

# Two cases of measles in pregnant women immediately preceding delivery (case reports)

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## Summary

Measles is an acute exanthema spread by airborne infection and still occurs sporadically in Japan. Its mortality rate is estimated to be 0.1% and it has no specific therapy. Here, we present two cases of measles in pregnant women immediately preceding delivery. It is required to prevent the perinatal spread of measles when pregnant women are infected immediately preceding delivery. We measured the measles antibody titer of 1,393 pregnant women by enzyme immunoassay between 2004 and 2008. The antibody-positive rate was 87.7%, but the antibody titer tended to be low in childbearing age. Preventive treatment with measles vaccination is extremely important before pregnancy in order to prevent perinatal measles.

**Key words:** Measles; Airborne infection; Vaccine; Antibody titer; Enzyme immunoassay; Gelatin particle agglutination test.

## Introduction

Measles is an acute exanthema spread highly by airborne infection. We describe two cases of measles in pregnant women immediately preceding delivery. If a pregnant woman develops measles in peripartum it is difficult to control and prevent the aggravation. We report and discuss the management of measles in pregnancy.

## Case Reports

### Case 1

The first case is that of a 29-year-old woman (gravida 1, para 1) who was admitted to our hospital for placenta previa at 28 + 5 weeks of pregnancy. There had been no abnormalities in the mother or fetus during the pregnancy. At 31 + 0 weeks, the appearance of warning bleeding led to emergency admission. At 31 + 1 weeks, a clinical diagnosis of measles was made by a dermatologist following the development of fever (39°C) and whole-body rash. The mother had no previous history of measles infection, and the measles antibody titer (hemagglutination inhibition (HI) test) was negative (less than eightfold increase) in the first trimester. She was placed in a private room on the obstetric ward and ritodrine was administered as a tocolytic agent along with fluid therapy. No anomalies were observed either with ultrasound (US) or fetal heart monitoring. However, two days later due to the continuation of warning bleeding, an abnormal skin condition and deteriorating hepatic function, an emergency cesarean section was carried out at 31 + 3 weeks. The infant was male, weighed 1,654 g, and had Apgar scores of 1 and 8 after 1 and 5 min, respectively. Immediately after birth, tracheal intubation was performed on the infant and 120 mg/kg surfactant was administered; however, there were no symptoms of respiratory distress syndrome and the infant was extubated at two days. Immunoglobulin (0.05 g; Mitsubishi Pharma Corporation) was intramuscularly administered to the infant to prevent measles infection; however, measles developed without onset of rash or pneumonia. The

mother's rash disappeared two days after delivery, and she was discharged eight days after delivery. The baby was admitted to the neonatal intensive care unit, and discharged on day 38 without complications.

In this case, both the mother and the child were quarantined but measurement of antibody titer for measles among medical staff or obstetric ward patients was not implemented. There was, however, no onset of measles symptoms in either staff or patients.

### Case 2

The second case is that of a 24-year-old woman (gravida 0, para 0) who was regularly examined at a local clinic and whose pregnancy had progressed without any major problems for both the mother and child. At 36 + 4 weeks, skin symptoms appeared and at 36 + 6 weeks, Koplik's spots, a slight fever of 37.1–37.4°C, and facial rash appeared. Following a diagnosis of measles by a dermatologist, the mother was admitted to our hospital for consultation at 37 + 1 weeks. The mother had no previous history of measles infection, and measles antibody titer (HI test) was negative (less than eightfold increase) in the first trimester. No anomalies were observed either with US or fetal heart monitoring and home treatment was prescribed. However, the next day, a temperature of 39.°C and the onset of uterine contractions led to emergency admission. To avoid measles transmission to other patients, she was placed in a negative pressure room. Immunoglobulin (5 g) was administered as transplacental treatment, together with 200 µg/min ritodrine and 1 µg/h magnesium as a tocolytic agent. However, the uterine contractions continued with the fetus in breech presentation and thus an emergency cesarean section was carried out the same day. The infant was male, weighed 2,784 g, and had Apgar scores of 9 and 10 after 1 and 5 min, respectively. Quarantine of the mother was required, but this was not possible at our hospital. The baby had to be transferred to another hospital. Two days after delivery, the mother's temperature decreased to 36°C and skin symptoms improved. The infant received preventive treatment of immunoglobulin for three days and was returned to this hospital five days after the transfer. The infant subsequently showed no symptoms of measles. Both the mother and the child were discharged from the hospital on day 8 after delivery.

Measles antibody titer measurement was carried out with

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informed consent among medical staff and patients admitted to the maternity ward, but no one tested negative. One member of the medical staff, however, developed measles symptoms but was immediately isolated and transmission to obstetric ward patients and newborn infants was successfully prevented.

## Discussion

Measles is highly infectious and causes acute exanthema with febrile illness to more than 90% of people who do not have immune antibodies. Since the start of routine immunization in Japan in 1978, there have been no major measles outbreaks. However, the retention of measles virus antibody in the adult population is around 80% and it is estimated that around 100,000 people are affected every year [1]. The reasons for this are thought to be the low immunization rate of around 70%, primary vaccine failure when live vaccines are used because of lack of conferment of immunity, and secondary vaccine failure when antibody titer decreases due to lack of efficacy of booster vaccination. During pregnancy, the mother's immunity decreases due to hormonal changes. There is sufficient potential for women to become infected with measles during pregnancy to necessitate a management strategy.

The measles vaccine is a live vaccine and contraindicated during pregnancy. It is essential that women who test negative for measles antibodies during pregnancy (less than eightfold increase) are prevented from coming into contact with measles patients. On the other hand, it is recommended that in the future women should be given the live measles vaccine post partum [2]. However, this may not be realistic because mothers give priority to child-rearing upon leaving the hospital and hospital visits may become more difficult after delivery. Thus, awareness programmes in obstetric units at the time of hospital discharge are necessary to promote postpartum immunization.

