

# Perinatal Mortality in Triplet Births in Japan: Time Trends and Factors Influencing Mortality

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Perinatal mortality rates (PMRs) in triplets were analyzed using Japanese Vital Statistics during the period of 1980–1998. The total number of perinatal deaths in triplets was 1051. The PMR significantly decreased from 214 per 1000 births in 1980 to 39 in 1998, a reduction of 82%. PMRs in triplets were 11.1-fold higher in 1980 and 6.9-fold higher in 1998 than in singletons, indicating that PMRs improved more in triplets than in singletons during the last two decades in Japan. The PMR was the highest in the third-born, followed by the second- and the first-born triplets in each period. As for maternal age, the PMR was 1.5–3.7 times higher in the < 25 years of age group than the other age groups. Additionally, the PMR was the lowest for birthweight (BW)  $\geq$  2000g during the entire period. In addition, the PMR decreased with gestational age (GA) of up to 38–39 weeks and increased thereafter. The effects of BW on the PMR were stronger than the effects of GA. The proportion of perinatal deaths in triplets with extremely low BW (< 1000g) was 74% in 1980–1989 and increased to 82% in 1990–1998. The declining PMR was unlikely to be due to the improvement in BW in triplets. It is likely that it was related to the improved medical management of triplets during the perinatal period and the first week of life. Information obtained in the present study may be useful in counseling pregnant woman about triplet births.

Triplet rates in Japan have increased 4.5-fold in the years from 1974 to 1996 (Imaizumi, 1998). The same tendency was also observed in 14 out of 15 countries in Europe, Canada, Australia, Singapore and Hong Kong (Imaizumi, 1998). According to Imaizumi (1994), the perinatal mortality rate (PMR) was 12 times higher in triplets (59 per 1000 livebirths) than in singletons (5) in 1991. Lipitz et al. (1989) reported that the PMR in triplets was 93 per 1000 deliveries during the period of 1975–1988. To reduce the overall PMR, medical management during the perinatal period is important for triplets and higher order multiple births as well as twins.

The purpose of this study is to quantify yearly changes of the PMR in triplets during the period of 1980–1998. It also deals with the effects of sex, birth order of triplets, maternal age, birthweight (BW), and gestational age (GA) on the PMR in triplets.

## Materials and Methods

Perinatal death data were obtained from the Vital Statistics of Japan for the Years 1980–1998 (Health and Welfare Statistics and Information Department, Ministry of Health

and Welfare, Japan), covering the entire population of Japan. The definition of perinatal deaths has changed since 1995 (*ICD-10*) in Japan. The PMR currently refers to the number of fetal deaths at 22 weeks or more ( $\leq$  22) GA and neonatal deaths  $\leq$  7 days of age, per 1000 births (livebirths and fetal deaths at  $\leq$  22). Before 1994, the fetal death rate (FDR) was considered to be the number of fetal deaths at  $28 \leq$  per 1000 livebirths. In the *ICD-10* (World Health Organization [WHO], 1992), the FDR refers to the number of fetal deaths at 22  $\leq$  per 1000 births. The early neonatal death rate (ENDR) refers to the number of neonatal deaths  $\leq$  7 days of age per 1000 livebirths. The definition of stillbirths in the Vital Statistics in Japan refers to the number of fetal deaths at  $\leq$  12 weeks. The number of fetal deaths at  $\leq$  22 in the period 1980 to 1994 was recomputed using a tape of the stillbirth record in Japan and the FDR was adjusted for the length of GA for fetal deaths at  $\leq$  22 during the period of 1980–1994.

In this connection, WHO (1977) recommended including all fetuses and infants who were delivered weighing at least 500g. In Japan, registration of all livebirths and stillbirths was made on an individual basis.

A least squares method was used to estimate parameters of the multiple regression analysis in which GA ( $X_1$ ) and BW ( $X_2$ ) were the independent variables. The PMR ( $Y$ ) was a dependent variable.

## Results

### Yearly Changes of Perinatal Mortality

Tables 1a and 1b show the number of perinatal deaths in triplets and Tables 2a and 2b shows the PMR during the period of 1980–1998. The PMR per 1000 triplet births decreased from 214 in 1980 to 39 in 1998. Table 2 also shows the FDR and the ENDR.

