



Measles Rubella  
Immunisation  
Campaign in  
England.

*'One Year On'*

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## Measles Rubella Immunisation Campaign in England

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### 1. Summary:

This report provides background to the reasons why the 1994 measles rubella immunisation campaign was necessary, reviews the implementation and provides information on the impact of the campaign in which 6.585 million children were immunised in England. Data for suspected adverse reactions to the measles rubella vaccine are presented for the whole of the UK.

A large measles epidemic had been predicted by independent researchers and action was planned in accordance with the recommendations of the independent Joint Committee on Vaccination and Immunisation; the epidemic has been averted. Laboratory confirmed cases of measles are now exceptionally rare. Early indications suggest a dramatic decline in laboratory confirmed rubella cases in children whose ages were targeted in the campaign.

Most reported adverse reactions were mild and self-limiting: only one child in every 6,700 immunised in the UK was reported to have any adverse reaction whatsoever. Immediate serious adverse reactions were either of an allergic type such as anaphylaxis or were described as convulsions; all these children recovered fully. From the descriptions provided, most of the reported immediate convulsions appeared to be associated with syncope. Later onset neurological reactions were reported at rates no higher than those expected from the background frequency of the illness.

### 2. Epidemiology:

In 1988, routine immunisation against measles was augmented by the introduction of measles, mumps and rubella (MMR) vaccine. Coverage by the second birthday rose progressively from 76% in 1988 to 92-93% by 1994. At the time of the change-over, MMR vaccine was recommended for those children who were having their pre-school DT and polio boosters, even if they had already had one dose of measles vaccine. As a consequence, many children born between 1983 and 1987 had two doses of measles

vaccine. This catch-up programme was designed to prevent children entering school still susceptible to rubella and mumps. Children who since October 1988 received a first dose of MMR at 13 months were not scheduled for a routine second dose. After 5 years of excellent control of measles, it became clear in 1994 that measles notifications were rising and the pattern of measles was changing. More cases were outbreak associated and were occurring increasingly in older children<sup>1</sup>.

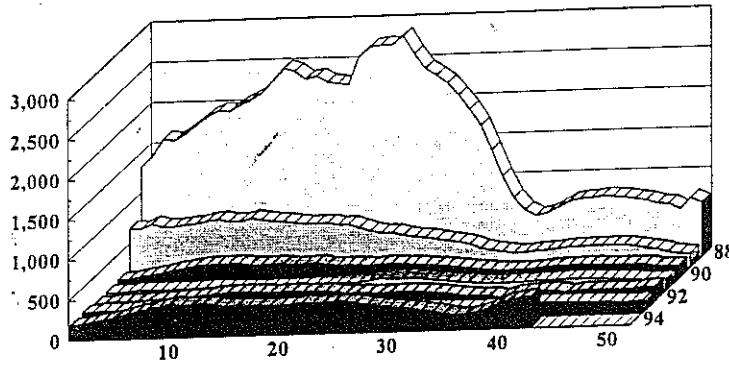


Figure 1. Measles notifications in England & Wales, 1988 to 1994 (OPCS data).

Laboratory confirmation of measles showed that the distribution of cases was indeed shifting to older groups.

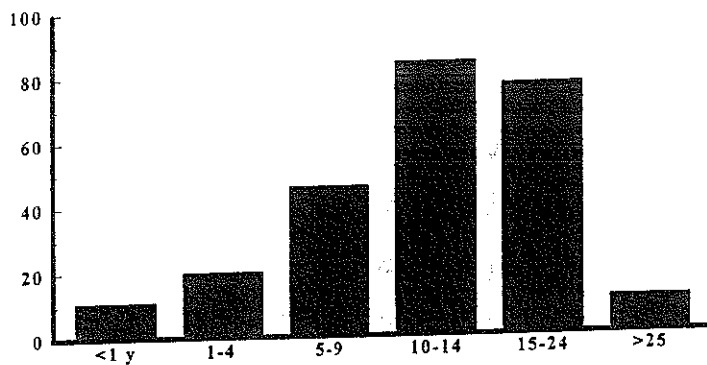


Figure 2. Proportion of notified measles cases, confirmed by laboratory testing by age band, 1992-93 (PHLS data).

