Epidemiology and surveillance of meningococcal disease in England and Wales

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Background

- The HPA Meningococcal Reference Unit (MRU) has been providing data on meningococcal disease for England and Wales since 1984
- The methods used to ascertain meningococcal disease, to characterise the organism, and to determine the incidence between 1995 – 2006 are described.
- Meningococcal serogroup C conjugate (MCC) vaccine was introduced into the UK population in November 1999

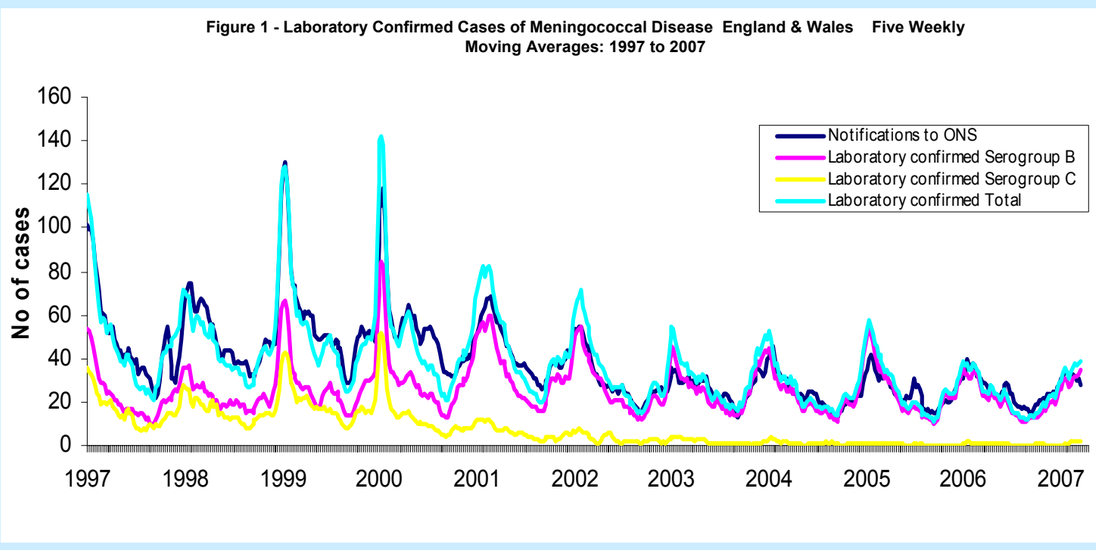
Methods

- Clinicians are required to notify all clinical cases of suspected meningococcal meningitis and septicaemia *via* the local Health Protection Units to the HPA Centre for Infections
- Since 1984, all microbiology laboratories have been encouraged to submit cultures of *N meningitidis* for characterisation to the MRU. Since October 1996, the MRU has provided a non-culture meningococcal PCR diagnostic service for England and Wales
- Isolates are characterised by serogroup, serotype and sero-subtype. MICs to therapeutic and prophylactic antibiotics (penicillin, cefotaxime, rifampicin and ciprofloxacin) are also determined.
- Non-culture confirmation is based on real-time Taqman® PCR assays; *ctrA* for detection, *siaD* for serogroup B, C, Y or W135 characterisation and *mynA* for serogroup A.
- Currently approximately 45% of cases are confirmed by PCR alone.

