C V I F O R U M

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Doubt over measles targets prompts new vaccination strategy

Infants under one year of age who survive acute attacks of measles have a higher risk of dying during the nine months after the attack.

December 31, 1995, is still 18 months away but it is beginning to loom large at WHO's Expanded Programme on Immunization (EPI). It is, among other things, a day of reckoning for measles, which kills more children than any other vaccine-preventable disease. It is the day when these deaths are supposed to be down by 95% compared with the estimated 7-8 million a year two decades ago, according to targets set by world leaders at the 1990 World Summit for Children. Numbers of cases, too, should fall by 90%, according to these targets.

For good measure, the EPI itself added two more targets: a reduction of the proportion of deaths among infected individuals – the so-called case-fatality rate – to less than 1% in all countries and immunization of at least 90% of children in their first year of life in all communities, districts and countries of the world.

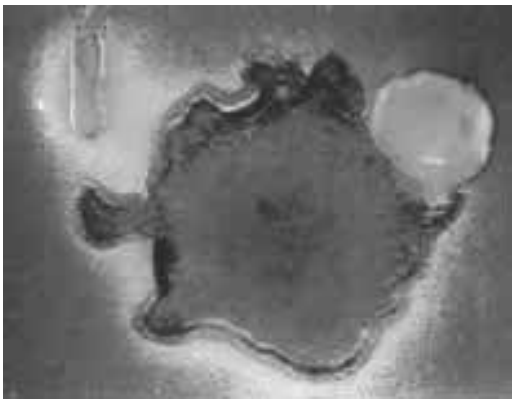
"We've a good chance of making the mortality target," says Medical Officer John Clements, who has been managing EPI's measles control efforts for the past two years. "Bringing down the numbers of cases is going to be much harder," he adds ruefully. "Without a special effort, many countries are just not going to make it."

His optimism about meeting the mortality target rests largely on a decline in estimated annual deaths over the past 20 years to a 1993 low of 1.1 million – a fall of around 85%. Of these deaths, 98% occur in developing countries.

The decline in measles deaths is also reflected, Dr Clements notes, in declining case-fatality rates. In the 1970s, a child living in a developing country and infected with the measles virus had an estimated 7% risk of dying from the infection. Today, the highest case-fatality rate, 6%, is reported by only 15 developing countries, 14 of them in sub-Saharan Africa (the 15th is Afghanistan). True, of the 157 developing countries or territories reporting cases and deaths to the EPI, only one, Singapore, has reached the under 1% EPI case-fatality rate target. But 86 of them, nearly all in the Americas, Eastern Mediterranean and Western Pacific, report rates between 1 and 2%.

Dr Clements' optimism about mortality targets is tempered, though, by two reservations. One is that "our baseline pre-immunization estimates of seven to eight million are just that, estimates, and so are our current data for deaths. We are confident our global estimates are correct. When it comes down to individual countries, we are less certain."

The other is that in recent years evidence from developing countries, particularly in Africa, has emerged that infants under one year of age who survive acute attacks of measles have a higher risk – twenty-fold higher in at least one study – of dying during



Len Sirman Photos

The measles virus.

Cover photo: UNICEF/ Sean Sprague

UNICEF/Jorgen Schytte

This Mozambican child receiving a measles shot has a good chance of not adding to the world's current toll of over a million measles deaths a year.

the nine months after the acute measles attack than infants who have never had measles. For children between one and two years of age, the risk of delayed measles mortality is also higher, but "only" about six-fold. Delayed measles mortality rates for under one-year-olds can be up to 300% higher than acute mortality rates, according to this same study, and up to 50% higher for the one-to-two-year-olds. "If this is the case," comments Dr Clements, "it suggests that measles is an even deadlier disease than we thought."

As for numbers of cases, currently estimated at 45 million a year, the target of a 95% reduction is unlikely to be met on time. Worldwide, current figures represent a drop of only 65% compared with the 130 million cases annually in pre-immunization days. However, 84 (43%) of the 195 countries and territories in the world reporting to EPI have already reached the target, 28 of them in Africa. Fifty-two countries – 42 in the developing world, including six in Africa – have even slashed case numbers by 95% or more compared with a 1975-1977 estimate (although 27 countries, all developing, have more cases than in the mid-1970s, seven of them showing increases of over 200%).

Targets or no targets, progress has been "impressive", Dr Clements says. Measles, he points out, "has virtually disappeared from much of the Americas". And, according to UNICEF estimates, nonfatal episodes of measles – associated with subsequent malnutrition, pneumonia, diarrhoea, vitamin A loss, blindness and deafness – have plummeted from about 75 million to about 25 million cases.

These achievements are due to the immunization programmes supported largely by the EPI and UNICEF over the past two decades. Today, thanks to these programmes, 78% of children under one year of age have been vaccinated against measles vs. 13% a decade ago.

Nevertheless, raising the immunization coverage rate to the 1995 target of 90% is going to be difficult. The global coverage rate has even fallen slightly, to 78%, from the 80% peak of 1990. It is true that 24 countries – 15 in the developing world – have coverage rates over 95%, but in some areas, coverage remains low: 18 of the 46 African countries, for example, have rates under 50%. In the view of Dr Jong-Wook Lee, head of the new Global Programme for Vaccines and Immunization (GPV), of which the EPI is a part (see page 13), "early successes...led some countries to let their guard down [and] donors' interest and support began to wane".

