

Review

Impact of anti-vaccine movements on pertussis control: the untold story

E J Gangarosa, A M Galazka, C R Wolfe, L M Phillips, R E Gangarosa, E Miller, R T Chen

To assess the impact of anti-vaccine movements that targeted pertussis whole-cell vaccines, we compared pertussis incidence in countries where high coverage with diphtheria-tetanus-pertussis vaccines (DTP) was maintained (Hungary, the former East Germany, Poland, and the USA) with countries where immunisation was disrupted by anti-vaccine movements (Sweden, Japan, UK, The Russian Federation, Ireland, Italy, the former West Germany, and Australia). Pertussis incidence was 10 to 100 times lower in countries where high vaccine coverage was maintained than in countries where immunisation programs were compromised by anti-vaccine movements. Comparisons of neighbouring countries with high and low vaccine coverage further underscore the efficacy of these vaccines. Given the safety and cost-effectiveness of whole-cell pertussis vaccines, our study shows that, far from being obsolete, these vaccines continue to have an important role in global immunisation.

Of the vaccine-preventable diseases, pertussis rivals measles and neonatal tetanus in importance and severity among young children in the developing world. Millions of cases and hundreds of thousands of deaths occur each year. Complications are common: pneumonia in 15% of infants under 6 months of age, and severe neurological sequelae in 0.1–4.0% of patients. Pertussis is an exhausting illness that often lasts months.¹ Because the disease is so serious and so difficult to treat, prevention is paramount.

Whole-cell vaccines, whether monovalent or in diphtheria-tetanus-pertussis (DTP), have been important in the control of pertussis.¹ The decrease in pertussis incidence resulting from vaccination may have created the impression that pertussis was becoming milder and more scarce owing to medical and social development.^{2,3} As pertussis became rarer, attention shifted from the disease to the adverse events—often unrelated—that sometimes follow vaccination.⁴ In several countries, publicity surrounding such adverse events gave rise to movements opposed to whole-cell pertussis vaccination. This paper describes these anti-vaccine movements, their impact on pertussis control, and the future role of whole-cell pertussis vaccines.

Methods

We searched the literature, studied English translations of contemporary news stories, and analysed country-specific incidence of pertussis, whole-cell vaccine coverage, and vaccination schedules from data compiled by the US Centers for Disease Control and Prevention, and by WHO. We also studied books and other publications intended for lay audiences written by advocates against vaccination. From available relevant data, we compared the pertussis experiences of two groups of

countries.

Group I includes countries in which use of whole-cell pertussis vaccine (in DTP) has lasted decades—eg, Hungary, the former East Germany, Poland, and the USA. These countries have provided comprehensive DTP coverage with little or no interruption by anti-vaccine movements.

Group II includes countries in which peer-reviewed publications documented that anti-vaccine movements affected pertussis-control programmes. We defined opposition to whole-cell pertussis vaccines as activities of groups that actively or passively opposed use of the vaccines. Sweden, Japan, the UK, and The Russian Federation had active opposition to whole-cell vaccines—that is, well-organised movements that sought to stop their use by means of news stories, television interviews, lectures, popular articles, books, and other writings. Distraught parents whose children suffered adverse events blamed on whole-cell pertussis vaccination featured prominently. Some outspoken medical authorities became leaders in these movements.

Italy, the former West Germany, Ireland, and Australia had less organised, passive movements against whole-cell pertussis vaccines, in which health-care providers withheld vaccines because of safety concerns. Religious groups that oppose vaccination have been most prominent in passive movements against the vaccines. Parents concerned about vaccine safety did not feature prominently in passive movements. Characteristics of active and passive movements often overlap. Practitioners and followers of natural, alternative, and chiropractic medicine, and homoeopathy, have been prominent in both active and passive anti-vaccine movements.

