Oral Fluid Testing during 10 Years of Rubella Elimination, England and Wales

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Surveillance of rubella in England and Wales has included immunoglobulin M testing of oral (crevicular) fluid from reported case-patients since 1994. The need for laboratory confirmation to monitor rubella elimination is emphasized by poor sensitivity (51%, 95% confidence interval 48.9%–54.0%) and specificity (55%, 95% confidence interval 53.7%–55.6%) of the clinical case definition. During 1999–2008, oral fluid from 11,709 (84%) of 13,952 reported case-patients was tested; 143 (1.0%) cases were confirmed and 11,566 (99%) were discarded (annual investigation and discard rate of clinically suspected rubella cases was 2,208/100,000 population). Incidence of confirmed rubella increased from 0.50 to 0.77/1 million population when oral fluid testing was included. Oral fluid tests confirmed that cases were more likely to be in older, unvaccinated men. Testing of oral fluid has improved ascertainment of confirmed rubella in children and men and provided additional information for assessing UK progress toward the World Health Organization elimination goal.

In 1970, rubella vaccination was introduced in the United Kingdom for prepubertal girls and nonimmune women of childbearing age to protect them from the risks for rubella during pregnancy. Although this selective vaccination policy effectively reduced the number of cases of congenital rubella syndrome (CRS) and terminations of pregnancy, rubella during pregnancy continued to occur. In 1988, measles, mumps, and rubella (MMR) vaccine was introduced for universal vaccination at 13–15 months of age with the goal of eliminating circulating rubella. A considerable decrease in rubella in young children followed, but in 1993, clinically diagnosed and laboratory-confirmed rubella increased; the increase occurred predominantly in older men who had previously not been offered a rubella-containing vaccine. Therefore, in November 1994, rubella vaccine was included in a school catch-up campaign to prevent a predicted measles epidemic. Approximately 92% of children 5–16 years of age received combined measles–rubella vaccine. In 1996, to maintain measles control, a second dose of MMR was recommended for children 5 years of age.

For any disease in the elimination phase, accurate surveillance is necessary to identify reservoirs of infection and susceptible groups. In 2005, the World Health Organization (WHO) European Region adopted a resolution to eliminate indigenous rubella by 2010 (elimination goal of confirmed rubella incidence <1 per 1 million population). WHO has developed a clinical case definition for rubella, but identification of cases based on clinical suspicion alone becomes less reliable as disease incidence decreases. Therefore, for countries trying to eliminate rubella, laboratory confirmation of all suspected cases is recommended.

Before 1994, surveillance of laboratory-confirmed rubella in England and Wales was based mainly on detection of immunoglobulin (Ig) M against rubella in serum. However, because rubella infection is usually mild, physicians are reluctant to obtain blood samples for serum confirmation, especially from young children. There is also some reluctance to obtain serum from men because the diagnosis is of major clinical significance. Oral or crevicular fluid is a noninvasively obtained clinical specimen that is likely to be more acceptable, especially for children, and is safe and easy to obtain. Transudates from the capillary bed situated beneath the margin between the tooth and gum are obtained by rubbing an absorptive device between the gum and the cheek. These samples, which are distinguishable...
from saliva samples, contain mucosal cells that enable detection of the rubella virus by PCR. Methods for obtaining, extracting, and storing oral fluid samples are well established (7,10–13). Detection of rubella IgM in oral fluid has been validated and shown to be ≈90% sensitive and 99% specific compared with detection in serum (2). Samples are also suitable for genome detection (14,15). Therefore, since late 1994, the enhanced surveillance program in England and Wales has relied on oral fluid testing to provide laboratory confirmation for clinically diagnosed cases of measles, mumps, and rubella (however, serum testing is still recommended for confirmation of infection during pregnancy).

An additional increase in rubella incidence occurred during 1995–1998. Reports of rubella peaked in 1996 (a total of 9,081 clinically diagnosed cases were reported) (16). This situation offered an opportunity to evaluate the sensitivity and specificity of the WHO clinical case definition for rubella. In addition, we describe the added value of oral fluid testing during the subsequent 10 years of rubella elimination (1999–2008).

