

Reproductive Effects on 65 Yusho Women - 35 Years After The PCBs/PCDFs Exposures -

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Introduction

It has been 35 years since the outbreak of Yusho. In 1968, a mass poisoning involving more than 10,000 people occurred in the western part of Japan from ingestion of rice oil contaminated by PCBs and PCDFs. Although the initial symptoms including acneform eruption, dermal pigmentation, and increased eye discharge were gradually faded by the lapse of time, exposed patients and their offspring still complain of various symptoms on different organs. Among the self-reported 12,270 patients who reported to the health center by Oct. 1968 as being exposed to contaminated oil, only 1872 people were officially approved as Yusho patients by Nov. 1999. There are still many patients who are in serious illness even now. In August 2002, we, the Yusho Support Center (NGO), conducted a retrospective health study of Yusho Women. The aim of this study is to investigate the long-term reproductive effects on Yusho Women directly or indirectly exposed in the uterus to PCBs and PCDFs by focusing the exposure age and their reproductive effects.

Method and Materials

We undertook a questionnaire study of their medical history and self reported symptoms. Individuals who self-reported were recruited via the Committee of Permanent Rescue of Yusho (NGO). Respondents were sent a mail-out/mail return questionnaire that covers the exposure event, exposure age, gynecological diseases ever diagnosed by physicians, experiences of hospitalization, operation by those diseases, abnormal menstruation, and adverse pregnancy outcomes. In addition, the questionnaire included their daughter's reproductive diseases and menstrual characteristics. The diseases of other organs ever diagnosed by physicians and chronic symptoms were also studied. All results collected were based on questionnaire responses without physical examination. The identification of the control group matched for age was not yet been done, as it was difficult to estimate how many exposed patients would return their questionnaires 35 years long after the incident.

Results and Discussion

Questionnaires of 150 were sent to the exposed population, 65 (43%) responded. Among 65 respondents, 51 (78%) were approved as Yusho patients, and 14 were not approved. As shown in Table 1, the ages of the respondents in August 2002 are from 19 to 80 years old. The respondents include 9 pairs of mothers and daughters and 1 pair of sisters. Among them, 5 daughters were exposed in the uterus, they are the second generation of Yusho. 44 (67 %) of the respondents answered their exposure ages: prenatal exposure to 41 years old. The table indicates that 10 (15%) women were diagnosed with diseases in the

thyroid gland: Basedow's disease (2), goiter (2), thyroid cancer (1), thyroprival (1), thyroid dysfunction (3), thyroid enlargement (1). 37(57%) of the respondents answered they had seen an obstetrician because of the diseases of reproductive organs. They were either hospitalized, operated, or had medical treatments. Their diseases include: endometriosis 6 (9 %), ovarian cancer (1), cervical erosion (2), uterine myoma (2), ovariectomy (2), uterectomy (1), amenorrhea (3), ovarian cyst (1), placenta praevia (1), menopausal disorder (1), dysmenorrhea (2), breast cancer (1), and other diseases. From the women who were exposed at the ages between 20-32, 9 cola-babies were born (3 stillbirths). Moreover, 87% of the respondents were found to have problem with one or more symptoms including abnormal menstruation cycles and bleeding, hypermenorrhea, dysmenorrhea, abnormal vaginal discharge, and other symptoms. In the case of Taiwan Yucheng, abnormal menstrual bleeding was found in 16% of the studied cohort.⁽¹⁾ Our Yusho's study shows high prevalence of menstrual abnormality as menorrhagia. There are 6 cases of endometriosis in this study, among them, three women who were exposed at the age of 2, 6, and 7 during their childhood developed endometriosis when they grew up. This fact shows that childhood exposure to these chemicals become apparent 20-30 years later. Moreover, there were two women with prenatal exposure who had no menstruation when they grew up. These cases suggest that trans-generational reproductive effect might have occurred.

Yusho has been approved as the patients who ingested the rice oil contaminated with PCBs/PCDFs and as those who have shown specific symptoms such as acneform eruption, dermal pigmentation and increased eye discharge. However, according to the present study, Yusho Women were suffered not only from endometriosis, but also from various diseases of the uterus and the ovary, as well as the diseases in the thyroid gland. Some of those diseases are also found in the second generation of Yusho. It is clear that these symptoms and diseases are the consequences of ingesting the contaminated oil. The level of PCDDs, PCDFs, and Co-PCBs in the causal rice oil were investigated by detailed study in 2002.⁽²⁾ Therefore, it is most probable that these symptoms and diseases result from PCBs and PCDFs.

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References

- (1) Y. L.Guo, Y.L.Hsu, C.C.Rogan, W.J (2000) Menstruation and reproduction in women with PCB poisoning: long-term follow-up interviews of the women from the Taiwan Yucheng Cohort. *Int. J. of Epidemiology*, **29**: 672-677.
- (2) Y. Yao, T. Takasuga, S. Masunaga, J. Nakanishi (2002) Detailed study on the levels of polychlorinated dibenzo-p-dioxins, polychlorinated dibenzofurans and polychlorinated biphenyls in Yusho rice oil. *Chemosphere*, **46**: 1461-1469.