We used country-specific incidences reported to WHO to compare pertussis-vaccination experiences. The numerator is number of cases, the denominator is per 100 000 of the total population. These data underestimate true incidence: pertussis is underdiagnosed, especially without classic whoop and paroxysmal cough; laboratory capabilities vary substantially; cultures are rarely undertaken for cases not admitted to hospital; reporting systems are usually passive; and surveillance efficiency varies from country to country. Although not quantitatively precise, surveillance data show overall trends and patterns.^{1,5}

Findings

Group 1: countries with sustained use of whole-cell pertussis vaccines

Hungary—Hungary's pertussis-control programme has been exemplary.⁶ Surveillance, including mandatory reporting, began in 1931. Immunisation with whole-cell pertussis vaccine has continued without interruption

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Gangarosa International Health Foundation and Rollins School of Public Health, Emory University, Atlanta, GA, USA

(Prof E J Gangarosa MD); **World Health Organization, Geneva, Switzerland** (Prof A M Galazka MD); **Centers for Disease Control and Prevention, Georgia (GA), USA** (C R Wolfe BA, R T Chen MD, L M Phillips MPH); and **PHLS Communicable Disease Surveillance Centre, London, UK** (E Miller FRCPATH)

Correspondence to: Prof E J Gangarosa, 5305 Greencastle Way, Stone Mountain, GA 30087-1427, USA

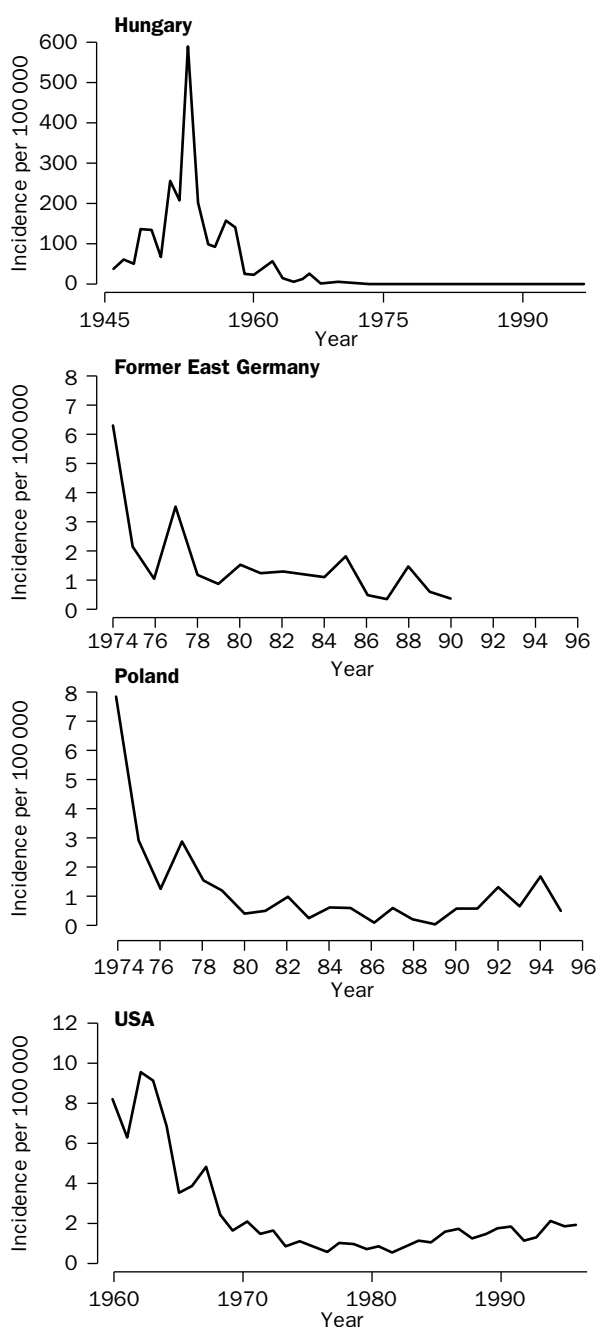


Figure 1: Incidence of pertussis in countries with sustained use of whole-cell vaccines

Note that scales vary.

since 1955. Vaccine coverage with three primary and two booster doses has been nearly 100%. Reported incidences fell from more than 100 per 100 000 in the prevaccine era to less than one per 100 000 after vaccination, where they have remained for almost 30 years (figure 1).

