The epidemiology of mumps in the UK: a preliminary study of virus transmission, herd immunity and the potential impact of immunization

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SUMMARY

Mathematical models and statistical analyses of epidemiological data are employed to assess the potential impact of mass vaccination on the incidences of cases of mumps infection and cases of mumps related complications. The analyses reveal that in the United Kingdom the average age at infection with the mumps virus is currently between 6–7 years and that the inter-epidemic period of the infection is approximately 3 years. The critical level of vaccine uptake to eliminate mumps virus transmission is predicted to be approximately 85% of each cohort of boys and girls by the age of 2 years. Analyses of published data show that the risk of complication arising from mumps infection is markedly age- and sex-related. Model predictions suggest that the incidence of orchitis will be increased, over the level pertaining prior to mass vaccination, by levels of vaccine uptake (by 2 years of age) that are less than 70% of each yearly cohort of boys and girls. Moderate (over 60%) to high (75%) levels of vaccine uptake, however, are predicted to reduce the overall incidence of cases of mumps related complications (especially those with CNS involvement).

INTRODUCTION

The last few years have seen much debate in the United Kingdom on the merits and inadequacies of our current vaccination programmes for the control of various viral and bacterial infections such as measles, rubella and pertussis (see for example, Walker, Carter & Jones, 1986; Miller & Miller, 1985; Anderson & Grenfell, 1986; Anderson & May, 1982 *a, b*). The major topics of these discussions have been the low levels of vaccine uptake in the United Kingdom compared with many other developed countries (in particular the United States, Canada and Sweden), the relative merits of one or two stage vaccination programmes for the control of congenital rubella syndrome (aimed at either boys and girls at around 2 years of age and/or girls between the ages of 11–15 years; Anderson & Grenfell, 1986) and the desirability of introducing a combined measles, mumps and rubella vaccine (MMR). The ideal target levels of vaccine uptake for measles, pertussis, mumps and rubella amongst young children to eliminate local transmission within the

Table 1. *Predicted levels of vaccination coverage (before the age of 2 years) for the elimination of various viral and bacterial infections in the UK*

Infection	Average age of infection prior to immunization (years)	Inter-epidemic period (years)	Vaccination coverage for elimination (%)
Measles	4–5	2	90–95
Pertussis	4–5	3–4	90–95
Mumps	6–7	3	85–90
Rubella	9–10	4–5	80–85

United Kingdom have been defined in recent years (via theoretical studies of virus transmission and control by mass vaccination). The predicted values for the UK (assuming uniform coverage in all areas of the UK) are listed in Table 1 (the figures indicate the desired level of cohort vaccination by the age of 2 years) (Anderson & May, 1985b).

A variety of approaches have been suggested to improve the current levels of uptake, which fall far short of the target figures listed in Table 1 (Measles uptake in England and Wales is currently around 60–65% by the age of 4 years.). At one extreme these include legislation to enforce the vaccination of all children prior to their attendance at primary schools (to mirror the USA vaccination policy) (Anderson & Grenfell, 1986) and at the other, changes in the pattern of vaccine administration such as the introduction of a combined MMR vaccine to encourage increased uptake amongst young children (Miller & Miller, 1985). The latter suggestion has prompted wide discussion amongst public health personnel and medical authorities.

This paper presents a preliminary analysis of the predicted impact of the introduction of a mumps vaccine (via the administration of a MMR vaccine to young children). The research is based on analyses of the available epidemiological data on mumps virus transmission in the UK, and the use of mathematical models that mimic viral transmission and the impact of mass immunization. In recent years, mathematical methods have been widely employed to assess the impact of artificially created herd immunity on the incidences of infectious diseases such as measles, rubella and pertussis (see Anderson & May, 1982a, 1983, 1985a, b; Anderson & Grenfell, 1986; Schenzle, 1984). However, very few attempts have been made to analyse the epidemiology and control of mumps by mass immunization (Schenzle, 1984; Donaghy, 1984). The present paper pays particular attention to the potential impact of mass immunization in the UK on the incidence of mumps and mumps-associated complications in a previously unvaccinated population.

Mumps is generally considered to be a relatively mild infection of children, the most common clinical symptoms being fever accompanied by parotitis which occurs in approximately 60% of all infections. Several complications are associated with mumps virus infection of which meningoencephalitis and orchitis are the most common (Centers for Disease Control, 1984). The former occurs in approximately 10% of all diagnosed clinical cases, and the latter in about 27% of clinical cases in post-pubertal males (Beard *et al.* 1977; Centers for Disease Control, 1984).

Case complication rates appear to be age- and sex-related (RCGP, 1974; Beard *et al.* 1977; IHE, 1985).

A vaccine against mumps infection was first licensed in the United States in 1967 and has since been used extensively. Inclusion of the mumps vaccine (via the introduction of MMR vaccine) in the US schools immunization programme has resulted in a 97% decrease in the incidence of mumps between the years 1968–82. Vaccination coverage in the USA is currently running at about 95% of each cohort prior to school attendance (Centers for Disease Control, 1984).

The levels of vaccine uptake achieved in the United States are admirable and present a target for the United Kingdom. However, the analyses presented in this paper assumes lower levels of uptake in line with current levels for measles vaccine (60–65% by the age of 4 years).

METHODS

(a) *Model structure*

The mathematical details of the model structure employed and the biological and epidemiological assumptions incorporated in it, plus methods of analysis, have been described in previous publications (Anderson & May, 1983, 1985*a*, *b*; Anderson & Grenfell, 1986). Briefly, the predictions of the impact of different vaccination strategies are based on a model of virus transmission in a large age- and sex-structured community. The model consists of a set of partial differential equations and is compartmental in structure. It describes changes in the densities of individuals classified into five sub-groups; infants with maternally-derived antibodies, susceptible individuals, incubators who are infected but are not yet infectious, infectious individuals and immune individuals (immunity may be acquired either by natural infection or by vaccination). It is assumed that immunity, once acquired (whether by vaccination or via infection), is lifelong. A central assumption of the model concerns the way in which the virus is transmitted between infectious and susceptible individuals. The *per capita* force of infection, λ, or the rate at which susceptible individuals of age a at time t acquire the infection is defined as;

$$\lambda(a,t) = \int_0^L \beta(a',a)\, Y(a',t)\, \mathrm{d}a'. \tag{1}$$

where L denotes the maximum lifespan (assumed to be 75 years in the following analyses), $Y(a', t)$ is the density of infectious people of age a' at time t, and $\beta(a', a)$ is the transmission coefficient arising from the contact of susceptibles of age a with infectious individuals of age a' (Anderson & May, 1985*a*, *b*; Schenzle, 1984).