The above graph provides an estimate of probability that notified cases were correctly diagnosed. When this probability was applied to the notified cases according to their age, it could be seen (from Figure 3) that the group at highest risk of measles was not children under 9 years, from whom most notifications were coming, but older children aged 10-14 years.

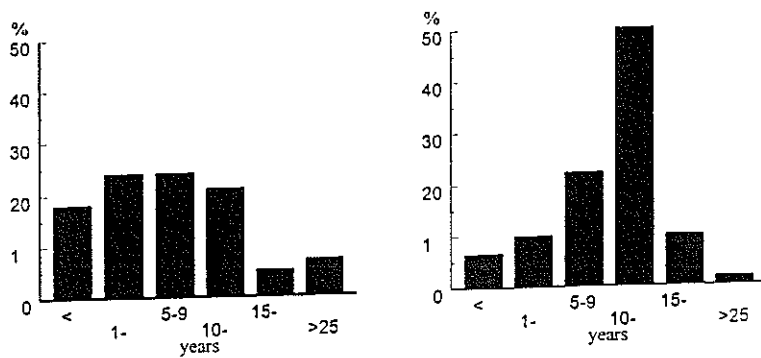


Figure 3. Left: Age distribution of notified cases of measles E & W 1993-1994. Right: Age distribution corrected for probability of correct diagnosis for each age band (as above at Fig 2).

In late 1993, based on age specific notification rates, age specific infection rates from laboratory reporting, age specific sero-epidemiology, coverage data and vaccine efficacy data, two independent groups using different mathematical models presented predictions<sup>2,3</sup> that a large epidemic was likely by 1996/7. The Joint Committee on Vaccination and Immunisation (JCVI) considered this and other evidence, including the experience of other countries, and recommended that a nation-wide school-based immunisation campaign should be carried out. Figure 4 shows the most recent epidemics from three European countries where high levels of immunisation coverage had been achieved but nevertheless after 5 to 7 years, further measles epidemics occurred<sup>4</sup>. The reason in each case was a growing accumulation of susceptible individuals who had either not been immunised or who were 'vaccine failures'.

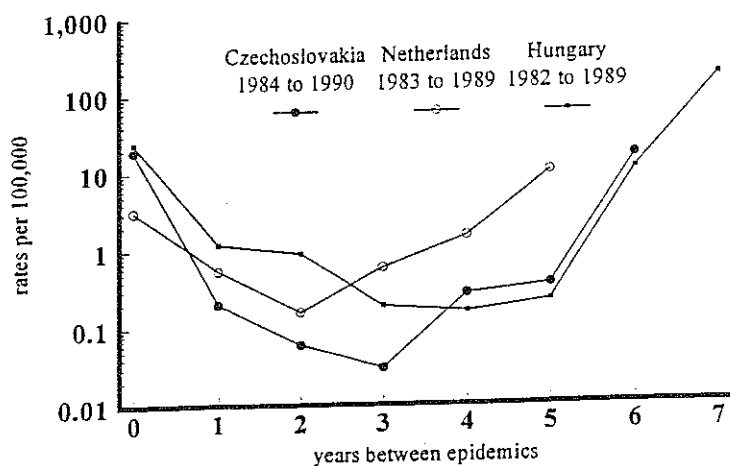


Figure 4. Intervals between most recent measles epidemics in European countries with high immunisation coverage (WHO data).