The former East Germany—Germany before unification provides striking contrast in pertussis experiences. The former West Germany adopted a non-compulsory vaccination policy, resulting in low coverage. The former East Germany, however, achieved control (figure 1) by requiring vaccination to consist of three primary doses and a single booster dose of DTP. Thus, in 1989, DTP coverage in the former East Germany was 95%. The

country had only one to two cases per 100 000 during 1980-90, whereas the former West Germany had an incidence well over 100 times higher.⁷

Poland—since 1960, pertussis has been controlled in Poland by means of a schedule of three primary doses and a single booster dose, resulting in more than 95% coverage. Reported incidence fell from 100-200 per 100 000 in the prevaccine era to about one per 100 000 after vaccination (figure 1).

USA—pertussis has been controlled in the USA, though there has been an upward trend in incidence since 1981 (figure 1). Concerns over safety of whole-cell pertussis vaccine peaked in the early 1980s after the television programme "Vaccine Roulette" and publication of the book *A Shot in the Dark*.⁸ These gave rise to a movement against whole-cell vaccines, instigated several lawsuits against vaccine manufacturers, substantially increased vaccine prices, and caused some companies to stop production of the vaccines.⁴ Nevertheless, several developments have favoured pertussis control. Vaccines manufactured in the USA have generally been highly efficacious.^{9,10} Paediatric and primary-care organisations have strongly advocated vaccination. School-entry immunisation requirements further contributed to 90-95% DTP coverage at primary-school entry. A strong infrastructure promotes vaccination, surveillance of adverse events, and, since 1988, compensation for post-vaccination injuries.^{4,11}

Group 2: countries with pertussis-control programmes affected by active or passive movements against whole-cell vaccines

This group initially had varying success in controlling pertussis—first with monovalent whole-cell vaccine, and subsequently with DTP. Reported incidence exceeded 100 per 100 000 in the late 1940s and early 1950s, when vaccination programmes began. Coverage accelerated during the 1960s, reaching roughly 80% during the 1970s. The consequent fall in reported incidence, ranging from ten-fold to 100-fold, set the stage for movements against whole-cell pertussis vaccines.

Sweden—pertussis vaccination began in the 1950s. A substantial drop in incidence followed. In 1967, an influential medical leader, Justus Ström claimed that pertussis had become a milder disease owing to economic, social, and medical progress; this claim led him to question the need for pertussis vaccines.² By 1975, Swedish paediatricians had lost confidence in the vaccine as the incidence of pertussis increased. Some cases occurred in immunised children, and some neurological events were blamed on the vaccine. DTP coverage decreased rapidly from 90% in 1974 to 12% in 1979.¹² In 1979, the Swedish medical society abandoned whole-cell pertussis vaccine and decided to wait for a new, safer, more effective vaccine—a strategy that was soon adopted as national policy. During 1980-83, annual incidence for children aged 0-4 years increased to 3370 per 100 000,¹² with rates of serious complications approaching global rates.¹ In subsequent years, Sweden reported more than 10 000 cases annually with an incidence exceeding 100 per 100 000, comparable to rates reported in some developing countries¹ (figure 2).

Japan—vaccination against pertussis began in 1947. By 1974, there were few cases and no deaths.¹³ During a

