Social epidemiology of chickenpox in two British national cohorts

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Abstract

Study Objective—To provide a quantitative description of factors independently predictive of reported chickenpox infections in two national cohorts of British children.

Design—Longitudinal cohort study design employing logistic regression analysis of data obtained in the 1970 British Births Survey (later to become the Child Health and Education Study, CHES), and the 1958 British Perinatal Mortality Survey (later to become the National Child Development Survey, NCDS).

Settings—One-week birth cohorts covering the whole of the United Kingdom.

Participants—Data were obtained from questionnaires administered to the carers of 10 196 children born in the UK between 5 and 11 April 1970 (CHES) and 10 927 children born in the UK between 3 and 9 March 1958 (NCDS). These numbers consist of the whole of the surviving cohorts excluding those for whom data were incomplete.

Measurements—Biological, social, and medical factors in the parents and children, as recorded by the child's principle carer or from clinical notes.

Main results—Chickenpox by the age of 10 years was reported to be more common in the children of advantaged families (higher social class, higher parental education levels), with a higher prevalence in those parts of the United Kingdom normally associated with affluence, such as the South East and South West of England, and lower rates in Wales and Scotland. Chickenpox by 10 years was also associated with more crowding in the home. A similar but less marked pattern occurred for chickenpox by the age of 11 years in the 1958 NCDS cohort. This social distribution apparently reflected overall rather than age-specific susceptibility.

Conclusions—The national and international pattern of chickenpox epidemiology indicate that both social and climatological factors may be important in defining groups at risk. Further research is indicated if a vaccination service is to be implemented in this country.

with relatively benign morbidity. Serious sequelae such as pneumonia, encephalitis, or cerebella ataxia are rare¹ unless an infant develops a neonatal infection contracted from a mother infected during pregnancy. Some reports have linked varicella with the development of cancer in animals^{2 3} but this association remains unproved in humans.

Data from the Royal College of General Practitioner's Research Unit indicate that in England and Wales 0.5% of the population, about 200 000 in all, contract chickenpox each year on average, of whom about 1000 (0.5%) are admitted to hospital as a result of associated complications.⁴ The average annual number of deaths from chickenpox between 1967 and 1985 was 20 in England and Wales. This period included the two epidemics around 1971 and 1980.⁴ As is the case with measles, it is often the immunosuppressed patient who suffers most. Despite the normally inconsequential course of the infection the overall national social and economic burden of chickenpox is substantial.⁵

From the clinical and epidemiological perspective, chickenpox is of great interest as the varicella-zoster virus has the capability of silent residence in a variety of neural ganglia for much of a lifetime. On reactivation by unknown factors it causes skin lesions known as "zoster" and also shingles, a painful neuralgia that afflicts many adults, especially the elderly. For these reasons the prospect of vaccination has been considered but as Joseph and Noah⁴ point out basic information on the incidence and severity of varicella and zoster disease remains to be collected. Several studies and numerous case reports have indicated that the population distribution of infections and susceptibility to chickenpox in developing countries contrasts substantially with the experience of the industrialised world.⁶ Additional information about the epidemiology of the disease and the identification of those most at risk in the industrialised nations, where vaccination is likely to be most cost effective, would aid such decisions. The present report is a contribution to this topic.

Methods

The present study uses data from the 1958 and 1970 national cohort studies henceforth called respectively the National Child Development study (NCDS) and the Child Health and Education Study (CHES). These were both started as cross sectional studies undertaken on all of the approximately 17 000 mothers who gave birth to babies throughout the UK, in one complete week in spring.⁷⁻⁹ The original objective was to understand better the factors associated with maternal and infant morbidity at and around the

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Chickenpox has received relatively little attention from public health doctors or epidemiologists either at home or abroad. It is generally perceived to be a common contagious childhood disease

time of birth. Later, the same cohorts of births were used in longitudinal studies as the surviving children were followed up at 7 and 11 years (NCDS) and 5 and 10 years (CHES).

At both 7 and 11 years of age (NCDS) and at 10 years (CHES), the mothers or carers of the children were asked whether their child had ever had chickenpox. These questions were asked by a health professional in the home who completed the questionnaire and could answer any queries. In the CHES questionnaire, the age at which the child had had chickenpox was also obtained.

1970 NATIONAL COHORT (CHES)

Social, demographic, and biological factors relating to reported chickenpox infection in the CHES cohort were initially investigated by cross tabulating 73 background variables with a history of the disease by 10 years of age. No prior selection of background variables was made as there was no a priori reason for favouring some social, demographic, or biological factors over others. The data on chickenpox used in this cohort include information from the 241 cases of chickenpox reported to have occurred shortly after the child's 10th birthday, representing the time between the questionnaire presentation date and its completion. From the original birth cohort of 16 120 (which excludes deaths <1 week post partum and babies born in Northern Ireland), 10 196 cases

were selected for study. This comprised all survivors with data available from each of the three time points (0, 5, and 10 years), where the child's immunisation history was known, and where chickenpox was either reported as having occurred at a specified age or was reported as not having occurred at all. The group lost to follow up in survivors in this cohort included a disproportionate number of unmarried mothers who smoked and mothers living in the South East of England. Only 121 cases were lost because the parent did not know whether the child had had chickenpox or not and 178 cases were lost because chickenpox had occurred but had not been reported at a specified age. Cases of chickenpox could not be validated by any independent procedure and therefore this study refers to "reported" chickenpox.