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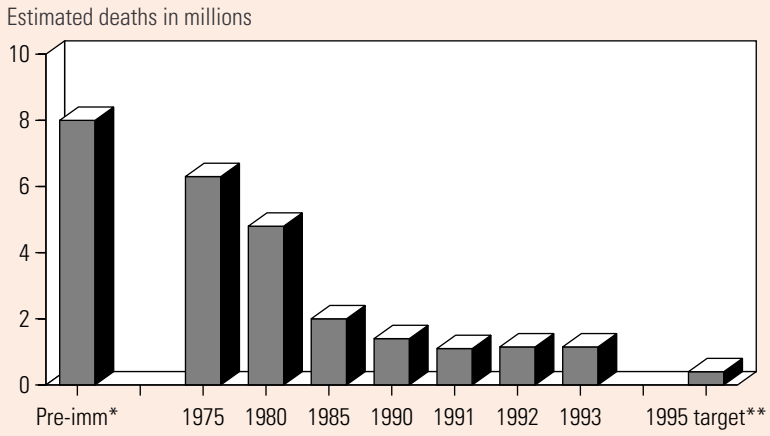
Reasons for low vaccine coverage vary from place to place, notes epidemiologist Harry Hull, who heads the GPV's Disease Control Task Force. They include a mix of inadequate funds, poor health service infrastructure, ineffective case surveillance, a high level of "missed opportunities" and lack of political commitment.

But in some places, even reaching the 90% coverage target may not be enough to bring case numbers down to the 1995 target. "The current measles vaccine is excellent," says Dr Hull, "but not perfect. At best it protects 80-85% of children against measles when administered before the age of 12 months. Given the extreme infectiousness of the virus, in areas of intense measles transmission the 15-20% of children who are not protected by vaccination could be a source of further outbreaks." Giving a second dose of vaccine to older children entering school would help to solve this problem. Indeed, a two-dose policy has been adopted by a number of developed countries, including Bulgaria, Czechoslovakia, Denmark, Finland, Israel, the Netherlands, Norway and Sweden. But for developing countries, where large numbers of children die from measles in their infancy, giving a second dose of measles vaccine to children entering school would have little impact on the disease.

One major drawback of the current vaccine is that its protective efficacy is neutralized by anti-measles antibodies that babies acquire from their mothers before birth. By nine months of age most children have lost enough of these antibodies to allow the vaccine to exert its protective effect. This is the age at which measles vaccination is recommended for children in developing countries. But even before nine months, maternally acquired antibodies have fallen to low levels in many children. In areas of intense measles transmission, these unprotected children run a high risk of potentially fatal measles infection. In some parts of Africa, for example, one-quarter to one-third of children under nine months of age contract measles. In such areas, immunization programmes are on the horns of a dilemma: if they vaccinate at six months, they protect children whose maternally acquired antibodies have fallen to low levels but they increase the numbers of vaccine failures in children with still too high levels of antibodies. In places where the infection is rampant, some programmes resolve the dilemma by

In some places, even reaching 90% coverage may not be enough to bring case numbers down to the 1995 target.

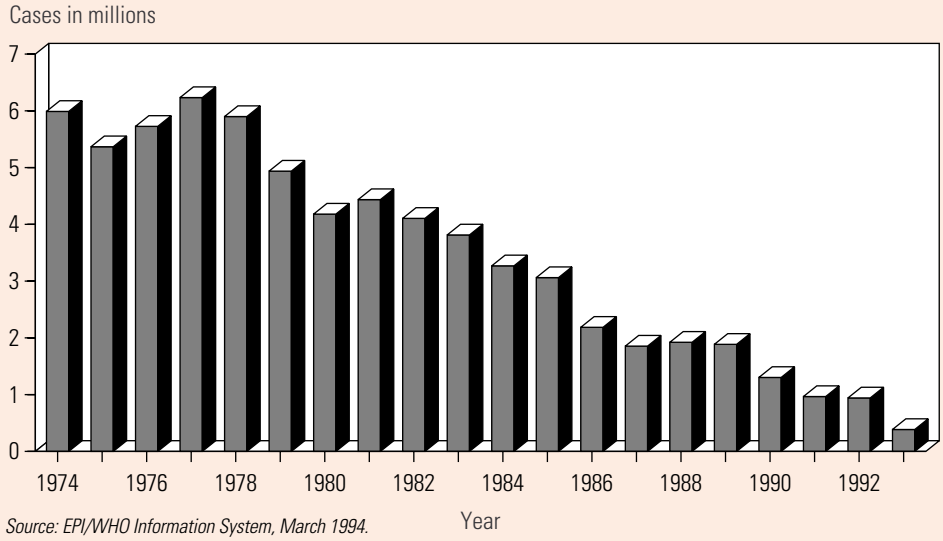
Progress towards reaching the 1995 global goal of 95% reduction in estimated measles deaths



**Pre-immunization rates of measles deaths applied to projected 1995 population statistics*

***95% reduction target applied to projected 1995 population statistics*

Number of cases of measles reported globally 1974 to 1993



Source: EPI/WHO Information System, March 1994.

vaccinating at six months and giving a second dose at 12 months to catch non-responders to the first vaccination.