Figure 1 shows yearly changes in the PMR, the FDR, and the ENDR during the period of 1980–1998. The FDR per 1000 triplet births decreased from 165 in 1980 to 21 in 1998, being 1/8. The ENDR per 1000 triplet live births

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decreased from 59 in 1980 to 19 in 1998, being 1/3. The FDR decreased more rapidly than the ENDR during the entire period. With eight exceptions, these rates were similar for both sexes in each year.

#### Effect of Birth Order of Triplets

Tables 2a and 2b show the number of perinatal deaths in triplets and the PMRs according to birth order of triplets during the period of 1986–1998. The PMR increased from the 1st-born to the third-born in each year group. The PMR was significantly higher in the 3rd-born than the first-born triplets between 1990–1991 and 1996–1998 and in the 3rd-born than the 2nd-born triplets in 1990–1991 and 1994–1995.

#### Effect of Maternal Age

Table 3a and 3b show the PMR according to maternal age group during the period of 1980–1998. The PMR in triplets was the lowest in the maternal age group of 25–29 years during the period from 1980–1983 to 1988–1991 and in the oldest maternal age group ( $\geq 35$  years) in 1992–1998. On the other hand, the PMR was the highest in the youngest maternal age group ( $< 25$  years) in the entire period. In each 4-year period, the PMR was 1.5–3.7 times higher in the youngest group than in the oldest group. With a few exceptions, the rate was significantly higher in the youngest group than the other age groups in each period (see Table 3b). The PMR in the oldest group decreased rapidly from 1980–1983 to

1996–1998, a reduction of 77%. Corresponding declining rates were between 66% to 70% in the other age groups. The relationship between the PMR and maternal age group indicated a U-shape in 1980–1991, but not in 1992–1998.

#### Birthweight-specific Mortality Rate

The number of BW-specific perinatal deaths and the BW-specific PMR per 1000 triplet births is shown in Table 4. The BW was categorized into 500g intervals except BW  $\geq 2000$ g. The PMR decreased by 10% from 1980–1989 (1011) to 1990–1998 (906) for BW  $< 500$ g. Corresponding values were a reduction of 56% (from 666 to 290) for 500–999g, of 76% (133 vs. 32) for 1000–1499g, of 84% (38 vs. 6) for 1500–1999g, and of 69% (16 vs. 5) for BW  $\geq 2000$ g, respectively. The PMR in 1980–1989 significantly decreased from 56% to 84% in 1990–1998 in each BW group for BW  $\geq 500$ g. With BW, the overall PMR decreased from BW  $< 500$ g (958) to BW  $\geq 2000$ g (9.6). The PMR decreased rapidly from 500–999g (417) to 1000–1499g (59), a reduction of 86%. From Table 4, a proportion of BW  $< 500$ g in perinatal deaths increased from 1980–1989 (91%) to 1990–1998 (94%).

#### Gestational Age-specific Mortality Rate

Table 5 shows GA-specific PMRs in triplets for two periods: 1980–1989 and 1990–1998. The PMR decreased with GA up to 34–35 weeks for both periods and increased thereafter. The PMR was significantly higher in the former period than in the recent period in each GA group.

**Table 1a**

Number of Perinatal Deaths, Perinatal Mortality Rates, Fetal Death Rates and Early Neonatal Death Rates in Triplets According to Sex, 1980–1998

Year	Perinatal deaths			Number of Deaths			Early neonatal deaths		
	Males	Females	Total <sup>b</sup>	Fetal deaths <sup>a</sup>			Males	Females	Total
				Males	Females	Total <sup>b</sup>			
1980	41	30	74	29	25	57	12	5	17
1981	27	42	70	16	28	45	11	14	25
1982	43	44	90	35	34	72	8	10	18
1983	37	29	68	21	22	45	16	7	23
1984	23	32	55	17	16	33	6	16	22
1985	31	23	56	23	17	42	8	6	14
1986	31	7	39	23	4	28	8	3	11
1987	19	29	49	16	27	44	3	2	5
1988	19	21	43	11	13	27	8	8	16
1989	15	28	44	12	21	34	3	7	10
1990	24	29	58	20	19	44	4	10	14
1991	20	24	47	9	12	24	11	12	23
1992	29	31	64	16	15	35	13	16	29
1993	33	13	52	16	8	30	17	5	22
1994	24	26	55	13	14	32	11	12	23
1995	28	15	54	17	11	39	11	4	15
1996	21	18	41	5	8	15	16	10	26
1997	20	29	54	17	20	42	3	9	12
1998	19	17	38	10	8	20	9	9	18