In 1988, the last epidemic year in England and Wales, there were 86,000 notifications. The predictions submitted to the JCVI in 1993 suggested an epidemic of the order of 150,000 cases. Because more cases would occur in older children than previously and measles case fatality rates increase with advancing age, as many as 50 deaths were predicted, an estimate based on case fatality rates from the 1980s. In the measles epidemic of 1988, 15 children died of measles but that epidemic predominantly affected younger children than would be affected in a forthcoming epidemic. In the US epidemic of 1989-91, 130 children died of measles, showing that despite modern facilities for intensive care, measles still has the potential for significant morbidity and mortality. At least 10% of measles cases suffer complications such as pneumonia, otitis media or encephalitis.

In early 1994, it became apparent that there was already an epidemic in Scotland: there were 138 admissions of mostly teenagers to one hospital alone (Ruchill Hospital, Glasgow). Since 1970, there has only been one year (1973) when measles epidemics occurred simultaneously in Scotland and England and Wales. The JCVI reviewed this evidence and recommended that a campaign should be implemented before an epidemic could occur in England, Wales, Northern Ireland and the parts of Scotland not yet affected. To achieve this, implementation would be necessary in 1994, a year earlier than had first been considered to deal with the epidemic originally expected in 1996-97. JCVI also recommended that the vaccine of choice was MR vaccine. The inclusion of rubella vaccine was recommended on the grounds of the already identified considerable window of susceptibility in teenagers, especially males, amongst whom there had been a large number of rubella infections in 1993. The target population, all school children aged 5 to 16 years, was chosen on the basis of age specific sero-epidemiology that identified that this was the group at greatest risk.

### **3. Strategic Alternatives:**

Mathematical modelling had given a clear indication that because of low coverage in the past, reduced circulation of measles recently, and the recognised failure rate of measles vaccine in routine use, this country faced the largest measles epidemic since the early 1980s. Similar experiences had been observed in Hungary, Czechoslovakia

and the Netherlands (Figure 4) where there had been measles epidemics despite high coverage, with the age of cases shifted to older groups with higher morbidity and mortality.

A range of strategic alternatives was considered, taking account of the likelihood of achieving the necessary coverage over the time available, and recognising that the use of a short intensive campaign was the most effective way to interrupt measles virus transmission. Target groups for consideration included children aged 1 - 5 years, primary school aged children (5 - 11 years), and all school aged children. Options included static regimens - i.e. second doses according to the passing of a particular age point by individual children (5 years or 11 years), or campaigns. Also considered were routes of service delivery for each option, - i.e. primary care services or school health services. Each option and each strategy was costed and tested against the mathematical models<sup>2,3</sup>.

It was clear to JCVI that the most cost effective use of resources was the implementation of an intensive school health service delivered campaign, targeted at all children aged 5 to 16 years, irrespective of previous history of measles or immunisation. A cost benefit analysis that compared the cost of a campaign with the cost of a measles epidemic was strongly in favour of prevention. A campaign was costed at approximately £20 million ( vaccine costs, publicity costs and notional costs for the staff time in providing the service) against the estimated approximate £60 million costs of an epidemic (health care costs and value of lives lost), along with 0.3 million working days lost to the economy from parents' time off work caring for their ill children. Studies had shown that when children under 5 years have measles, parental time off work is minimal: if the child is over 5, one parent frequently has to take considerable amounts of time off work.

Before the national campaign was implemented, a pilot campaign was undertaken in one district and high coverage was achieved. The experiences from that district were used in the development of the information materials and were available to the advisory group planning the campaign implementation. The staff/service cost per immunised child was £0.83.

#### **4. Implementation:**

In the summer of 1994, an implementation group was set up with representation from NHS management, pharmacists, medical and nursing professions, Public Health Laboratory Service, National Institute for Biological Standards and Control, Health Education Authority, Department for Education, Immunisation Co-ordinators and the Department of Health. In July 1994, the NHS Executive Board agreed that the campaign should be implemented as soon as was practicable through the NHS and agreed this could be achieved in November 1994. Costs of vaccine, distribution and publicity were borne centrally.

Post codes of 27,000 schools were provided by the Department for Education. These were re-aggregated according to District Health Authorities and issued to District Immunisation ~~Co-ordinators~~. Co-ordinators obtained school rolls for each school and these formed the basis for identification of the target population, and were used for allocation of vaccine and consumables (syringes, needles, sharps' boxes).

