Publicity linking eggs with salmonellosis probably did not affect the results. Much of the press coverage referred to the situation in the United States. That there was no significant difference between reported egg consumption in subjects interviewed before or after the median date of interview implies that neither government statements or media coverage influenced people in their reporting.

England and Wales are experiencing an epidemic of food poisoning caused by *S enteritidis* phage type 4. This study supports previous findings that eggs, egg products, and precooked chicken are significant vehicles of infection and for the first time in a large national study confirms their importance in indigenous sporadic cases. The proportion of eggs contaminated is low,[16] but because as many as 30 million eggs are consumed daily the number of human infections caused nationally represents an important public health problem. Whether imperfect practice in kitchens has contributed to the striking increase in *S enteritidis* food poisoning or not there is no evidence that standards have declined in recent years; the best solution is to combine public health education with a reduction in contamination of eggs and infection of poultry with salmonella. This will require the eradication of *S enteritidis* from layer and broiler flocks, and the first stage in this strategy must be to identify infected flocks.

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Fetal infection after maternal reinfection with rubella: criteria for defining reinfection

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Abstract

Five cases of asymptomatic maternal reinfection with rubella are described that occurred in England and Wales during 1985-8 and resulted in intrauterine infection. The criteria for diagnosing reinfection are described. In four cases the rubella contact was with the woman's own children. Two women had therapeutic abortions, rubella virus being recovered from the products of conception, and three were delivered of infants with congenitally acquired disease.

Though the risks associated with maternal reinfection with rubella are very small and being measured in a prospective study, it is hoped that the recently introduced augmented programme of rubella vaccination will reduce rubella in the community and therefore this small risk still further.

Introduction

Reinfection with rubella may occur and has been reported after both naturally acquired and vaccine induced infection. Reinfection is usually subclinical and is detected serologically, most commonly among pregnant women who have had close and prolonged contact with rubella at home. Reinfection in pregnancy has been considered to present a minimal risk to the fetus, and mothers are usually reassured that there is no risk or only a minimal one to the fetus.[1,2] Nevertheless, there have been several isolated reports of fetal infection and malformation resulting from maternal reinfection (reviewed by Morgan-Capner[3]). We report five such cases.

Patients and methods

Cases were referred by obstetricians, paediatricians, and microbiologists or were identified from reports to the Communicable Disease Surveillance Centre by laboratories in England and Wales during 1985-8. Standard techniques were used for serological testing of mothers and infants and for isolating rubella virus from the products of conception or from throat swabs taken from infants.[4] When possible the avidity of specific IgG1 was measured; high avidity suggests recent reinfection.[5]

Results

The table shows details of the five cases; all five women were without symptoms throughout pregnancy. Three women (cases 1-3) were serologically investigated after contact with rubella between four and eight weeks' gestation, when their children had symptoms like rubella. IgM antibody (specific for rubella) was detected in serum samples taken from all three women after contact; subsequent samples from two of them (cases 1 and 2) showed a decline in titre. Reinfection was diagnosed because antibody had been detected by radial haemolysis at >15 000 IU/l on two occasions before the affected pregnancy; these serum samples were not available for retesting. The results of

Serological results and outcome of pregnancy in five cases of confirmed maternal reinfection with rubella during pregnancy, 1985-8

Case No	Mother's age (years)/ parity	Vaccination history	Year rubella antibodies previously detected*	Rubella contact early in pregnancy	Maternal results in affected pregnancy: Avidity IgG	Maternal results in affected pregnancy: IgM antibodies (arbitrary units)	Outcome of pregnancy (year)	Virus isolated from products of conception or infant
1	26/2	1973 (documented)	1984 1985	Own child	High	19	Therapeutic abortion (1988)	Yes
2	26/2	None	1981 1986	Own children	High	17	Therapeutic abortion (1988)	Yes
3	28/4	Not known	1981 1983	Own child	NA	>40	Infant with virologically confirmed congenital rubella syndrome (1986)	NA
4	31/2	1978 (History only)	1980† 1981†	Own child	NA	NA	Infant with virologically confirmed congenital rubella syndrome (1985)	Yes
5	32/1	1974 (documented)	1980†	None reported	NA	NA	Infant with virologically confirmed congenital rubella syndrome (1986)	Yes

