FIG 2—Needle biopsy specimen of liver six months after stopping herbal challenge. The inflammatory changes shown in fig 1 have resolved.

authenticated.² Mistletoe, however, contains several potential toxins (β -phenylethylamine, tyramine, acetylcholine, and propionylcholine). The herbal tablets used by our patient contained 90 mg mistletoe extract, which is not a large dose—for example, Potters' *Cyclopaedia of Botanical Drugs and Preparations* recommends 2–8 g.

We have found no record of any toxic reactions to mistletoe in man, and it has not been implicated in drug-induced hepatitis,³ though other herbs may cause severe liver injury.^{4 5} Although

mistletoe was the most likely toxin in this case, we thought that trying to obtain definitive proof with a second challenge test using mistletoe extract alone was not justifiable because of the severity of the histological change after the first challenge test.

Mistletoe is widely used in herbal remedies and until May 1978 a bronchodilator preparation (Felsol) containing mistletoe extract was listed in MIMS. Herbal remedies may be purchased without prescription and are much more commonly consumed than many doctors realise. This case shows that active hepatitis may result from their consumption, but there may well be cases in which the hepatitis remains subclinical and so progresses insidiously. Herbal remedies might also be an aetiological factor in the development of so-called cryptogenic cirrhosis.

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Congenital rubella affecting an infant whose mother had rubella antibodies before conception

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Abstract

A woman who had had high titres of rubella antibodies some months before she became pregnant gave birth to an infant in whom congenital rubella was confirmed at 4 months.

Rubella haemagglutination inhibition tests, complement fixation tests, and immunofluorescence tests with anti-human IgG were carried out on sera from the mother. Rubella antibody titres in sera obtained in March 1971, seven and a half months before conception, were equivalent to 400 units, which is usually taken as indicating good immunity. Rubella virus was isolated from the baby's nose and throat in July 1973 but was not isolated from a cervical swab taken from the mother in December 1973; tests of her immunological competence did not show any definite abnormality.

The presence of high levels of rubella haemagglutina-

tion inhibition antibodies does not invariably confer immunity or exclude the possibility of congenital rubella in a subsequent pregnancy.

Introduction

Virologically confirmed rubella reinfections, with disease of a fetus, are rare.^{1–3} We describe a baby severely affected by congenital rubella whose mother had high titres of rubella antibodies some months before she became pregnant. This case may be important with regard to current policies in rubella prophylaxis and the diagnosis of congenital rubella.

Case report

The baby was born in March 1973 and died in October 1976, the first child of healthy, unrelated parents who were both laboratory technicians. The mother had been told that she had contracted rubella when aged 7; she had not been immunised. Because she was considering becoming pregnant she deliberately came into contact with a colleague with suspected rubella in early October 1971. She did not develop any symptoms and arranged to have her rubella haemagglutination inhibition titre estimated at East Birmingham Hospital on 30 October. The titre (400 units) suggested good immunity, but rubella-specific IgM antibodies were not estimated. Blood samples for laboratory reference purposes taken from her in September 1970 and March 1971 were later found to have similar antibody levels. She

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became pregnant seven and a half months after the last estimation of antibodies. During the pregnancy she was not in known contact with rubella and was well apart from slight malaise and sickness at two and a half months' gestation. On 8 March 1973 she was delivered normally of an infant girl weighing 2400 g at 39½ weeks' gestation.

The baby was small with head circumference 31 cm, length 45 cm, and disproportionately small hands and eyes. She fed with difficulty and remained in the special-care nursery for three weeks, being tube-fed with expressed breast milk.

At 3½ months bilateral lens opacities were noted. The baby was slow at feeding and unresponsive and had increased limb muscle tone. The head circumference had only slightly increased to 34 cm, and she gained weight slowly. Rubella virus was isolated from nose and throat swabs collected when she was 4 months old, and congenital rubella was diagnosed.

Subsequently, she made only slow progress in growth and development and had severe thoracic kyphoscoliosis, coxa vara, spastic quadriplegia, and microcephaly. She responded only to loud sounds and was visually inattentive, with anterior cataracts and pigmented retinas. No abnormality was detected in the cardiovascular system. After a series of chest infections she died in October 1976, aged 3 years 7 months. Necropsy was not performed.

In January 1979 the mother was delivered of a normal infant with no signs of congenital rubella.