Any given value of the transmission coefficient $\beta(a', a)$ encapsulates two components; the degree of contact between individuals in two different age classes, and the likelihood that a contact between a susceptible and an infectious individual in those age classes will give rise to a new case of infection. The model assumes that mixing (and hence transmission) is heterogeneous between age-classes and that the population is divided into a series of age-classes such that the function $\beta(a', a)$ adopts a series of values defined as β_{ij} which represent the transmission coefficient between susceptibles of age class i and infectious individuals of age class j. As described in previous publications, the matrix of β_{ij} values represents 'who
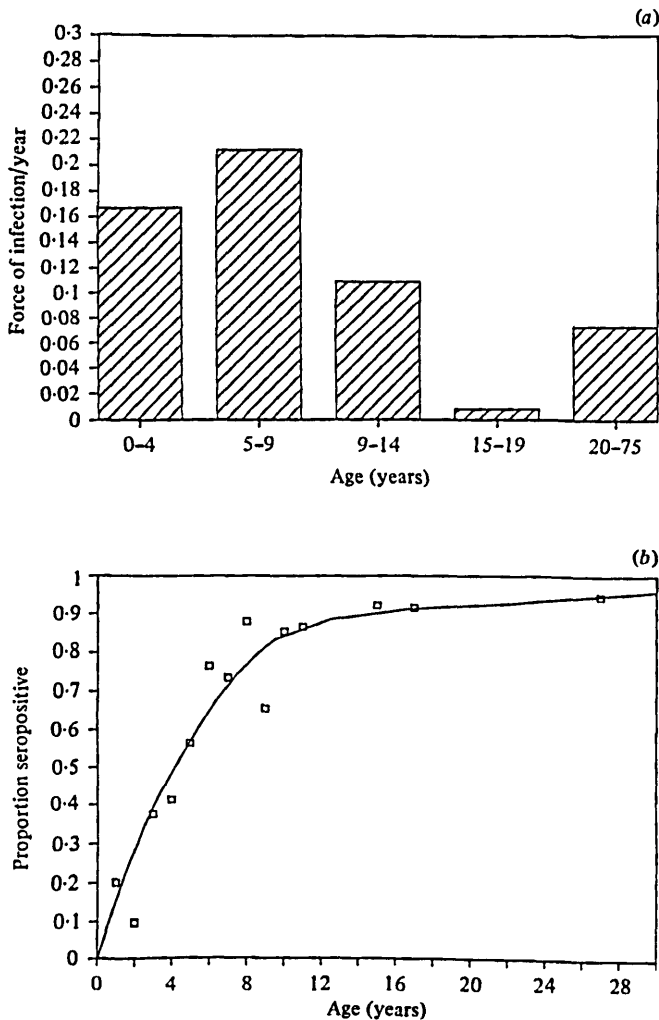
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Fig. 1. Age related changes in the *per capita* force of infection (the rate at which susceptibles acquire infection per unit of time) derived from serological data collected in London and the Home Counties in 1977–8 (data from Mortimer, 1978). (a). The average values of $\lambda(a)$ (defined per year) for various age classes estimated by the maximum likelihood technique described in Grenfell & Anderson (1986). (b). Age-related changes in the proportion seropositive for antibodies to the mumps virus: □, observed values; ——, values predicted on the basis of the average forces of infection recorded in (a).

acquires infection from whom' (WAIFW matrices) (see Anderson & May, 1985b). The particular matrix employed in this study represents a high degree of inter-mixing within the child-age class representing ages 5–9 years; it corresponds to the WAIFW 1 matrix defined in Anderson & Grenfell (1986).

(b) Epidemiological data

The age specific forces of infection (the rates at which susceptibles acquire infection) used throughout this study were based on a serological survey (sample
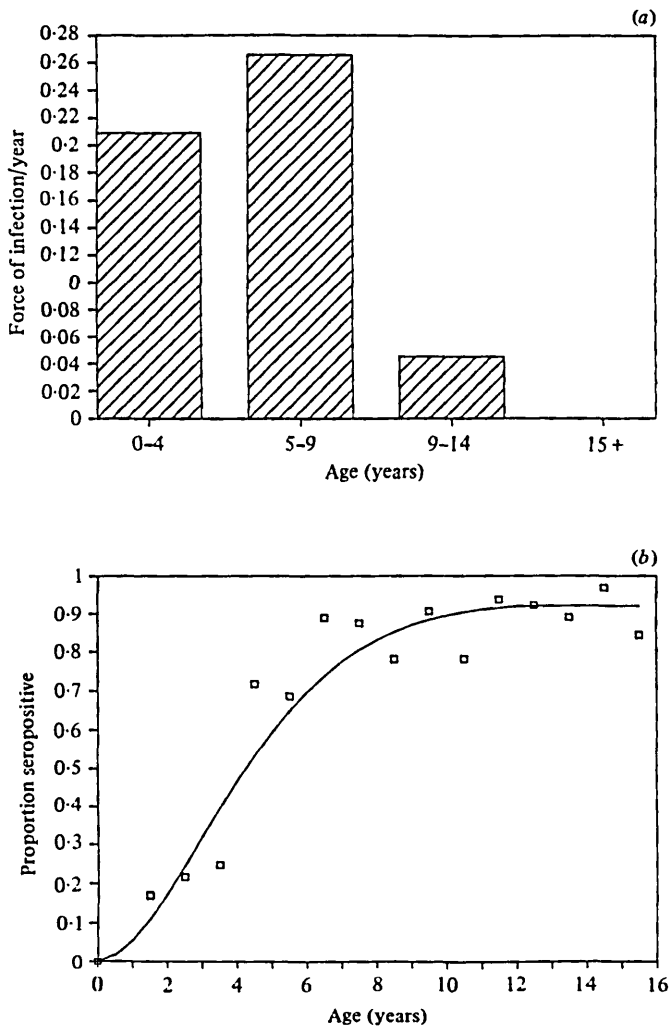
Fig. 2. Age-related changes in the force of infection derived from serological data collected in the Netherlands (Wagenvoort *et al.* 1980). (*a*) The average values for $\lambda(a)$ for various age classes. (*b*) Age-related changes in the proportion seropositive for antibodies to mumps virus: □, observed values; ——, values predicted on the basis of the forces of infection defined in (*a*).

