Rubella antibody status of patients attending a south-west London antenatal clinic, 2007–2012

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ABSTRACT

Mass vaccination with the measles-mumps-rubella (MMR) vaccine for children aged 12–15 months was introduced in 1988; schoolgirl vaccination was discontinued in 1996 and replaced by a second dose of MMR for preschool children and post-partum vaccination of susceptible women identified through antenatal testing. In the UK, declining uptake rates due to concerns about the MMR vaccine, and increasing numbers of cases in some European countries where rubella surveillance and preconceptional vaccination are inadequate, coupled with poor uptake rates, has started to show in the number of rubella-susceptible patients presenting at antenatal clinics (ANCs). In this study, samples were collected in serum separator tubes at the West Middlesex University Hospital (WMUH) ANC and sent to the laboratory. Rubella status was determined using a third-generation rubella IgG enzyme immunoassay. Any negative results were retested and confirmed using an alternative method. The concentrations were expressed as iu/mL (World Health Organization [WHO] standard). Over a five-year period, the number of rubella-susceptible patients increased from 4.1% to 6.8% of the total number of specimens tested. The current population susceptibility levels seem to be influenced by a number of factors: the target population, age at vaccination and the level of coverage, and exposure to wild virus.

KEY WORDS: Pregnancy.
Rubella.
Vaccination.

Introduction

Infection with the rubella virus typically causes a mild disease (German measles) in children and young adults. The disease is characterised by a rash that starts on the face and neck then spreads to the trunk and limbs, usually waning after three days (Fig. 1). Other symptoms include low-grade fever, nausea, swollen glands (suboccipital and posterior cervical lymphadenopathy), arthritis and joint pains, as well as conjunctivitis.[1]

Although rubella infection is usually mild, it can cause serious problems in fetal growth and development. In fact, rubella was the first virus shown to be a teratogen. In the first and second trimesters of pregnancy, fetal rubella infection often leads to severe abnormalities, which are collectively known as rubella embryopathy or congenital rubella syndrome (CRS; Gregg's syndrome). Congenital rubella syndrome has been associated with serious damage to the heart, ears and eyes of the newborn.[1,2]

In the UK, the rubella vaccine has been offered to schoolgirls since 1970 and mass vaccination with the measles-mumps-rubella (MMR) vaccine of children aged 12–15 months was introduced in 1988. Although the schoolgirl vaccination programme was discontinued in 1996, it was replaced by a second MMR vaccination for preschool children. Post-partum vaccination of susceptible women, who are identified through antenatal testing, continues.[3,4]

As a result of these measures, maternal rubella infection is now rare in many developed countries. Unfortunately, in some developing countries or in countries with inadequate rubella surveillance and preconceptional vaccination, rubella infection in pregnancy can still result in miscarriage, stillbirth or newborns with CRS.[5,6]

Uptake rates for the MMR vaccine fell in the UK in the 1990s following speculation that it might be linked with autism and Crohn's disease (the articles proposing this association were later retracted by *The Lancet*). These concerns were firmly refuted after investigation by the Health Protection Agency (HPA; now Public Health England [PHE]), among others, with the conclusion that the MMR

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Fig. 1. The disease is characterised by a rash that starts on the face and neck then spreads to the trunk and limbs, usually waning after three days.

Table 1. Immune status distribution among pregnant women screened at the antenatal clinic from 2007 to 2012.

Immune status	2007	2008	2009	2010	2011	2012	Total
Susceptible	52	231	210	282	373	390	1538
Low-level immune (LLI)	7	21	17	70	70	95	280
Immune	1374	4751	4913	5169	5187	6629	28023
Other	2	5	2	3	1	16	29
Total	1435	5008	5142	5524	5631	7130	29870
Susceptible (% of total)	3.6	4.6	4.1	5.1	6.6	5.5	5.1
Susceptible + LLI (% of total)	4.1	5.0	4.4	6.4	7.9	6.8	6.1
Fisher two-tailed *P* value	>0.9999			Not significant			

vaccine remained the safest and most effective means of protecting children against the dangerous diseases caused by measles, mumps, and rubella infections.[7,8] Recently, the number of rubella cases in some European countries has been increasing; this coupled with poor vaccine uptake rates may start to jeopardise the progress of rubella immunisation.[9–11]

