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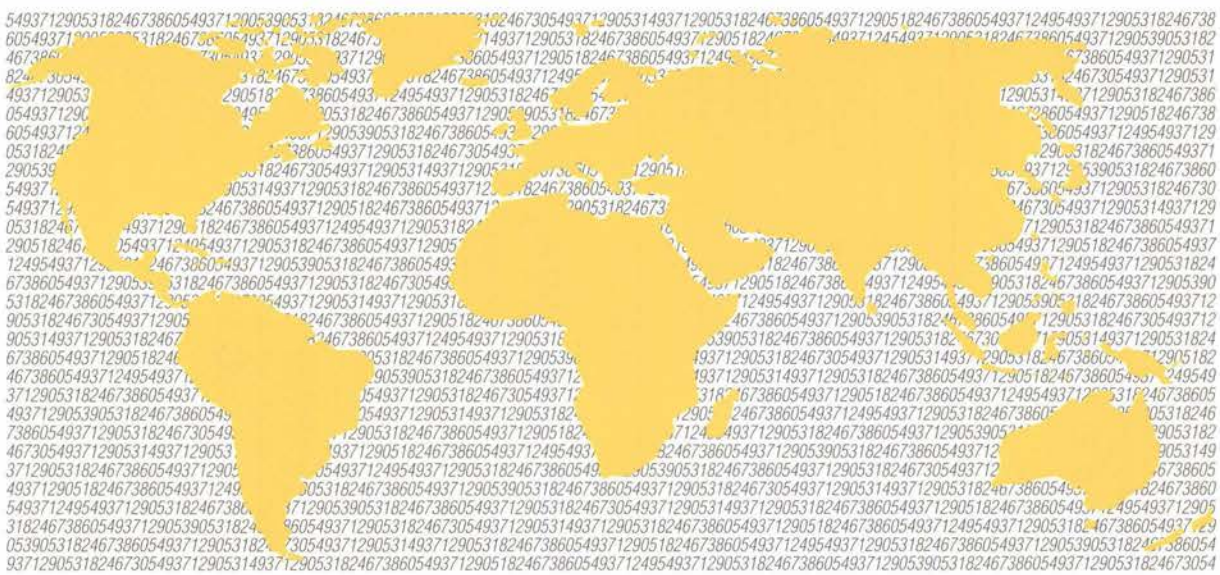

Epidemiology and control of infectious diseases

Maladies infectieuses: épidémiologie et lutte

World Health Organization
Organisation mondiale de la Santé
Genève

The *World health statistics quarterly* replaces (since 1978) the monthly *World health statistics report* (published since 1967) and its forerunner the *Epidemiological and vital statistics report* (published since 1947). It deals with the detailed analysis of selected health topics of current interest. Starting with Vol. 41 (1988), the *Quarterly* contains articles in *either* French *or* English with a summary in both languages.

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Symbols used in tables

- • Preliminary, approximate or estimated data
- ... Data not available
- — Nil or magnitude negligible
- .. Category not applicable
- T Total
- M Male
- F Female
- N Absolute numbers

Explication des signes

- • Donnée préliminaire, approximative ou estimative
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- .. Catégorie non applicable
- T Total
- M Masculin
- F Féminin
- N Nombres absolus

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Infectious diseases: epidemiology and control

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Contents

Sommaire

Emerging and other infectious diseases: epidemiology and control

David L. Heymann[a]

Infectious diseases emerge or re-emerge when bacteria, viruses and parasites take advantage of flaws in our defences against them. This is what happened in the Democratic Republic of the Congo (DRC, former Zaire) in the late 1990s when the monkeypox virus, hitherto only responsible for rare and sporadic disease, caused extensive outbreaks among humans. The declining coverage of the vaccine which eradicated smallpox and also protected against monkeypox could have contributed to the emergence. Furthermore, civil unrest and poverty incited people to penetrate deeper into the rainforest in search of food, exposing them to increased contact with animals harbouring the virus.

Underlying factors

Population increase and rapid urbanization have resulted in the breakdown of sanitation and water-supply systems in large coastal cities in Latin America, Asia and Africa, thus promoting the transmission of cholera and shigellosis. In 1991, cholera, not reported from Latin America in over 100 years, re-emerged in Peru and rapidly spread throughout the continent, causing well over 1 million cases in a continuing and widespread epidemic. Legionellosis, first identified in North America in 1976, is now known to occur worldwide and posing a threat to travellers exposed to poorly maintained air conditioning systems.

Breakdown in mosquito control in Latin America resulted in vast epidemics of dengue fever in 1996 and 1997. Dengue haemorrhagic fever, rare in the Americas before 1981, spread widely along with dengue during these epidemics. The deterioration in immunization programmes contributed to the re-emergence of diphtheria and polio in Eastern Europe, while neglect of yellow fever vaccination led to outbreaks in Africa and Latin America in the 1990s.

Modified production methods for animal feed may have triggered the emergence of a new disease in cattle – bovine spongiform encephalopathy (BSE), identified in Europe in 1986, associated in time and place with the emergence of a previously unknown variant of Creutzfeldt-Jakob disease in humans. Poor hygiene in large scale food production contributed to making *E. coli* O157 a food safety concern in Japan, Europe, and in the Americas in the 1990s.

The viruses causing hepatitis C, Ebola haemorrhagic fever and AIDS can be transmitted by infected blood. Hepatitis C was first identified in 1989 and is now thought to be present in at least 3% of the world population. Ebola virus was identified for the first time in 1976, causing a disease which has come to symbolize emerging diseases. At the time of the first Ebola outbreak in the Democratic Republic of the Congo, AIDS had not yet been diagnosed but it has been shown retrospectively that HIV was present in almost 1% of the population in some rural parts of the country in 1976. Since then, AIDS has become a global public health problem. Nosocomial transmission has been implicated in the transmission of HIV in Eastern Europe, and poor hospital practice with malfunctioning barrier nursing transformed the relatively slow spreading Ebola outbreaks into major epidemics.

The effects of human intervention or of natural processes on the environment contribute to the emergence and re-emergence of infectious diseases. These range from global warming and consequent extension of vector-borne diseases, to ecological changes due to deforestation that increase contact between man and animals and also the possibility for micro-organisms to breach the species barrier. For example, zoonotic diseases such as Lassa fever, first identified in West Africa 1969, are now known to infect man through food supplies contaminated with the urine of rats in search of food as their natural habitat can no longer support their needs. The hantavirus pulmonary syndrome, first diagnosed in the Americas in 1983, may be transmitted to humans by inhalation of droplets from droppings, urine and saliva of infected rodents. Lyme borreliosis in Europe and North America is transmitted to humans through contact with ticks that normally feed on rodents and deer. As drought extends in sub-Saharan Africa, epidemic *Neisseria meningitidis* has emerged south of the meningitis belt in countries such as Uganda and the United Republic of Tanzania, while outbreaks of malaria and other vector-borne diseases have been linked to woodcutting in rainforest areas.

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Human behaviour also plays a role in the emergence and re-emergence of infectious diseases, as evidenced by the increase in gonorrhoea and syphilis during the late 1970s, and the emergence and spread of HIV worldwide, directly linked to unsafe sexual practices.

Further boost to infectious diseases

Two major factors can amplify the emergence and re-emergence of infectious diseases: the progression of antimicrobial resistance, and the tremendous increase of international travel. Antimicrobial agents are the basis for the management of important public health problems such as tuberculosis, malaria, sexually transmitted diseases and lower respiratory infections. Soon after penicillin became widely available in 1942, the first warnings of the potential importance of resistance were sounded. In the 1990s, penicillin-resistant *Staphylococcus aureus* had attained levels > 80% both in hospitals and in the community, and the bacterium is increasingly resistant to other antimicrobials. By 1976, chloroquine-resistant *Plasmodium falciparum* malaria was highly prevalent in South-East Asia; resistance has now been recorded in all parts of the world along with high level resistance to two back-up drugs, Fansidar and Mefloquine. In the early 1970s, *Neisseria gonorrhoeae* resistant to usual doses of penicillin was observed in Europe and the United States, presumably imported from South-East Asia. By 1996, penicillin-resistant *N. gonorrhoeae* had spread worldwide, and strains resistant to all major families of antibiotics had been identified wherever these antibiotics had been widely used.

The selection and spread of resistant strains is facilitated by human behaviour, such as over-prescribing antimicrobials, poor compliance, and the unregulated sale of the drugs. Large amounts of antimicrobials are used in animal husbandry and agriculture; this may facilitate the selection of resistant strains in animals which then transfer resistance factors to human pathogens, or infect humans in the form of zoonotic disease. There is direct evidence that four multi-resistant bacteria infecting humans (*Salmonella, Campylobacter, Enterococci* and *Escherichia coli*), are directly linked to resistant organisms in animals.

The role of travel in the spread of infectious diseases has been known for centuries, but today, travellers, like mosquitoes, have become important vectors of disease. Over 500 million people travelled by air in 1995 according to the World Tourism Organization.

Disease eradication

It is now 20 years since smallpox was eradicated. This unparalleled public health accomplishment resulted in immeasurable savings in human suffering, mortality and financial resources, and encouraged other eradication initiatives. Poliomyelitis is expected to be eradicated during the coming decade and transmission of the virus has already been interrupted in the Americas. Reported cases of dracunculiasis have decreased from > 900 000 in 1989 to < 200 000 in 1996 when most cases occurred in countries that are still endemic. Leprosy and Chagas disease likewise continue their downward trend towards elimination.

The eradication of smallpox boosted an already growing feeling that infectious diseases were no longer a threat, at least to industrialized countries. This optimism had prevailed since the 1950s encouraged by unprecedented developments of vaccines and antimicrobial agents, and sometimes leading to a transfer of resources and public health specialists away from infectious disease control. Eventually, it became clear that the infrastructure for infectious disease surveillance and control had suffered. Population movements, combined with changes in environment and human behaviour, have created weaknesses in the defence systems against infectious diseases in both industrialized and developing countries.

Public health control

Eradication and regulation may contribute to the containment of infectious diseases, but do not replace sound public health practices. Eradication or elimination can be applied to very few infectious diseases, namely, only those which have no reservoir other than humans, which trigger solid immunity after infection, and for which affordable and effective intervention strategies exist.

Attempts at regulations to prevent the spread of infectious diseases were first recorded in 1377 in quarantine legislation to protect Venice from plague-carrying rats on ships from foreign ports. From then on, countries have joined in adopting and enforcing a series of regulations aimed at maximum protection against the international spread of infectious diseases, with minimum restriction.

Today the International Health Regulations (IHR) provide a universal code of practice ranging from strong national disease detection systems and measures of prevention and control, including vaccination, to disinfection, disinfestation and de-ratting. Currently the IHR require the notification of three infectious diseases – cholera, plague and yellow fever, but, once these diseases are reported, the Regulations are often misapplied, resulting in the disruption of international travel and trade, and huge economic losses. This was experienced both by Peru when the present pandemic of cholera reached the country in 1991 and by India, during the outbreak of plague in 1994. Both countries suffered multi-million dollar losses in trade and travel.

Many infectious diseases, including those which are new or re-emerging, are not covered by the present IHR in spite of their great potential for international spread. The insufficient coverage and application of the Regulations are now addressed in a thorough revision to make them more applicable to infection control in the 21st century. The revised IHR will replace the reporting of specific diseases such as cholera, with the reporting of syndromes such as epidemic diarrhoeal disease with high mortality. Their scope will be broadened to include all infectious diseases of international importance, and will clearly indicate what measures are appropriate, or inappropriate, internationally.

However, regulations and eradication or elimination of a disease are no substitute for good public health practice: rebuilding of the weakened public health infrastructure and strengthening of water supply and sanitation systems; minimizing the impact of natural and man-made environmental changes; effectively communicating information about prevention of infectious diseases; and using antibiotics appropriately. The challenge in the 21st century will be to continue to provide resources to strengthen and ensure more cost-effective infectious disease control while also providing additional resources for other emerging public health problems such as those related to smoking and aging.

Global situation of dengue and dengue haemorrhagic fever, and its emergence in the Americas

Fransisco P. Pinheiro[a] & Stephen J. Corber[b]

Introduction

Clinically, dengue fever has been recognized for more than 200 years, and a disease similar to dengue haemorrhagic fever (DHF) was first described in northern Australia at the end of the past century *(1)*. Although several dengue epidemics or pandemics have been described in previous centuries and in the first half of this century, a remarkable increase of the incidence of the two diseases has been noted since the 1950s. A main concern was the appearance of an epidemic of DHF in the Philippines in 1954, which rapidly spread to Thailand, Viet Nam, Indonesia and to other Asian and Pacific countries, becoming endemic and epidemic in several of them *(1)*. The first DHF epidemic in the Americas occurred in Cuba in 1981 *(2)*; subsequently 24 other countries in the Region have reported DHF. Also of great concern has been the occurrence of several pandemics and countless epidemics of dengue fever over the past 40 years, with considerable health, social and economic consequences.

Present situation

About two-thirds of the world's population live in areas infested with dengue vectors, mainly *Aedes aegypti*. All four dengue viruses are circulating, sometimes simultaneously, in most of these areas. It is estimated that up to 80 million persons become infected annually, although marked underreporting results in the notification of much smaller number of cases *(3)*.

Currently dengue is endemic in all continents except Europe and epidemic DHF occurs in Asia and in the Americas. The incidence of DHF is greater by far in Asia than in the Americas. In the Americas, the emergence of epidemic DHF occurred in 1981, nearly 30 years after its appearance in Asia and its incidence is showing a marked upward trend.

Asian countries

DHF continues to be a serious public health problem and a major cause of hospitalization and death among children in many Asian countries, with over 100 000 deaths estimated to have occurred in 1995. The disease continues to affect children predominantly. All four dengue serotypes are in continual circulation, which characterizes a situation of hyperendemicity. DHF continues to occur mainly in urban centres but rural areas have also been affected. In the 1990s DHF has continued to show a higher incidence in South-East Asia, particularly in Viet Nam and Thailand. These two countries account for more than two-thirds of the DHF cases reported in Asia despite the fact that a significant decline of their reported cases was observed during the period 1991-1995 compared to the previous 5-year period *(Table 1)*. In contrast, an increase in the number of reported cases was noted in the Philippines, Lao People's Democratic Republic, Cambodia, Myanmar, Malaysia, India, Singapore, and Sri Lanka, when the two periods are compared. In Indonesia the incidence of DHF was similar in both periods. No epidemics have been reported in Maldives since 1988, when a very severe outbreak of dengue and 9 deaths from DHF occurred in Male. Serological surveys indicate that dengue fever is endemic in Bangladesh and although an outbreak of DHF apparently occurred in 1964, DHF is not considered at present to be a public health problem in Bangladesh *(4)*.

India and Sri Lanka represent countries where epidemic DHF is becoming a potential threat. Since the late 1980s several outbreaks have occurred in both countries and at least two outbreaks were detected in India during the period 1991-1995 *(5)*. A dengue-3 strain genetically distinct from other dengue-3 viruses previously circulating in those countries has been considered the major cause of these outbreaks *(6)*. In 1996 (as of 29 October) 7 247 cases of dengue and DHF of which 297 were fatal were reported in New Delhi, and dengue-2 virus was isolated *(7)*. A report from Pakistan documented the occurrence in 1994 of laboratory-confirmed dengue cases, 3 of which were associated with benign haemorrhagic manifestations 2 of them being due to dengue-1 and the other to dengue-2 *(8)*.

Pacific countries

Epidemics of dengue fever with sporadic cases of DHF have been reported recently in several Pacific islands, including Vanuatu, New Caledonia, Tahiti, Rarotonga, Fiji, American Samoa, Western Samoa,

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[b] Director, Division of Disease Prevention and Control, WHO Office for the American Region.

Table 1
Dengue haemorrhagic fever cases (and deaths) reported in selected countries in Asia[a]

Tableau 1
Nombre de cas de dengue hémorragique (et de décès) notifiés dans certains pays d'Asie[a]

	Philippines		Viet Nam		China – Chine		Thailand – Thaïlande		Lao P.D.R. – R.p.d. Lao		Cambodia – Cambodge	
	C	D	C	D	C	D	C	D	C	D	C	D
1956-1980	25 738	1 670	208 590	3 780	21 227	459	236 364	5 923	...	...	...	...
1981	123	8	35 323	408	...	...	25 670	198	287	...	442	...
1982	305	31	39 806	361	...	...	22 250	159	...	...	711	...
1983	1 684	130	143 380	1 798	85 293	3 032	30 225	229	204	5	4 286	...
1984	2 545	89	30 496	368	...	...	69 101	496	22	14	912	...
1985	...	...	45 107	399	...	...	80 076	542	1 774	15	6 420	...
1986	839	30	46 266	511	...	...	27 837	236	365	43	2 458	...
1987	859	27	354 517	1 566	...	...	174 285	1 007	9 699	295	5 536	...
1988	2 922	68	85 160	826	51 510	1 529	26 926	179	1 212	27	1 981	...
1989	305	14	40 205	289	37 886	807	74 391	290	...	...	...	...
1990	588	27	54 767	246	376	0	92 005	419	60	3	7 241	403
1991	...	...	111 817	445	902	...	43 511	137	0	...	1 882	134
1992	...	...	51 311	271	46 095	...	41 125	136	138	...	4 800	172
1993	5 715	...	53 674	157	359	...	67 017	222	343	...	3 913	189
1994	5 603	...	44 944	...	2	0	51 688	140	2 585	2	1 498	...
1995	7 413	...	80 447	...	6 114	0	59 911	164	7 781	...	10 199	...
1996	13 613	...	86 621	...	7	...	34 618	102	8 197	...	1 433	...
1981-1985	4 657	258	294 112	3 334	85 293	3 032	227 322	1 624	2 287	34	12 771	...
1986-1990	5 513	166	580 915	3 438	89 772	2 336	395 444	2 131	11 336	368	17 216	403
1991-1995	18 731	...	342 193	873	53 472	0	263 252	799	10 847	2	22 292	495
Total[b]	68 252	2 094	1 512 431	11 425	249 771	5 827	1 157 000	10 579	32 667	404	53 712	898

	Myanmar		Malaysia – Malaisie		Singapore – Singapour		Indonesia – Indonésie		India – Inde		Sri Lanka	
	C	D	C	D	C	D	C	D	C	D	C	D
1956-1980	30 191	1 339	8 588	357	5 167	48	49 499	2 683	...	...	69	17
1981	1 524	90	524	17	133	0	5 909	231	...	...	...	...
1982	1 706	49	3 006	35	216	0	4 665	255	...	...	...	...
1983	2 856	83	790	5	205	2	13 875	491	...	...	...	...
1984	3 232	39	702	5	86	0	12 710	382	...	...	...	...
1985	2 666	134	367	12	126	2	13 588	460	...	...	...	...
1986	2 192	111	1 408	8	354	1	16 529	608	...	...	...	...
1987	7 424	233	2 025	8	436	2	23 864	1 105	...	...	...	...
1988	1 181	65	1 428	3	245	0	44 573	1 527	...	...	10	...
1989	1 196	52	2 564	16	944	2	10 362	464	...	...	203	20
1990	6 318	182	4 880	21	1 733	3	22 807	821	...	...	1 350	54
1991	8 055	305	6 628	39	2 179	6	21 120	578	6 291	3	1 048	31
1992	1 678	37	5 473	24	2 878	4	17 620	509	2 683	12	656	15
1993	2 297	67	5 589	23	837	0	17 418	418	11 125	36	750	7
1994	11 050	444	3 133	13	1 216	0	18 783	471	7 494	4	582	7
1995	2 221	48	6 543	28	2 008	0	35 102	885	7 847	10	440	11
1996	1 621	18	14 255	...	3 128	0	44 650	1 192	13 069	460	1 244	28
1981-1985	11 984	395	5 389	74	766	4	50 747	1 819	...	...	...	...
1986-1990	18 311	643	12 305	56	3 712	8	118 135	4 525	...	...	1 563	74
1991-1995	25 301	901	27 366	127	9 118	10	110 043	2 861	35 440	65	3 476	71
Total[b]	87 408	3 296	67 903	614	21 891	70	373 074	13 080	48 509	525	6 352	190

[a] Data reported by WHO Regional Offices for South-East Asia and the Western Pacific. – Données notifiées par les bureaux régionaux de l'OMS pour l'Asie du Sud-Est et le Pacifique occidental.
[b] 1956-1996

Yapa and Palau; all 4 serotypes are circulating in these islands but usually a single serotype causes the epidemics *(9)*. In Australia a small outbreak associated with dengue-1 occurred in 1990-1991, and a large outbreak due to dengue-2 affected Townsville during 1992-1993; 21% of the patients presented minor haemorrhagic manifestations *(10)*. In 1995 an epidemic of dengue-3 affected several islands of New Caledonia; dengue-3 was the predominant serotype during the last epidemic which affected these islands in 1989 *(11)*. In 1995 increased dengue activity associated with serotype 2 was reported in the island of Rarotonga *(12)*.

African countries

All four dengue serotypes are known to circulate in Africa, but the presence of clinical dengue is documented by a few reports only. Recently outbreaks of dengue fever were described in Djibouti and the Comoro islands. The episode in Djibouti occurred in 1991-1992; it was associated with dengue-2 and the estimated number of cases was 12 000 *(13)*. During an outbreak associated with dengue-1 on Grand Comoro Island in 1993, it was estimated that between 56 000 and 75 000 persons became infected *(14)*. Dengue epidemics have also been recorded in the Seychelles, Kenya, Mozambique and Somalia, and cases compatible with DHF were observed in Mozambique *(6)*. Nevertheless no epidemics similar to those in Asia and in the Americas have been recorded.

Middle Eastern countries

An outbreak of dengue occurred in Jeddah, Saudi Arabia, in 1994, during which 2 fatal cases of DHF were recorded and were confirmed as dengue-2 infections by virus isolation. Both patients were adults, one died in shock and the other with hepatorenal failure. Genetic analysis of the isolate from one of the fatal cases showed a close relationship to other dengue-2 isolates from East Africa *(15)*. Prior to this event, dengue-2 transmission had been confirmed in Yemen.

The re-emergence of dengue and the emergence of DHF in the Americas

Historical overview

The first description of a dengue-like disease in the Americas relates to an outbreak that occurred in Philadelphia, United Sates, in 1780 *(1)*. In the following century 4 large epidemics affected Caribbean countries and the southern United States during the periods 1827-1828, 1850-1851, 1879-1880 and 1897-1899 *(16)*. Small-joint arthritis including swelling, commonly found in infections associated with the arboviruses Chikungunya and Mayaro, was among the clinical manifestations observed exclusively during the dengue outbreaks between 1827 and 1880. In the first half of this century 4 epidemics were reported in the same countries, the last one during the period 1941-1946, affecting cities in the Texas Gulf, several Caribbean islands including Cuba, Puerto Rico and Bermuda, Mexico, Panama and Venezuela *(16)*. In Brazil, epidemics of dengue were recorded during 1846-1848 and 1851-1853. From then until 1982 only 2 outbreaks were reported, in 1916 and 1923 *(17,18)*. Peru reported cases of dengue during the 1950s but not in the following 3 decades *(19)*. In 1953 dengue virus which was identified as serotype 2 was isolated for the first time in the Americas in the island of Trinidad. Several isolates of dengue-2 were obtained from persons in the same island during 1953-1954 but no outbreaks were reported in this period in Trinidad nor in any other Caribbean island *(20)*.

Re-emergence of dengue

During the 1960s two extensive pandemics of dengue affected the Caribbean and Venezuela. The first one which broke out in 1963 was due to dengue-3 and swept the Caribbean after almost 20 years of silence. Jamaica, Puerto Rico, islands of the Lesser Antilles and Venezuela were among the countries affected, although Cuba, Hispaniola and Trinidad were spared in this outbreak. The second epidemic occurred in the Caribbean and in Venezuela during 1968-1969 and although dengue-2 was predominantly isolated, dengue-3 was also recovered from persons in some islands *(16)*. During the 1970s these two serotypes caused extensive epidemics in Colombia where dengue had not been recognized since 1952 *(21)*. The first epidemic occurred during 1971-1972 and was due to dengue-2, whereas the 1975-1977 epidemic was associated with dengue-3. It was estimated that more than half a million persons became infected, although both outbreaks occurred "silently" for the most part or were confused with other illnesses and did not draw much attention on the part of the health authorities.

