has been cloned using a different embryo splitting method and several groups have announced plans to clone humans. One group already has over 700 applicants and "unlimited funds" but it is not clear where they will operate. Human cloning was initiated but stopped a few years ago in New Zealand, where it is now banned, along with two dozen other countries. Some form of human cloning to provide stem cells for repairing damaged tissue will be allowed in countries like Britain and Denmark and if the results are good, other restrictions may be lifted. We could devote an entire Newsletter to discussing the debate dealing with moral, religious, and scientific aspects of human cloning and may provide an update on this in a subsequent issue in view of recent developments.

We are much more likely to see perpetual pets in the near future. When Richard Denniston announced plans to clone a cat this year, one woman dug up her beloved pet that had been buried for three days after a car ran over her. She rushed the body to her vet who removed some skin and sent the tissue to Denniston who induced the cells to multiply. Millions of them now live on, frozen in liquid nitrogen, awaiting resurrection. Several companies are preserving pet cells for cloning with preparation costs ranging from $600 to $1,400 and $10 a month for storage. A satisfactory clone will probably cost $20,000 and they are flooded with clients. **One person paid $1500 to preserve cells from her three dogs so they could all be together again.**

Pacemakers For The Brain And Heart

Researchers are now exploring the use of implanted brain pacemakers for epilepsy and mental illnesses such as obsessive-compulsive disorder as well as depression and addiction. The actual device is implanted in the patient's chest and a wire is threaded through a small hole in the skull to targeted sites in the brain. A small electrical impulse is delivered either in occasional bursts or as a steady current depending on the disorder and delivery destination. In the planning stage are **devices that will detect different types of aberrant electrical brain activity and respond in an appropriate fashion to restore normalcy**. One of the most promising applications appears to be an implanted device that monitors brain waves and can not only predict an impending epileptic seizure because of distinctive abnormal activity patterns but also intervene to prevent it. Despite medications, some patients with severe epilepsy can suffer from seizures on almost an hourly basis around the clock. Preliminary studies show a 75 percent reduction in such seizures using a prototype of this feedback device.

In addition to the tremors of Parkinson's, the FDA is expected to approve pacemakers to control other symptoms such as rigidity, gait and balance disturbances, falling spells, and uncontrollable twisting motions. A small system placed under the skin is already in use for the treatment of severe pain. It sends mild electrical impulses through a strategically placed wire to the spinal cord that blocks pain signals from reaching the brain. Researchers are also trying to determine if deep electrical brain stimulation could revive patients who are in a vegetative state following a stroke or severe brain trauma.

Many of the above devices have been designed by Medtronic, the company that pioneered the first practical implantable cardiac pacemaker to correct abnormally slow heart rates. They have now perfected pacemakers that can immediately detect and correct other potentially fatal disturbances in rate and rhythm and prevent heart failure.

Bioelectromagnetic Medicine In The Millennium

> In the decade to come, it is safe to predict, bioelectromagnetics will assume a therapeutic importance equal to, or greater than, that of pharmacology and surgery today. With proper interdisciplinary effort, significant inroads can be made in controlling the ravages of cancer, some forms of heart disease, arthritis, hormonal disorders, and neurological scourges such as Alzheimer's disease, spinal cord injury, and multiple sclerosis. This prediction is not pie-in-the-sky. Pilot studies and biological mechanisms already described in primordial terms, form a rational basis for such a statement.

Andy Basset wrote this in 1992, but unfortunately did not live long enough to see that much of his prediction had come true well ahead of schedule. Weak but precise electrical and electromagnetic signals that stimulate specific brain structures will likely significantly relieve a wide range of neurological and mental disorders and replace drugs within the next ten years. As previously noted, some implanted electrical devices are already being used to treat the tremors of Parkinson's disease and to provide relief for patients suffering from severe pain.

In general, **magnetotherapy devices are non-invasive and thus not associated with infections and other complications that can accompany surgical procedures**. Bone stimulation devices have been approved for decades to heal fractures that failed to unite normally and may have other applications. Certain types of cranioelectrical stimulation have long been used to augment the analgesic effect of TENS devices and some have been allowed to make claims for relieving depression, anxiety and insomnia. A fairly recent repetitive transcranial magnetic stimulation technique using a hand held device that is targeted to an area of the frontal lobe has been found to improve severe depression resistant to medication, and new non-convulsive electric shock approaches may replace conventional shock treatment. Neuroelectric therapy (NET) based on acupuncture principles has been found to be effective in reducing substance abuse and withdrawal symptoms in drug addicts. The Symtonic device has been shown in polysomnography trials to effectively and safely reduce insomnia without the side effects, tolerance and rebound associated with hypnotic medications. Other double blind studies have demonstrated that it is also effective in alleviating anxiety disorders. Treatment is administered by a weak signal in the CB radio range via an electrode to the hypothalamic region for 20 minutes three times a week.

As noted in previous Newsletters, a metabolic-magnetotherapy approach has resulted in remarkable reversal of terminal metastatic malignancies and end stage cardiomyopathy. Pulsed Signal Therapy (PST) has been proven to be effective for relieving pain and restoring mobility in severe osteoarthritis in double blind and other rigid studies in over 100,000 patients. Treatment consists of just nine daily one- hour sessions and long-term follow-up confirms sustained benefits and safety. **However, worthless copycat devices abound, so caveat emptor** - and stay tuned!

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