There is an additional drawback, however, to waiting even six months before giving the measles vaccine. All the other EPI vaccines – against tuberculosis, diphtheria, tetanus, pertussis and polio – are generally given between birth and 14 weeks of age. "Many mothers in developing countries," notes Dr Hull, "have difficulty bringing their children back for any kind of immunization six months after childbirth." In fact, the EPI "loses" about 25% of children between their last regular immunization session at three-to-four months of age and their scheduled measles vaccination at six-to-nine months.

Jean-Marc Olivé, who is responsible for the measles control activities of the Pan American Health Organization in Washington, D.C., dreams of a better vaccine. "One that could be given just after birth. And that could be given orally, like the polio vaccine, so that it could be administered easily by volunteers in immunization campaigns, without the costs and risks of injection. And that could withstand heat and not require a costly, complicated cold chain." Development of such a vaccine is a high CVI priority and research on at least two promising prototypes is under way. But it is early days yet.

For Dr Olivé, though, waiting for a better vaccine is not the answer. "Our current vaccine is enough. It's a superb vaccine. And we have evidence from the Americas that, used properly, it can make a profound impact on numbers of cases and deaths from measles." Used properly, this vaccine, he believes, could still bring all the 1995 targets within reach.

To help define just what "properly" means, the GPV and the CVI organized last April a meeting of experts in Washington, D.C. They recommended that the EPI's single-minded attempt to deliver one dose of measles vaccine to every child should give way to a more flexible, multi-pronged strategy adapted to differing local circumstances. This strategy calls, among other measures, for mass vaccination campaigns at

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Measles: not to be taken lightly

For many people in the industrialized world, measles is just another of those annoying but not too serious diseases that children catch at school: a bit of fever, a few spots, a cough, a sniffle, and that's it.

What makes measles dangerous, though, are its complications. The list is long and daunting: diarrhoea, pneumonia, otitis media, blindness, encephalitis and laryngotracheobronchitis. In developing countries, according to UNICEF data, these complications occur in up to 80% of children with measles, causing up to 40% of deaths in children under five years of age. But they are by no means rare in developed countries, where they occur in as many as 10% of children with measles. In the United States, for example, during the surge in measles that occurred in 1989 and 1990, 9% of the 46,000 people who came down with the disease developed serious complications requiring hospitalization and 130 of them died. More than half of the measles cases were in school-age children and about a third in pre-school-age children. Otitis media and diarrhoea accounted for 71% of the complications. In 90% of the measles deaths, the victims had not been vaccinated – despite a vaccine coverage rate at that time of over 95% for the United States as a whole.

Recovery from measles, though, does not end the risk of complications. In developing countries, there is evidence of increased mortality in children over the nine months following an attack (see text). And in developed countries 1 in 100,000 children who have come down with measles risk a fatal degenerative brain disease called subacute sclerosing panencephalitis that can develop years after the original attack.

The moral? Don't underestimate measles wherever you live. And vaccinate your children. For WHO, measles vaccination is one of the most cost-effective public health interventions available today.

"When the world decides to put enough effort and resources into controlling measles, we can start making plans for eradication."

least once every year or two years in areas with intense measles transmission or with immunization coverage levels under 80%, whether or not this means vaccinating children who have already received a first dose of vaccine. It calls for mass vaccination of children living in ideal conditions for measles transmission – densely populated urban slums, refugee camps, war zones, schools, hospitals, even health centres. It calls for more effective monitoring of outbreaks. And it calls for better treatment – including administration of vitamin A, which can halve deaths from measles.

Is there enough vaccine available to do the job? GPV's Vaccine Supply and Quality Unit says vaccine manufacturers have the capacity to increase production but need a year's notice to do so.

Are the funds available? To raise vaccine coverage rates from the current 78% to 90% would cost US$8-10 million for the vaccine alone, the EPI estimates. Plus about the same amount for delivery, logistical and other costs. Plus mass immunization campaigns, which cost about 50-75 US cents a child.

Who will pay? WHO, UNICEF and other CVI partners agreed at the Washington meeting to put their fund-raising efforts into high gear for the new measles strategy.

Reaching the 1995 targets is, for Dr Hull, a first step on the road to eradication of measles.

"This first step is one of controlling the disease, bringing down the numbers of deaths and cases."

The second step is elimination, whereby local transmission of the infection ceases and the only new cases are those imported from outside a country or area. The English-speaking Caribbean countries have declared their intention to eliminate measles by 1995, the Central American countries, by 1997 and WHO's European Region, by 2000. As more and more countries in more and more areas enter the "elimination mode" over the next ten years, eventually, says Dr Hull, these areas could move into a global eradication mode.

He is confident that, although "we're not yet thinking seriously about it", eradication is possible. Part of the problem, he says, is epidemiological. The virus is one of the most infectious pathogens around. It thrives in densely populated urban environments, and the world is becoming increasingly urban. Its weak point is that it has only one host: man.

Part of the problem is also political. "When the world decides to put enough effort and resources into controlling measles, we can start making plans for eradication."

Where there's a will ….

A Forum brief on… nucleic acid vaccines

Transferring foreign genes into human cells for vaccination purposes – known scientifically as "nucleic acid vaccination" – is being acclaimed as "one of the hottest areas of vaccine research", "one of the most exciting new developments in vaccine science", "the biological equivalent of cold fusion". A meeting held last May at the Geneva headquarters of WHO confirmed current interest in the subject among vaccine researchers and manufacturers.