From the set of all the 49 factors significantly associated ($p < 0.05$) with a history of chickenpox, groups were formed with a maximum of 10 independent categorical variables which were clearly related to one another through their subject similarity or through their chronological importance in development (table I). Recoding within variables was undertaken to group together adjacent or logically related levels that showed similar associations with chickenpox. Thus Yorkshire and the East Midlands were grouped together (similar chickenpox incidence and geographically close) but not with the South West despite similar rates of chickenpox. The six groups formed are listed in table I and forward stepping logistic regression by BMDP-PLR were undertaken, initially on each group separately, with chickenpox by age 10 as the dependent variable. The probability criterion for entering the model within each group was set at 0.01 and two moves were allowed into or out of the model in each round. Factors entering the model within each group are superscripted "1" in table I.

A hierarchical set of further regressions was then undertaken to eliminate covarying factors and select the most significant independent predictors of chickenpox. This was done initially by recombining groups using those factors entering the model in the initial round of the six logistic regressions. Factors in groups 1 and 2 (total $n=10$) and groups 4, 5, and 6 (total $n=10$) were combined into two new groups and a similar procedure was completed. Factors again entering the interim model from the two "second round" of regressions are superscripted "2" in table I. Group 3 factors were held over to be regressed together with those factors entering the interim model from groups 1 and 2. Those entering the interim model on this occasion are superscripted "3" in table I. Finally, all the remaining 12 surviving factors from all the original groups were included in a single regression leaving six independent variables predictive of chickenpox by 10 years of age. These factors are superscripted "4" in table I (see discussion). The model produced by this procedure generated a decile based, Hosmer-Lemeshow goodness of fit χ^2 of 8.4 with 8 degrees of freedom ($p=0.399$) indicating a satisfactory fit.¹⁰

1958 NATIONAL COHORT STUDY (NCDS)

Factors similar to those determined to be most predictive of chickenpox by age 10 years in the

Table I Background factors significantly ($p < 0.05$) associated with reported chickenpox by 10 years of age in the CHES cohort

Group	Factor*
(1) Mother's background	Region of delivery ^{1 2 3 4} Place of birth of infant Place of birth of mother ¹ Age mother left full-time education ^{1 2 3 4} Mother's occupational class ^{1 2 3} Mother's age Mother's height Highest educational qualification (1975) ¹
(2) Father's background	Place of birth of father ¹ Age father left full-time education Father's ethnic origin ^{1 2 3 4} Father's occupational class (1970) ^{1 2 3 4} Father's occupational class (1975) Father's age ¹ Father's employment status Highest educational qualification (1975) Either parent's highest qualification (1975) ¹
(3) Circumstantial	Present marital status Marital status at conception ¹ Number of rooms in household in 1975 Number of persons in household in 1975 ^{1 3 4} Persons per room ratio in 1975 ^{1 2}
(4) Reproductive history	Number of previous pregnancies Number of previous early neonatal deaths Number of older children in household (1975) Parity ^{1 2} Interval between births ^{1 2 4} Interval between pregnancies Contraceptive method previously used ^{1 2} Certainty of last menstrual period dates Believability of last menstrual period dates
(5) Present pregnancy	Present smoking habits Present or past smoking habits Lowest haemoglobin count Date of first antenatal care visit ¹ Person responsible for antenatal care ¹ Mother's asthma or hayfever Any labour preparation class attendance ^{1 2} Attended labour classes in health clinic Place of delivery ¹ Antenatal visit rate
(6) Birth	Birth weight Resuscitation of infant Separation of mother from infant after birth Gestational age at delivery ¹ Attempted breastfeeding Feeding pattern in first week Breastfeeding during first 3 months ^{1 2} Feeding pattern over first 3 months

*Superscripts refer to the round of regressions the factor remained in the model for. Factors in *italics* remained in the final model—see text.

1970 cohort data were identified in the 1958 cohort study. Equivalent variables were present in NCDS for "region of residence", "occupational class of father", "ethnic origin", and "interval between births". Similarity was assumed between the CHES factor "age mother left full-time education" and the dichotomised NCDS factor "did father stay at school past minimum school leaving age", as maternal and paternal educational levels usually correlate highly. Similarly, the CHES factor "number of persons in the household" (in 1975) was represented in NCDS analysis by the "number cooked for in household" at the beginning of the index pregnancy. Only cases for which information was available at both 7 and 11 years were used for analysis.

Levels within each background variable were combined according to the same principles as in the CHES cohort analysis and a single regression was performed with reported chickenpox by age 11 as the dependent variable.

