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The Future of Public Health

Special Centennial Edition



The Next 100 Years

The months leading up to the centennial of the Pan American Health Organization (PAHO) have offered an extraordinary opportunity for reflection, for examining the deep public service roots of what is today the oldest ongoing international public health agency in the world. We know well how, at the turn of the last century, the nations of the Americas faced plague, yellow fever, malaria and cholera. We are awed by and salute those who fought back and made a difference. In founding PAHO in 1902, these Pan American health pioneers saw, in the words of World Health Organization Director-General Gro Harlem Brundtland, “that no country—not even the strongest among them—will benefit from standing alone.”

Throughout the past century, public health workers across the continent joined forces in a grand venture to make the Americas a better place to live. They healed the sick and halted epidemics, traveling by horse, boat or foot, delivering vaccines, looking for signs of new diseases, cleaning up pestilent swamps, teaching the poor how to avoid disease and assessing health conditions. Their successes were legion even as their challenges mounted. They fought to reduce the pernicious inequalities that resulted in unacceptable numbers of children and mothers dying, and they lobbied to underscore the links between health and development.

The century of important achievements in health in the Americas is worthy of celebration, but we must continue to look ahead to the daunting challenges we still face. In this special issue of *Perspectives in Health*, the focus shifts to the future, honoring PAHO's centennial by looking at the future of public health. These glimpses of the future are imaginative and authoritative, written by distinguished authors who have agreed to share not only their knowledge but also their bold willingness to prophesy developments that might affect the future of public health.

The tone of this special centennial edition is set by PAHO Director George Alleyne, who assesses the prospects for another century of Pan American cooperation in health by first surveying the current state of public health in the Americas. Far from predicting Armageddon, Dr. Alleyne's analysis leads him to conclude that “the trends we have observed in the recent past can be used as portents of a much rosier health future” for the Region.

Sir Gustav Nossal, Australia's eminent vaccinologist, draws on the nearly two centuries of efforts to develop vaccines against all manner of disease, the most notable being smallpox globally and polio in the Americas. In forming predictions, Dr. Nossal points to promising new alliances, particularly the public-private philanthropic partnerships for vaccine research and development that have taken root in the last several years. He discusses the importance and likelihood of developing and delivering new vaccines, especially for HIV/AIDS, malaria and tuberculosis.

Following the ebola outbreaks in Africa several years back, the world seemed consumed by fears of hemorrhagic fevers and other emerging and reemerging diseases. Dr. C.J. Peters, the “virus hunter” who was called on to confirm those outbreaks, makes no effort to quiet our fears in predicting a future full of “microbial surprises.” His essay highlights the critical links between health and the environment and the pressing need to bolster public health infrastructure.

The burgeoning field of genomics, perhaps as no other, allows us to see today some of the marvelous possibilities of the future. Juan Enriquez and Rodrigo Martínez, of Harvard Business School's Life Sciences Project, point out that DNA-embedded silicon biochips can already screen for individual genetic defects, while in the near future the antigens in mosquito saliva could deliver vaccines instead of disease. Yet availing ourselves of the marvels of the so-called life sciences revolution, they warn, will require major investments in science, technology and research.

Dr. Ilona Kickbusch, a leader in the field of health promotion, notes that in the late 20th century, public health increasingly turned its focus toward prevention of disease and promotion of healthy lifestyles. Building on its successes, health promotion in the new century will incorporate community participation, individual and social empowerment, and the actions of diverse stakeholders in a reoriented health system. Dr. Kickbusch questions where our health choices might take us and just how far the search for better health should go. Asking, “How do we want to live?” she poses perhaps *the* question for the future, not just for public health, but for humanity.

The authors in this issue lay a solid foundation for further discussion by posing questions, positing predictions and offering suggestions about the paths we might take to the future. But in describing new visions, their words also recall those who came before us: the men and women who strove to make sure that children would not be scarred by smallpox, who set out to vaccinate whole countries on a single day. As we in international public health brave the future, we follow in the footsteps of those pioneers, heeding the words of Winston Churchill: “We shall not fail or falter; we shall not weaken or tire. Neither the sudden shock of battle nor the long-drawn trials of vigilance and exertion will wear us down. Give us the tools, and we will finish the job.”

Bryna Brennan
Executive Editor



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The Pan American Health Organization celebrates its 100th anniversary in 2002. This special centennial issue honors that anniversary by looking forward to PAHO's next 100 years and to future developments in immunization, emerging diseases, the life sciences, health promotion and international cooperation in public health.

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A New Guard

by Sir George Alleyne

A Second Century

As it celebrates its 100th anniversary, the Pan American Health Organization can take a lesson from the game of cricket. Now is the time to take stock of the surroundings, reassess one's strengths and focus even more closely on the work at hand.



Many images and ideas are associated with the concept of a century. The most widely known and accepted is that a century refers to a period of 100 years, and here at the Pan American Health Organization (PAHO) at this time, the association is with the 100 years of our existence. We celebrate the 100 years of health in the Americas, and we celebrate the progress the countries of the Americas have made with PAHO's support.



But to many of us who grew up in the English-speaking Caribbean, steeped almost from birth in the intricacies of the arcane but beautiful game of cricket, a century also refers to 100 runs and it is a goal to which every batsman in every class of cricket aspires. It means that he has withstood the onslaught and wiles of the bowlers from the opposing team and has registered 100 runs. It is a time for celebration with one's teammates, and in the gentlemanly spirit in which the game is played, it implies being congratulated by the opposing team as well.

But the really great batsmen—those who are revered in circles where the game is really understood, those whose names and feats are the lore of national pride—are never content with scoring a single century. The really great batsmen are not satisfied with the applause and the congratulations. They settle down, take a new guard and try to score another 100 runs. They go for another century. When they take a new guard, they assess the surroundings, look at their position at the wicket, assess their strengths anew and try to focus their

concentration even more closely on the business at hand.

So it is with PAHO. Having scored a century, we must accept with modesty the plaudits of all those who wish us well and now dedicate ourselves with the maximum concentration possible to the business of the next 100 years. It is reasonable to savor the moment, and it is appropriate for us to assess the strengths that allowed us to reach this stage and ponder whether the auguries are good for another 100 years. But we also must focus clearly on the work we are here to do.

Some have predicted apocalyptic failures in global public health systems. But in the Americas recent trends point to a much brighter future for health.

divine in general terms some of the difficulties that may be faced and reflect on how we will have to adjust our style and strokes.

We could suggest the unlikely appearance of an Armageddon-like situation in which famine and pestilence follow the collapse of the public health systems of the countries. We could predict scenarios close to the real-life situations depicted by Laurie Garrett in her book *Betrayal of Trust*, which tells of governments betraying the trust of the people and not maintaining public

quent appearance of yet unknown diseases. Conflicts of varying types would dominate the international scene, leading to armies of displaced persons invading other lands and places. Poverty would deepen across the Americas and be the cause of a deterioration of the social fabric, with malnutrition becoming rife. The sum of all this would be a rapid and profound retrogression in all the health indicators.

But I do not see any possibility that this apocalyptic situation will ever occur. Even in the grimmest days of



PAHO is a creature of the health situation of the Americas. We did not spring full-blown from the head of some mythical Zeus. We started slowly and grew slowly, adapting as we went along to the health needs of the countries of the Americas. Or more correctly, we adapted to those health needs that required our technical cooperation. It is quite clear that no one can predict the future health situations that will call for our support, but we can try to

health systems. No early warning systems would alert us to epidemics that might cause havoc with all aspects of people's lives. We could suggest that the dire predictions about the shortage of potable water might become fact, and countries would fight not for territory but for the water that would become a commodity more scarce than gold. We could think that extreme global warming would become a reality, with attendant increases in cancers and the invasion of ecological niches by agents and vectors that were alien to those places, with the conse-

the economic crisis of the decade of the eighties, there was nothing even remotely approaching such a desolate state. It is far more likely that the trends we have observed in the recent past can be used as portents of a much rosier health future that will affect our technical cooperation with the countries.

The first trend that we must note is the demographic transition, which is very marked in the Americas. Mortality rates will continue to fall, partly as a result of improved economic conditions, but perhaps more important, as

a result of the growth and spread of technology. We have seen how technologies for improving child health, such as immunization and the use of oral rehydration materials, have decreased child mortality. Newer vaccines will become available, and the combining of technologies into schemes such as the Integrated Management of Childhood Illness (IMCI) will become a standard part of the public health agenda. The fall in fertility that follows the decrease in mortality is a constant phenomenon. The rationale

For the past 30 years it has been fashionable to speak of the epidemiologic transition as if epidemiologic stages progressed steadily from one to another. Vivid accounts described the three stages of a transition: the age of pestilence and famine would be followed by the age of the receding pandemics, until finally we would reach the age of chronic diseases such as cancer and cardiovascular diseases. In fact, the

health development of our countries shows more of a mosaic pattern. We now have to confront the mosaic of chronic diseases that are increasingly important, while at the same time we must cope with new and emerging infections. It has been a salutary lesson for us that microbes will never go away, and we have to learn to inhabit the earth with them.

We can expect that new discoveries in science will shed more light on the relation of life in utero to the future development of a wide range of diseases, thus introducing the possibility of genuine early intervention and prevention. But we must never lose sight of the possibility that new diseases or new forms of old diseases may come to haunt us.

I can see the improvement of the environmental conditions that impact on health. The past decade has brought an improvement in the availability of potable water to the population. I am cheered by the recent efforts at collaboration between ministers of health and ministers of the environment that are focused specifically on joint approaches to improving human health.

I can see the health sectors of our countries accepting the need for their efforts in health sector reform to result in a more equitable distribution of health goods, and the state accepting the responsibility for the discharge of essential public health functions. We will see a wider acceptance of the thesis that health is an important contributor to human development, and national as well as international development agencies will direct their attention even more to the health of the people and ways to improve it. Those of us who see gender inequality as a societal issue will take heart from the wider acceptance of the belief that gender diversity is essential for health development, and women will assume roles in health beyond their traditional ones.



for the sequence is unclear, but the phenomenon has been universally observed. With this fall in fertility will come a decrease in the rate of population growth. In addition, we can predict that as infant and child health conditions improve, an increase in life expectancy will occur, and we can look forward to an increasing graying of the population. There are now about 100 million persons in the Americas over the age of 60; in 50 years we expect that figure to be 300 million, with the increase most marked in Latin America and the Caribbean.

Life expectancy in the Americas will increase, and science will discover new cures and preventions. Yet chronic and new diseases will continue to challenge us.

Having surveyed the surroundings and taken a new guard, we can now ask, What are the characteristics of PAHO that will make for its continued existence and increase the possibility that it will score another century in fine style?

First, its hemispheric character is a strength. We are more fortunate than other regions in that we have a geo-

Health sector reform should lead to greater equity in the next century, and health should be increasingly recognized as a key contributor to our countries' development.

and caliber of human resources. Over the years we have seen a greater disciplinary diversity as the nature of the health problems we face has changed. We have a greater appreciation of what is meant by our technical cooperation and of the means by which such cooperation is played out not only between ourselves and our countries but also between our countries. The deployment of these human resources such that the Organization has a physical presence in the countries must be another one of our strengths. The



graphically defined limit, and the notion of pursuing a Pan American ideal has a long history. The importance of the hemispheric approach and the concept of health as a hemispheric venture has been emphasized repeatedly in various presidential summits that have also validated the usefulness of the inter-American institutions.