Q *What is nucleic acid vaccination?*

A It is a new method of vaccination that consists of taking a gene – a segment of the nucleic acid DNA, for example – from a disease-causing virus or bacterium (*pathogen*) and injecting it into the person to be vaccinated in such a way that the person's cells produce a vaccinating molecule (*antigen*) and so provoke a protective immune response against future infection by the pathogen.

Q *You mean the person's body produces its own vaccine?*

A In a sense, yes. The gene gives the body instructions on how to produce its own protective, vaccinating molecule against a disease.

Q *How does the technique work?*

A The gene chosen for the procedure is one that codes for an antigen known to stimulate protective immunity. Once inside a host's cell, the gene makes the cell produce the antigen. The host's immune system recognizes the antigen as foreign, mounts an attack to block or destroy it and at the same time puts its "armed forces" – antibody-producing cells, killer cells, etc. – on alert against future infection by the pathogen. And the host is protected against the disease.

Q *Are nucleic acid vaccines ready for use in human subjects?*

A No. The technique has so far only been carried out in animals – mice, rats, ferrets, rabbits, dogs, cattle, chickens, fish, monkeys and chimpanzees.

Q *How promising have the results been so far?*

A Prototype versions of nucleic acid vaccines using DNA or RNA, the other nucleic acid that cells use to make a "working copy" of DNA, have provoked the two main types of immune responses needed to protect against most infections, antibody and cellular responses. In mice, these responses were still detectable up to 19 months after a single, minute dose of nucleic acid.

Q *But have nucleic acid vaccines actually protected animals against disease?*

A Yes. They have given some degree of protection in animals against influenza, malaria, tuberculosis and leishmaniasis and have produced promising immune responses against hepatitis B and SIDS, the monkey equivalent of AIDS.

Q *Can a single injection protect against several diseases?*

A In principle, yes. Part of the excitement over nucleic acid vaccines is their potential to carry a large number of foreign genes and to have the recipient cells produce many antigens against many different diseases. And that's one reason for the CVI's

Part of the excitement over nucleic acid vaccines is their potential to carry a large number of foreign genes.... And that's one reason for the CVI's interest, since it fits in with the CVI's ultimate goal of a single vaccine for all major childhood diseases.

interest, since it fits in with the CVI's ultimate goal of a single vaccine for all major childhood diseases. But we're still in the early stages of work on this new vaccination approach. So far, in the different animal experiments, the technique has been used to insert only a single gene coding for a single antigen. That's step one and it's showing immense promise.

Q *How is the vaccination procedure carried out?*

A Suppose you want to make a nucleic acid vaccine against malaria. You take from a malaria parasite's DNA a gene that codes for a protein known to stimulate immunity. You stick that gene chemically onto a piece of bacterial DNA and add on the other bits of DNA – so-called promoters, activators, enhancers, and so on – needed to switch on the gene and keep it switched on. You then simply inject this DNA package (*construct*) into the host's muscle tissue. Within a few days you'll find the malaria protein in the host's cells, as well as antibodies and immunologically competent cells specifically directed against the antigen. And if you challenge the host with malaria parasites, the chances are it will be protected against the infection.

"It's not so much a revolution as a step forward in vaccine technology."

Q *Why use bacterial DNA?*

A The bacterial DNA is just a vehicle or backbone on which you can stick genes and shuttle them into cells. It is not chromosomal DNA, but a strand of circular (*plasmid*) DNA, which bacteria use, among other things, to transfer genes – particularly drug-resistance genes – among themselves. And bacterial DNA is inert in mammalian cells: it only replicates in bacteria.

Q *Why inject the DNA into muscle rather than other tissues?*

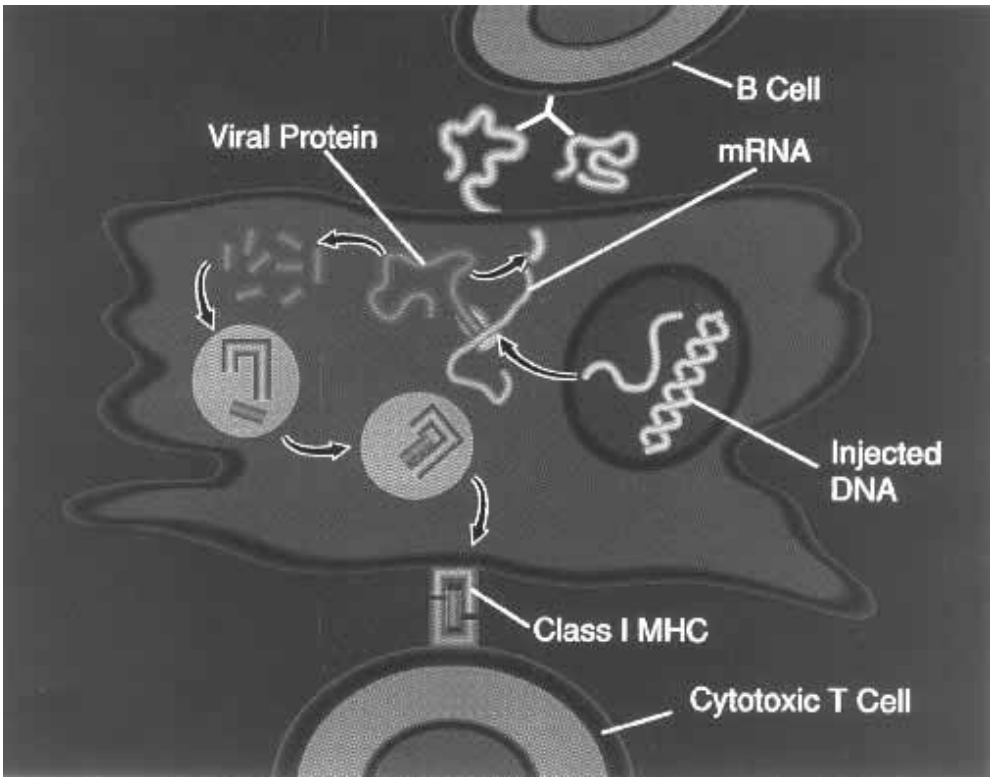
A Other tissues have been tried but so far muscle cells – either skeletal muscle, as in the arms or legs, or heart muscle – and skin cells seem to express the foreign gene best, giving the largest quantities of vaccinating antigen in stable amounts for the longest period of time. The cells secrete the vaccinating antigen into the bloodstream, where it is carried throughout the body.