Methods

Since 1988, physicians in England and Wales have been required by law to report clinically suspected cases of rubella to the proper officer at the local health authority (usually a public health consultant in a Health Protection Unit [HPU]). Since late 1994, when a report is received, the HPU sends an oral fluid kit to the primary-care physician or patient for confirmatory testing. The kit is then returned by prepaid envelope to the Virus Reference Department at the Health Protection Agency Centre for Infections, for analysis. A request form contains vaccination history and, until July 2003, some brief clinical features (presence of a rash, fever, conjunctivitis, cough, and lymphadenopathy [type not specified]). Oral fluid testing was also used to test cases that were not formally reported as part of outbreaks in 3 universities associated with imported virus from Greece in 1999 (17). A similar process is used for measles (and mumps) (18,19). If there is a strong clinical or epidemiologic suspicion of rubella in samples tested for measles and for measles in samples tested for rubella, dual testing is performed.

Oral (crevicular) fluid specimens, obtained by wiping a specially designed sponge swab (oral test kit [Oracol; Malvern Medical Developments, Worcester, UK]) around the gum margins, were tested for rubella-specific IgM initially by using a solid-phase IgM–antibody capture radioimmunoassay (20). After 2002, an in-house assay for rubella IgG was introduced (21), and after 2003, all samples taken within 1 week after symptom onset that were negative for rubella IgM and rubella IgG were tested by reverse transcription–PCR for rubella virus (14). In 2006, the rubella solid-phase IgM–antibody capture radioimmunoassay was replaced by a commercial enzyme immunoassay (22).

Results

Accuracy of Clinical Case Definition

During January 1995–July 2003, of 29,825 reported case-patients, oral fluid from 17,042 (57%) was tested for IgM; complete clinical information was obtained for 12,220 (72%) patients who submitted oral fluid samples. The overall sensitivity of the clinical case definition of maculopapular rash and fever and lymphadenopathy was 51% (95% confidence interval 48.9%–54.0%) and the specific-


ity was 55% (95% confidence interval 53.7%–55.6%). The sensitivity and specificity of this case definition did not show significant variation by age, sex, and year of reporting (Table 1). However, the positive predictive value was significantly higher for persons ≥15 years of age (71% for persons 15–24 years of age compared with 1% for persons 5–9 years of age), for men (21% compared with 5% for women), and during the 1995–1998 epidemic period (20% compared with 1% in January 1999–July 2003).

Enhanced Surveillance, 1999–2008

During 1999–2008, a total of 13,952 clinically suspected rubella cases were reported, and the number of cases per year (1,000–2,000) remained stable (Figure). Oral fluid was tested for 11,709 (84%) case-patients; 143 (1.0%) positive results (1,000–2,000) remained stable (Figure). Oral rubella cases were reported, and the number of cases per year presented in Table 1.

Table 1. Accuracy of World Health Organization–modified clinical case definition for rubella, England and Wales, 1999–2008*

| Characteristic   | Sensitivity | Specificity | Positive predictive value |
|-----------------|-------------|-------------|----------------------------|
|                 | No. positive/ no. tested | % (95% CI) | No. positive/ no. tested | % (95% CI) | No. positive/ no. tested | % (95% CI) |
| Age, y          |             |             |                           |             |                           |             |
| <1              | 22/37       | 59.5 (43.6–75.3) | 1,467/2,804 | 52.3 (50.5–54.2) | 22/1,359 | 1.6 (1.0–2.3) |
| 1–4             | 34/75       | 45.3 (34.1–56.6) | 2,303/4,522 | 50.9 (49.5–52.4) | 34/2,253 | 1.5 (1.0–2.0) |
| 5–9             | 7/11        | 63.6 (35.2–92.1) | 1,006/1,640 | 61.3 (59.0–63.7) | 7/641   | 1.1 (0.3–1.9) |
| 10–14           | 10/32       | 31.3 (15.2–47.3) | 298/426    | 70.0 (65.6–74.3) | 10/138  | 7.2 (2.9–11.6) |
| 15–24           | 433/871     | 49.7 (46.4–53.0) | 281/462    | 60.8 (56.4–65.3) | 433/614 | 70.5 (66.9–74.1) |
| ≥25             | 256/455     | 56.3 (51.7–60.8) | 257/439    | 58.5 (53.9–63.2) | 256/438 | 58.4 (53.8–63.1) |
| Sex             |             |             |                           |             |                           |             |
| M               | 649/1,278   | 50.8 (48.0–53.5) | 2,877/5,326 | 54.0 (52.7–55.4) | 649/3,098 | 20.9 (19.5–22.4) |
| F               | 112/202     | 55.4 (48.6–62.3) | 2,744/4,954 | 55.3 (54.0–56.8) | 112/2,322 | 4.8 (3.95–5.7) |
| Year of report  |             |             |                           |             |                           |             |
| 1995 Jan–1998 Dec | 743/1,435 | 51.8 (49.2–54.4) | 3,630/6,677 | 54.4 (53.2–55.6) | 743/3,790 | 19.6 (18.3–20.9) |
| 1999 Jan–2003 Jul | 18/46     | 39.1 (25.0–53.2) | 1,983/3,616 | 54.8 (53.2–55.6) | 18/1,651 | 1.1 (0.6–1.6) |