Results

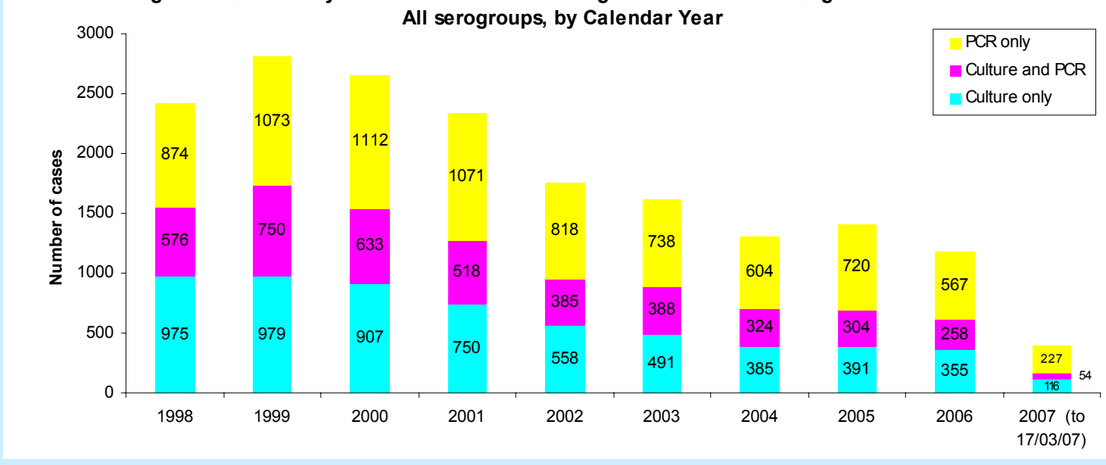
Good case ascertainment of meningococcal disease is demonstrated in Figure 1 by the close correlation between the number of clinical notifications and of laboratory confirmed cases, particularly in more recent years.

Figure 1 - Laboratory Confirmed Cases of Meningococcal Disease England & Wales Five Weekly Moving Averages: 1997 to 2007



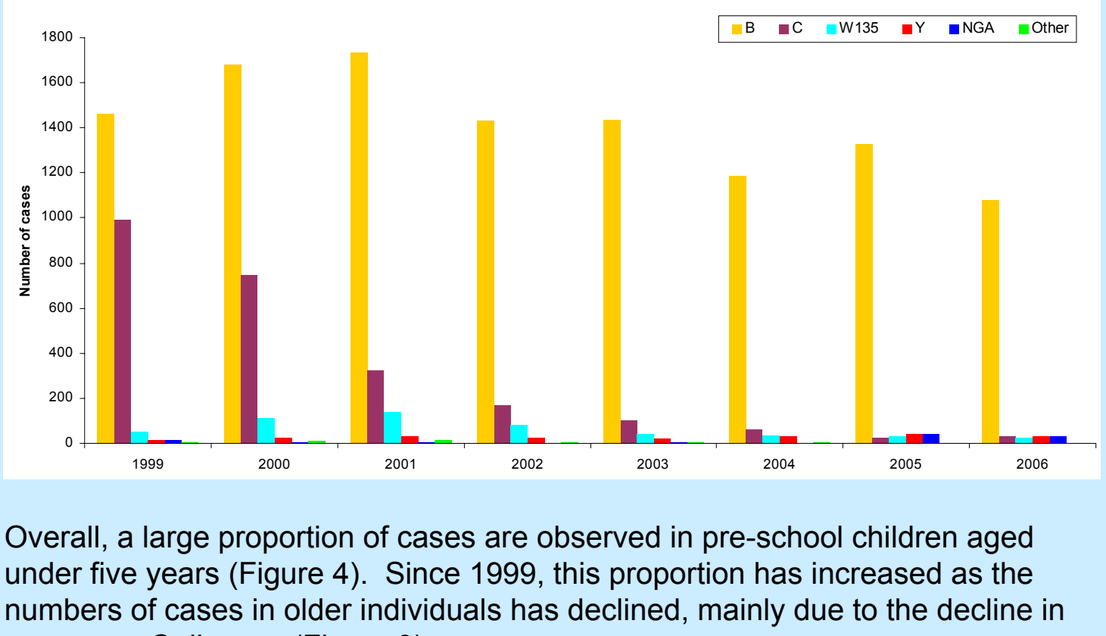
The incidence and numbers of laboratory-confirmed cases was highest in 1999, and has been steadily decreasing since (Figure 2).

Figure 2 - Laboratory Confirmed Cases of Meningococcal Disease in England and Wales All serogroups, by Calendar Year



The increase in 1999 was partly explained by better ascertainment resulting from the use of PCR. The decrease from 2000 is due to a major reduction in serogroup C cases resulting from MCC vaccination (Figure 3).