The focus of PAHO on information and the use of information as a tool of technical cooperation has been one of our Organization's strengths from its inception and will continue to be such. The growth in the importance of infor-

mation as power, coupled with the ever expanding availability of technology, will further strengthen our capacity to assist countries in knowing what problems the people face and what measures must be taken to address those problems. Our use of information and the accompanying technologies will not merely be passive, but will also contribute to changes in the behaviors that account for so much of the morbidity and mortality from the diseases that appear within the epidemiologic mosaic.

Another strength must be the nature

countries see the face of PAHO and feel its presence beyond the cold documents that are the inevitable product of any bureaucracy.

Our presence in the countries enhances the capacity to respond to situations of disaster and emergency. Disasters are a normal part of our landscape, and our ability to see them as the result of lack of prepared-

ness for the occurrence of natural hazards has been and must continue to be one of our strengths. Our focus on the continuum from preparedness through prevention, mitigation, succor and subsequent development has been and must continue to be one of our strengths into the next century. Natural hazards are by definition largely unpredictable, but we can limit the extent to which they become disasters.

Part of the landscape that will influence the guard we take will be the increasing number of actors who will

be involved in health. It will be part of our strength to discern the nature of the partnerships that will be optimally productive and be complementary to our own actions. This will demand a flexibility and openness that can only come from a self-confidence born of having already scored a century and seen the value of partnerships in specific fields.

But in the final analysis, I believe that our ability to take a new guard and score another century will depend, more than anything else, on the power

U ndoubted benefits accrue to all countries from such joint efforts, but in addition I wish to see greater

Pan American collaboration in support of countries in the Region that are less well endowed and have poorer health.

My hope is that future generations of Americans will be seized, as we are, by the importance of the past century, and be as convinced of the nature of the



Pan Americanism has led to great feats in health. The future challenge is to extend this spirit in support of countries that are less well endowed and have poorer health.

of the principles we espouse. In recent years I have promoted as vigorously as I could the concepts of equity and the pursuit of the Pan American ideal. The idea that we can help identify the inequalities in health that exist, and at the same time help to identify the inequality in the distribution of the determinants of that health, is a noble one. It is one that is worthy of an organization that has been at the service of the Americas for 100 years. Abundant evidence shows that the countries of the Americas can perform great feats in health when they work together.

challenges and the possibilities of PAHO addressing them based on some of the strengths I have outlined. If my hope is realized, then the prospects for at least another century of service are good.

Sir George Alleyne will conclude his second term as director of the Pan American Health Organization in early 2003, culminating a 22-year career at PAHO. He was made knight bachelor by Her Majesty Queen Elizabeth II in 1990 for his services to medicine and in 2001 received the Order of the Caribbean Community, the highest honor that can be conferred on a Caribbean national.

Protecting Our Progeny

The Future of Vaccines

by Sir Gustav Nossal

It took 181 years from Edward Jenner's introduction of a smallpox vaccine for public health efforts to succeed in eradicating that disease from the globe. Even today, the gap between the introduction of a vaccine in the industrialized countries and its use in the poorer nations remains dauntingly long. Yet vaccines have proven themselves to be the most cost-effective public health tools in history.

How will progress in vaccines affect public health in the next 100 years? What lingering diseases will they help us conquer? How will their global use be financed? What lessons from experience can be applied to future vaccination campaigns?

If one had a crystal ball to look at the future of vaccines, it would no doubt reveal some important and heartening milestones, possibly including the following:

- By 2005, significant progress toward—if not achievement of—the global eradication of polio
- By 2010, vaccines against meningitis, pneumonia, rotavirus-caused diarrhea and human papilloma virus (the cause of cervical cancer)
- By 2015, vaccines against AIDS, malaria and pulmonary tuberculosis, and the global control of measles
- By 2025, the ability to protect infants against at least 20 pathogens throughout their lives



Vaccines have helped us conquer some of humanity's worst scourges in the past century. In the future they will help us control and even eliminate many more.

In reality, we can only speculate meaningfully on the future by thoroughly analyzing the past and present. Yet even in that real-life context, the prospects look bright indeed for a major impact of vaccines on global human health.

Smallpox is an important and encouraging case study. Though the vaccine has been around for more than two centuries, it took a mere 11 years for a disciplined campaign that was

80 percent coverage by 1990. This overall statistic, however, hides the fact that coverage was quite uneven. In countries with per capita GDP of less than \$1,000, coverage reached a mean of just over 50 percent. In the Americas, coverage was much better (often spectacularly) than the global average.

Unfortunately, since 1990 no real further progress has occurred, and indeed coverage has slipped in a number of countries, with coverage in the poorest countries now at just over 40 percent. EPI has saved many millions

three additional strategies: national immunization days (NID), a global system for surveillance, and “mop-up” operations, that is, intense vaccination efforts around the last few index cases.

National Immunization Days represented a huge effort in social mobilization, receiving extraordinary help from Rotary International, the news media, the government sector and, particularly, highly involved health ministries. On a single day, all of a country’s children under 5 were lined up and given the oral Sabin vaccine. This succeeded



adequately financed and brilliantly led to achieve eradication. What came as an encore?

Just as smallpox was nearing eradication in the late 1970s, the World Health Organization (WHO) launched the Expanded Programme on Immunization (EPI), which included six infant vaccines: against diphtheria, pertussis, tetanus, poliomyelitis, measles and tuberculosis. Although EPI got off to a slow start, the concept of universal childhood immunization was embraced seriously from 1984 on.

As a result, global immunization of infants rose progressively to just under

of lives and must be counted as a success. Yet globally there are still at least 2 million vaccine-preventable deaths every year in children under 5.

Polio eradication

With the Americas once again in the lead, global polio eradication efforts began in earnest in 1988. It was soon realized that routine infant immunization, although essential, could not do the job alone. It was buttressed by

in finding many hard-to-reach children who, for one reason or another, had not been caught in the routine immunization net.

As it turned out, it was necessary to have two NID a month apart, and to repeat the effort yearly for at least three years, turning Rotary’s Polio Plus campaign into a monumental task. As polio gradually came under control, it became important to detect

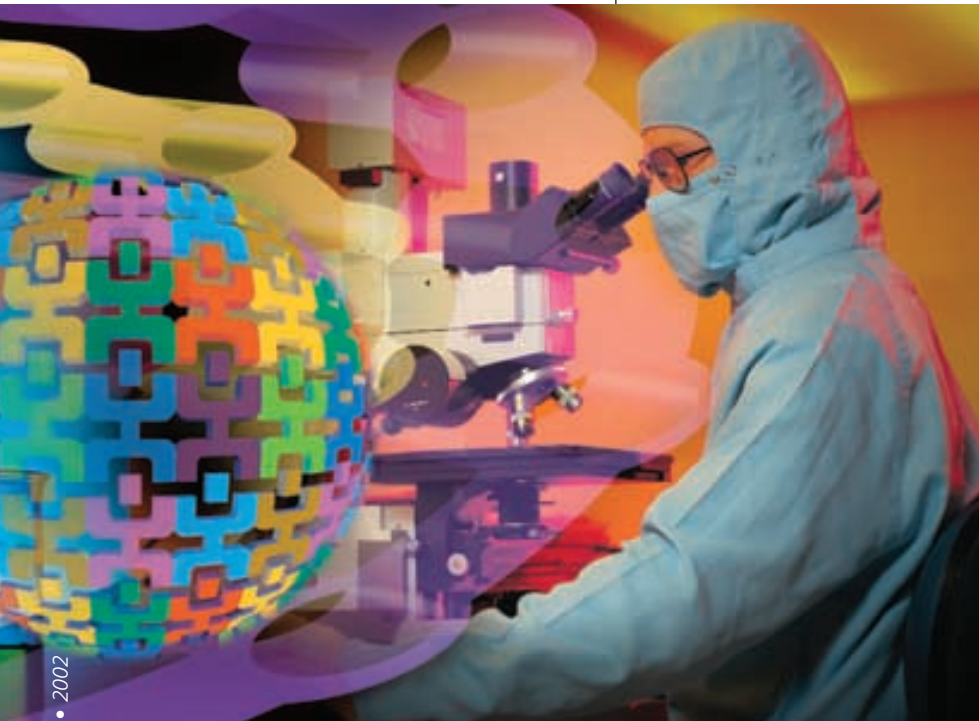
the residual cases. Therefore, a surveillance system was instituted to bring all cases of acute paralysis (technically termed flaccid to distinguish them from strokes) to the notice of health authorities. When cases were found, two stool samples were sent to accredited laboratories to see if the polio virus could be grown. This tedious but vital surveillance task has been absolutely crucial.

Finally, “mop-up” operations, consisting of dwelling-to-dwelling immunization around the last known cases,

We should see rapid progress in the “low-hanging fruit.” Vaccines against meningitis, rotavirus and pneumococcus may be available within the next five to seven years.

Global alliance

The experiences of both smallpox and polio show the extraordinary power of the vaccine approach. But what about the present state of play? In 1998, there was a sense that new energies were needed in global immunization efforts. Donor interest in EPI was fading, the vaccine infrastructure in many countries was deteriorating, and research was lagging on new vaccines for diseases occurring only in poor countries.



are the last step toward eradication. Thanks to this quadruple strategy, there have been no indigenous wild polio cases in the Western Hemisphere since 1991, none in the Western Pacific Region since 1997, and none in the European Region since 1998. Even in India, wild polio is now essentially confined to two northern states.

Over the next couple of years, WHO will be concentrating on 10 countries in Africa and South Asia, five of which are conflict ridden and five others “reservoir countries” because of high population density and very poor living

standards. The target year for the global eradication of the wild polio virus is 2005.

Although the Polio Plus campaign is a vertical program (as opposed to horizontal programs, which seek to provide primary health care across a broad front), it has broader implications. First, in many cases vitamin A supplements are administered simultaneously. Second, it provides a contact point between remote and disadvantaged rural poor and national health systems, often leading to a greater awareness of other available health interventions.

But as WHO, UNICEF, the World Bank and leading academics were searching for a new dynamic, help came from an unexpected source: William H. Gates III and his wife, Melinda French Gates. The Gates Foundation made an initial pledge of \$100 million to a Children’s Vaccine Program, at first designed to determine and overcome the chief roadblocks to the introduction of important new vaccines into the EPI. Within two years,

the Gates' extraordinary generosity had led to a total of \$1.4 billion committed to vaccine-related projects, including considerable research and development funds and a \$750 million gift earmarked for a Global Fund for Children's Vaccines, administered by UNICEF. The Vaccine Fund, as it is now known, targets the 74 poorest countries in the world, namely, those with per capita GDP of less than \$1,000 per annum. Several countries have added pledges to the fund, and it now stands at more than \$1 billion.



After extensive consultation with all stakeholders, the Global Alliance for Vaccines and Immunization (GAVI) was launched in 2000 as an unincorporated

We have good ideas about how to craft an AIDS vaccine. But testing these one by one will be a very slow process.

alliance of WHO, UNICEF, the World Bank, the Gates and Rockefeller foundations, and other nongovernmental organizations, along with bilateral donors, developing country health authorities and vaccine manufacturers from both developed and developing countries.

