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Discovery and Epidemiology of PCB Poisoning in Taiwan: A Four-Year Followup

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An outbreak of polychlorinated biphenyl (PCB) poisoning from the consumption of contaminated rice oil, covering four counties in central Taiwan, was investigated. There were 1843 cases by the end of 1980. The highest frequency of incidence occurred during the period from March to July 1979. The severity of clinical manifestations varied. Most patients showed symptoms of mild or moderate severity. The major age group affected was between 11 and 20 years old. Most of the victims were students and factory workers. The amount of PCB intake in each victim was estimated to be 0.7 to 1.84 g and the latent period from the time of intake to the onset of clinical manifestations was approximately 3 to 4 months. The patients' blood PCB concentrations ranged from 3 ppb to 1156 ppb; 44.27% of 613 patients had levels of 51 to 100 ppb and 27.6% PCB blood levels over 100 ppb. In the course of 3.5 years, 2061 persons were determined to be PCB poisoning victims. Now, except for a few severe cases, their skin symptoms are very much improved. Thirty-nine babies showing hyperpigmentation were born from PCB-poisoned mothers. The fatality rate was high: eight of them died. Another 24 deaths were reported among the PCB-poisoned group, almost half of them (12) from hepatoma, liver cirrhosis or liver diseases with hepatomegaly.

On May 21, 1979, a local health bureau in Taichung County was informed by the Hui-Ming School for Blindness that a strange disease, characterized by acne-like skin eruptions, had been occurring with increasing frequency among students and staff since the end of March. Samples of cooking oil, soy sauce and water were collected from the school. Unfortunately, routine toxicologic screening tests for cyanide, phosphorus, heavy metals, aflatoxin, pathogens and organic phosphates did not identify the cause of the disease. Meanwhile, biochemists and clinicians could not clarify the etiology of the disease either. Almost at the same time, 85 of 150 workers from a nearby plastic shoe factory also suffered from the same symptoms and reported to the local health bureau in the beginning of September 1979. Besides acneform eruptions, follicular accentuations, pigmentation of the skin and nails and hypersecretion of the Meibomian gland were found. An extensive epidemiological investigation was soon started in order to find a common agent. Victims in both outbreaks were found to have consumed the same brand of cooking rice oil manufactured by C-Company, purchased from the F-H oil store. The rice oil (C-rice oil) was then highly suspected of causing the disease.

A thorough investigation of C-rice oil was undertaken immediately. Illegal mixing of inedible animal oil or industrial oil to the cooking rice oil by some merchants was suspected, but could not be proved. On September 18, 1979, two more companies in a neighboring township of Taichung County reported that their workers (85 out of 233 and 19 out of 58, respectively) encountered the same problems. Meanwhile, there were cases reported in some other communities and households. All shared a common characteristic of consuming C-rice oil. Despite our endeavors, the etiology of the disease was unclear; the only conclusion we reached at that time was that the disease must have been related to adulteration of the rice oil.

Symptomatologically, the mysterious disease was quite similar to the Japanese Yusho, a major rice oil poisoning outbreak in northern Kyushu in 1968. Yusho was due to polychlorinated biphenyl (PCB) poisoning after consuming rice oil contaminated by Kanechlor-400 during the manufacturing process. But the dermatologists consulted in Taiwan could not recognize chloracne at that time and thus they did not provide any information suggesting PCB as the cause of the disease. Then we consulted S.

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Yamamoto and Gen Ohi, professors of Hygiene, University of Tokyo, Medical School. Samples of C-rice oil and patients blood samples were analyzed, and PCB contamination was proved in Tokyo on October, 6, 1979. Health authorities in Taiwan soon announced the exact cause of the disease and immediately prohibited further distribution of C-rice oil.

The laboratory analysis showed that the C-rice oil from both the Hui-Ming School for Blindness and the F-H Oil Store contained a Kanechlor-400, 500 mixture at concentrations as high as 65 and 108 ppm, respectively. These findings were also confirmed by M. Kuratsune and Y. Masuda of Kyushu University. However, PCBs were not detected in the newly purified rice oil from C-Company, and the owner claimed in defense that he had not used PCBs as a heat conductor in the deodorizing process since 1976. But both soil samples and workers' blood samples of the C-Company were proved by Y. Masuda to have abnormally high levels of PCBs.