Supplies of vaccine were issued in advance of the campaign, with every single district being appropriately resourced for vaccine and consumables in advance of the start of the campaign. There were no supply problems.

Information was sent to doctors in July, September and October. There was high profile national advertising, in October, of the need for the campaign and parents were reminded to complete the consent forms that had been distributed through the schools. Each health district or NHS Trust brought together teams of nurses, medical and clerical staff to plan the immunisation of all the appropriate children through a school based programme. These teams, often nurse-led, involved school nurses, community child health nurses and health visitors, who worked intensively. Most Health Authorities ran their campaigns during November with mop-up activities in December. In some cases, the campaign ran through December with mopping-up being completed by early February.

#### **5. Results:**

The target population for England was 7.17 million children, whose ages ranged from 5 to 16 years. Districts and NHS Trusts submitted their final returns for the November phase of the campaign and the mop-up activities. 92% of the target children have

been immunised in England. The following table shows the coverages achieved by District Health Authority or NHS Trust.

Coverage(%)	DHAs/Trusts (%)
>95	37 (21.5)
90 - 95	96 (55.8)
85 - 90	31 (18.0)
80 - 85	6 (3.5)
<80	2 (1.2)
<b>Mean coverage: 92%</b>	<b>Total: 172</b>

Table 1. Immunisation coverages achieved by DHAs or NHS Trusts.

### 6. Outcome:

In the autumn of 1994, notifications were rising much as they had before the 1988 epidemic. Within approximately three weeks of the start of the campaign, notifications levelled off, and subsequently have declined.

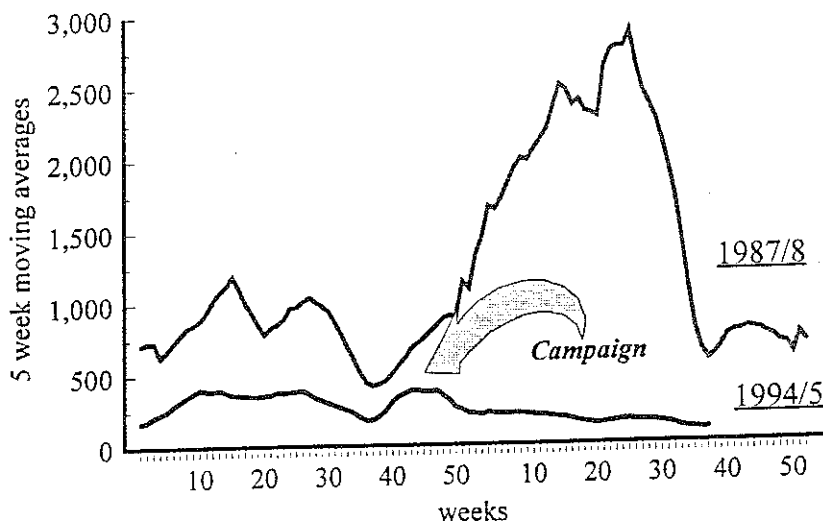


Figure 5. Measles notifications E & W 1987/8 and 1994/5 (OPCS reports).

Previous experience has demonstrated that measles notification data shows useful trends but individual notifications are highly unreliable, especially in younger



children<sup>5</sup>, as shown in Figure 2 earlier; here the specificity of notification in the under 5s is considerably less than 20%. After pilot studies in 1993/4, from the beginning of November 1994, the Public Health Laboratory Service has been able to provide salivary antibody diagnosis<sup>6</sup> to confirm measles in suspected cases. Before the campaign, almost 40% of investigated cases were positive. There were more than 100 positive reports in November and December 1994. During 1995, there have been between 200 and recently 100 notifications each week. Over half of these notified cases are tested for confirmation of the diagnosis. The most recently available results show that less than 1% of the tested cases are measles; before the campaign, when there were more notified cases, 38% were measles. However, more than 2000 samples have been tested but only 49 have been confirmed with serological or saliva testing; these include 8 importations. One indigenous case was nosocomially linked with an imported case. Only two cases have occurred in children whose ages were covered by the campaign; neither child had been immunised in the campaign. All other cases were in children under the age of routine immunisation, those under 5 years who had received one dose of MMR vaccine previously, or who were over 16 years. Reports of laboratory confirmed rubella cases have declined dramatically in 1995 in children whose ages were targeted in the campaign (PHLS data).