The GAVI board was chaired initially by WHO Director-General Gro Harlem Brundtland and is now chaired by Ms. Carol Bellamy, executive director of UNICEF, ensuring commitment of their respective organizations at the highest level.

GAVI has set itself three major goals. The first is to improve infrastructure for immunization in countries where it is inferior through cash grants dependent on a demonstrable increase in vaccination coverage.

The second is to purchase, for selected countries, vaccines beyond the traditional six, primarily hepatitis B, yellow fever and *Hemophilus influenzae B*, or Hib, for meningitis, pneumonia and septicemia.

The third and longer-term goal is to do applied research and development work for newer vaccines already well down the track, such as against pneumococcus and rotavirus.

Already two-thirds of GAVI's target countries have grants and/or vaccine supplies flowing to them. Yet sustainability is a real worry, as the beneficiary countries will gradually have to subsume the costs of the vaccines into their own health budgets.

Future vaccines

Despite the amazing progress of immunological science, there are many diseases for which we do not yet have an effective vaccine. We could see rapid progress in the so-called "low-hanging fruit," those vaccines-in-research whose underlying principles have largely been established and that seem

to require relatively straightforward development work to become available. This is probably the case for the A subtype of meningococcus, responsible for horrible meningitis epidemics in sub-Saharan Africa; for rotavirus, an important cause of infantile diarrhea; and for pneumococcus, which will involve major expense because each of many different disease-causing types will need to be included in an eventual vaccine.

It would be surprising if vaccines for these pathogens were not available within five to seven years. Again, we must seek public sector funds for their early introduction.

Somewhat more speculative are vaccines against shigellosis, or bacillary dysentery, a cause of some 800,000 deaths per year, nearly all in very poor countries; and against *Helicobacter pylori*, the cause of peptic ulcer disease, chronic gastritis and a big proportion of gastric cancers. It is doubtful whether the pharmaceutical industry will come up with sufficient research funding to drive these vaccines all the way to registration. The chances are better for a vaccine against human papilloma virus (HPV), the cause of cervical cancer and genital warts, because industrialized countries have a major interest in preventing these problems.

From a public health viewpoint, there are three "future vaccines" of even greater interest: those against HIV/AIDS, malaria and tuberculosis. These are so important that each deserves some discussion.

So far, an AIDS vaccine has eluded us, primarily because the human immunodeficiency virus has such devilishly clever tricks up its sleeve to foil the host's natural defense system. It chooses to live in and destroy one of the most important cells of the

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immune system, the so-called CD4+, or helper T cell. It also infects scavenger cells important in initiating immune responses. It can go underground in these cells, only to emerge much later. Being an RNA (ribonucleic acid) virus, it is subject to a very high rate of mutation, so that when the immune system does manage to polish off most of the virus, a mutant form with a different antigenic signature pops up, needing to be dealt with in turn. Finally, the active recognition sites on the grappling hooks that the virus uses to hang onto its target cell are skillfully hidden from the prying eyes of antibody molecules until the very moment of docking and entry.

Despite these challenges, progress is being made toward a vaccine. Strategies have been devised to evoke antibodies that are broadly active against different subtypes of the virus. During the long latent period of the disease, while the patient is still well, the body's killer T cells do fight against the virus, keeping the total load in the body relatively low. If a vaccine can provoke those T cells into intense activity before infection occurs, the very small virus load entering the body might be destroyed completely.

We have good ideas about how to craft such a vaccine; it is now necessary to trial these one by one in the clinic, a process that is necessarily very slow. An alliance known as the International AIDS Vaccine Initiative (IAVI) has raised sizable funds to speed clinical

trials, so that several different vaccine candidates can be assessed simultaneously. Much of this trial work will have to be conducted in developing countries, given their higher incidence of infection.

Targeting malaria

Malaria is the worst of the human parasitic diseases, killing between 1 million and 2 million people every year, chiefly in Africa. People living in endemic areas eventually develop partial immunity, such that they do not get attacks despite having parasites in their blood. If they move to a non-malarial area for several years, they gradually lose their immunity.

Here, scientists will have to do better than nature.

There are four susceptible points in the parasite's life cycle when it may be vulnerable. First, a motile form known as a sporozoite is introduced into the skin by the night-feeding female *Anopheles* mosquito. Within less than half an hour, sporozoites reach and enter liver cells. Up to that point, antibodies directed to the sporozoite surface might lead to their destruction. Once in the liver, the parasite multiplies, during the process shedding bits that will reach the surface of the cell. If a killer T cell recognizes these bits (called peptides or T cell epitopes), the affected liver cell is attacked and destroyed before it can release its progeny into the bloodstream. Infection is thus aborted.

But once the progeny (known as merozoites) are in the blood, they quickly attach to and infect red blood cells. They then multiply, rupture the red cell, and enter a new one. It is this blood-stage cycle that is responsible

for the symptoms of the disease. In its transit from one red cell to the next, the merozoite is briefly susceptible to antibody.

Finally, some merozoite-infected red cells release gametocytes, sexual forms of the parasite, which can mature within the mosquito into male and female gametes. When these unite, the life cycle is completed. If one were to make antibodies to these gametocytes, one would not help the patient, but at a population level, transmission would be blocked, and eventually the disease might be brought under control.

Experimental vaccines incorporating each of these four sets of ideas have been shown to work in model systems. It is now a question of subjecting them to phased human trials. One of the many Gates Foundation programs, the Malaria Vaccine Initiative, is planning to do just that. So far, some partial success has been achieved in human trials with a sporozoite vaccine and a combination blood-stage antigen vaccine.

Attacking TB

Why do we need a tuberculosis vaccine other than the BCG (Bacillus Calmette-Guerin) vaccine? Simply because this live, attenuated bacterium can protect infants from tuberculosis but appears incapable of coping with the real problem, namely, pulmonary tuberculosis in adolescents and young adults.

Though not as far advanced as it is for AIDS and malaria, research toward a new TB vaccine is exploring plenty of bright ideas, including both live attenuated and molecular approaches. A recently completed tubercle bacillus genome project is speeding the search.

One of the biggest problems, not only with the "big three" but also with other vaccines, is the fact that pure protein molecules—made by genetic engineering—do not by themselves induce a

strong immune response. For this we need immune-strengthening substances called adjuvants. Many are under development, but these tend to be toxic, and the search for more satisfactory adjuvants is intense.

Alternatively, we need new and craftier ways of delivering the vaccine. For example, we can take the gene for an important vaccine molecule (or antigen) and transplant it into a virus, then inject that virus, which will strongly alert the immune system. We can also inject DNA coding for antigens, which enters cells and then creates a factory where the body itself is manufacturing vaccine molecules over a considerable period. One highly promising strategy is known as “prime-boost,” in which a DNA vaccine is injected first and an engineered virus next. This has worked well in animal models of both HIV/AIDS and malaria.

Genomics has opened up other entirely new avenues as well. Plants can be engineered to produce antigens, so an edible vaccine is feasible. This would have to be constructed so that either a mucosal adjuvant or some other immune-enhancing factor was also present. Vaccines can also be applied to the skin and, amazingly, find their way into the body, yielding a transdermal vaccine. Here again, immune enhancers will represent the problem area.

Within a 100-year time frame, many of these ideas will seem clumsy; third and fourth generation developments will then be in use. Special attention will have to be given to noninjectable vaccines—no one wants their babies to become pincushions.

Vaccine combinations will become increasingly important. Some companies are already working on a seven-valent vaccine against diphtheria, per-

In a world sobered by Sept. 11, 2001, it is no longer naïve to hope that grave social inequities around the globe will finally be addressed.

tussis, tetanus, poliomyelitis, hepatitis B, Hib and meningococcus C all mixed together. A measles-mumps-rubella-chickenpox vaccine is already on the horizon. There is little doubt that a century from now, infants will be protected against most of today’s most prevalent infectious diseases and even more.

How many of these diseases will we eradicate completely? The Pan American Health Organization has targeted measles as the next one for the Americas and has already made tremendous progress toward that goal. Given the problems encountered with polio eradication efforts in Africa and South Asia, global control of measles may be more realistic than total eradication. In principle, however, any microorganism against which there is a highly effective vaccine, which has no animal reservoir, and which (unlike tetanus and anthrax) does not persist long term in soil or water, is eradicable.

The two major challenges are cost and the fact that an organism against which infants are not being immunized because it has been eradicated, such as smallpox, could be used for bioterrorism. Short of eradication, it is encouraging to note how rapidly a disease can be brought under control. For example, in Taiwan the widespread use of hepatitis B vaccine has dramatically lowered the carrier rate and has already diminished the incidence of liver cancer in relevant cohorts.

A golden century?

In a world sobered by the events of Sept. 11, 2001, it is no longer naïve to hope that grave social inequities around the globe will finally receive the attention they deserve. There is growing recognition that a reservoir of communicable disease in any country represents a global threat, given the extent of international travel. Prevention of infection is not only better than cure, it is much cheaper.

Yet for the splendid examples of Rotary International and Bill and Melinda Gates to be followed more extensively, one additional realization is needed. That is the nexus between health and economic development. In the words of Harvard economist Jeffrey D. Sachs and his colleagues: “The linkages of health to poverty reduction and to long-term economic growth are powerful, much stronger than is generally understood. The burden of disease in some low-income regions stands as a stark barrier to economic growth.”

Sachs estimates that \$30 billion per year of additional donor support could save 8 million lives each year and provide direct economic benefits of \$186 billion per year. Over the next 100 years, that adds up to truly astounding progress for the human race. As far as vaccines are concerned, the long journey from Edward Jenner to William H. Gates III would then have represented only the beginning of a golden era in public health.

Sir Gustav Nossal is professor emeritus of the University of Melbourne and was named Australian of the Year in 2000. He chairs the Strategic Advisory Council of the Bill and Melinda Gates Children’s Vaccine Program and the Strategic Advisory Group of Experts of the World Health Organization’s Vaccines and Biologicals Program.

Hurrying Toward Disaster?

by C. J. Peters

A

young man—a trained athlete in the prime of life—lies on his sofa with aches that penetrate to his bones. He turns up the air conditioner as his fever drenches him in sweat. He drinks a little water but has no appetite after vomiting throughout the night. He feels as bad as he has ever felt in his life. The weight of his lethargy presses him down into the couch. Soon, he begins to feel short of breath. In a few hours, he will go to the hospital, but it won't matter. Even state-of-the-art intensive care cannot revive his failing heart, suction his edematous lungs fast enough or replace the fluid with sufficient oxygen for him to breathe. Within 48 hours, the young man will have drowned in his own blood plasma.

As human impact on the earth increases exponentially, the chances for unpleasant surprises from the microbial world will also grow.