Similar cases were also reported in May 1979 by Changhua County, and on inspection on September 18, 1979, we ascertained that this was a similar skin disease. After our announcement on October 8, 1979, Changhua Christian Hospital reported that victims, including school children and residents, were found in several townships in Changhua County. An epidemiological survey through local health bureau and hospitals was then done extensively. Clinical study and service teams were organized to give better medical care. This episode of PCB poisoning with rice oil as a vehicle as the second disastrous outbreak in the world.

Materials and Methods

The PCB victims in this study comprised (1) patients visiting and registering in the local hospitals and local health bureaus in Central Taiwan and (2) self-reported asymptomatic persons having ingested the contaminated C-rice oil.

The clinical severity of the disease was graded 0-IV according to the criteria specified in Table 1.

Except for the initial samples assayed in Tokyo, determination of PCBs with gas chromatography was done by the Food and Drug Bureau of Department of Health, Executive Yuan, R.O.C. and the Taiwan Plant Protection Center. The gas chromatograph was fitted with an electron capture detector (Ni^{63} – ECD) and a glass column (3 mm × 2 mm) packed with Chromosorb WHP (80/100 mesh) coated with 3% OV-1. The temperatures of the inlet, column, and detector were maintained at 230°C, 200°C and 280°C, respectively. For quantitative analysis of PCBs, Ugawa's peak height method (*2*) and Webb's formula (*3*) were followed.

The total amount of PCB intake for each person was estimated by using the formula:

$$TC/n = \text{Total PCB intake per person}$$

where T is the total amount of C-rice oil consumed in each community, C is the concentration of PCBs in each oil sample and n is the number of persons ingesting the oil.

Table 1. Criteria of clinical severity grading of patients with PCBs poisoning.[a]

Grade	Main criteria	Reference criteria
0	Abnormal blood level of PCBs without clinical maifestation	
I	Increased cheeselike discharge from Meibomian gland, pigmentation of nails	Increasing sweating, dry skin, pigmentation of lips gingiva and mucus membrane of oral cavity
II	Grade I plus comedo	Hair follicle keratosis on the extensor side of extremity joints
III	Grade II plus acneform eruption, cyst formation of sebaceous gland in genital and evidence of follicular opening in the site of neck and upper chest	Swelling of eye lids, swelling and pain at joints
IV	Enlarged and elevated follicular opening all over the body and extensive distribution of acneform eruption	Swelling of face and limbs, extensive distribution of acne with purulent infection

[a]As defined by Guto and Higuchi (*1*).

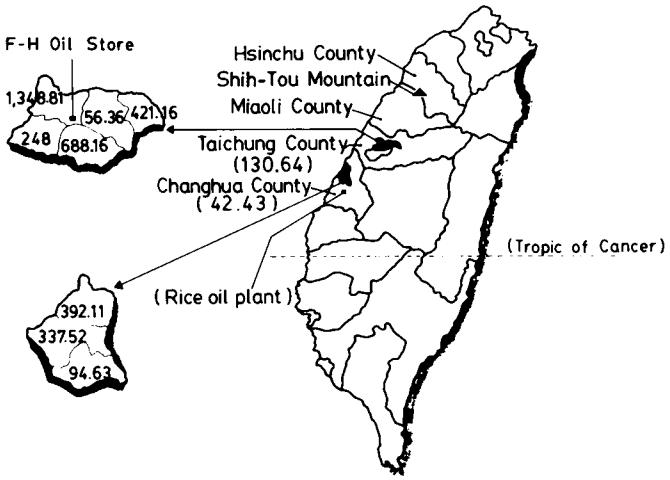

FIGURE 1. Geographical distribution of PCB-poisoned patients.

Results

Geographically, the distribution of PCB-poisoned victims covered Taichung, Changhua, Hsinchu and Miaoli counties (Fig. 1). of 1843 cases recorded from December 1978 to November 1980, 1252 (130.64 morbidity per 100,000) persons in Taichung and 487 (42.43 morbidity per 100,000) persons in Changhua County were involved. Cases were less frequently found in Hsinchu (14 cases) and Miaoli Counties (90 cases) and they were from two sources. One was from an outbreak in the temples of Shih-Tou Mountain located at the junction of Hsinchu and Miaoli Counties. Most of them were monks and nuns. The second outbreak was in students who returned from their technique-practicing courses in the factories of Taichung County. The morbidity per 100,000

Table 2. Distribution of clinical severity grading of PCB-poisoning patients.

