CHAPTER 1

SMALLPOX

eradicating an ancient scourge

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When countries gather for the World Health Assembly each year one question often comes up: whether or not to destroy the last remaining stocks of the smallpox virus. That is a choice we have thanks to the relentless pursuit of the smallpox virus by health workers across the world.

Eastern Nigeria, December 1966. The message came through on the radio – a crackly transmission carrying news of a smallpox outbreak in the bush. The missionaries had set up a ham radio network covering parts of the Ogoja region of eastern Nigeria where they were working in support of the country's national smallpox campaign. Every day at 7 pm they tuned in to share news and check that none of them had fallen ill. The report ended with a request for Dr William Foege to come out to the village and take a look. Foege had his doubts. He had been working in Nigeria as a medical missionary long enough to know that chickenpox was sometimes mistaken for the far more serious disease. However, he knew that only around 35% of the population was supposed to have been vaccinated against smallpox in that region. And an outbreak, even if only rumoured, was too important to be ignored. So Foege and his team set off that day, bumping their way over rutted roads, eventually finding the village 15 km from the highway.

Photo 1.1. Somalia, 1970s. A mother holds a child whose body is almost entirely covered with smallpox pustules

WHO/J. Breman

As always when the imposing two-metre tall Foege showed up, a crowd gathered. Foege spoke to the head of the village and was taken from hut to hut, registering the scared faces and looking for the tell-tale signs of smallpox. As with chickenpox and measles, a person with smallpox develops a rash.

Unlike the chickenpox rash which develops over a couple of days, smallpox comes up very quickly in a rash that is also more dense on the face, hands and feet. The red spots swell, filling with fluid until the pea-sized poxes become hard. As the disease progresses, the pustules continue to erupt under the skin, spreading over the face, body and hands until the victim's body is almost entirely covered (Photo 1.1).

It didn't take long for Foege to validate the report. This was indeed smallpox, and now he had a problem: fresh supplies of the vaccine and more vehicles were not due to arrive for several weeks. Whatever Foege and his team were going to do, they would have to do it quickly. That night he and his colleagues decided that the first step was to get a picture of the extent of the outbreak. They started by using a map to divide the area around the affected village into manageable sections. Then they got on the radio and called on other missionaries to send runners to the surrounding villages to find out if they had more cases.

Once they had an accurate map of the epidemic, Foege and his team went into the affected villages and, using the limited supplies, vaccinated people who hadn't yet caught the disease, ring-fencing the hot spots with a barrier of immunity. It was a good start, but on its own was not going to be sufficient to stop the disease. There were going to be travellers who had no idea they were infected and who would spread the virus around the region. Foege knew that the battle against smallpox would be won or lost depending on how well his team handled these cases.

Foege learnt that people regularly traded goods at designated locations, each market serving several villages. With this information, he mapped out local transportation and trade routes. What was left of the vaccine was committed to building rings of resistance in the areas he had mapped out that were most likely to see new cases. At the end of the first week Foege's response to the outbreak was in place. Now all he could do was watch and wait.

When WHO was founded

In 1948, when the World Health Organization (WHO) came into being, the smallpox virus was infecting about 50 million people a year – the equivalent of the population of South Africa. In many ways, it was exactly the kind of adversary that WHO was expected to take on – a global heavyweight of disease that was beyond the scope of any individual nation to combat.

Caused by the variola virus, smallpox is one of the most devastating diseases known to humankind (see Box 1.1 Fact file – smallpox). Prior to 1960, smallpox ranked with malaria and tuberculosis as the main causes of death due to infectious disease. In 1967, there were around 10–15 million cases of smallpox in the world each year, a figure which had dropped from around 50 million cases a year in the 1950s. One group of experts has estimated the global death toll from smallpox during the 20th century to have been around 300 million. This contrasts with, for example, a recent estimate by the *New York Times* that 100 million people died during the 20th century either directly or indirectly as a result of war and armed conflict.

The fear that smallpox struck in people was extraordinary. Until the vaccine was developed and widely available in the 20th century, many societies – independently of each other – developed a technique known as variolation. This involved inoculating a healthy person with the dried scabs of someone with smallpox, giving that person a mild form of smallpox. But the method was not without risk, 1–2% of those variolated in this way died, compared with up to 30% of people who died when they contracted the disease itself. Smallpox was so frightening that people were prepared to risk death to become protected.

Box 1.1. Fact file – smallpox

What is smallpox? Acute contagious disease caused by a virus.

Origin: 3000 years ago in Egypt or India.

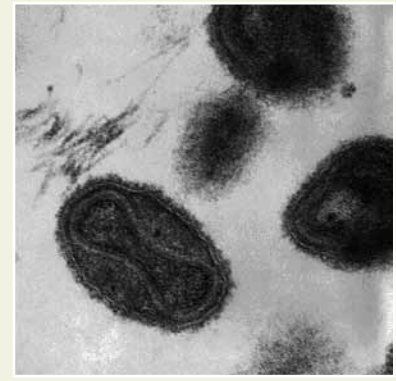
Virus family: *Poxviridae* or poxvirus.

Forms: Variola minor (killed one in 100). Variola major (killed one in three).

Transmission: Airborne droplet.

Cure: There is no cure, but vaccination can be used very effectively to prevent infection from developing if given during a period of up to four days after a person has been exposed to the virus.

Life after eradication: Virus stocks kept in high-security Russian and USA laboratories.