Notes: <sup>a</sup> Fetal deaths after 22 weeks of gestation

<sup>b</sup> Including unknown sexes

**Table 1b**

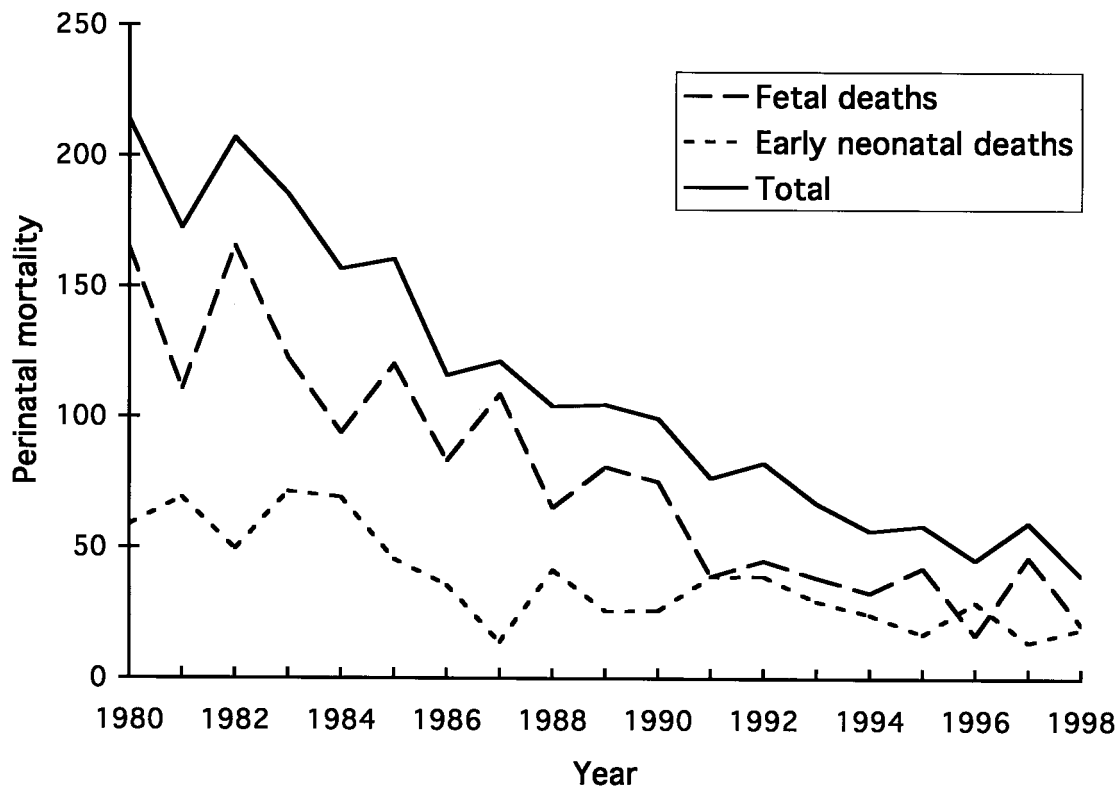
Perinatal Mortality Rate per 1000 Births According to Sex, 1980–1998