Titration methods include the enzyme immunoassay (EIA) and gelatin particle agglutination (PA) test. The PA method is cheap and highly sensitive, and is recommended for screening. The average adult antibody titer is assumed to be 1:512-1024 as determined by the PA method. EIA is also highly sensitive, but care in its interpretation must be taken because of different cutoff values with each diagnostic kit.

We measured measles antibody titers using EIA in 1,393 pregnant women between 2004 and 2008. Detection of IgG antibody to measles was done by a commercial EIA kit (SRL Inc, Tokyo, Japan). Approval for the study was obtained from our institution's ethics committee. We found a positive rate of 87.7%, which was defined as an antibody titer greater than 8.0 (Table 1). However, with EIA, there is a large bias in the interpretation of the antibody titer ( $34.1 \pm 31.7$  (mean  $\pm$  S.D.)). It is difficult to know what level of antibody titer can prevent the onset of measles. We used the two-tailed Student's t-test for comparison of measles antibody titer between different age groups and found that the antibody titer tends to be low in childbearing age (Figure 1). On

Table 1. — Detailed results of the study population.

Age	≤ 19	20-24	25-29	30-34	35-39	40 ≥	Total
<i>Antibody titer</i>							
negative (< 4)	1	16	24	21	6	1	69
equivocal (4-8)	2	17	32	34	17	1	103
positive (> 8)	15	114	297	457	276	62	1221
Positive rate	83.3%	77.6%	84.1%	89.3%	92.3%	96.7%	87.7%

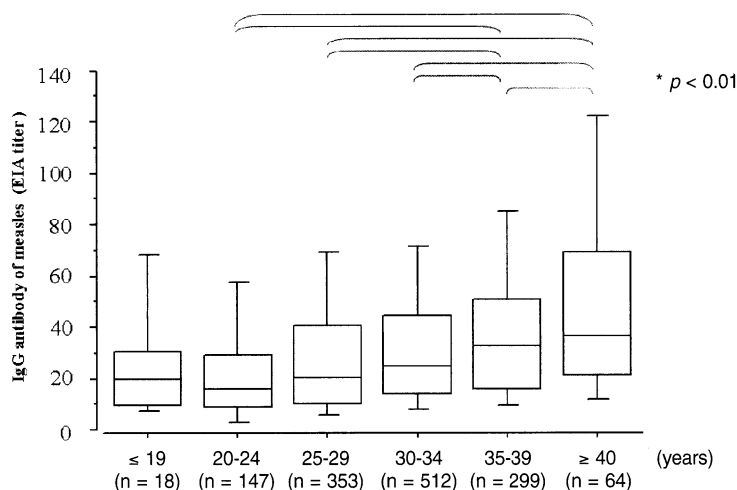


Figure 1. — Measles antibody titer in different age groups.

the other hand, measles infection is a concern in pregnant women.

In the event of contact with a measles patient during pregnancy, it is important that antibody levels are checked immediately. Those testing negative, with a less than eightfold increase should receive 15-50 mg/kg immunoglobulin intramuscularly within six days to prevent the onset or minimize the severity of the illness [3].

Even if measles develops during pregnancy, there is still no clear evidence for teratogenicity even in the first trimester. However, because the combined rate of miscarriage or premature birth within two weeks of onset is 30% [4], treatment to suppress uterine contractions is frequently required. In particular, in addition to reduced humoral immunity during pregnancy, infection with measles reduces cellular immunity for approximately one month, and pneumonia and other complications can easily develop concurrently. In such cases, the mother and child can develop serious illness, and intensive care and isolation are necessary.

Congenital measles in an infant was first reported in 1920 [5]. It is assumed that the fatality rate of congenital measles in infants reaches 27% because there is insufficient transmission of maternal antibody to the child [6]. If a pregnant woman develops measles, tocolysis should be performed for as long as possible. Importantly, it is necessary to prevent the onset of measles in the perinatal period.

Furthermore, it is necessary to take preventive measures against infection of other mothers, infants and hospital staff. Regular measurement of antibody titer in

medical staffs and immediate inoculation of those testing negative is particularly desirable. If medical staff come into contact with a pregnant woman with measles, their antibody levels should be checked immediately. Live vaccine should be administered within 72 hours of exposure, and steps must be taken to prevent infection of other patients.

We diagnosed two cases of measles on the basis of clinical findings alone (fever, Koplic's spots, and whole body rash). However, because measles may be confused with other diseases, the World Health Organization (WHO) has recommended that the diagnosis of measles should be confirmed by laboratory testing [7]. A laboratory diagnosis is most frequently made serologically. The WHO Global Measles Laboratory Network uses serum IgM alone as the standard test to confirm the diagnosis of measles [8, 9]. However, in countries with a very low prevalence of measles, such as the US, this approach has a high likelihood of yielding false-positive results [8]. Thus, in countries with a low prevalence of measles, use of paired acute- and convalescent-phase sera for anti-measles IgM and IgG is a reasonable approach [8]; at least a fourfold increase in anti-measles antibody titer is indicative of infection [10].

There is currently a global movement toward the eradication of measles, which has been limited to around ten cases per year in Europe and the US. However, it is estimated that around 100,000 people in Japan are affected each year and there are calls from both within the country and outside for stronger measures to be taken. It is recommended that the live measles vaccine be administered twice- at one year of age and on commencing elementary education, to acquire measles immunity. The opportunity for adults to receive a booster vaccination at an appropriate point should also be considered for long-term immunity.

In the case of occasional outbreaks in obstetric wards as described above, care should be taken to prevent mother to child infection, and medical staff should take steps to maintain their own immunity.

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