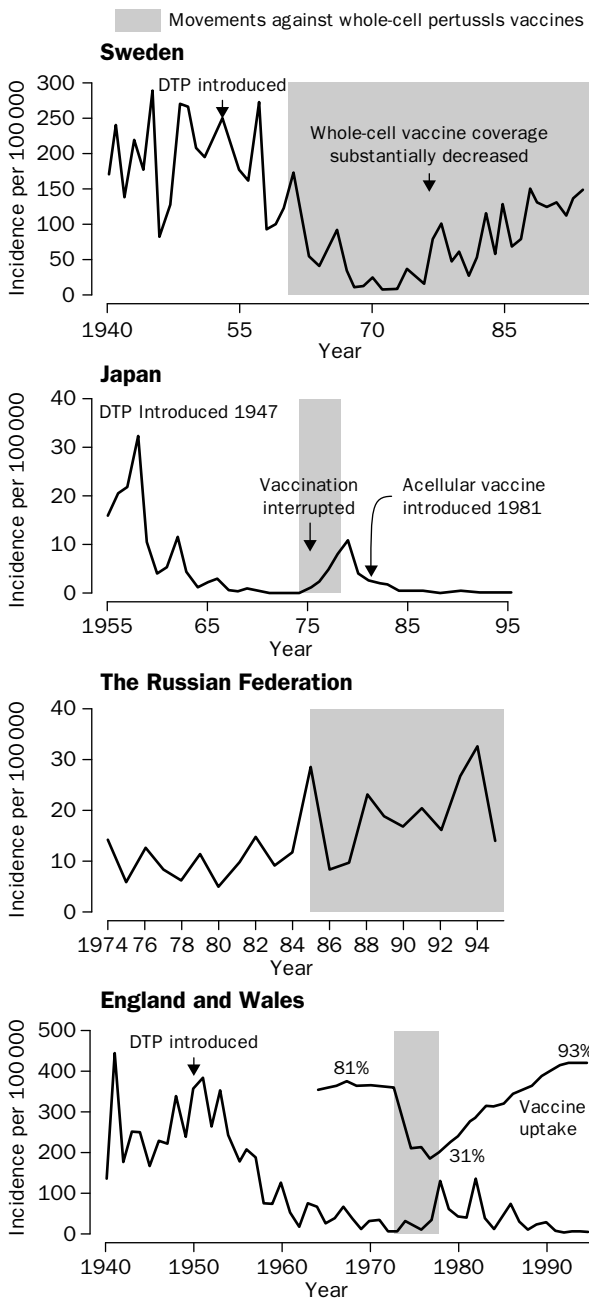


Figure 2: Incidence of pertussis in countries affected by active anti-vaccine movements
 Note that scales vary.

national debate about adverse events resulting from smallpox vaccine, news reports of neurological reactions after DTP vaccination gave rise to Japan's movement against whole-cell pertussis vaccines. Activists alarmed the public with "unbalanced arguments concerning vaccine risks" and claimed that "vaccination would no longer be needed" because "there was practically no more pertussis in the community".¹⁴ This national debate effectively created "a social problem".¹⁵ In response, the Okayama Prefectural Medical Association switched from DTP to diphtheria-tetanus vaccine (DT) only. After two infants died within 24 h of receiving DTP, the Ministry of Health and Welfare eliminated whole-cell pertussis vaccine altogether. They later allowed it only for children

older than 2 years. Pertussis coverage for infants fell from nearly 80% in 1974 to 10% in 1976.¹³ A pertussis epidemic occurred in 1979 with more than 13 000 cases and 41 deaths. Japan began replacing whole-cell with acellular pertussis vaccines in 1981, and a striking fall in pertussis incidence followed (figure 2).

UK—after a 1974 report, ascribing 36 neurological reactions to whole-cell pertussis vaccine,¹⁶ persistent television and press coverage interrupted a successful vaccination programme (figure 2). A prominent public-health academic, Dr Gordon Stewart, claimed that the protective effect of the vaccine was marginal and did not outweigh its danger.³ Others reached opposite conclusions based on the fall in pertussis incidence after introduction of the vaccine in the 1950s.¹⁷ Although health authorities resisted pressure to withdraw the vaccine, loss of confidence in it led to a sharp reduction in coverage. Pertussis epidemics followed (figure 2). Confidence was restored after publication of a national reassessment of vaccine efficacy that showed "outstanding value in preventing serious disease".¹⁸ Provision of financial incentives for general practitioners who achieved the target of vaccine coverage contributed to the recovery.¹⁹ Disease incidence declined dramatically, and has since been low (figure 2).