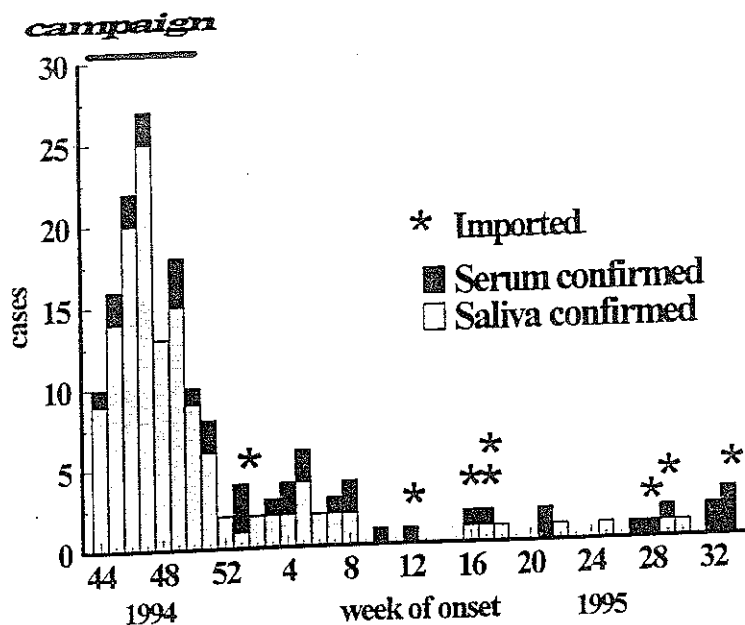


Figure 6. Cases of measles (E & W) confirmed by serum and salivary antibody testing (PHLS data), weeks 44/1994 - 33/1995.

## 7. Adverse reactions:

### 7.1 Planning:

Before the start of the campaign, the Post-Licensing Division of the Medicines Control Agency (MCA) agreed that all suspected adverse reactions to MR vaccine would be handled with high priority. Doctors were reminded by the CMO of the importance of reporting all suspected adverse reactions before the start of the campaign. Yellow Card reports were classified and entered into the MCA database within 24 hours of receipt and reviewed by a medical assessor within 36 hours. The MCA database was electronically linked with the measles team database and all reports relating to MR vaccine were transferred on a daily basis. Requests for follow-up information were sent to doctors reporting serious ~~suspected~~ adverse reactions if inadequate information was provided on the Yellow Card.

### 7.2 Adverse reaction results:

*8 million children have been immunised in the UK campaign and the following figures relate to the whole of the UK. These data will change if any further reports are submitted.* By the end of October 1995, 2,735 adverse reactions have been reported affecting 1,202 children (more than one reaction was reported in some children), a reporting rate of 1 affected child for approximately 6,700 immunisations. Most of the reports were of minor conditions, many of which were unlikely to be linked to immunisation, or of no likely consequence. The report of a reaction does not necessarily imply that it was caused by the vaccine.

There were **no** deaths. 530 reports of serious reactions were received. These serious adverse reactions fell into two groups - those occurring immediately or soon after the immunisation and those occurring later.

### 7.3 Allergic type reactions:

There were 123 reports of immediate allergic type reactions, such as anaphylaxis or bronchospasm. 52% of children with anaphylaxis received adrenaline. Some were admitted briefly to hospital but no serious or long lasting effects are known to have

resulted. The overall reporting rate for anaphylactic or acute allergic reactions was 1 in 65,000 injections; the rate for anaphylaxis was 1 in 100,000 injections.