CDC

The smallpox virus

Photo 1.2. USA, 1960. Russian scientist Viktor Zhdanov (right)

WHO/M. Rude

Photo 1.3. India, 1962. Freeze-dried smallpox vaccine being prepared at the King Institute of Preventive Medicine in Madras (today Chennai) in the Indian state of Tamil Nadu

WHO/P.N. Sharma

Governments first seriously discussed the possibility of eradication in 1953 at the annual World Health Assembly, but there was little enthusiasm for the idea. Sceptics pointed to several failed attempts to eradicate other diseases, including hookworm at the turn of the 20th century, while efforts to stamp out yellow fever had been called off in 1932, when scientists discovered that monkeys were regularly being infected with the virus, thus putting it out of reach of an eradication campaign targeting humans. The World Health Organization's own campaign to eradicate malaria was just getting under way in the 1950s – a massive undertaking that succeeded in some countries of the Americas, Asia and Europe, but failed in Africa.

Given widespread doubt in the 1950s that any disease could be eradicated, it required someone with more than just technical knowledge of smallpox control to give WHO's programme its first real impetus. Soviet scientist, Viktor Zhdanov, was just such a man. Speaking at the World Health Assembly in 1958, Zhdanov, an epidemiologist by training and deputy health minister of the what was the Soviet Union at the time, called for the total eradication of the virus (Photo 1.2).

Inspired by Soviet success

Coming from anyone else, this might have seemed like a dream, but Zhdanov carried considerable influence. He had seen smallpox contained in the Soviet Union in the 1930s, and although the disease remained a problem in the central Asian republics where cases were coming in from Afghanistan and Iran (today the Islamic Republic of Iran), Zhdanov saw no reason why Soviet successes could not be repeated elsewhere. He proposed a four-year global vaccination campaign starting in 1959.

Apart from his own experience of running an eradication campaign, Zhdanov also brought his belief in a technique known as lyophilization or freeze-drying (Photo 1.3), which had been developed during the Second World War to meet demand for reliable stocks of dried blood plasma. Research in the 1950s had shown that several pharmaceutical products could be preserved in this way. Smallpox vaccine was one of them.

Freeze-dried vaccine is easily transported and can be reconstituted when needed, unlike polio vaccine, for example, which has to be refrigerated, greatly

complicating the task of getting it into the field. Zhdanov believed that freeze-dried vaccine would be an essential tool in WHO's smallpox eradication programme, and said his own government was ready to furnish WHO with supplies.

The Soviet Union was not the only country to have contained smallpox. Most other industrialized nations had done so by this time too, but the disease remained endemic in many developing countries (see Box 1.2 From widespread to wiped out). Zhdanov convinced WHO Member States of the merits of his plan and at the next World Health Assembly, also in 1959, they voted unanimously in favour of starting a global smallpox eradication campaign. The idea was for countries to take the lead in terms of carrying out the eradication programme with technical support from WHO. In the years that followed, many less developed countries embarked on their own mass vaccination campaigns and several, including China, eliminated the disease at home, but elsewhere it continued to take lives (see Box 1.3 A virtuoso performance). This was especially true of India, Indonesia and Pakistan and countries in sub-Saharan Africa. Meanwhile WHO's campaign was hampered by a lack of funding.

Box 1.2. From widespread to wiped out

Diseases that infect large numbers of people in a certain area and that can remain stable over a period of time are called 'endemic' diseases. A disease may have been eliminated from one country or region while remaining endemic in another. For example, China eliminated endemic smallpox by 1961, but the disease remained endemic throughout the Indian subcontinent.

So how do public health experts know when a disease has finally been destroyed for good? According to the World Health Organization, disease eradication – when a disease has been completely wiped out worldwide – means that "no further cases of a disease occur anywhere, and continued control measures are unnecessary". Smallpox was eventually eradicated in 1977 based on joint measures of disease control and surveillance.

Box 1.3. A virtuoso performance

What do Chinese opera, ice-cream coolers and chalkboards have in common? These – and other unusual devices – were deployed to tackle the last major outbreak of smallpox in China.

When the disease broke out in the county of Cang Yuan, in the province of Yunnan in 1959, one of the biggest challenges health workers faced was to reach the communities affected. Vaccinators had to cross the remote, mountainous region on horseback to get to these isolated villages because there was no public transport system.

Ministry of Health, China

China, 1961. A doctor vaccinates children in Taihu Hospital, Jiangsu Province

People living along the 4061-km border between the Chinese province and Myanmar, the Lao People's Democratic Republic and Viet Nam, were particularly affected by the killer disease. Armed with ice-cream coolers to store the vaccine, health workers set about vaccinating the entire population.

They faced many difficulties. There were not enough health workers, so they had to train locals to do the vaccinations. Some people resisted vaccination because they believed that local healers could cure smallpox by chanting – a tradition known as *koradji* – to drive out spirits. It wasn't easy to explain to the people – most of whom were illiterate – how smallpox was prevented. So to educate them, the lyrics of local songs were changed and Chinese opera performances were staged to explain how vaccination worked. Health workers also used chalkboards and posters to educate people about the disease.

Their efforts were not in vain. In March 1961, China's last case of smallpox was confirmed – a 23-year-old man, Hu Xiaofa.

Campaign gets a boost

Photo 1.4. Ethiopia, 1972. Dr Donald A. Henderson (right) examining vaccination scars on children during case-finding operations

WHO

By the end of 1966, smallpox was still circulating in 31 countries and territories. Frustrated by the lack of progress, in 1966 governments finally secured annual funding of US$ 2.4 million for what was termed an intensified global smallpox eradication effort. It wasn't a huge amount of money and governments didn't allocate the funds with any great enthusiasm. At that time, the public health community had plenty of reasons to be sceptical about stamping out diseases – the struggling malaria campaign being just one of them.

Fortunately, positive forces were at work. For one thing, the United States of America had stepped up its commitment to the programme. In 1965, President Lyndon B. Johnson announced that his country would fully support a programme to eradicate smallpox in 20 countries of west and central Africa and backed the idea of global smallpox eradication. In 1966, he sent one of the country's top epidemiologists, Dr Donald A. Henderson, to Geneva to head WHO's Smallpox Eradication unit (Photo 1.4).