The Russian Federation—The Soviet Union assigned high priority to compulsory immunisation, thereby achieving control of vaccine-preventable diseases, including pertussis. The anti-government bias of Perestroika gave rise to an active anti-vaccine movement that targeted DTP. Inspired by the virologist Galina Chervonskaya, the mass media initiated an active campaign to discredit vaccination. Another prominent physician, A V Pichnohkov, asserted that the vaccine would cause leukaemia and was "stressful" for the child's system. Chervonskaya, Pichnohkov, and other paediatricians have propounded an excessive list of contraindications, specifying more than 50 diagnoses in which DTP vaccine should not be given. A series of "unbalanced statements" about the dangers and ineffectiveness of vaccines were featured in medical journals, on radio, on television, and in the popular press. Parents and physicians lost confidence in vaccines, and chose not to immunise children. DTP coverage fell by 30%, setting the stage for diphtheria and pertussis epidemics.²⁰ Along with perhaps the largest postwar diphtheria outbreak, The Russian Federation has reported one of the highest incidences of pertussis in the developed world (figure 2).

Ireland—Ireland's vaccination programme initially lowered pertussis incidence from 79 per 100 000 in 1955 to about ten per 100 000 in the mid-1970s. The trend reversed in the mid-1970s with opposition to whole-cell pertussis vaccine in the UK.²¹ Vaccine coverage fell from more than 60% in the early 1970s to 30% after 1976. Epidemics occurred in 1985 and 1989. In 1990, only 65% of infants had received three primary doses. Incidence remained higher than ten per 100 000 through 1993 (figure 3).

Italy—Binkin and colleagues²² studied pertussis in Italy (figure 3) using a national vaccination-coverage survey done in 1985, sales data from vaccine manufacturers, and Italy's infectious-diseases surveillance system. Fewer than 40% of children under 5 years were vaccinated, and

about 25% had experienced clinical pertussis by the age of 5 years. Among children younger than 1 year, one in 14 was admitted to hospital for pertussis, and one in 850 of these admissions died. The reported annual incidence between 1980 and 1989 was 22 times higher than in the USA. A seroepidemiological study of pertussis by Stroffolini and colleagues confirmed "a great exposure of children" and "extremely low" vaccine coverage in Palermo.²³ In a 1991 telephone survey,²² Binkin found that paediatricians' attitudes about whole-cell pertussis vaccine varied widely. In some regions, only 20% of paediatricians recommended DTP, compared with 100% in other regions. By contrast, another survey showed that mothers accepted the vaccine—87% perceived pertussis as a dangerous disease, 69% were aware that the vaccine was available, 90% believed that the vaccine was protective, and 87% said they would accept their paediatrician's advice on vaccination. Binkin reported that the factors that gave rise to Italy's pertussis dilemma were the attitudes, knowledge, and practices of physician providers.²² In 1995, only 50% of children in Italy had received three primary doses and a single booster as part of their routine schedule.

Australia—Australia controlled pertussis during the 1970s, with an incidence rate as low as one per 100 000 (figure 3). However, confidence in the vaccine waned when news was received from the UK about alleged neurological reactions associated with the vaccine.²⁴ In a postal survey from the early 1990s, McIntyre and Nolan found that up to 58% of randomly selected vaccine providers would give DT when DTP was indicated.²⁵ In 1993, Lester and Nolan warned that "geographically clustered populations of children who have inadequate pertussis protection could promote epidemic outbreaks".²⁵ A large outbreak with more than 5000 cases occurred in 1994 (figure 3).

Dr Viera Scheibner, Australia's prominent opponent of whole-cell pertussis vaccines, claims that these vaccines are ineffective and "constitute an assault on the immune system". Her 1996 book has been marketed as "the most well documented evidence against vaccines to be found anywhere in the world".²⁶

The former West Germany—the contrast between the former West Germany and East Germany provides perhaps the most striking example of the national danger of antivaccine movements. Finger and colleagues analysed vaccination histories and incidence of pertussis among West German children at school entrance.⁷ Coverage with whole-cell pertussis vaccine was fairly constant at 11.0% and 11.2% for children born in 1976 or 1983, respectively. Pertussis was reported in 35% (1976) and 37% (1983) of these children. The authors estimated that incidence in West Germany was 180 per 100 000 during this period. They attributed the high incidence to health-care providers who believed the disease to be a "normal" childhood illness.