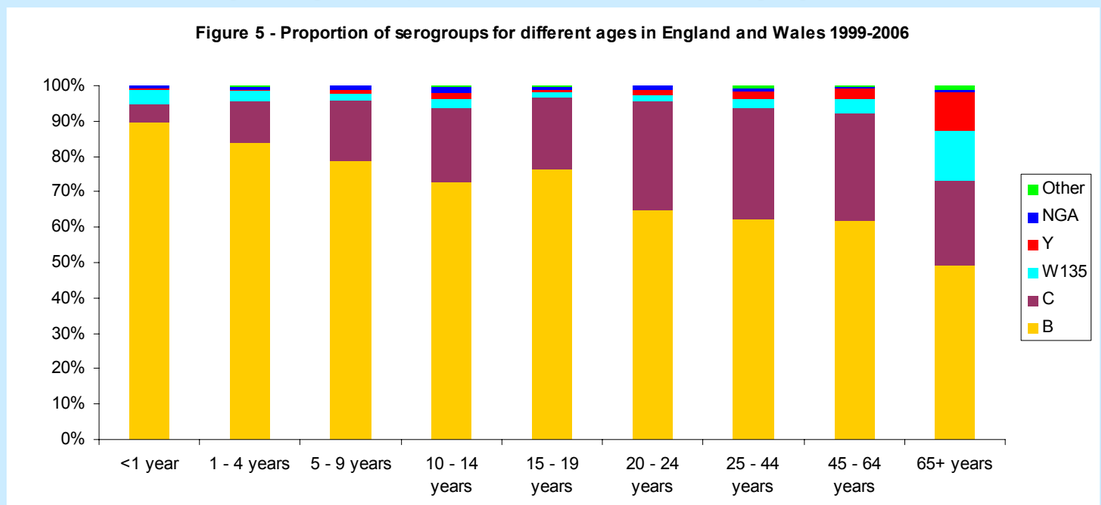
Figure 3 - Serogroups present in England and Wales 1999 -2006



Overall, a large proportion of cases are observed in pre-school children aged under five years (Figure 4). Since 1999, this proportion has increased as the numbers of cases in older individuals has declined, mainly due to the decline in serogroup C disease (Figure 3).

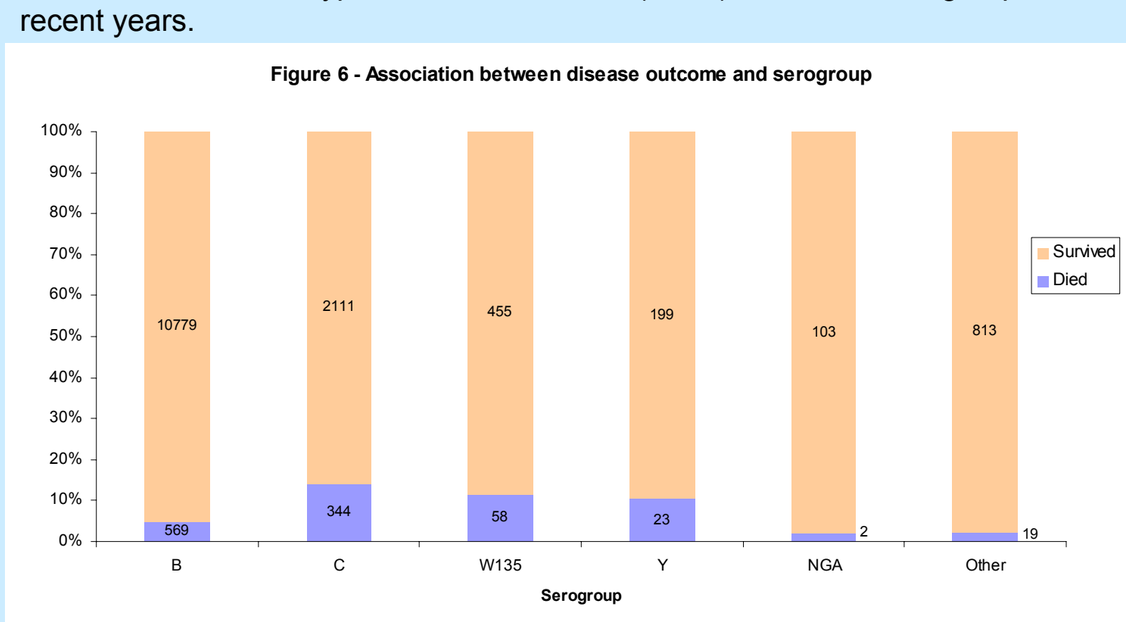
Serogroup distribution is also related to age (Figure 5), with non-serogroup B infections forming a larger proportion of cases in older age groups.