Like Zhdanov, Henderson had considerable experience in the field. He had been the head of disease surveillance at the Centers for Disease Control and Prevention (CDC) in Atlanta, USA, with particular responsibility for the planning of smallpox eradication and measles control programmes to support countries in west and central Africa. A forceful man, he was just the kind of person needed to push the programme forward.

But he did not join WHO willingly. "I was reluctant to take on the job because of my commitment to the smallpox and measles eradication campaign, which had just been launched only a year before in west and central Africa, and which I was running," Henderson recalls. "Secondly, there wasn't a lot of money assigned to this – US$ 2.4 million wasn't even enough to buy the vaccine we needed. Beyond that, nearly half the delegates in the World Health Assembly were doubtful about undertaking the programme in the first place." The delegates were not alone. WHO's director-general at the time, Dr Marcolino Gomes Candau, believed that smallpox eradication was unachievable, a programme which "could serve only to undermine the organization's credibility". Candau had been informed by experts that to eradicate smallpox, at least eight in 10 people had to be vaccinated. From his

own experience in his native country, Brazil, he knew this was impossible in vast, inaccessible places, such as the Amazon region.

Despite his misgivings, Henderson went to work at WHO headquarters in Geneva where he launched the Intensified Smallpox Eradication Programme on 1 January 1967 that was to provide technical assistance to countries' smallpox eradication campaigns. From the outset, Henderson considered the accurate and timely reporting of cases to be an essential element of a successful campaign. At that time, this systematic collection and analysis of data known as surveillance was not the standard approach it is today. Surveillance and containment are in other words the identification and isolation of known cases and vaccination of their close contacts. These were the key approaches that Henderson and his team recommended in a manual they published in preparation for CDC's campaign in west and central Africa, to provide support to countries working to eradicate smallpox. In contrast, however, the WHO campaign Henderson took over was, at least to begin with, a programme committed to traditional mass vaccination of populations thought to be at risk in countries where the disease was still established.

Mass vaccination means pretty much what it says: vaccinating, as far as possible, every man, woman and child, although WHO experts at the time recommended vaccinating at least 80% of the population to achieve protection in a given population known as herd immunity. It was an approach that had proved successful in western Europe and North America, as well as in Japan and other countries. Indeed, many vaccine-preventable diseases, like smallpox, are controlled by achieving this high level of immunization known as herd immunity (see Box 1.4 Herd immunity).

For the campaign to work, WHO needed to be sure of two things: that the vaccine was of good quality, and that it was reaching all the areas where it was needed. Donations of vaccine were coming in from several

Box 1.4. Herd immunity

Vaccines have been proved to be one of the safest biological preparations. Millions of people have been vaccinated all over the world against numerous diseases with relatively few adverse reactions. However, there are some people for whom vaccination may not be safe. These include pregnant women and people with allergies, some skin conditions and diseases that weaken the immune system, such as HIV/AIDS.

That is why the concept of herd immunity is important. It means that even if a small proportion of the population is not vaccinated, by vaccinating most and reaching herd immunity, the unvaccinated people have a very low risk of becoming infected. This is because the chain of transmission of the disease has been reduced to a level that is too low to maintain.

So, for example, about 90–95% of the population has to be vaccinated to prevent measles from spreading to the remaining 5–10% who are unvaccinated. For polio, this level – known as the herd immunity threshold – is 60–97%. For smallpox, the level was about eight people in every 10.

countries, but not all of it was usable. To boost its stocks, WHO persuaded laboratories in Canada and the Netherlands to act as quality control centres, testing samples of all vaccine for the programme. Meanwhile, designated vaccine manufacturers produced a manual that laboratories in front-line countries could use to manufacture their own vaccine. As early as 1973, more than 80% of all vaccine for the programme was coming from countries where the disease was endemic.

Of course, it was one thing to have plentiful supplies of good vaccine, quite another to make sure that the vaccine was getting to and getting *into* the people who needed it. Vaccination technique hadn't changed much since the 18th century, when the smallpox vaccine was first discovered (see Box 1.5 Vaccinia – the first vaccine).

At the beginning of WHO's smallpox eradication campaign, vaccination was a crude scratching process that sometimes caused serious wounds. Whether it worked or not depended largely on the skill of the person doing the scratching. What WHO needed was a technique that didn't require expert delivery.

Box 1.5. Vaccinia – the first vaccine

Smallpox is famous for being the first disease that humankind eradicated, but it will also be remembered as the first disease for which we created a vaccine.

But before we had a vaccine, a technique known as variolation had been in use for centuries. People in China, India, Turkey and other parts of the world would introduce scrapings of smallpox sores into healthy people. Most of them became immune, but between about 1% and 2% of those variolated in this way died.

WHO/S. Furnell

Switzerland, 2008: A cow

The discovery of smallpox vaccination is generally attributed to the English physician Edward Jenner, who in 1796 noticed that milkmaids never seemed to get smallpox because they had caught what he thought was cowpox. Jenner set out to prove this. He scratched the arm of an eight-year-old boy called James Phipps and deliberately infected him with cowpox pus taken from a blister on the hand of a milkmaid. A few months later, he infected the boy using pus taken from a smallpox patient. The boy didn't develop the disease. The cowpox had made him immune. It was not until 1938 that another scientist, Allan Watt Downie, realized that cowpox did not make people immune from smallpox but a related virus, called vaccinia virus.

Jenner coined the term 'vaccination' from the Latin word for cow, *vaccus*. In the 1870s, almost a century after Jenner's work, French scientist Louis Pasteur developed preparations that protected people against rabies and anthrax. He coined the term 'vaccine' for this type of preparation in honour of Jenner's accomplishments.