size: 1354) carried out in London and the Home Counties in 1977–8 (Mortimer, 1978) (Fig. 1*a*). Such surveys provide a more reliable source for estimating the force of infection than case notifications since an estimated 30% of mumps infections are thought to be asymptomatic (Ho, 1979; Centers for Disease Control, 1984). Furthermore, mumps is not a notifiable disease in the UK at present and extensive unbiased case notification records are therefore unavailable. The estimation of the forces of infection was carried out as described in previous publications and employed a maximum-likelihood technique (Grenfell & Anderson, 1986; Nokes, Anderson & Anderson, 1986; Anderson & May, 1985*a*). Fig. 1(*a*) gives the estimates of the age-specific forces of infection derived from the serological data. Note that these estimates were derived from data for a community
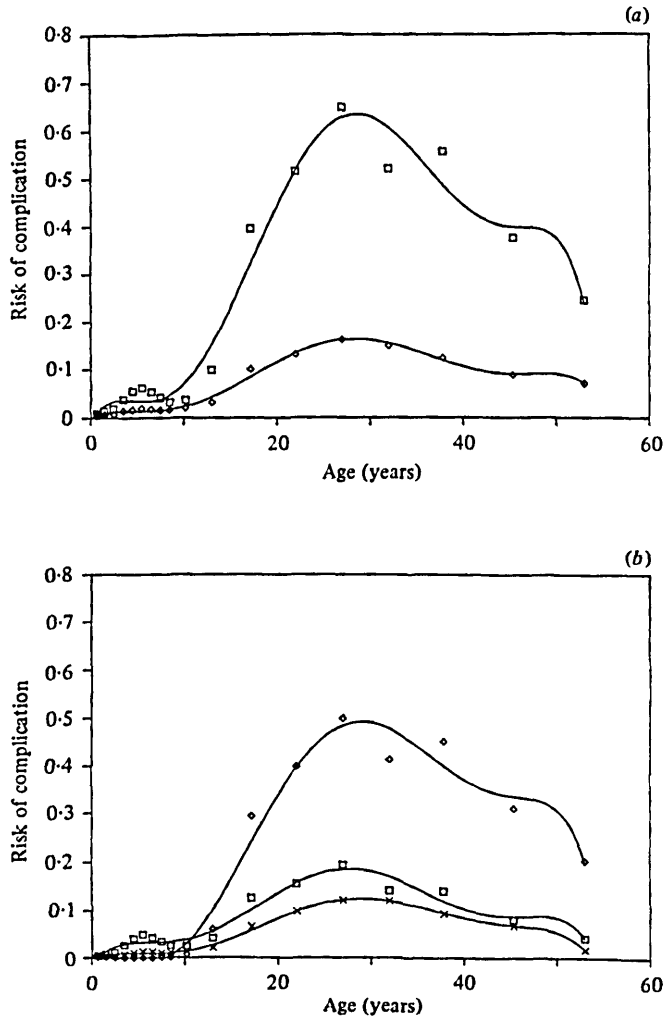
Fig. 3. The age- and sex-dependent risk of serious complications arising from infection by the mumps virus. The points represent the proportion of cases of mumps, admitted to hospitals in England and Wales in 1958–9, that presented with complications (data from RCGP, 1974), adjusted to mirror the proportion of the total number of cases of mumps in each age class (see text for further details). The recorded risk values denote relative as opposed to absolute changes with respect to age. ——, best fit polynomials of the form $m(a) = b_0 + b_1 a + b_2 a^2 + b_3 a^3 + b_4 a^4 \cdots b_n a^n$. (a) □, males; and ◇, females, denote the total relative risk of complications. Parameter values:

Males
$$b_0 = -0.11490606 \times 10^{-1}; \quad b_1 = 0.36169458 \times 10^{-1}, \quad b_2 = -0.97006201 \times 10^{-2},$$
$$b_3 = 0.10518546 \times 10^{-2}, \quad b_4 = -0.43306240 \times 10^{-4}, \quad b_5 = 0.761954865 \times 10^{-6},$$
$$b_6 = -0.48703892 \times 10^{-8}.$$

Females,
$$b_0 = -0.28200953 \times 10^{-2}, \quad b_1 = 0.111582798 \times 10^{-1}, \quad b_2 = -0.270945607 \times 10^{-2},$$
$$b_3 = 0.279145872 \times 10^{-3}, \quad b_4 = -0.112244828 \times 10^{-4}, \quad b_5 = 0.193848598 \times 10^{-6},$$
$$b_6 = -0.121660899 \times 10^{-8}.$$

(b) Complications divided into the risk of meningitis and/or encephalitis in males (□) and females (×), and the risk of orchitis in males (◇). Parameter values:

that has had no previous experience of mass vaccination against mumps. They reveal a high force of infection in young children, particularly in the 5 to 9 year-olds, with lower values in the very young children and teenage and adult age classes. These estimates are in accord with the often-made observation that the incidence of mumps infection tends to be highest in the 5 to 9 year-old children (Kalen & McLeod, 1977; Centers for Disease Control, 1984). The low estimated value of the force of infection in the 15–19 age range is probably due to the scarcity of observations in the serological profile in this region (Fig. 1*b*).

Additional serological data for the presence or absence of antibodies to the mumps virus, stratified by age, are available from surveys carried out in the Netherlands (Fig. 2) and the USA. Analysis of these data reveals similar age-related trends to those derived from the UK serological survey.

(c) *Other epidemiological parameters*

Other parameters of importance in the study of viral transmission within communities are the duration of immunity provided by maternally derived antibodies, the latent period of infection (the time from infection to the beginning of the state of infectiousness) and the infectious period (Anderson & May, 1985). From a literature survey we have taken the following values for mumps infection: average duration of maternal antibody protection, 91·25 days (Wagenvoort *et al.* 1980; Sato *et al.* 1979; Kalen & McLeod, 1977), the latent period, 13 days; the infectious period, 6 days (Benenson, 1975). The value for the infectious period may appear to be an under-estimate as it is generally quoted as 7–10 days. However, viral shedding usually occurs for up to 6 days prior to the onset of symptoms (and hence diagnosis) at which time the infectious individual is usually effectively removed from circulation by quarantine within the home as a consequence of illness (Kalen & McLeod, 1977). Immunity, either acquired naturally or by immunization is assumed to be lifelong (Wagenvoort *et al.* 1980).

(d) *The risk of serious disease*

A major concern in the introduction of a mass vaccination programme centres on the issue of whether or not low-to-moderate levels of immunization will actually increase the numbers of susceptibles in the older age-classes over the level pertaining before its introduction (Anderson & May, 1985*a*). This concern arises from the observation (from theoretical and empirical studies) that mass vaccination tends to decrease the rate of virus transmission and hence increase the average age

Male meningitis:
$b_0 = -0.164\,899\,301 \times 10^{-1}$, $b_1 = 0.273\,542\,445 \times 10^{-1}$, $b_2 = -0.537\,609\,808 \times 10^{-2}$,
$b_3 = 0.472\,619\,323 \times 10^{-3}$, $b_4 = -0.179\,809\,177 \times 10^{-4}$, $b_5 = 0.305\,023\,371 \times 10^{-6}$,
$b_6 = -0.190\,992\,816 \times 10^{-8}$;
Male orchitis:
$b_0 = 0.507\,006\,146 \times 10^{-2}$, $b_1 = 0.467\,381\,499 \times 10^{-2}$, $b_2 = -0.384\,407\,621 \times 10^{-2}$,
$b_3 = 0.577\,472\,105 \times 10^{-3}$, $b_4 = -0.260\,529\,638 \times 10^{-4}$, $b_5 = 0.476\,991\,894 \times 10^{-6}$,
$b_6 = -0.311\,901\,886 \times 10^{-8}$;
Female meningitis:
$b_0 = -0.604\,900\,121 \times 10^{-2}$, $b_1 = 110\,808\,205 \times 10^{-1}$, $b_2 = -0.256\,707\,397 \times 10^{-2}$,
$b_3 = 0.248\,831\,814 \times 10^{-3}$, $b_4 = -0.976\,500\,836 \times 10^{-5}$, $b_5 = 0.167\,477\,371 \times 10^{-6}$,
$b_6 = -0.105\,503\,832 \times 10^{-8}$.

at which a susceptible individual typically acquires infection. Whether this concern is of practical significance depends critically on the way in which the risk of serious complications resulting from infection changes with age. More precisely, it depends upon the exact form of age dependency in the case complication rate (defined as the ratio of the number of cases in which complications arise within a specified age class divided by the total number of cases of infection in that age class).