Results

PREVALENCE

The history of chickenpox in young children from these two national cohort studies indicates that notwithstanding occasional epidemics, the underlying trend of chickenpox prevalence may have been down in the later study or that its age distribution had shifted. In NCDS by age 7 years, 61% of the cohort had been infected, increasing to 77% by age 11 years. In the CHES a total of 64% of the cohort were reported as having had the disease by age 10 years. The period of sus-

ceptibility for the CHES children (1970–80) included epidemics peaking in 1971 and 1980.⁴ Although no equivalent national data are available for the NCDS children between 1958 and 1966, the 1967 and 1968 chickenpox rates were relatively high and a slight trend towards a lower overall prevalence in the later period may be reasonably suspected. As discussed below a far higher proportion of the susceptible child population contracted chickenpox by 7 years in NCDS than in CHES. More recently a returning shift towards earlier infections has been proposed⁴ and this again seems to be associated with an increasing overall prevalence.¹¹

No information on the precise age of contracting the disease is available from NCDS but CHES data on age specific rates recalled by the mother when the child was 10 years are probably reliable (figure). These show the exponential increase in susceptibility to the disease up to age 10 when data collection ended.

FACTORS PREDICTIVE OF CHICKENPOX BY 10 YEARS (CHES)

The six factors independently predictive of reported chickenpox by age 10 years in the 1970 cohort are presented, together with the odds of chickenpox in each category and adjusted for other factors in the model, in table II. This table also lists the prevalence of chickenpox by age 10 in each level of each of the final model independent variables.

Taking the criteria of selection of categories whose 99% confidence intervals lie below or above unity, or whose trends across adjacent categories are clear, or both, conclusions about the social epidemiology of reported chickenpox by age 10 in the cohort can be drawn. Firstly, contracting chickenpox by 10 years of age shows a strong significant inverse association with occupational class of the father with an 87% higher odds of chickenpox by age 10 in children whose fathers were in the professional and managerial groups compared with unskilled labouring groups, when other factors are taken into account. European parents were two and a half times as likely to report chickenpox by age 10 in their children as non-Europeans or parents of mixed origin, whereas children whose parental ethnicity was not known or not stated also had a high odds of reported chickenpox. Chickenpox by 10 years was reported to be significantly more likely to occur in children who were delivered in the standard regions of Yorkshire and Humberside, East Midlands, East Anglia and the South East (including Greater London). The odds of the reported disease was twice as high in children whose mothers had left full-time education at 19 years or later compared with those who left at age 14 years. The adjusted odds of the disease was significantly and positively related to the interval between the birth (or end of pregnancy) of the previous and index children up to 5 years and significantly negatively related thereafter. First children were less likely to succumb to chickenpox but only at the 5% level of significance. A clearer pattern was presented by the association between chickenpox and the number of people in the household where a trend up to five persons was apparent but no higher.

Table II Factors predictive of chickenpox by 10 years in the CHES cohort

	% with Chickenpox	Adjusted odds ratio*	(99% CI)	χ^2
Father's social class:				
I	76.7	1.50	(1.15, 1.96)	32.98***
II	69.0	1.17	(0.99, 1.39)	
III (non-manual)	67.6	1.13	(0.96, 1.32)	
III (manual)	61.7	0.98	(0.87, 1.09)	
IV	57.6	0.89	(0.76, 1.03)	
V	54.7	0.80	(0.65, 1.00)	
Unsupported	56.8	0.83	(0.62, 1.11)	57.91***
Unknown	60.9	0.97	(0.64, 1.20)	
Ethnic origin:				
European	63.7	1.28	(1.12, 1.46)	211.73***
Non-European, mixed	41.3	0.52	(0.42, 0.65)	
Unknown, not natural parents	63.2	1.50	(1.27, 1.78)	
Region of birth:				
Scotland	49.8	0.61	(0.52, 0.71)	211.73***
North, North West	59.7	0.93	(0.83, 1.05)	
Yorks and Humber, East Midlands	66.1	1.25	(1.09, 1.43)	
West Midlands	55.1	0.82	(0.70, 0.95)	
East Anglia, London	69.6	1.44	(1.25, 1.67)	
South East	73.0	1.59	(1.39, 1.81)	
South West	64.1	1.05	(0.87, 1.27)	
Wales	54.1	0.72	(0.59, 0.87)	
Mother's age (y) at leaving full-time education:				
≤14	57.9	0.72	(0.59, 0.88)	34.48***
15	61.1	0.89	(0.80, 0.98)	
16	64.9	0.97	(0.85, 1.11)	
17, 18	69.4	1.13	(0.97, 1.32)	
≥19	75.4	1.43	(1.14, 1.78)	
Interval between births (y):				
No previous pregnancies	60.2	0.91	(0.82, 1.02)	56.55***
<2	64.8	1.12	(0.99, 1.25)	
2–3	69.0	1.25	(1.09, 1.43)	
3–5	67.1	1.22	(1.06, 1.40)	
>5	54.4	0.76	(0.64, 0.89)	
Suspect dates/unknown	57.5	0.85	(0.69, 1.04)	
No in household				
2, 3	55.4	0.80	(0.70, 0.93)	22.16***
4	64.7	1.07	(0.98, 1.17)	
5	65.5	1.16	(1.04, 1.28)	
≥6	58.7	1.00	(0.89, 1.13)	

***=p<0.001

*Odds highlighted in bold deviate significantly (p<0.01) from 1.