A milestone in the re-emergence of dengue in the Americas was the introduction of dengue-1 in 1977. This was followed by a devastating pandemic that lasted until 1980 *(22)*. The virus was initially detected in Jamaica, possibly having been imported from Africa, and from there the epidemic spread to virtually every island in the Caribbean. The epidemic in South America began in 1978, affecting Venezuela, Colombia, Guyana, Surinam and French Guiana. The epidemic in Central America was also detected in 1978, affecting Honduras initially and subsequently El Salvador, Guatemala and Belize. Spreading to the north, the epidemic reached Mexico at the end of 1978 and during 1979-1980 continued to affect other Mexican states, and reached the state of Texas in

the second half of 1980. About 702 000 cases were reported to the Pan American Health Organization (PAHO) for the period 1977-1980, but the incidence was much higher since estimates from Colombia, Cuba and Venezuela alone indicated that over 5 million persons became infected. In 1981 dengue-4 strain probably imported from Pacific islands emerged in the Americas causing a series of outbreaks in the Caribbean, northern South America, Central America and Mexico; with some exceptions, dengue-4 infection has generally been associated with mild disease *(22)*.

During the 1980s five countries in South America namely Brazil, Bolivia, Paraguay, Ecuador and Peru, that had not experienced dengue before or had been free of the disease for several decades were affected by explosive epidemics caused by serotype 1 *(22)*; in the epidemic in Peru serotype 4 was also isolated *(23)*. The first epidemic which occurred in northern Brazil in 1982 was associated with serotypes 1 and 4 *(24)*; vector control measures were implemented, and since then no dengue activity has been reported in this area. In 1986, dengue 1 was introduced in Rio de Janeiro, Brazil, causing major outbreaks *(25)*. It was subsequently disseminated to most states in Brazil. Following its introduction in those countries, dengue-1 virus has continued to cause major epidemics in Brazil, Ecuador and Peru in subsequent years.

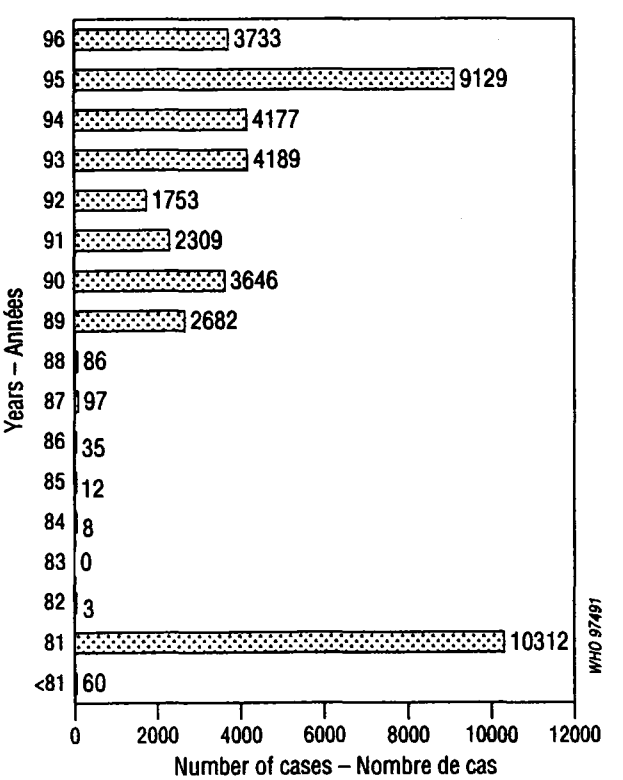
During 1993, the last two tropical Latin American countries which had been free of dengue for several decades, namely Costa Rica and Panama, reported indigenous transmission of dengue; the serotype was dengue-1 and its introduction in Costa Rica was associated with severe outbreaks in this year and in subsequent years *(26)*. In 1994 dengue-3 was reintroduced in the Americas for the first time since 1978 when it had been isolated in Puerto Rico *(27)*. This serotype was initially detected in Panama and Nicaragua and in the following year it spread to other Central American countries and to Mexico, causing numerous epidemics of dengue. In Nicaragua, in 1994, the introduction of dengue-3 was associated with a countrywide epidemic of dengue/DHF but dengue-1 was also present. The introduction of dengue-3 in Mexico in 1995 coincided with an increased number of DHF cases; however, only dengue-1 and particularly dengue-2 were associated with DHF *(28)*. It should be noted that this dengue-3 virus belongs to the genotype that has caused major epidemics of DHF in Sri Lanka and India *(27)*. As of June 1997, dengue-3 has not been isolated outside Central America and Mexico. Over 250 000 cases of dengue were reported in the Region in each of 1995 and 1996.

The emergence of DHF

In 1981, Cuba reported the first major outbreak of DHF in the Americas *(2)*. Prior to this, suspected cases of DHF or fatal dengue cases had been reported by 5 countries or territories namely Venezuela, Jamaica, Honduras, Curacao and Puerto Rico, but only a few of them fulfilled the WHO criteria for diagnosis of dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS) and most were not laboratory confirmed *(22)*. During the Cuban epidemic, a total of 344 203 cases of dengue were notified, of which 10 312 were classified as severe cases (WHO grades II-IV) and 158 were fatal; a total of 116 143 patients were hospitalized, the majority of them during a 3-month period *(2)*. The DHF Cuban epidemic was associated with a strain of dengue-2 virus and it occurred 4 years after dengue-1 had been introduced in the island causing epidemics of dengue fever and infecting almost half of the population.

The outbreak of DHF/DSS in Cuba is the most important event in the history of dengue in the Americas. Since then, in every year except 1983, confirmed or suspected cases of DHF have been reported in the Americas *(Fig. 1)*. The figure shows that a marked increase in the annual incidence occurred in 1989 which was due to a countrywide epidemic in Venezuela. This was the second major DHF epidemic in the Americas with 3 108 DHF cases and 73 deaths being reported between

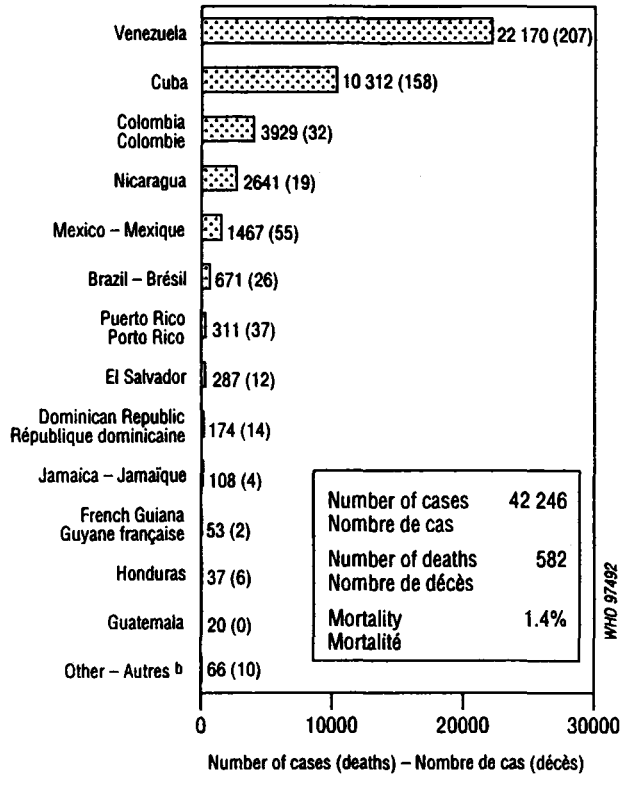
Fig. 1
Cases of dengue haemorrhagic fever in the Americas, 1981-1996[a]
Cas de dengue hémorragique dans les Amériques, 1981-1996[a]



[a] Provisional figure for 1996 – Chiffre provisoire pour 1996

Fig. 2
Number of reported cases (deaths) of dengue haemorrhagic fever in the Americas by country/territory, 1981-1996[a]

Nombre de cas (décès) de fièvre hémorragique notifiés dans la Région des Amériques, par pays/territoire, 1981-1996[a]



[a] Provisional figures for 1996. – Chiffres provisoires pour 1996.

[b] Martinique 17 (1), Suriname 11 (0), Dominica – Dominique 11 (0), Guadeloupe 7 (3), Trinidad and Tobago – Trinité-et-Tobago 7 (1), Panama 3 (1), Grenada – Grenade 3 (0), Aruba 2 (2), Barbados – Barbade 2 (1), Costa Rica 1 (0) Saint Lucia – Sainte-Lucie 1 (0), Saint Kitts and Nevis – Saint Kitts-et-Nevis 1 (0).

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Between 1981 and 1996 a total of 42 246 cases of DHF and 582 deaths were reported by 25 countries in the Americas. *Fig. 2* shows the distribution of cases by country where it can be observed that 22 170 (53%) of the reports originated from Venezuela. It can also be seen that excluding Cuba and Venezuela, the number of cases by country varies from 1 to 3 740. Colombia, Nicaragua and Mexico have each reported over 1 000 cases, most of which during the period 1992-1996. About 74% of the Colombian cases were notified during 1995-1996 whereas 97% of the Mexican cases were reported during 1995-1996. In Brazil, 4 fatal cases which exhibited fever, haemorrhages and shock occurred during 1986-1987 and were associated with dengue-1 virus; confirmation was obtained by virus isolation or by antigen detection *(22)*. In 1990-1991 an outbreak of DHF was recorded in Rio de Janeiro, Brazil *(30)* and 24 cases with 11 deaths occurred in the Brazilian State of Ceara in 1994 *(31)*.

Studies of DHF cases in the Americas *(32, 29, 33, 34)* revealed similarities to the clinical manifestations exhibited by DHF patients in Asia. However, the incidence of gastrointestinal haemorrhages observed in Cuba and Puerto Rico seem to be higher than that seen in Thai children *(35)*. Liver necrosis was described in 70% of 72 children who died of DHF in Cuba in 1981 *(35)*. Severe neurological manifestations, renal failure and myocarditis have been occasionally reported in the Americas *(31, 36, 37)*.

The age distribution of DHF cases in the Americas is different to that observed in Asia. In the outbreaks in Cuba and Venezuela the disease has occurred in all age groups, although children under 15 years of age have comprised about two-thirds of the fatalities. Studies of DHF cases that fulfilled WHO's criteria done in Brazil *(34)* showed a modal age range of 31-45 years. Observations made in Puerto Rico showed distinct age distribution patterns of cases that fulfilled WHO's criteria: in 1986 two-thirds of the cases were under 15 years of age, but during 1990-1991 the mean age of patients was 38 years *(37, 33)*. This age distribution pattern is different from that found in South-East Asia where young children are affected predominantly. It should be noted, however, that a marked increase in the number of DHF cases in people over 15 years old has been observed in the Philippines and Malaysia during recent years *(38)*. Regarding the sex distribution, Cuba reported no significant female predominance, a finding that is in contrast with observations from Asia.

The epidemics in Cuba and Brazil were clearly associated with dengue-2 virus. In both countries dengue-1 had been introduced 4 years earlier, after a period of several decades of absence of dengue virus circulation. However, a major epidemic occurred in Cuba while only relatively small outbreaks have been observed in Brazil. Other countries such as Peru and Ecuador have experienced a similar sequence of dengue infections with these serotypes, but no DHF epidemics were recorded. A distinct epidemiological pattern was observed in Venezuela and in French Guiana where dengue was endemic for over 20 years before the emergence of the first epidemics of DHF in 1989-1990 and 1990-1991 respectively. Dengue-2 was predominant in Venezuela *(29)* and in French Guiana *(39)* and the only serotype found in the

tissues of fatal cases in Venezuela *(29)*. In French Guiana, the dengue-2 strains isolated during the DHF outbreak and during an outbreak of dengue fever that occurred in 1986 were genetically similar and belonged to the Jamaican genotype which in turn has a genome sequence very close to dengue-2 strains from Viet Nam where DHF is highly endemic *(39)*. These findings illustrate the complexity of the factors responsible for triggering DHF. Studies in Cuba suggested that individual risk factors for DHF include chronic diseases such as bronchial asthma, diabetes mellitus and sickle cell anaemia, and that race seems also to be important, since DHF/DSS was more prevalent in white than in black persons *(40)*.

Overall, the case-fatality rate (CFR) of DHF in the Americas is 1.4% *(Fig. 2)*. However, a marked variation has been observed among countries. In 1995, the CFR ranged from 8.3% in Puerto Rico to 0.8% in Venezuela. This variation could be due to several factors such as reporting criteria, viral strain, case management, host genetic factors and possibly other causes.

Causes of the emergence/re-emergence

In 1947, PAHO was entrusted by its Directing Council to organize a hemispheric campaign to eradicate the mosquito *Aedes aegypti*. By 1962, 18 continental countries and several Caribbean island countries had successfully eradicated the vector. Unfortunately, after 1962 only 3 additional countries eliminated the vector. Even more serious, however, was that the countries that had achieved eradication became reinfested in the 1960s and in subsequent decades. Countries still infested (the United States, Cuba and some other Caribbean islands, Venezuela) became sources of reinfestation for those that had eradicated the vector. Other reasons for the programme's failure include reduced political support, resulting in inadequate management and scarcity of trained technical personnel; resistance of *A. aegypti* to chlorinated insecticides and high cost of materials, equipment and wages. There was progressive dissemination of the vector so that by 1997 with the exception of Canada, Chile and Bermuda, all countries in the Americas are infested. *Map 1* shows the distribution of *A. aegypti* before and after the achievements of the eradication programme, where it can be seen that the mosquito has regained most of its original distribution. The practice of water storage in domestic settings due to the problems of water supply and the exponential growth of containers that can hold water (tires, disposable containers) greatly contribute to the increase of vector densities favouring virus transmission. Other factors contributing to the emergence/re-emergence of dengue/DHF include the rapid growth and urbanization of populations in Latin America and the Caribbean, and increased travel of persons which facilitates dissemination of dengue viruses. At present, all 4 dengue serotypes are circulating in the Americas, thus increasing the risk for DHF in this region.

Map 1 Distribution of *Aedes aegypti* in the Americas, 1930, 1962 and 1997

Carte 1 Répartition d'*Aedes aegypti dans* les Amériques, 1930, 1962 et 1997

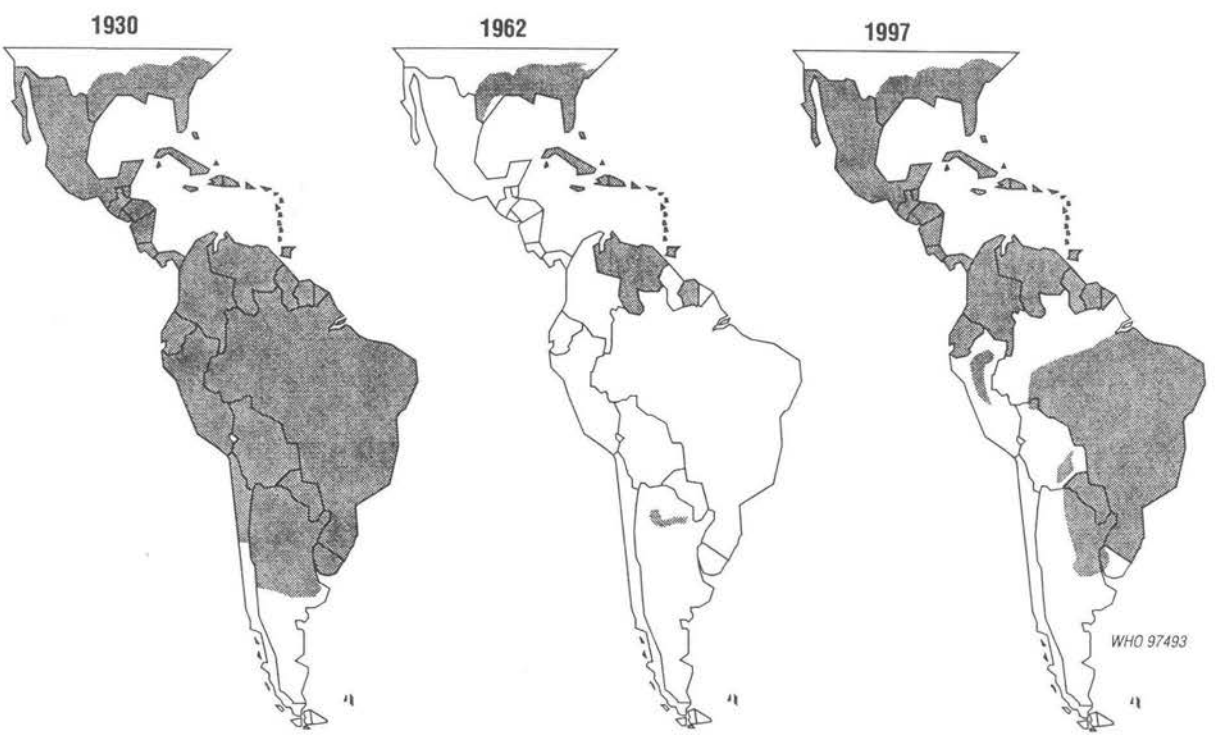
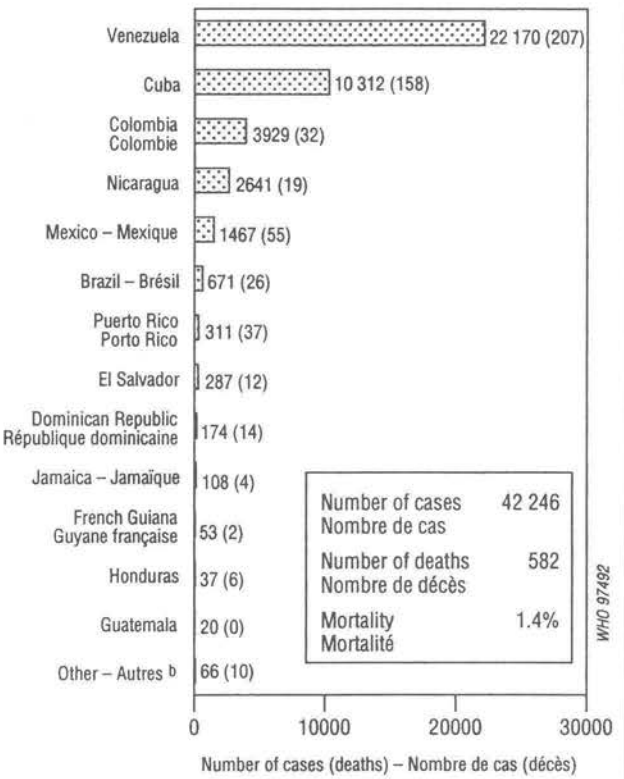


Fig. 2
Number of reported cases (deaths) of dengue haemorrhagic fever in the Americas by country/territory, 1981-1996[a]

Nombre de cas (décès) de fièvre hémorragique notifiés dans la Région des Amériques, par pays/territoire, 1981-1996[a]



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Prevention and control

The high number of dengue and DHF cases, the presence of all 4 dengue virus serotypes in the Region, and the extensive range of the vector make it necessary to intensify disease prevention and control activities.

Unfortunately a vaccine against dengue is not available at present. A live attenuated tetravalent vaccine developed in Thailand looks promising, but field efficacy trials have not yet been undertaken. In parallel, efforts are being made to develop a genetically engineered dengue vaccine. Different approaches are being explored such as chimeric infectious clone using dengue-2 attenuated or 17D yellow fever strains as backbones, and a DNA naked vaccine. Despite these efforts it may take 5-10 years before a vaccine safe and efficacious for the immunization of children becomes available.

Therefore vector control is at present the only approach to combat dengue/DHF. Recent discussions concerning a new effort to eradicate the vector from the Americas have not been well received by Member countries generally because of high cost, the need for hemispheric commitment and implementation, and various operational obstacles (such as difficulties in establishing vertical programmes and problems accessing certain slum areas). At a meeting in Caracas, Venezuela, in April 1997, experts recommended a 5-step approach beginning with control programmes and leading to eventual eradication.

PAHO has developed guidelines *(35)* for the prevention and control of dengue/DHF and *A. aegypti* which include several components that should be implemented together. These components are as follows: *(a)* epidemiological surveillance (active, with laboratory support); *(b)* education of the medical community to recognize and properly treat dengue/DHF cases; *(c)* entomological surveillance; *(d)* vector control with emphasis on source reduction utilizing environmental management (improvement of water supply, adequate solid waste management, naturalistic methods), chemical methods and biological control; *(e)* community participation with efforts oriented towards the elimination or proper handling of potential breeding sites, physical protection of water storage areas and clean up campaigns; and *(f)* emergency plans to cope with epidemics of dengue/DHF.

There is a lack of well organized and effective control programmes at present as evidenced by the frequent outbreaks/epidemics of dengue fever and the increase of DHF in several countries. Emergency measures to combat the epidemics have had limited impact. A reliance on emergency as the basis for response to this disease cannot be successful. Rather, countries must dedicate themselves to coordinated prevention and control programmes in order to be effective.

Summary

About two-thirds of the world's population live in areas infested with dengue vectors, mainly *Aedes aegypti*. All four dengue viruses are circulating, sometimes simultaneously, in most of these areas. It is estimated that up to 80 million persons become infected annually although marked underreporting results in the notification of much smaller figures. Currently dengue is endemic in all continents except Europe and epidemic dengue haemorrhagic fever (DHF) occurs in Asia, the Americas and some Pacific islands. The incidence of DHF is much greater in the Asian countries than in other regions.

In Asian countries the disease continues to affect children predominantly although a marked increase in the number of DHF cases in people over 15 years old has been observed in the Philippines and Malaysia during recent years. In the 1990's DHF has continued to show a higher incidence in South-East Asia, particularly in Viet Nam and Thailand which together account for more than two-thirds of the DHF cases reported in Asia. However, an increase in the number of reported cases has been noted in the Philippines, Lao People's Democratic Republic, Cambodia, Myanmar, Malaysia, India, Singapore and Sri Lanka during the period 1991-1995 as compared to the preceding 5-year period.

In the Americas, the emergence of epidemic DHF occurred in 1981 almost 30 years after its appearance in Asia, and its incidence is showing a marked upward trend. In 1981 Cuba reported the first major outbreak of DHF in the Americas, during which a total of 344 203 cases of dengue were notified, including 10 312 severe cases and 158 deaths. The DHF Cuban epidemic was associated with a strain of dengue-2 virus and it occurred four years after dengue-1 had been introduced in the island causing epidemics of dengue fever. Prior to this event suspected cases of DHF or fatal dengue cases had been reported by five countries but only a few of them fulfilled the WHO criteria for diagnosis of DHF. The outbreak in Cuba is the most important event in the history of dengue in the Americas. Subsequently to it, in every year except 1983, confirmed or suspected cases of DHF have been reported in the Region. The second major outbreak in the Americas occurred in Venezuela in 1989 and since then this country has suffered epidemics of DHF every year.

Between 1981 and 1996 a total of 42 246 cases of DHF and 582 deaths were reported by 25 countries in the Americas, 53% of which originated from Venezuela and 24 % from Cuba. Colombia, Nicaragua and Mexico have each reported over 1 000 cases during the period 1992-1996. About 74% of the Colombian cases and 97% of the Mexican cases were reported during 1995-1996.

A main cause of the emergence of DHF in the Americas was the failure of the hemispheric campaign to eradicate *Aedes aegypti*. Following a successful period that resulted in the elimination of the mosquito from 18 countries by 1962, the programme began to decline and as a result there was a progressive dissemination of the vector so that by 1997 with the exception of Canada, Chile and Bermuda, all countries in the Americas are infested. Other factors contributing to the emergence/

re-emergence of dengue/DHF include the rapid growth and urbanization of populations in Latin America and the Caribbean, and increased travel of persons which facilitates dissemination of dengue viruses. Presently, all four dengue serotypes are circulating in the Americas, thus increasing the risk for DHF in this region.