If the risk of serious disease (defined by the case complication rate) decreases with age, all levels of vaccination coverage will be beneficial in the sense that they will reduce the incidence of infection and the incidence of serious complications. However, if the case complication rate increases with age (either monotonically or in some more complex non-linear manner) then all levels of vaccination coverage will decrease the incidence of infection but some levels (i.e. low to moderate coverage) may actually increase the total incidence of serious complications over the level pertaining prior to the start of mass vaccination.

Whether this problem is likely to arise for a specific infection and any given level of vaccination coverage can be quantitatively assessed by reference to a *risk ratio*, $w(a_1, a_2, t)$ which defines the ratio of the number of cases in which complications arise over the age range a_1 to a_2 at time t under a given vaccination programme (a defined level of vaccine uptake) divided by the number of cases in which complications arise in the same age range prior to the introduction of mass vaccination. More formally,

$$w(a_1, a_2, t) = \frac{\int_{a_1}^{a_2} m(a)\,\lambda'(a,t)\,Y'(a,t)\,\mathrm{d}a}{\int_{a_1}^{a_2} m(a)\,\lambda(a,o)\,Y(a,o)\,\mathrm{d}a}. \tag{2}$$

Here, $m(a)$ is the age-dependent case complication rate, $\lambda'(a, t)$ is the age-dependent force of infection under the vaccination programme, $Y'(a, t)$ is the number of infectious people of age a under the vaccination programme, $\lambda(a, o)$ is the age dependent force of infection prior to mass vaccination and $Y(a, o)$ is the number of infectious people of age a prior to mass vaccination (for further details see Anderson & May, 1983, 1985b). Note that since the function $m(a)$ (the case complication rate) enters in the numerator and denominator of eqn. (2), estimates of $m(a)$ need not reflect the exact magnitude of the complication rate. The function $m(a)$ must simply reflect relative (as opposed to exact) changes in the incidence of case complications with respect to age.

In this study five separate risk functions are employed. They represent total risk for males and for females (any form of case complication), the risk of meningitis and/or encephalitis for males and for females and the risk of orchitis for males. Meningitis, encephalitis and orchitis normally represent 85% of the total cases of complications (RCGP, 1974).

Information on age-related case complication rates is limited at present but data are available (of varying quality and varying age stratification) from studies in the UK, the USA and Belgium. Our analyses are based on the UK data which was collected by the Association for the Study of Infectious Disease under the auspices of the Royal College of General Practitioners (RCGP, 1974). The study
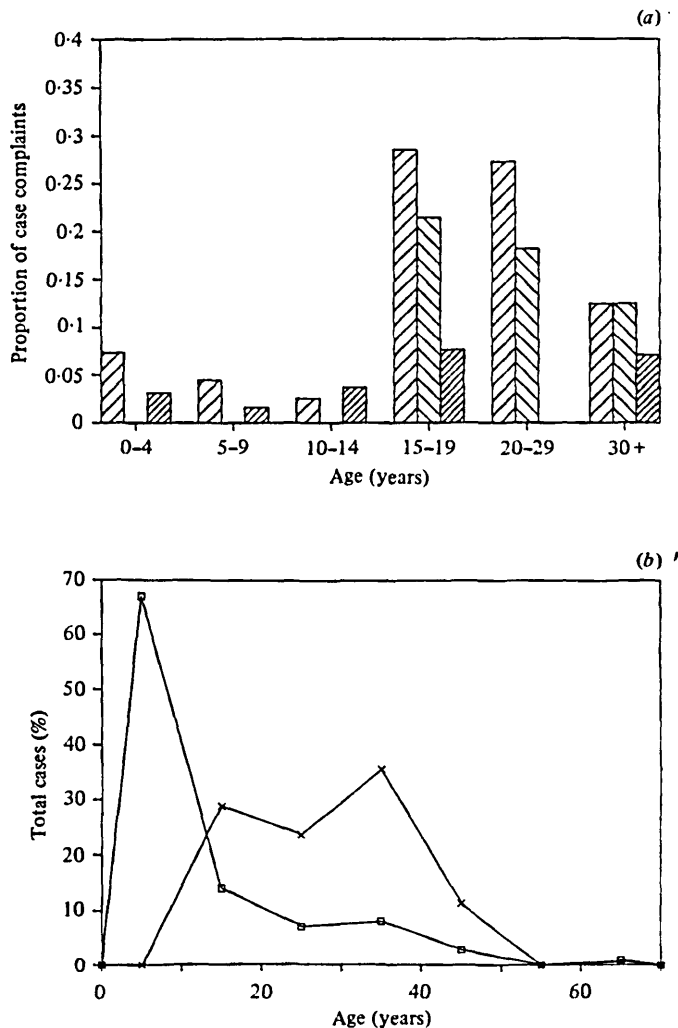
Fig. 4. Age-related risks of complications arising from mumps infection. (a) Data from Belgium (IHE, 1985) total risk for males (▨), total risk for females (▱), risk of orchitis (▧). (b) Data from the USA (Beard *et al.* 1977) percentage of mumps cases (□) and orchitis (×).

collated the number of cases of mumps-related complications admitted to 16 hospitals in England and Wales over the period 1958–59. The data contains a strong bias in reporting efficiency since only the more serious cases tend to be admitted to hospital. However, this observation does not invalidate its use in the context of assessing age-related risks and their significance to the introduction of mass immunization. The collated age- and sex-stratified data were employed to calculate a relative risk (relative between age classes) by multiplying the proportion of cases of mumps related complications (the proportion of the total number of cases of complications) within an age class, by the proportion of the total number of mumps cases that occur within the same age class. The latter proportions were estimated from the serological data recorded in Fig. 1. Note that

the derived estimate is a *relative* risk function describing the chance that a case of mumps infection in a given age class results in serious complications relative to the chance in other age classes. In the analyses reported in this paper, the impact of vaccination on the incidence of mumps related complications is assessed via the risk ratio $w(a_1, a_2\ t)$ defined in eqn (2) and hence, the relative risk function described above suffices due to its presence in the numerator and denominator of eqn (2).

The five age-dependent risk functions calculated from the RCGP data (RCGP, 1974) and the serological study of Mortimer (1978) are displayed in Fig. 3 (again note that the scale on the vertical axes reflects relative not actual risk). The recorded patterns reveal that males experience a much higher risk of complication as a result of mumps infection than do females. However, when the data are dissected to reveal complications in both sexes due to meningitis and encephalitis (these are considered together since the distinction relies on clinical judgement and is often arbitrary (Centers for Disease Control, 1980; RCGP, 1974), and orchitis in males, it becomes apparent that the age-related relative risk functions for CNS involvement are similar for both males and females. Much of the total risk experienced by males is due to orchitis in post-pubertal individuals.

