BREVIA

Measles Outbreaks in a Population with Declining Vaccine Uptake

V. A. A. Jansen,[1]* N. Stollenwerk,[1] H. J. Jensen,[2] M. E. Ramsay,[3] W. J. Edmunds,[3] C. J. Rhodes[1]

Measles is a highly infectious and potentially dangerous disease. Before mass vaccination was started in the United Kingdom, measles caused an average of 100 deaths per year (*1*). Since the introduction of vaccination, vaccine uptake has risen from around 50% in 1968 to 76% in 1988. After the introduction of the combined measles, mumps, and rubella (MMR) vaccine in 1988, vaccine uptake rose rapidly to a national average of 91% by 1998 (*2*), at which time the alleged side effects of the MMR vaccine began to be widely discussed. Although all of the claims of serious side effects have been refuted, there has been a decline in the uptake of the MMR vaccine in the United Kingdom leading to a growing pool of susceptible individuals (*2*). The drop in vaccine uptake has coincided with a number of large measles outbreaks (Fig. 1A).

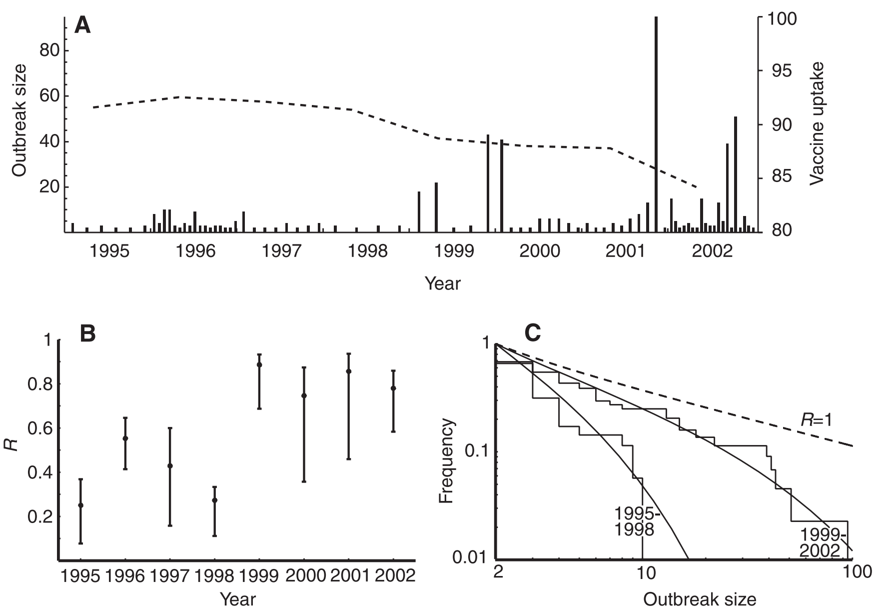

Fig. 1. (**A**) Recent measles outbreaks in England and Wales. Cases were assigned to the same outbreaks if they had had epidemiological contact. Isolated cases and outbreaks caused by deliberately bringing susceptible and infected children together were excluded. Dashed line, the vaccine uptake measured as the percentage of children that had completed a primary course with the MMR vaccine at their second birthday [from (*2*)]. (**B**) The reproductive number per year; bars indicate 90% bootstrap confidence intervals. (**C**) The frequency distribution of outbreaks of a certain size or larger (stepped lines) for the years 1995–1998 and 1999–2002 and the theoretically predicted distributions (curved lines). Dashed line, distribution for $R = 1$.

Although the population biology of measles depends on many factors, such as seasonality of transmission and the social, spatial, and age structure of the population, the fate of an epidemic can be predicted by a single parameter: the reproductive number R, defined as the mean number of secondary infections per infection (*3, 4*). The reproductive number is approximately proportional to the fraction of the population that is not immunized (*5*). If the reproductive number is smaller than one, the disease will not persist but will manifest itself in outbreaks of varying size triggered by importations of the disease. If the reproductive number approaches one, large outbreaks become increasingly likely, and, if it exceeds one, the disease can become endemic. If the reproductive number equals one, the situation is said to be at criticality. A decline in vaccine uptake will lead to increasingly large outbreaks of measles and, finally, the reappearance of measles as an endemic disease (fig. S1).

We used data on recent outbreaks in England and Wales to estimate the reproductive number. Isolated cases were excluded because they tend to be misrepresented in the data. The reproductive number depends on the average size of outbreaks m, as $R = 1 - 2/m$ (*5*). The estimated reproductive number for the years 1995–1998 and 1999–2002 were $R = 0.47$ and $R = 0.82$, respectively [with 90% bootstrap confidence intervals of (0.36, 0.55) and (0.71, 0.87), respectively]. This is a significant increase (bootstrap method, $P < 0.00011$). Estimates of the reproductive number per year show that the increase in the reproductive number occurred almost immediately after the decrease in the MMR vaccine uptake in 1998 (Fig. 1B), although the residual effects of previous changes to the vaccination program might have contributed to this effect (*1*). An indication that the situation is close to criticality, i.e., reproductive number equal to one, is provided by the distribution of outbreak sizes. At criticality, the probability of an outbreak of size x or larger is approximately proportional to $x^{-1/2}$ (*5*). By comparing the distribution of outbreak sizes before 1999 with the distribution for the years 1999–2002, it can be seen that the shape of the distribution is close to the distribution at criticality (Fig. 1C). Similar power laws have been observed in the distribution of measles outbreaks in small islands (*6*).

If the current low level of MMR vaccine uptake persists in the UK population, the increasing number of unvaccinated individuals will lead to an increase in the reproductive number and possibly the re-establishment of endemic measles and accompanying mortality. In their attempt to avoid the perceived risk associated with vaccination, parents' behavior collectively results in a substantial increase in the real risk of exposure to measles.

References and Notes

1. N. J. Gay, L. M. Hesketh, P. Morgan-Capner, E. Miller, *Epidemiol. Infect.* **115**, 139 (1995).
2. See www.doh.gov.uk/public/sb0121 and www.doh.gov.uk/public/sb0218.htm for National Health Service immunization statistics [cited 15 April 2003].
3. D. J. D. Earn, P. Rohani, B. M. Bolker, B. T. Grenfell, *Science* **287**, 667 (2000).
4. R. M. Anderson, R. M. May, *Infectious Diseases of Humans* (Oxford Univ. Press, Oxford, 1992).
5. Methods are available as supporting material at *Science* online
6. C. J. Rhodes, R.M. Anderson, *Nature* **381**, 600 (1996).
7. V.A.A.J. and N.S. were supported by The Wellcome Trust (grant no. 063134).

Supporting Online Material
www.sciencemag.org/cgi/content/full/301/5634/804/DC1
Methods
Fig. S1
References

12 May 2003; accepted 7 July 2003

[1]School of Biological Sciences, Royal Holloway University of London, Egham, Surrey TW20 0EX, UK. [2]Department of Mathematics, Imperial College London, 180 Queen's Gate, London SW7 2BZ, UK. [3]Health Protection Agency, CDSC, 61 Colindale Avenue, London, NW9 5EQ, UK.

*To whom correspondence should be addressed. E-mail: vincent.jansen@rhul.ac.uk