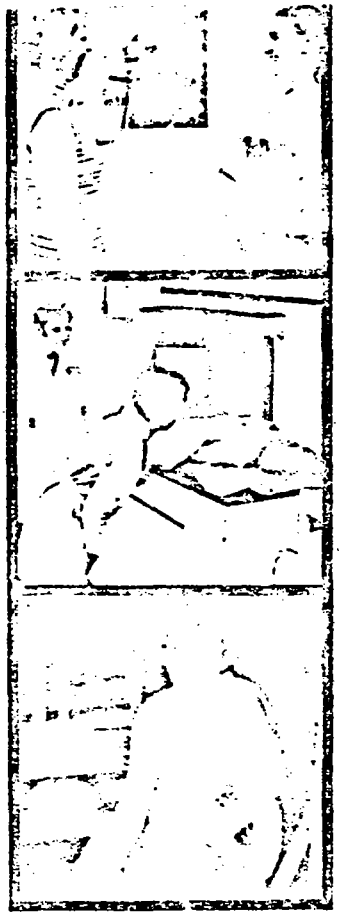

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U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
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Yusho, a poisoning caused by rice oil contaminated with polychlorinated biphenyls

MASANORI KURATSUNE, M.D., TAKESUMI YOSHIMURA, M.D., JUNICHI MATSUZAKA, M.D., and ATSUKO YAMAGUCHI, M.D.

SPORADIC outbreaks of a peculiar skin disease were reported in Fukuoka-Ken (Fukuoka Prefecture), Japan, in early October 1968. It was characterized by such symptoms as follicular accentuation, acneform eruption, pigmentation of the skin and nails, and hypersecretion of the Meibomian gland. Staff members of the department of dermatology of the Faculty of Medicine, Kyushu University, Fukuoka, who examined some of the early patients suspected they had chloracne. A possible causal relationship between the disease and ingestion of a certain brand of rice oil was also suspected in view of the distinct familial aggregation of the patients and their common use of the oil (*1*). This relationship was subsequently proved, and the disease was called Yusho, or rice oil disease.

To clarify the cause of the epidemic, a study group headed by Prof. S. Katsuki of the Kyushu University Faculty of Medicine was organized by the staff of that university, the School of Medicine of Kurume University, and local health departments. An epidemiologic study subgroup was set up within the study group on October 19, 1968, which was directed by Kuratsune and also included the other three authors. This subgroup immediately designed and carried out a series of extensive surveys in close cooperation with the department of hygiene of our faculty of medicine and the departments of public health of the Prefecture of Fukuoka and of the cities of Kitakyushu, Fukuoka, and Ohmuta.

The epidemic spread not only over Fukuoka-Ken but also over 20 other prefectures in the western part of Japan. It produced 1,001 patients —502 males and 499 females—according to the latest tabulation by the section of food hygiene, Ministry of Welfare. Although our study of the epidemic was confined to Fukuoka-Ken, and the epidemic proved to be caused by accidentally contaminated oil, we believe that publication of our results will help prevent similar food poisonings. These incidents can occur anywhere in the world if sufficient care is not exercised.

The authors are with the department of public health, Faculty of Medicine, Kyushu University, Fukuoka, Japan. Dr. Kuratsune is a professor of public health, Dr. Yoshimura and Dr. Matsuzaka are working toward doctoral degrees in public health, and Dr. Yamaguchi is a research student. *The study on Yusho was supported by a special research grant from the Japanese Government.* *Tearsheet requests to Masanori Kuratsune, M.D., Faculty of Medicine, Kyushu University, Fukuoka, Japan.*

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Most of the results of our study have already been published in Japanese (*2–5*). We refer also, when necessary, to some important observations made by a clinical study subgroup headed by Prof. K. Higuchi of the department of dermatology at our university and also to studies by a chemical study subgroup headed by Prof. H. Tsukamoto of the Faculty of Pharmaceutical Sciences.

Clinical Symptoms

The subjective symptoms of the 89 male and the 100 female patients whose cases of Yusho had been diagnosed by the end of October 1968 are listed in table 1. Most of these symptoms related to the skin and eyes. Detailed clinical examinations of these 189 persons by the clinical study subgroup revealed many of the clinical characteristics of Yusho (*1,6–9*).

Dermatological observations. Acneform eruption—marked enlargement and elevation of the follicular opening; pigmentation of the skin, lips, gingiva, the mucous membrane of the oral cavity, and nails; formation of hyperkeratotic plaque on the soles of the feet and palms of the hands; hyperhidrosis; hypertrichosis; swelling of Montgomery's gland in the breast; cyst formation of the sebaceous gland in the genital region; dry skin; and, in children, milia near the joints.