Résumé

La situation mondiale de la dengue et de la dengue hémorragique et leur émergence dans les Amériques

Près des deux tiers de la population mondiale vivent dans des régions infestées par les vecteurs de la dengue, et principalement par *Aedes aegypti*. Les quatre virus de la dengue circulent, parfois simultanément, dans la plupart de ces régions. On estime que jusqu'à 80 millions de personnes seraient infectées chaque année, bien qu'une nette sous-notification se traduise par la déclaration de chiffres beaucoup moins importants. Actuellement, la dengue sévit à l'état endémique sur tous les continents sauf en Europe, et la dengue hémorragique sévit sur le mode épidémique en Asie, dans les Amériques et dans certaines îles du Pacifique. L'incidence de la dengue hémorragique est beaucoup plus importante dans les pays d'Asie que dans d'autres régions.

Dans les pays d'Asie, la maladie continue de toucher principalement les enfants, bien que l'on ait observé une augmentation sensible du nombre de cas de dengue hémorragique chez les personnes de plus de 15 ans aux Philippines et en Malaisie ces dernières années. Dans les années 90, l'incidence de la dengue hémorragique est restée plus élevée en Asie du Sud-Est, en particulier au Viet Nam et en Thaïlande, où l'on dénombre plus des deux tiers des cas notifiés en Asie. Toutefois, une augmentation du nombre de cas notifiés a été enregistrée aux Philippines, en République démocratique populaire lao, au Cambodge, au Myanmar, en Malaisie, en Inde, à Singapour et au Sri Lanka pendant la période 1991-1995 par rapport à la période de 5 ans précédente.

Dans la Région des Amériques, la dengue hémorragique épidémique a fait son apparition en 1981, soit une trentaine d'années après l'Asie, et son incidence accuse une tendance marquée à la hausse. En 1981, Cuba a signalé la première flambée d'importance de dengue hémorragique aux Amériques. Pendant l'épidémie survenue à Cuba, 344 203 cas de dengue ont été notifiés, dont 10 312 classés comme cas graves et 158 mortels. L'épidémie de dengue hémorragique à Cuba était associée à une souche du virus de la dengue 2 et s'est produite 4 ans après que le virus de la dengue 1 eut fait son apparition sur l'île, entraînant des épidémies. Avant cela, des cas suspects de dengue hémorragique ou des cas mortels de dengue avaient été déclarés par cinq pays, mais seuls quelques-uns répondaient aux critères de diagnostic de la dengue hémorragique établis par l'OMS. La flambée de Cuba est la plus importante manifestation survenue dans l'histoire de la dengue aux Amériques. A la suite de celle-ci, chaque année, sauf en 1983, des cas suspects ou confirmés de dengue hémorragique ont été notifiés dans la Région. La deuxième flambée majeure aux Amériques s'est produite au Venezuela en 1989 et, depuis, ce pays a connu des épidémies de dengue hémorragique chaque année.

Entre 1981 et 1996, 42 246 cas de dengue hémorragique et 582 décès ont été signalés par 25 pays des Amériques, dont 53% par le Venezuela et 24% par Cuba. La Colombie, le Nicaragua et le Mexique ont chacun signalé plus de 1 000 cas au cours de la période 1992-1996. Environ 74% des cas survenus en Colombie et 97% des cas survenus au Mexique ont été notifiés en 1995-1996.

L'une des principales causes de l'émergence de la dengue hémorragique dans les Amériques a été l'absence de campagnes d'éradication d'*Aedes aegypti* à l'échelle du continent. Après une période de succès qui s'est traduite par l'élimination du moustique dans 18 pays en 1962, le programme a commencé à décliner et, de ce fait, le vecteur a commencé à se disséminer progressivement, au point qu'en 1997, à l'exception du Canada, du Chili et des Bermudes, tous les pays des Amériques étaient infestés. Parmi les autres facteurs contribuant à l'émergence/réémergence de la dengue/dengue hémorragique figurent la croissance rapide et l'urbanisation des populations d'Amérique latine et des Caraïbes, et les mouvements accrus de personnes qui facilitent la dissémination des virus de la dengue. A l'heure actuelle, les quatre sérotypes circulent dans les Amériques, accroissant ainsi le risque de dengue hémorragique dans cette région.

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Meningococcal disease: public health burden and control

Eugene Tikhomirov[a], *Maria Santamaria*[b] & *Karin Esteves*[c]

Introduction

Meningococcal disease is one of the most important medical emergencies demanding early diagnosis and effective therapy. Although effective, nontoxic and affordable antibiotics are available worldwide, the disease is still associated with a very high mortality and persistent neurological defects, particularly among infants and young children.

Sporadic meningococcal meningitis occurs throughout the world, with seasonal variations, and accounts for 10-40% of endemic bacterial meningitis. Epidemic meningitis also occurs in any part of the world, but the largest and most frequently recurring outbreaks have been in the semi-arid area of sub-Saharan Africa, designated the "meningitis belt".

The socioeconomic implications of epidemic meningitis can be disruptive. The control and prevention of cerebrospinal meningitis (CSM) outbreaks requires a massive amount of vaccine, medicines, injection material, and logistic support from the national health authorities of the affected countries. Most countries face great difficulties in responding appropriately to these needs. In addition, routine health services and other important activities are disrupted.

The current pandemic in the meningitis belt in Africa, causing thousands of deaths, has again focused global attention on meningitis. To respond to the current situation and the expected spread of the disease, WHO, in collaboration with its Member States and various governmental and non-governmental agencies, has developed a sustainable plan of action for preparedness and control of meningococcal disease in the region.

Endemic disease

Meningococcal disease is a contagious disease caused by the meningococcus *(N. meningitidis)*, a gram-negative bacterium. Thirteen serogroups based on the specificity of the capsular polysaccharides are currently recognized (A, B, C, D, H, I, K, L, W135, X, Y, Z and Z'). Meningitis is the most common clinical expression of the infection, particularly during epidemics, while meningococcal septicaemia (meningococcaemia), is less common but highly fatal.

In its endemic form, meningococcal disease causes sporadic cases or small clusters. The rates of endemic meningococcal disease range from 1 to 5 per 100 000 population in Europe and North America. In developing countries, particularly in the sub-Saharan arid area, the incidence rate between epidemics varies from <10 to >20 per 100 000 *(1)*. In many countries, endemic meningococcal disease cannot be distinguished from other causes of purulent meningitis because laboratory facilities are lacking, and meningococcal meningitis is thus reported as part of bacterial meningitis. Over 80% of cases of bacterial meningitis are caused by three bacteria: *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae* type b. Meningococcal meningitis or cerebrospinal meningitis (CSM), caused by *N. meningitidis*, is the only one which occurs in epidemic form. Apart from epidemics, at least 1.2 million cases of bacterial meningitis are estimated to occur every year; 135 000 of them are fatal *(Table 1)*. Approximately 500 000 of these cases and 50 000 of deaths are due to meningococcus.

During non-epidemic conditions in developed countries, 50-60% of the cases occur in children 3 months to 5 years of age, but cases are also seen in teenagers and young adults under 25-30 years of age. In countries within the meningitis belt the maximum incidence is usually found among children aged 5-10 years. Household contacts of patients with meningococcal disease have a risk of acquiring infection equal to approximately 600-1 000 times the age-specific incidence in the general population. Meningococcal infection affects both sexes but males have a higher incidence. Young people living in closed communities, such as boarding schools, are affected more than other individuals. Meningococcal disease is also considered a military disease, as its incidence among non-vaccinated recruits is at least 4-10 times higher than in the general population. In the northern hemisphere, including subtropical countries, a seasonal upsurge in meningococcal disease occurs in winter and spring, beginning in December-January and culminating in March-April *(1)*.

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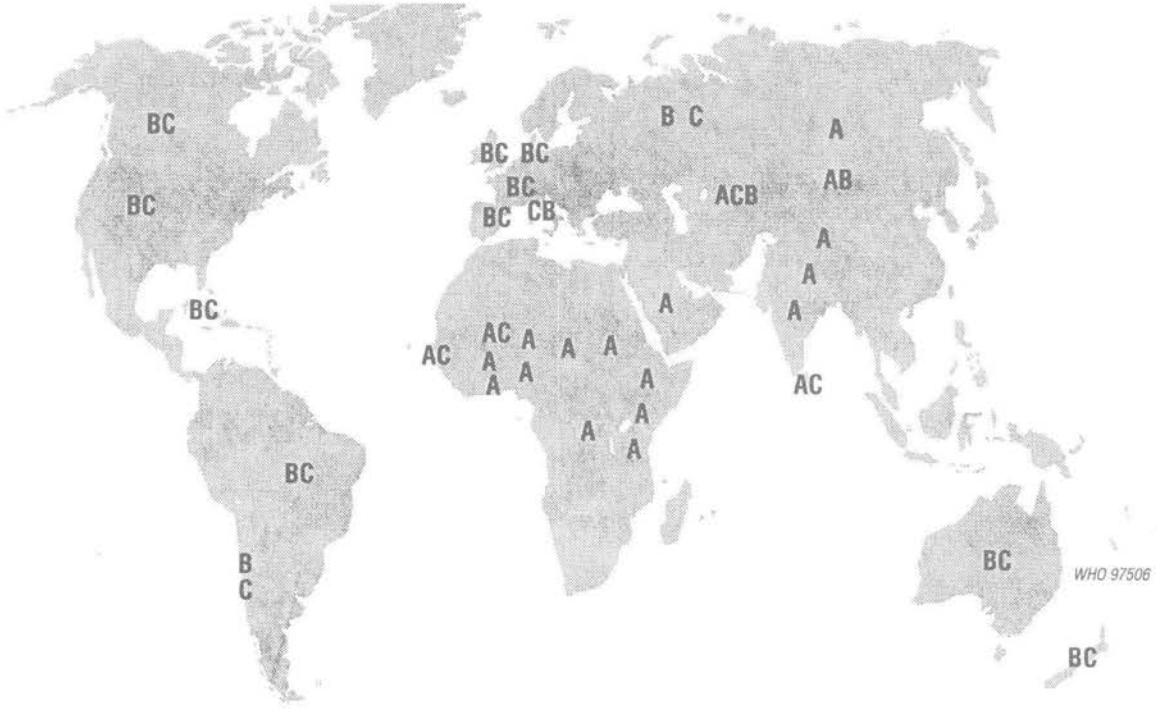
Table 1
Estimated global number of cases and deaths from bacterial meningitis by WHO Region, 1997

Tableau 1
Nombre mondial estimé de cas de méningite bactérienne et nombre de décès, par Région OMS, 1997

WHO Region – Région OMS	Bacterial meningitis – Méningite bactérienne			Meningococcal meningitis – Méningite à méningocoque		
	All – Nombre total	Disabled – Nombre d'incapacités	Fatal – Nombre de décès	All – Nombre total	Disabled – Nombre d'incapacités	Fatal – Nombre de décès
Africa – Afrique	500 000	75 000	60 000	250 000	31 000	27 000
America – Les Amériques	80 000	9 000	9 000	30 000	5 000	2 500
Eastern Mediterranean – Méditerranée orientale	150 000	20 000	16 000	50 000	6 000	5 000
Europe	100 000	10 000	10 000	40 000	2 000	3 000
South-East Asia – Asie du Sud-Est	160 000	20 500	17 000	55 000	7 500	5 500
Western Pacific – Pacifique occidental	210 000	25 500	23 000	75 000	8 500	7 000
Total	1 200 000	160 000	135 000	500 000	60 000	50 000

Of the 13 serogroups of *N. meningitidis*, serogroup B is a predominant agent causing systemic disease, followed in frequency by serogroup C both in Europe and in the Americas *(Map 1)*. Serogroup A meningococcus, historically the main cause of epidemic meningococcal disease all over the world, still dominates in Africa and Asia during both endemic and epidemic periods. Although reporting is incomplete, available information clearly indicates a global increase of meningococcal disease. In industrialized countries, where statistics are available, both overall increased incidence and series of local outbreaks were associated with serogroup C meningococci, e.g. in the Czech Republic, England and Wales, Finland, France, Israel, Spain and the United States since the early 1990s. An upsurge of meningococcal serogroup C disease was due to the emergence and spread of particular

Map 1. Distribution of predominant *N. meningitidis* serogroups (A, B & C), 1996–1997
Carte 1. Répartition des sérogroupes de *N. meningitidis* prédominants (A, B et C), 1996–1997



strains (phenotypes) such as C:2a:P1.2,5 and C:2b:P1.2,5.

Epidemic disease

In the 1960s, meningococcal infection was no longer considered to be a serious problem in Europe and North America. It was still a permanent public health problem in countries situated in the African meningitis belt where large outbreaks used to occur every 8-12 years. The intervals between epidemics have now become shorter and more irregular, particularly in regions with extensive mixing and communication between populations. Outside the meningitis belt, no evident periodicity has been observed.

The increasing trend noted in a number of countries of the Americas, Asia and Europe since the early 1970s, shows a characteristic pattern of recurrent epidemics and persistent sporadic cases. Although the epidemics are far less severe outside the African meningitis belt, it is evident that epidemic meningococcal disease in the past two decades has become a worldwide problem which can affect any country regardless of climate *(Map 2)*.

Several countries in Europe (Belgium, France, Italy, Portugal, Spain, United Kingdom and the former Yugoslavia) reported significant increases or outbreaks (Finland, Norway, Russia) in the 1970s. Increased activity was also reported in Argentina, and outbreaks in Algeria, Brazil, Chile, Mongolia, and Vietnam. In the 1980s, an epidemic wave of meningococcal disease spread over vast territories in Asia (India, Nepal) and in Africa *(Map 2)*. Approximately 1 500 cases of meningococcal meningitis occurred in the Kathmandu Valley, Nepal, in 1982-1984 with an annual attack rate of 103 cases per 100 000 population. In 1985, New Delhi experienced an outbreak after a lapse of almost 20 years; 6 133 cases were reported, and the overall case-fatality rate was 13%, the highest occurring in children under 1 year of age (25.5%). An epidemic of group B meningococcal disease occurred in Cuba in 1982-1984, and in Chile in 1986 and 1993. An epidemic of group A meningococcal disease occurred in Mongolia in 1994-1995 and local outbreaks due to group C meningococcus were reported in Canada and the United States in 1992-1993 *(3)* and in Spain in 1995-1997.

Meningococcal disease is particularly severe across sub-Saharan Africa where large epidemics occur periodically with attack rates that may exceed 500 per 100 000 population. *Table 2* presents the reported and estimated number of CSM cases (per decade) in this hyperendemic area, during the period 1970 to September 1997. These numbers are not far from the 340 000 cases with 53 000 deaths reported in the 10-year period, 1951-1960 *(2)*.

In the 1980s epidemics of meningococcal disease occurred throughout the meningitis belt in Benin, Burkina Faso, Chad, the Gambia, Ghana, Mali, Niger, Nigeria, Senegal and Togo, culminating in severe epidemics in Ethiopia and Sudan in

Map 2. Major outbreaks of meningococcal meningitis, 1971–1997
Carte 2. Principales épidémies de méningite à méningocoques, 1971–1997

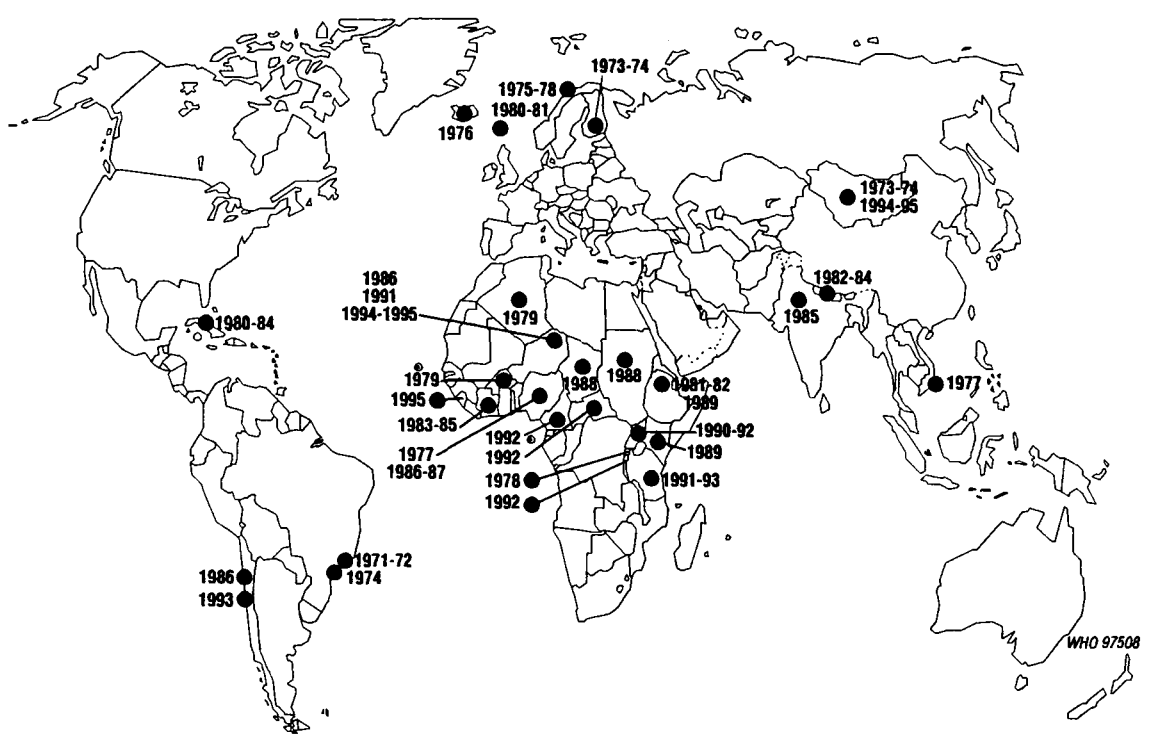


Table 2
Number of cases of cerebrospinal meningitis reported in the African meningitis belt, 1970-1997

Tableau 2
Nombre de cas de méningite cérébrospinale signalés dans la ceinture africaine de la méningite, 1970-1997

Year – Année	Number of cases – Nombre de cas	Adjusted for incomplete reporting – Après ajustement pour tenir compte des données incomplètes
1970-1979	236 608	298 850
1980-1989	388 762	389 540
1990-1997	379 992[a]	> 500 000[b]

[a] Reported up to 1 October 1997. – Notifiés au 1er octobre 1997.
[b] By 31 December 1999. – Au 31 décembre 1999.

Table 3
Cases (and deaths) of cerebrospinal meningitis reported in selected African countries, 1996 and 1997

Tableau 3
Nombre de cas de méningite cérébrospinale (et nombre de décès) signalés par différents pays africains en 1996 et 1997

Country – Pays	1996 Cases – Cas	1996 Deaths – Décès	1997 Cases – Cas	1997 Deaths – Décès
Benin – Bénin	699	84	360	54
Burkina Faso	42 129	4 226	21 504	2 426
Burundi	138	32	...	...
Cameroon – Cameroun	178	30	...	...
Central African Republic – République centrafricaine	155	22	10	3
Chad – Tchad	1 079	109	158	17
Côte d'Ivoire	...	...	...	...
Democratic Republic of the Congo – République démocratique du Congo	86	11	1 210	...
Eritrea – Erythrée	...	...	7	1
Ethiopia – Ethiopie	771	11	...	...
Gambia – Gambie	...	...	913	120
Ghana	479	41	18 551	1 403
Guinea – Guinée	89	15	51	4
Malawi	269	29	...	...
Mali	7 254	10 960	10 960	1 106
Mauritania – Mauritanie	...	...	11	2
Mozambique	2 132	121	101	18
Niger	16 145	1 502	3 922	442
Nigeria – Nigéria	77 089	8 651	...	...
Senegal – Sénégal	...	...	13	4
Sudan – Soudan	301	...	176	...
Togo	517	100	2 845	427
United Republic of Tanzania – République-Unie de Tanzanie	1 286	204	...	...
Zambia – Zambie	1 897	194	69	...
Total	152 693	16 213	60 861	6 027

1987-1989 *(Map 2)*. More than 30 000 cases were reported in Sudan in 1988, the year of peak incidence, and over 40 000 cases in Ethiopia in 1989.

Since the mid-1990s epidemics in the African meningitis belt have been on an unprecedented scale *(Table 3)*. Over 150 000 cases were reported to WHO during the 1996 season, of which about 16 000 were fatal. Nearly 95% of all cases and deaths in Africa in 1996 occurred in 4 countries: Burkina Faso, Mali, Niger and Nigeria. The anticipated continuation of CSM epidemics during the 1997 season materialized, with large outbreaks in

Burkina Faso, the Gambia, Ghana, Mali, Niger and Togo *(Table 3)*.

The epidemics that occurred towards the end of the 1980s through the 1990s in Burundi, Central African Republic, Democratic Republic of the Congo (formerly Zaire), Kenya, Rwanda, United Republic of Tanzania, Uganda and Zambia are examples of the spread of the disease outside its usual boundaries. If this is truly a new characteristic of the epidemiology of meningococcal disease, it could be due to climate change with subsequent extension of drought areas, or increased mobility of the population whether by voluntary travel, or because of massive migration of internally displaced and refugee populations. The outbreaks may also reflect the introduction of a new meningococcal strain into susceptible populations.

Epidemics in Africa spread rapidly and reach their peak within weeks, but can last for several months in the absence of vaccination. Often the epidemic recurs for 2-3 years starting with a local outbreak in a city or a rural region in the first year followed by a more widespread and intense epidemic the next year. Incidence rates then often remain elevated during the subsequent 1-2 years with successive seasonal outbreaks separated by periods of remission. This pattern seen at the provincial or national level may result from the combination of a number of local outbreaks, spreading from place to place throughout the country, in particular along the transport axes. In regions without marked seasons, epidemics can last for 6 months or more in the absence of vaccination. While sporadic cases generally occur among young children, the epidemics often result in broader age distribution involving older children, teenagers and young adults.

Conditions favouring epidemics

Epidemics are favoured by multiple factors related to the microorganism, the host and the environment. Interactions between these factors may explain the periodicity and seasonal patterns of epidemics, as well as the unusual age distribution among individuals who contract meningitis during an epidemic *(4)*.

Microorganism

The risk of epidemic meningococcal disease differs between serogroups. The most explosive epidemics have been almost exclusively associated with serogroup A, but B and C serogroups can also cause outbreaks. Certain strains of meningococci are more virulent and more likely to cause outbreaks. The spread of a single clone of serogroup A *N. meningitidis* designated as an epidemic clone III.1 has been associated with the current pandemic. This particular strain may be linked to the epidemic which started in China and, after passing through Nepal and Northern India, caused a large outbreak in Mecca in 1987 *(5)*. It subsequently caused a CSM pandemic in Africa and has been identified in Burundi, Central African Republic, Chad, Democratic Republic of the Congo, Ethiopia, the Gambia, Guinea, Kenya, Mali, Niger, Nigeria, Rwanda, Sudan, South Africa, United Republic of Tanzania and Zambia *(5, 6, 7)*. Particular clones of *N. meningitidis* serogroups B and C have been responsible for clusters and local outbreaks in Australia, Canada, New Zealand, United Kingdom and the United States *(3, 8)*.