From January 2007 to December 2012, Quest Diagnostics provided antenatal rubella antibody screening for the West Middlesex University Hospital (WNUH). A review of patient reports showed that the number of patients reported as non-immune or susceptible (<10 iu/mL) increased during this time period. The screening cut-off level of 10 iu/mL used to identify women at risk, was determined in 1995 on the basis of early epidemiological studies. This cut-off value now needs to be reviewed for correlation with immunity in a young, immunised, antenatal population.[12]

Materials and methods

Samples were collected in serum separator tubes in the antenatal clinic at WMUH and sent to the laboratory. Rubella immunity was determined using the Bioelisa Rubella IgG Colour assay (Biokit, Barcelona, Spain) supplied by Launch Diagnostics, and performed on the automated Best 2000 platform (Dynal/Invitrogen, Carlsbad, CA, USA). Negative results were retested and confirmed using the miniVIDAS Rubella IgG II assay (bioMérieux, Marcy l'Etoile, France). Both kits are CE-marked, having been standardised against the World Health Organization (WHO) international rubella virus serum standard,[13] with concentration expressed as iu/mL. The laboratory participates in the UK NEQAS scheme and the USCAP equivalent, and consistently produces results above the mean for its peer group.

Results

From 2007 to 2012, Quest Diagnostics tested 29,870 patients who attended the antenatal clinic for rubella antibodies. Of these, 1538 (5.1%) were reported as rubella-susceptible (<10 iu/mL, 'susceptible') and 280 (~1.0%) showed a modest immune response (10–15 iu/mL; 'low-level immune'); the remainder showed good immunity to rubella ('immune'). The numbers of susceptible, low-level immune and immune patients over the five-year period are presented in Table 1. In 2007, the number of susceptible and low-level immune patients accounted for 4.1% of the samples received. By 2011, this proportion had increased to 7.9%. The age distribution of the susceptible patients is shown in Table 2. Patients in the 21–25 age group showed the greatest increasing trend (11% increase from 2007 to 2010) and those in the 31–40 age group showed the greatest decreasing trend (8.9% decrease from 2008 to 2010). Figure 2 shows the ethnic distribution of the patients. No change in the proportion of susceptible patients was observed in any of the 14 ethnic groups.

Discussion

Rubella infection and congenital rubella are comparatively rare in the UK. However, sporadic cases do occur and are often associated with travel abroad. Elimination of rubella infection in Europe has progressed over the past 10 years, and the goal is complete elimination of the virus by 2015.[14]

In recent years, however, concern has grown about the possibility of a re-emergence, with potentially serious implications for susceptible pregnant women. Of particular concern are communities with relatively high rubella susceptibility rates due to several years of poor vaccine

Table 2. Age distribution of susceptible pregnant women from 2007 to 2012.

Age range	2007	2008	2009	2010	2011	2012
<20	9 (17%)	35 (15%)	30 (14%)	48 (17%)	77 (20%)	48 (12%)
21–25	9 (17%)	38 (17%)	49 (23%)	80 (28%)	84 (23%)	103 (26%)
26–30	19 (37%)	87 (38%)	86 (41%)	97 (34%)	117 (31%)	142 (36%)
31–40	13 (25%)	65 (28%)	41 (20%)	54 (19%)	89 (24%)	93 (24%)
40+	2 (3.8%)	6 (2.6%)	4 (1.9%)	3 (1.1%)	6 (1.6%)	4 (1.0%)
All ages	52	231	210	282	373	390