Saved by a 'sewing needle'

Scientists at CDC had developed a hydraulic-powered jet injector that could do 1000 vaccinations in an hour. It was impressive in the right conditions, but had a tendency to break down. The jet injectors were used in Brazil and west and central Africa in the first year of the intensified programme, but were soon pushed aside in favour of a simpler instrument – an industrial

sewing needle that delivered the vaccine not with the point, but with the eye, which was ground down to produce a two-prong fork (Photo 1.5). This became a perfect receptacle for holding a droplet of vaccine. All the field worker had to do was dip the fork into the reconstituted vaccine then make 15 rapid jabs on the upper arm with the needle held at a right angle to introduce the vaccine underneath the skin. Village volunteers required less than an hour's training to get it right, after which they were able to vaccinate as many as 500 people per day. The bifurcated needle had the added advantage of requiring only a quarter of the vaccine that the jet injector needed to deliver immunity (Photo 1.6).

In the first year of the intensified programme, 44 countries reported 131 789 cases of smallpox. The countries where the disease was endemic were Afghanistan, Brazil, India, Indonesia, Nepal, Pakistan and most of the countries in sub-Saharan Africa. Staggeringly, it later emerged that only about 1% of all cases were being reported in 1967, suggesting that a more realistic figure for smallpox cases that year was somewhere between 10 and 15 million. But as already stated, health data were less reliable and abundant than they are today.

To say that what WHO and the endemic countries were trying to achieve was daunting would be a serious understatement. Even homing in on a single country such as India, which at the time had a population of around 600 million people, many of whom lived in rural areas, the challenge of mounting a successful mass vaccination campaign was enormous. Sceptics pointed out that even if one could vaccinate everyone in India, it was going to be impossible to cope with each year's wave of 20 million or so newborn babies, all prime candidates for infection.

Such arguments carried considerable weight until December 1966 and what happened in eastern Nigeria.

Photo 1.5. The bifurcated needle was about five centimetres long

WHO

Photo 1.6. Bangladesh, 1975. A volunteer vaccinates a small child with a bifurcated needle

CDC/WHO/S. Foster

Breakthrough in Nigeria

Foege's response to the eastern Nigeria outbreak was based on careful case reporting or surveillance and close containment, through targeted vaccination. That way, he and his colleagues managed to shut down the smallpox outbreaks in a matter of five months. Everyone located in the radius of an outbreak was vaccinated, encircling the disease to form a ring of immunity around it and to

prevent it spreading. The population of eastern Nigeria was about 12 million at that time and Foege and his colleagues stopped the outbreaks across the vast region by vaccinating only 750 000 of them. It was a remarkable achievement.

Foege was not the first to argue that eradication based on surveillance–containment could work. A similar approach had been used to control outbreaks in England in the 19th century. The approach, known as the Leicester system, relied on the same isolation or ring-fencing of known smallpox cases from the general population to break the chain of transmission.

But Foege succeeded in providing convincing evidence of how effective surveillance– containment could be in field conditions. Perhaps even more extraordinary and significant was the work of Dr A. Ramachandra Rao in the Indian state of Tamil Nadu a year later. With funds from WHO, Rao led a single team in surveillance–containment work across the state. Within six months they had halted smallpox transmission among its 41 million inhabitants. The eastern Nigeria experiment and the experience in Tamil Nadu pointed the way forward and set WHO's global eradication campaign on a new course. As Henderson puts it: "Even though we had been talking about surveillance–containment in 1966, we hadn't realized how effective it could be in the field."

Lessons were being learnt. Important information was flowing into WHO's head office in Geneva from campaigns across the globe. The increasing emphasis on surveillance containment began to bear fruit in country after country as smallpox began to recede across the world.

In Brazil, where the campaign had been run on a mass vaccination basis, people such as Dr Ciro de Quadros, who was working in Parana state in the south, started surveillance–containment campaigns that were pursued with extraordinary zeal. Almost four decades later Henderson recalls de Quadros's personal commitment with considerable warmth: "This man used to get reports from every single health unit and hospital in the state, then head out with his driver and vaccinator to do the containment vaccination." By 1971 smallpox had disappeared in Brazil.

Indonesia was also getting to grips with the problem. The government set up four 'fire-fighting teams' to tackle the disease in central Java where cases continued to arise. In a matter of months, cases dropped from several hundred a month to zero. Smallpox was also on the run in Africa, where by 1970 it had been extinguished in 20 African countries.

But as long as the disease remained at large, it could re-appear anywhere. This chilling fact was brought home in 1972 in Kosovo (when it was part of the Socialist Federal Republic of Yugoslavia). In February of that year, a 38-year-old man returned home from a pilgrimage to Iraq. He started to feel sick but was only diagnosed with smallpox after he had been in contact with his family. The result was an epidemic that infected 175 people and killed 35. The authorities launched a campaign to vaccinate the whole country – 21 million people. They worked so fast that 18 million were vaccinated in just 10 days. A combination of military roadblocks and intensive vaccination brought the outbreak to an end.

At the end of the decade, WHO was faced with a tantalizing prospect – that the surveillance–containment approach might be sufficient to stamp out the disease for good. But big doubts remained. It was one thing to contain outbreaks in sparsely populated eastern Nigeria, quite another to attempt the same thing in heavily populated India.