The most important point to note from Fig. 3, however, is the trend for the relative risk measure of the case complication rate to increase with age over the age span 0 to 30 years. Analysis of comparable data collected in the United States and Belgium reveal broadly similar qualitative trends (Fig. 4) (Beard *et al.* 1977; IHE, 1985).

RESULTS

Our analyses of the predicted impact of vaccination on the incidence of mumps and mumps-related complications employ the model described in Anderson & May (1985*b*) and the parameter estimates detailed in the methods section. In a manner similar to that described for analyses of vaccination against measles and rubella (Anderson & May, 1983, 1985*b*; Anderson & Grenfell, 1986) we consider two types of predictions:

Long-term steady-state predictions

In this section we examine predicted developments after many decades of cohort vaccination in which each cohort of boys and girls is immunized at around 2 years of age. We record these long-term or steady-state predictions by means of a graph showing the ratio of cases of mumps-related complications after many decades (the equilibrium state) of cohort vaccination (at 2 years of age at various levels of vaccine uptake) over the age range 0–75 years divided by the identical quantity prior to the start of immunization (as defined in eqn (2) in the methods section) as a function of the level of vaccination coverage at age 2 years (Fig. 5). The age-dependent risk function ($m(a)$) and the age-dependent forces of infection employed in these calculations are as defined in Fig. 3 and Fig. 1 respectively.

The first point to note from Fig. 5 is the prediction that the elimination of mumps virus transmission is predicted to occur at a vaccination coverage of approximately 86% of 2-year-old boys and girls. The five functions recorded in Fig. 5 denote the value of the ratio $w(a_1, a_2)$ (where $a_1 = 0$, $a_2 = 75$ years) under
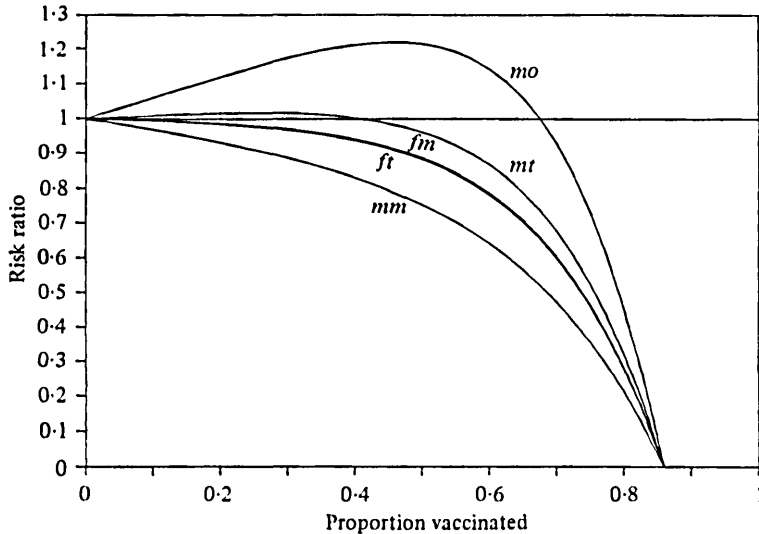
Fig. 5. The equilibrium or steady state risk ratio $w(a_1, a_2)$ (where $a_1 = 0$ and $a_2 = 75$ years), denoting the ratio of cases of serious disease after the introduction of mass vaccination divided by cases prior to immunization, as a function of the proportion of 2 year old boys and girls immunized each year. The five curves denote model predictions of the equilibrium ratio for five separate age-related risk functions: *mo*, male orchitis; *mt*, total complications, males; *ft*, total complications, females; *mm*, meningitis in males; *fm*, meningitis in females (see text). A value of unity reflects no change after the start of mass vaccination.
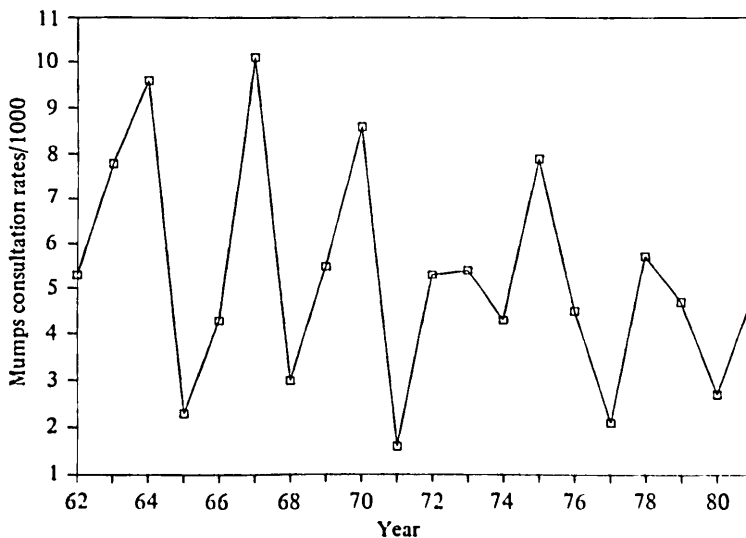

Fig. 6. Temporal changes in the incidence of mumps in England and Wales over the period 1962–81 (data from Galbraith *et al.* 1984). Note the 3 year incidence cycle.

different levels of vaccine uptake for orchitis in males (*mo*), total mumps complications in males (*mt*), cases of CNS involvement in males (*mm*), cases of CNS involvement in females (*fm*) and total mumps complications in females (*ft*). The predictions are that vaccination coverage in excess of 40% at 2 years of age will reduce the number of cases of mumps complications with respect to CNS in-
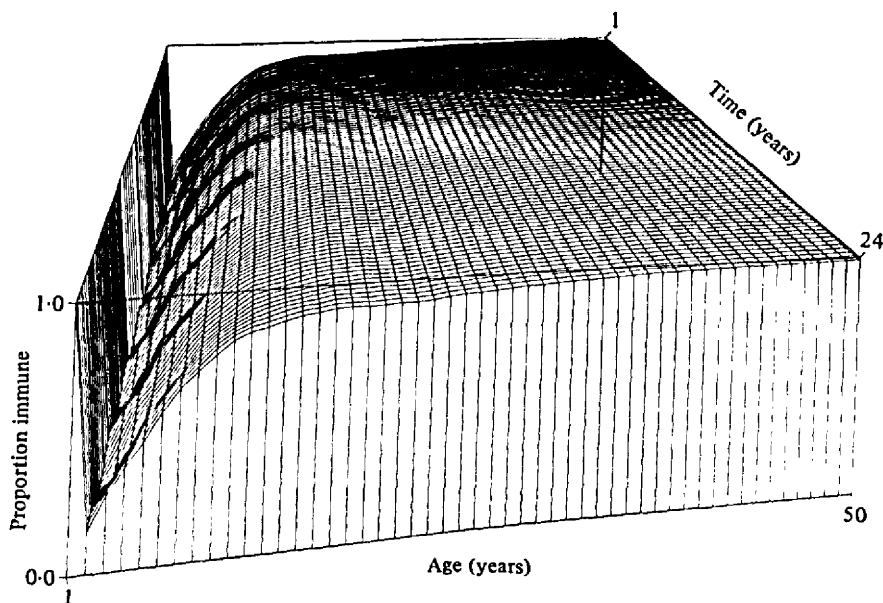
Fig. 7. The predicted serological surface (the proportion seropositive for antibodies to the mumps virus stratified according to age and projected through time) in the absence of immunization.

volvement in males and females and the total numbers of case complications below the levels prior to immunization. In the case of orchitis in males, however, the prediction is that vaccination coverage in excess of 70% at 2 years of age is required to reduce the incidence of this complication below pre-vaccination levels.