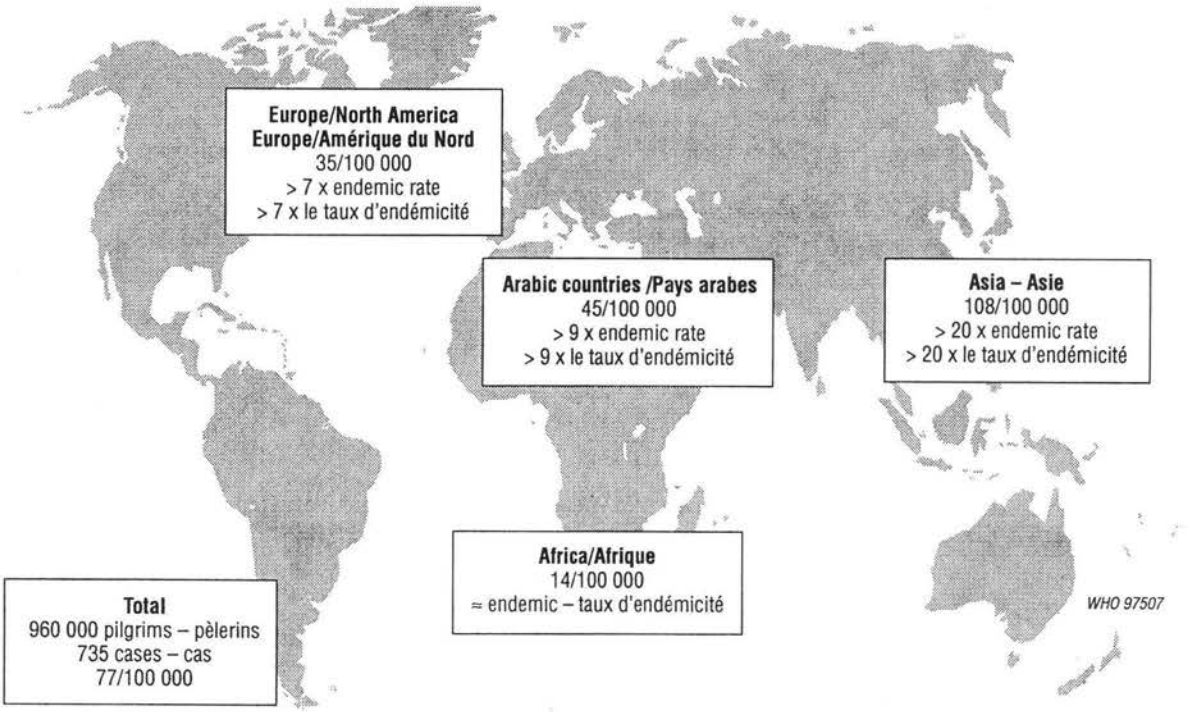
Host

Nasopharyngeal carriage permits the infection to persist in the community. Although an increasing carrier rate could raise the risk of infection among non-immune individuals there is no constant and close relationship between the carrier rate and the incidence of disease *(9)*. Humoral immunity is an essential factor in the prevention of meningococcal disease. Waning herd immunity to a particular strain in a population may be necessary for an outbreak to occur and could contribute to the regularity of epidemic cycles in sub-Saharan Africa *(4)*. Concurrent infections may predispose to meningococcal infection. During a group A meningococcal epidemic in Chad in 1988, patients with meningococcal meningitis were about 23 times more likely than matched control patients to have nasopharyngeal shedding of respiratory pathogens, including *Mycoplasma hominis*, adenoviruses, parainfluenza viruses, rhinoviruses and respiratory syncytial virus *(4)*. In temperate countries, an increase in the incidence of meningococcal disease has been observed to follow outbreaks of influenza.

Environment

Climate factors play an important role in the seasonal upsurge of meningococcal disease. Peak activity is in general in periods of low absolute humidity, such as the winter in temperate climate zones and the dry season in Africa. Drought and dust storms in sub-Saharan Africa can help the spread of infection while the onset of the rainy season often leads to the end of the epidemic. Poor living conditions and overcrowded housing are linked with a higher incidence of meningococcal disease. During a recent epidemic in Nairobi, the highest attack rates occurred in two districts, Kasarani and Kibera, where the city's largest slums are located *(10)*. Travel and migration facilitate the circulation of virulent strains within a country or between countries. Imported cases of group A meningococcal disease in Moscow in 1996 (WHO data), in Canada in 1997 *(11)* and a cluster of cases of meningococcal disease during an international youth football tournament in Belgium *(12)* are recent examples. Large population movements such

Map 3. Meningococcal meningitis associated with Haj, 1987
Carte 3. Méningite à méningocoques associée au Hadj, 1987



as a pilgrimage play a major role in the spread of infection and disease. The outbreak which occurred in Mecca in 1987, at the end of the pilgrimage period, caused more cases among pilgrims than among the Saudi population. The incidence rates of meningococcal disease among pilgrims originating from Asia, North America, Europe, and the Eastern Mediterranean far exceeded the endemic rates in these areas (see *Map 3*). Other large population displacements, e.g. refugees, may pose similar risks *(13)*.

Group A epidemics have almost disappeared from memory of both the medical community and the general public in industrialized countries during a quiescent phase which has lasted half a century. The tremendous increase in international travel resulting in people moving further and quicker across the globe has accelerated the speed with which bacteria move from population to population and the potential for epidemic meningitis in industrialized countries is becoming alarmingly real as well.

From epidemic response to epidemic preparedness

The recent epidemics of meningococcal disease were exceptionally severe and few of the affected countries in Africa were adequately prepared to cope with these emergencies. The need to reinforce national capacity for preparedness, detection and control of epidemic meningitis, particularly in the African meningitis belt, recognized as a public health priority by governments and the international community, has been addressed in an international initiative led by WHO together with its Member States, collaborating centres and various governmental and non-governmental institutions.

This initiative focuses on strengthening national and regional health systems in key areas, such as:

- surveillance to monitor communicable diseases in the community and detect outbreaks early;
- laboratory capacity to diagnose communicable diseases and confirm outbreaks and their cause promptly;
- policy guidelines for the use of vaccine; the creation of a contingency stock of vaccine and injection material to ensure the timely protection of the population at risk; and
- protocols for the appropriate management of cases, particularly in remote areas deprived of adequate health services.

Governments of 16 African countries committed to the initiative meet in Burkina Faso in October 1996 to develop national plans of action. These plans include a national estimate of needs of vaccine and drugs based on criteria of population at risk, the epidemiological pattern of the disease, and available stocks of vaccine and other supplies at the country level. Similar steps were taken in countries at risk in the WHO Region for the Eastern Mediterranean. The plans mark a shift from the epidemic response of the past to epidemic preparedness.

In December 1996, an *ad hoc* working group further developed the WHO strategy for provision of vaccine while the two principal manufacturers of

CSM vaccine assigned to WHO the responsibility for assuring the best use of the vaccine available for epidemic control in 1997, some 14 million doses. An international coordinating group was established in mid-January 1997 with representatives of the Federation of the International Red Cross and Red Crescent Societies, Médecins sans Frontières, UNICEF, Association pour l'Aide à la Médecine préventive, and technical partners including WHO collaborating centres in France, Norway and the United States, as well as manufacturers of vaccine and autodestruct injection material. The coordinating group started with an assessment of the anticipated need for meningococcal vaccine, treatment drugs, injection and other material for the control of epidemic meningitis in Africa in the 1997 season. The assessment, presented to the international donor community in March 1997, received a response which made it possible to implement epidemic control activities in Africa in 1997 with an adequate and timely supply of vaccine and drugs along with autodestruct injection material.

Although this international initiative was triggered by the emergency resulting from the severe epidemics of meningococcal meningitis in Africa, it is sufficiently broad in scope to include other communicable diseases of public health importance at the local and national levels.

Summary

Meningococcal disease which is increasing globally is still associated with a high mortality and persistent neurological defects, particularly among infants and young children. Sporadic meningococcal meningitis occurs throughout the world, with seasonal variations, and accounts for 10-40% of endemic bacterial meningitis. Epidemic meningitis occurs in any part of the world but the largest and most frequently recurring epidemics have been in the semi-arid area of sub-Saharan Africa where the current pandemic is associated with attack rates exceeding 500 per 100 000 population and thousands of deaths. In the Americas and Europe serogroup B is the predominant agent causing systemic disease, followed in frequency by serogroup C. Serogroup A meningococcus was historically the main cause of epidemic meningococcal disease globally and still predominates in Africa and Asia. A range of internal and external factors predispose for epidemics such as strain virulence, carriers, humoral immunity, co-infections, low humidity and drought, population movements and crowding. To respond to the current situation and the expected spread of the disease, WHO, in collaboration with its Member States and various governmental and non-governmental agencies, has developed a sustainable plan of action for preparedness and control of meningitis.

Résumé

Affections méningococciques: importance pour la santé publique et efforts de lutte

Les affections méningococciques dont la fréquence augmente dans le monde sont toujours associées à une forte mortalité et à des troubles neurologiques persistants, surtout chez le nourrisson et le jeune enfant. La méningite à méningocoque est observée sporadiquement dans le monde entier avec des variations saisonnières et représente 10 à 40% de la méningite bactérienne endémique. La méningite épidémique est observée dans toutes les parties du monde, mais les épidémies récurrentes les plus importantes et les plus fréquentes touchent la zone semi-aride de l'Afrique subsaharienne où la pandémie actuelle avec des taux d'atteinte dépassant 500 pour 100 000 habitants, provoque des milliers de décès. Dans les Amériques et en Europe, le principal agent étiologique de la maladie généralisée est le sérogroupe B suivi du sérogroupe C. Le méningocoque du sérogroupe A était auparavant l'agent principal des épidémies à méningocoque dans le rnonde entier et l'est encore en Afrique et en Asie. Il existe toute une série de facteurs internes et externes de prédisposition aux épidémies, par exemple la virulence des souches, la présence de porteurs, le déficit de l'immunité humorale, les co-infections, une faible humidité et la sécheresse, les mouvements de population et le surpeuplement. Pour faire face à la situation actuelle et à l'extension prévue de la maladie, l'Organisation mondiale de la Santé, en collaboration avec ses Etats Membres et différents organismes gouvernementaux et non gouvernementaux, a mis au point un plan d'action durable pour se préparer aux épidémies et les combattre.

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Yellow fever in Kenya: the need for a country-wide surveillance programme

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The emergence of yellow fever (YF) as a public health concern in 1992 took Kenya by surprise. Between 1966 and the 1992-1993 YF epidemic in Kenya, no human cases of YF had been recorded in East Africa. In September 1992, 3 cases of haemorrhagic fever were reported to the Kenya Ministry of Health from the the southern part of the Kerio Valley, Keiyo District, and from Baringo and Koibatek Districts (formely Elgeyo-Marakwet and Baringo Districts) of the Rift Valley Province. Early in 1993 the disease was confirmed as YF *(1)*. The official number of patients reported was 54, including 29 fatalities *(2)*. Medical record review and hospital-based disease surveillance identified persons with haemorrhagic illness from three districts of the Rift Valley Province in the period between 10 September 1992 and 11 March 1993. Twenty-six persons had serological and/or virological evidence of recent YF infection, and 5 confirmed YF cases died, resulting in a case-fatality rate of 19% (E.J. Sanders – personal communication, 1997). All patients with confirmed YF lived in rural areas. The potential risk for an urban outbreak was underscored by the recognition of YF cases outside the area affected by the 1992-93 outbreak *(3, 4, 5)*. Surveillance through 1995 identified 4 persons with confirmed YF infection who lived south of Eldama Ravine along the borders with the Kericho and Nakuru Districts, districts that were not targeted by the 1993 YF vaccination effort. These findings highlighted the value of a sentinel surveillance system in detecting continued low-level transmission of YF in Kenya and also increased awareness to the threat of YF. Continued YF surveillance, including expansion of the surveillance network, will provide vital information regarding the "wandering epizootics" that are believed to maintain YF transmission *(6)*.

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Yellow fever

Yellow fever, as the type species of the Flaviviridae, is a mosquito-borne illness that exists in two distinct cycles, the sylvatic or jungle cycle and the urban cycle, the latter of which is often characterized by explosive epidemics usually transmitted by the mosquito vector *Aedes aegypti*. The maintenance cycle of YF virus relies on mosquito-monkey-mosquito transmission (the sylvatic cycle) whereby a non-immune monkey is fed on by a YF infected mosquito and the monkey becomes viraemic. During the viraemic phase, mosquitoes feeding on the primate may, in turn, become infected and after an extrinsic incubation period of about 10-12 days, that mosquito too will become an effective vector of YF. This cycle is maintained largely in the tree canopies of forested areas and man becomes accidentally infected when venturing into the forested area. Once a mosquito is infected, it remains so for life. Moreover, there is evidence of vertical transmission of YF in mosquitoes, albeit it at a low level; hence it is impossible to eradicate YF from a country once it has become established, i.e. the virus becomes endemic.

The history of yellow fever in Kenya

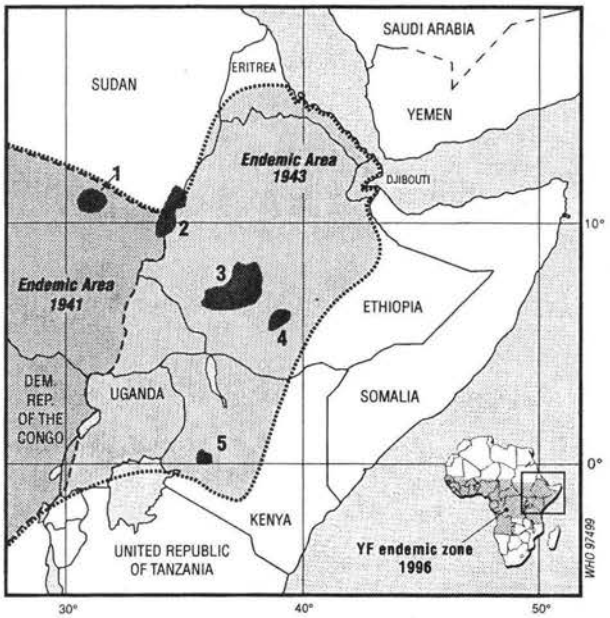
Periodic outbreaks of YF have been reported in East Africa since 1940 *(Fig. 1)*, but none occurred in Kenya until 1992 *(7-11)*. Comparison of nucleotide sequences indicate that the virus isolated in the Kenya outbreak was closely related to previous isolates from the Sudan (1940), Ethiopia (1961) and Uganda (1964) *(12)*. Another interesting observation is that all YF epidemics in East Africa occurred within the endemic transmission zone that was delimited by sero-surveys conducted between 1933 and 1943. Uganda and Eritrea lie within the transmission zone but have not documented epidemic YF transmission *(Fig. 1) (13, 14)*.

Serosurveys conducted between 1940 and 1970 identified four areas in Kenya where YF transmission had been active prior to the 1992-1993 epidemic, but only one human case was documented in 1943 *(14-17)*. These areas were: Nairobi (1943), Coastal (1952), Marsabit and Kenya's border with Ethiopia (1967) *(Fig. 2)*. No YF isolate was obtained from mosquito collections from any of these locations *(18)*.

It is clear from these surveys that YF activity was occurring at a very low level and that human infection was a rare occurrence. It has to be kept in

Fig. 1
Yellow fever epidemic and endemic areas in East Africa

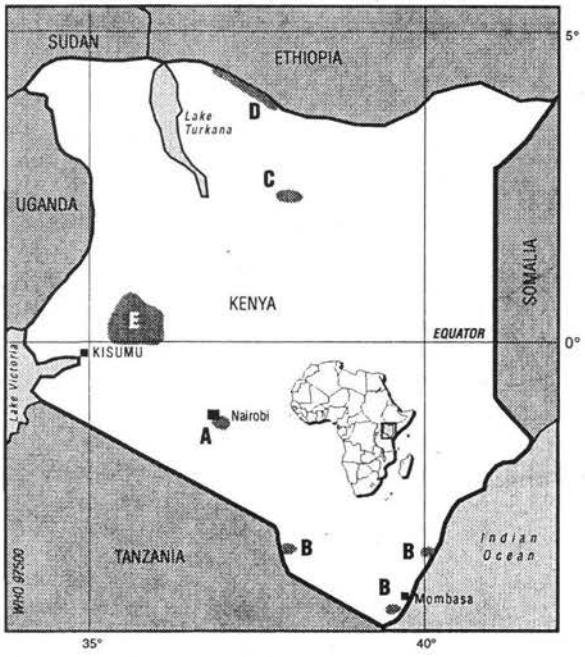
Zones où la fièvre jaune sévit à l'état endémique ou sur le mode épidémique, Kenya, 1940 à 1992-93



1. Nuba Mountains – Monts Nuba	1940
2. Southern Fung & Upper Nile – Bas Fung et Haut Nil	1959
3. Omo River – Rivière Omo	1960-62
4. Arba-Minch	1966
5. Kerio Valley – Vallée du Kerio	1992-93

Fig. 2
History of yellow fever transmission, Kenya, 1943 to 1992-93

Historique de la transmission de la fièvre jaune, Kenya, 1943 à 1992-93



Infected areas – Zones d'infection

A. Nairobi	1943
B. Coast Province – Province de Coast	1952
C. Marsabit	1967
D. Turkana District – District de Turkana	1967-70
E. Kerio Valley – Vallée du Kerio	1992-93

mind that isolated cases of YF can be difficult to diagnose and cases of clinical YF may have been occurring and simply gone unnoticed. This does not itself explain the apparent lack of clinical YF in Kenya prior to 1992. People may not have put themselves at risk of infection by encroaching into areas where the sylvatic cycle of YF is active, a situation that has changed today with increasing needs placed on the land for farming, housing and road construction. What happened in 1992 to produce an outbreak of YF in Kenya? Studies conducted following the YF epidemic pointed to a number of factors that may have been important in the emergence of YF virus in the human population (P. Reiter – personal communication, 1993). There was an exceptionally severe drought during the period 1991-1992 which would have led to a concentration of both primates and vectors at watering holes, coupled with the extensive rainfalls following the end of the drought which would favour increased mosquito populations. In addition, road construction and agricultural expansion into previously forested areas and cattle movement into the YF endemic area, potentially introducing *Amblyomma* ticks (implicated as potential reservoir vectors of YF in Central Africa) may have been determining factors *(19)*. Entomological surveys in the affected areas of the Rift Valley were successful in isolating YF virus from *Aedes africanus* and *Aedes keniensis*, and blood samples from primates showed 37% (13 of 35) seropositivity against YF although no virus was isolated.

To prevent infection with YF, vaccination is the only effective public health intervention. In west African countries experiencing multiple YF epidemics, consideration has been given to include YF vaccination in the Expanded Programme of Immunizations (EPI). A cost-effectiveness model developed with data from Nigeria defined the age-specific prevalence of immunity resulting from vaccination of infants and from natural endemic infection. The data were used to predict the number of cases and deaths during hypothetical epidemics in 2006 and 2026, representing the historic periodicity of epidemics. It was found that routine immunization, as part of the EPI, would be 7 times more efficient in terms of yellow fever cases and deaths prevented, compared to the emergency mass vaccination campaigns *(20)*. Conversely, the cost-effectiveness of emergency control is significantly greater in the case of an epidemic of limited scope. Despite these considerations, health planners have often concluded that the infrequent occurrence of YF epidemics does not justify annual assignment of scarce resources to a prevention programme. Since country-wide vaccination of the Kenyan population may be unlikely in the immediate future, surveillance for suspect cases of YF remains the only approach to identify unknown areas with YF transmission for which a selective vaccination programme should be put into action *(21)*.

Yellow fever surveillance in Kenya

The country-wide surveillance programme for YF has five components: active surveillance, diagnostic services, research, training, and prevention.

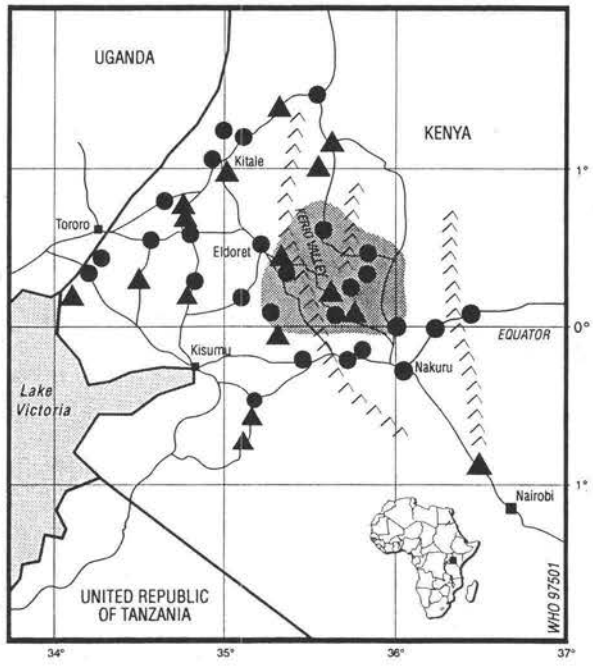
Active surveillance

The Kenya Ministry of Health supports YF surveillance at the national level and recognizes the important role of the Virus Research Centre of the Kenya Medical Research Institute (VRC-KEMRI) in monitoring disease activity. The surveillance activity itself is undertaken at the district level with close liaison with the Provincial Medical Officer (PMO) and the Provincial Public Health Officer (PPHO). The health care system in Kenya at the district level consists of: government hospitals, health centres and dispensaries. In addition there are a number of mission hospitals and private hospitals offering an independent service throughout the country. A unique feature of the active YF surveillance system in Kenya is the involvement of government health facilities, mission and private hospitals. Perhaps the single most important element of surveillance is the recognition of cases of YF by front-line health care workers. Here, however, lies a significant problem as the differential diagnosis of early or mild cases of YF is often difficult, especially where malaria, typhoid, leptospirosis, and viral hepatitis (hepatitis A and hepatitis B) are common. In addition, many health care workers are simply not aware that YF is a problem in Kenya, and some believe that because the people of Keiyo, Baringo and Koibatek districts have been vaccinated, the problem has gone away.

To assist front-line health care workers in making a clinical diagnosis, a YF case definition form has been produced by VRC-KEMRI to help identify suspected cases of YF. The case investigation form has been in use since the inception of the YF surveillance programme in 1993. A suspected case of YF is any patient with a complex of any two of the following symptoms: fever of >38 °C, jaundice, haemorrhage, signs of encephalitis or renal involvement *(5)*. A simplified version of the case investigation form is now in use. The original 18 sentinel surveillance sites have been increased to 43, and the areas under surveillance include districts in west Kenya that border the YF endemic area *(Fig. 3)*. Each new surveillance site has to be developed into an effective reporting centre by promoting awareness of YF and the surveillance programme of VRC-KEMRI. Each surveillance site is given visual presentations on YF, its endemicity in Kenya, the modes of transmission, diagnosis, VRC-KEMRI, the need for surveillance and the positive benefits of the programme for the local community in the way of vaccination against YF if cases are discovered. This programme of education is targeted at clinical officers, nursing and laboratory staff. The laboratory staff also get

Fig. 3
Yellow fever/haemorrhagic fever surveillance health facilities, Kenya, 1996

Services de santé chargés de la surveillance de la fièvre jaune et des fièvres hémorragiques, Kenya, 1996



training in how to process and store specimens for analysis by VRC-KEMRI. Due to the very high staff turnover, a problem common to all health care facilities, training and education is a continuing feature of the work.

The delivery of specimens from the field location to VRC-KEMRI in Nairobi produces its own set of problems. Most sites do not have the funding capacity to send specimens by courier so it is the job of VRC-KEMRI to collect the samples from the reporting station. This is no easy task as a number of the sites are in remote locations and the cost-effectiveness of driving to collect a single specimen is way too high. Therefore, in most cases the specimen(s) are collected during the monthly visit that is made to each surveillance site, which creates problems with the sensitivity of the the system to detect early transmission.

The surveillance programme in Kenya is complicated, as the influx of people from surrounding countries could tip the balance at anytime by introducing YF at an unsuspected point. In this respect, the northern regions of Kenya are home to thousands of refugees who are housed in large encampments. Refugee camps have often been the sites of

numerous communicable diseases and because of overcrowding and remoteness, an outbreak can often take hold before the proper authorities can be informed. YF is a threat also in these situations because many refugees come from countries with documented YF activity, e.g. Sudan and Ethiopia. Therefore, the network of surveillance centres in Kenya must take into account the whole country to build up greater knowledge of disease potential.