County	Grade 0		Grade I		Grade II		Grade III		Grade IV		Total
	No.	%	No.	%	No.	%	No.	%	No.	%	
Taichung	82	7.66	508	47.48	236	22.06	164	15.33	80	7.48	1070
Changhua	68	13.71	98	19.76	244	49.19	64	12.90	22	4.44	496
Miaoli	2	2.22	65	72.22	15	16.67	6	6.67	2	2.22	90
Hsinchu			12	85.71	2	14.28					14
Total	152	9.10	683	40.89	497	26.16	234	14.01	104	6.22	1670

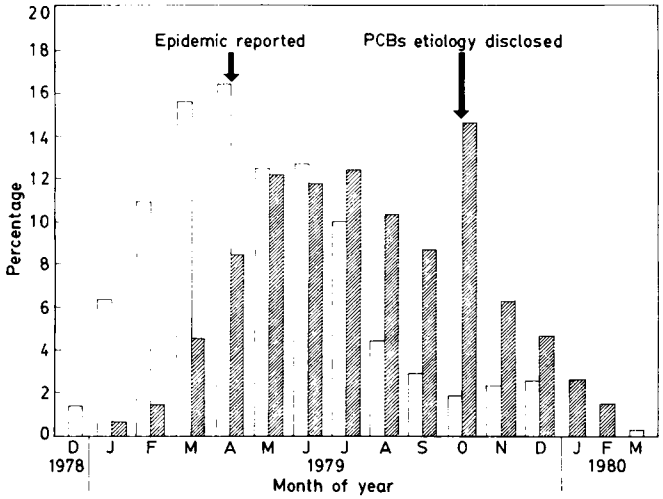

FIGURE 2. Monthly distribution of new patients in (□) Taichung and (▨) Changhua Counties.

Table 3. Age and sex distribution of PCBs-poisoned patients in Taichung and Changhua Counties.

Age, yr.	Taichung County[a]		Changhua County[b]		Total	
	No.	%	No.	%	No.	%
0–5	33	3.39	23	4.85	56	3.87
6–10	60	6.16	58	12.23	118	8.15
11–15	113	11.60	129	27.21	242	16.71
16–20	201	20.63	57	12.02	258	17.81
21–25	119	19.21	29	6.11	148	10.22
26–30	88	9.03	32	6.75	120	8.29
31–35	58	5.95	19	4.00	77	5.32
36–40	60	6.16	29	6.11	89	6.15
41–45	60	6.16	29	6.11	89	6.15
46–50	44	4.51	25	5.27	69	4.76
> 50	121	12.42	40	8.44	161	11.12
Not specified	17		4		21	
Total	294	100.00	474	100.00	1448	100.00

[a]M:F = 450:524.
[b]M:F = 245:229.

at five townships in Taichung County varied from 56.36 to 1348.81. The patients were mainly workers from three factories, and students and staff in the Hui-Ming School for Blindness. Three townships in Changhua County were surveyed, and the morbidity per 100,000 was 94.63, 337.52 and 392.11, respectively. Because of early prohibition of the distribution of C-rice oil, the involved area was limited only to the central part of Taiwan.

As to the clinical severity of the PCB poisoning, of 1670 persons diagnosed in 1979 to 1980, 152 (9.10%) were of grade 0, 683 (40.89%) of grade I, 497 (26.16%) of grade II, 234 (14.01%) and 104 (6.22%) of grade III and IV (Table 2).

The monthly distribution of new patients in Taichung and Changhua between December 1978 and March 1980 is shown in Figure 2. The earliest cases occurred at the end of 1978 and were identified by retrospective studies in Changhua County. In both counties, new cases increased steadily to a peak in the first 5 and 8 months, respectively. In Changhua, only one peak (16.4%) appeared in April 1979, whereas in Taichung, there were two peaks, the first (12.4%) in July 1979 and the second (14.6%) in October 1979.