Age specific infection rates for chickenpox (Child Health and Education Study)

Seen together the association between reported chickenpox by age 10 years and higher occupational class, European origin, longer maternal education, and longer birth spacing intervals are consistent with social conditions of advantage and relative affluence.

Further analysis was undertaken to obtain more detail on these relationships. The contingency that the disease was associated with urban life was assessed by reviewing the odds of chickenpox in both rural and urban communities as defined by the health visitor's report of the type of neighbourhood the child lived in at the age of 5 years. These indicate clearly that once an adjustment had been made for existing predictors no additional variance was explained by this factor (adjusted odds ratio of chickenpox in rural neighbourhoods=1.00; 99% confidence interval 0.94, 1.08; $\chi^2=0.14$, 1df, NS). Secondly, the possibility that unadjusted regional groupings were distorting actual geographical patterns of the disease when controlled for other independent factors was examined by restoring the individual standard regions to the regression. This showed that no distortion had occurred and that all parts of the South and East had high levels of reported chickenpox infection by age 10 while Scotland and Wales were areas with the lowest geographical prevalence (table III).

CHICKENPOX BY AGE 11 IN THE NCDS COHORT

When factors similar to those predictive of chickenpox by 10 years in the CHES cohort were applied to the NCDS data the results showed some similarity, although variation was noticeably

less evident (table IV). Despite slightly different independent variable definitions there were higher odds in professional than in manual occupational classes, in Europeans than in non-Europeans, and in the economically privileged parts of the UK (South and East compared with the North, Scotland, and Wales). A weak positive association existed between chickenpox and the level of parental education. While in both cohorts the odds dropped with the longer pregnancy to birth intervals and the number of people in the household, both variables exhibiting U shaped trends of association in both cohorts, the positions of the peaks and troughs differed slightly. Thus, the higher rate occurred when the interval between the end of the previous pregnancy and birth of the index child in CHES was two to three years whereas in NCDS it was one to two years. Both cohorts showed the drop in the odds of infection in the index child when the end of the previous pregnancy occurred at least five years before the index child's birth. For the number of household members, the CHES variable related to the "total number who live in the same address and are catered for by the same person" in 1975. For NCDS the comparable variable referred to the "number resident in the house at the beginning of pregnancy of the index child excluding lodgers and those eating separately". As 47% of the women in CHES had at least one child between 1970 and 1975 the category comparisons between the two cohorts should be adjusted for this factor. Furthermore, the ranges are different and it seems likely that this to some extent reflects changing living conditions (that is, improved housing) in the UK as a whole. Nevertheless the risk of reported chickenpox in small households seems to be higher (and in large households seems to be lower) in the NCDS cohort than in the CHES. This could be accounted for by the age distribution differences of reported chickenpox in the two cohorts (see below).

SPLIT AGE ANALYSIS ON THE TWO COHORTS

Because of the very high ultimate seroconversion rates in adult populations, which indicate prior chickenpox exposure or infection, or both, it is pertinent to question whether the social distribution we observed reflects trends in contracting the disease by a certain (that is, young) age rather than differences in overall susceptibility. To explore this contingency the odds of chickenpox were compared in the same factors for two different age groups in each cohort. For purposes of cohort comparison the 7th birthdate was taken as the cohort dividing line for the two age groups. The proposed hypothesis was that if socially advantaged conditions were associated with chickenpox being contracted at earlier ages then the odds obtained for reported chickenpox infections at an earlier age would differ substantially from the odds of reported chickenpox at later ages, the former being more extreme in their social distribution.

The CHES cohort

Further separate logistic regressions using the same factors were run for those reported to have had the disease before and after their 7th birthday

Table III Standard regional variation in chickenpox by 10 years of age adjusted for factors predictive of chickenpox (CHES)

	Adjusted odds ratio*	(99% CI)
Scotland	0.61	(0.51, 0.72)
South Wales	0.67	(0.53, 0.86)
North Wales	0.78	(0.54, 1.12)
North	0.92	(0.76, 1.12)
Yorkshire, Humberside	1.13	(0.95, 1.35)
North West	0.89	(0.77, 1.04)
East Midlands	1.30	(1.05, 1.63)
West Midlands	0.80	(0.68, 0.94)
South West	1.04	(0.85, 1.27)
East Anglia	1.36	(1.03, 1.79)
South East	1.56	(1.35, 1.80)
London	1.46	(1.22, 1.74)
No	10.123	
χ^2 11df	209.38	
p	<0.0001	

*Odds ratios of chickenpox in each standard region adjusted for other predictors
Odds significantly ($p<0.01$) deviant from 1 are highlighted in bold

Table IV Odds of a child having chickenpox by 11 years (NCDS) adjusted for factors independently predictive of chickenpox by 10 years (CHES).