Q *Is injection the only way to administer this vaccine?*

A No, the DNA can be coated onto tiny gold particles that are "shot" into skin cells using a special DNA "gun", and the results are almost as good as with intramuscular injection. The foreign gene is expressed by cells far from the site of the injection. Other methods involve linking the DNA to fatty substances called cationic lipids and administering them by aerosol into the nose or throat, routes that could be useful for vaccination against respiratory infections. The same DNA-lipid complexes have been given intravenously or intraperitoneally with some success.

Q *What is revolutionary about nucleic acid vaccination?*

A It's not so much a revolution as a step forward in vaccine technology. Vaccines in use today fall into four main groups. First there are those using whole live bugs – viruses, bacteria, parasites. The second group uses whole bugs weakened (*attenuated*) to reduce the risk of side-effects but not their immune-stimulating activity. Then there are vaccines using bugs that are totally inactivated or killed but whose molecular structures are recognized and attacked by the immune system. And fourth, thanks to modern molecular immunology and biology, there are now vaccines that contain only those bits (*subunits*) of bugs – their antigen molecules or the antigenic structures (*epitopes*) on the molecules – needed to produce a protective immune response.



Courtesy Donnelly, Ulmer and Liu, Merck Research Laboratories

Schematic representation of how nucleic acid vaccination works. A segment of nucleic acid, here DNA, that codes for proteins* (antigens) *belonging to a viral pathogen is injected into human tissue and finds its way to nucleus of a cell. There it is copied* (transcribed) *onto another nucleic acid, RNA, which is "translated" in the cytoplasm to produce the viral protein antigens. One type of antigen is then broken down inside the cell by enzymes and carried to the cell surface by special molecules* (MHC Class I molecules) *that "present" the antigen to killer immune cells* (cytotoxic T cells). *Other antigens are transported intact to the cell surface where they stimulate another type of immune cell, a B cell, to produce antibodies against the foreign proteins. The immune system "remembers" this two-way stimulation and responds quickly if the real virus and its proteins show up.

With all these vaccines, you're giving the body a ready-made antigen – giving it a controlled infection, as it were – and telling the immune system to wake up, pay attention and remember the antigen for future reference. With nucleic acid vaccines, you're giving the body the genetic information to make its own antigen. Strictly speaking, you're not infecting the body but, as it is scientifically termed, "transfecting" it with a foreign gene.

There's a fifth type of vaccine that goes a step further – recombinant vaccines. These consist of attenuated bacteria or viruses into whose genetic fabric *(genome)* one or more genes coding for the desired antigens have been spliced. When such bacterial "vectors" infect the body, they express the foreign genes and produce the vaccinating antigens. Viral vectors go right inside the host's cells and take over their genetic machinery so that they produce the proteins coded by the virus' own nucleic acids and by the "cuckoo" DNA it is carrying.

Q How is this viral vector technique different from nucleic acid vaccination?

A With viral vectors, you're still infecting the body with a whole foreign organism, even though you're only using the virus as a guided missile to carry genetic information into the body's cells. So it does closely resemble the nucleic acid technique. But nucleic acid vaccination crosses an important demarcation line in that it altogether avoids introducing infectious organisms into the body. The DNA is both vector and source of the antigen. And it's pure – or "naked", as some people have called it. It contains only instructions for producing a vaccine, without all the extra information carried by a whole virus, even one that's been deprived of its potency and replicating ability.

Nucleic acid vaccination crosses an important demarcation line in that it altogether avoids introducing infectious organisms into the body. The DNA is both vector and source of the antigen.

Q *What will the practical advantages of nucleic acid vaccines be compared with other vaccines?*

A If this new approach fulfils its promise, we can hope for many advantages. It should avoid, for example, the risk of side-effects – including unwanted immune reactions – associated with whole organism vaccines or vaccine vectors, particularly viruses used as vectors which have their own genes to express.

Also, the antigen produced by the transfected cells is the body's own "product", so it is more likely than the antigens on subunit vaccines to have the right molecular shape and chemical "packaging" to produce a strong, protective immune response.

