S. pneumoniae is an important childhood pathogen worldwide. It causes a wide spectrum of clinical illness ranging from otitis media to fatal meningitis. It is the most common cause of acute otitis media, sinusitis, bacteraemia, pneumonia, and meningitis.

Recognised risk factors for IPD in children include: anatomical or functional asplenia, congenital or acquired immunodeficiency, chronic renal disease, receipt of immunosuppressive chemotherapy, and ethnicity (for example, Native American, Australian aboriginal, and Polynesian children).

More recently, reports have suggested that children attending day care and those with frequent episodes of otitis media may be at increased risk.

Although specific factors increase the risk of IPD for the individual child it is not known what proportion of children with IPD have an underlying abnormality. The reported percentage of children in developed countries with IPD and a preceding health problem ranges from 22% to 64%.

As well as children with primary and secondary immunodeficiency, children with central nervous system malformations, congenital heart disease, chromosomal abnormalities, and physical malformations appear in one or more of the series. To what extent these other preceding problems are associated with an increased risk of IPD is not known.

The aim of this study was to describe a series of children with invasive pneumococcal disease and to identify factors associated with an increased risk of IPD.

**METHODS**

This was a case series of all children up to 18 years of age hospitalised at the John Radcliffe Hospital with IPD from July 1985 to May 2001, and residing in Oxfordshire. Patients presenting to other hospitals and referred to the John Radcliffe were excluded. Invasive pneumococcal disease was defined as the isolation of S. pneumoniae from a normally sterile body fluid in someone with a clinical diagnosis such as meningitis, pneumonia, or otitis media.

Cases were identified from laboratory surveillance data. From 1985 to 1995 cases were identified from the microbiology logbooks used to record pneumococcal isolates sent for serotyping. From 1995 to 2001 cases were identified from the enhanced notification statistics between 1986 and 1999. The children's paper and electronic medical records were reviewed. Data describing past medical history, presenting illness, and subsequent inpatient and outpatient management were abstracted using a structured pro forma.

Social deprivation was measured using the Jarman index. This index uses eight variables from the national census to produce a social deprivation score for each of the 9265 wards in England and Wales. The mean score for all wards in England and Wales is zero, with a higher score indicating a more socially deprived ward.

Data were double entered into a Microsoft Access 97 database and analysed using SAS version 8.2 (SAS Institute Inc., Cary, NC, USA); 95% confidence intervals were calculated using exact methods where necessary.

The proportion of children with a congenital abnormality was compared with the proportion of congenital abnormalities among live births in England and Wales based on notification statistics between 1986 and 1999.

**RESULTS**

One hundred and forty cases of IPD in children 18 years of age or younger resident in Oxfordshire and presenting to the John Radcliffe Hospital between July 1985 and May 2001 were identified from medical records. Of the 140 children with IPD, 75 (53%) had one pneumococcal disease focus, 64 (46%) had two disease foci, and one (1%) had three disease foci. One hundred and nineteen (85%) of the children had bacteraemia, 45 (32%) had meningitis, 39 (28%) had pneumonia, and three (2%) had osteomyelitis. Full medical record and electronic hospital data were available on 136 (97%); demographic, hospital utilisation, and microbiological data on the remaining 14 children were obtained from hospital data.

**Abbreviations:** CI, confidence interval; IPD, invasive pneumococcal disease
four were obtained from the hospital electronic records and laboratory databases.

Table 1 summarises the demographic features of the study sample. The distribution of cases across the four seasons was examined for the years 1986 to 2000 (n = 131). A greater proportion of cases occurred during the winter (31%) compared with the summer (21%), but this seasonal effect was not statistically significant.

The median age of cases was 1.5 years. Forty four (31%) cases were less than 1 year of age and 39 (28%) were between 1 and 2 years of age. Eighty two (59%) cases were males.