India – the last bastion

Foege went to India in 1970, joining Dr Nicole Grasset at WHO's South-East Asia Regional Office in New Delhi. Grasset had gained her field experience in Biafra, Nigeria, during the civil strife there (Photo 1.7). While employed at the Pasteur Institute in Paris, she organized, at the request of the International Committee of the Red Cross, three major immunization programmes for the prevention of measles, tuberculosis and smallpox. Grasset was a formidable presence, combining intelligence and drive with an absolute belief in the campaign's ultimate success. For Grasset, Henderson's and Foege's contribution was invaluable. To understand this, it is necessary to realize the extent to which experts in the early 1970s were bitterly divided over which approach to eradicating smallpox was the most effective: "One of the biggest problems we had in India," Grasset recalls, "was the view of some in the health ministry and other high-level health officials saying that what we should be doing was vaccinating in areas where the disease was not yet established," the idea being that these areas would then become bastions against the disease. But as Grasset points out, you don't fight fires by dousing the area around the burning building, you target the flames, and the hot spots where the flames are most likely to develop.

Photo 1.7. India, 1960s. Dr Nicole Grasset

WHO

Photo 1.8. India, 1963. Schoolboys take part in a national vaccination campaign

WHO/Satyan

In India, until the 1950s, more than a million people died of smallpox annually, while the disease blinded and disfigured many more, according to Dr Mahendra Dutta, who was a senior member of the health ministry's smallpox eradication department (Photo 1.8). Working with India's central and state governments, and a handful of nongovernmental organizations (NGOs), WHO provided India with technical support as it stepped up its surveillance–containment effort, and by the end of 1973 had chased the disease into four remaining states: Bihar, Uttar Pradesh, West Bengal and Madhya Pradesh. Despite progress, doubts remained about the global eradication campaign's ultimate success. "We were doing very well," recalls Henderson, "Latin America was free. Indonesia was free. It looked like Africa was pretty much free except for Ethiopia. But where we had the problem was India. So in 1973 we sat down with the Indian government and worked out a plan to visit every village in India, every house within a space of seven to 10 days. The idea was that if we could intervene early enough it would interrupt the chain of transmission."

The Intensified National Smallpox Eradication Programme was launched in India in 1973, and introduced, among other things, a set of surveillance and containment standards. They required 75% of cases to be discovered within two weeks of the first case and for containment proceedings – in other words targeted vaccination – to begin within two days of that case being identified. What this meant was that the veritable army of health workers committed to the India campaign – more than 135 000 people each week – had to work even harder.

India's health workers were supported by epidemiologists from diverse backgrounds. One was Dr Larry Brilliant, who in true 1970s style, was told by his guru that eradication of smallpox was God's gift to the world, and that he should get involved. Brilliant, who once headed the Google philanthropic foundation, was one of many WHO health-care professionals who joined the India campaign in 1972. Brilliant's co-workers searched schools and markets as well as Shitala Mata temples. People entering the temple to make an offering to Shitala Mata, the Goddess of smallpox, were followed back to their houses where his co-workers often found people with smallpox (Photo 1.9).

At times, the efforts in India looked like a military campaign. Occasionally WHO workers were called upon to use strong-arm tactics and forced vaccination, when there was resistance. But in general such methods were not

advised as they often resulted in villagers running away into the fields or fighting with vaccinators. And such incidents were rare. Moreover, Dutta recalls that rumours of resistance to vaccination were often unfounded: "Day after day in every village visited, the people were found panicky, as a number of cases, several of them fatal, had occurred, and they pleaded [with us] to provide vaccination."

The results of the intensified eradication programme were astounding. "Search teams found 10 000 cases immediately," Henderson recalls. For critics of the campaign, the sudden increase in reported cases was proof that the eradication efforts were not working, and never could work. But Henderson, Grasset and Foege knew the statistics simply reflected more accurate reporting of cases. They were convinced that by continuing to contain the outbreaks reported, better days would come, which they did.

The number of cases rose rapidly from January through May, eventually reaching the largest monthly total of cases since 1951. However, for Henderson, January and February were the turning point in the global campaign. "We had a structure and teams in place and I knew we were getting on top of it," he says. "And we knew that if we could defeat it in India, we could defeat it anywhere – in Bangladesh, in Pakistan and in Ethiopia."

And then came Bihar – a fertile state in north-eastern India. At the beginning of 1974 smallpox had burned through the north of the state, and, in the heat of the summer, a WHO team arrived in the industrial city of Jamshedpur (at that time a part of Bihar) where it was greeted with gruesome stories. In four days of intensive searching the WHO team, led by Brilliant, registered more than 2000 smallpox victims. To prevent the disease from spreading further, almost the entire city of Jamshedpur, which had a population of 600 000 at that time, was quarantined. Buses and cars were stopped at the city gates while vaccinators boarded trains leaving the city and worked through the carriages.

Convinced this time that the best way to get the wheels turning in India was to go right to the top, Grasset went to see Jehangir Ratanji Dadabhoy Tata, head of Tata Industries, and explained the situation. With the go-ahead from the prime minister Indira Ghandi, Tata committed a large number of his staff to the project – from assembly-line workers to nurses and managers – to search for and isolate smallpox cases, and then vaccinate the people who had recently come into contact with them.

Photo 1.9. Shitala Mata is the Hindu Goddess of smallpox – both the disease and the cure. She rides on a donkey and carries in her four hands a broom, a fan, a small bowl and a pot of water, which she uses to cure the disease. Shitala Mata means "cooling mother" in the Hindi language

WHO/S. Khamsi

The situation was complicated by the fact that people in hundreds of villages around the city had also become infected. One of these villages, occupied by members of the Ho tribe, refused to be vaccinated on religious grounds. With the support of local police, Brilliant once recalled how sometimes he and his co-workers had to forcibly vaccinate people, occasionally having to break down doors in the middle of the night to do so.

Operation Smallpox Zero

WHO launched Operation Smallpox Zero in 1975. This tightened the noose further, and the last case of the disease was reported on 17 May that year in Bihar. There had been many critics of the campaign. One – a WHO official – had even told Henderson that if the India campaign were successful, he would "eat a tyre off a jeep". At the successful conclusion of the campaign Henderson sent that person a jeep tyre. "I don't know if he ever tried to eat it," he says.