Year	PMR per 1000 births			FDR per 1000 births			ENDR per 1000 livebirths		
	Males	Females	Total <sup>b</sup>	Males	Females	Total <sup>b</sup>	Males	Females	Total
1980	231.6	180.7	213.9	163.8	150.6	164.7	81.1	35.5	58.8
1981	145.2	191.8	172.4	86.0	127.9	110.8	64.7	73.3	69.3
1982	197.2	205.6	206.9	160.6	158.9	165.5	43.7	55.6	49.6
1983	207.9	155.1	185.3	118.0	117.6	122.6	101.9*	42.4	71.4
1984	132.9	179.8	156.7	98.3	89.9	94.0	38.5*	98.8	69.2
1985	198.7*	120.4	160.5	147.4	89.0	120.3	60.2	34.5	45.6
1986	191.4*	40.5	116.1	142.0*	23.1	83.3	57.6	17.8	35.7
1987	105.0	130.6	121.3	88.4	121.6	108.9	18.2	10.3	13.9
1988	102.2	93.8	104.1	59.1	58.0	65.4	45.7	37.9	41.5
1989	68.2*	140.7	104.8	54.5	105.5	81.0	14.4	39.3	25.9
1990	88.2	94.8	99.5	73.5	62.1	75.5	15.9	34.8	26.0
1991	67.6	76.4	76.7	30.4	38.2	39.2	38.3	39.7	39.0
1992	70.4	86.1	82.5	38.8	41.7	45.1	32.8	46.4	39.1
1993	79.3*	36.8	67.1	38.5	22.7	38.7	42.5*	14.5	29.5
1994	49.7	53.7	56.6	26.9	28.9	32.9	23.4	25.5	24.5
1995	57.7	35.2	58.6	35.1	25.8	42.3	23.5	9.6	17.0
1996	46.6	40.0	45.4	11.1	17.8	16.6	35.9	22.6	29.3
1997	45.1	63.6	59.7	38.4	43.9	46.5	7.0	20.6	13.9
1998	38.5	36.3	39.4	20.2	17.1	20.8	18.6	19.6	19.1

Notes: <sup>a</sup> Fetal deaths after 22 weeks of gestation

<sup>b</sup> Including unknown sexes

\* Comparison of male vs female rate:  $p < 0.05$ .



**Figure 1**

Yearly changes in the PMR, the FDR, and the ENDR, 1980–1998.

**Table 2a**

Number of Perinatal Deaths and Perinatal Mortality in Triplets According to Birth Order of Triplets, 1986–1998

	Number of perinatal deaths			PMR per 1000 births		
	1st-born	2nd-born	3rd-born	1st-born	2nd-born	3rd-born
1986–87	25	27	36	101.6	109.3	145.8
1988–89	23	30	34	83.0	107.5	122.7
1990–91	30	30	45	75.0	75.2	113.4
1992–93	33	34	49	64.0	65.5	95.0
1994–95	26	30	53	41.3	47.5	83.7
1996–98	33	43	57	36.0	46.8	62.1

**Table 2b**

Odds Ratio (95% Confidence Interval) for Perinatal Mortality Rates in Triplets According to Birth Order of Triplets, 1986–1998

	1st- vs. 2nd-born	1st- vs. 3rd-born	2nd- vs. 3rd-born
1986–87	1.09 (0.61–1.95)	1.58 (0.91–2.74)	1.45 (0.85–2.48)
1988–89	1.37 (0.77–2.42)	1.62 (0.93–2.84)	1.19 (0.70–2.00)
1990–91	1.02 (0.60–1.73)	1.66* (1.02–2.71)	1.63* (1.00–2.65)
1992–93	1.03 (0.62–1.68)	1.59* (1.00–2.51)	1.55 (0.98–2.44)
1994–95	1.16 (0.68–1.99)	2.21* (1.36–3.58)	1.90* (1.19–3.01)
1996–98	1.32 (0.83–2.11)	1.81* (1.16–2.80)	1.36 (0.91–2.05)

Note: \* Comparison of PMRs in triplets among birth order of triplets,  $p < 0.05$ .**Table 3a**

Perinatal Mortality Rate in Triplets According to Maternal Age per 1000 births, 1980–1998

	Number of deaths					Perinatal mortality rate per 1000 births				
	Maternal age					Maternal age				
	< 25	25–29	30–34	35 ≤	Total	< 25	25–29	30–34	≤ 35	Total
1980–83	65	133	88	16	302	300.9	174.3	177.4	202.5	194.3
1984–87	37	85	62	15	199	228.4	113.6	145.9	142.9	138.2
1988–91	32	70	74	16	192	155.3	82.2	93.3	89.9	94.6
1992–95	30	72	107	16	225	146.3	52.5	72.9	40.0	65.3
1996–98	16	47	48	22	133	100.6	59.2	54.1	45.8	48.3
Total	180	407	379	85	1051	189.9	89.9	93.1	68.4	93.7

**Table 3b**

Odds Ratio for Perinatal Mortality Rate in Triplets According to Maternal Age per 1000 births, 1980–1988