Contrasting experiences of neighbouring countries with high and low DTP protection, 1985-95

The efficacy of whole-cell vaccine is also evident in the comparison of experiences in adjacent countries with different DTP protection—measured by the percentage of infants covered and the number of primary and booster doses in immunisation schedules. Without complete information, we assume a generally uniform whole-cell

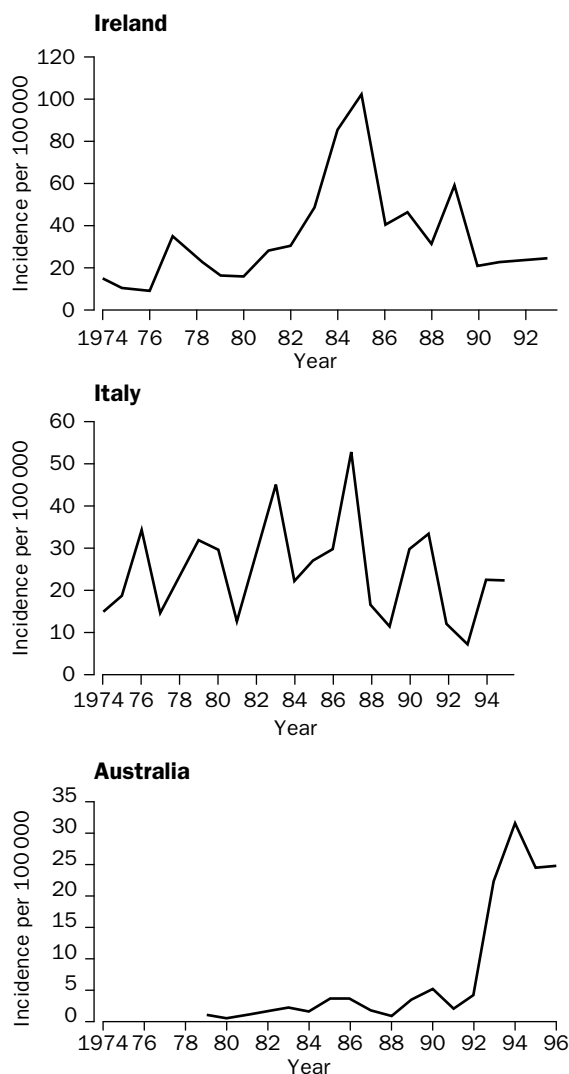


Figure 3: Incidence of pertussis in countries affected by passive anti-vaccine movements

Note that scales vary.

vaccine efficacy with the exception of reported anomalies²⁷—eg, low efficacy in Canada²⁸ and in a 1996 field trial in Europe.²⁹ Higher vaccine coverage in Norway, Portugal, Hungary, and the USA corresponded to a pertussis incidence ten to 100 times smaller than in each country's respective lower-protected neighbour—ie, Sweden, Spain, Greece, and Canada (figure 4). The most striking comparison, between the former West Germany and East Germany, cannot be quantified because pertussis was not reportable in West Germany.

Discussion

Our findings provide strong evidence of a causal relation between movements against whole-cell pertussis vaccine and pertussis epidemics, based on Hill's criteria:³⁰ strength of association (eg, incidence ratios exceeding 100 to 1, Sweden *vs* Norway; 150 to 20 comparing peak incidence for Sweden in 1990 during antivaccine era *vs* Sweden in 1972 with highest whole-cell vaccine coverage); consistency of findings under different surveillance systems, time periods, and populations; specificity of infection affecting primarily unvaccinated or undervaccinated individuals; temporal relation