*By radial haemolysis. †Serum samples not available for retesting. NA=Serum sample not available.

avidity testing in two of the three women (cases 1 and 2) supported the diagnosis of reinfection. These two women had therapeutic abortions and rubella virus was isolated from the products of conception. The third woman (case 3) continued to term and IgM antibodies specific for rubella were detected in blood samples from her infant; follow up showed bilateral deafness, retinopathy, and mental retardation. The remaining two cases (4 and 5) were identified after the birth of an infant with confirmed congenital rubella, with such clinical features as congenital heart defects, cataracts, retinopathy, and deafness. Further details of these cases will be reported elsewhere.

Discussion

The risks associated with maternal reinfection with rubella cannot be assessed unless clear criteria for diagnosing reinfection are established. Many previous reports of reinfection with rubella in pregnancy apparently resulting in fetal malformation are difficult to interpret accurately as evidence of pre-existing rubella antibodies was not adequate.[3] A working party of the Medical Research Council's subcommittee on rubella vaccines, which included us, recommended that evidence of reinfection would be accepted if a person with pre-existing rubella antibodies showed a significant rise in antibody concentration or a rubella specific IgM response, or both. If serum samples obtained before reinfection were not available for retesting evidence of pre-existing antibody would be accepted if there were at least two laboratory reports of antibody detected by radial haemolysis or other reliable technique at a concentration >15 000 IU/l. A documented history of rubella vaccination followed by at least one test for rubella antibodies giving positive results by radial haemolysis or an alternative reliable technique would also be acceptable. The five cases reported here fulfil these criteria.

How common is fetal damage after maternal reinfection? Studies in 41 women with asymptomatic reinfection early in pregnancy in whom booster antibody responses or specific IgM antibodies, or both, were detected showed that neither fetal infection nor damage occurred.[1,2] Our five cases, however, confirm that fetal damage may occasionally result from maternal reinfection. A further five cases that apparently resulted from reinfection have also been reported in other countries,[6-10] and we are aware of other cases that are yet to be reported in Britain. Nevertheless, fetal damage after maternal reinfection with rubella is likely to be rare. The five cases we report were among 554 rubella infections in pregnancy and 24 cases of congenital rubella reported to the Communicable Disease Surveillance Centre from 1985 to 1988; 9% (50) of the women were reported to have rubella antibody on previous screening or had a documented history of vaccination. There may therefore have been other cases of reinfection during this time. Most women, however, had only one previous test giving positive results for rubella antibodies, and this could have been falsely reported as positive owing to technical or clerical errors.[11] Failure of the vaccine may be the reason for rubella occasionally occurring in vaccinated women.

We receive many inquiries from obstetricians, general practitioners, and virologists from Britain and abroad seeking advice about the risks associated with maternal reinfection in pregnancy. Until the risks of fetal damage are measured it is difficult to counsel patients satisfactorily or advise those responsible for their management. To define the risks of reinfection accurately a prospective study has been set up in which laboratories conducting diagnostic tests for rubella report cases to the Communicable Disease Surveillance Centre. When mothers elect for termination of pregnancy it will entail determining whether the fetus has been infected and when pregnancies proceed to term whether the infants have any clinical or virological evidence of infection.

A technique for the prenatal diagnosis of intrauterine infection with rubella for women who have serological evidence of reinfection would be invaluable in identifying pregnancies at risk. Although IgM antibody specific for rubella can be detected in fetal blood in most cases of congenital infection, it may not appear until as late as 23 weeks' gestation,[12,13] which inevitably limits the practical value of this technique. Reliable techniques that are applicable in early pregnancy are not yet available, although preliminary studies using nucleic acid hybridisation to detect rubella virus RNA in chorionic villus samples are promising.[14] Further well controlled studies to validate this technique are required, as well as studies to evaluate more sensitive techniques, such as the polymerase chain reaction.[15]