Year	< 25 vs. 25–29	< 25 vs. 30–34	< 25 vs. ≤ 35	25–29 vs. 30–34	25–29 vs. ≤ 35	30–34 vs. ≤ 35
1980–83	2.04*	2.00*	1.69	0.98	0.83	0.85
1984–87	2.31*	1.73*	1.78	0.75	0.77	1.02
1988–91	2.05*	1.79*	1.86	0.87	0.91	1.04
1992–95	3.10*	2.18*	4.11*	0.70*	1.33	1.89*
1996–98	1.78	1.96*	2.33*	1.10	1.31	1.19
Total	2.37*	2.28*	3.19*	0.96	1.34*	1.40*

Note: \* significant at the 5% level.

**Table 4**

Perinatal Mortality Rate of Triplets According to Birthweight (g), 1980–1989 and 1990–1998

birthweight (g)	Number of perinatal deaths			PMR per 1000 births			Odds Ratio (95% CI)
	1980–89	1990–98	Total	1980–89	1990–98	Total	
< 500	182(31)	163(35)	345(33)	1011.1	905.6	958.3	—
500–999	255(43)	216(47)	471(45)	665.8	289.5	417.2	4.89* (3.75–6.37)
1000–1499	82(14)	54(12)	136(13)	132.9	31.9	58.8	4.66* (3.26–6.66)
1500–1999	45(8)	18(4)	63(6)	37.9	6.3	15.5	6.24* (3.60–10.82)
2000 ≤	23(4)	9(2)	32(3)	15.9	4.8	9.6	3.37* (1.56–7.32)
Total <sup>a</sup>	588(100)	460(100)	1048(100)	153.5	62.3	93.5	2.73* (2.40–3.10)
<1500	519(88)	433(94)	952(91)	439.8	165.2	250.5	3.97* (3.40–4.60)
1500 ≤	68(12)	27(6)	95(9)	25.8	5.7	12.8	4.64* (2.97–7.27)

Notes: <sup>a</sup> Including unknown birthweight.  
 \* Comparison of PMRs for 1980–89 and 1990–1998, *p* < 0.05.  
 The figures in parentheses indicate percentages.

**Table 5**

Number of Perinatal Deaths and Perinatal Mortality in Triplets According to Gestational Age, 1980–1989 and 1990–1998

Gestational age (weeks)	Perinatal deaths			PMR per 1000 births			Odds ratio (95% confidence interval)
	1980–89	1990–98	Total	1980–89	1990–98	Total	
22–23	189	136	325	1000.0	850.0	931.2	—
24–25	96	94	190	827.6	458.5	591.9	5.67* (3.26–9.87)
26–27	57	46	103	575.8	161.4	268.2	7.05* (4.24–11.72)
28–29	62	40	102	280.5	82.6	144.7	4.33* (2.80–6.70)
30–31	48	30	78	145.9	33.9	64.3	4.86* (3.02–7.82)
32–33	41	42	83	75.2	25.9	38.3	3.06* (1.96–4.75)
34–35	31	29	60	39.7	13.0	19.9	3.14* (1.88–5.24)
Over 36	62	41	103	40.2	27.1	33.7	1.51* (1.01–2.25)
Total	586	458	1044	153.2	62.0	93.1	2.74* (2.40–3.11)

Note: \* Comparison of PMRs in triplets for two periods, *p* < 0.05.

**Table 6**

Perinatal Mortality in Triplets According to Birthweight and Gestational Age, 1980–1998

Gestational age (weeks)	Birthweight (g)				Total
	< 500	500 ≤	1000 ≤	1500 ≤	
22–27	243	362	8	5	618
28–29	20	49	32	0	102
30–31	19	15	33	11	78
32–33	16	20	28	16	83
34+	43	20	38	61	163
Total	341	466	139	93	1044
	Perinatal mortality rate per 1000 births				
22–27	952.9	500.7	112.7	1000.0 <sup>a</sup>	586.3
28–29	909.1	219.7	71.3	0.0 <sup>a</sup>	144.7
30–31	1187.5	194.8	40.6	36.3	64.5
32–33	941.2	327.9	47.8	10.7	38.3
34+	1000.0	454.5	96.5	10.9	26.9
Total	966.0	413.1	60.1	12.6	93.2

Note: <sup>a</sup> The denominator was under 15 triplet births.