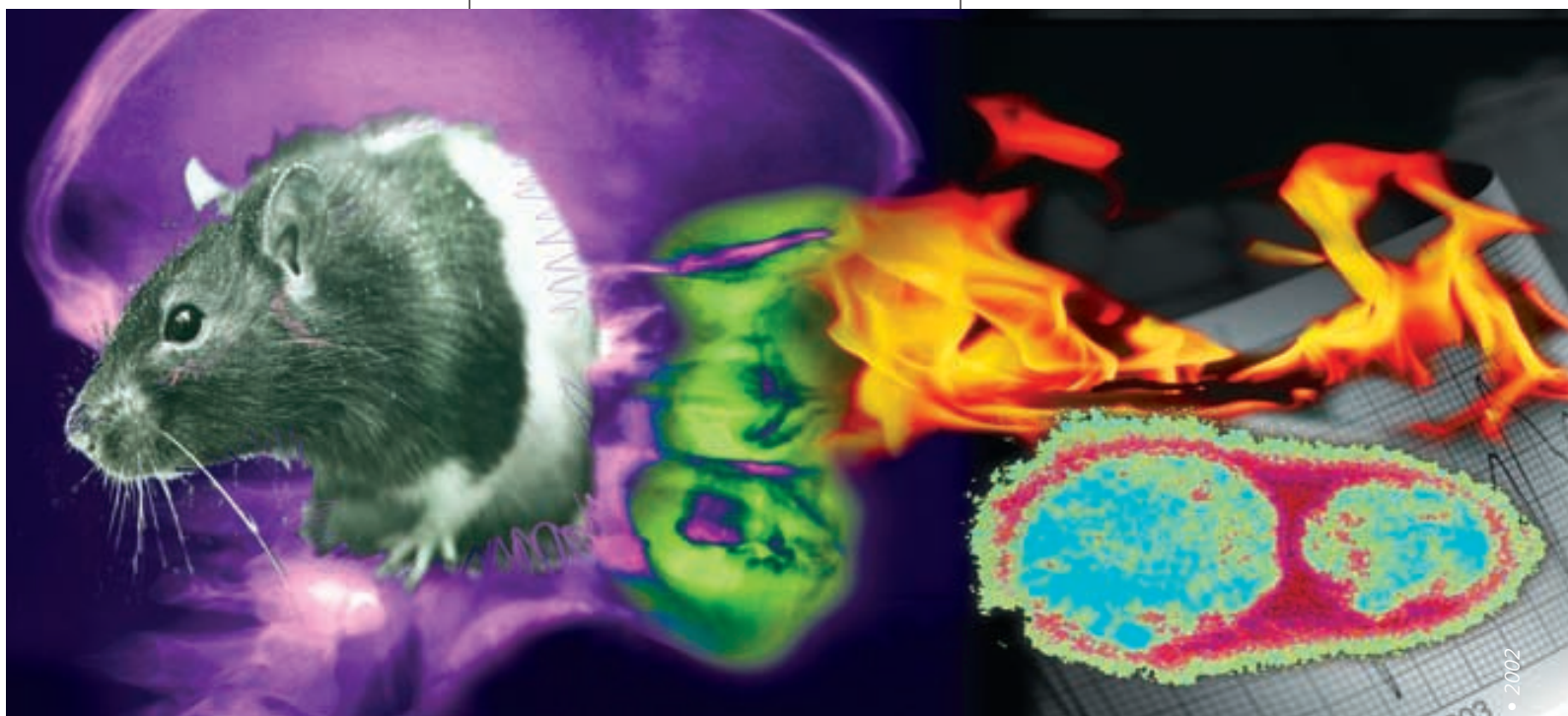
It may sound like a fiction writer's overheated imagination, but this is what really happened in the southwestern United States in 1993. Cases of the "mystery disease" piled up. Newspapers alarmingly reported the "experts stumped." Local physicians quickly realized they were up against something beyond their knowledge, and even the accumulated scientific wisdom at the nearby university proved little help. State public health authorities were unable to solve the problem, and when officials of the U.S. national Cen-

are not just a media invention; they are real and significant. The main components of the problem are the emergence of "new" organisms, shifting tactics of known infectious agents and the growing resistance of pathogens to existing antimicrobial drugs.

Although the threat of emerging and reemerging infectious diseases is greatest in the developing countries of the tropics, countries with higher incomes face the danger as well. Two other "new" hantaviruses were discovered after people died in small, poor

Amerindian communities in Paraguay and in one of the most expensive neighborhoods on Long Island, New York, in the United States.

While the industrialized world has more resources to prepare for these threats, its impressive health progress over the last century has led to widespread complacency about diseases that seem to affect primarily the world's poor. Yet with the growth of global travel, changes in the earth's ecology and natural viral mutation, one country's emerging disease is potentially



ters for Disease Control and Prevention were called in, they had nothing to offer but an investigation. Finally, after a concerted effort, authorities discovered the root of the malady was a virus carried by a local rodent, which showed no signs of illness itself. This new hantavirus caused a new disease, hantavirus pulmonary syndrome, or HPS, which to this day we do not know how to prevent or treat.

The story of HPS exemplifies our increasing awareness of threats from the microbial world and our halting efforts to confront them. The dangers

Given the growth of global travel, changes in the earth's ecology and natural viral mutation, one country's emerging disease is potentially another's next epidemic.

another's next epidemic. What's more, the factors that favor emerging diseases are also present—in some cases even accentuated—in the developed world.

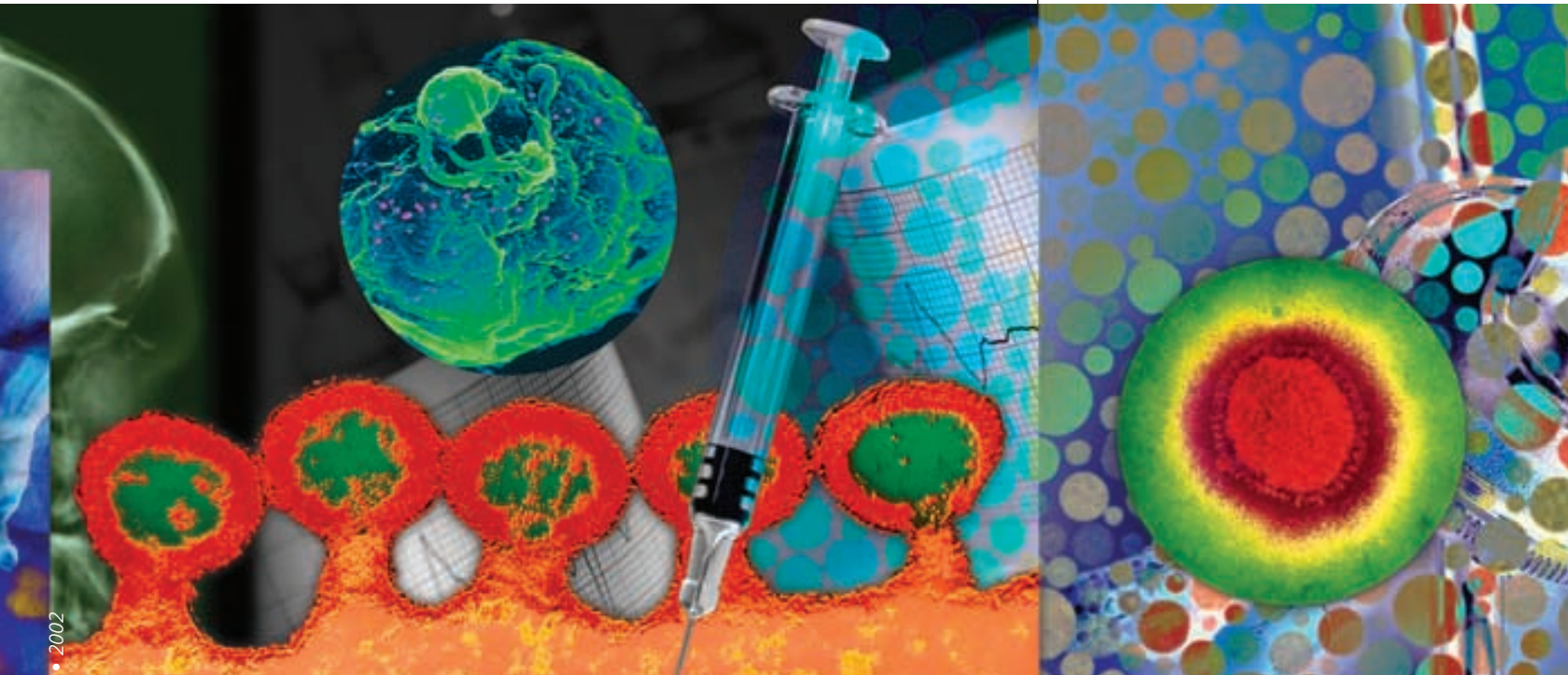
“New,” but not so new

The evolution of pathogens is measured in centuries or millennia, so truly “new” organisms do not simply burst upon the scene from nothing. Usually, they have undergone quiet periods of development in nonhuman hosts, then

Health progress in richer countries has led to widespread complacency about diseases that seem to affect primarily the world's poor. Yet the factors that favor emerging diseases are also present—in some cases even accentuated—in the developed world.

of the countries of the Americas and is considered a significant threat to the Region's public health.

Another "recently emerged" virus, HIV (human immunodeficiency virus), illustrates a different process. The simian version was a chronic infector of chimpanzees in Africa before crossing species and infecting humans, causing acquired immune deficiency syndrome, or AIDS. Transmitted primarily by sexual intercourse, unsterilized needles and blood transfusions, AIDS has spread rapidly worldwide by capitaliz-



changes in ecology or human society lead to their emergence as killers and their recognition by medical science.

Such was the story of the rodent-borne hantaviruses: they have been parasites of native rodents in the Americas for at least 30 million years, but in 1993, climate changes caused by the El Niño southern oscillation led to increased breeding and rapid growth of rodent populations in the southwestern United States—and a

subsequent spillover of the virus into human populations.

Cases of the disease had occurred but gone unrecognized for many years until more accurate tests for viruses allowed us to define a "new" disease that had not been diagnosed previously. More important, scientists found that in the Americas, more than 20 different viruses could cause this new clinical disease. Each virus is carried by a different rodent species, with distinct epidemiological patterns dependent on the host species and its interaction with people. HPS has now been recognized in most

ing on its chronic nature and the long period during which carriers show no symptoms but can transmit the virus. In spite of its stealth strategy, AIDS claims the lives of virtually everyone it infects within a decade or so. Some will be able to stave off its lethal effects by taking expensive and toxic medications, but the majority of the 40 million people infected today will die without even this benefit. In all likelihood, HIV will be the most significant infectious agent of the 21st century—barring the emergence of something even worse.

A more agile offender is the influenza A virus. We tend to think of influenza as a minor illness that comes to torment us every winter. But this is only partially true. The virus circulates in humans and gradually changes its covering proteins to escape protective responses from our immune system. We monitor those changes through a global surveillance system coordinated

tion, a worldwide epidemic, or pandemic, results. The virus spreads quickly because no one has any significant immunity to the novel strain, and the illness it causes can be unusually severe. The worst pandemic was in 1918, when more than 20 million people died worldwide from a particularly virulent influenza strain. The last was the 1968–69 “Hong Kong flu,” which killed 700,000. Since flu pandemics tend to occur every 10 to 40 years, we are statistically overdue for a new one. In 1997 we had a very close call: a virus

appeared in domestic fowl in Hong Kong and killed nearly one-third of the people subsequently infected. Fortunately, it proved to be of limited transmissibility between humans, and prompt surveillance and disposal of infected birds eliminated the threat.

What would happen in a new pandemic? It is questionable whether we could detect a new virus in time to prepare a new vaccine in quantity. We might turn to antiviral drugs, but stocks are low, and expanding them rapidly would not be feasible. The death toll from a new pandemic might be “only” a million or so—or it could rival or exceed the 20 million deaths in 1918.