Virological and immunological investigations

A haemagglutination inhibition test was carried out according to the method described by Stewart *et al.*⁴ Sera were pretreated with 25% kaolin to remove non-specific inhibitors. Erythrocytes from day-old chicks or pigeons were used as indicator cells; haemagglutinin and standard reference sera were obtained from the Public Health Laboratory Service (PHLS) standards laboratory and the microtitre (Dynatech) system used. A complement fixation test was performed using the overnight fixation technique described by Bradstreet and Taylor⁵ modified to use the microtitre system. The antigen was obtained from the PHLS standards laboratory. Tests to detect neutralisation antibody to rubella virus were not performed.

Rubella virus was isolated in RK13 cells maintained in 5% fetal calf serum, which were incubated on a roller drum at 36°C for 15 days. Isolates were identified using a neutralising serum provided by PHLS standards laboratory.

An immunofluorescence test was carried out using baby hamster (BHK 13) cells infected with rubella virus. The patient's sera were allowed to react with them. Antigen-antibody reactions were detected by the "sandwich" method, using fluorescein-labelled anti-human IgG preparations.

Two samples of serum from the mother, taken in September 1970 and March 1971, were retrieved; they had been stored as "normal controls" in the endocrinology laboratory where she had worked. The titres in these, as in the serum taken in October 1971, were calculated as equivalent to 400 units, which is usually taken as indicating good immunity (table I).

Rubella virus was isolated from the baby's nose and throat in July 1973 but could not be isolated from a cervical swab from the mother in December 1973. Tests of the mother's immunological competence did not show any definite abnormality (table II). Immunoglobulin concentrations were normal (IgG 11.4 g/l, IgA 1.8 g/l, IgM 1.43 g/l) when measured on 8 January 1974.

TABLE I—Results of virological tests in mother and baby

Date	Haemagglutination inhibition titre (units)	Complement fixation titre	Rubella- specific IgG titre*	Rubella- specific IgM*
<i>Mother's serum</i>				
8 September 1970	400	256	512	
2 March 1971	400	128	512	
30 October 1971	400			
21 June 1973	50†	1/4†	64	
13 September 1973				Negative
<i>Baby's serum</i>				
21 June 1973	400†			
13 September 1973	50	1/16	128	Negative

* Tested in Manchester Public Health Laboratory.

† Tested in both East Birmingham and Coventry Laboratories.

TABLE II—Results of lymphocyte transformation tests carried out on 8 and 30 January 1974 (ratios of test to control results)

	Results in:		Comment
	Mother	Normal subject	
<i>8 January</i>			
Mitogens:			
Phytohaemagglutinin 2.0 µg	13	322	} Response reduced from normal
Phytohaemagglutinin 0.2 µg	0.6	21	
Pokeweed	9.7	33	
Antigens			
Purified protein derivative	5.7	1.7	} Normal response
<i>Candida albicans</i>	2.1	2.0	
Tetanus toxoid	2.0	0.9	
Rubella antigen	0.3	0.9	No response
<i>30 January</i>			
Phytohaemagglutinin 2.0 µg	60	162	} Normal response
Phytohaemagglutinin 0.2 µg	44	60	
Live rubella virus	—	—	
Inactivated rubella virus	—	—	

Discussion

The clinical features in the baby were clearly those of congenital rubella. This diagnosis was confirmed by the isolation of virus from the infant, even though several months before conception the mother had had an antibody titre usually assumed to signify immunity.

Immunity against rubella was once thought to be lifelong, but it is now recognised that reinfection is not uncommon. Reinfection is usually subclinical and is especially likely after rubella immunisation, though it also occurs after naturally acquired infection.⁶ Previous detection of high titres of rubella haemagglutination inhibition antibodies does not invariably confer protection, as our case, and one other, show.²

Reports of presumed reinfection during pregnancy suggest that the fetus may be severely affected,¹⁻² may have evidence of infection without congenital malformation,³ or may be uninfected.⁷ Such events are rare: two cases were detected in 40 000 sera from pregnant women.²

Rubella antibody levels must be interpreted with care when used as a means of deciding whether rubella infection has occurred in pregnancy. High levels before conception do not exclude the possibility of congenital rubella in a subsequent pregnancy. Pregnant women should avoid unnecessary contact with rubella even when they believe themselves immune. In the cases reported we could not find any evidence of a woman having more than one infant severely affected by congenital rubella.

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