Diagnostic services

One of the goals of the Division of Emerging and other Communicable Diseases Surveillance and Control of the World Health Organization (WHO/EMC) is to establish a global network of surveillance and reporting centres to monitor communicable diseases and to avail national and international response to contain epidemics. Global surveillance is based on a network of (WHO) Collaborating Centres of which VRC-KEMRI is designated a WHO Collaborating Center for Arbovirus and Haemorrhagic Fever Reference and Research. As part of the WHO/EMC directive to establish enhanced viral diagnostics in Kenya, the virology laboratory of VRC-KEMRI is being strengthened with the help of the US Centers for Disease Control and Prevention (CDC) by the addition of modern diagnostic techniques (including polymerase chain reaction [PCR]) to supplement the techniques already available, and modernization of the diagnostic facility. In order to promote self-sufficiency, this also includes the production of reagents used in the serological tests. Reagents such as virus antigens and immune serum can be produced with relative ease, but their quality must be carefully controlled and standardized. The VRC-KEMRI laboratory will call on another WHO Collaborating Centre at the Division for Vector Borne Infectious Diseases of CDC located in Fort Collins, Colorado to independently test the reagents produced in Kenya. Reagents produced at VRC-KEMRI will be made available to reference laboratories in neighbouring countries to promote collaboration and surveillance for arboviral diseases such as YF. Virus isolation from patient serum or from field-caught mosquitoes is possible at VRC-KEMRI because of a reliable tissue culture facility. With respect to the diagnosis of flavivirus disease (of which YF is just one of many present in Africa) which is notoriously difficult because of cross-reactivities within the group, the definitive diagnosis is by virus isolation. These isolates are then forwarded to CDC for further characterization. The laboratory, whilst being able to diagnose YF, is also in a position to develop diagnostic capability to screen serum samples against a range of other arboviral diseases that are common to East Africa *(Table 1)*. Importantly, any suspect positive serum identified by VRC-KEMRI must be confirmed before the relevant authorities are contacted. Again, the expertise of CDC is called upon to provide confirmation. This acts as an effective quality control of the diagnostic activities in Kenya and VRC-KEMRI will become part of a quality control programme to be initiated by CDC to routinely check the performance of VRC-KEMRI. VRC-KEMRI will also, in the near future, make itself available as a reference laboratory for neighbouring countries to enhance the speed at which the diagnosis of diseases, such as YF, can be made. This will promote links be-

Table 1
Arbovirus diagnostic test capabilities at VRC-KEMRI

Tableau 1
Moyens de diagnostic des arbovirus au Centre de recherche sur les virus de l'Institut de la Recherche médicale du Kenya (VRC-KEMRI)

Alphaviruses	Flaviviruses	Bunyaviruses
Chikungunya	Banzi	Bunyamwera[a]
Middelburg[a]	Dengue 1-4	Bwamba[a]
O'nyong-nyong	Ilheus	Crimean-Congo HF – FH de Crimée-Congo
Semliki Forest – Forêt de Semliki	Spondweni[a]	Dugbe[a]
Sindbis	Uganda S – Ouganda S	Germiston
	Usutu[a]	Ilesha
	West Nile	Matariya[a]
	Yellow fever – Fièvre jaune	Nairobi sheep disease[a] – Maladie du mouton de Nairobi[a]
	Zika	Nyando[a]
		Rift Valley fever – Fièvre de la vallée du Rift
		Sandfly fever-Naples[a] – Fièvre à phlébotomes-Naples[a]
		Sandfly fever-Sicilian[a] – Fièvre à phlébotomes-Sicile[a]
		Shokwe[a]
		Tahyna[a]
		Tataguine[a]

[a] Viruses for which diagnostic capability will soon be available. – Virus pour lesquels des moyens de diagnostic seront rapidement disponibles.

tween countries within East Africa and foster possible research collaborations and the transfer of techniques. The main focus is to make a reliable and rapid diagnosis of YF (and other arboviral diseases) and to report the findings to the appropriate authorities for direct action.

Research

Information on YF in Kenya has remained fragmentary 5 years following the emergence of the first recorded YF epidemic. Are there other areas in Kenya experiencing YF transmission not yet covered in the active surveillance? What is the public health threat of an urban epidemic in areas relatively near the endemic area *(Fig. 3)*? The key element to address these questions is the implementation of a country-wide, laboratory-based, active surveillance system. Surveillance for clinical YF cases should be expanded with focussed studies of fever of unknown origin to include mild presentations of YF in selected geographical areas. Based on human case finding, additional important research projects will be conducted in Kenya to analyse YF enzootic/endemic cycles. West Kenya is the most densely populated area of Kenya and an earlier entomological survey showed that the concentration of the urban YF mosquito vector, *Aedes aegypti* exceeds the threshold limits for effective human transmission (Reiter – personal communication, 1993). Needless to say, if YF virus became established in the Lake Victoria basin, the potential for a large YF epidemic exists. In conjunction with the above study, *Ae. aegypti* mosquitoes that are caught and mosquito larvae that are hatched will be analysed for YF virus by virus isolation and PCR. In collaboration with the Primate Research Institute in Kenya, sero-surveys of the monkey populations in areas that have been targeted for mosquito isolations will also be made. It is interesting to note here that migrations of large numbers of primates from the YF endemic areas of the Kerio Valley, Baringo and Koibatek districts are known to have taken place. During the YF outbreak of 1992-1993, the inhabitants of the afore mentioned districts became aware of the relationship between monkeys, mosquitoes, YF virus and its transmission to man. The result was an active culling of primates by locals who drove the primates in large groups to other areas. The arrival of numerous primates in new locations may be one reason for the expansion of the YF endemic area in Kenya as the sylvatic cycle of YF virus became established in these new districts. Any virus isolates made by VRC-KEMRI will be analysed by CDC to provide information on the virus strain (East African YF and West African isolates of YF are genetically distinguishable). CDC will play a major role in the provision of reagents that cannot be produced locally in Kenya (e.g. primers for PCR) and in the confirmation of serological and virological data generated by VRC-KEMRI.

VRC-KEMRI has recently hosted students from the London School of Hygiene and Tropical Medicine (LSHTM) for a period of study in fulfilling the "Control of Infectious Diseases" course offered at the LSHTM. The surveillance programme was analysed in detail in discussions with each clinical and nursing staff at each of the surveillance locations and a number of constructive alterations are being implemented to improve the functioning of the operation. Collaboration with the LSHTM will be strengthened by the enrolment of Kenyans in a Ph.D. programme, to be based at VRC-KEMRI. The Ph.D. programme will focus on aspects of YF epidemiology in Kenya and also on the effects of YF vaccination in immunocompromized individuals.

Training

The training of staff at VRC-KEMRI, and in neighbouring countries, in the diagnosis of YF is an important part of the programme. To reliably diagnose YF by using standard serological techniques, to interpret the results accurately, and to 'troubleshoot' when problems arise, requires a high degree of competency in the staff running the test systems. Two staff members at VRC-KEMRI have received training from CDC in YF virology and serology systems and VRC-KEMRI has hosted a CDC/WHO-sponsored workshop for East Africa in 1995 to transfer YF diagnostic serology to neighbouring countries. However, some of the countries that attended the workshop have had difficulties in establishing the techniques as a routine procedure due to shortcomings of laboratory facilities. It is here that VRC-KEMRI can play a role in helping to overcome the problems experienced by laboratories in other East African countries by providing for an expert to visit the laboratory and to spend time training staff in the environment in which the tests will be performed. It would also be possible for members of other laboratories to visit and to spend time at VRC-KEMRI to learn the techniques in question and to be provided with reagents, produced at VRC-KEMRI, for use in their own laboratories. Quality control of each laboratory's activities is essential and this could be provided by being incorporated into the performance analysis network of CDC.

Prevention

The ultimate goal of the surveillance programme is to prevent YF infection in the Kenyan population. At present, the incorporation of YF vaccination into the Kenya EPI is not expected in the immediate future, hence active surveillance to monitor YF activity becomes imperative for the population of Kenya. Surveillance has already shown that the YF-endemic area apparently expanded in Kenya as cases have been occurring in districts to the southwest of the vaccinated zone *(5)*. Sanders et al. *(5)*

raised the point that the surveillance programme should be incorporated into one of the existing Kenya's EPI target disease surveillance programmes, for example, the polio eradication campaign. The polio eradication programme has a high profile in Kenya as part of the programme to free Kenya of the disease by the year 2000. However, inclusion of YF in the surveillance would be seen by some as confusing a concentrated effort to tackle a disease which can be eradicated. Further discussions and more active collaboration with the Kenya Ministry of Health are planned to ensure cooperation of all the provinces included within the YF surveillance programme. Plans are also being formulated to establish a YF outbreak response team within Kenya that could mobilize available vaccine stocks within the country at a moment's notice of the diagnosis being made and independently confirmed.

A recent review of the YF surveillance programme in Kenya questioned whether the system could exist as anything more than a research programme, based on the fact that YF surveillance has not been integrated into one of Kenya's existing disease control programmes *(5)*. To be effective in the long term, the programme of surveillance must be integrated as it cannot exist as a research concern alone. How this could be effectively implemented is a difficult question. There exists in Kenya a disease reporting system which comprises 37 infectious diseases. Incorporation of a case definition for YF should be included in this list of notifiable diseases and clinical staff made aware of the importance of recognizing signs and symptoms of YF. A case definition based on jaundice and haemorrhages will effectively detect 3% of the YF cases *(20)*. Expanding the case definition to viral syndrome will enable to detect mild cases of YF, in addition to cases of dengue fever and other arboviral syndromes for which laboratory diagnosis can be provided at VRC-KEMRI. Detailed discussions with the Ministry of Health of Kenya will be necessary to produce a workable case definition to detect as many suspect cases of YF as possible without putting too great a burden on the clinical staff and the diagnostic facility. A further possibility would be to follow the anticipated eradication of polio from Kenya in the year 2000 by transferring resources to promote a Kenya-wide awareness of YF targeted at the recognition of disease, diagnosis and reporting. The manpower currently directed to the polio eradication programme would have a great impact on YF surveillance in Kenya, given the expertise gained during the polio campaign, and could also function as a response team to outbreaks of YF and be responsible for coordinated vaccination programmes.

The support and funding by international concerns such as WHO and CDC are crucial to the success of the programme of YF surveillance in Kenya and it is not only the people of Kenya who benefit from such information provided by surveillance, but East Africa as a whole, since the surveillance programme for YF can be used as a model for neighbouring countries. The ultimate goal of the programme is to generate sufficient data on YF transmission in Kenya to justify YF vaccination of the entire population. In the immediate future, the usefulness of the surveillance programme will be monitored by the timely provision of YF vaccine for areas with confirmed YF cases and the protection of populations known to live within areas that are endemic to YF.

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Summary

Since the emergence of yellow fever (YF) as a public health threat in Kenya in 1992-1993, low level transmission of the virus to humans has continued to occur. A programme of YF surveillance has been instrumental in the monitoring of YF activity and has clearly demonstrated an expansion of the zone of virus activity into regions that were not affected in the 1992-1993 epidemic. This is of major concern for the approximately 29 million Kenyans who are unvaccinated and therefore at risk of infection. A revision of the surveillance programme is underway to create a more efficient system of recognition of suspect YF cases, laboratory diagnosis and reporting to the appropriate authorities for action. In addition, a research programme to study YF ecology in Kenya will benefit the surveillance programme, enabling it to target potential 'hotspots' of YF activity. As it may not be possible, for financial reasons, to incorporate YF vaccination into the Kenya Expanded Programme of Immunization in the immediate future, the need for continued surveillance to monitor the emergence of YF in Kenya is vital.

Résumé

La fièvre jaune au Kenya: importance d'un programme de surveillance à l'échelle du pays

Depuis l'émergence de la fièvre jaune comme problème de santé publique au Kenya en 1992-1993, de faibles niveaux de transmission du virus à l'homme persistent. Un programme de surveillance de la fièvre jaune a permis de suivre l'activité du virus et a clairement mis en évidence une extension de la zone d'activité virale dans des régions qui n'avaient pas été touchées par l'épidémie de 1992-1993. Cela est un sujet de préoccupation majeur pour les quelque 29 millions de Kenyans qui ne sont pas vaccinés et sont donc exposés à l'infection. Une révision du programme de surveillance est en cours afin de mettre en place un système plus efficace de reconnaissance des cas suspects, de diagnostic au laboratoire et de notification aux autorités habilitées à prendre les mesures qui s'imposent. En outre, le programme de surveillance pourra se prévaloir d'un programme de recherche sur l'écologie de la fièvre jaune au Kenya, ce qui lui permettra de viser les «points chauds» éventuels de l'activité virale. Etant donné qu'il ne sera peut-être pas possible, pour des raisons financières, d'introduire la vaccination antiamarile dans le programme élargi de vaccination du Kenya dans un avenir proche, il est essentiel de poursuivre la surveillance afin de contrôler l'émergence de la fièvre jaune au Kenya.

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Disease eradication as a public health strategy: is measles next?

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Disease eradication as a public health strategy

Since the turn of the 20th century, 6 major initiatives have been launched to eradicate infectious diseases, targeting yellow fever, yaws, malaria, smallpox, poliomyelitis and dracunculiasis. Following the ultimately unsuccessful conclusion of the first 3 efforts, support for eradication programmes waned, particularly as attention shifted to improving basic health services worldwide, a pursuit felt by many to be incompatible with the 'vertical' nature of eradication *(1)*. The successful smallpox eradication programme, however, and the progress of the ongoing initiatives against poliomyelitis and dracunculiasis have somewhat rehabilitated the concept of disease eradication *(1)*. There is increasing evidence that, in addition to eliminating an infectious disease and its related costs, such programmes can substantially benefit health services in general *(2, 3)*.

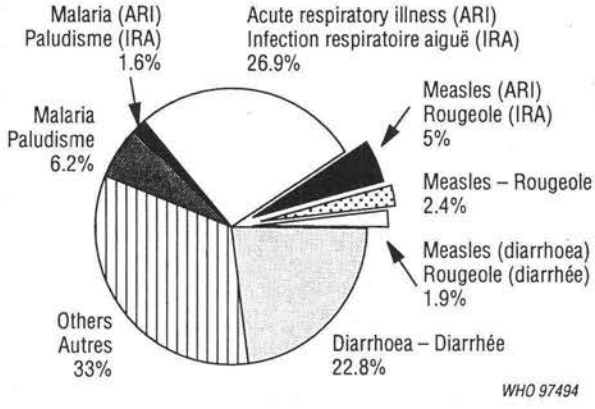
The prominence of recent eradication initiatives has led some to promote the concept as a *public health strategy*, calling for similar initiatives to be launched against other diseases of public health importance. In a number of countries, political leaders, health authorities and the general public are increasingly suggesting that measles, the leading cause of vaccine-preventable childhood morbidity and mortality, should be the next organism targeted for eradication.

Measles as a public health problem

Despite the widespread opinion that measles constitutes a 'normal' disease of childhood, nearly 10% of the mortality among children aged less than 5 years worldwide is due to this disease *(Fig. 1)* *(4)*. In 1996 alone, it was estimated that over 1 million children died of measles or one of its complications *(5)*. The majority of this mortality is taking place in the world's poorest countries, particularly in sub-Saharan Africa where a combination of factors such as crowding, a lower age at exposure and, possibly, malnutrition contribute to substantially higher case-fatality rates than seen in industrialized countries *(6)*. In some developing countries, measles case-fatality rates still reach over 10%, especially during outbreaks *(7)*.

Fig. 1
Distribution of 12.2 million deaths among children aged less than 5 years in all developing countries, 1993

Répartition des 12,2 millions de décès parmi les enfants de moins de 5 ans dans les pays en développement, 1993



Even in industrialized nations, measles continues to cause considerable morbidity, the economic consequences of which can be substantial *(8)*. In many of these countries, the financial costs of measles-related treatment and lost productivity alone have been a major factor in decisions to pursue a very high degree of control of the disease. In the mid-1990s, cost-effectiveness studies in the United Kingdom and Canada demonstrated the fiscal advantage of undertaking supplementary immunization activities to prevent nationwide measles epidemics *(9, 10)*.

A new direction: measles outbreak prevention and elimination

The decision to target a disease for global eradication is based on a number of biological, epidemiological, social, political and economic factors *(1)*. Of particular importance is the demonstration that control strategies can eliminate the organism over a wide geographical area for a sustained period of time. Although several industrialized countries adopted measles elimination goals in the 1970s, few managed to interrupt transmission for prolonged periods due to either the strategies chosen

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or the operational constraints in their implementation.

Much of the recent interest in measles eradication is the result of the progress toward regional elimination of the disease in the Americas. Building on the success of the regional polio eradication initiative and experience with measles elimination in Cuba, Chile and the English-speaking Caribbean, the 1994 Pan American Sanitary Conference adopted a goal of regional measles elimination by the year 2000. The strategy combined a one-time mass campaign for all children aged 9 months to 14 years with high routine immunization coverage and regular catch-up campaigns *(11)*. Following the widespread implementation of this strategy, the number of reported measles cases fell from 49 000 in 1993 to less than 2 200 in 1996, the lowest number ever reported in the Region. This decline occurred despite marked improvements in surveillance, including the introduction of IgM testing of all suspected measles cases.

Outside the Americas, an increasing number of industralized and developing countries have adopted aggressive measles control goals ranging from outbreak prediction and prevention to nationwide interruption of transmission *(5, 12)*. In the United Kingdom, for example, a nationwide measles-rubella campaign was conducted in 1994 to prevent an outbreak that was predicted for the following year. Similar strategies have been employed in countries of southern Africa, the Eastern Mediterranean, South-East Asia and the Western Pacific.

Global eradication of measles: unanswered questions

Despite the interest in a global measles eradication initiative, a number of issues remain to be resolved. Additional observation is needed to determine whether the successful interruption of transmission in many countries of the Americas can be sustained despite the regular reintroduction of the virus from other regions and the gradual but inevitable increase in susceptible individuals. The occurrence of a large urban outbreak in both the child and adult populations of Brazil in 1997 demonstrated that widespread circulation can be quickly re-established if the virus is reintroduced into a population whose level of susceptibility has been allowed to exceed the epidemic threshold of the disease *(13)*. High quality surveillance is needed not only to identify rapidly and investigate infected areas, but to determine the accumulation and distribution of measles-susceptible individuals in a population in order to guide routine and supplementary immunization activities.

A concerted effort will be needed to demonstrate the benefits that a global eradication initiative holds for countries where there has been a very low burden of measles-related disease for many years. High level commitment within the political, medical and general communities of industrialized countries in particular would be essential to ensuring that the appropriate strategies were fully implemented and that sufficient resources are available. At least US$1 billion would be needed in external support over a 5-10 year period to facilitate measles eradication in developing nations.

Of particular importance to the future of a measles eradication effort is the successful conclusion of the ongoing polio eradication initiative. Not only will such an achievement ensure the management, immunization and surveillance infrastructure needed to eradicate measles, but it will further strengthen the political support required at all levels for a new eradication initiative. As demonstrated in the Americas, the introduction of measles elimination activities soon after polio transmission has been interrupted may play an important role in sustaining high quality poliovirus surveillance after the disease has disappeared *(11)*. Regardless of the target disease, robust mechanisms must be established to ensure that the impact of such initiatives on health services in general can be monitored and optimized.

Conclusion

There is increasing evidence that the sustained interruption of measles transmission is possible with existing vaccines *(12)*. However, questions concerning the optimal immunization strategies for countries with differing levels of measles control and economic development must continue to be addressed. Immunization and surveillance programmes worldwide must be strengthened to ensure that there will be a minimal accumulation of susceptibles between mass campaigns. The political commitment and both human and financial resources that are needed to launch a globally coordinated effort must be identified.

The eradication of measles offers an opportunity to achieve a substantial and permanent impact on worldwide childhood morbidity and mortality. Although this goal now appears biologically and epidemiologically feasible, before launching a global initiative, further attention must be given to the remaining social, political and financial obstacles to ensure that the benefits of such an initiative would ultimately be realized.

Summary

Following the failure of disease eradication efforts in the first half of this century, the success of smallpox eradication and the ongoing initiatives against poliomyelitis

and dracunculiasis are re-establishing eradication as a viable disease control strategy. The perpetual benefits of eradication, together with the positive impact that such initiatives can have on health services in general, are changing the world's perception of these endeavours. Among the most obvious examples of this changing trend is the recent enthusiasm in both industrialized and developing countries for re-exploring the eradicability of measles. Increasingly, it appears that measles, the single leading cause of vaccine-preventable childhood morbidity and mortality worldwide, may be the next major organism targeted for global eradication.

Résumé

L'éradication en tant que stratégie de santé publique: bientôt la rougeole ?

Après l'échec des efforts d'éradication de la maladie au cours de la première moitié de ce siècle, le succès de l'éradication de la variole et des initiatives en cours contre la poliomyélite et la dracunculose fait à nouveau de l'éradication une stratégie viable de lutte contre la maladie. Le caractère définitif de l'éradication et ses avantages, et l'impact positif que ces initiatives peuvent avoir sur les services de santé en général, sont en train de modifier la façon dont ces efforts sont perçus dans le monde. Parmi les exemples les plus flagrants de cette évolution, on dénote l'enthousiasme manifesté récemment par les pays industrialisés comme les pays en développement désireux de reconsidérer «l'éradicabilité» de la rougeole. De plus en plus, il semble que la rougeole, principale cause de morbidité et de mortalité évitable par la vaccination de l'enfant, pourrait bien être la prochaine cible d'une campagne mondiale d'éradication.

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Current status of the global eradication of poliomyelitis

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Substantial progress towards the global eradication of poliomyelitis by the year 2000 has been achieved since May 1988 when WHO Member States adopted this goal at the Forty-first World Health Assembly. Virtually all polio-endemic countries have now begun to implement the WHO-recommended strategies to eradicate polio *(1)*. This article describes the scientific basis of the strategies used, the current degree of strategy implementation, and the status of polio eradication in the world.

Polio eradication strategies and their implementation

The WHO-recommended strategies for polio eradication are as follows: *(a)* high routine immunization coverage with at least 3 doses of oral polio vaccine (> 80% OPV3); *(b)* annual National Immunization Days (NIDs), during which 2 supplemental OPV doses are given to all children < 5 years; *(c)* laboratory-based surveillance for all cases of acute flaccid paralysis (AFP) in children under 15 years of age, with the collection and virological examination of stool specimens from every case, and *(d)* 'mopping-up' immunization campaigns to administer supplemental OPV doses through house-to-house campaigns in areas with persisting transmission of wild poliovirus.

Routine immunization coverage

Reaching and maintaining the highest routine immunization coverage with OPV at all administrative levels remains the foundation on which the polio eradication initiative is built. In temperate, industrialized countries, high levels of seroconversion and interruption of poliovirus transmission have been attained with 3 doses of OPV in the routine immunization programme *(2)*. Although high routine OPV3 coverage has resulted in high levels of control in many tropical developing countries, wild virus transmission has often persisted owing to a number of factors which affect both the intensity of transmission (low sanitation levels, high population density) and seroconversion rates (high maternal antibody, competing enterovirus infections, diarrhoea) *(3)*. For these reasons, high routine coverage often only reduces transmission to low levels, requiring supplemental doses of OPV to interrupt transmission.