Table 1. Reproductive effects on 65 Yusho women and diseases in the thyroid gland

No.	A	B	C	D	E	F	G
	age in 2002	age at exposure	approved as Yusho	diagnosed by physician gynecological diseases	self-reported abnormalities of menstruation	adverse pregnancy outcomes	diseases in the thyroid gland
1	80	41	yes	breast cancer	menoxenia/ menorrhagia	miscarriage	
2	78	41	yes	#	#		
3	77	43	yes		hypermenorrhea		
4	77	+	yes	ovariotomy	#		
5	75	40	yes	abnormal bleeding	#		
6	72	37	yes				thyroid enlargement
7	70	37	yes	#	#	miscarriage	
8	70	33	yes			delivery by forceps	thyroprival
9	70	35-36	yes		#		
10	70	36	yes				
11	68	34	yes				thyroid disfunction
12	67	27	yes				
13	67	+	yes			semi cola-baby	
14	67	28-29	yes		menorrhagia	premature baby	
15	66	31	yes	#			
16	66	+	yes	#	menorrhagia	2cola-baby/ stillbirths	
17	66	32	yes	hypermenorrhea	blood lump		goiter
18	66	+	yes				
19	65	+	yes		#		
20	65	31	yes	#	blood lump		
21	65	31	yes	cervical erosion	#		
22	65	31	yes	abnormal virginal discharge	darkish blood bleeding		
23	65	30	yes	uterectomy	abn.bleeding/severe menorrhagia	2 miscarriages	
24	64	30-31	no	#	abdominal pain	cola-baby/stillbirth	
25	63	28	yes	herpes in genital area	#		thyroid disfunction
26	63	28	yes	myoma of uterus/ ovariotomy	abn.bleeding/ dysmenorrhea	cola-baby	
27	62	28	no	#	abn.bleeding./ dysmenorrhea	cola-baby/ early delivery	
28	62	28	yes	endometriosis/myoma uterus	blood lump		thyroid cancer
29	60	+	no	myoma of uterus	darkish blood	cola-baby	
30	60	21	yes		menorrhagia/ dysmenorrhea	cola-baby	
31	58	23	yes		menorrhagia/ hypermenorrhea	cola-baby	
32	56	34-35	no	amenorrhea	irregular cycle/ abn.bleeding	abortion	thyroid disfunction
33	55	+	no	cervical erosion	hypermenorrhea		
34	54	20	yes		irregular cycle/ hypermenorrhea	cola-baby	basedow's disease
35	52	17-18	no	endometriosis	irregular cycle/ abn.bleeding	many miscarriages	
36	51	13	yes	abnormal virginal discharge	abn.virginal discharge		
37	48	+	yes	abnormal virginal discharge		no pregnancy	thyroptosis

Table 1. Reproductive effects on 65 Yusho women and diseases in the thyroid gland (continued)

No.	A	B	C	D	E	F	G
	age in 2002	age at exposure	approved as Yusho	diagnosed by physician gynecological diseases	self-reported abnormalities of menstruation	adverse pregnancy outcomes	diseases in the thyroid gland
38	46	8	yes			no pregnancy	
39	46	12	yes	ovarian cancer	abn.bleeding		
40	45	+	no	ovarian cyst		early delivery	
41	44	4	yes			no pregnancy	
42	44	+	yes				
43	44	9	yes		irregular cycle		
44	44	7	yes	endometriosis	menorrhagia		
45	43	6	yes	endometriosis	menorrhagia	faint labour	
46	42	+	yes	menopausal disorder		no pregnancy	
47	42	5	yes			4miscarriages	
48	41	+	yes			miscarriage	
49	41	+	yes				
50	41	+	yes	cervical erosion		no pregnancy	
51	40	+	yes	endometriosis			
52	40	6	no	placenta praevia		2 miscarriages	
53	40	2	yes			toxemia of pregnancy	
54	39	4	yes			sesarean	basedow's disease
55	39	+	yes			no pregnancy	
56	38	4	yes			semi-cola baby	
57	37	2	yes	endometriosis		faint labour/sesarean	
58	37	3	no		menorrhagia	no pregnancy	
59	36	+	yes		irregular cycle		
60	35	+	yes	menoxenia	abn.virginal discharge		
61	34	0	no	amenorrhoea	blood lump		
62	30	+	no	dysmenorrhoea	abn.bleeding	semi-cola baby	
63	29	-6	no		menorrhagia	jaundice	
64	20	+	no	dysmenorrhoea	severe menorrhagia	not married	
65	19	+	no	amenorrhoea		not married	

A age in August 2002

B age at exposure

+ not mention exposure age

C approved as Yusho

D gynecological diseases diagnosed by physician experiences of: hospitalization/operation/treatment

E self-reported abnormalities of menstruation

F adverse pregnancy outcomes miscarriage: abortion/stillbirth/early delively/cola-baby/semi cola-baby/neonatal death/premature baby

G diseases in the thyroid gland

shaded abnormalities

not mention name of the diseases/symptoms