*CI, confidence interval.
The annual incidence based on reported cases was highest in the North East region and lowest in Wales, whereas the annual incidence based on laboratory reports of serum confirmation was highest in London. Incidence based on oral fluid test results also differed, even after adjustment for the proportion of reported cases tested. The estimated overall incidence of confirmed rubella increased by 54% (from 0.50 cases/1 million population to 0.77 cases/1 million population) when data for oral fluid testing were included. Oral fluid data also changed the ranking of regions; the Eastern region overtook London in reporting the highest overall incidence. Although the West Midlands and Yorkshire and Humberside regions reported the lowest incidence on the basis of serum testing alone, after oral fluid testing was included, the East Midlands region reported the lowest overall incidence.

Discussion

Before vaccination was introduced, epidemics of rubella occurred regularly and caused mild rash illness, predominantly in children. In 1970, introduction of a selective vaccination policy in the United Kingdom aimed to reduce the risk for infection in early pregnancy and the risk for fetal death and CRS. Despite the success of the selective policy, MMR was adopted into the routine childhood vaccination schedule to eliminate circulating rubella and to further reduce the risk for CRS.

Since 1988, a clinical diagnosis of rubella has been reportable by registered medical practitioners in England and Wales under the statutory Notification of Infectious Diseases; there is no case definition. When an infection is commonly occurring in an area, the positive predictive value of a clinical diagnosis may be sufficient for accurate surveillance (24). However, because rubella has become less common, an increasing proportion of reported cases are likely to be caused by other infections that have similar clinical manifestations. The rash of rubella may be temporary and can resemble the rash caused by other viruses. For example, infection with parvovirus B19, human herpesvirus 6 (roseola infantum), and human herpesvirus 7 all involve rash and fever and may be misdiagnosed as rubella (25,26).

We have confirmed the low sensitivity and specificity of the clinical case definition and that this definition is not affected by age, sex, and period of reporting. Despite some missing clinical information and the absence of information about arthralgia, this finding suggests that the WHO clinical case definition is not sufficiently accurate for surveillance in the postvaccine era. This finding also emphasizes the need to have laboratory confirmation of all clinically diagnosed cases to accurately monitor rubella elimination (27).

Over the 10-year period of elimination, only ≈1 of 100 persons reported with clinically diagnosed rubella and who underwent oral fluid testing had confirmed cases. In addition, reported cases differed from laboratory-confirmed cases with respect to patient age, sex, vaccination status, and geographic distribution. We have therefore shown that surveillance based only on clinical reports would substantially overestimate the true incidence of rubella, particularly in children, and therefore give a misleading epidemiologic picture. Furthermore, we have shown that testing of oral fluid is acceptable in the United Kingdom and can be used to augment routine serologic diagnosis. Approximately one third of confirmed rubella cases were diagnosed by testing of oral fluid, which improved ascertainment of confirmed infections in children and men. In addition, by using

| Age, y | Total no. reports | No. cases confirmed by oral (crevicular) fluid testing | No. additional cases confirmed by serum testing |
|-------|------------------|-----------------------------------------------------|-----------------------------------------------|
|       | M    | F    | UNK | Total no. (%) | M    | F    | UNK | Total no. (%) | M    | F    | UNK | Total no. (%) |
| <1    | 1,823 | 1,674 | 23  | 3,520 (25.0) | 10   | 10   | 1   | 21 (15.0) | 4    | 2    | 1   | 7 (2.7) |
| 1–4   | 3,406 | 2,882 | 37  | 6,325 (45.0) | 14   | 9    | 1   | 24 (17.0) | 19   | 10   | 1   | 30 (11.0) |
| 5–9   | 1,083 | 1,005 | 14  | 2,102 (15.0) | 2    | 3    | 0   | 5 (3.5) | 2    | 2    | 0   | 4 (1.5) |
| 10–14 | 339   | 298   | 4   | 641 (4.6) | 3    | 1    | 0   | 4 (0.3) | 7    | 3    | 1   | 11 (4.2) |
| ≥15   | 506   | 729   | 7   | 1,242 (8.9) | 63   | 26   | 0   | 89 (62.0) | 93   | 109  | 7   | 209 (79.0) |
| UNK   | 54    | 56    | 12  | 122   | 0    | 0    | 0   | 0     | 0    | 2    | 0   | 2     |
| Total no. (%) | 7,211 | 6,644 | 97  | 13,952 | 92   | 49   | 2   | 143 | 125 | 128 | 10 | 263 |