Short-term predictions

In this section we consider model predictions of the impact of cohort vaccination on the incidence of cases of mumps related complications in the short term after the introduction of immunization and before the system has settled to its long term steady-state. Vaccination is applied to both boys and girls such that varying proportions are immunized at the age of 2 years. The level of vaccination uptake has an important influence on the short term projections and we consider three different levels of uptake, namely; 40, 60 and 75%. These represent respectively low, moderate and high levels of vaccination. The moderate level of 60% is of particular relevance to the situation in the UK since uptake of measles vaccine is presently on average approximately 60% of 2 to 3 year old children (although considerable variation occurs between different regions in the UK).

Prior to the introduction of mass vaccination, the model predicts an oscillatory pattern in the incidence of mumps cases with an inter-epidemic period of approximately 3 years. This prediction is in close agreement with observed trends (see Anderson, Grenfell & May, 1984; Galbraith *et al.* 1984). (see Fig. 6). The serological surface predicted by the model (the proportion seropositive for antibodies to the mumps virus), reflecting changes in seropositivity with respect to age and time in the absence of vaccination, is presented in Fig. 7. Note that the 3 year cycles in
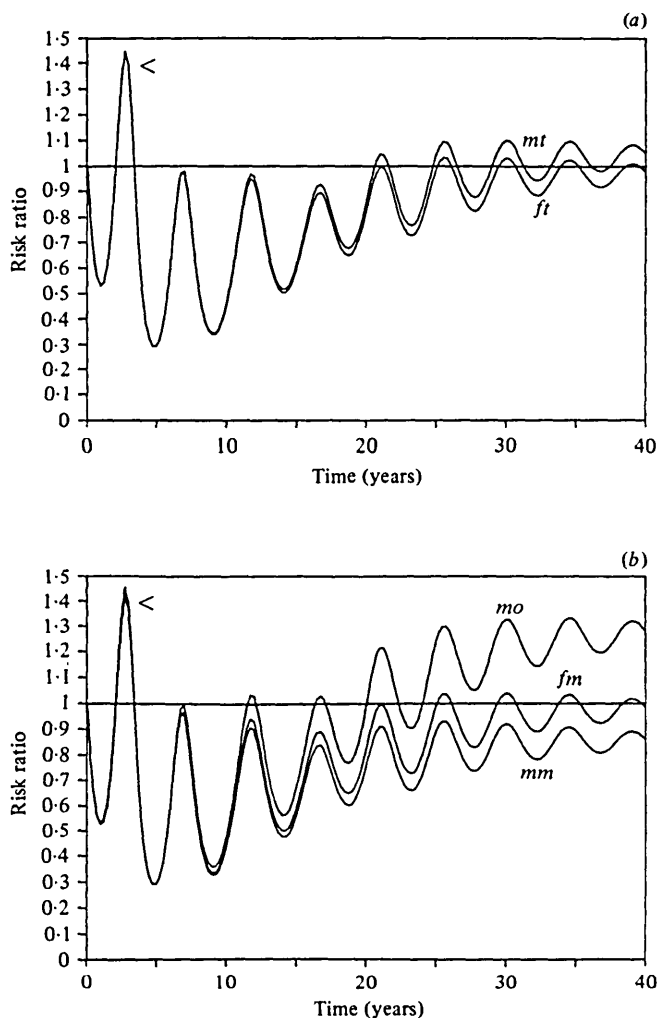
Fig. 8. Short-term temporal changes in the risk ratio $w(a_1, a_2, t)$ after the start of mass vaccination (< denotes the start of cohort immunization). (*a*) and (*b*) record predicted changes under 40% coverage of 2-year-old boys and girls. (*a*) Temporal changes in the ratio calculated on the total risk of mumps-associated complications in males (*mt*) and females (*ft*). (*b*) Similar to (*a*) but recording predicted changes in the risk ratio based on orchitis in males (*mo*) meningitis in males (*mm*) and meningitis in females (*fm*). The population size was set at 49·7 million (to mirror England and Wales) in all the numerical simulations displayed in this and subsequent figures.

the incidence of mumps create 3 year 'ripples' on the surface. Their magnitude, however, is probably too small to be detectable in longitudinal, cross-sectional serological surveys.

In a manner similar to that described in the section on long-term predictions, we examined the predicted impact of the three different levels of vaccination by reference to the risk ratio $w(a_1, a_2, t)$ at time t reflecting cases of complications after immunization divided by cases of complications before immunization, over the age range 0 to 75 years. Temporal projections over a 40 year time span for vaccination coverages of 40, 60 and 75% are shown respectively in Figs. 8, 9 and
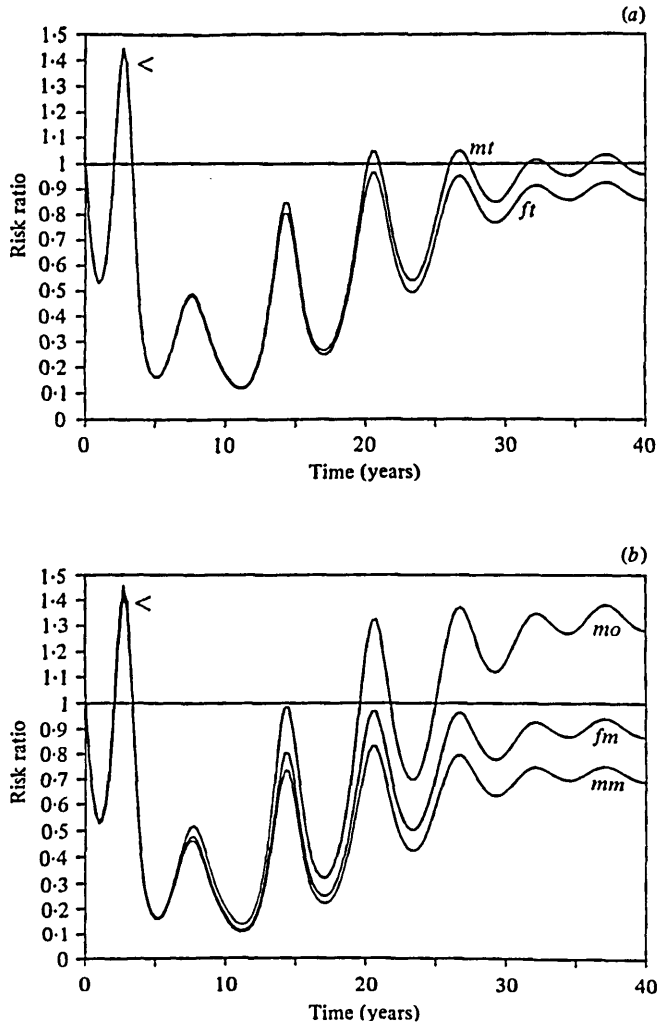
Fig. 9. Similar to Fig. 8 except that it records the predicted changes under the impact of 60% coverage of boys and girls at 2 years of age. (a) Total risk for males (mt) and females (ft). (b) Risk of orchitis (mo), meningitis in males (mm) and meningitis in females (fm).