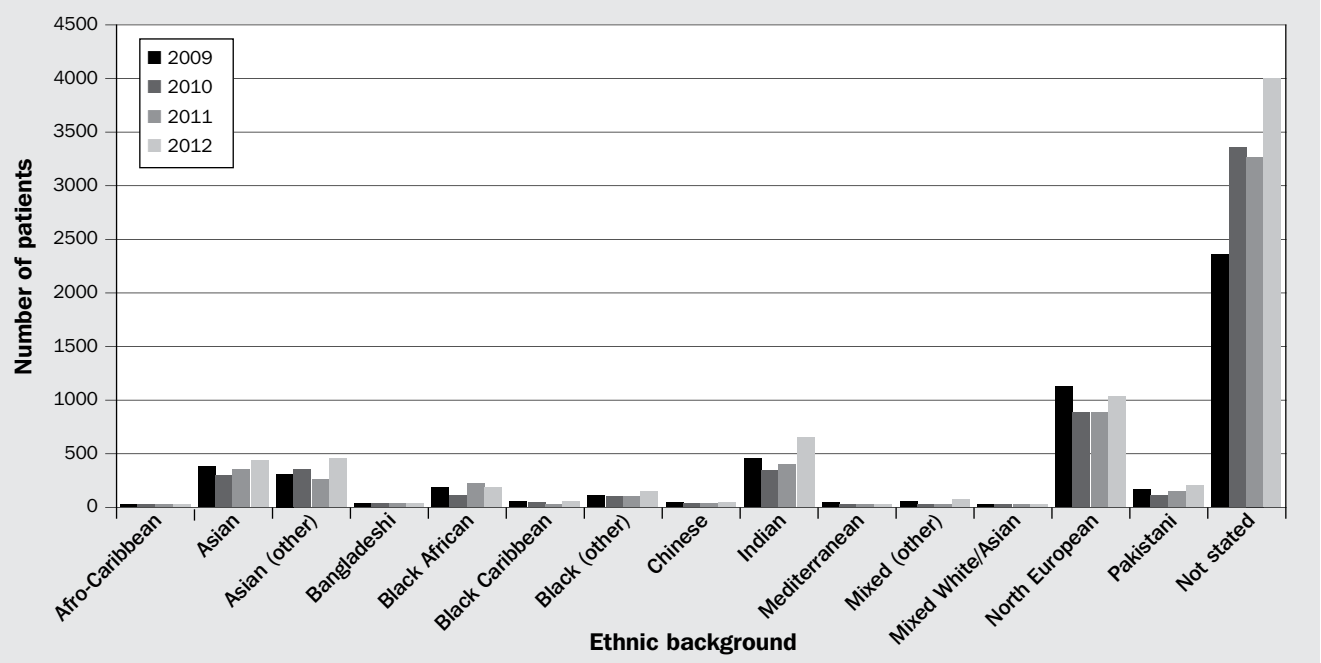

Fig. 2. Ethnic origin.

uptake, or the significant numbers of recent immigrants from countries lacking routine rubella vaccination programmes. Uptake rates of the combined MMR vaccine did decline due to poor publicity, and studies have shown that non-immunisers were more concerned about unknown, long-term side-effects of vaccines than about the diseases. Vaccines were often perceived as placing stress on the immune system rather than strengthening it.[15] On the other hand, those who did immunise believed the risk from vaccines was lower than the risk from disease, although they thought that the likelihood of contracting many of these diseases was low.

Over a five-year period, Quest Diagnostics reported on the rubella immune status of nearly 30,000 rubella samples obtained from women attending an antenatal clinic. What was apparent was the increasing number of women who were susceptible or had low-level immunity (10–15 iu/mL): in 2007, this group comprised 4.1% of the total number tested; by 2012 its proportion had increased to 6.8% (Table 1). Was there a single factor responsible for this rise? A review of the proportion of susceptible patients in each age group over the study period showed different trends among the age groups, with the largest increasing trend in the 21–25 age group.