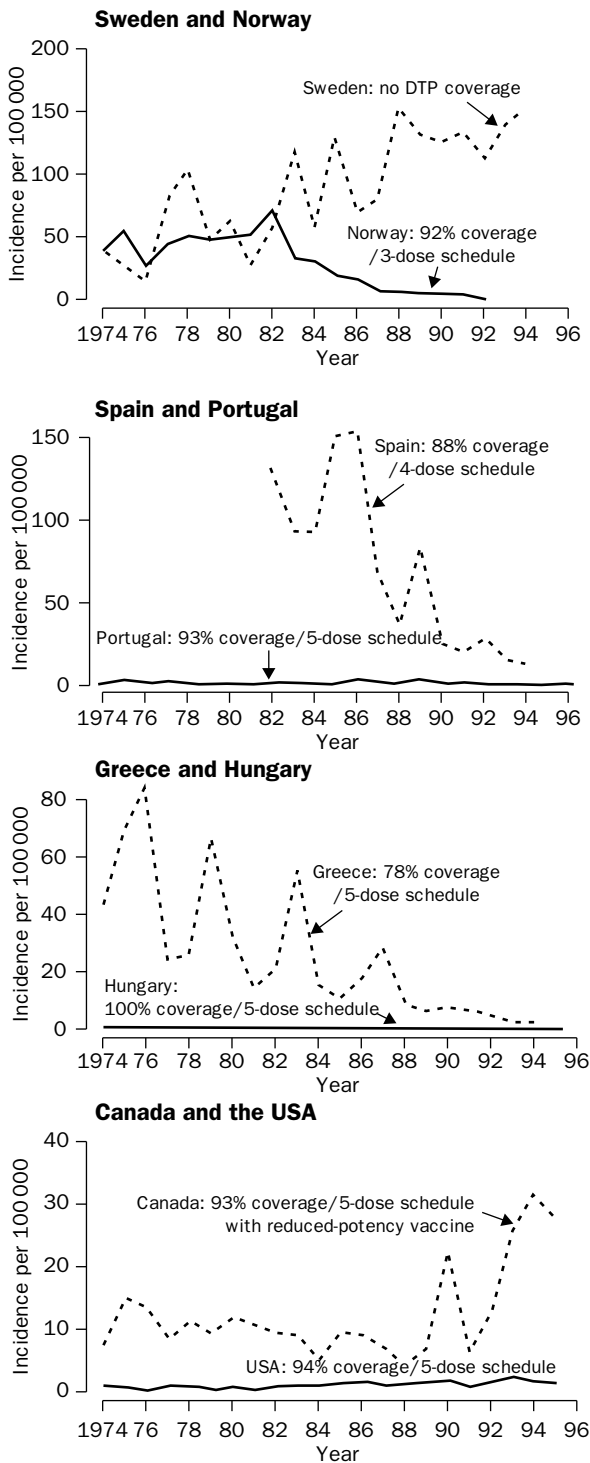


Figure 4: **Incidence of pertussis in neighbouring countries with high vs low DTP vaccine coverage**
 Note that scales vary. Information on coverage and dose schedules based on 1993-95 data.

(epidemics follow cessation of vaccination and recede with resumed vaccine coverage); biological gradient (dose-response effect seen—eg, in incidence *vs* vaccine coverage in the UK, 1963-95); plausibility that vaccination is protective, that herd immunity suppresses transmission, and that successful disease-control encourages complacency⁴; coherence of evidence—ie, no conflict with the natural history of pertussis; and experimental evidence plus analogy—eg, smallpox

eradication, in which high vaccine coverage prevents disease through mass vaccination and surveillance-containment strategies.

This study shows overall trends, though not a precise comparison of reported incidence, since practices of pertussis diagnosis and surveillance differ according to country.¹ A policy against whole-cell pertussis vaccination had a qualitatively similar adverse impact in Sweden, Japan, the UK, The Russian Federation, Ireland, Italy, the former West Germany, and Australia. Conversely, sustained vaccination has controlled pertussis in Hungary, Poland, the former East Germany, and the USA. A dose-response relation is evident: extremes of vaccination coverage (eg, Hungary *vs* Sweden) spanned reported incidence of ten to 100 times, whereas smaller differences in coverage or efficacy (eg, USA *vs* Canada) showed intermediate effects.