At this point the only country in the world still seeing outbreaks of variola major – the worst type of smallpox – was Bangladesh, India's eastern neighbour. Local fighting had broken out in the newly independent, but still fragile state, and the United Nations had evacuated all of its staff apart from its smallpox eradication team. The team searched for months, but found no more cases to report. In November 1975, WHO announced at a press conference that two months had passed since the last case in Bangladesh had been reported. At that time there were no known cases anywhere in the world. The following day, however, a cable arrived from Bhola Island, off the country's southern coast, to report new cases in the village of Kuralia.

A WHO team set off on a 24-hour journey by speedboat, steamer, jeep and finally on foot to reach the village, expecting to find cases of chickenpox. It turned out that a medical officer had failed to report several smallpox outbreaks. Indeed, when the team searched they found there had been outbreaks in three other villages that had since burnt themselves out. After narrowing their search, they found a three-year-old girl named Rahima Banu, who had become ill on 16 October.

To make quite sure she was the last case in Asia, the WHO team put Rahima in quarantine, posting guards at her home 24 hours a day while food and money were supplied to the family so that they would not need to leave the house. Everyone within a mile and half – about 18 000 people – was vaccinated and

every house was searched within a five-mile radius of Rahima's house. The team found dozens of cases of measles and chickenpox, not one of smallpox. Rahima survived. No other smallpox cases were found. It seemed that little Rahima Banu was indeed the last case in Asia.

Doctors from WHO collected six of Rahima's pox scabs – the last relics of a once mighty disease, which are now kept in a laboratory in the USA (see Box 1.6 Genie in a bottle).

After Bangladesh, the only country with smallpox was Ethiopia. It was already difficult, but when the civil war broke out in 1974 the challenge for vaccinators was daunting. Some rebel forces supported the eradication campaign, providing teams with a military escort. Others attacked smallpox workers and on one occasion killed two of them.

Smallpox teams travelled by helicopter, braving grenades and bullets to reach remote areas. One team was kidnapped with their Canadian pilot. They were released four days later. Petrus Koswara, a 43-year-old doctor from Indonesia, died in the field of a heart attack attributed to the emotional and physical strain. "This was one of the most difficult countries for the smallpox eradication effort," Henderson says.

While civil war raged in Ethiopia, WHO was about to fight its last battle

Box 1.6. Genie in a bottle

The eradication of smallpox, while clearly a blessing, has left one dilemma – what to do with the remaining stocks of the virus. As far as we know, they are kept in only two places on the planet: the Russian Federation's virology institute called VECTOR outside the city of Novosibirsk in Siberia and the Centers for Disease Control and Prevention (CDC), in Atlanta, USA. In both institutions, the virus is kept frozen and stored securely. So, it is nevertheless still with us – like a bottled genie with appalling powers.

In 1979, when WHO announced that smallpox had been eradicated, it recommended that vaccination against the disease should stop. By 1986 it had ceased everywhere. Then, WHO's Expert Committee on Orthopoxvirus Infections asked whether all stocks of variola virus should be destroyed. In preparation, scientists prepared a library of cloned DNA fragments of selected strains, and fully or partially sequenced the genomes of several prototype strains.

However, several developments have made governments reluctant to deliver the virus the final blow. In particular, they fear that terrorists might obtain smallpox virus stocks illegally and build biological weapons or 'bioweapons' that are designed to spread disease deliberately to kill whole populations. As far as we know, no 'smallpox bombs' have been built successfully. Such a bomb would be devastating because most people born since 1970 have not been vaccinated against smallpox.

Since eradication, some people fear that the bodies of those who died of smallpox in the permafrost wastelands of Siberia could thaw – due to global warming – unleashing the virus on the nearby population. That could cause a local outbreak that would spread fast across the globe, given today's unprotected populations. There are also fears that a laboratory somewhere in the world may have kept smallpox virus stocks – deliberately or simply without realizing it. In this case, a laboratory accident could also unleash the virus on an unprotected world.

In 1999, WHO's expert committee decided that the virus should be destroyed. But given these and other risks, the World Health Assembly decided that the stocks should be kept for research purposes. That's why the Russian Federation kept its stocks at VECTOR and the USA kept its stocks at CDC. Just in case the genie manages to leap back out of the bottle.

WHO

Container to keep smallpox virus stocks in high-security laboratory at the Centers for Disease Control and Prevention in Atlanta, USA

WHO/S. Marennikova

Soviet Union, 1987. Smallpox virus strains are stored in a sealed refrigerator at VECTOR, the State Research Center of Virology and Biotechnology, which was in the former Soviet Union and is today located in the Russian Federation

Box 1.7. The last case

Ali Maow Maalin was working as a hospital cook in the busy port of Merca, Somalia – a town of some 30 000 people on the Indian ocean. Maalin, aged 23 at that time, had worked as a vaccinator in the smallpox eradication programme, but he himself had not been vaccinated. On 12 October 1977, two children with smallpox from a nomad encampment were sent to an isolation camp near the town. The driver stopped at the hospital to ask for directions.

Maalin offered to accompany the driver. "He asked me if I had been vaccinated," says Maalin, now working for the Polio Eradication Programme in Somalia. "I said: 'don't worry about that. Let's go.'" Maalin says he was in contact with the infected children for no more than 15 minutes. But that was enough.

WHO

Somalia, 1977. Ali Maow Maalin, the last person to have naturally occurring smallpox in the world

Nine days later Maalin started to feel sick. After developing a rash, he was diagnosed with chickenpox and sent home. But Maalin had seen enough smallpox posters to know that what he had was not chickenpox. Even so, he was too scared to check in to the isolation camp. "I thought that I would die there," he says. In the end a male nurse from the hospital reported that Maalin was sick. Maalin did not go to the hospital, but remained at home.