Ecological change

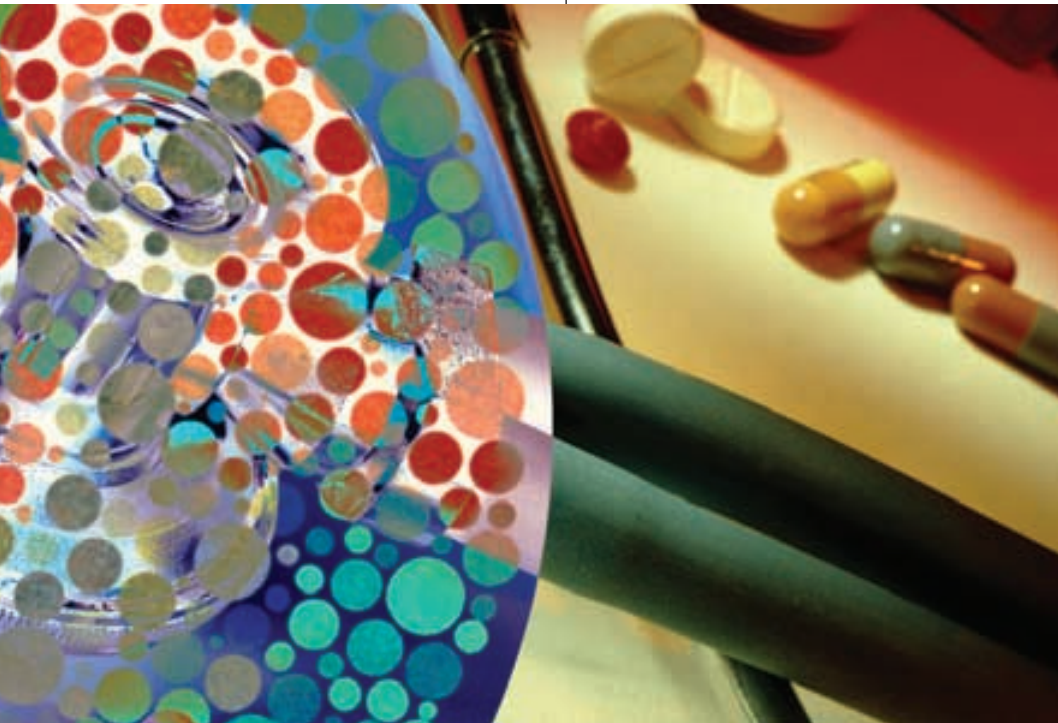
The driving forces behind these problems are in great part related to population growth and human behavior. Satellite images show that people have modified more than half the world’s surface, leading to profound changes in land use, water availability and even climate. As agriculture occupies progressively larger zones, flora, fauna and associated infectious disease agents are shifting rapidly. The movement of species from one ecosystem to another in these disrupted ecological zones can result in an overrun by a new invader.

In North America, we think of this most frequently with plants such as kudzu and dandelions, but many animals were also introduced. The most dangerous of these are the ubiquitous *Rattus norvegicus* (the urban gray rat) and *Mus musculus* (the domestic house mouse), which were introduced into the Americas from the Old World, bringing with them plague, rickettsialpox, Seoul virus and lymphocytic choriomeningitis virus. *Aedes aegypti*, the mosquito vector of dengue and yellow fever, was also introduced into the

by the World Health Organization (WHO), and in an annual WHO meeting, a new vaccine formula is devised to fight the emerging strains. We are fairly successful in coping with the evolutionary changes of the virus, yet every year some 20,000 people die of the flu in the United States alone.

Independent of this slow strain drift is another process that occurs outside humans, in which many different influenza strains randomly exchange their genes. When a highly virulent and transmissible combination occurs and makes its way into the human popula-

We are statistically overdue for a new influenza pandemic. Its death toll might be “only” a million, or it could rival the 20 million deaths of 1918.



Americas, carrying those viruses and making possible their spread across the entire Region. More recently, in 1999, West Nile virus was introduced, probably via a stowaway mosquito on an airplane, into New York from the Middle East. Dr. Robert Tesh, at the University of Texas Medical Branch in Galveston, recently isolated the virus from a Houston blue jay, confirming its spread as far west as Texas. Nationwide, the virus has caused 149 human cases, including 18 deaths, and will probably reach Central and South America in the near future.

By far the most common underlying causes of emergence can be found in changes in the ecology of the infectious disease or its hosts.

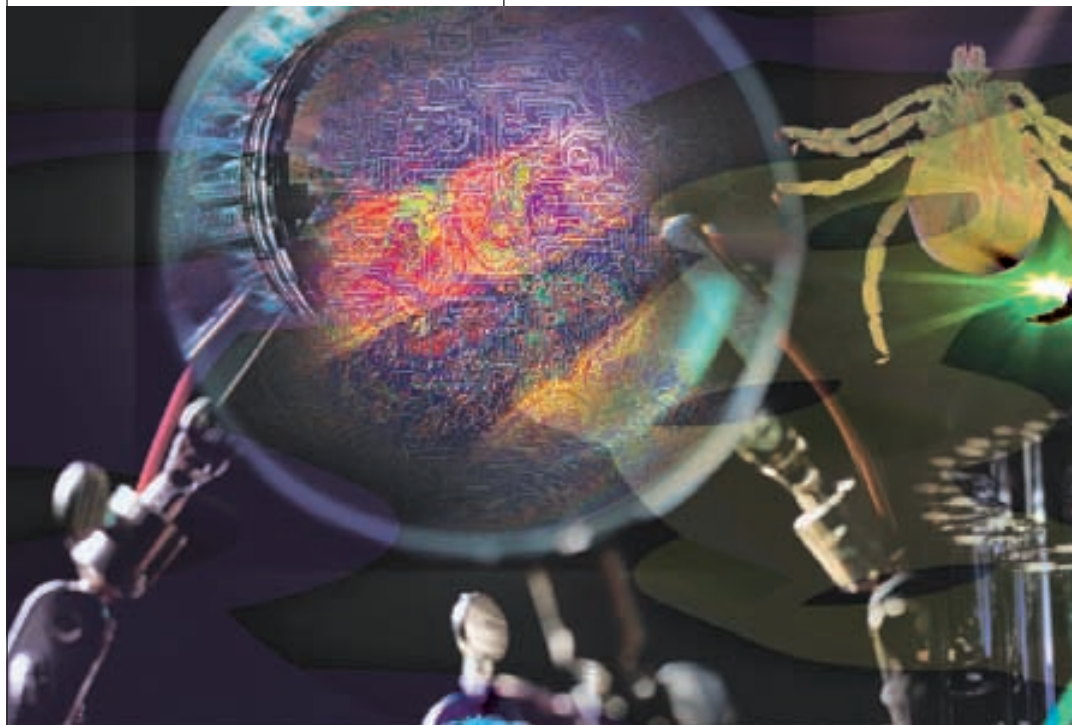
A classic example is Bolivian hemorrhagic fever, which emerged in the 1960s. Machupo virus, which causes this dangerous disease, is carried by rodents, and settlements in new areas of Bolivia's department of Beni led to its emergence as a concentrated human health problem. The cause of the disease was unknown, but it invaded small towns, causing high death rates and often prompting the abandonment of entire settlements. When authorities discovered that the disease was caused by a rodent-borne virus, the animals were eliminated and the towns were safe again. However, rodents continue to live in clearings where isolated houses are built and in fields where crops are planted to sustain nearby towns. The well-fed animals in the fields remain a constant threat to the rural people who work there.

The need to provide increasing amounts of food and water for the world's burgeoning population also contributes to the emergence of new diseases. Intensive agricultural methods often mean that a single, genetically homogeneous species is raised in a

limited area, creating a perfect target for emerging diseases, which proliferate happily among a large number of like animals in close proximity. The growing impoundment of water and expanding irrigation are important elements in the emergence of mosquito-borne diseases, and the lack of potable water for consumption and washing in poorer populations leads to increasing transmission of intestinal diseases such as cholera and typhoid. The problem is not only that these ecological changes are occurring, but that they are occur-

coming back to haunt us. Plague, pneumococcal meningitis and pneumonia, tuberculosis and typhoid are only a few of the once-subjugated bacteria now reemerging as significant pathogens that we can no longer successfully deal with. Future generations may be impressed with our discoveries of powerful drugs to fight lethal bacteria, but they are likely to be less impressed with the way we squandered these drugs' life-saving qualities by using them in ways that predictably lead to resistance.

The problem is clear in evolutionary



ring at an accelerated rate. Indeed, the rate of increase is itself increasing. In this sense, it is very possible that we are hurrying toward an appointment with disaster.

Drug resistance

Up to now, we have successfully battled many of the classic bacterial infectious diseases through the use of antibiotics such as penicillin to treat them. Yet many pathogens are now

terms: using antibacterial drugs selectively and with proper controls minimizes the emergence of resistant organisms. But their widespread use for trivial infections or against viruses that are not inhibited by the drugs destroys the sensitive bacteria in hosts and assures that the next infections will be with bacteria that have evolved ways to escape the drugs' action.

Some very important infections fall into this category, among them typhoid fever. Thanks in large part to the widespread use of inexpensive antibiotics for uncertain indications,

the typhoid bacterium has developed resistance to all three drugs that have been used successfully to treat the disease in the past. Typhoid is also rapidly developing resistance to a newer, expensive class of drugs that is currently the last bastion of defense. In poorer countries, the effect on people who lack access to clean water will be devastating; but the impact will also flow over to the more affluent in our global society who travel or otherwise come in contact with carriers of resistant typhoid bacteria. A similar situa-

tion is evolving with tuberculosis and many other bacteria. Meanwhile, the pharmaceutical industry faces declining profits from the production of antimicrobials, and both science and industry are lagging in the development of new drugs to replace those that have been lost. We can save the remaining ones only by improving doctors' prescribing practices and patients' attitudes, by controlling over-the-counter sales and by eliminating the most important drugs from use in livestock production. If the antibacterial drug situation is

bleak, antiparasitic drugs present an even more distressing problem. Profit margins for critical compounds used to treat parasitic diseases in tropical countries are even lower than for antibacterial drugs. Malaria—which kills 1 million people annually—economically justifies a small continuing effort by the pharmaceutical industry, but lesser killers, such as trypanosomiasis and schistosomiasis, do not provide sufficient incentive. As for antivirals, few drugs are available other than for HIV because mar-

ket forces are too weak to spur development and production. This is also true for new pesticides that could curb disease vectors in the world's poorest countries.

is likely to become more acute. So far, most recently emerging diseases do not pass readily from human to human. But infectious diseases of the future are a big unknown, and pathogens—emerging or reemerging—are likely to bring new surprises. The specter of the return of smallpox through a deliberate act of bioterrorism is a particularly sobering example raised by the Sept. 11, 2001, attacks and their aftermath. How can we prepare for diseases of the future?

First, we must jump-start the



process of developing new anti-infective drugs, vaccines and pesticides. If development is not economically feasible for the private sector, we must involve the public sector in their development. This does not represent a socialization of private enterprise, but rather a recognition that there is insufficient motivation for the private sector and that there is a pressing need to accomplish a common good.