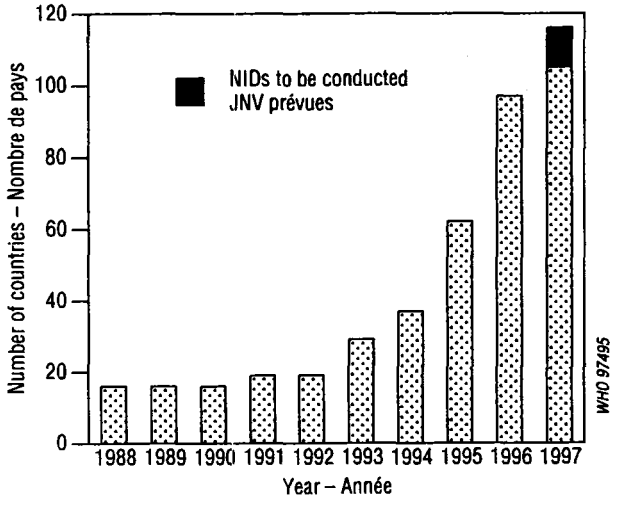
At the start of the polio eradication initiative in 1988, global coverage with 3 doses of OPV (OPV3) was 67% *(Table 1)*, as compared to less than 10% in 1974. OPV3 coverage peaked in 1990 at 85%, stabilized near 80% in the first half of the 1990s and was 81% in 1996. OPV3 coverage in 1996 was lowest in the African Region, but doubled in that Region from 32% in 1988 to 60% in 1996.

National Immunization Days (NIDs)

Immunization strategies for global polio eradication in endemic countries are based on the work of Chumakov *(4)* and others who first used mass immunization campaigns to control polio epidemics in Hungary *(5)* and the former USSR. Based on refinements of this strategy in Cuba and Brazil *(6)*, the Pan American Health Organization recommended National Immunization Days (NIDs) for polio eradication in endemic countries in the

Fig. 1
Cumulative number of countries conducting NIDs

Nombre cumulatif de pays ayant organisé des journées nationales de vaccination (JNV)



Data as of 24 June 1997 – Données au 24 juin 1997

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Table 1
Reported poliomyelitis cases and oral polio vaccine (OPV) coverage 1988 and 1996, and acute flaccid paralysis (AFP) surveillance performance indicators 1996, by WHO Region

Tableau 1
Cas de poliomyélite notifiés et couverture par le vaccin antipoliomyélitique buccal (VPO), 1988 et 1996, et indicateurs d'efficacité de la surveillance de la paralysie flasque aiguë (PFA), 1996, par Région OMS

WHO Region – Région OMS	No. of reported polio cases – Nombre de cas de poliomyélite notifiés		% reduction 1988-1996	OPV3 coverage – Couverture VPO3		AFP surveillance quality 1996 – Qualité de la surveillance de la PFA 1996	
	1988	1996		1988	1996	Non-polio AFP rate[a] – Taux de PFA non poliomyélitique[a]	% AFP with 2 stool specimens – % de cas de PFA pour lesquels l'on dispose de 2 échantillons de selles
Africa – Afrique	4 563	2 071	55%	32%	60%	<0.1	NA
America – Les Amériques	308	0	100%	85%	88%	1.2	76%
South-East Asia – Asie du Sud-Est	25 741	1 125	96%	66%	84%	< 0.1	39%[b]
Eastern Mediterranean – Méditerranée orientale	2 339	528	77%	67%	78%	0.7	65%
Europe	204	193	5%	60%	92%	0.7	63%
Western Pacific – Pacifique occidental	2 126	194	91%	85%	88%	1.2	80%
Global – Niveau mondial	35 251	4 111	88%	67%	81%	0.6	–

[a] Number of AFP cases (not attributed to polio) per 100 000 children aged <15 years. – Nombre de cas de PFA (non attribués à la poliomyélite) pour 100 000 enfants âgés de moins de 15 ans.
[b] Percentage excludes India, for which these data are not available. – Ce pourcentage exclut l'Inde, pays pour lequel ces données ne sont pas disponibles.

Americas. The effectiveness and global applicability of the NIDs strategy was further established through experience in China and other countries *(7, 8)*.

NIDs are conducted during the season of low poliovirus transmission in 2 rounds, 4 to 6 weeks apart. During each round, OPV is administered to all children <5 years of age, regardless of prior immunization status. NIDs interrupt poliovirus circulation by rapidly increasing systemic and intestinal immunity in the population, thereby limiting spread of the virus *(1, 9, 10)*.

The number of countries conducting NIDs worldwide has risen since the early 1990s, as the polio eradication initiative became operational in WHO regions *(11)*. By the end of 1996, a cumulative total of 97 countries had conducted NIDs or Sub-NIDs (see *Fig. 1*), including all polio-endemic countries in the Americas, Asia and Europe, and 25 of 42 endemic countries in the African Region *(14)*. Globally, 419 million children < 5 years were immunized during NIDs in 1996, approximately two-thirds of the world's children in that age group. In India, 127 million children < 5 years were immunized during the second round of 1996 NIDs, making this the largest single immunization campaign in history *(12)*.

Increasingly, NIDs are being coordinated between countries and WHO regions to rapidly interrupt poliovirus transmission and ensure coverage of migrant populations in border areas. Between December 1996 and January 1997, 257 million children were immunized during NIDs in 11 countries of the Eastern Mediterranean, South-East Asian and Western Pacific regions of WHO. "Operation MECACAR" *(13)*, conducted in 1995, 1996 and 1997, synchronized NIDs among 18 countries of the European and the Eastern Mediterranean regions, achieving immunization coverage of 95%.

Surveillance for acute flaccid paralysis (AFP)

The goals of the surveillance strategy for polio eradication are to monitor progress, identify remaining areas of wild virus transmission for 'mopping-up' immunization, and eventually provide the basis for certification of eradication.

To achieve these goals, two stool specimens are collected from all AFP cases in children < 15 years and examined for the presence of wild poliovirus. Surveillance for cases of AFP, instead of clinical polio, increases the sensitivity of the surveillance system to detect polio cases, because clinical criteria alone are not sufficient to diagnose polio reliably. Atypical presentations of paralytic polio may be mistaken clinically for Guillain-Barré syndrome, transverse myelitis, or other paralytic conditions *(15)*, and vice versa. For reporting purposes, the following AFP case definition is used: "All children < 15 years of age with acute flaccid paralysis, includ-

ing those considered to have Guillain-Barré syndrome, and persons of any age in whom polio is suspected".

The most important indicators for the quality of AFP surveillance are the annual rate of non-polio AFP cases in children < 15 years, and the percentage of AFP cases from whom 2 specimens were collected within 2 weeks of paralysis onset ('adequate specimens'), since viral shedding is most intense during the first 2 weeks after onset. For effective AFP surveillance, the non-polio AFP rate should be at least 1 case per 100 000 children < 15 *(16)* and at least 80% of AFP cases should have adequate specimens taken.

A global network of polio laboratories has been developed, which is capable of detecting wild poliovirus when and where it occurs. The laboratory network currently consists of 67 national laboratories, 16 regional reference laboratories, and 6 specialized reference laboratories *(17)*. National laboratories perform primary virus isolation, referring any polioviruses detected to regional reference laboratories where tests are performed to differentiate vaccine strains from wild virus strains. Specialized laboratories perform genomic sequencing studies on poliovirus isolates to determine the exact geographical and temporal origin of a particular virus. A process of formal accreditation of national laboratories began in 1996 to ensure quality and facilitate the use of standardized procedures and reagents.

By the end of 1996, AFP surveillance was being conducted in 126 (86%) of 146 countries where polio is or recently was endemic *(11)*. In 1996, the global rate for non-polio AFP was at 0.6/100 000, although rates varied substantially by WHO region (see *Table 1*). Rates of non-polio AFP were still < 0.1 in the South-East Asian and African Regions, where AFP surveillance is just being established. The proportion of AFP cases with adequate specimens shows similar variation (see *Table 1*).

Mopping-up immunization

Despite NIDs, small foci of circulation of wild polioviruses often continue to persist. Continued transmission in these areas is often facilitated by high population density, poor sanitation levels and the presence of children missed by both routine and supplementary immunization. Good surveillance is essential to identify these final reservoirs of wild virus infection. Intensive, localized immunization campaigns, also known as 'mopping-up' campaigns, are required in these areas. In contrast to the strategy of immunizing at fixed posts as in NIDs, mopping-up must be done on a house-to-house basis to ensure that every single child in the area is found and immunized *(1)*. Mopping-up immunization was first used during polio eradication in the Americas to target the last remaining foci of wild-virus transmission *(18)*. Experience has shown that mopping-up operations are most effective if planned well ahead of time and conducted during the low-transmission phase. Large mopping-up immunization campaigns targeted the last remaining foci of transmission in 199 coastal counties of Colombia *(19)* in 1991 (850 000 children immunized), and in 13 coastal departments of Peru in 1992 *(20)* (1.9 million children immunized).

Mopping-up campaigns have also been conducted in the Western Pacific Region of WHO. During 1995-1996, approximately 3 million children < 5 years were immunized in border counties of Yunnan province, China, where 4 paralytic polio cases imported from Myanmar had been identified. Another large mopping-up campaign was conducted in May-June 1997 in the Mekong river areas of Viet Nam and Cambodia, targeting mainly the migrant population living on boats. A total of 2 million children were immunized.

Mopping-up campaigns are more intense and require even more resources than NIDs on a per-capita basis. Immunizing about one-third of Cambodia's target population < 5 years during the recent mopping-up was as costly as the full NID earlier in the year.

Certification of polio eradication

The process for certification of polio eradication has been established in each WHO region and at the global level. In 1994, the International Commission for Certification of Poliomyelitis Eradication (ICCPE) certified that indigenous wild polioviruses had been eradicated from the Region of the Americas *(21)*. Despite continuing high quality AFP surveillance, indigenous wild poliovirus has not been isolated in the Region since September 1991. The Global Commission for the Certification of the Eradication of Poliomyelitis was set up in 1995 and has met twice since (1995, 1997). The Global Commission stated that WHO regions will only be certified as poliomyelitis-free after all countries and areas of the region have met the following criteria[d]: *(a)* absence of circulation of indigenous wild polioviruses for at least a 3-year period in which surveillance activities have been maintained at the levels of performance needed for certification; *(b)* a national certification committee in each country has validated and submitted the documentation required by the regional commission; and *(c)* appropriate measures are in place to detect and respond to any importations of wild poliovirus. Regional commissions have now been appointed in all 5 other WHO regions where they will oversee the certification process, aided by

[d] *Report of the first meeting of the Global Commission for the Certification of the Eradication of Poliomyelitis, WHO, Geneva, 1995* (Document WHO/EPI/GEN/95.6).

national certification committees in all countries. Regional certification will be based on detailed documentation of surveillance and immunization activities to be submitted by each country.

The polio eradication coalition

To achieve polio eradication, a global partnership was formed involving, among others, Rotary International, the United Nations Children's Fund (UNICEF), WHO, the Centers for Disease Control and Prevention (CDC), other donor governments, non-governmental organizations, and ministries of health in the polio-endemic countries. AUSAID, DANIDA, JICA and USAID have made significant contributions. Over the past decade, these partner agencies have provided funding as well as technical expertise, advocacy support and volunteers. Support from Rotary International has been crucial for the initiative. Rotary continues to play an important advocacy role, it has funded the procurement of large quantities of oral polio vaccine and increasingly supports surveillance activities. In many countries, Rotary volunteers are directly involved in planning and implementing NIDs and surveillance activities. UNICEF facilitated the procurement of more than 700 million doses of OPV for NIDs in 1996, and also played a key role in negotiating a series of cease-fires in conflict zones to allow the immunization of children. The CDC provides funds for vaccine as well as a wide range of technical expertise, particularly to develop surveillance systems for AFP and wild poliovirus.

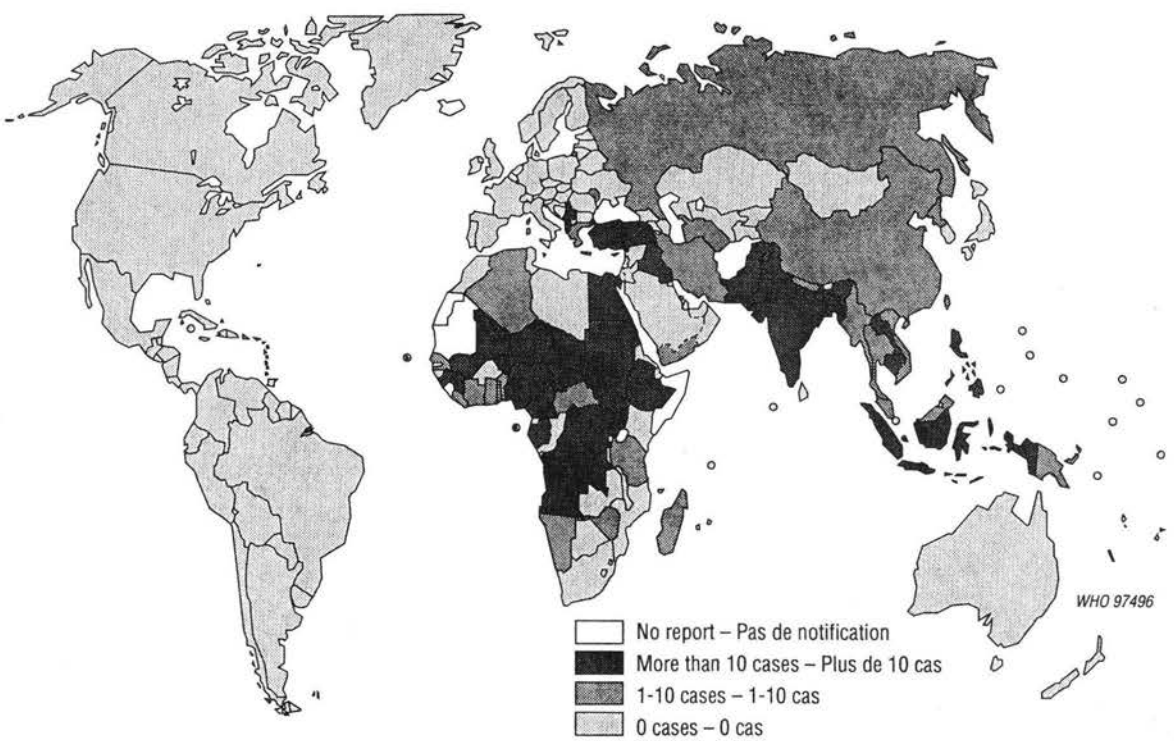
Although substantial funding for polio eradication has been provided by donor governments and other agencies, many polio-endemic countries underwrite most of the cost of polio eradication activities themselves: for example, it was estimated that over 80% of polio eradication costs in the Americas were met by individual countries, and in China, outside funding was used for less than 10% of NID costs. In the poorest countries (i.e., sub-Saharan Africa), however, external support is needed for more than 80% of polio eradication costs. Significant external funding, as well as international and interregional cooperation, need to continue to achieve success. Projected resource requirements include approximately US$ 175 million in external support to sustain polio eradication activities globally during 1997, and US$ 1 billion for the period 1997-2005 *(11)*.

Impact on polio incidence

Polio has been eradicated from the western hemisphere (WHO Region of the Americas) for more than 5 years *(22)*. The last case of polio caused by wild poliovirus in South America was in a 2-year old Peruvian boy paralyzed in August 1991. The Western Pacific Region is close to eradication *(23)*, with only one known remaining reservoir of wild virus circulation in the Mekong area of Cambodia and

Map 1 Global reported incidence of indigenous poliomyelitis, 1996[a]

Carte 1 Incidence de la poliomyélite autochtone notifiée au niveau mondial, 1996[a]



[a] 4 111 polio cases reported as of 25 August 1997. – 4 111 cas de poliomyélite notifiés au 25 août 1997.

the Southern Region of Viet Nam. Global polio incidence has decreased in recent years due to the implementation of NIDs. In 1996, a total of 4 111 polio cases were reported globally (data as of 4 August 1997), a decrease of 88% from the 35 251 cases reported in 1988 *(Table 1, Map 1)*.

In the African Region, 1996 was the first year in which a significant number of NIDs were conducted as part of the "Kick Polio out of Africa" campaign. The impact of these NIDs on polio incidence should be evident in 1997.

Despite improvements in surveillance, the number of polio cases reported from the Eastern Mediterranean Region declined 77% from 1988 to 1996 (2 339 to 528). However, wild poliovirus continues to circulate in Pakistan and Egypt. A recent polio outbreak, after the 1997 NIDs, was reported from the North-West Frontier Province in Pakistan in May/June 1997.

In 1988, 204 polio cases were reported from 5 countries of the European Region; this included reported polio cases from 11 of 15 Republics of the former USSR. Several polio outbreaks occurred during the early 1990s following the break-up of the USSR, mainly in the Caucasus area and the Central Asian Republics. Of the 193 cases reported in the European Region in 1996, 167 were associated with a large outbreak which resulted from a wild poliovirus importation into Albania *(24)*. The outbreak primarily affected Albania, but also spread into Greece and the neighbouring Kosovo Region. The number of cases reported from countries in the European Region participating in Operation MECACAR *(13)* decreased from 53 in 1995 to 19 in 1996.

In the South-East Asia Region, the number of reported cases declined from 25 711 in 1988 to 1 125 in 1996, a 96% decrease. The rapid improvement of AFP surveillance now has highest priority for polio eradication in this region, particularly in those 6 countries in which AFP surveillance has recently been initiated.

In the Western Pacific Region, confirmed polio cases declined by 91% between 1988 (2 126) and 1996 (194). Of the 194 cases reported in 1996, only 21 (11%) were confirmed, based on wild poliovirus isolation, and no indigenous wild poliovirus was isolated in China during 1996.

Conclusions

There has been remarkable progress since the polio eradication goal was established in 1988, with an 88% decrease in the number of reported cases globally. By the end of 1997 it is expected that virtually all endemic countries in the world will have conducted full National Immunization Days, providing supplemental OPV to almost two-thirds of all children < 5 years globally. An increasing number of countries participate in multinational, synchronized NIDs to target the remaining foci of transmission most effectively. As a result of increased supplementary immunization activities, the number of reported polio cases rapidly decreased in many countries. Surveillance data indicate that the first NIDs in India, which until recently contributed the largest number of reported cases annually, had a significant impact on polio incidence.

By comparison, efforts to develop AFP surveillance have lagged behind. The rapid development of complete and timely AFP surveillance and continuation of effective NIDs, particularly in the remaining countries with endemic polio in the African, South-East Asian and Eastern Mediterranean regions, is an urgent priority for the global eradication initiative.

The countries which now remain endemic for polio include countries affected by civil unrest or military conflict, or politically isolated countries (e.g., Democratic People's Republic of Korea, Somalia, Sudan, the Democratic Republic of Congo), which serve as important remaining reservoirs from where wild poliovirus continues to spread into bordering or even distant polio-free countries. Expansion of the eradication initiative into these countries is critical to achieve global eradication.

External support will continue to be required by those countries and regions where the incidence of polio has reached low levels, to ensure that final chains of poliovirus transmission are interrupted and to permit the eventual certification of eradication. Sufficient external support will ensure continued implementation and improvements of the recommended strategies. The year-2000 objective for achieving poliomyelitis eradication remains a feasible target.

Summary

Substantial progress towards the global eradication of poliomyelitis by the year 2000 has been achieved since May 1988 when WHO Member States adopted this goal at the Forty-first World Health Assembly. Virtually all polio-endemic countries have begun to implement the WHO-recommended strategies to eradicate polio and it is expected that, by the end of 1997, all endemic countries in the world will have conducted full National Immunization Days (NID), providing supplemental oral polio vaccine (OPV) to nearly two-thirds of all children < 5 years. In contrast, although globally acute flaccid paralysis (AFP) surveillance was being conducted in 126 (86%) of 146 countries where polio is or recently was endemic, surveillance remains incomplete and untimely. A global network of polio laboratories, capable of detecting wild poliovirus when and where it occurs, has been developed. Furthermore, in countries where polio virus circulation has been limited to focal areas, and

surveillance is adequate, mopping-up campaigns are being conducted to eliminate the final chains of transmission. The process for certification of polio eradication has been established in each WHO region as well as at the global level. The impact of the eradication initiative is evident, with an 88% decrease in the number of reported cases globally since 1988. In order to achieve the goal of eradication, the rapid development of complete and timely AFP surveillance and the continuation of effective NIDs constitute an urgent priority. This is of particular relevance in the remaining polio-endemic countries, especially in those that are affected by war or politically isolated and are important remaining reservoirs from where wild poliovirus continues to spread into bordering or even distant polio-free countries. External support will continue to be required by those countries and regions where the incidence of polio has reached low levels to ensure that final chains of poliovirus transmission are interrupted and to permit the eventual certification of eradication. The year 2000 objective for achieving poliomyelitis eradication remains a feasible target.

Résumé

Situation actuelle de l'éradication de la poliomyélite dans le monde

Des progrès importants en vue de l'éradication mondiale de la poliomyélite d'ici l'an 2000 ont été réalisés depuis mai 1988, date à laquelle les Etats Membres de l'OMS ont adopté ce but lors de la Quarante et Unième Assemblée mondiale de la Santé. Pratiquement tous les pays d'endémie ont commencé à mettre en œuvre les stratégies recommandées par l'OMS afin d'éradiquer la poliomyélite et l'on espère que, d'ici la fin de 1997, tous les pays d'endémie auront organisé des journées nationales de vaccination (JNV), administrant des doses supplémentaires de vaccin antipoliomyélite buccal (VPO) à près des deux tiers des enfants âgés de moins de 5 ans. En revanche, même si, au niveau mondial, une surveillance de la paralysie flasque aiguë (PFA) est en vigueur dans 126 pays (86%) sur les 146 où la poliomyélite sévit ou sévissait encore récemment à l'état endémique, la surveillance demeure incomplète et n'est pas effectuée en temps opportun. Un réseau mondial de laboratoires de la poliomyélite capable de déceler le poliovirus sauvage quand et là où il sévit a été mis en place. Par ailleurs, dans les pays où la circulation du virus a été limitée à des zones localisées, et où la surveillance est suffisante, des campagnes de vaccination de rattrapage sont organisées pour éliminer les dernières chaînes de transmission. Le processus de certification de l'éradication de la poliomyélite a été établi dans chacune des régions de l'OMS aussi bien qu'au niveau mondial. L'impact de l'initiative en faveur de l'éradication est évident, puisqu'une diminution de 88% du nombre de cas notifiés dans le monde a déjà été observée depuis 1988. Pour atteindre le but de l'éradication, la mise en place rapide d'une surveillance complète en temps opportun de la PFA et la poursuite des JNV constituent une priorité urgente. Cela est particulièrement important dans les pays d'endémie restants, en particulier dans les pays touchés par la guerre ou isolés politiquement et qui constituent des réservoirs importants, d'où le poliovirus sauvage continue de se propager dans des pays indemnes de poliomyélite voisins ou plus éloignés. Une aide extérieure continuera d'être nécessaire dans les pays et les régions où l'incidence de la poliomyélite est tombée à des niveaux peu élevés pour s'assurer que les dernières chaînes de transmission du poliovirus sont interrompues et permettre la certification de l'éradication. L'objectif de l'éradication de la poliomyélite en l'an 2000 reste une cible réalisable.

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Progress towards the elimination of transmission of Chagas disease in Latin America

Alvaro Moncayo[a]

Chagas disease, named after the Brazilian physician Carlos Chagas who first described it in 1909, exists only on the American Continent. It is caused by a flagellate protozoan parasite, *Trypanosoma cruzi*, transmitted to humans by triatomine insects known popularly in the different countries as "vinchuca", "barbeiro", "chipo" etc. The geographical distribution of the human *T. cruzi* infection extends from Mexico to the south of Argentina. The disease affects 16-18 million people and some 100 million, i.e. about 25% of the population of Latin America, is at risk of acquiring Chagas disease.

There are two stages of the human disease: the acute stage which appears shortly after the infection and the chronic stage which appears after a silent period that may last several years. The lesions of the chronic phase irreversibly affect internal organs namely the heart, oesophagus and colon and the peripheral nervous system. After several years of an asymptomatic period, 27% of those infected develop cardiac symptoms which may lead to sudden death, 6% develop digestive damage – mainly megaviscera, and 3% will present peripheral nervous involvement.