**Birthweight and Gestational Age**

Table 6 shows the PMR by BW and GA during the period 1980–1998. Excluding small numbers of births, the highest PMR was for BW < 500g and every GA (909–1000), and followed by BW of 500–999g and 22–27 weeks GA (501). On the other hand, the lowest PMR was for BW ≥ 1500g and ≤ 32 weeks GA (11), and followed by BW ≥ 1500g and 30–31 weeks (36), and at 1000–1499g and 30–31 weeks (41).

As mentioned in Material and Methods, least squares method was used to estimate parameters of the multiple regression analysis. The following equation was obtained as the best fitted model for a dependent variable PMR (Y) and two independent variables: GA (X<sub>1</sub>) and BW (X<sub>2</sub>).

$$Y = 1659.87 - 23.52 X_1 - 525.09 X_2$$

in which the adjusted R-square of the multiple correlation coefficient was 0.53, with the estimated parameter (X<sub>2</sub>) being significant at the 1% level, but with no significant independent relationship with X<sub>1</sub> (GA). Thus, BW was the more effectively correlated parameter considered with the PMR.

## Discussion

Imaizumi (1994) studied the PMR in triplets during the period of 1980–1991 in Japan. However, as mentioned previously, the definition of the PMR has been changed since 1995. In the present study, the FDR was adjusted for the length of GA for fetal deaths  $\geq 22$  weeks GA during the period 1980–1994. Therefore, the PMR was higher in the present study than the previous study (Imaizumi, 1994) during the period from 1980 to 1991. The PMR was 214 per 1000 births in 1980 and 39 in 1998 decreasing by 82% during the 18 years.

In Japan, the PMR was 12-fold higher in triplets than singletons (Imaizumi, 1994). According to Imaizumi (2001), the PMR in twins was 55.2 per 1000 births during the period of 1980–1998. Using the Vital Statistics of Japan and Table 1 from Imaizumi (2001), the PMR in singletons was obtained as 11.9 per 1000 births (298341/25097959) during the period of 1980–1998. Therefore, the PMR was 4.6-fold higher in twins than in singletons and 7.9-fold higher in triplets than in singletons during that period. The PMR in singletons and the relative risk of the PMR for triplets compared to singletons were 19.3 (30502/1582502) and 11.1-fold in 1980 and 5.7 (6742/1186391) and 6.9-fold in 1998, respectively.

In Table 5, the PMR was 1011.1 per 1000 births for BW < 500g in the period 1980–1989. For BW < 500g, the number of livebirths and fetal deaths after 22 weeks were 180 and the number of perinatal deaths were 182 for 1980–1989. Probably, two triplets were born in 1979 and died in 1980 due to early neonatal deaths. Therefore the denominator (livebirths and FD after 22 weeks) was smaller than the numerator.

Based on the findings of several studies Bakketeig et al. (1984) concluded that the association of overall PMR was stronger with BW than with GA. The same result was obtained for twins in Japan (Imaizumi, 2001) and for triplets in the present study. To reduce the PMR in triplets, BW is an important factor. For the 10-year period from 1985 (see Table 4), the PMR decreased 10% for BW < 500g, 57% for BW 500–999g, 76% for BW 1000–1499g, 83% for BW 1500–1999g, and 70% for BW  $\geq 2000$ g. These values were smaller for extremely low BW (< 1000g). From Table 4, the proportion of triplets with extremely low BW increased from 74% (437/588) of the total number of perinatal deaths in 1980–1989 to 82%

(379/460) in 1990–1998, increasing by 8% during the observed period.

Although extremely low BW increased, overall PMRs decreased rapidly year by year. Therefore, the declining PMR was probably not the result of an improvement of BW in triplets. It seems that it may be attributed to the improvement in medical antenatal and neonatal care. The same result was also obtained in twins (Imaizumi, 2001).

From Table 1 and the Vital Statistics of Japan in 1980 and 1998, a proportion of the total number of triplet perinatal deaths was 0.23% (74/32422) in the former and 0.51% (38/7447) in the latter, increasing 2.2-fold during the 18 years. To reduce the overall PMR further, intensive management of triplet and higher order multiple births will be very important during the antenatal period and the first week of life.

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