Table 1. Percent distribution of symptoms of Yusho reported by 189 patients examined before October 31, 1968

Symptoms	Males (N=89)	Females (N=100)
Dark brown pigmentation of nails	83.1	75.0
Distinctive hair follicles	64.0	56.0
Increased sweating at palms	50.6	55.0
Acnelike skin eruptions	87.6	82.0
Red plaques on limbs	20.2	16.0
Itching	42.7	52.0
Pigmentation of skin	75.3	72.0
Swelling of limbs	20.2	41.0
Stiffened soles in feet and palms of hands	24.7	29.0
Pigmented mucous membrane	56.2	47.0
Increased eye discharge	86.8	83.0
Hyperemia of conjunctiva	70.8	71.0
Transient visual disturbance	56.2	55.0
Jaundice	11.2	11.0
Swelling of upper eyelids	71.9	74.0
Feeling of weakness	58.4	52.0
Numbness in limbs	32.6	39.0
Fever	16.9	19.0
Hearing difficulties	18.0	19.0
Spasm of limbs	7.9	8.0
Headache	30.3	39.0
Vomiting	23.6	28.0
Diarrhea	19.1	17.0

Ophthalmic observations. Hypersecretion of the meibomian gland and abnormal pigmentation of the conjunctiva.

Neurological observations. Numbness, pain, hypoesthesia, and lowered sensory conduction by the radial and sural nerves.

Other observations. Elevated serum triglyceride.

Epidemiologic Data Available

When the epidemiologic study subgroup began to act, it had several pieces of information that appeared to be important but whose implications were uncertain, such as the following:

1. The familial aggregation of patients was notable, and the disease showed no distinct age and sex preference.

2. All the patients seemed to have used one brand of rice oil (abbreviated as K rice oil because it was produced by K Company). An emergency survey undertaken by the health department of the city of Fukuoka had disclosed that some of the patients in a certain area had, as a group, purchased a can of K rice oil and divided it among the group members. Those who did not buy the oil seemed to be unaffected even though they lived next door to the patients.

3. The patients seemed to be broadly distributed throughout Fukuoka-Ken.

These data of course were valuable, but we knew that if we relied on them alone, they might mislead us. We exercised particular caution, therefore, to avoid such a risk, always seeking possible antitheses when interpreting any result.

Descriptive Epidemiologic Studies

The epidemiologic study subgroup first tried to learn how the 325 patients were distributed by place of residence and time of onset of the disease (*2*). Those persons who thought they were suffering from Yusho were asked to report to their local health departments. From October 1968 until the epidemic practically terminated in January 1969, a total of 6,611 persons in Fukuoka-Ken had reported that they were affected. Among them, 325 cases of Yusho were diagnosed by the clinical study subgroup. An early analysis of a portion of the 325 persons with confirmed cases, carried out in late October 1968, revealed several peculiar features in the geographic distribution of cases, features which did not basically change during the epidemic. Therefore, only the results of

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analysis of these 325 cases will be presented to illustrate these peculiarities.

Familial aggregation. The 325 patients belonged to 112 families, a result indicating a distinct familial aggregation, which is considered one of the most important characteristics of Yusho.

Time of occurrence. Ninety-nine percent of the patients were affected during 1968, and 55 percent of the cases were concentrated in the 3 months from June to August (table 2). The monthly distribution of the cases was alike for both sexes. These results indicated that exposure to the causal agent or agents was probably temporal and indifferent to sex.

Sex and age. Distribution of the 325 patients by sex and age revealed no significant sex difference (table 3). Age-specific incidence rates per 100,000, calculated by using the census population of 1965, indicated lower risks for both males and females in the age group over 60 years, but again no marked sex difference (table 4).

Geographic distribution. We calculated crude incidence rates of Yusho for three large cities (Kitakyushu, Fukuoka, and Ohmuta) and for the jurisdictional areas of the 22 local health departments of Fukuoka-Ken. A very marked difference was noted in their rates. Ten health departments reported no cases of Yusho while extremely high incidence rates per 100,000 were noted for the area covered by the health department of Soeda (58.9) and that covered by the health department of Tagawa (44.5); intermediately high rates, from 7 to 14, were observed for the three large cities and the area of the Kasuya health department.

There are many coal mines, most of which have recently been abandoned, in the jurisdictional areas of the Soeda and Tagawa health departments. The city of Kitakyushu has big steel and chemical industries, Fukuoka is a seat of commerce, and Ohmuta has big coal mines and chemical industries. In contrast, the Kasuya health de-

Table 2. Distribution of 325 patients with Yusho diagnosed by January 20, 1969, by sex and month when symptoms appeared