†UNK, unknown.
PCR, we obtained genotype information on 12 samples that would have otherwise not been available.

Currently, there is only 1 commercial assay for testing rubella IgM in oral fluid, and this assay does not have an In Vitro Diagnostics license, thus limiting its use in some countries. However, in many regions, WHO is evaluating this assay as a tool for surveillance of infection (29). In the United Kingdom was 0.14/100,000 live-born infants (32), which was far below the WHO elimination goal of 1/100,000 live-born infants (4).

In recently published surveillance guidelines, WHO has recommended IgM detection, which can be performed with serum and oral fluid (31). These guidelines also describe performance indicators to assess the quality of national surveillance systems in the elimination phase. These indicators include a laboratory investigation rate (proportion of clinically suspected cases with adequate specimens for IgM testing) >80% and a detection rate for the number of clinically suspected rubella cases investigated and discarded by laboratory testing >2/100,000 population/year.

Data from the enhanced surveillance program show that for ∼84% of reported cases, oral fluid was tested, and results for 2,208 clinically suspected rubella cases per 100,000 population were investigated and discarded. This high discard rate would be feasible only with noninvasive testing and contributes to the high quality of the UK enhanced surveillance program. Information about the low rate of rubella supplements surveillance that confirms that CRS incidence in the United Kingdom was 0.14/100,000 live-born infants in 2007 (32), which was far below the WHO elimination goal of 1/100,000 live-born infants (4).

We confirmed that a clinical case definition alone is not sufficiently specific for surveillance of rubella in the elimination era and that laboratory confirmation by testing serum samples is biased and incomplete. Since 1999, a substantial proportion of confirmed cases of rubella identified through the enhanced surveillance scheme have occurred in unvaccinated men. With the availability of oral fluid testing, a high number and high proportion of suspected cases have been tested. However, numbers of confirmed rubella cases in children remain low, which is consistent with high levels of vaccine coverage and low levels of susceptibility in this younger age group (33). The enhanced oral fluid

**Table 3. Regional variation in rubella reports by oral (crevicular) fluid testing and confirmed cases from oral fluid and serum, England and Wales, 1999–2008**

| Region                  | No. cases confirmed by oral fluid testing (%) | No. cases confirmed by serum testing | Annual incidence of confirmed cases* |
|-------------------------|----------------------------------------------|-------------------------------------|---------------------------------------|
|                         | confirmed cases† | confirmed cases‡ | Total | Confirmed by oral fluid testing† | Confirmed by serum testing | Total |
| East Midlands           | 1,336            | 319              | 1,655 (80) | 3 | 9 | 0.09 | 0.21 | 0.29 |
| Eastern                 | 1,212            | 224              | 1,232 (102) | 44 | 32 | 0.80 | 0.59 | 1.41 |
| London                  | 1,653            | 226              | 1,452 (88) | 32 | 67 | 0.67 | 0.92 | 1.35 |
| North East              | 840              | 331              | 574 (68) | 0 | 12 | 0.00 | 0.47 | 0.47 |
| North West              | 1,662            | 245              | 1,505 (91) | 12 | 13 | 0.25 | 0.19 | 0.37 |
| South East              | 2,363            | 295              | 2,350 (99) | 18 | 48 | 0.34 | 0.60 | 0.82 |
| South West              | 1,109            | 224              | 857 (77) | 13 | 40 | 0.31 | 0.81 | 1.07 |
| West Midlands           | 1,235            | 234              | 821 (66) | 12 | 10 | 0.33 | 0.19 | 0.42 |
| Wales                   | 639              | 220              | 518 (81) | 1 | 10 | 0.02 | 0.34 | 0.38 |
| Yorkshire and Humberides | 1,903          | 382              | 1,260 (66) | 7 | 22 | 0.20 | 0.44 | 0.58 |
| Total                   | 13,952           | 266              | 11,709 (84) | 143 | 263 | 0.31 | 0.50 | 0.77 |

*Incidence per 1 million population. Annual incidence calculated by using 2001 census population figures.
†Adjusted for proportion of cases tested.
‡Several oral fluid tests were conducted for cases that were not formally reported during university outbreaks in 3 regions in 1999, including the South West, Eastern, and North West regions (17).
surveillance system has proven valuable for accurately assessing circulating rubella and CRS from the population of England and Wales.