And third, nucleic acid vaccines consist of pure DNA and don't require all the expensive, time-consuming purification steps needed to produce whole-organism or subunit vaccines.Nor do they require the oil emulsions and other accompanying substances needed for subunit vaccines. So, they should be quicker and cheaper to make.

It does look as if we've found a way of bringing the CVI's one-vaccine-for-many-diseases vision a little closer to realization.

Q *Any drawbacks with this new technique?*

A So far, in the animal studies that have been carried out over the past couple of years, the only problems have been instances where the plasmid DNA hasn't produced enough antigen or where the results have been highly variable between different animals. But no adverse effects to date.

Q *Are there any fears, though, that side-effects or other problems could occur?*

A Nucleic acid vaccination is a gene transfer technique, involving genetic manipulation. And tampering with genes raises all kinds of fears and fantasies in the public mind, from talking tomatoes to resuscitated dinosaurs. Don't forget, it's taken 50 years for gene therapy to go from the lab to early human application. No doubt, nucleic acid vaccination will have to run a fairly stiff regulatory gauntlet.

Q *What kind of scientific doubts does the technique raise?*

A One question is what happens, in the long run, to the foreign DNA in the host's body – especially as the transfected cells seem capable of expressing the DNA for relatively long periods. Could it be integrated into the genomes of some individuals, alter the genetic workings of their host cells and turn on genes that are better left dormant, such as oncogenes with their cancer-causing potential? Or could it turn off genes that suppress this potential? And could the foreign DNA itself – as distinct from the antigen it codes for – provoke an immune or auto-immune response?

Q *Are there any answers?*

A From mice to men is a big step, but so far there is no evidence to support or confound these fears. In animals studied to date the plasmid DNA does not replicate and is not integrated by host cells into their genomes. As for causing immune or auto-immune reactions, DNA itself is a poor immune stimulator and unlikely to provoke the formation of anti-DNA antibodies.

Q *How does the CVI view the advent of nucleic acid vaccines?*

A As a door that has opened in vaccine science. We don't know at this stage if we will find a real Pandora's box of possibilities on the other side. But it does look as if we've found a way of bringing the CVI's one-vaccine-for-many-diseases vision a little closer to realization.

A Moroccan priority – making success sustainable

Morocco's national immunization programme is the pride and joy of the health ministry. For the ministry's Secretary General Abderrahmane Zahi, "it is a spectacular programme, a complete programme. It is the first Moroccan health programme to involve the entire country. It is everybody's programme."

UNICEF/Amy Zuckerman

A mother comforts her child who is about to be vaccinated in a Moroccan national immunization campaign.

The results, it is true, speak for themselves. Coverage of under-five-year-olds with the major children's vaccines is up from 40% in 1986, a year before the programme began, to 91% for 1993. Figures for the individual vaccines are also high: 93% for tuberculosis (vs. 87% for the region and 85% for the world), 87% for diphtheria-pertussis-tetanus (vs. 76% and 79%), 87% for polio (vs. 76% and 80%), 82% for measles (vs. 75% and 78%). Immunization of pregnant women with tetanus immunization is the only blemish on the list, with 34% (vs. 40% and 43%).

Disease incidence has nosedived for pertussis (from 1,078 cases in 1987 to 43 in 1992), measles (26,621 to 6,008) and tetanus (189 to 49). And in 1992, there were no cases of diphtheria or polio (last heard of in 1989).

So successful has the programme been that the ministry is using it as model for other programmes about to be launched – family planning, safe water and sanitation, and diarrhoea.

Dr Zahi believes the programme's success is the result of its efforts to mobilize "our entire society" – the media, health care

"It is a spectacular programme, a complete programme. It is the first Moroccan health programme to involve the entire country. It is everybody's programme."

IN A NUTSHELL	
Population (estimate 1993):	26 million
No. of births a year:	666,000
Infant mortality rate (<1 yr):	57 per 1,000 live births
Child mortality rate (<5 yr):	76 per 1,000 live births
% of 1-yr-olds fully immunized (1992):	78
% of national budget for health:	5
Human development rank:	111
Main immunization thrusts:	Polio, neonatal tetanus, measles
Major health problems:	Poorly accessible rural areas
Major ongoing health measures:	Reach and sustain >90% immunization coverage of <1-yr-olds and >80% of pregnant women with tetanus toxoid

"The national campaigns... have enjoyed the active support of the King and... have been crucial to making immunization a national priority."

Abderrahmane Zahi

professionals, politicians, rural communities. This "social mobilization" is in turn, he says, the result of the programme's emphasis in recent years on immunization campaigns, both national campaigns and "mini-campaigns" in geographically more remote areas. The national campaigns, begun in 1987 and organized since 1989 with the other member-states of the Maghreb Arab Union – Algeria, Libya, Mauritania and Tunisia – have enjoyed the active support of the King and, says Dr Zahi, "have been crucial to making immunization a national priority."

They have been costly, though, involving some 4,000 immunization teams, 4,000 vehicles and 28,000 health workers to staff the country's 12,000 vaccination posts. For this reason and the fact that some population groups remain out of reach, the ministry is now building a more permanent, "sustainable" health system, with a mix of fixed and mobile services.

An additional boost to the immunization programme is its recent adherence to UNICEF's Vaccine Independence Initiative, whereby the Moroccan Government buys all its vaccines through a revolving fund supported by the United States Agency for International Development. All part of a current thrust, says Dr Zahi, "to build on and go beyond the immunization programme's success story".