#### 7.4 Neurological reactions

91 neurological reactions were categorised as serious, although many fell outside the appropriate time periods which would be compatible with the replication rates of the viral components of the vaccine, making it less likely that these were related to the viral effects of the immunisation. For example, the onset of 37 out of 61 convulsions was within 24 hours of the injection. Furthermore, most of the 29 reactions reported as convulsions occurring within 1 hour of immunisation, followed symptoms of syncope (there were 8 convulsions occurring between 1 and 24 hours after immunisation).

The reporting rate of convulsions ~~known to have~~ occurred 4-28 days after immunisation was 1 in 600,000 injections; this rate will include both suspected vaccine related reactions and causally unrelated events.

Late onset reactions may be linked to replication of the viral components of the vaccine and are usually expected at approximately 4-10 and 10-28 days post immunisation for the measles and rubella virus components respectively. 52 convulsions were reported to have occurred within 4 weeks of immunisation. Using computerised hospital discharge diagnosis data from one health region, it has been estimated that over any 4 week period, in the absence of an immunisation campaign, at least 300 admissions for convulsions would be expected among 8 million children aged 5 to 16 years. There were three cases of Guillain Barre Syndrome (GBS) reported; one of which was an atypical sensory form. Available epidemiological data from the UK suggest that 1-7 cases of GBS would be expected over a 4 week period for this age group, in the absence of immunisation.

One case of Sub-acute Sclerosing Panencephalitis (SSPE) was reported but the clinical details suggest that the likely cause was natural measles infection, and not the measles virus component of the vaccine. Since the introduction of measles immunisation, SSPE rates have declined dramatically.

There were 11 reports of encephalitis or encephalopathy and two of meningitis. The onset after immunisation varied from three days to 7 weeks. One boy was left with a slight hemiparesis; all the other patients recovered completely. The doctor who

reported the case of hemiparesis noted that the titre of measles antibodies did not change, implying pre-existing immunity; this makes it unlikely that the encephalitis was causally linked to the measles virus component of the vaccine.

#### 7.5 Arthropathies and other reactions:

Rubella infection or immunisation can be associated with arthropathy, especially in adults. This can be expected to begin approximately 14-21 days after immunisation. Only one report of arthritis was received with onset within this period. In all, there were 6 reports of arthritis. Analysis of the time of onset of the 47 reported cases of arthropathy (arthritis and arthralgia) after MR immunisation shows that the onset for most cases was outside the expected time, (see Figure 7) suggesting that many cases were ~~unlikely to be~~ causally associated with the rubella virus component of the vaccine.

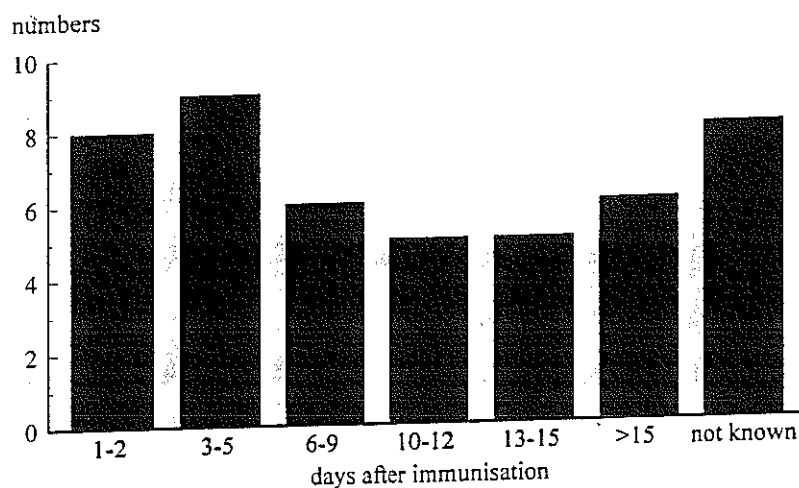


Figure 7. Time of onset of reported cases of arthropathy.