The risk of infection with Chagas disease is directly related to poverty: the blood-sucking triatomine bug which transmits the parasite finds a favourable habitat in crevices in the walls and roofs of poor houses in rural areas and in the peripheral urban slums. The rural/urban migration movements that occurred in Latin America in the 1970s and 1980s changed the traditional epidemiological pattern of Chagas disease, transforming it into an urban infection that can be transmitted by blood transfusion. The rates of infection of blood in blood banks in some selected cities of the continent vary between 3% and 53% thus showing that the prevalence of *T. cruzi*-infected blood is higher than that of HIV infection and hepatitis B and C.

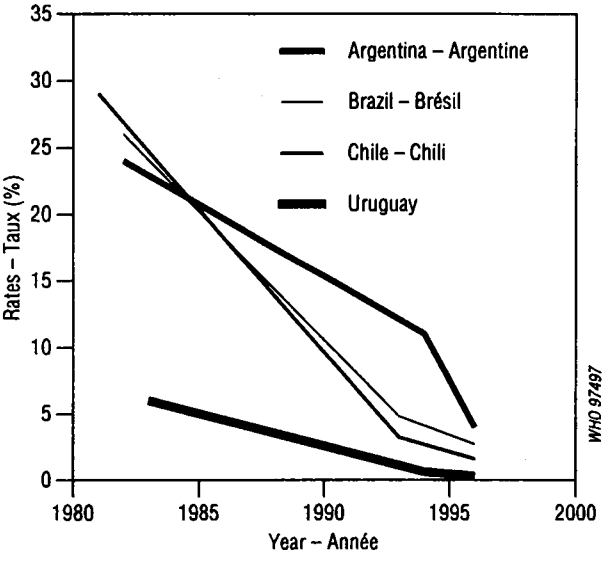
From a global perspective, Chagas disease represents the third largest tropical disease burden after malaria and schistosomiasis. According to the UNDP Human Development Report *(1)*, the estimated average annual per capita gross domestic product in Latin America, is US$ 2 966. Thus, the economic loss for the continent due to early mortality and disability by this disease in economically most productive young adults currently amounts to US$ 8 156 millions which is equivalent to 2.5% of the external debt of the whole continent in 1995.

Southern Cone Initiative

In 1991, the Ministers of Health of Argentina, Bolivia, Brazil, Chile, Paraguay and Uruguay, launched the "Southern Cone Initiative for elimination of transmission of Chagas disease". The progress towards elimination of vectorial and transfusional transmission of Chagas disease in Uruguay, Chile, Argentina and Brazil has been extensively documented *(2-5)*. Current data on disinfecting of houses, coverage of screening in blood banks and serology in children and young adults indicate that the interruption of the vectorial and transfusional transmission of Chagas disease will be achieved in these countries as follows: Uruguay and Chile in 1999, Brazil and Argentina in 2003. By eliminating the transmission of Chagas disease in the above countries, the incidence of the disease in the whole of Latin America will be reduced by more than 70% (see *Figs. 1 & 2*).

Fig. 1
Southern Cone Initiative for the elimination of transmission of Chagas disease: house infestation by triatomines, 1982-1996

Initiative du Cône Sud pour l'élimination de la transmission de la maladie de Chagas : infestation des habitations par des triatomes, 1982-1996



Source: Reports from national Chagas disease control programmes, 1993-1996. – Rapports des programmes nationaux de lutte contre la maladie de Chagas, 1993-1996.

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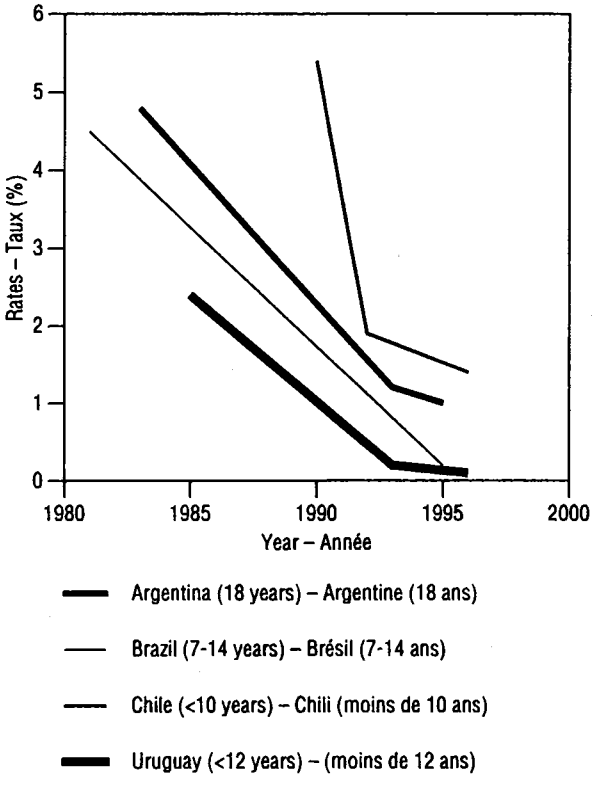
Fig. 2
Southern Cone Initiative for the elimination of transmission of Chagas disease: incidence of infections 1980-1996

Initiative du Cône Sud pour l'élimination de la transmission de la maladie de Chagas : incidence des infections, 1980-1996



Source: Reports from national Chagas disease programmes, 1993-1997. – Rapports des programmes nationaux de lutte contre la maladie de Chagas, 1993-1997.

Control activities are progressing as scheduled in Bolivia and Paraguay, but at this stage there are no entomological or epidemiological data available to assess the impact of the control programmes in these two countries and to estimate a date for achievement of interruption of transmission. These data should be available in 1999, after 4-5 years of continued control activities and completion of cross-sectional entomological and serological surveys. Peru joined in March 1997 as the southern area of this country is also infested by *T. infestans*. The detailed epidemiological situation, country by country is as follows:

Argentina

The area of transmission of Chagas disease in Argentina includes the zones north of latitude 44° 45′, covering about 60% of the territory of the country. The main vector is *Triatoma infestans* which is a domiciliated species.

The cumulative number of houses sprayed between 1992 and 1996 completed the attack phase of the control strategy. This has led to important reductions in the house infestation rates from 24% in 1983 to 4% in 1996 – equivalent to 84% decrease in the period. As a consequence, there was a reduction of 80% in the incidence of human infection in the group of 18 year old males between 1983 and 1996.

To prevent the transfusional transmission of Chagas disease, the screening of *T. cruzi*-infected blood is compulsory since 1983 and the coverage of the screening in the blood banks of the country was 98% in 1996.

Brazil

In 1970, the endemic area included over 36% of the country, with 2 493 municipalities being infested by *T. infestans*, the main vector of the disease. A total of 49 million persons lived in the endemic zone, 53% of whom in rural areas. *T. infestans*, the most important species responsible for the vectorial transmission of the disease, is exclusively domestic.

In 1983, there were 711 municipalities infested by *T. infestans* in the endemic states, while in 1995 only 75 municipalities were infested, representing a 90% reduction. In 8 of the 11 endemic states, a reduction of house infestation rates of 71% is observed. Focal areas still infested with *T. infestans* remain only in the states of Bahia, Tocantins and Rio Grande do Sul, which gives a house infestation rate of 2.7% for the whole country.

Seroepidemiological surveys carried out between 1994 and 1996 in 10 endemic states among population samples of individuals 7-14 years old showed that the incidence of infections in this age group is 0.23% in the country as a whole, indicating a reduction of 95% as compared to the 1981 rates.

Similar trends are observed in relation with the decreasing proportion of *T. cruzi*-infected blood in blood banks between 1982 and 1995. A proportion of 6.5% of infected blood was found in the whole country in 1982, whereas in 1995 this proportion was only 0.7%. The coverage of screening in blood banks reached 98% in 1995.

Chile

Chile has a population of 13 380 000, including 1 654 000 who live in the endemic rural area from parallel 18° 30′ to parallel 34° 35′ and hence are at risk of contracting the infection and further evolve to chronic myocardiopathy or megaviscera. The main species of triatomines responsible for the vectorial transmission of Chagas disease in Chile is *T. infestans*, a domestic insect.

In 1981, the proportion of infected persons in all age groups in the country was 17% and the average house infestation rate was 29%. The countrywide prevalence of infected subjects among blood donors in 1984 was 3.6%.

The vector control operations with residual activity insecticides carried out between 1982 and 1996 have reduced the house infestation rates by *T. infestans* to 1.6%, which is equivalent to a decrease of 95%. Transmission through blood transfusion is under control due to the 100% coverage since compulsory blood screening in the endemic regions was introduced in 1995.

A countrywide seroepidemiological study, completed in 1996, showed a prevalence rate of 1.4% in the age group <10 years as compared to 5.4% in the same age group in 1990, indicating the advanced degree of control and imminent interruption of vectorial transmission in Chile *(6)*.

Uruguay

Chagas disease is endemic in Uruguay where vectorial domiciliary transmission is effected through the triatomine insect *T. infestans*. In 1983, this insect infested human dwellings and their peridomestic annexes in 80% of the national territory. Sustained spraying helped eliminate the infestation by *T. infestans* in Artigas, Colonia, Durazno and Soriano, and markedly decreased the rate of house infestation in the remaining areas to the current figure of 0.3% for the entire country.

In 1985, a countrywide serological survey to detect human *T. cruzi* infection, showed a prevalence rate of 3.4% for the total population, and of 2.4% for the school-age group of <12 years old.

A seroepidemiological survey carried out in 1995 in different rural areas of the endemic departments in children <12 years old showed 0-0.1% infection rates in this age group. This could be interpreted as the confirmation of the interruption of the vectorial transmission of Chagas disease in Uruguay. In addition, there is 100% coverage of compulsory blood screening in the country.

Summary

From a global perspective, Chagas disease represents the third largest tropical disease burden after malaria and schistosomiasis. The estimated average annual per-capita gross domestic product in Latin America is US$ 2 966. The economic loss for the continent due to early mortality and disability by this disease in economically most productive young adults currently amounts to US$ 8 156 million which is equivalent to 2.5% of the external debt of the whole continent in 1995.

In 1991, the Ministers of Health of Argentina, Bolivia, Brazil, Chile, Paraguay and Uruguay, launched the Southern Cone Initiative for elimination of transmission of Chagas disease. The progress towards elimination of vectorial and transfusional transmission of Chagas disease in Uruguay, Chile, Argentina and Brazil has been documented by reports from the national control programmes of the above countries. Current data on disinfestation of houses, coverage of screening in blood banks and serology in children and young adults indicate that the interruption of the vectorial and transfusional transmission of Chagas disease will be achieved in these countries as follows: Uruguay and Chile in 1999, Brazil and Argentina in 2003. By eliminating the transmission of Chagas disease in the above countries, the incidence of the disease in the whole of Latin America will be reduced by more than 70%.

Résumé

Progrès sur la voie de l'élimination de la transmission de la maladie de Chagas en Amérique latine

D'un point de vue mondial, la maladie de Chagas est la troisième maladie tropicale par son importance, après le paludisme et la schistosomiase. Le produit national brut moyen par habitant et par an de l'Amérique latine est estimé à US $2 966. Les pertes économiques pour le continent dues à la mortalité précoce et aux incapacités provoquées par cette maladie chez des jeunes adultes économiquement les plus productifs s'élèvent à l'heure actuelle à US $8 156 millions, soit l'équivalent de 2,5% du montant de la dette extérieure de l'ensemble du continent en 1995.

En 1991, les Ministres de la Santé de l'Argentine, de la Bolivie, du Brésil, du Chili, du Paraguay et de l'Uruguay ont lancé l'initiative du Cône Sud pour l'élimination de la transmission de la maladie de Chagas. Les progrès accomplis sur la voie de l'élimination de la transmission vectorielle et transfusionnelle de la maladie de Chagas en Uruguay, au Chili, en Argentine et au Brésil ont été attestés dans des rapports publiés par les programmes nationaux de lutte des pays concernés. Les données actuelles concernant la désinsectisation des habitations, le dépistage par les banques de sang et la sérologie chez l'enfant et le jeune adulte indiquent que la transmission vectorielle et transfusionnelle de la maladie de Chagas sera interrompue en Uruguay et au Chili d'ici 1999, et au Brésil et en Argentine en 2003. L'élimination de la transmission de la maladie de Chagas dans les pays susmentionnés permettra de réduire l'incidence de la maladie dans l'ensemble de l'Amérique latine de plus de 70%.

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The lot quality technique: a global review of applications in the assessment of health services and disease surveillance

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Introduction

Health programme managers need up-to-date information to enable health systems to work effectively. Today, with increasing decentralization of health services, the need for information at the local level is growing. In particular, health programme managers need to know which communities are meeting particular targets and goals, and which are not. In this paper, the potential of the lot quality (LQ) sampling technique to provide useful, inexpensive programmatic information at the community level is explored. The paper begins with a brief description of the LQ method, reviews 34 health surveys which have used the LQ method, and discusses future applications of the LQ method for health assessments.

The LQ method (also called Lot Quality Assurance Sampling or Lot Quality Assessment) was developed in the 1920s as a quality control technique for goods produced on a factory assembly line *(1)*. The idea was to examine a small number of units randomly selected from each lot. If the number of defective items in that small sample exceeded a predetermined number, the lot was discarded. Otherwise, the lot was accepted. The number of units tested and the maximum allowable number of defects were determined statistically to ensure that there was a high probability that the lots accepted contained relatively few defective goods, if any, and that the lots rejected contained a relatively high proportion of defective goods.

Interest in applying the LQ method to health assessment has been growing since the mid-1980s *(1-5)*. In 1991, an international meeting on epidemiological and statistical methods for rapid health assessment concluded that LQ was one of the more practical methods, and encouraged further studies *(6-8)*. General guidelines on use of the LQ method were published by WHO in 1991 *(9)*. In 1995, special guidelines on LQ surveys for salt iodization programmes were released *(10)* and in 1996 a WHO manual on using the LQ technique to monitor immunization programmes[c] became available.

For the evaluation of health care services, lots can take many forms, including villages and communities, catchment areas of hospitals or health centres, groups of health care workers, or even batches of health records. In factories, manufactured goods are classified as "defective" or "not defective". In health services studies, individuals may be classified as "failed to receive appropriate treatment" or "received appropriate treatment". In immunization studies, individuals are classified as "unimmunized" or "immunized".

Description of the lot quality method

The LQ method combines two standard statistical techniques: *(a)* stratified random sampling for data collection, and *(b)* one-sided hypothesis testing for data analysis. The hypothesis testing technique provides a minimal amount of information from each lot or stratum, namely whether the level of defective goods is likely to be above or below a given threshold. Because of this, the size of the sample selected from each lot can be relatively small.

Defining the lots

The first step in the LQ method is to divide the population under study into lots which may consist of villages, urban zones, or health facility catchment areas. Performance across lots should differ since the purpose of the survey is to identify poorly performing lots. However, within a single lot the population should have the same exposure to disease and the same health care opportunity. The more homogeneous the population within each lot, the more likely it is that the results from only a few persons will be indicative of the entire lot. After selecting the lots, a random sample of size "n" is selected from each lot for inspection. The lot is either "accepted" or "rejected" depending upon whether the number of "defects" found in the sample exceeds a preset limit, "d".

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The role of threshold levels

In LQ, the procedure for determining whether to accept or reject a lot is equivalent to performing a one-sided hypothesis test for the null hypothesis, H_0, that the proportion of defects in the lot is greater than or equal to a predetermined upper threshold, P_0 (P_0 can be thought of as the maximum proportion of defects allowed). Rejecting the null hypothesis means accepting the lot and accepting the null hypothesis means rejecting the lot.

To have a hypothesis testing system that rejects almost all lots which have many defects, it is necessary to set an upper threshold, P_0, for the proportion of allowable defects within a lot, and to define α, the risk of misclassifying a lot as below P_0. In statistical terms, α refers to the risk of a type 1 error. The LQ method will reject all lots for which the probability is greater than α that the proportion of defects is greater than or equal to P_0. For example, if a health administrator wishes to identify lots with less than 75% vaccine coverage, the upper threshold (P_0) would be 25%. α is often set at 5%: this means that there would be less than a 5% chance that a lot which is accepted has not attained at least 75% coverage.

At the same time, it is important that lots with high coverage rates are not rejected, since this would result in a waste of valuable resources. To guard against this happening, a lower threshold for the proportion of defects, P_a, is set, along with a second critical value, β. The LQ method has a probability of $(1-\beta)$ of rejecting lots in which the proportion of defects (or unimmunized persons) is less than P_a. In statistical terms, β refers to the risk of a type 2 error, and $(1-\beta)$ is known as the power of the test. β is often set at a higher level than α, because it is usually considered that the consequences of accepting a lot with poor coverage are more significant than those of rejecting a lot with high coverage.

Thus, the programme manager should choose an upper threshold for the proportion of allowable defects in accepted lots and a lower threshold for the proportion of defects in rejected lots. In the above example, the programme manager would set 25% as the maximum proportion of allowable unimmunized persons in accepted lots. However, suppose that the health administrator considers that $\geq 90\%$ coverage is excellent and consequently would not wish to put resources into any community that had such high coverage rates. In this case, the lower threshold for the proportion of allowable defects in rejected lots (β) could be set at 10%. With these threshold levels, the lots accepted would include no more than 5% of all lots with underlying coverage $< 75\%$, and the lots rejected would include at most 10% of lots with underlying coverage of 90% or more.

Practical considerations in choosing appropriate thresholds

Selecting appropriate thresholds is a crucial step in setting the LQ design. The usual reason for doing an LQ survey in health care is to improve target resources. To do this, it is necessary to divide the lots into two groups – those with "good performance" which would not get additional resources, and those with "poor performance" which would get additional resources. Ideally, the majority of lots would be accepted, and a limited number of lots would be rejected. Additional resources could then be targeted to the rejected lots to bring them up to a more acceptable level of performance. An LQ exercise that either accepted all lots or rejected all lots would not be particularly helpful to a programme manager; therefore, the threshold levels should be set somewhere between the performance levels expected to be found in the best and worst lots. Any information about performance levels in the area under study, even informed guesses, can be useful in this context.

Determining sample size and allowable defects

Based on the upper and lower threshold levels for defects, and their associated critical values, the LQ method allows for the calculation of pairs of values "n" and "d", where "n" is the size of the sample to be drawn from each lot and "d" is the maximum number of allowable defects. LQ tables, which provide values of "n" and "d" corresponding to various upper and lower threshold levels, and common values of α and β, can be found in a number of publications *(9)*.

A second way to select the sample size and maximum allowable defects is to use operating characteristic (OC) curves found in books of statistical tables *(11)*. These curves plot the probability of accepting a lot, against the underlying proportion of defects in the population. Each pair of values "n" and "d" has its own OC curve. Therefore, by selecting a particular OC curve, one is also selecting upper and lower thresholds, and their associated α and β values. OC curves are somewhat more difficult for the non-statistician to use and interpret than LQ tables, but they have the advantage of allowing the researcher to more easily examine the effects of different thresholds and confidence levels on sample size.

Once the "n" and "d" values are set, a random sample of size "n" is taken from each lot. The lot is rejected if the number of defects exceeds "d"; otherwise, the lot is accepted. It is possible to stop the survey as soon as the number of defects exceeds "d", since at this point the lot is automatically rejected. However, in most surveys, the programme manager not only wants to identify poorly performing lots, but also to obtain an overall estimate of performance for the entire study area. In this situation, it is necessary to sample "n" subjects in every lot.

Estimating coverage levels with the LQ method

If "n" subjects are selected from every lot, the results from the individual lots can be combined into an estimate of coverage for the study area as a whole by weighting the results from each lot by the size of the target population in the lot and then taking the mean. Provided that the estimates of the size of the target population in each lot are reliable (this should be the case, since an assessment of the target population size is needed to set the size of the survey), the estimate of coverage obtained from the LQ method will usually have greater precision than that obtained with the 30-cluster method *(12)*. This is because stratified random samples generally have narrower limits than cluster samples of the same size. In fact, stratified samples often have narrower confidence intervals than simple random samples. This is because some subjects are selected from each and every strata, making it impossible to miss some strata completely.

Terminology of the LQ method

The terminology of the LQ method has several problems. First it is confusing, since accepting a lot is synonymous with rejecting the null hypothesis. Second, the LQ method uses the words "accept" and "reject" in different ways than they are used in everyday language. It is important to keep in mind that no value judgment is being made about the absolute level of performance when a lot is accepted or rejected.

Global review of LQ surveys

This section reviews the global experience with surveys which used the LQ method to evaluate preventive services or to estimate disease incidence. These studies are either published in the scientific literature or had reports forwarded to WHO as of February 1997.

Number of surveys, location, sample size

A total of 34 LQ health surveys, conducted from 1984 through 1996, were identified *(Table 1)*. Twenty (59%) were conducted between 1992 and 1996. These surveys provide experience from countries in the WHO African, American, European, South-East Asia, and Western Pacific Regions; no surveys were reported from countries in the WHO Eastern Mediterranean Region.

Of the 34 LQ surveys, 14 (41%) were conducted in an urban area, 16 (47%) took place in a predominantly rural province, region or district, and 4 surveys (12%) covered the entire country. The size of the total population in the sampling frame ranged from 8 000 to 1.2 billion persons. Lots were defined as: health centre (or subcentre) catchment areas, townships, villages within a single district, zones or wards of a city, or districts within a province. For 5 surveys, lots were defined as physicians or individual community health workers. The number of lots per study ranged from 2 to 870. Of the 34 surveys, 17 (50%) had ≤ 15 lots, 8 (24%) had 16-30 lots, 7 (21%) had 31-100 lots, and 2 (6%) nationwide surveys had > 100 lots. The total sample size ranged from 70 to 25 230 *(Table 1)*.

Types of health assessments

Health care parameters assessed in the surveys varied and some surveys assessed more than 1 health parameter: 24 surveys assessed immunization coverage, 9 surveys examined women's health issues such as family planning and antenatal care, 5 surveys assessed ORT use, 5 surveys estimated disease incidence, and 3 surveys evaluated health worker performance.

Use of LQ method to measure immunization coverage. Twenty-three surveys examined immunization coverage for young children: most assessed the age group 12-23 months. Nine surveys examined tetanus toxoid coverage for women: most assessed mothers of children aged 0-11 months. All LQ coverage surveys in this review obtained an overall estimate of immunization coverage with confidence intervals narrower than ± 10%; 8 surveys had confidence intervals of ± 6% or less. In 4 surveys *(13-16)* the overall level of immunization coverage determined by the LQ method was less than 10% above the lower threshold, indicating that the original coverage figures used to set the lower threshold were overestimates.

Use of LQ for women's health services assessments. Nine surveys explored the LQ method to assess women's health services. Four surveys assessed antenatal care: the usual indicators assessed were number of antenatal visits and place of delivery of the infant. Three LQ surveys assessed family planning methods. Two LQ surveys in Belgium determined the proportion of women in several private physicians' practices who had been appropriately screened for cervical cancer or breast cancer.

Use of LQ for ORT assessments. Five surveys assessed ORT use. For example, an LQ survey in Mozambique examined the quantity of liquids administered to children with diarrhoea and mothers' knowledge and use of ORT (P. Tabard, unpublished data, 1993).

Use of LQ for disease surveillance, including serosurveys. The LQ method has been adapted for disease surveillance in a variety of settings. The WHO Global Programme for Vaccines and Immunization has developed a protocol[f] which uses the

[f] Stroh, G. *Guidelines: assessment of neonatal tetanus elimination.* Global Programme for Vaccines and Immunization, Geneva, World Health Organization, 1995.