Why some women experience reinfection with a sufficient viraemia to affect the fetus is unknown. Those with immunity induced by vaccination may be more susceptible to reinfection than those with naturally acquired immunity because of qualitative differences in the immune response.[16] Some women may have a defect in their rubella specific immune responses, such as an inability to produce antibodies to the protective epitope of the virus or a defect in their rubella specific lymphoproliferative response. A defective cytomegalovirus specific lymphoproliferative response has been suggested as a possible explanation for why some mothers transmit cytomegalovirus to the fetus.[17]

Cases in which fetal damage results from maternal reinfection by rubella may raise medicolegal issues. If an affected baby was born to a woman with evidence of pre-existing immunity fulfilling the criteria described

the doctor or manufacturer of the vaccine could not be considered to have been negligent. Nevertheless, unless a no fault compensation scheme is established such cases are likely to entail parents in considerable expense over a prolonged period and create considerable adverse publicity for rubella vaccination. Indeed, this has occurred recently; it would be unfortunate if such adverse publicity destroys the public's confidence in a remarkably effective and safe vaccine.

The selective rubella vaccination programme in the United Kingdom was recently augmented by the introduction of a combined measles, mumps, and rubella vaccine for children of both sexes.[18] Although this programme will reduce the circulation of rubella in the community and thereby decrease the risk of exposure of pregnant women to the virus, cases of reinfection will probably continue to be diagnosed for some years. Until rubella infection is eradicated consideration must be given to testing all pregnant women who have contact with or develop illnesses like rubella, even if they have a history of rubella vaccination and have been reported previously to have rubella antibodies.

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Cusum plotting of temperature charts for assessing antimicrobial treatment in neutropenic patients

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Patients with severe neutropenia are at risk of life threatening infection in proportion to their neutrophil count.[1] They are treated empirically on developing fever with a combination of broad spectrum antibacterial agents. The interpretation of their temperature charts, which are commonly chaotic, causes added confusion.

We compiled temperature charts for patients requiring antibiotics to assess the usefulness of cusum plotting in monitoring patients' progress and to determine the merit of modifying treatment during the febrile episode.

Cumulative sum (cusum) is a statistical manoeuvre that permits rapid analysis and identification of trends in a series of data. Cusum plots may be performed on any data gathered serially; their main use is in quality control in medical laboratories.[2] Their value in analysing clinical data has been outlined.[3-5] To apply cusum plots to temperature measurements a reference temperature is selected, which is subtracted from each successive temperature recording and the remainder (which may be positive or negative) is added arithmetically to the previous sum. This cumulative sum is plotted against time. If successive temperature readings are the same as the reference temperature the plot remains at zero; if the temperature rises or falls the plot does likewise. Changes to a sustained higher or lower temperature result in a plot with an upward or downward gradient respectively. In interpreting cusum plots changes in gradient (not plot height) and inflection points are important, but these may be disguised slightly by the reference temperature chosen.

Patients, methods, and results

We retrospectively analysed by cusum plots conventional temperature charts of 25 neutropenic patients (neutrophil count $<1{\cdot}0\times10^9$/l) who had developed a fever. These were calculated in two ways. In 14 patients (group A) the reference temperature was calculated as the mean of five temperature readings before the fever; all subsequent values were then plotted as a cusum plot. In 11 patients (group B) we chose four reference temperatures (37·2 °C, 37·6 °C, 38·2 °C, and the mean of the first six febrile points); the cumulative sum was then continued with successive temperature recordings.

Of the 14 charts of patients in group A, five showed a clear inflection associated with starting antimicrobial chemotherapy; no other useful information was obtained. Of the 11 charts of patients in group B, eight showed an association between starting treatment and resolution of the fever. In three patients the upward trend in temperature continued despite treatment and reversed only with an increasing granulocyte count $>1{\cdot}0\times10^9$/l. The trend was most easily interpreted with either 37·6°C or the mean of the first six temperature points during the fever as the reference. In five patients the cusum distribution showed clearly that the temperature trend was improving; further antimicrobial agents, however, had been given on the basis of a perceived non-response from the conventional temperature charts (figure.)