10. In each particular case the level of vaccination uptake is assumed to be constant through time. At a 40% level of vaccination the model predicts little change in the total risk ratio for both males (mt) and females (ft) after an initial reduction following the introduction of mass immunization (the value of $w(a_1, a_2, t)$ eventually oscillates around a value of unity) (Fig. 8). When the total risk is dissected into risk of complications due to CNS involvement and orchitis in males a different pattern emerges. The model predicts a slight reduction in cases of CNS involvement in both males (mm) and females (fm) but an increase in cases of orchitis (mo) (Fig. 8b). A comparison of Fig. 8(a and b) reveals that the total risk for males is unchanged in the long term (Fig. 8a) as a result of the decrease in the number of cases of CNS involvement being balanced by a rise in cases of orchitis (Fig. 8b).
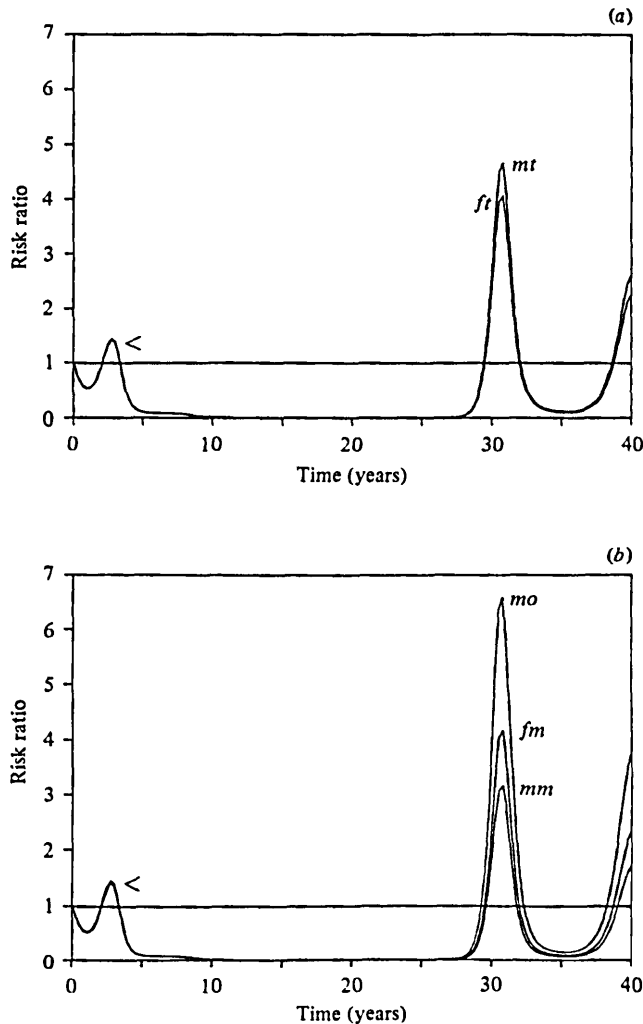
Fig. 10. Similar to Fig. 8 except that it records the predicted change under the impact of 75% coverage of boys and girls at 2 years of age (a) and (b) are as defined in the legend to Fig. 8.

At a 60% level of vaccination the model predicts a substantive initial reduction in total mumps related complications for both females and males followed by a rise to a level just below the pre-vaccination situation (Fig. 9a). At a finer level, a 60% coverage is predicted to reduce the incidence of cases of CNS complications in both males and females and to increase the incidence of cases of orchitis in males (Fig. 9b).

At the highest level of vaccination (75% of boys and girls by 2 years of age), the model predicts a very marked reduction in the incidence of total complications and cases involving CNS complications and orchitis (Fig. 10a and b). High levels of vaccination, however, are predicted to lengthen the inter-epidemic period greatly such that outbreaks of high incidence of case complications occur approximately 25 years after the introduction of mass immunization. The inter-epidemic period, and the average age of infection of those still susceptible to the
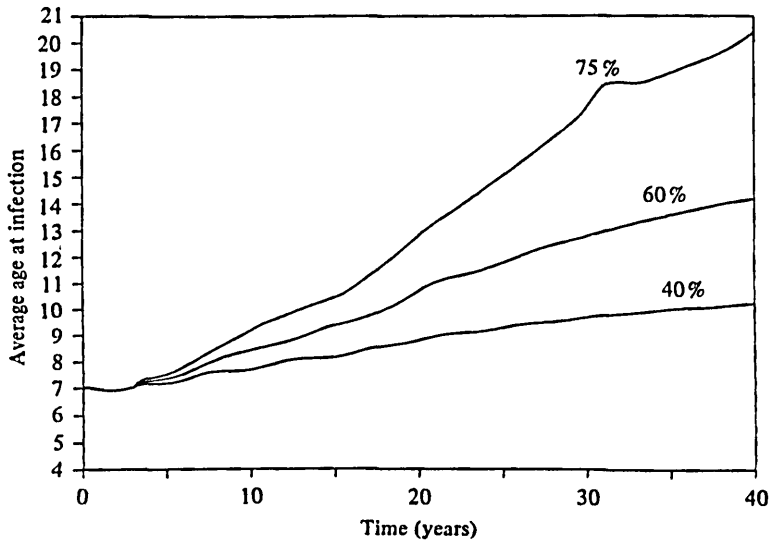
Fig. 11. Predicted temporal changes in the average age at infection with mumps under the impact of three different levels of vaccination coverage (40, 60 and 75%). Vaccination was initiated in year 3.

mumps virus, are predicted to rise as the level of vaccination coverage increases. This point is demonstrated in Fig. 11 which records the progressive increase through time from the start of mass vaccination of the average age at infection under the three levels of immunization. Note that under a 75% coverage level the average age at infection among those still susceptible is predicted to rise from roughly 7 years of age (the pre-vaccination state) to 21 years of age.

A clearer picture of the impact of mass vaccination in the population can be obtained by inspection of the predicted changes in seropositivity for antibodies to the mumps virus in different age classes as cohort immunization proceeds through time. Two serological surfaces denoting the predicted impact of 40 and 60% levels of vaccination are portrayed in Fig. 12. Time 0 represents the pre-vaccination situation in these graphs. Note that mass vaccination is predicted to have little impact on the overall proportion susceptible to infection in the population. The model simply suggests that mass vaccination changes the age distribution of the proportions susceptible such that a higher fraction remain susceptible in the older teenage and adult age classes than was the case prior to immunization (Fig. 12). The epidemiological principles underlying this observation have been discussed in detail in previous publications (see Anderson & May, 1983, 1985a, b; Anderson & Grenfell, 1986). One consequence of this altered age distribution of susceptibility is the increase in the inter-epidemic period.