Table 1
Summary of lot quality studies conducted, worldwide, 1984-1996

Tableau 1
Récapitulatif des études sur le contrôle de la qualité des lots à l'échelle mondiale, 1984-1996

	Country/Area – Pays/Zone	Year – Année	Area/City – Région/Ville	Total population in sampling frame – Population totale dans la base d'échantillonnage	Number of lots – Nombre de lots	Total sample size – Taille de l'échantillon	Purpose of survey – But de l'enquête	Reference – Référence
1	Bangladesh	1992	Khulna City Corporation	676 000	29 city wards – quartiers	406 children – enfants 406 mothers – mères	Immunization coverage – Couverture vaccinale Tetanus toxoid coverage, breastfeeding, family planning – Couverture par l'anatoxine tétanique, allaitement maternel, planification familiale	*(22)*
2	Bangladesh	1994	Khulna City Corporation	676 000	31 city wards – quartiers	434 children – enfants 434 mothers – mères	Immunization coverage – Couverture vaccinale Tetanus toxoid coverage, breastfeeding, family planning – Couverture par l'anatoxine tétanique, allaitement maternel, planification familiale	B. Roy & M. Carnell, 1994[a]
3	Bangladesh	1994	Gazipur Zila District – District de Gazipur Zila	1 600 000	40 villages	1 000 births – naissances 1 000 mothers – mères	Neonatal tetanus mortality – Mortalité par tétanos néonatal Tetanus toxoid coverage – Couverture par l'anatoxine tétanique	G. Stroh, 1996[a]
4	Belgium – Belgique	1996	Brussels, medical records of 2 general practitioners – Bruxelles, dossiers médicaux de 2 médecins généralistes	8 000	2 physicians – médecins	70 women – femmes	Cervical cancer screening coverage – Couverture par le dépistage du cancer du col	M. Boutsen, 1996[a]
5	Belgium – Belgique	1996	Brussels, medical records of 2 general practitioners – Bruxelles, dossiers médicaux de 2 médecins généralistes	8 000	2 physicians – médecins	70 women – femmes	Breast cancer screening coverage – Couverture par le dépistage du cancer du sein	M. Boutsen, 1996[a]
6	Burkina Faso	1994	Bobo Dioulasso	150 000	11 city wards – quartiers	121 children – enfants 121 mothers – mères	Immunization coverage – Couverture vaccinale Tetanus toxoid coverage – Couverture par l'anatoxine tétanique	*(16)*
7	Burkina Faso	1994	Ouagadougou	441 514	13 city wards – quartiers	143 children – enfants	Immunization coverage – Couverture vaccinale	A. Roisin, 1994[a]

						143 mothers – mères	Tetanus toxoid coverage – Couverture par l'anatoxine tétanique	
8	China – Chine	1994	Zheijiang Province, Lanxi City –Province de Zheijang,Lanxi	50 000	3 townships – quartiers	192 children – enfants	Immunization coverage – Couverture vaccinale	*(23)*
9	China – Chine	1996	Nationwide – Niveau national	1 200 000 000	870 townships – quartiers	25 230 children – enfants	Immunization coverage – Couverture vaccinale	K. Wang, 1996[a]
10	Costa Rica	1987	Nationwide – Niveau national	1 600 000	758 health worker catchment areas – 758 zones couvertes par agents de santé	15 160 children – enfants	Immunization coverage – Couverture vaccinale	*(15)*
11	Costa Rica	1988	Nationwide – Niveau national	1 600 000	60 health worker catchment areas – 60 zones couvertes par agents de santé	1 680 children – enfants	Immunization coverage, oral rehydration therapy, antenatal care – Couverture vaccinale, traitement par réhydratation orale, soins prénatals	*(25)*
12	Costa Rica	1988-1990	6 outposts in different health regions – 6 postes périphériques dans différentes régions sanitaires	...	18 health workers – agents de santé	108 health worker observations – 108 observations de l'agent de santé	Injection safety – Sécurité des injections	*(19)*
13	Costa Rica	1988-1990	6 health regions, urban & rural areas – 6 régions sanitaires, régions rurales et urbaines	...	12 health workers – agents de santé	230 health worker observations – 230 observations de l'agent de santé	Growth monitoring – Surveillance de la croissance	*(18)*
14	Democratic Republic of the Congo – République démocratique du Congo	1988	Kinshasa	3 500 000	31 zones	423 children – enfants 423 mothers – mères	Immunization coverage – Couverture vaccinale Tetanus toxoid coverage – Couverture par l'anatoxine tétanique	*(28)*
15	Georgia – Géorgie	1996	Tbilisi – Tbilissi	1 255 000	10 rayons	120 children – enfants	Immunization coverage – Couverture vaccinale	*(h)*
16	India – Inde	1992	Health center catchment area, Saharanpur District – Zone desservie par le centre de santé, district de Saharanpur	52 688	9 subcenters – centres subsidiaires	97 children – enfants 97 mothers – mères	Immunization coverage – Couverture vaccinale Tetanus toxoid coverage – Couverture par l'anatoxine tétanique	*(26)*

Table 1 (*Continued*)

Tableau 1 (*Suite*)

17	India – Inde	1992	Health center catchment area, Alwar District – Zone desservie par le centre de santé, district d'Alwar	168 000	27 subcenters – centres subsidiaires	311 children – enfants 311 mothers – mères	Immunization coverage – Couverture vaccinale Tetanus toxoid coverage – Couverture par l'anatoxine tétanique	*(13)*
18	Indonesia – Indonésie	1986	Bali Province, Gianyar District – Province de Bali, district de Gianyar	337 000	30 villages	209 children – enfants	Immunization coverage – Couverture vaccinale	*(3)*
19	Indonesia – Indonésie	1986	Jakarta City, East Municipality – Jakarta, municipalité est	2 000 000	29 villages	209 children – enfants	Immunization coverage – Couverture vaccinale	*(3)*
20	Indonesia – Indonésie	1996	Bali Province, Buleleng and and Karangesem Districts – Province de Bali, districts de Buleleng et de Karangesem	900 000	50 villages	1 000 births – naissances	Neonatal tetanus mortality – Mortalité par tétanos néonatal	F. Gasse, 1996[a]
21	Indonesia – Indonésie	1996	West Java Province, Mojokerto Municipality, Mojokerto and Kediri Districts – Province de Java occidentale, municipalité de Mojokerto, districts de Mojokerto et Kediri	2 300 000	50 villages	1 000 births – naissances	Neonatal tetanus mortality – Mortalité par tétanos néonatal	F. Gasse, 1996[a]
22	Malawi	1984	Nationwide – Niveau national	8 000 000	6 surveillance sites – zones de surveillance	224 children – enfants	Response to antimalarial treatment regimen – Réaction au schéma de traitement antipaludéen	*(2)*
23	Malawi	1992	Mbalachanda	28 100	14 health workers – agents de santé	266 health worker record observations – 266 observations enregistrées par les agents de santé	Check records of village health workers for registration, oral rehydration therapy, immunizations – Vérification des dossiers des agents de santé de village (enregistrement, traitement par réhydratation orale, vaccinations)	*(20)*
24	Mozambique	1992	Maputo	1 200 000	18 health center catchment areas – 18 zones couvertes par agents de santé	234 children – enfants	Immunization coverage – Couverture vaccinale	*(21)*

25	Mozambique	1993	Tete Province – Province de Tete	350 704	12 health center catchment areas – 12 zones couvertes par agents de santé	144 children – enfants 141 mothers – mères	Immunization coverage, diarrhoea prevalence – Couverture vaccinale, prévalence de la diarrhée Oral rehydration therapy, tetanus toxoid coverage, antenatal care – Thérapie par réhydratation orale, couverture par l'anatoxine tétanique, soins prénatals	P. Tabard, 1993[a]
26	Peru – Pérou	1984	Lima City (periurban area), pre-campaign – Lima (zone périurbaine) pré-campagne	85 927	12 districts	108 children – enfants 108 mothers – mères	Immunization coverage – Couverture vaccinale Oral rehydration therapy, antenatal care – Thérapie par réhydratation orale, soins prénatals	*(14)*
27	Peru – Pérou	1984	Lima City (periurban area), post-campaign – Lima (zone périurbaine), post-campagne	85 927	12 districts	108 children – enfants 108 mothers – mères	Immunization coverage – Couverture vaccinale Oral rehydration therapy, antenatal care – Thérapie par réhydratation orale, soins prénatals	*(14)*
28	Peru – Pérou	1988	Huarez Region, pre-campaign – Région de Huarez, pré-campagne	81 031	12 health areas – régions sanitaires	111 children – enfants	Immunization coverage – Couverture vaccinale	*(27)*
29	Peru – Pérou	1988	Huarez Region, post-phase 1 of campaign – Région de Huarez, post-phase 1 de la campagne	81 031	12 health areas – régions sanitaires	160 children – enfants	Immunization coverage – Couverture vaccinale	*(27)*
30	Peru – Pérou	1988	Huarez Region, post-phase 2 of campaign – Région de Huarez, post-phase 2 de la campagne	81 031	12 health areas – régions sanitaires	250 children – enfants	Immunization coverage – Couverture vaccinale	*(27)*
31	Senegal – Sénégal	1996	Dakar City, Pikine area – Dakar, zone de Pikine	...	2 city wards – quartiers	80 married women – femmes mariées	Contraceptive use – Contraception	M. Boutsen, 1996[a]
32	Turkey – Turquie	1996	Kahramanmara Province – Province de Kahramanmara	860 803	16 districts	384 children – enfants	Immunization coverage – Couverture vaccinale	S. Sener, 1997[a]
33	Turkey – Turquie	1996	Kars Province – Province de Kars	313 339	35 health catchment areas – 35 zones couvertes par agents de santé	385 children – enfants	Immunization coverage – Couverture vaccinale	S. Sener, 1997[a]
34	Uganda – Ouganda	1996	Terego County – Comté de Terego	53 056	16 parishes – localités	944 persons – personnes	Trypanosomiasis serosurvey – Enquête sérologique sur la trypanosomiase	C. Pacquet, 1996[a]

[a] Unpublished data – Données non publiées.
[b] Tsereteli, Z. & Varsimashvili, Z. *EPI coverage survey with add on questions in Georgia.* Tbilisi, Ministry of Health and UNICEF Georgia Country Office, 1996.

LQ method to assess whether the incidence of neonatal tetanus is below the "elimination threshold" of 1 death due to neonatal tetanus per 100 000 live births. A field test was conducted in Gazipur Zila District, Bangladesh in 1994. This district was selected because it had high levels of tetanus toxoid coverage of women (about 80%) and had reported no neonatal tetanus cases during the year. Some 5 459 households were surveyed to obtain information on the survival of 1 000 live births. Sixteen neonatal deaths were detected, 7 of which were determined to be due to neonatal tetanus. Thus, Gazipur Zila District, with a neonatal tetanus mortality rate of 7/1 000 live births, had not reached neonatal tetanus elimination (G. Stroh, unpublished data, 1994). Two surveys conducted in 1996 in Indonesia found neonatal tetanus mortality rates below the elimination threshold (F. Gasse, unpublished data, 1996).

A survey in Tete Province, Mozambique explored the use of the LQ method to obtain prevalence of diarrhoeal disease reported by mothers of children aged 12-23 months: 8% of children had diarrhoea on the day of the survey, 19% had an episode in the previous 2 weeks, and every child had at least 1 episode in the previous year (P. Tabard, unpublished data, 1993).

LQ sampling is also being used for serosurveys. In 1984, a survey in Malawi assessed the response of children <5 years of age to a chloroquine treatment regimen for prevention of malaria *(2)*. In 1996, a trypanosomiasis serosurvey was conducted in Uganda (C. Pacquet, personal communication 1996). Several authors have proposed that the LQ method could be readily extended to a sentinel serosurveillance system for HIV infection in low-prevalence areas *(8, 17)*; however, no studies are reported to date.

Use of LQ for health worker supervision. Studies in Costa Rica used the LQ method as a supervisory tool to assess the quality of health worker performance related to nutrition programmes *(18)* and injection safety techniques *(19)*. In these studies each lot is a health worker and certain aspects of the health worker's performance are observed multiple times. To examine performance, the investigators must define a series of tasks. For example, the tasks for injection safety were: identification of children requiring vaccination; preparation of the syringe and a sterile work area; educating mothers on vaccines and their potential side effects; delivery of the vaccine and clean-up; and maintenance of the cold chain. Health workers identified as performing below standard should receive training, and subsequent LQ studies can be used to monitor improvements in health worker performance.

In Malawi, the LQ method was used to evaluate the accuracy of data in health records maintained by community health workers, and thereby identify health workers in need of further supervision *(20)*. Poor performance was easy to detect: 9 of 14 health workers had failed to acceptably update information on ORT, whereas only one health worker had failed to properly update immunization data.

Use of LQ for nutrition programmes. In 1995 guidelines were released on use of the LQ method to monitor salt iodization programmes *(10)*; studies should be forthcoming over the next few years. The LQ method has been proposed to assess vitamin A deficiency; however, no surveys are yet reported.

Costs

The LQ method remains relatively inexpensive and provides data much more rapidly than standard surveys: many LQ surveys can be completed and analyzed in a few weeks. Information from 9 LQ surveys indicated that 30 to 150 person-days of field work were needed per survey *(Table 2)*.

The LQ method provides better precision and more detailed information than a standard 30-cluster survey *(12)*, but at the cost of randomly selecting the individuals in the survey. Two surveys directly compared the two methods *(Table 2)*. In Maputo, Mozambique, the per lot cost of an LQ survey (US$ 5 400) was higher than for 30-cluster survey (US$ 2 600-3 000) *(21)*. The manpower required for the Maputo LQ survey was 144 person-days, as compared to 60 person-days for the 30-cluster survey. However, each lot could be judged as passing or failing, and the precision achieved by the LQ method (confidence interval, ± 2-3%) was greater than that of the 30-cluster method (confidence interval, ± 5-8%). In Saharanpur District, India, an LQ survey cost 18 850 Rupees, compared with 12 050 Rupees for a 30-cluster survey in the same area *(13)*. As with the Maputo survey, the increased costs for the Saharanpur LQ survey were associated with increased precision in the coverage estimate and information about each lot.

Discussion

A decade ago, statisticians and epidemiologists foresaw that the LQ method could be suitable for assessing a variety of primary health care services. Since 1984, 34 LQ surveys have been carried out; 59% of these were conducted in 1992-1996, indicating increasing use of this method.

A majority of LQ surveys have been used to measure immunization coverage. This is because the LQ method overcomes several limitations of the 30-cluster method promoted by the WHO Expanded Programme on Immunization (EPI)[g] *(12)*.

[g] *The EPI coverage survey: Training for mid-level managers.* (Document WHO/EPI.MLM 91.10).

Table 2
Person-days of work required for selected lot quality surveys

Tableau 2
Journées-personnes de travail requises pour la réalisation de certaines enquêtes sur la qualité des lots

Country – Pays	Urban/Rural – Zone urbaine/ Zone rurale	Year – Année	Lot quality survey – Enquête sur le contrôle de qualité des lots		30-cluster survey – Enquête dans 30 grappes		Reference – Référence
			Person/days of field work – Journées/ personnes de travail sur le terrain	Sample size – Taille de l'échantillon	Person/days of field work – Journées/ personnes de travail sur le terrain	Sample size – Taille de l'échantillon	
Democratic Republic of the Congo – République démocratique du Congo	Urban – Zone urbaine	1988	50	423			*(28)*
India (Alwar) – Inde	Rural – Zone rurale	1992	150	311	90	212	*(13)*
Indonesia – Indonésie	Rural – Zone rurale	1996	150	1000			F. Gasse, 1996[a]
Mozambique	Urban – Zone urbainee	1992	144	234	60	212	*(21)*
Bangladesh	Urban – Zone urbaine	1992	120	406			*(22)*
Indonesia – Indonésie	Urban/Rural – Zone urbaine/ Zone rurale	1996	100	1000			F. Gasse, 1996[a]
Indonesia – Indonésie	Rural – Zone rurale	1987	36	209			*(3)*
Indonesia – Indonésie	Urban – Zone urbaine	1987	33	209			*(3)*
Peru – Pérou	Urban – Zone urbaine	1984	20	108			*(14)*

[a] Unpublished data – Données non publiées.

For a given level of precision, an LQ immunization coverage survey requires about half the size of an EPI 30-cluster coverage survey. This is because of the design effect, which is assumed to be 2 for an EPI cluster sample, but is no more than 1 for a stratified random sample. One of the most attractive features of the LQ technique is that it provides a qualitative result ("pass" or "fail") for each lot, whereas a 30-cluster survey does not allow data to be interpreted from individual clusters. Thus, the LQ survey allows the manager to identify poorly performing pockets and to direct supervision to areas most in need. The surveys we reviewed provide information about performance at the level of individual health centre catchment areas, single villages, or even for individual health workers. Moreover, the LQ method can interpret data as soon as it is collected from a lot, e.g., data do not have to be collected from all lots before action can be taken. The fact that LQ assessments can be set up to provide information useful at the community level is particularly important in an era of increasing decentralization. It is also important for programmes with high performance, such as many immunization programmes (immunization coverage is 80% or higher in many countries), where attention needs to be focused on identifying pockets where the programme is not working well.

The major drawback of the LQ method is the requirement of visiting every lot. Depending on the number of lots, this could be somewhat more costly and time-consuming than a traditional 30-cluster coverage survey. If it is already known that there is very little variation in coverage among lots, or if a manager requires no other information than a rough estimate of the coverage levels achieved over the study area as a whole, a traditional 30-cluster survey may be more appropriate than an LQ survey. However, if more detailed information on coverage at the community level is required, then the LQ method offers a practical alternative to the 30-cluster survey. When choosing

the most appropriate method, the investigators must balance the extra cost of carrying out an LQ survey with the additional information the LQ survey will yield.

The LQ method has been used to examine a number of other health care parameters, ranging from ORT use to growth monitoring, antenatal care, health worker performance, and disease surveillance. The above studies are promising and further health assessments based on the LQ method would be useful.

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Summary

Since the mid-1980s, there has been growing interest in adapting the lot quality (LQ) technique to monitor the quality of health care services, especially in developing countries. This global review has identified a total of 34 LQ surveys conducted from 1984 to1996 in Africa, the Americas, Europe, South-East Asia, and the Western Pacific. Health care parameters assessed in the surveys varied and some surveys assessed more than 1 health parameter: 24 surveys assessed immunization coverage, 9 examined women's health issues such as family planning and antenatal care, 5 assessed use of oral rehydration therapy, 5 estimated disease incidence, and 3 others evaluated health worker performance. These studies indicate that LQ is a practical, relatively low-cost field method which is increasingly being applied in health programmes.

Résumé

Etude mondiale des applications de la technique du contrôle de la qualité des lots pour l'évaluation des services de santé et la surveillance de la maladie

Depuis le milieu des années 80, on s'intéresse de plus en plus à l'adaptation de la technique de contrôle de la qualité des lots pour la surveillance de la qualité des services de santé, notamment dans les pays en développement. Cette étude mondiale a répertorié au total 34 enquêtes sur le contrôle de la qualité des lots effectuées de 1984 à 1996 en Afrique, dans les Amériques, en Europe, en Asie du Sud-Est et dans le Pacifique occidental. Les paramètres relatifs aux soins de santé évalués dans les enquêtes n'étaient pas les mêmes et certaines enquêtes ont évalué plusieurs paramètres: 24 enquêtes ont porté sur la couverture vaccinale, 9 sur des problèmes de santé des femmes, telles que la planification familiale et les soins prénatals, 5 enquêtes sur l'utilisation de la thérapie par réhydratation orale, 5 sur l'incidence de la maladie et trois autres sur la qualité du travail des agents de santé. Ces études montrent que le contrôle de la qualité des lots est une méthode de terrain pratique et d'un coût relativement bas de plus en plus utilisée dans les programmes de santé.

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Corrigendum
Vol. 49, No. 3/4, 1996
Pages 232 and 233
Replace by:

Rectificatif
Vol. 49, No. 3/4, 1996
Pages 232 et 233
Remplacer par ce qui suit :

Table 2
Rates[a] of violent death among children <15 years of age. United States and 25 other industrialized countries/areas

Tableau 2
Taux[a] des décès violents chez les enfants âgés de moins de 15 ans, Etats-Unis d'Amérique et 25 autres pays/zones

Age (years – années)	Homicide	Suicide	Firearm deaths – Décès par armes à feu				
			Homicide	Suicide	Unintentional – Non intentionnel	Unknown intention – Intention inconnue	Total
0-4							
United States – Etats-Unis	4.1	0.0	0.43	0.0	0.15	0.01	0.59
Non-US – Autres pays/zones	0.95	0.0	0.05	0.0	0.01	0.01	0.07
Ratio US/Non-US – Rapport Etats-Unis/autres pays	4.3		8.6		15	1	8.4
5-14							
United States – Etats-Unis	1.75	0.84	1.22	0.49	0.46	0.06	2.23
Non-US – Autres pays	0.30	0.40	0.07	0.05	0.05	0.01	0.18
Ratio US/Non-US – Rapport Etats-Unis/autres pays	5.8	2.1	17.4	9.8	9.2	6.0	12.4
0-14							
United States – Etats-Unis	**2.57**	**0.55**	**0.94**	**0.32**	**0.36**	**0.04**	**1.66**
Non-US – Autres pays	**0.51**	**0.27**	**0.06**	**0.03**	**0.04**	**0.01**	**0.14**
Ratio US/Non-US – Rapport Etats-Unis/autres pays	**5.0**	**2.0**	**15.7**	**10.7**	**9.0**	**4.0**	**11.9**

[a] Rates per 100 000 and for 1 year between 1990 and 1995. – Taux pour 100 000 et pour un an entre 1990 et 1995.

Table 3
Rates[a] of non-firearm related violent death for children <15 years of age, United States of America and 25 other industrialized countries/areas

Tableau 3
Taux[a] des décès violents dus à d'autres causes que les armes à feu pour les enfants âgés de moins de 15 ans, Etats-Unis d'Amérique et 25 autres pays/zones industrialisés

Age (years – années)	Homicide (non-firearm –autres que par armes à feu)	Suicide (non-firearm – autres que par armes à feu)
0-4		
United States – Etats-Unis	3.67	0.0
Non-US – Autres pays/zones	0.9	0.0
Ratio US/Non-US – Rapport Etats-Unis/autres pays	4.1	
5-14		
United States – Etats-Unis	0.53	0.35
Non-US – Autres pays	0.24	0.35
Ratio US/Non-US – Rapport Etats-Unis/autres pays	2.2	1.0
0-14		
United States – Etats-Unis	**1.63**	**0.23**
Non-US – Autres pays	**0.45**	**0.24**
Ratio US/Non-US – Rapport Etats-Unis/autres pays	**3.6**	**1.0**

[a] Rates per 100 000 and for 1 year between 1990 and 1995. – Taux pour 100 000 et pour un an entre 1990 et 1995.

World Health Statistics Quarterly

Rapport trimestriel de statistiques sanitaires mondiales

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Annual table of contents

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Table annuelle des matières

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Les maladies infectieuses : épidémiologie et lutte

Malgré les progrès de la science, de la santé publique et de la médecine observés depuis un demi-siècle, les maladies infectieuses demeurent un problème de santé publique important, étant responsables du tiers des décès qui surviennent dans le monde chaque année. On a assisté depuis dix ans à la fois à l'émergence de nouveaux organismes pathogènes, tels que les agents responsables du SIDA, de la fièvre hémorragique à virus Ebola et de la maladie de Lyme, et à la réémergence de plusieurs maladies, dont la fièvre jaune en Afrique orientale, la dengue hémorragique et le choléra dans les Amériques, et la méningite méningococcique en Afrique. Le présent numéro du *Rapport trimestriel de Statistiques sanitaires mondiales* s'intéresse plus particulièrement à trois de ces maladies réémergentes. La situation mondiale n'est pas entièrement sombre, cependant, et ce numéro passe également en revue les progrès accomplis en matière d'éradication de la poliomyélite et d'élimination de la transmission de la maladie de Chagas. Y sont évoquées aussi les possibilités d'une éradication de la rougeole et le dernier article décrit comment un instrument mis au point par l'industrie pour évaluer la qualité des lots peut être utilisé pour contrôler la qualité des services de santé.