The hospital had stopped taking patients while everyone inside, including the staff, had been vaccinated and were in quarantine. Meanwhile, a team set about vaccinating everyone in the 50 houses surrounding Maalin's home, later expanding this to the 792 houses. In all, 54 777 people were vaccinated in the following two weeks.

Isolated, the virus was unable to leap into a new victim. The cook from Merca was the last case of smallpox – variola minor to be precise – in a small outbreak that flared up just one year past

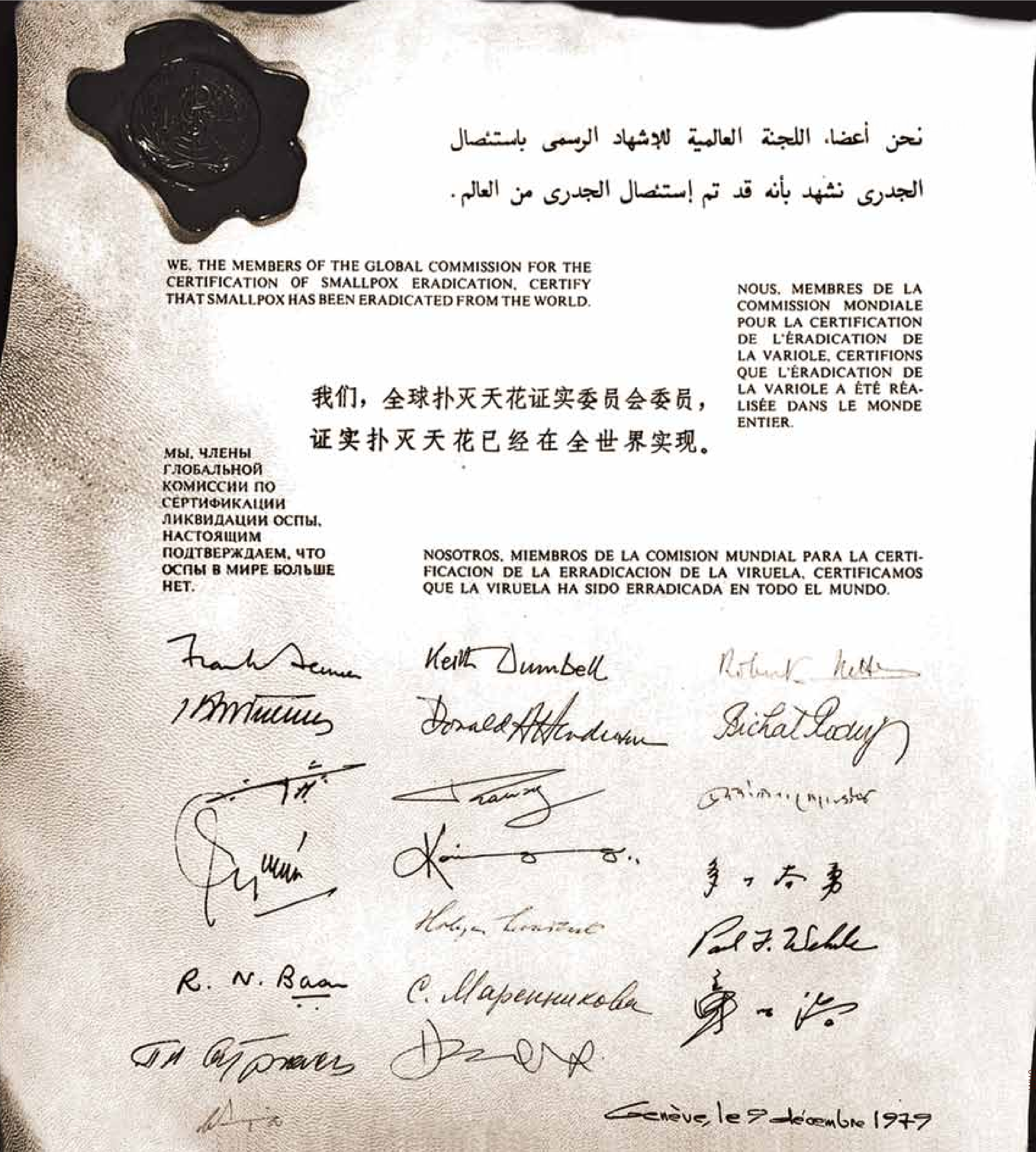
WHO's originally projected 10-year eradication target date. Since then, as far as we know, there have been no other cases of smallpox apart from a laboratory accident in the United Kingdom that triggered a small outbreak and caused one death in 1978. Smallpox was officially declared eradicated in 1979, two years after Maalin became ill. Maalin is the last person in the world to have contracted naturally occurring smallpox.

against smallpox on the country's border with Somalia. Teams had hunted down the last cases among the dispersed groups of nomads across the Ogaden Desert. In October 1976, WHO announced that Ethiopia was free of smallpox.

Seven weeks later, however, another outbreak was reported just over the border in Somalia, possibly brought by nomads from Ethiopia, and in 1977 an epidemic took hold. The Organization mounted an intensive search and containment programme in the spring and summer of that year, finally hunting down the last case of variola minor, the less lethal form of the disease, in the port town of Merca. The person carrying the virus was a 23-year-old hospital cook by the name of Ali Maow Maalin (see Box 1.7 The last case).

For the next few years, international commissions assembled by WHO visited each of the endemic countries to confirm that eradication was a reality, and in May 1980 the World Health Assembly announced that eradication had been achieved across the globe (Photo 1.10). For the first time in history, a major disease had been completely destroyed by human endeavour. The overall cost was around US$ 300 million, of which just under one third, or US$ 98 million, represented international assistance.