	% with chickenpox	Adjusted odds ratio*	(99% CI)	
Father's social class:				
I	81.4	1.11	(0.83, 1.49)	
II	81.2	1.19	(0.99, 1.43)	
III	77.5	1.05	(0.93, 1.19)	
IV	73.0	0.84	(0.71, 1.00)	
V	72.6	0.86	(0.71, 1.04)	
No husband	76.0	1.00	(0.67, 1.48)	$\chi^2=19.63$, $p=0.0015$
Mother's place of birth:				
European	77.2	1.12	(0.88, 1.41)	
Non-European	75.4	0.89	(0.71, 1.13)	$\chi^2=1.44$, $p=0.2305$
Old standard region:				
Scotland	70.7	0.74	(0.63, 0.86)	
North Western	76.1	0.95	(0.81, 1.12)	
Northern	72.0	0.78	(0.65, 0.95)	
East/West Riding, North Midlands	79.4	1.16	(0.99, 1.35)	
Midlands	77.3	1.04	(0.87, 1.24)	
South East, South West, London	79.9	1.17	(1.03, 1.34)	
Southern	82.3	1.35	(1.04, 1.74)	
Eastern	79.9	1.15	(0.94, 1.42)	
Wales	73.1	0.82	(0.66, 1.03)	$\chi^2=63.85$, $p<0.0001$
Did father stay at school after earliest school leaving age?				
No	76.0	0.93	(0.86, 1.01)	
Yes	75.0	1.07	(0.99, 1.17)	$\chi^2=5.11$, $p=0.0238$
Last pregnancy to birth interval (y):				
No previous pregnancies	75.7	1.01	(0.83, 1.23)	
<1	76.6	1.03	(0.72, 1.47)	
1-2	80.3	1.24	(1.07, 1.44)	
2-3	81.0	1.21	(1.03, 1.43)	
3-4	78.1	1.00	(0.82, 1.21)	
4-5	76.5	0.93	(0.74, 1.17)	
>5	70.7	0.69	(0.59, 0.81)	$\chi^2=59.34$, $p<0.0001$
No in household (excluding baby and lodgers)				
None	76.5	1.13	(0.87, 1.46)	
1, 2	75.1	1.01	(0.84, 1.21)	
3	82.1	1.51	(1.31, 1.74)	
4-5	76.5	1.15	(1.00, 1.33)	
6-7	72.9	0.96	(0.78, 1.18)	
8+	60.5	0.53	(0.40, 0.70)	$\chi^2=77.76$, $p<0.0001$

*Odds significantly ($p<0.01$) deviant from 1 are in bold.

Table V Comparison of odds of chickenpox (CHES) at different ages adjusted for predictors of chickenpox by 10 years (CHES)

	Chickenpox <7y		Chickenpox 7-10y	
	Adjusted odds ratio	(99% CI)	Adjusted odds ratio	(99% CI)
Father's occupational class:				
I	1.40	(1.11, 1.78)	1.35	(1.00, 1.82)
II	1.13	(0.96, 1.34)	1.15	(0.94, 1.36)
IIINM	1.08	(0.91, 1.27)	1.13	(0.94, 1.36)
IIIM	0.96	(0.85, 1.08)	1.00	(0.88, 1.13)
IV	0.82	(0.70, 0.97)	0.96	(0.81, 1.14)
V	0.79	(0.62, 1.02)	0.86	(0.67, 1.11)
No father figure	0.91	(0.66, 1.27)	0.82	(0.59, 1.16)
Not known	1.03	(0.74, 1.42)	0.83	(0.58, 1.21)
	$\chi^2=29.1$, 7df, $p=0.0001$		$\chi^2=14.81$, 7df, $p=0.0385$	
Parent's ethnic origin:				
European	1.17	(1.01, 1.36)	1.27	(1.08, 1.49)
Non-European	0.63	(0.48, 0.82)	0.55	(0.42, 0.72)
Unknown/adopted	1.36	(1.13, 1.64)	1.44	(1.17, 1.75)
	$\chi^2=23.41$, 2df, $p<0.0001$		$\chi^2=35.01$, 2df, $p<0.0001$	
Region of child's delivery:				
Scotland	0.73	(0.61, 0.88)	0.62	(0.52, 0.75)
North/North West	0.91	(0.80, 1.04)	0.97	(0.85, 1.17)
Yorks and Humb/East Midlands	1.08	(0.94, 1.25)	1.29	(1.10, 1.50)
West Midlands	0.98	(0.83, 1.16)	0.77	(0.64, 0.92)
East Anglia/London	1.49	(1.30, 1.72)	1.27	(1.07, 1.50)
South East	1.47	(1.29, 1.67)	1.45	(1.25, 1.70)
South West	0.99	(0.81, 1.21)	1.09	(0.88, 1.36)
Wales	0.65	(0.51, 0.82)	0.82	(0.66, 1.03)
	$\chi^2=137.09$, 7df, $p<0.0001$		$\chi^2=119.38$, 7df, $p<0.0001$	
Age mother left full-time education (y):				
≤14	0.75	(0.60, 0.93)	0.78	(0.62, 0.99)
15	0.89	(0.80, 0.99)	0.92	(0.81, 1.03)
16	0.95	(0.83, 1.09)	1.00	(0.86, 1.16)
17, 18	1.15	(0.99, 1.34)	1.08	(0.91, 1.30)
≥19	1.38	(1.13, 1.69)	1.29	(1.00, 1.66)
	$\chi^2=30.59$, 4df, $p<0.0001$		$\chi^2=13.07$, 4df, $p=0.0109$	
Last pregnancy to birth interval (y):				
No previous pregnancies	0.64	(0.57, 0.72)	1.15	(1.01, 1.30)
<2	1.00	(0.89, 1.13)	1.19	(1.04, 1.36)
2-3	1.22	(1.07, 1.39)	1.20	(1.02, 1.40)
3-5	1.39	(1.21, 1.59)	1.07	(0.90, 1.26)
>5	1.09	(0.80, 1.13)	0.70	(0.57, 0.85)
Not known/uncertain	0.97	(0.79, 1.21)	0.82	(0.64, 1.05)
	$\chi^2=142.19$, 5df, $p<0.0001$		$\chi^2=38.34$, 5df, $p<0.0001$	
No in household:				
2 or 3	0.94	(0.80, 1.10)	0.79	(0.67, 0.93)
4	0.95	(0.87, 1.04)	1.13	(1.02, 1.25)
5	1.07	(0.96, 1.19)	1.17	(1.04, 1.32)
≥6	1.05	(0.92, 1.19)	0.95	(0.85, 1.10)
	$\chi^2=5.64$, 3df, $p=0.1305$		$\chi^2=24.52$, 3df, $p=0.00016$	