Second, we must employ new science more effectively. The huge advances in molecular and structural biology and genomic science have

ket forces are too weak to spur development and production. This is also true for new pesticides that could curb disease vectors in the world's poorest countries.

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Population growth continually challenges our ability to deal with emerging infectious diseases. We must make intelligent choices so that we have the least possible impact on our natural environment.

given us tools that have already enlarged our understanding of emerging diseases and the recurring problems of the tropics. Yet we have seen few direct benefits for drug development or vaccines. These will be available only when we address a complex nexus of social, economic and regulatory barriers.

Third, we must devise new strategies to fight and prevent the spread of infectious diseases. We have already seen impressive results from some simple but innovative approaches targeted at critical weaknesses in the propagation of infectious diseases. For example, in tuberculosis treatment, the use of directly observed therapy (DOTS) has been highly effective in increasing cures and limiting the emergence of further antibacterial drug resistance. Insecticide-treated bed nets represent a radical change in the traditional approach to malaria amelioration. While questions remain about sustainability and the development of resistance to insecticides, this approach exemplifies the kind of solutions we need to develop and implement.

We must also find ways of strength-

ening public health infrastructure, which is critical to surveillance—what’s happening with old diseases as well as new ones—and to prevention and control. While public health is invisible to most of us, and so gets little attention and inadequate funding, it is critically important to keeping us safe from infectious diseases, including the threat of bioterrorism. Public health infrastructure is weak in almost all countries but is particularly at risk in the developing world. We must find new ways to augment our greatest protection

ligent choices so that we have the least possible impact on our natural environment.

What to do, in fact, may be less of an unknown than how to accomplish it. The work of physicians, public health officials, government agencies and the private sector must be coordinated. Both professionals and the public must be better educated to attack these difficult problems. Only a coordinated effort—sufficiently funded—by governments, foundations, scientific establishments and international organiza-



against infectious disease worldwide and particularly in those countries with greatest need.

Other factors loom even larger and will be even more difficult to address. The earth’s growing population continually challenges our ability to deal effectively with emerging infectious diseases. Land use, water availability and likely even climate change are driven by population expansion. Moreover, the increasing use of resources leaves us with fewer alternatives to address problems when they inevitably arise. At the least, we must make intel-

tions will allow us to keep infectious diseases of the future in check.

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The Next Revolution

Who's Ready? Who's Not?

by Juan Enríquez and Rodrigo Martínez

Genomics is creating a revolution in health and medicine. But only those countries that prepare their populations to join it will be able to fully reap its benefits.



Imagine you are sitting at an outdoor café in a European city, sipping tea and discussing the future of the world with some friends. Now imagine it is Oct. 12, 1492, the day Columbus landed in the Americas and changed the course of world history forever. Even if you had heard a news report of that event, you and your friends would have little idea of what it meant or of its enormous implications for the future. Yet if you did understand even part of it—and could act on your knowledge—the benefits could well be great.

Something similar is happening today at the dawn of the 21st century. Since Feb. 12, 2001, it has been possible for any one of us to go on line and browse the entire human genome, the map of the code that makes us human. Yet few of us can grasp much of what it means or what to do about it. Those who do—from individuals to countries and regions—will clearly be in a better position to reap the benefits.

Genomics has created a revolution in the life sciences, one that will change the way we look at and live in our world. Already, it has had a major impact on agriculture, and its influence will soon extend to everything from chemicals and energy to insurance, cosmetics and the military. But nowhere will its effects be greater than in medicine and health.

We have already begun to learn much about ourselves, even though we remain ignorant of what most of the data mean and what functions many genes play. As we learn more over the next two or three decades, what will happen? Health care will shift significantly from a reactive to a proactive endeavor. Doctors and technicians will increasingly focus on specific conditions in individual genotypes and phenotypes, and on probabilities rather than symptoms. They will know what diseases we are predisposed to and what we might do to prevent the onset of illness, as well as the reactions we are likely to have to specific drugs. We will carry genetic ID cards and consume ever more personalized medicines. We will need fewer and fewer surgeons. We will live much longer and remain much healthier throughout our lives.

We can already see some of these fundamental changes in the works. A number of biotechnology companies are successfully developing DNA-

embedded silicon biochips that can test for thousands of genetic conditions. Eventually, these coin-sized chips may be able to screen for most diseases and defects known to have genetic roots.

Such diagnostic tools will lead to a shift toward highly personalized medical care. They will also turn our focus toward prevention rather than intervention. As a result, there could be a major change in the ratio of doctor bills to drug costs: from the current 9:1 to something approaching 1:1 over the next quarter century.

Genomics should also spur novel ways of delivering “medicines.” Consumer products such as soaps, shampoos, cosmetics, aerosols, foods and beverages may provide our daily doses of medicines. Genetically engineered health products could be purchased in supermarkets and health clubs, not just hospitals and pharmacies.

Future benefits

These developments occur mostly in, and may seem likely to benefit primarily, the world’s richer countries. But developing countries should not be isolated from the life sciences revolution. By allowing us to better map out microbes and viruses, genomics will teach us more about the diseases and epidemics that plague the developing world and will help us develop more and better treatments to cure them.

Already, more than 250 million people throughout the world have been helped by more than 130 drug products and vaccines produced by biotechnology companies, according to the Biotechnology Industry Organization. And there are more than 350 biotech products and vaccines currently in the industry’s pipeline. Meanwhile, supercomputing and “bioinformatics”—the use of software

to facilitate drug discovery—promise to further accelerate advances in pharmaceuticals that will benefit both rich countries and poor.

The potential for genetically modified food crops to benefit poorer countries is widely acknowledged, but an equally important area of genomics for both developed and developing countries is the convergence between food and medicine. Just as crops can be genetically engineered to resist insects or to have enhanced nutritional value, they can also be genetically engineered



to possess specific medicinal qualities.

For example, agribusiness firms already are trying to tap the exceptional cancer-fighting qualities of wild Italian broccoli and engineer those into commercial varieties. Others are working on bioengineered corn that can attack cancer cells, fight osteoporosis and reduce heart disease.

Elsewhere, research is under way to reprogram the genes of certain fruits and vegetables to turn them into vaccines against tetanus, diphtheria, hepatitis B and cholera. To the delight of the world’s children, getting a vac-

cine may soon mean eating an apple, a banana or a potato rather than getting a shot.

The link between agriculture and medicine will not be limited to plants. Already, some biotechnology companies are genetically engineering goats to produce milk containing antibodies and proteins that are known to fight human diseases, including cancer. Other companies are trying to produce antigens in mosquito saliva, turning pests into living vaccines for a variety of human diseases.

Thanks to genomics, health care will become more personalized and proactive. We will need fewer and fewer surgeons. We will live longer, much healthier lives.

of an agriculturally based global economy into an industrial one (having 12 children and a lot of land suddenly mattered much less when one had access to a thousand horsepower). Countries that prepared their citizens to understand and adapt to the industrial revolution became the dominant global players. Thus England—a little island on Europe’s periphery—was able to out-produce all and run the world’s largest empire, while China’s and India’s relative importance simply collapsed.



Of course, there is no guarantee that the benefits of the life sciences revolution will be shared equally across the globe. Indeed, the incalculable opportunities this revolution opens up are matched only by the enormous challenges entailed in sharing its benefits equitably. Political, social and economic structures—along with public policy choices—determine the evolution of any technology and its applica-

tions. What will the life sciences revolution mean for the future of public health in the Americas? How can we make sure that Latin America and the Caribbean will participate in this revolution and enjoy its benefits?

Equally momentous revolutions of the past have shed some light on this question. The agricultural, industrial and information revolutions all showed the importance of understanding the rules of the game and developing a working knowledge of the “dominant language.” Some people, countries and regions understood the transformation

Today, just as then, those who understand how technology is changing the rules and the dominant language—and those who prepare their populations for these changes—are the ones who will reap the benefits. All the others risk getting left further behind.

A new language

The life sciences revolution is based on the single most powerful language humans have ever tried to unravel, the

language of life, in which every living thing on our planet is coded. This revolution actually started 49 years ago, in 1953, when James Watson and Francis Crick deciphered the structure of DNA. Their work introduced a new alphabet based on A's, T's, C's and G's (for Adenine, Thiamine, Cytosine and Guanin), the four nucleotides that form DNA.

Today the language of genomics is increasingly merging with the language of the digital revolution, which itself transformed the global economy over

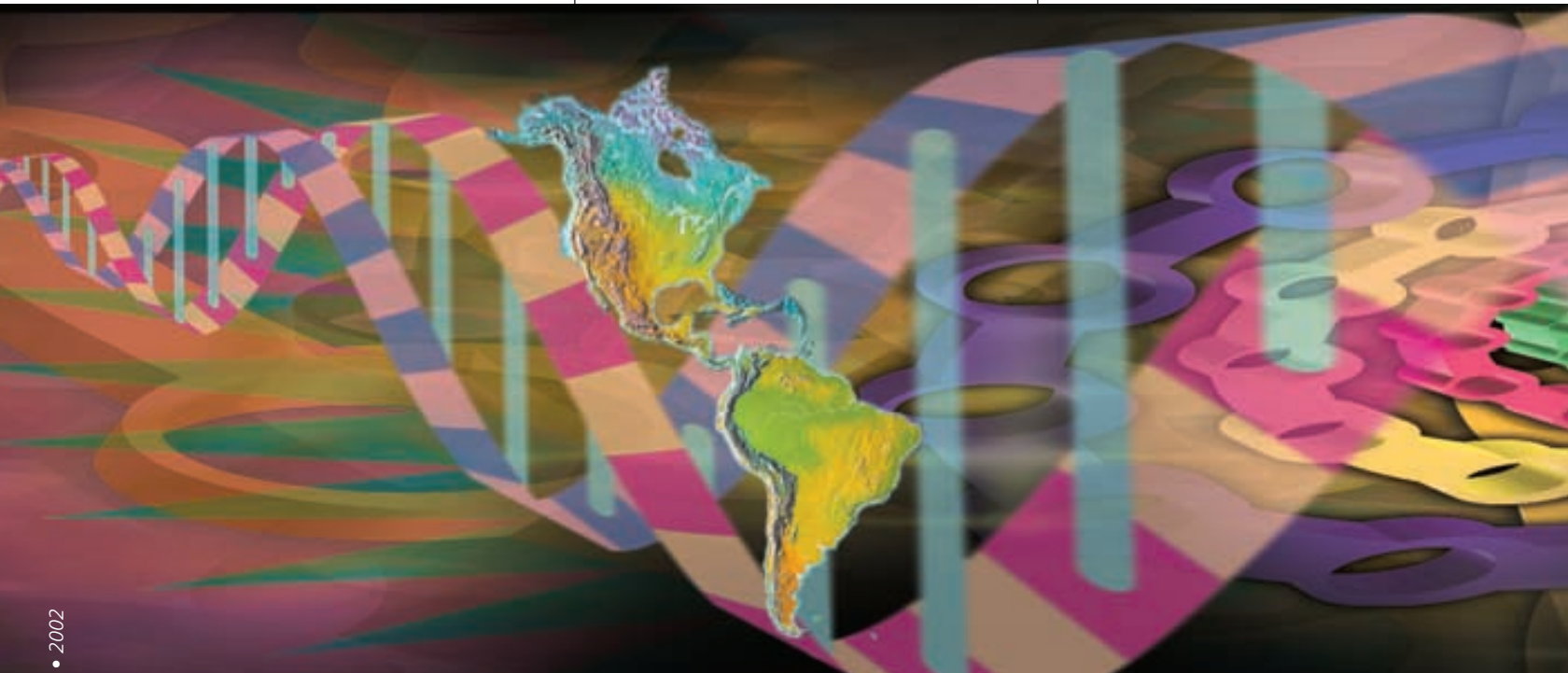
and today they are much better off. Examples include Singapore, Taiwan and South Korea—all of which in 1965 were much poorer than Mexico.