Determining the relationship between ethnicity and susceptibility to rubella infection was difficult because electronic capture of ethnic origin was not available before 2009, and a large proportion of patients (55% over the four years) did not report their ethnic background. However, there was no definitive trend in any of the 14 ethnic groups. This seems to agree with the findings of other studies which showed that no single factor is solely responsible for an increase in susceptibility.[16–19]

The increase in percentage of susceptible patients in recent years could open the door to a re-emergence of rubella infection in the UK. If such a re-emergence were to occur, women who had emigrated to Britain in later childhood or in adulthood would be at higher risk of acquiring infection during pregnancy than would be the case for indigenous women. Appropriate local and national strategies should be implemented to ensure that all such women are offered rubella vaccination at the earliest opportunity. □

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References

1 World Health Organization. *Rubella Fact Sheet*. Geneva: WHO, 2013 (http://who.int/mediacentre/factsheets/fs367/en).
2 Lambert SR. Congenital rubella syndrome: the end is in sight. *Br J Ophthalmol* 2007; **91** (11): 1418–9.
3 Pebody RG, Edmunds WJ, Conyn-van Spaendonck M *et al*. The seroepidemiology of rubella in Western Europe. *Epidemiol Infect* 2000; **125** (2): 347–57. Erratum in *Epidemiol Infect* 2001; **126** (2): 333.
4 Tookey P. Rubella in England, Scotland and Wales. *Euro Surveill* 2004; **9** (4): 21–3.
5 Derrough T, Bacci S, Lopalco PL. Letter to the editor: commitment needed for the prevention of congenital rubella syndrome in Europe. *Euro Surveill* 2012; **17** (10): pii: 20106.
6 Usonis V, Anca I, Andre F *et al*. Rubella revisited: where are we on the road to disease elimination in Central Europe? *Vaccine* 2011; **29** (49): 9141–7.
7 Seagrott V. MMR vaccine and Crohn's disease: ecological study of hospital admissions in England, 1991 to 2002. *BMJ* 2005; **330** (7500): 1120–1.
8 Farrington CP, Miller E, Taylor B. MMR and autism: further evidence against a causal association. *Vaccine* 2001; **19** (27): 3632–5.
9 Owens SR. Injection of confidence. The recent controversy in the UK has led to falling MMR vaccination rates. *EMBO J* 2002; **3** (5): 406–9.
10 Fleck F. MMR controversy raises questions about publication ethics. *Bull World Health Organ* 2004; **82** (4): 311–2.
11 Lopalco P, Sprenger M. Do European doctors support measles,

mumps, rubella vaccination programmes enough? *Euro Surveill* 2011; **16** (39): pii: 19979.
12 Skendzel LP. Rubella immunity. Defining the level of protective antibody. *Am J Clin Pathol* 1996; **106** (2): 170–4.
13 Dimech W, Panagiotopoulos L, Francis B *et al*. Evaluation of eight anti-rubella virus immunoglobulin G immunoassays that report in international units per milliliter. *J Clin Microbiol* 2008; **46** (6): 1955–60.
14 Nardone A, Tischer A, Andrews N *et al*. Comparison of rubella seroepidemiology in 17 countries: progress towards international disease control targets. *Bull World Health Organ* 2008; **86** (2): 118–25.
15 Alfredsson R, Sensson E, Trollfors B, Borres MP. Why do parents hesitate to vaccinate their children against measles, mumps and rubella? *Acta Paediatr* 2004; **93** (9): 1232–7.
16 Matthews LA, Lawrance LM, Gray D, Gray S. An audit of rubella IgG antibody status in antenatal women in a NHS Trust over 5 years (2005–2009). *Epidemiol Infect* 2011; **139** (11): 1720–6.
17 Byrne L, Brant L, Reynolds C, Ramsey M. Seroprevalence of low rubella IgG antibody levels among antenatal women in England tested by NHS Blood and Transplant: 2004–2009. Is rubella susceptibility increasing? *Vaccine* 2012; **30** (2): 161–7.
18 Tookey PA, Cortina-Borja M, Peckham CS. Rubella susceptibility among pregnant women in North London, 1996–1999. *J Public Health Med* 2002; **24** (3): 211–6.
19 Lawman S, Morton K, Best JM. Reasons for rubella susceptibility among pregnant women in West Lambeth. *J R Soc Med* 1994; **87** (5): 263–4.