"Dream manager"

An interview with Jong-Wook Lee

Openness. Participation. Cohesion. Who could find fault with a management style embracing these principles? Certainly, when Jong-Wook Lee slides into a chair to answer questions about his plans as the CVI's first Director – if only Acting Director for the moment – and the first Director of WHO's brand-new Global Programme for Vaccines and Immunization (GPV), there is a frankness and easy-going efficiency about him that gives credibility to his quest for openness.

Jong-Wook Lee

As for participation and cohesion, "I want everyone working for these programmes to feel a sense of participation, of belonging," he says. "And I want both to run in a tighter, more streamlined manner."

Certainly, teamwork and cohesion are needed, he says, for a programme like the GPV that spans such a wide range of activities, from vaccine research and development through supply and quality assurance to vaccine delivery in the field and disease control.

For his CVI role, Dr Lee adds a fourth principle: "Facing reality". His eyes crinkle into a disarming smile: " My job, as I see it, is to bring the CVI vision down-to-earth so that it will be grounded in the real world."

Dr Lee is Korean and has worked in the Western Pacific since joining WHO in 1983. Over the past four years he headed the disease prevention and control activities of WHO's Regional Office for the Western Pacific in Manila, Philippines. As leader of a task force on polio eradication in the Western Pacific, he earned a reputation as an ardent "polio devotee".

To the exclusion of all else? "Not at all," he demurs. "As GPV Director, my top priorities for disease control are neonatal tetanus and measles – as well as polio, of course." For the CVI, his two immediate priorities are

"Finding more than US$1 billion to meet short-term needs over the next ten years ... should bring us close to achieving the CVI's single-vaccine goal and should make the CVI a force to reckon with."

"Running teams is my forte. With the CVI, I'm going to have to run dreams. To make them real. To make them work."

"getting the funds to pay for the dream" and "putting some sound management principles" into the running of the initiative.

Paying for the CVI dream, Dr Lee says, means finding more than US$1 billion to meet short-term needs over the next ten years. "That should bring us close to achieving the CVI's single-vaccine goal and it should make the CVI a force to reckon with." Right now, to get the initiative off the ground, he reckons that US$200 million is needed, of which US$10 million for the global coordinating activities of the secretariat in Geneva. "What we have now is just US$100 million."

His second CVI priority is "streamlining the mode of working of the organization". Up to now, he says, the CVI has been "a loose alliance of activities and programmes". He plans to bring these activities and programmes into a "more cohesive, coordinated whole."

In practice, this will mean forging closer working relationships between the CVI's operational units – its Task Forces and Product Development Groups. "Up to now, these units have been operating successfully, but independently. I would like to see frequent, regular meetings and open discussion between them. And I would like all the members of these units to feel that they belong to the CVI, whatever their everyday professional allegiances."

It will also mean "eliminating gaps and overlaps" , as Dr Lee puts it, between the GPV and the CVI. As current head of both programmes, he sees himself in an ideal position to broker "an efficient working marriage" between the two, with a sharing of the same governing and technical bodies.

How does Dr Lee, whose GPV/WHO hat sits squarely and firmly on his head, see his more tentative CVI role in relation to the other sponsoring agencies – UNICEF, the United Nations Development Programme, the Rockefeller Foundation and the World Bank?

The GPV, Dr Lee points out, although created within WHO as a WHO programme, is slated to become a "special programme" with many different sponsors. "It will never have the broad umbrella scope of the CVI, but it will have a firm budgetary basis and will itself provide funds to the CVI." His GPV role, he says, "is to open the new programme to the outside world and to the CVI in particular, to ensure that it becomes a major partner within the CVI." He wants the GPV to provide the expertise and technical input needed by the CVI, while keeping its sights firmly on the CVI's long-term visionary goals, "without forgetting the more immediate needs of countries to control and eradicate disease".

His CVI role, he says, is to "provide a management base for the CVI's working units and ensure that there is an efficient two-way communication between them and the different working parts of the GPV". This, he adds, will mean dealing with "everyday problems that call for everyday solutions" and are on a different plane from the overall guidance provided by the CVI's sponsoring agencies through its governing bodies.

Dr Lee gazes for a moment at the shadows of the trees playing on the window blinds. "You know, running teams is my forte. With the CVI, I'm going to have to run dreams. To make them real. To make them work."

MEETING CALENDAR

3-6 September 1994
Le Bischenberg

European Science Foundation: therapeutic immunomodulation – tolerance induction in the adult, means and mechanisms

Centre d'Etudes et de Formation, 17, rue Raiffeisen, B.P. 79, Bischoffsheim 67210, Obernai, France.
Tel: (33) 88.76.71.35;
Fax: (33) 88.36.69.87

14 September 1994
London, UK

British Society for Parasitology Autumn Symposium: parasite vaccines

Dr H. Hurd, Centre for Applied Entomology and Parasitology, Dept of Biological Sciences, Keele University, Keele, ST5 5BG UK

1-5 October 1994
Banff, Canada

2nd international cytokine conference

Convention Dimensions, 5050 Pare, Suite 202, Montreal, Quebec, Canada H4P 1P3. TelL (1-514) 344-1818;
Fax: (1-514) 344-1565