Social deprivation as measured by the Jarman index could be estimated for 128 (91%) of the 140 cases. The median Jarman score for the 129 cases was −2.5 (interquartile range −8.1 to 9.7). The median for all wards in the Oxfordshire region was −7.3 (interquartile range −13.0 to 0.4). This difference was statistically significant (Wilcoxon rank sum test, p < 0.001). The Jarman index did not vary with age, being similar for children less than 2 years of age (median −2.13, interquartile range −9.24 to 19.25) and without past problems (median −1.84, interquartile range −8.13 to 9.50) were similar (Wilcoxon rank two sample test, p = 0.70).

Table 3 compares the proportion of children with a congenital abnormality in the study group with the proportion of children in England and Wales born with a congenital abnormality. Congenital abnormalities of the central nervous system and heart, chromosomal abnormalities, eye malformations, and deafness were all more common in the children with IPD than expected from the national data. Odds ratios ranged from 32 (95% CI 6.6 to 96) for chromosomal abnormalities to 99 (95% CI 31 to 236) for central nervous system malformations.

A recent event immediately prior to the episode of IPD was present in 54 (40%) of the 136 children for whom the full medical records were reviewed. These events included a chest infection in two, a coughing illness of three or more weeks duration in four, otitis media in seven, other respiratory infections in 17, other infections in three, chemotherapy in three, a recent head injury in one, and a recent general anaesthetic and surgical procedure in two. Three infants presented within one day of birth.

DISCUSSION
The observed association between risk of infection and social deprivation is not new, but provides an important reminder of the health impact of social inequality. These findings extend the recent observations from the North Thames Region that social deprivation and crowding remain significant risk factors for bacterial meningitis in all age groups. Social deprivation scores did not differ between those with or without preceding health problems. Therefore it seems unlikely preceding problems. Table 2 shows the preceding health problems and median ages of cases with each type of problem. The children with preceding health problems were significantly older at the time of presentation with IPD than children without preceding health problems. The age at presentation with IPD varied significantly by type of preceding problem. When comparisons were made by specific previous problem, children with immunodeficiency, chromosomal abnormalities, cancer, and asthma were significantly older than children with no preceding health problem. The social deprivation score for those with (median −2.13, interquartile range −9.24 to 19.25) and without past problems (median −1.84, interquartile range −8.13 to 9.50) were similar (Wilcoxon rank two sample test, p = 0.70).
that the social deprivation effect is caused by the economic impact on a family of having a child with increased health needs. In addition to the likely increased exposure to invasive pneumococcal associated with household crowding, poorer access to health care, poorer quality housing and hygiene, increased exposure to cigarette smoke and poorer nutrition are all potential mechanisms by which social deprivation may increase the risk of invasive pneumococcal disease.

The strong associations between central nervous system, eye, ear, heart, and chromosomal abnormalities, and an increased risk of IPD is notable and has not been previously reported. The comparison with national congenital malformation rates at birth is crude but seems more likely to underestimate than overestimate the association—death from congenital malformation during childhood is not uncommon and is likely to outweigh the converse effect of recognition of abnormality after birth and of immigration of children with congenital malformations from other countries. However, the John Radcliffe Hospital is a tertiary referral centre for a number of congenital abnormalities, and children with pneumococcal disease may be more likely to be referred to the hospital if they have a congenital abnormality—resulting in the observed association.

The mechanism by which these congenital abnormalities might be associated with an increased risk of IPD is speculative. It is consistent with the concept of host genetic polymorphisms being associated with an increased risk of invasive pneumococcal infections. Alternatively they may result in anatomical or physiological abnormalities which increase the risk of IPD, such as aspiration in association with central nervous system disease, hypoxia in association with congenital heart disease, or craniofacial abnormalities, which in turn predispose to upper respiratory tract infections. This study sample included a wide age range of children. Social deprivation appeared to have an effect that was present across the age range. In contrast the increased risk of IPD associated with preceding health problems varied with age. Children with preceding health problems were significantly older than those without. The specific preceding health problems for which the age at presentation with IPD was increased—immunodeficiency, chromosomal abnormalities, cancer, and asthma—are all likely to be associated with impaired immune function or increased risk of a respiratory infection. Malignancies and chemotherapy are already recognised indications for pneumococcal vaccine. Whether or not asymptomatic children are also a group with a specific indication for pneumococcal immunisation needs to be confirmed.

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