A region short-changed

Unfortunately, most of Latin America and the Caribbean failed to make the required adjustments, and today we see some of the results. In every country of the Region, large numbers

had few natural resources—invested in human capital, and by 1999 the average South Korean could expect to live 73 years, two more than someone living in Latin America.

We see a similar pattern in infant mortality. For the last 40 years, Latin American and Caribbean countries have reduced infant mortality by 70 percent, while Singapore and South Korea have seen a 90 percent decrease. In the 1960s, an Argentine baby had about a one-third higher chance of survival than the average South Korean



the last 50 years. The ability to transmit data through ones and zeroes (or light and no light) has shifted economic activity from commodities and manufacturing toward services and knowledge. In the 1960s, one-third of the global economy was agriculture, one-third was industry and one-third was services and knowledge. Today, services and knowledge account for two-thirds of the global economy, while agriculture represents less than 4 percent.

These shifts allowed some poor countries to reeducate their own populations and reinvent their economies,

of people live in critical conditions. In rural areas of Argentina, Brazil, Bolivia, Chile and Mexico, more than three-quarters of the population has no access to clean drinking water, much less good health care.

While life expectancy has increased during the past half-century in most parts of the world, other regions have done better than Latin America and the Caribbean. In 1960, someone living in the Region could expect to live 58 years—about four years longer than someone living in South Korea. In subsequent decades, South Korea—which

child. Today, an Argentine baby is twice as likely to die as a South Korean baby (and South Korea is not the richest country in Asia, nor is Argentina the poorest one in Latin America).

These gaps, unfortunately, could soon widen. According to World Bank data, health expenditures in Latin America increased from 5.8 percent of GDP to 6.4 percent during the first half of the 1990s. Yet this is less per capita than in Asia: in 1995, Latin American countries spent \$192 per capita on health, while Singapore spent \$926 and South Korea \$551.

For decades, perhaps centuries, education and health have been trumpeted as official priorities by virtually every Latin American government. Many countries' constitutions "guarantee" these as inalienable rights. We have often heard, "We will not rest until every child has access to decent doctors and good teachers." But are health and education really priorities in Latin America and the Caribbean, and are

If Latin America and the Caribbean are to reap the benefits of the life sciences revolution, they must rediscover the importance of science and scientists in development.

School Information and Management Systems. Those who remain functionally illiterate in Microsoft or Linux have a much harder time making a living.

Many bureaucrats and policymakers argue that you can't have it all; either you invest in basic health care and basic education or you shift resources to R&D. This is a false dichotomy. Striving to improve basic health conditions and investing in R&D are not mutually exclusive; on the contrary, they eventually reinforce each other. While this may seem a distant objective in places like Africa or poorer parts of Latin America today, it should be remembered that South Korea had the same income per capita as Ghana in 1960.

If Latin Americans are to reap the benefits of the life sciences revolution, they must rediscover the importance of science and scientists as a key component of development. Development summits, like the recent United Nations-hosted International Conference on Financing for Development in Monterrey, Mexico, will have no impact if science and technology are not at the core of any development strategy.

Patenting knowledge

One good barometer of a country's ability to produce knowledge, apply it and have it generate wealth is its ability to get patents. Unfortunately, Latin America and the Caribbean do not do well by this measure. Of the 13,566 patent applications presented in Mexico in 2001, for example, only 5 percent actually came from Mexicans. From 1997 to 2001, Argentine, Brazilian and Mexican universities failed to obtain even one patent per year, on average, in the United States. Yet over the same period, the Yissum Research Development Company at Hebrew University in Israel was granted 191 U.S. patents. The University of Cali-

priorities in and of themselves enough?

Some have argued that the citizens of economically successful countries simply work harder. That is false. The average Mexican works longer hours than the average Japanese (the average number of hours worked annually in Mexico has increased by more than 100 since 1990). Indeed, throughout Latin America, people are working longer and harder than ever. The key difference is productivity. And productivity depends on whether a country's workers get enough to eat, whether they are healthy, and whether they

understand and have the education to use the dominant economic language.

Investing in public health is essential. But it is not sustainable without parallel investments in science, technology and corporate R&D. A society has to generate wealth to be able to invest more in its human resources. And today, one rarely generates widespread wealth in a knowledge economy without developing a digitally literate population. More than 90 percent of all information produced in 1999 was in digital format, according to the University of California at Berkeley's



The majority of Latin American countries missed the digital revolution. They cannot afford to miss the next revolution, in the life sciences.

California was granted more than 1,800 patents between 1997 and 2000.

This dismal record on patents is not surprising if you consider that Mexico has, for every 1 million people, 214 scientists engaged in R&D, and Argentina has 660 per million. By contrast, Korea has 2,235 and Singapore 2,318. Not surprisingly, the average South Korean worker today earns three times more than the average Mexican (even though as recently as 1975, Mexican workers earned five times as much as their South Korean counterparts).

Increasingly, investments, information technology, patent and licensing activities, and other commercial activities are related to advances in the life sciences. The ability to speak and work with the new language of ATCGs is changing almost every industry throughout the world: agribusiness, chemicals, pharmaceuticals, health provision, insurance, energy and military, among others. Today, most of the patents granted in the United States are related to biotechnology, not information technology or telecommunications.

The majority of Latin American countries missed the digital revolution; they cannot afford to miss the life sciences revolution by betting their future on exporting commodities and cheap labor. Neither countries nor people can continue to do what they have always done without falling further and fur-

ther behind. This does not mean that every country must become a biotech cluster. But what it does mean is that at least some citizens and companies have to be literate in this new language, and the more the better. Every time Latin American countries reduce their already miniscule R&D budgets, they have less chance of participating in the new economy, and it gets harder to improve their long-term economic and social conditions. Mexico decreased its expenditures in R&D from 1985 to 1995 from 0.44 percent to 0.33 percent of GDP. In 2001, expenditures of the National Council for Science and Technology (CONACYT) were cut by almost one-third.

We in Latin America and the Caribbean must generate more knowledge in our own countries and patent more knowledge in the United States and Europe. Lowering inflation and further decreasing public expenditures can help stabilize the Region's economies, but these are stopgap measures that rarely generate much new wealth. Only highly trained individuals can do this rapidly and consistently.

There are three fundamental lessons of the past decades. First, investing in massive natural resource recovery projects is not a path to riches. Consider the oil-rich states of Iran, Iraq, Saudi Arabia, Nigeria, Venezuela, Mexico and the former Soviet Union. Second, countries need to invest primarily in people, particularly in public health and science-based education. Third, science-based literacy has to lead to profitable companies; otherwise incomes and investments in people tend to collapse.

As World Health Organization (WHO) Director-General Gro Harlem Brundtland wrote in the WHO report *Genomics and World Health* published earlier this year: "It is a reality that most genomic and biotechnology research is presently carried out in the industrialized world, and is primarily market-driven. Genomics also needs to

be applied to the health problems of the developing world. It is crucial that we actively seek means to involve developing country scientists in innovative biotechnology."

For Latin America and the Caribbean, the future of public health could become much brighter, and quality of life in general much better, as a result of the life sciences revolution—but only if the Region's countries invest in their people and prepare them, not just to adapt, but to truly capitalize on change.



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Brave New Brazil

When the history of the life sciences revolution is written—sometime later this century—will Latin American and Caribbean countries figure as central characters in the narrative or be relegated to the footnotes? The experience of Brazil suggests that the Region need not be shut out if countries make a concerted effort to invest in R&D.

Brazil in fact has already secured itself a world-class leadership role in the field of genomics. Researchers from a São Paulo consortium became the first in the world, in July 2000, to decode the genome of a plant pathogen, *Xylella fastidiosa*, a bacterium that infects citrus plants. Soon after, members of the same group announced they had successfully mapped some 800,000 human expressed sequence tags (ESTs)—small pieces of DNA sequence—in malignant tumors.



In 2001, scientists at the Brazilian Agricultural Research Corporation (EMBRAPA) became the first in the developing world to successfully clone an animal, a calf named Vitoria. Earlier this year, Brazilian researchers successfully sequenced the genomes of two bacteria of the genus *Xanthomonas* that cause citrus canker and produce substantial economical losses around the world.

Most of these successes can be traced to an initiative of the State of São Paulo Research Foundation (FAPESP) launched in 1997, which created a "virtual genomics institute" linking laboratories and researchers across the state. Initially the network—called the Organization for Nucleotide Sequencing and Analysis, or ONSA—linked some 200 scientists working in 30 research laboratories.

By now, it has expanded to about 400 researchers and 60 labs.

Seed financing for the project came from FAPESP itself, which by law is guaranteed 1 percent of São Paulo's state tax revenues. Funds have also come from the Brazilian citrus growers' association, the Swiss-based Ludwig Institute for Cancer Research, and Brazilian sugar growers (for a project to sequence the sugarcane genome), as well as the U.S. Department of Agriculture and California winegrowers, who contracted ONSA researchers to sequence a strain of *Xylella fastidiosa* that has wreaked havoc on California vineyards.

Recent developments include the expansion of Brazil's cancer genome efforts into a "clinical genome project" focusing on gene expression and its correlation with clinical

evolution, therapeutic response and survival in cancer patients. Also in its final phase is a project to sequence ESTs from the parasite *Schistosoma*, a major cause of illness in South America, the Caribbean, Africa and the Middle East.

All these successes "have boosted the confidence of Brazilian scientists and strengthened this model for organizing collaborative research in the country," says Dr. Marco A. Zago, professor of clinical medicine at the University of São Paulo and an ONSA affiliate. "Obviously this way of using the available resources and distributing acquired competency more efficiently should interest other countries," says Zago, "especially developing countries that need to make the most of their scarce resources."
—the editor

The Future Value of Health

by *Ilona Kickbusch*

In the 21st century, health promotion will find new allies among consumers, communities, even industry. But how will health be seen? As a social resource, a consumer good or the ultimate goal of life?



Will a child born today survive and be a healthy adult in the year 2050? Will he or she live to see the year 2102, when the Pan American Health Organization celebrates its second centennial? What life options and life choices will today's child have in either a resource-poor or a supportive environment? Who decides if he or she will live or die, be healthy or be sick?

It lies in the very nature of health that how we act today defines the future. But what vision of health holds the most promise for the future and should be driving public health actions as we forge ahead?

The answers to these questions are not easy to come by, not only because they entail speculation but also because the context in which we ask them has undergone—and is undergoing—revolutionary change. We can only speculate, for example, on the future impact of the unprecedented progress in

around a much broader question, one that sociologist Ulrich Beck has called the key political question of the 21st century: “How do we want to live?”