Age and sex distribution of 1448 PCB-poisoned patients in Taichung (974 cases) and Changhua Counties (474 cases) from December 1978 to March 1980 is shown in Table 3. The highest rate was found in the 16 to 20 age range (17.81%) and the next was in the 11 to 15 age range (16.71%). The ages of 21 patients were not recorded. The ratio of male to female in Taichung County was 0.855 (M:F = 450:524) and in Changhua County 1.07 (M:F = 245:229). The difference was not statistically significant ($\chi^2 = 3.773$, $p > 0.05$). Their occupations are shown in Table 4. In Taichung, 586 (60.16%) of 974 patients were factory workers. In Chunghua, most patients were students (39.24%), and workers were the next most frequent category of cases. (18.56%).

The network of distribution of C-rice oil was investi-

Table 4. Distribution of occupations in PCB-poisoned patients in Taichung and Changhua Counties.

County	No. (%) of cases							Total
	Farmer	Worker	Merchant	Government employee	Student	House-wife	Other	
Taichung	9	586	9	15	148	71	136	974
	(0.92)	(60.16)	(0.92)	(1.54)	(15.19)	(7.28)	(13.96)	
Changhua	64	88	10	5	186	77	44	474
	(13.50)	(18.56)	(2.10)	(1.05)	(39.24)	(16.24)	(9.28)	
Total	73	674	19	20	334	148	180	1448
	(5.04)	(46.54)	(1.31)	(1.38)	(23.07)	(10.22)	(12.43)	

gated. The wholesale oil dealers and retail stores related to the outbreaks are shown in Figure 3. Outbreaks in Taichung occurred in the Hui-Ming School for Blindness, C-F Plastic Show Factory, C-Y Fabric Company, I-Y Industrial Company, as well as some sporadic cases in households and other communities. Oil samples collected from the outbreaks in Taichung, Hsinchu and Miaoli were heavily contaminated with PCBs (31 to 300 ppm). All the rice oil consumed was purchased from the F-H Oil Store in Taichung County. Except for one sample (30 ppm), an extensive search for PCBs in hundreds of rice oil samples from stores and the victims' home in Changhua County failed to disclose PCB contamination.

The period of ingestion of PCB-contaminated oil, dosage and latent period of the intoxication were investigated in the Hui-Ming School for Blindness, C-Y Fabric Company, I-Y Industrial Company and C-F Plastic Shoe Factory. The period of PCB intake ranged from 3 to 9 months. The estimated average total PCB intake in each person varied from 0.77 to 1.84 g. The average latent period from intake to onset of illness was 3 to 4 months (range: 1.5 to > 6 months) (Table 5).

The blood levels of PCBs in 613 patients within the first year of outbreak ranged from 3 ppb to 1156 ppb (*17*). Most (82.54%) of the blood levels ranged from 11 to 150 ppb with a peak frequency in 51 to 100 ppb (44.37%); 169 (27.57%) patients had PCB levels of more than 100 ppb (Table 6).

Discussion

Although chloracne has been reported as an occupational disease sporadically (*4,5*), the Japanese Yusho in 1968 was the first recognized outbreak in the world of PCB poisoning via contaminated cooking rice oil. It involved more than 1600 victims, mainly the residents of Fukuoka and Nagasaki Prefectures (*6,7*). Unfortunately, the same rice oil disease recurred in Central Taiwan 11 years after the Japanese Yusho outbreak. The epidemic here was spread over Taichung, Hsinchu, Miaoli and Changhua Counties. The number of reported cases was 1843 at the end of 1980 and it has now reached

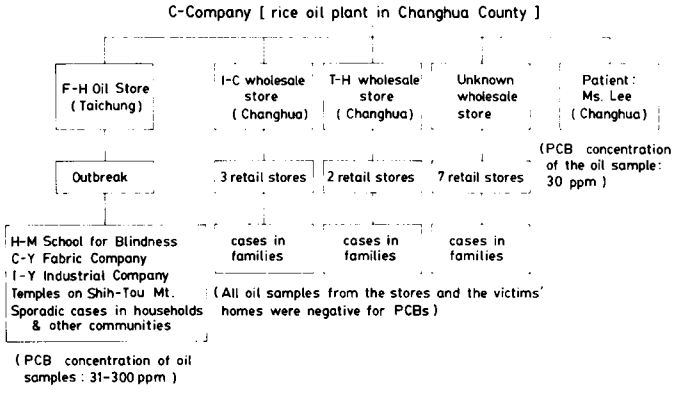

FIGURE 3. Sources of rice oil consumed by PCB-poisoned patients.