Figure 5 - Proportion of serogroups for different ages in England and Wales 1999-2006



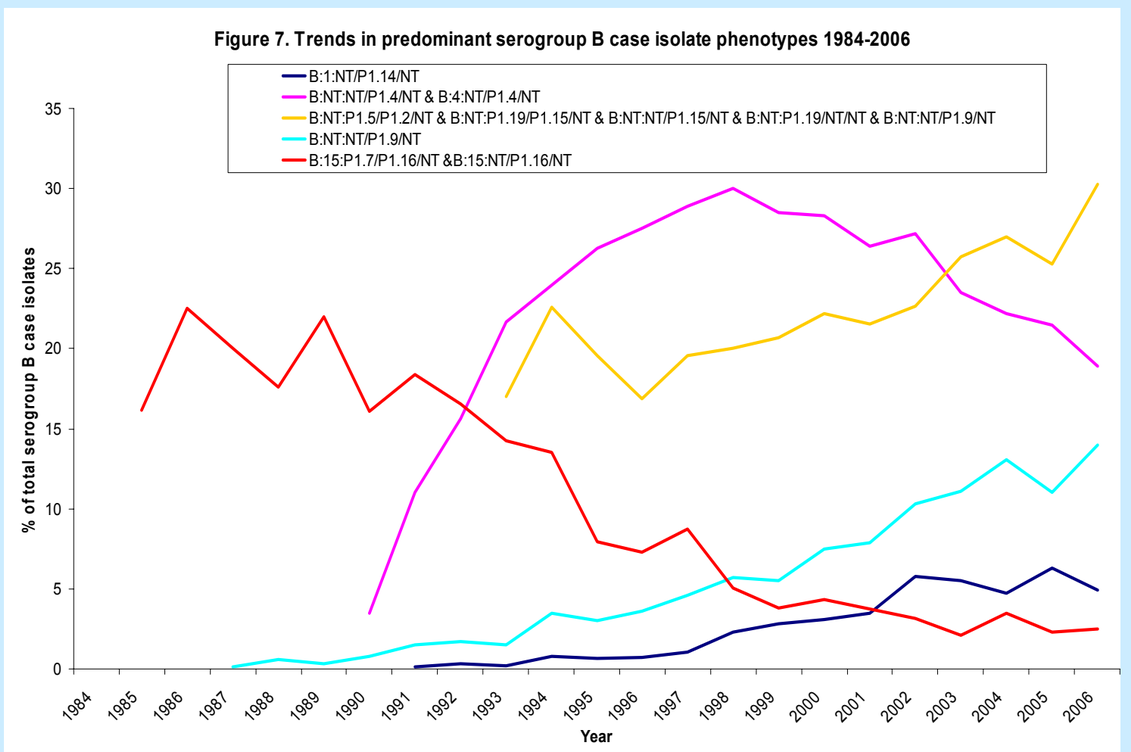
Serogroups C and W135 are most likely to result in adverse outcome with case fatality rates of 16.3% and 12.8% respectively (Figure 6). This is probably due to the association of 'hypervirulent' CC ST-11 (ET37) with these serogroups in recent years.