The context in which we ponder these and other questions is indeed extraordinary. The changes under way in public health, wellness and biotechnology are all significant enough to warrant the term “revolution.” At the same time, the very nature of our underlying social organization is changing as well, as we move from industrial to knowledge-based societies

Health as a social resource

Revolutions rarely happen overnight; sometimes it is only with hindsight that we realize they have taken place. The two public health revolutions that have changed the face of health and disease in the 19th and 20th centuries are the control of infectious disease through health protective measures and the consequent battle against noncommunicable disease through behavior modification. These have taken place over



health during the 20th century, including extraordinary gains in child survival and life spans. We cannot yet know the health effects of changing family patterns or of the changing nature of work. We cannot fathom the future consequences of the AIDS pandemic, of genetically modified food or of the increasing health gap between countries in different parts of the world.

Yet we can say with certainty that much of future health development will depend on political choices and decisions that reach far beyond the health sector. These choices revolve

characterized by increasing global interdependence.

Although some skepticism is always appropriate when revolutions are declared, it is clear that three seminal social trends will shape the future of health promotion: (1) the epidemiological shift, (2) new economic forces in the health arena and (3) developments in the life sciences. All of these will contribute to a change in our understanding of health and in the strategies we apply to ensure and improve the health of individuals and populations.

several decades. As a result of these revolutions, something momentous has been occurring in many societies: people are living longer and healthier lives, and they are becoming participants in health creation and health decision making. This has led to a new understanding and a new practice of public health.

Today, the Ottawa Charter for Health Promotion, adopted at a conference of the World Health Organization in 1986, is seen as the signal of a third public health revolution. We can now, in the words of social

Our future health will depend in large part on political choices that revolve around the question, “How do we want to live?”

gies have recently been confirmed by two major state-of-the-art reviews on health promotion and health behavior research conducted under the auspices of the U.S. Institute of Medicine in 2000 and 2001. These reports conclude that future action in public health and health promotion must be based on an ecological model and a social environmental approach to health, one that addresses underlying factors that influence susceptibility to a whole range of diseases.

One strategy is to address health

ments now so often required by national and local laws.

A third approach is to recognize that health literacy and social capital are important for societal development and call for investments at the community level. This is reflected in the growing movements for “healthy cities” and “healthy municipalities.”

Much of the future of health promotion lies in the systematic application of all three strategies as they gain increasing recognition and are supported by a mounting evidence base.



epidemiologist Lester Breslow, “turn more attention to the nature of health and regard it... as a resource for living.” We can now focus health promotion strategies on “capacity building for health.” In other words, *empowerment*—of individuals, communities and entire societies—is today the key factor in promoting health.

The Ottawa Charter defines five key action areas: healthy public policy, supportive environments, community action, personal skills and a reoriented health system. Its concepts and strate-

determinants by adding health as a valued resource to existing social organizations through what has been called the “settings approach.” This underlies the promotion of healthy workplaces and healthy schools.

A second strategy is the development of tools and methodologies that address the health effects of policies in areas other than health, holding a wide range of public and private actors accountable for the health impacts of their policies. These would include the use of public health impact statements, akin to the environmental impact state-

Health as an industry

Yet these strategies, like the Ottawa Charter itself, do not take sufficient account of what has become one of today’s most significant social trends: the promotion of health as a product in a growing private market of health goods and services. In this arena, change will be spearheaded by the private sector and by large numbers of individual consumers who will embark on a “wellness revolution.” Increasing

consumer awareness and an increasingly proactive approach to health will open up opportunities for a new type of health industry that will affect almost every aspect of modern life. Its goal will be to persuade people to voluntarily become consumers of “health” in order to feel better, to reduce the effects of aging and to avoid becoming consumers in the “sickness business.”

The goods and services that make up this expanded industry include the fitness market, cosmetic surgery, lifestyle drugs (such as, for some, Viagra) and

vitamins, minerals and health foods. They also include new types of health insurance, which would pay for health services instead of sickness services and reimburse the tools and services this new industry has to offer.

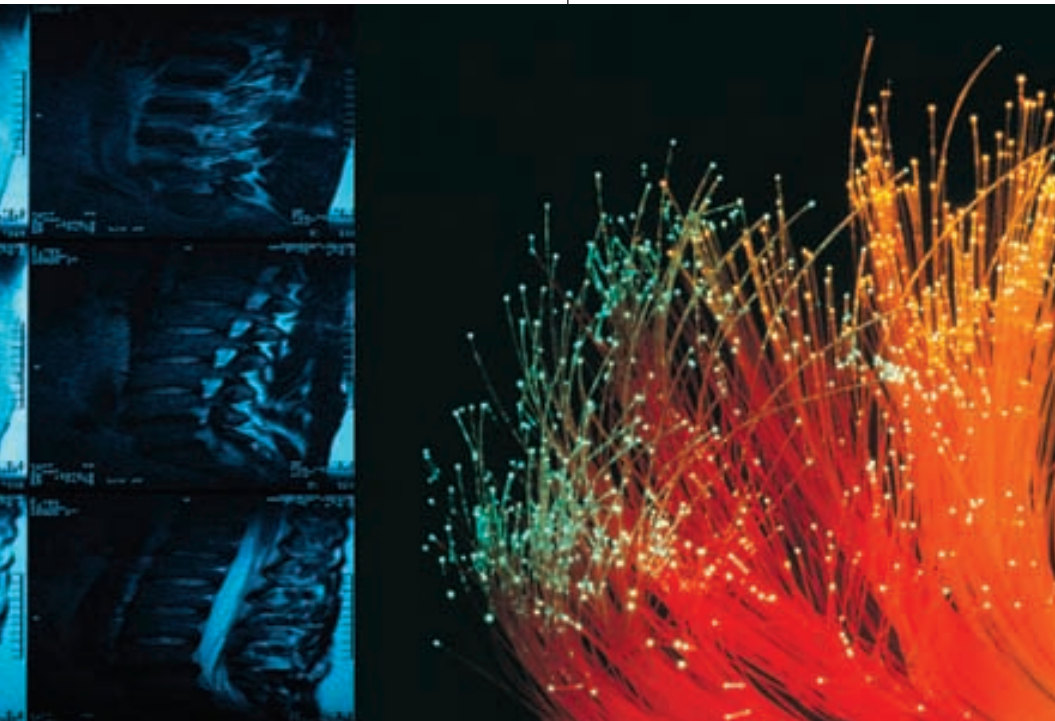
Some U.S. economists already consider the \$1.3 trillion health care industry as one of the few drivers of growth in the years ahead. By 2010, health care is expected to account for 16 percent of U.S. economic output; some say that by 2040, this could grow to 20–30 percent. Calculations

Will the health gap grow, as rich countries embark on a trillion-dollar wellness industry while poorer countries cannot afford basic care?

supplements and product enhancements. In short, health sells. In this perspective, increasing the health literacy of consumers by providing access to information on health and new health products and services lays the foundation for some of the greatest business opportunities of the foreseeable future.

This move toward making health a private, commercial and individual endeavor is an expression of larger trends in modern societies. The wellness revolution places economics as a driving force behind health by making it good business and providing the consumer with products that enhance well-being and quality of life. Unlike industries such as tobacco and alcohol, which require regulation to mitigate their adverse effects on consumers, the new wellness industry fosters a consumer movement toward products and services that create health. As Pilzer suggests, it means we can “fix the problems” using the same entrepreneurial skills that created them.

Yet all this raises serious questions about equity. As the wellness industry booms, the public health sector faces a critical shortage of public funding at the local, national and global levels, and the danger of a widening health gap grows. While the healthy and better off buy an ever-increasing amount of products and services that promote health, cuts in the public sector not only reduce prevention and health education services for the poor (such as



People are increasingly becoming participants in health creation and decision making. This has led to a new understanding and practice of public health.

indicate that in the United States alone, the sales of the wellness industry have already reached approximately \$200 billion and that it is set to achieve sales of \$1 trillion within 10 years. In his book *The Wellness Revolution*, P. Z. Pilzer defines health as “the next big thing of the 21st century... which promises to revolutionize our lives and offers opportunities for tremendous wealth building over the next 10 years.”

For many existing industries, health has become an “active added value” either as a sales pitch or in the form of

nutrition education) but also weaken public safeguards on harmful goods and services (such as access to and advertising of soft drinks and junk food in U.S. schools).

The debates around access to healthy nutrition, on the one hand, and safe food, on the other, in view of rising obesity and increasing food-borne illnesses will be one of the big public health battlegrounds of the future—but these will also provide a unique opportunity for combined public and private sector action on health. A key challenge to the future of health promotion will lie in devising strategies for harnessing the private sector for population health without increasing inequalities by making health a strictly individual concern, defined as a private good with no social dimensions or responsibilities.

Health: the ultimate value?

As health has become one of the defining dimensions of modern societies, an increasing number of social issues are being defined in health terms and addressed through the health system. In some areas, such as rape and other types of violence, this is a welcome trend, one that can promote a more victim-friendly response.

But in other areas, the trend is more dangerous, leading us to take a standard medical approach to social adjustment and social functioning, often responding with neuropharmacological solutions. Particularly in the broad area of mental health, the line between prevention and treatment, between social norms and medical prescriptions, is ever more difficult to draw. The extensive use of Ritalin to treat U.S. schoolchildren is a case in point.

Even addressing social determinants may take health promotion into the realm of social control. Many public health strategies must constantly strive

Health should be seen as a resource for living and a process toward empowerment, not as an ultimate goal in itself.

to achieve a balance between ensuring population health and providing choices. Indeed, the human capabilities approach—as advocated by the philosopher Martha Nussbaum—states explicitly that the individual must have the freedom to choose not to function.

The larger question, both in the domain of public health and in the health marketplace, will be what social, political and financial price we will be willing to pay for better health, individually and as a community, at both the local and global levels. Although it may seem benign to buy better health by joining a fitness club or choosing nutritional supplements, can the same be said of buying healthier and better children? Although it seems appropriate to strive for more health, should we not also critically consider the limits of this quest? Pilzer's list of the components of the nascent wellness industry includes genetic engineering, under which he classifies sex selection and fertility enhancement.

In his analysis of the consequences of the biotechnology revolution, Francis Fukuyama points out that genetic engineering presents a challenge not only to our assumptions about human nature but also to democracy, which is premised on the notion that all are created equal. What if, in an unregulated

marketplace, I have the means to buy my (perhaps sex-selected) child more intelligence through genetic engineering, instead of having her coached by expensive consultants for her college admissions tests? What new inequalities will we add to the great health divide as one part of the world embarks on a trillion-dollar wellness industry while the other cannot afford basic primary care?

These examples indicate that the future of health promotion lies in areas of social, economic and scientific development that the Ottawa Charter was not able to consider. But the charter can bring a vision and orientation to these new debates that is deeply humanitarian and equity oriented, and which is firmly rooted in the U.N. Declaration of Human Rights. Health promotion has always maintained that health is a social concept, a process toward empowerment—not an ultimate goal in itself.

The possibilities for improving public health are great as we enter the 21st century. But the task of improving people's control over their health is more difficult and forces us to ask tough ethical questions about health and its role in modern society. The answers will not be obvious or easy under the pressure of new markets and new technologies. Health promotion must be willing to question the value of ultimate health, just as the savage in Aldous Huxley's *Brave New World* questions the value of a life without disease, death and pain because it would deprive him of compassion, joy and human dignity.

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