*Values significantly different from 1 given in bold.

(table V). Approximately one half the cases of chickenpox in this cohort occurred in each of the two time periods. The cases used in these logistic regressions were cases before the 7th birthday compared with all those who had not contracted the disease by age 7 (the at risk population), and cases between 7 and 10 years compared with all those who had not contracted chickenpox by 10 (the at risk population).

The results indicate that the same social trends already reported characterise the incidence of the disease over both age periods. Patterns of association between reported chickenpox and father's occupational class, ethnic origin, maternal education, and geographical region were similar in the two age groups. Relationships with birth interval and household size, however, differed. Index children were more likely to catch the disease earlier if their next oldest sibling was at least two years older with a peak at three to five years difference in ages. Those index children who caught chickenpox later, however, were more likely to have older siblings closer in age to themselves. This may reflect the higher susceptibility of 2, 3, or 4 years olds to infection from older siblings returning home from school compared with the 6 or 7 year old whose exposure derives more from classmates.

The NCDS cohort

A similar analysis was conducted on the NCDS chickenpox data. Cases of chickenpox by 7 years and between 7 and 11 years were compared with the rest of the population at risk for their association with the same set of background factors found to be predictive of chickenpox by 10 years in CHES. In this analysis cases of reported chickenpox by 7 years which were denied at age 11 years ($n=500$) were omitted on the basis that the precise age of the child's chickenpox was uncertain. The "split age" analysis on the NCDS cohort produced less informative results (table VI). In NCDS, significant ($p<0.01$) variation for each independent variable was reached only for "region of birth" and "household size" (both 0-7 years chickenpox), and for "birth interval" (both age groups). For chickenpox between 0 and 7 years the higher odds in London, the South East, and South West and the lower odds in Scotland reached significance at the 1% level, with low odds in Wales falling between the 5% and 1% significance bands. For the children who caught chickenpox after age 7 years, significantly ($p<0.01$) high odds were seen in the Southern region with low odds in Scotland and Northern standard regions approaching significance ($p<0.05$). These results are broadly consistent with those of CHES and argue against a strong interaction between the age of infection and background social factors, although a trend towards the weakening of the odds in the older age group exists. For both age groups the birth interval remained a significant factor in the distribution of chickenpox in the population. As in the CHES data, the first child was protected against early but not later infection, with a sibling aged one to five years older increasing the odds of an early infection. Household size was a significant factor only for early chickenpox infection and was apparently more important than in CHES.

Direct comparison of the CHES and NCDS results are confounded by the appreciably different age specific susceptibility of chickenpox in the two cohorts. Although the prevalences of reported chickenpox by age 10 years in CHES (62%) and by 11 years in NCDS (77%) were not too dissimilar, the proportions of the population with a reported history of the disease by age 7 years differed substantially (CHES 30.4%, NCDS 61.8%).

Discussion

The data presented seem to indicate that reported chickenpox infections more commonly affect the more advantaged sectors of society. Furthermore, the risk of contraction of the disease in early childhood is slightly more dependent on social factors than later infections although similar trends are apparent. These data are distinct from another common infectious disease, measles, whose social distribution clearly follows lines of deprivation and poorer economic circumstances.¹² What explanations can account for this pattern?