The predicted rise in seronegativity in the older age classes, over the levels pertaining prior to immunization, is only worrying if levels of vaccine uptake decline during the course of a mass vaccination programme. In these circumstances, a major epidemic of mumps would occur shortly after the decline in vaccine uptake (in a manner similar to that recorded for pertussis in the UK following the decline in vaccine uptake in the mid-1970s).
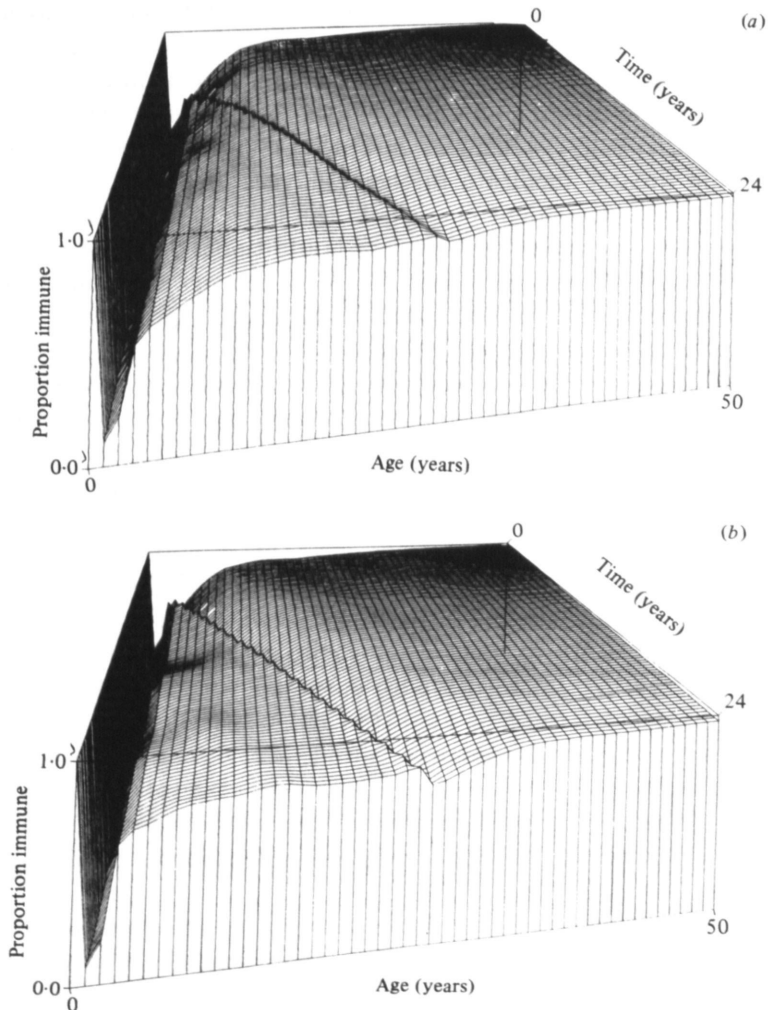
Fig. 12. Predicted changes in the proportion seropositive for mumps virus antibodies, stratified according to age, through time after the start of cohort vaccination in year 1. (a) 40% vaccination of 2 year old boys and girls. (b) 60% vaccination of 2-year-old boys and girls.

DISCUSSION

The accuracy of the model predictions presented in this paper are in part dependent on the quality of the available epidemiological data that describes the transmission of mumps in the UK (this data base provided estimates of the parameters of the model). For example, as shown in a previous publication in the context of rubella transmission (Anderson & Grenfell, 1986), predicted trends are particularly sensitive to changes in the magnitudes of the age-dependent forces of infection. The parameter estimates employed in this paper were derived from a single serological survey (Fig. 1) of 1354 individuals over the limited age range 1–27 years (Mortimer, 1978). There is clearly an urgent need to improve upon this

data base by the acquisition of further serological profiles, finely stratified according to age, which are based on much larger sample sizes and which cover a much broader age range. Ideally, this information should be acquired prior to the introduction of mass vaccination in the UK (the introduction of a combined measles, mumps and rubella vaccine is currently under discussion). Such additional data would greatly facilitate further analyses of the sensitivity of the model predictions to age-dependent changes in the force of infection.

A further and equally important requirement is additional data on the incidence of mumps related complications based on finely stratified age structured case and case complication reports. Ideally, such data should be collected such that the risk of complications arising from mumps infection can be defined per case of infection. The manner in which the complication rate changes with age is a central determinant of the way in which mass vaccination alters the incidence of serious disease resulting from infection.

The paucity of the available data argues for caution in the uncritical acceptance of the predictions detailed in this paper. However, in the absence of better quantitative information, and in the light of current discussions concerning the desirability of introducing MMR vaccine in the UK, it is clearly important to provide some assessment of the benefits and risks associated with different levels of mass vaccination. Model predictions are, broadly speaking, encouraging. At a 60 % level of vaccine uptake (in accord with current levels of acceptance of the measles vaccine), the analyses predict a substantive reduction in the incidence of mumps, an increase in the inter-epidemic period, a rise in the average age at infection and most importantly, a decrease in the incidence of total mumps-related case complications. The only worrying aspect of the predictions is the suggested rise in the incidence of orchitis over the level pertaining prior to the introduction of mass vaccination (see Fig. 9b).

Whether this observation should influence opinion on the desirability of the introduction of the MMR vaccine is questionable. Mumps is a relatively benign disease and it is rare that permanent sequelae follow a mumps virus infection. In the RCGP survey of 1958–69, no permanent sterility or testicular atrophy were recorded following orchitis (RCGP, 1974). In a study of mumps orchitis in Rochester, USA over the period 1935–74 only two patients had bilateral testicular atrophy after having mumps orchitis out of a sample of 47 patients (Beard et al. 1977). Of the cases involving the CNS, encephalitis although rare, may give rise to persistent sequalae, but meningitis is thought to be self limiting (RCGP, 1974).

In summary therefore, even at moderate levels of vaccine uptake (say, 60 %) the benefits accruing from the introduction of the mumps vaccine (as MMR vaccine) are predicted largely to outweigh the risks associated with an increase in the average age at infection in the vaccinated population. Whether the predicted increase in the incidence of orchitis is of sufficient concern to inhibit the introduction of MMR vaccine is a matter for medical judgement on the seriousness of this type of complication arising from infection by the mumps virus. In forming this judgement there is a clear need for more precise quantitative epidemiological data on age-stratified case complication rates, the incidence of unilateral and bilateral testicular atrophy in cases of mumps orchitis and the proportion sero-

positive for antibodies to the mumps virus in finely stratified age classes in the currently unvaccinated population in the UK.

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