2061 patients, as registered in the Health Department of the Taiwan Provincial Government.

Most patients within the first year of the outbreak showed symptoms of mild (grade I: 40.89%) or moderate (grade II: 26.16%) severity. PCBs tended to be retained in adipose tissues and were almost not excreted from body. Many of our patients still suffered from the intoxication after more than 2 years. Hyperpigmentation in babies due to PCB intoxication during pregnancy was also found. Most of the infants affected also had obvious growth retardation.

The earliest cases of PCB intoxication in Taiwan could be traced back to December 1978. The highest frequency of incidence occurred during the period from March to July 1979. After the health authorities announced the cause of the outbreak on October 6, 1979, new cases in October increased conspicuously in Taichung but not in Changhua, probably because patients in Changhua purchased contaminated rice oil several months earlier than those in Taichung. Most patients in Changhua had developed symptoms and had already shown up at hospitals or local health bureaus at the time of announcement, but quite a number of victims in Taichung were possibly still in the latent period. They would not have known themselves to be PCB victims if C-rice oil had not been detected and announced to be contaminated by PCBs. Therefore, most of the new cases which increased in October 1979 were self-reported victims from Taichung.

Oil samples from Taichung proved to be contaminated with PCBs but all except one oil sample from Changhua were negative for PCBs. In Taichung, the F-H Oil Store was the only store suspected, and the oil samples from both the F-H Oil Store and community sources were collected at the beginning of the outbreak. In Changhua, PCB intoxication occurred mainly in families. They had used up the contaminated rice oil by

Table 5. Period of intake and dosage of PCBs.[a]

	Period of intake, months	Average dosage, g/person
Hui-Ming School for Blindness	6	0.77
C-Y Fabric Company	3–4	1.38–1.84
I-Y Industrial Company	9	1.2
C-F Plastic Shoe Factory	9	1.09

[a]Latent period: Average 3–4 months, Range: 1.5 – >6 months.

Table 6. Blood PCB levels in patients.

Blood level, ppb	Cases	
	No.	%
<10	29	4.73
11–50	143	23.73
51–100	272	44.37
101–150	91	14.84
151–200	28	4.57
201–300	24	3.92
301–400	17	2.77
401–500	4	0.65
>500	5	0.82
Total	613	100.00

the time of oil sample collection. In addition, oil stores in Changhua might have discarded the suspected rice oil before inspection in order to avoid responsibility. This might be the reason why the vast majority of oil samples collected in Changhua were free from PCB contamination.

The blood PCB level of our patients has been reported recently. The mean value varied from 39 ppb to 101.7 ppb (*8–11*), which was much higher than that in the Japanese Yusho outbreak [mean ± SD: 5.9 ± 4.5 ppb (*12*); 6.7 ± 5.3 ppb (*11*)]. The difference is presumably due to the time of sampling, that is, the blood samples of our patients were collected at the early stage of the outbreak in contrast to five years after the outbreak in Japanese Yusho patients. Another factor was the C-rice oil contained larger percentages of PCB molecules with high numbers of chlorines (such as 5, 6, and 7) than the PCBs involved in the Japanese incident (*11,13*). These highly chlorinated PCBs, i.e., penta-, hexa-, and heptachlorobiphenyls, are generally retained in tissues longer than the lower chlorinated PCBs.

Furthermore, C-rice oil was contaminated not only by PCBs but also by polychlorinated dibenzofurans (PCDFs) and polychlorinated quaterphenyls (PCQs) (*11,14,15*). Masuda et al. indicated (*11*) that both rice oils, i.e., those from Japan and Taiwan, contained the same major components of PCDFs which were the very toxic 2,3,4,6,7-penta-CDF and 2,3,4,7,8-penta-CDF. These penta-CDFs showed strong reducing activity of drug-metabolizing enzyme (*16*).

PCB intoxication is a man-made health hazard in Taiwan. Synthesis, import or use of PCBs have been prohibited since this outbreak, but environmental contamination by PCBs may still exist. Sufficient caution and further investigations are necessary.