One possibility that urban lifestyle is implicated has already been discounted as unlikely. Another is that reports of chickenpox are positively biased in the better educated, socially advantaged sectors of the population. This could be the case, for example, if other social groupings ignore or fail to

recognise the disease when symptoms are mild. However, although this factor might be responsible for social bias in seeking medical attention, it is much less likely to significantly affect responses to questions asked by health professionals in the home. The CHES questionnaire furthermore, had a "Not Known" category which, unless the mother was certain the child had either had or not had chickenpox, was available for recording an uncertain response. The proportion of "not known" responses was only 1.2% (n=121).

Alternatively, chickenpox may have a higher real prevalence in the more privileged groups. This was apparently the case, for example, for cases of appendicitis and paralytic poliomyelitis in the past. For appendicitis higher rates of subclinical infection (and hence immunological protection) in early childhood in poorer socioeconomic groups, because of more insanitary living conditions, statistically contrasted with reduced immunity and therefore increased susceptibility to acute disease in more advantaged sectors in society as domestic conditions improved.^{12 13} Should such a phenomenon apply to chickenpox, social stratification in titres of varicella-zoster immunoglobulin should be demonstrable in infancy.

IgG antibody to varicella-zoster virus antigen has been detected in the umbilical cord sera of infants delivered of women with maternal IgG antibody of a similar concentration assessed at delivery.¹⁴ This raises another epidemiological possibility—that women re-exposed to chickenpox in adulthood may be boosting an immunological response that is transferred passively to the fetus during pregnancy. Should this form of adult exposure be more prevalent in poorer socioeconomic groups then an epidemiological pattern like that of polio may emerge. There is no evidence, however, that late transfer of passive immunity from breast feeding confers any protection against chickenpox either in the population as a whole or in socially disadvantaged groups. In the CHES cohort chickenpox rates by age 10 years in breast-fed children who were born into socially disadvantaged circumstances according to a social index scale¹⁵ were similar to a comparable bottle-fed group ($\chi^2=0.41$, 1df, $p=0.524$).

Within the United Kingdom, regional variation in the prevalence of reported chickenpox illustrated by these data may be consistent with other reports about the international geographical distribution of the disease and the age at which it occurs. It has been known for some time that exposure to varicella in the industrialised world, as measured by a reported history of infection or the presence of anti-varicella antibodies, is almost universal by early middle age. In Britain, studies have shown that almost 80% of children are seropositive by 15 years of age¹⁶ while in the United States 82% of infections are recorded in children by 9 years⁶ and seroreactivity in urban, native born people approaches 100% by age 60.¹⁷ In Japan, seropositivity plateaued at 100% at 25 years of age.¹⁸

Unlike measles, however, which is almost universally a disease of early childhood throughout the world, there are accumulating reports of

Table VI Odds of chickenpox at different ages (NCDS) adjusted for factors independently predictive of chickenpox by 10 years (CHES)

	Chickenpox <7y		Chickenpox 7–11y	
	Adjusted odds ratio	(99% CI)	Adjusted odds ratio	(99% CI)
Father's social class:				
I	0.89	(0.70, 1.14)	1.14	(0.79, 1.66)
II	1.11	(0.95, 1.29)	1.15	(0.90, 1.46)
III	1.08	(0.97, 1.21)	0.99	(0.84, 1.17)
IV	0.94	(0.80, 1.10)	0.90	(0.71, 1.13)
V	1.01	(0.85, 1.20)	0.82	(0.62, 1.07)
No husband	0.98	(0.69, 1.39)	1.05	(0.63, 1.76)
	$\chi^2=9.37$, $p=0.0953$		$\chi^2=7.05$, $p=0.2167$	
Mother's place of birth:				
European	1.03	(0.83, 1.26)	0.92	(0.66, 1.28)
Non-European	0.97	(0.79, 1.20)	1.09	(0.78, 1.52)
	$\chi^2=0.05$, $p=0.8151$		$\chi^2=0.49$, $p=0.4929$	
Old standard region:				
Scotland	0.85	(0.73, 0.98)	0.84	(0.68, 1.04)
North Western	1.04	(0.91, 1.20)	0.90	(0.73, 1.13)
Northern	0.93	(0.79, 1.11)	0.78	(0.60, 1.02)
East and West Rid, North Midlands	1.12	(0.98, 1.28)	1.05	(0.85, 1.29)
Midlands	1.07	(0.91, 1.25)	0.99	(0.78, 1.27)
Eastern	1.01	(0.85, 1.20)	1.09	(0.83, 1.43)
South East, South West, London	1.13	(1.01, 1.26)	1.05	(0.88, 1.26)
Southern	1.03	(0.84, 1.27)	1.42	(1.02, 1.98)
Wales	0.86	(0.70, 1.05)	0.99	(0.73, 1.34)
	$\chi^2=24.76$, $p=0.0017$		$\chi^2=17.66$, $p=0.0236$	
Did father stay at school after earliest school leaving age?				
No	0.96	(0.89, 1.03)	0.96	(0.86, 1.07)
Yes	1.04	(0.97, 1.12)	1.04	(0.93, 1.16)
	$\chi^2=2.45$, $p=0.1173$		$\chi^2=0.79$, $p=0.3726$	
Last pregnancy to birth interval (y):				
No previous pregnancies	0.70	(0.59, 0.84)	1.17	(0.90, 1.52)
<1	1.13	(0.82, 1.54)	1.07	(0.64, 1.80)
1–2	1.26	(1.11, 1.43)	1.20	(0.97, 1.48)
2–3	1.17	(1.01, 1.35)	1.10	(0.87, 1.40)
3–4	1.19	(1.00, 1.41)	0.82	(0.61, 1.09)
4–5	1.09	(0.88, 1.34)	0.90	(0.64, 1.27)
>5	0.66	(0.57, 0.77)	0.82	(0.65, 1.03)
	$\chi^2=116.84$, $p<0.0001$		$\chi^2=17.02$, $p=0.0092$	
No in household excluding baby and lodgers:				
None	1.01	(0.81, 1.27)	1.18	(0.84, 1.65)
1, 2	0.98	(0.84, 1.15)	1.00	(0.79, 1.26)
3	1.50	(1.32, 1.69)	1.09	(0.89, 1.32)
4–5	1.18	(1.04, 1.34)	1.03	(0.84, 1.25)
6–7	0.87	(0.66, 1.15)	1.11	(0.83, 1.49)
8+	0.66	(0.50, 0.87)	0.69	(0.45, 1.04)
	$\chi^2=80.16$, $p<0.0001$		$\chi^2=7.35$, $p=0.1956$	