3-6 October 1994
Paris, France

Annual meeting on molecular biology of hepatitis B viruses

Mme Claude Volkerick, Institut Pasteur, 25 rue du Dr. Roux, 75724 Paris Cedex 15, France.
Tel: (33-1) 45-68-82-72;
Fax: (33-1) 45-68-89-72

5-9 October 1994
Cold Spring Harbor, NY, USA

Molecular approaches to the control of infectious diseases

Meetings Office, Cold Spring Harbor Laboratory, 1 Bungtown Road, Cold Spring Harbor, NY 11724-2213, USA.
Tel: (1-516) 367.83.16

9-10 November 1994
Amsterdam, Netherlands

4th meeting of the CVI Consultative Group

Secretariat, Children's Vaccine Initiative, WHO/GPV, 1211 Geneva 27, Switzerland.
Tel. (41-22) 791-4801;
Fax: (41-22) 788-2071

12-14 October
Boston, MA, USA

Conference on artificial self-assembling systems for gene transfer

Ms Rebecca Lee, CBR Laboratories, 800 Huntington Ave., Boston, MA 02135. Tel: (1-617) 787-8108;
Fax: (1-617) 787-7909

12-17 October 1994
Montreal, Canada

7th international conference of comparative and applied virology

Prof Edouard Kurstek, Dept of Microbiology and Immunology, Faculty of Medicine, University of Montreal, P.O. Box 6128, Station A, Montreal, QC, H3C 317, Canada.
Tel: (1-514) 343.62.85;
Fax: (1-514) 343.57.01

21-25 October 1994
Orlando, FLA, USA

Receptor activation by antigens, cytokines, hormones and growth factors

Ms G. Busacco, Conference Department, The New York Academy of Sciences, 2 East 63rd Street, New York, NY 10021, USA.
Tel: (1-212) 838.02.30;
Fax: (1-212) 838.56.40

23-26 October 1994
Siena, Italy

Molecular mechanisms of microbial (bacterial and viral) pathogenesis, strategies of microbial attack, host response, immune response and prophylaxis

M. Rossini, Via Fiorentina, 1, 53100 Siena, Italy. Tel: (39-577) 293.483;
Fax: (39-577) 293.564

23-27 October 1994
Nairobi, Kenya

2nd African immunology conference

KEMRI, P.O.Box 54840, Nairobi, Kenya.
Tel: (254-2) 722-541; Fax: (254-2) 720-030

26-27 October 1994
Gothenburg, Sweden

Vaccines for the year 2000

Camille Johannesson, The Swedish Society of Medicine, P.O. Box 738, S-104 35 Stockholm, Sweden.
Tel: (46-8) 243-350; Fax: (46-8) 244-348

2-4 November 1994
Langen, Germany

Replacement, reduction and refinement of animal experiments in the development and control of biological products

Dr K. Cussler, Paul-Ehrlich Institute, Paul-Ehrlich-Str. 51-59, P. O. Box 1740, D-63207 Langen, Germany.
Tel: (49-6103) 777.401;
Fax: (49-6103) 777.254

16-19 November 1994
Niagara Falls

5th annual international meeting on rabies control in the Americas: coping with invading rabies epizootics

Sarah Crosgrey, Ontario Ministry of Natural Resources, Midhurst District Office, Midhurst, Ontario, Canada.
Tel: (1-705) 722-3663:
Fax: (1-705) 722-5720

17-20 November 1994
Monte Carlo, Monaco

Advances in gene technology: molecular biology and human disease

Christine Jones, The Miami Bio/Technology European Symposium at Monaco, 4 Little Essex Street, London WC2R 3LF, UK.
Tel: (44-71) 836-6633 x2593;
Fax: (44-71) 379-5417

5-7 December 1994
Harrogate, UK

2nd annual congress of the British Society for Immunology

BSI Office, Triangle House, Broomhill Road, London SW18 4HX, UK.
Tel: (44-81) 877-9920;
Fax: (44-81) 877-9308

16-23 January 1995
Keystone, CO, USA

Mucosal immunity: new strategies for protection against viral and bacterial pathogens

Keystone Symposia, Drawer 1630, Silverthorne, CO 80498, USA. Tel: (1-303) 262-1230

16-23 January 1995
Keystone, CO, USA

Molecular aspects of viral immunity

Keystone Symposia, Drawer 1630, Silverthorne, CO 80498, USA. Tel: (1-303) 262-1230

19-23 February 1995
Nice, France

7th European congress on biotechnology

Mrs L Cohen, Société de Chimie Industrielle, 28, rue St Dominique, 75007 Paris, France

16-22 March 1995
Taos, NM, USA

Control and manipulation of the immune response

Keystone Symposia, Drawer 1630, Silverthorne, CO 80498, USA. Tel: (1-303) 262-1230

7-11 May 1995
Eilat, Israel

39th OHOLO conference on vaccines: novel strategies in design and production

The Secretariat, 39th OHOLO Conference, P.O. Box 19, 70450 Ness-Ziona, Israel. Tel.: (972-8) 381-656; Fax: (972-8) 401-404

23-28 July 1995
San Francisco, CA, USA

9th international congress of immunology

Congress Secretariat, 9650 Rockville Pike, Bethesda, MD 20814, USA. Tel: (1-301) 530-7178; Fax: (1-301) 530-1816

PICTURE POSTSCRIPT

UNICEF/Lauren Goodsmith

Mule trip for two women and a child near Azrou in Morocco's Ifrane province.

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