Photo 1.10. Switzerland, 1979. Scroll of the Declaration of Smallpox *(overleaf)*



نحن أعضاء اللجنة العالمية للإشهاد الرسمى باستئصال
الجدرى نشهد بأنه قد تم إستئصال الجدرى من العالم.

WE, THE MEMBERS OF THE GLOBAL COMMISSION FOR THE CERTIFICATION OF SMALLPOX ERADICATION, CERTIFY THAT SMALLPOX HAS BEEN ERADICATED FROM THE WORLD.

NOUS, MEMBRES DE LA COMMISSION MONDIALE POUR LA CERTIFICATION DE L'ÉRADICATION DE LA VARIOLE, CERTIFIONS QUE L'ÉRADICATION DE LA VARIOLE A ÉTÉ RÉALISÉE DANS LE MONDE ENTIER.

我们，全球扑灭天花证实委员会委员，
证实扑灭天花已经在全世界实现。

МЫ, ЧЛЕНЫ ГЛОБАЛЬНОЙ КОМИССИИ ПО СЕРТИФИКАЦИИ ЛИКВИДАЦИИ ОСПЫ, НАСТОЯЩИМ ПОДТВЕРЖДАЕМ, ЧТО ОСПЫ В МИРЕ БОЛЬШЕ НЕТ.

NOSOTROS, MIEMBROS DE LA COMISION MUNDIAL PARA LA CERTIFICACION DE LA ERRADICACION DE LA VIRUELA, CERTIFICAMOS QUE LA VIRUELA HA SIDO ERRADICADA EN TODO EL MUNDO.

Genève, le 9 décembre 1979

The smallpox legacy

Photo 1.11. Mexico, 1987. A child wearing a brace to support her leg that has been weakened by polio

WHO/L. Solmssen

Dr Halfdan Mahler, WHO director-general at the time, later described the smallpox programme as "a triumph of management, not of medicine". But given the numerous problems that had to be overcome, including shortages of funds and vaccine, dysfunctional or non-existent national health services, infected refugees fleeing civil war and famine, traditional beliefs, and all the problems posed by climate and difficult terrain, it might be said that the programme was also an extraordinary triumph of the human will – the kind of determination that was in evidence when doctors, carrying vaccination equipment on their heads, swam across rivers, emerging on the other side "with leeches clinging to their bodies," as Grasset recalls.

The lessons learnt during the smallpox eradication campaign were put into practice by doctors working in other fields. Years later, Grasset and eye doctors in Nepal applied surveillance–containment to successfully tackle xerophthalmia, an eye condition that can lead to blindness in young children.

Dr David Heymann, who was with WHO for many years, worked on the smallpox eradication campaign in the 1970s in India. He points out that a couple of years after the world was declared free of smallpox, a new, lethal disease that weakened the body's ability to fight disease by attacking the immune system reared its head – HIV/AIDS.

"If HIV/AIDS had fully emerged to its present prevalence while smallpox was still circulating, I am not sure if we would have been able to eradicate smallpox using the smallpox vaccine," Heymann says, recalling how a US soldier in the 1980s became ill and died after being vaccinated for smallpox, because he was HIV positive. Since then, no new smallpox vaccines have been developed that are suitable for people with weak immune systems. If HIV had become widespread earlier, smallpox itself may have become lethal for people with HIV, just as tuberculosis and pneumonia are today.

The smallpox campaign was not only an achievement in itself, it also inspired other major public health successes. For example, the Expanded Programme of Immunization which covered vaccination for six major

childhood diseases – diphtheria, pertussis (whooping cough), tetanus, polio, measles and tuberculosis when it was launched in 1974 and to which many countries have recently added vaccination for hepatitis B and *Haemophilus influenzae* type b or Hib (Photo 1.11).

Of those, polio – a viral disease that can cause paralysis particularly in children – is the next major target for eradication. As Heymann points out, smallpox was easier to eradicate in many ways. "Smallpox was easy to diagnose. Once someone was infected, the symptoms appeared quickly and were clear. Polio, for example, often shows no symptoms, making it harder to track and vaccinate the people who are in contact, or at risk of contact, with those who are infected." The vaccine for smallpox was effective, protecting around 95% of the people, and easy to administer. The polio vaccine cannot be freeze-dried and reconstituted, like that for smallpox, and requires refrigeration.

Despite the difficulties, the polio campaign has gone well. In 1988, when the initiative began, there were more than 350 000 cases in 125 countries. Since then, the number of cases has fallen by more than 99%, and the polio virus continues to circulate in four countries – Afghanistan, India, Nigeria and Pakistan, which have in turn re-infected a number of other countries that had been polio free. But snuffing out the last remaining traces of the disease is proving difficult. With about 181 cases reported in the first six months of 2011, public health officials are hopeful that a final push by the remaining endemic and re-infected countries could see an end to the disease in the near future (Photo 1.12). A new vaccine targeting wild poliovirus serotypes in a single dose was launched in 2010 to tackle these last remaining strongholds.

The smallpox campaign laid the foundation – based on a mixture of surveillance and containment and mass vaccination – for controlling other vaccine–preventable diseases. "Many of those who run immunization programmes are former smallpox eradication leaders. Indeed, the emphasis given to immunization today is largely a result of the deliberate efforts made with one of the most cost-beneficial interventions available in medicine – immunization!" Heymann says, adding: "Immunization programmes have been some of the most successful and cost-effective means of fighting diseases in the last few decades."

Those programmes are ongoing. ■

Photo 1.12. Côte d'Ivoire. Child proudly holds up her vaccination certificate

WHO