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References

1. Health Protection Agency. General information on rubella (German measles). London: The Agency; 2009. 2–2-0009.
2. Ramsay ME, Brugha R, Brown DW, Cohen BJ, Miller E. Salivary diagnosis of rubella: a study of notified cases in the United Kingdom, 1991–8. Epidemiol Infect. 1998;120:315–9. DOI: 10.1017/S0950268898008838
3. Ramsay M, Gay N, Miller E, Rush M, White J, Morgan-Capner P, et al. The epidemiology of measles in England and Wales: rationale for the 1994 national vaccination campaign. Commun Dis Rep CDR Rev. 1994;4:R141–6.
4. Regional World Health Organization Office for Europe. Strategic plan for measles and congenital rubella infection in the WHO European Region. Copenhagen: The Organization; 2003.
5. World Health Organization Vaccine Assessment and Monitoring team DoVaB. WHO-recommended standards for surveillance of selected vaccine preventable diseases. Geneva: The Organization; 2003.
6. Malamud D. Oral diagnostic testing for detecting human immunodeficiency virus-1 antibodies: a technology whose time has come. Am J Med. 1997;102:9–14. DOI: 10.1016/S0002-9343(97)00032-6
7. Mortimer PP, Parry JV. The use of saliva for viral diagnosis and screening. Epidemiol Infect. 1988;101:197–201. DOI: 10.1017/S095026880004108
8. Parry JV, Mortimer PP. Non-invasive virological diagnosis: are saliva and urine specimens adequate substitutes for blood? Review of Medical Microbiology. 1991;1:73–8.
9. Parry JV. Simple and reliable salivary tests for HIV and hepatitis A and B virus diagnosis and surveillance. Ann NY Acad Sci. 1993;694:216–33. DOI: 10.1111/j.1749-6632.1993.tb18355.x
10. Nokes DJ, Enqueselassie F, Vyse A, Negatu W, Cutts FT, Brown DW. An evaluation of oral-fluid collection devices for the determination of rubella antibody status in a rural Ethiopian community. Trans R Soc Trop Med Hyg. 1998;92:679–85. DOI: 10.1016/S0035-9203(98)90811-2
11. Eckstein MB, Brown DW, Foster A, Richards AF, Gilbert CE, Vijayalakshmi P. Congenital rubella in south India: diagnosis using saliva from infants with cataract. BMJ. 1996;312:161.
12. Nokes DJ, Enqueselassie F, Negatu W, Vyse AJ, Cohen BJ, Brown DW, et al. Has oral fluid the potential to replace serum for the evaluation of population immunity levels? A study of measles, rubella and hepatitis B in rural Ethiopia. Bull World Health Organ. 2001;79:588–95.
13. Jin L, Vyse A, Brown DW. The role of RT-PCR assay of oral fluid for diagnosis and surveillance of measles, mumps and rubella. Bull World Health Organ. 2002;80:76–7.
14. Vyse AJ, Jin L. An RT-PCR assay using oral fluid samples to detect rubella virus genome for epidemiological surveillance. Mol Cell Probes. 2002;16:93–7. DOI: 10.1006/mcpn.2001.0390
15. Abernathy E, Cabezas C, Sun H, Zheng Q, Chen MH, Castillo-Solorzano C, et al. Confirmation of rubella within 4 days of rash onset: comparison of rubella virus RNA detection in oral fluid with immunoglobulin M detection in serum or oral fluid. J Clin Microbiol. 2009;47:182–8. DOI: 10.1128/JCM.01231-08
16. Miller F, Waight P, Gay N, Ramsay M, Vurdien J, Morgan-Capner P, et al. The epidemiology of rubella in England and Wales before and after the 1994 measles and rubella vaccination campaign: fourth joint report from the PHLS and the National Congenital Rubella Surveillance Programme. Commun Dis Rep CDR Rev. 1997;7:R26–32.
17. Rubella in university students. Commun Dis Rep CDR Wkly. 1999;9:113, 116.