Anti-vaccine advocates do not mention, minimise, or deny the consequences of compromised immunisation programmes.^{8,26} This article documents those consequences. Cases among children deprived of vaccine may have exceeded hundreds of thousands, and disease-related clinical complications (eg, pneumonia, encephalopathy, and seizures) may have numbered tens of thousands. Anti-vaccine movements have had some beneficial effects. Their call for safer vaccines underscored the need for acellular vaccines against pertussis, and their efforts have encouraged surveillance of adverse events and development of vaccine-injury compensation programmes.

Our findings also corroborate Fine and Clarkson's analysis³¹ that once high vaccine uptake and herd immunity are attained, perceived vaccine risks tend to deter individuals from being vaccinated. The result is a lowering of vaccine uptake, contrary to the community's common interest in maintaining high numbers of immunised individuals. What follows is a "tragedy of the commons"—a loss of confidence in vaccine and a resurgence of disease.³² These tragedies were abetted by anti-vaccine advocates through unbalanced news media accounts of perceived vaccine risks.³³ Some of these advocates have been prominent figures in science and medicine.^{2,3,26,34} They have argued that vaccines compromise the immune system, inappropriately questioned vaccine efficacy when sporadic cases occurred in immunised children,³⁵ advocated a long list of unwarranted contraindications to vaccination, warned that adverse events to the vaccine might be more common than reported, and attributed "disappearance" of pertussis to social and medical developments rather than vaccination. These messages undermined confidence in whole-cell pertussis vaccines, and, though discredited in medical literature, are still commonly cited in anti-vaccine literature.^{8,26}

Severe side-effects of whole-cell pertussis vaccines are so rare that they defy measurement. The American Academy of Pediatrics, the USA's National Vaccine Advisory Committee, and the Advisory Committee on Immunization Practices, concur that whole-cell pertussis vaccine is not a proven cause of brain damage, sudden infant death syndrome (SIDS), infantile spasms, or Reye's syndrome.^{36,37} Anaphylactic reactions to DTP components are exceedingly rare. In the USA, lawsuits have favoured plaintiffs alleging complications related to whole-cell pertussis vaccination, but the High Court of the UK ruled that a causal link had not been proven.³⁸

Mild local and systemic reactions (fever, fussiness, drowsiness, and brief loss of appetite) are fairly common with the vaccine, whereas moderate reactions (long periods of crying, sometimes at an unusually high pitch, limpness, and pallor) are rare.

Since acellular vaccines cause fewer side-effects,^{9,27,29} some developed countries (eg, the USA) plan to switch to such vaccines after using up existing supplies of whole-cell pertussis vaccines. However, use of whole-cell pertussis vaccines in the UK will probably continue pending studies of acellular pertussis vaccine's relative efficacy, reactivity, and compatibility with *Haemophilus influenzae* type-B vaccine.³⁹ The choice between whole-cell and acellular pertussis vaccines involves trade-offs between safety, efficacy, practicality, and cost. In addition to fewer mild or moderate reactions, acellular vaccine could interrupt disease transmission by means of its potential use in adolescents and adults. However, the best acellular vaccines may not provide protection equal to that of the best whole-cell vaccines.²⁷ Replacement of whole-cell pertussis vaccines with acellular vaccines might conceivably lead to less effective control at substantially higher costs. Despite the advantages of acellular vaccines, we believe that lower costs and better protection are compelling reasons for use of whole-cell pertussis vaccines to continue in many countries, particularly those with limited resources.⁴⁰ Scientists and physicians who choose acellular vaccine for their country have a special responsibility to strengthen their surveillance to monitor disease impact, costs, and rare adverse events—information that will guide others in the future.

Whereas our study focused on morbidity following anti-vaccine movements against whole-cell vaccines, other reports indicate that pertussis mortality also increased. Excess sudden postperinatal deaths were inversely related to vaccination coverage during pertussis outbreaks in several observational studies and in two ecological studies—one in the UK⁴¹ and the other in Scandinavia.⁴²

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