*Values significantly different from 1 given in bold

different chickenpox age distributions in tropical countries of the South compared with the temperature North. Studies conducted both within developing countries themselves and those reporting the susceptibility to chickenpox of migrants from those countries in the North support this conclusion. The mean age of chickenpox in one small West Bengal village was 23.4 years with 63% of cases over 15.¹⁹ In Somalia 46% of cases occurred in people over the age of 15.²⁰ Adolescent and young adult creoles in French Guiana were the most susceptible groups according to Poveda *et al*²¹ and Barss²² documented the susceptibility of adults in Papua New Guinea and its islands to chickenpox infections. In Angoda, Sri Lanka, hospital admission records between 1955 and 1959 showed that 71.5% of chickenpox cases were aged 20 or over.²³ Only 30% of student nurses aged 17–20 years possessed complement fixation antibodies to varicella-zoster antigen in Vellore, India²⁴ compared with 70–100% of similar age groups in England,²⁵ the United States,²⁶ and Canada.²⁷

Visitors to western countries from the tropics may be poorly protected against the disease and there are well documented outbreaks of chickenpox in Sri Lankan refugees²⁸ and Puerto Rican army recruits.²⁹ Nosocomial chickenpox infections affecting immigrant nurses from Sri Lanka and India³⁰ and the Philippines³¹ have also been reported. It may be no coincidence that most of these reports relate to islands where the circulation and transmission of the virus may be reduced. Alternatively, it raises the possibility that early exposure to varicella is associated with a more industrialised lifestyle, better conditions of sanitation and nutrition, and economically advantaged living conditions.

While inhabitants of tropical islands may be less exposed to the disease and may contract it late, if at all, this epidemiological pattern, together with the strong seasonal peaks in winter and spring,^{31 32} suggests that both ambient heat and humidity are associated with constraints on the activity of the virus. While seasonal patterns in infection may reflect changes in human behaviour, viral transmission or infectivity, or both, may be sensitive to environmental conditions. It has been suggested, for example, that varicella-zoster virus is sensitive to high ambient temperatures³³ and according to Venkitarama and John²³ varicella seems to be relatively uncommon in India in the hot months. Mean monthly chickenpox admission to the Fever Hospital in Angoda, Sri Lanka, during the hot monsoon period between 1955 and 1959 was 300.5 compared with the cooler dry season figure of 664.²³ The geographical prevalence figures determined in the present study and the regional death rates secondary to chickenpox between 1967 and 1985 prepared by the CDSC (Joseph personal communication) are consistent with a west (low)—east (high) gradient and a more efficient transmission in the drier parts of the UK. Tropical islands may not only constitute physical barriers to transmission but are also notably humid throughout the year.

A quite different hypothesis has been presented by Sinha¹⁹ who adopted the “epidemiological interference” hypothesis of Bang³⁴ to propose that the high prevalence in early childhood of respira-

tory Herpes infections in some developing countries, together with a degree of conferred, cross specific serological protection, postpones chickenpox infection to a later stage. The patchy serological profile data from the developing world, however, is more consistent with a lack of exposure to the antigen itself.

In conclusion the social epidemiology of chickenpox in two large representative cohorts of British schoolchildren shows patterns of susceptibility linked to measures of social advantage. The international distribution of chickenpox may reflect a similar trend on a wider scale, although it is possible that climatological parameters may also be involved. More research is indicated in accounting for these findings in view of the move towards providing a vaccination service against varicella-zoster. It would seem to be appropriate to recommend the closer monitoring of the disease in the UK before and in the event of a widespread vaccination service in order to assess differential susceptibility and to evaluate the immunisation protocols.

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