Figure 6 - Association between disease outcome and serogroup



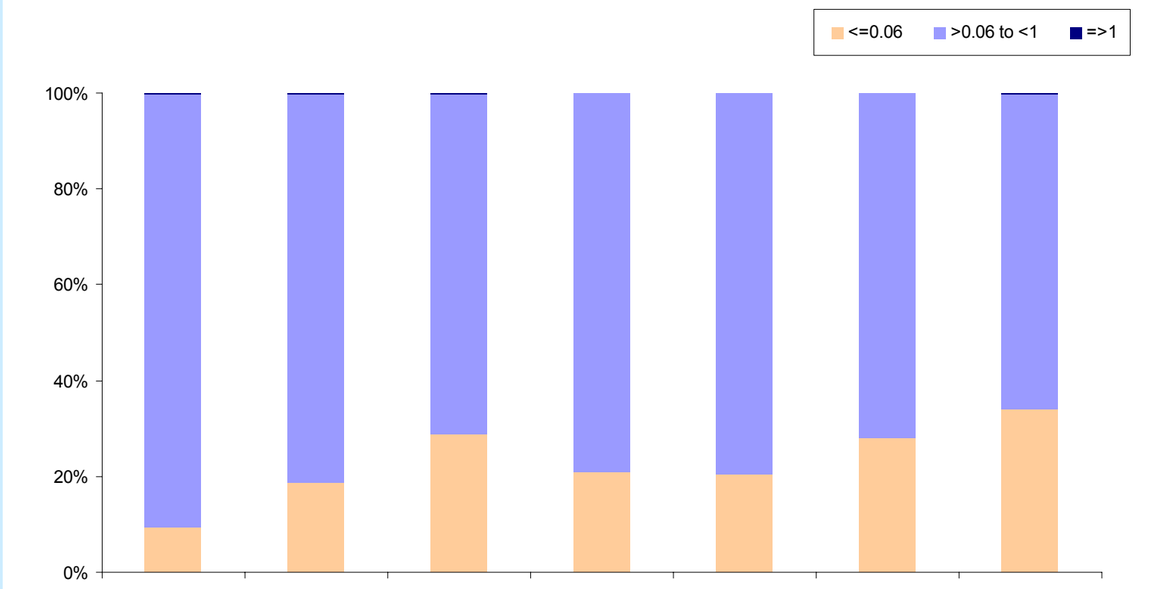
The predominant serogroup B phenotypes (Figure 7) varied over the years. Some strains such as B:15:P1.7 and B:15:P1.7,16 (representing CC ST-32), and B:4:P1.4 and B:4:NT, (representing CC ST-41/44) have declined naturally, while others such as B:NT:P1.9, B:NT:P1.19, B:NT:P1.15,19, B:NT:P1.15, B:NT:P1.5,2 (representing CC ST-269) have increased. Specifically, B:NT:P1.9 rose from 1.5% (1993) to 14% (2006). B:1:P1.14 isolates (representing CC ST-213) have also shown a steady increase from <0.5% (1992) to 5% (2006).

Figure 7. Trends in predominant serogroup B case isolate phenotypes 1984-2006



The proportion of cases with penicillin MIC of < 0.06µg/ml has remained fairly stable between 2001 and 2006, and there have been very few case isolates > 1µg/ml. (Figure 8). The highest proportion of case isolates are those with intermediate resistance ("less susceptible") to penicillin. The methodology used to determined MIC was changed in March 2006 from agar incorporation to Etest.

Figure 8 - Penicillin MIC (µg/ml) of England & Wales case isolates 2001 - 2006



Conclusions

- There has been major reduction of serogroup C disease following the introduction of MCC vaccine and there is evidence of herd immunity
- Serogroup B disease is now responsible for 90% of laboratory confirmed cases
- The increase in serogroup B observed up to 1999 has now reversed and cases fell by 45% between 2001 and 2006
- There is natural phenotypic and genotypic variation amongst all serogroups but particularly serogroup B