By the end of February 1983, there were 2,061 recorded cases of PCB poisoning, including infants showing hyperpigmentation. In total, 39 babies showing this symptom were born from those intoxicated mothers. They showed a very high infant mortality rate: eight of them died from pneumonia, bronchitis, sepsis, and premature and congenital weakness (Tables 7–9). The remaining children grew up and gradually recovered close to average lengths and body weights. Another 24 deaths were reported among the PCB-poisoned group (Table 8). Almost half of them died from hepatoma, liver cirrhosis or liver diseases with hepatomegaly (Fig. 4). The diagnoses were made from clinical symptoms and laboratory examinations. None

Table 7. Births and deaths of hyperpigmented babies between October 1979 and February 1983.

	1979	1980	1981	1982	1983	Total
No. of births	10	13	11	4	1	39
No. of deaths	0	2	3	3	0	8

Table 8. Distribution of deaths by age groups among PCB-poisoned patients between October 1979 and February 1983.

Age	1979	1980	1981	1982	1983	Total
≤19[a]	0	1	3	1	0	5
20–29	0	0	3	1	0	4
30–39	0	0	1	1	0	2
40–49	0	0	0	2	0	2
50–59	0	1	1	1	0	3
60–69	0	1	2	1	0	4
70–79	0	1	1	1	0	3
≥80	0	0	1	0	0	1
Total	0	4	12	8	0	24

[a]Includes infants with hyperpigmentation.

Table 9. Geographic distribution of death among PCB-poisoned patients between October 1979 and February 1983.

Geographic area	1979	1980	1981	1982	1983	Total
Taichung County	0	0	4	3	0	7
Chang Hua County	0	3	4	2	0	9
Miao Li County	0	0	3	3	0	6
Other counties[a]	0	1	1	0	0	2
Total	0	4	12	8	0	24[b,c]

[a]Patients in other counties originated from three affected areas. They had moved after the poisoning.
[b]Death of infants with hyperpigmentation are excluded.
[c]Male 15; female 9.

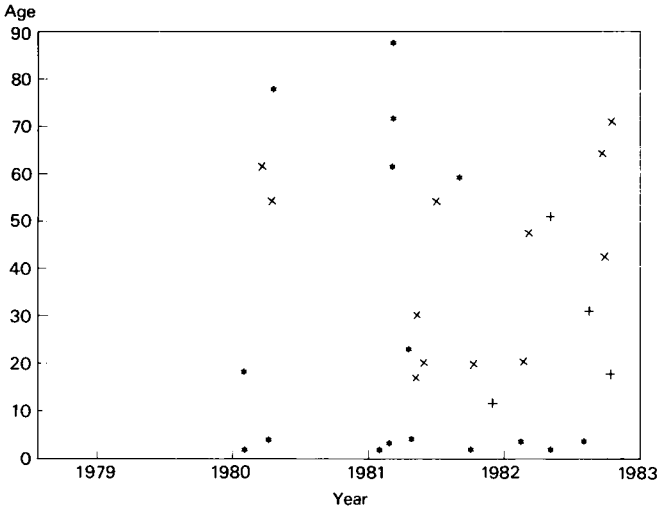

FIGURE 4. Death by age among PCB-poisoned patients (32 persons) between October 1979 and February 1983: (×) hepatic disease; (*) other diseases, (+) traffic accident.

Table 10. PCB content of the viscera: autopsy results on a 23-year-old male.

Organ	PCB, ppm
Lung	94
Tongue	640
Kidney	443
Blood	85
Liver	668
Stomach	629
Heart	3317
Bladder	10,208
Brain	222
Colon	5889
Spleen	222
Small intestines	656
Vein and arterial jugulars	5320

of them were autopsied. Four males died in traffic accidents. One 23-year-old male suddenly died on March 20, 1981. He was an in-patient at Veterans Hospital from May 13 to June 5, 1980, due to multiple acneform lesions on the face. His PCB blood level was 80.7 ppb. He received treatment with 13-*cis*-retinoic acid, Terramycin, Airol topical, Hostacycline and Multivita. Because the cause of death was unclear, the court ordered an autopsy. However, the autopsy did not reveal the cause of death, leaving the case open. Table 10 documents the high PCB content of the viscera.

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