18. Ramsay ME, Jin L, White J, Litton P, Cohen B, Brown D. The elimination of indigenous measles transmission in England and Wales. J Infect Dis. 2003;187(Suppl 1):S198–207. DOI: 10.1086/368024
19. Savage E, Ramsay M, White J, Beard S, Lawson H, Hanjan R, et al. Mumps outbreaks across England and Wales in 2004: observational study. BMJ. 2005;330:1119–20. DOI: 10.1136/bmj.330.7500.1119
20. Perry KR, Brown DW, Parry JV, Panday S, Pkipkin C, Richards A. Detection of measles, mumps, and rubella antibodies in saliva using antibody capture radioimmunoassay. J Med Virol. 1993;40:235–40. DOI: 10.1002/jmv.1890400312
21. Vyse AJ, Brown DW, Cohen BJ, Samuel R, Nokes DJ. Detection of rubella virus–specific immunoglobulin G in saliva by an amplification-based enzyme-linked immunosorbent assay using monoclonal antibody to fluorescent isothiocyanate. J Clin Microbiol. 1999;37:391–5.
22. Vijaylakshmi P, Muthukkaruppan VR, Rajasundari A, Korukluoglu G, Negatu W, Warrener LA, et al. Evaluation of a commercial rubella IgM assay for use on oral fluid samples for diagnosis and surveillance of congenital rubella syndrome and postnatal rubella. J Clin Virol. 2006;37:265–8. DOI: 10.1016/j.jcv.2006.09.005
23. Thomas HI, Morgan-Capner P, Enders G, O'Shea S, Caldicott D, Best JM. Persistence of specific IgM and low avidity specific IgG1 following primary rubella. J Virol Methods. 1992;39:149–55. DOI: 10.1016/0166-0934(92)90133-X
24. Vyse AJ, Gay NJ, White JM, Ramsay ME, Brown DW, Cohen BJ, et al. Evolution of surveillance of measles, mumps, and rubella in England and Wales: providing the platform for evidence-based vaccination policy. Epidemiol Rev. 2002;24:125–36. DOI: 10.1093/epirev/mxf002
25. Tait DR, Ward KN, Brown DW, Miller E. Exanthem subitum (roseola infantum) misdiagnosed as measles or rubella. BMJ. 1996;312:101–2.
26. Hogan PA. Viral exanthems in childhood. Australas J Dermatol. 1996;37(Suppl 1):S14–6. DOI: 10.1111/j.1440-0960.1996.tb01071.x
27. de Oliveira SA, Camacho LA, Medeiros Pereira AC, Bulhoes MM, Agius AF, Siqueira MM. Performance of rubella suspect IgM assay for use on oral fluid samples for diagnosis and surveillance of congenital rubella syndrome and postnatal rubella. J Clin Virol. 2008;40:64–7. DOI: 10.1016/j.jcv.2008.05.002
28. Recommendations from an ad hoc meeting of the WHO Measles and Rubella Laboratory Network (LabNet) on use of alternative diagnostic samples for measles and rubella surveillance. MMWR Morb Mortal Wkly Rep. 2008;57:657–60.
29. Centers for Disease Control and Prevention. Mumps epidemic—United Kingdom, 2004–2005. MMWR Morb Mortal Wkly Rep. 2006;55:173–5.
30. United Kingdom Department of Health. The MMR catch-up programme. 2008 Aug 7 [cited 2010 Jul 7]. http://www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Professionalletters/Chiefmedicalofficerletters/DH_086837

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31. Regional World Health Organization Office for Europe. Surveillance guidelines for measles, rubella and congenital rubella syndrome in the WHO European Region. Copenhagen: The Organization; 2009.
32. EUVAC. Rubella surveillance report 2000–2007 [cited 2010 Jul 7]. http://www.euvac.net/graphics/euvac/pdf/rubella_report.pdf
33. Vyse AJ, Gay NJ, Hesketh LM, Pebody R, Morgan-Capner P, Miller E. Interpreting serological surveys using mixture models: the seroepidemiology of measles, mumps and rubella in England and Wales at the beginning of the 21st century. Epidemiol Infect. 2006;134:1303–12. DOI: 10.1017/S0950268806006340

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