Other serious suspected reactions that have been reported include erythema multiforme (9), herpes zoster (7), Henoch Schonlein purpura (5) and thrombocytopaenia (2).

#### 8. Evaluation:

The impact of the campaign has been evaluated from coverage and surveillance data. The coverage data has been analysed by locality and has been disaggregated according to the age bands of the immunised children. Further correlations are being

made between coverage in the campaign and previous MMR coverage by locality, as well as by socio-demographic indices that may influence vaccine acceptance. Reasons for refusal to give consent were also recorded for all children; so far, the commonest reason to withhold consent was that the child had already had measles and MMR vaccines.

In addition to the surveillance initiatives described above, molecular techniques are also available through the PHLS to identify strains of measles viruses to attempt to identify persistence of 'old' circulating strains or emergence of new strains, especially importations.

The Health Education Authority has undertaken market research of the awareness and information gained from the advertising: reports suggest very high awareness of the campaign publicity. Before the campaign, measles had been rated by the public as one of the least serious of the childhood infectious diseases. Market research amongst parents and older children showed that the most convincing approach would be to highlight the potential seriousness of measles. Post campaign evaluation suggests that the parental awareness of the seriousness of measles had shifted considerably. Only 3% of the parents interviewed said that they had withheld consent; the commonest reason was that their child had already had measles and MMR vaccines. This figure matches the district returns on refusal to consent rates.

In association with the Royal College of Nursing, a distance learning module was prepared on the MR campaign, transmitted by BBC Select and made available on video to all District Co-ordinators. This and other information provided to nurses, and their impressions of the organisation of the campaign have been evaluated by the Queen's Nursing Institute. The overall conclusions of the report recognise the success of the involvement of nurses and the enhancement of their roles in community child health services. The arrangements for vaccine and consumables have also been audited and found to be satisfactory.

#### **9. Campaign conclusion:**

Despite high coverage with a single dose of measles vaccine, the high probability of a measles epidemic was recognised in advance. The anticipation was supported by extensive surveillance of age specific notification rates, age specific infection rates

from laboratory reporting, age specific sero-epidemiology, coverage data and vaccine efficacy data, as well as experience of other countries.

Despite the short period of time available between the decision to run the campaign and its implementation, an enormous amount of preparation was necessary against very tight deadlines. In the face of an impending epidemic, an intensive school based campaign was the only way of getting large numbers of children immunised sufficiently quickly. The campaign approach also offered the prospect of interruption of virus transmission.

There were some unexpected difficulties, such as the concern of some sections of the community about the origins of the cell line used to grow rubella vaccine viruses, but notwithstanding such problems, very high coverage was achieved in the allotted period of time.

On the basis of spontaneous reporting, only one in every 6,700 children immunised with MR vaccine in the UK were reported to have experienced any adverse reaction whatsoever. Spontaneous reporting systems are vulnerable to under-reporting, but favour reporting of acute and serious reactions. The reports of suspected adverse reactions do not necessarily imply a causal relationship. In some cases, the association of these reactions and MR vaccine will have been coincidental. Even allowing for previous immunity against measles in many children, the balance of risks and benefits associated with MR vaccine is extremely favourable compared with the incidence of serious sequelae after wild measles virus infection.

The impact of the campaign is already apparent. There has been no measles epidemic in 1995 and there are clear signs that measles transmission has been interrupted in much of the country. Measles notifications are at historic low levels and confirmed cases, especially indigenously acquired ones, are remarkably few. The UK now has measles surveillance of world leading class. The next steps will be to consolidate the gains achieved through the campaign.

A very large number of health professionals played their part. GPs clearly dealt with many enquiries from parents: a gratifying sign of the trust that parents have in their GPs as sources of such advice. The PHLS, Immunisation Co-ordinators, school health services, especially nurses, schools and pharmacists made an invaluable contribution to a most successful campaign.

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