Month	Males		Females		Total	
	Number	Percent	Number	Percent	Number	Percent
Before 1968	2	1.3	2	1.2	4	1.2
1968						
January	0	.0	0	.0	0	.0
February	4	2.5	6	3.6	10	3.1
March	8	5.1	12	7.2	20	6.2
April	15	9.5	10	6.0	25	7.7
May	18	11.4	15	9.0	33	10.2
June	23	14.6	33	19.8	56	17.2
July	27	17.1	32	19.2	59	18.1
August	34	21.5	30	18.0	64	19.7
September	17	10.8	12	7.2	29	8.9
October	8	5.1	14	8.4	22	6.8
November	1	.6	1	.6	2	.6
December	1	.6	0	.0	1	.3
Total	158	100.0	167	100.0	325	100.0

Table 3. Distribution of 325 patients with Yusho diagnosed by January 20, 1969, by sex and age group

Age group (years)	Males		Females		Total	
	Number	Percent	Number	Percent	Number	Percent
0–9	37	23.4	27	16.2	64	19.7
10–19	38	24.1	28	16.8	66	20.3
20–29	28	17.7	36	21.6	64	19.7
30–39	30	19.0	39	23.4	69	21.2
40–49	11	7.0	23	13.8	34	10.5
50–59	9	5.7	11	6.6	20	6.2
60–69	4	2.5	3	1.8	7	2.2
70–79	1	.5	0	.0	1	.3
Total	158	100.0	167	100.0	325	100.0

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partment covers an area that is primarily agricultural. Most areas where few Yusho patients were seen were agricultural. No other common socioeconomic or environmental factor was observed that might explain the geographic distribution of patients.

Oil Used by Patients

As stated, K rice oil had been suspected as the possible cause of the epidemic. K rice oil is a high-quality salad oil, made from rice bran by the procedure shown in the chart. It was popular in Fukuoka-Ken, even though it was slightly more expensive than other oils on the market. A thorough investigation was undertaken to determine whether the patients with Yusho had actually used this brand of oil before they were affected and if so, whether there were any common characteristics in regard to the container of the oil (bottle or can), date of production, date of purchase, or route of marketing. To seek information on these points, an investigation was conducted in cooperation with the local health departments. All patients and their wives were visited and interviewed in their homes. In addition, all the available shipping records of K Company and all available records of purchases and sales of K rice oil at wholesale oil dealers' offices and at retail stores were carefully examined.

These followup surveys soon disclosed an astonishing fact. All the persons with Yusho had used, for varying periods, K rice oil which came either from 16.5 kg. cans or 1.65 kg. bottles. One hundred seventy of the 325 patients—49 households—had used only canned oil, while the remaining 155 patients—63 households—had used only bottled oil (table 5). We were able to confirm the shipping dates for the oil used by all but four of these 170 patients. No matter where the persons lived or what their age was, 166 of the 170 had apparently used rice oil that was shipped by the K Company on February 5 and 6, 1968, according to the lot numbers on the few remaining cans. Even the four patients for whom we could not confirm shipping dates of the oil had also undoubtedly used a canned rice oil produced by the K company.

The shipping or production dates could not be confirmed, however, for the bottled K oil that 155 patients had used exclusively, because they had no old bottles at home. Purchasers of oil in bottles return the empty ones to retail stores when they buy new oil. Nevertheless, all the shipping, purchase, or selling records at K Company, at the oil dealers, and at the retail stores were examined to learn whether any bottled K rice oil had been shipped to, and had reached, the retail stores from which the 155 patients bought their oil. All shipments of oil to the stores used by the patients were further investigated to determine whether any of them had been made on February 5 or 6, 1968, or immediately before or after these dates.

By this method, we discovered that 143 of the 155 patients might have bought the bottled oil shipped from the K Company in the period February 6–15, 1968. Whether the remaining 12 patients might have also purchased oil shipped in this period remains in doubt because of lack of records. Thus, nearly all of the patients had a distinguishing characteristic—they all had a common experience of use, or possible use, of rice oil shipped by one company in a specific period. Such a coincidence could hardly be expected to happen by chance.

Table 4. Age-specific incidence rates for Yusho, by sex of patient

Age group (years)	Incidence rates per 100,000	
	Males	Females
0–9	11.4	8.6
10–19	8.9	6.6
20–29	9.1	10.3
30–39	9.6	11.9
40–49	5.4	9.3
50–59	5.4	7.2
60–69	3.5	2.4
70 and over	1.7	.0
All ages	8.3	8.1

Table 5. Distribution of 325 patients and 112 households that used K rice oil, by type of oil container and shipping dates of oil

Container and shipping dates	Patients		Households	
	Number	Percent	Number	Percent
Users of canned oil	170	52.3	49	43.8
Shipped February 5 and 6	166	51.1	47	42.0
Shipping dates unknown	4	1.2	2	1.8
Users of bottled oil	155	47.7	63	56.3
Probably used oil shipped February 5–15	143	44.0	56	50.0
Shipping dates unknown	12	3.7	7	6.3
Total	325	100.0	112	[1] 100.1

[1] Does not add to 100.0 percent because of rounding.

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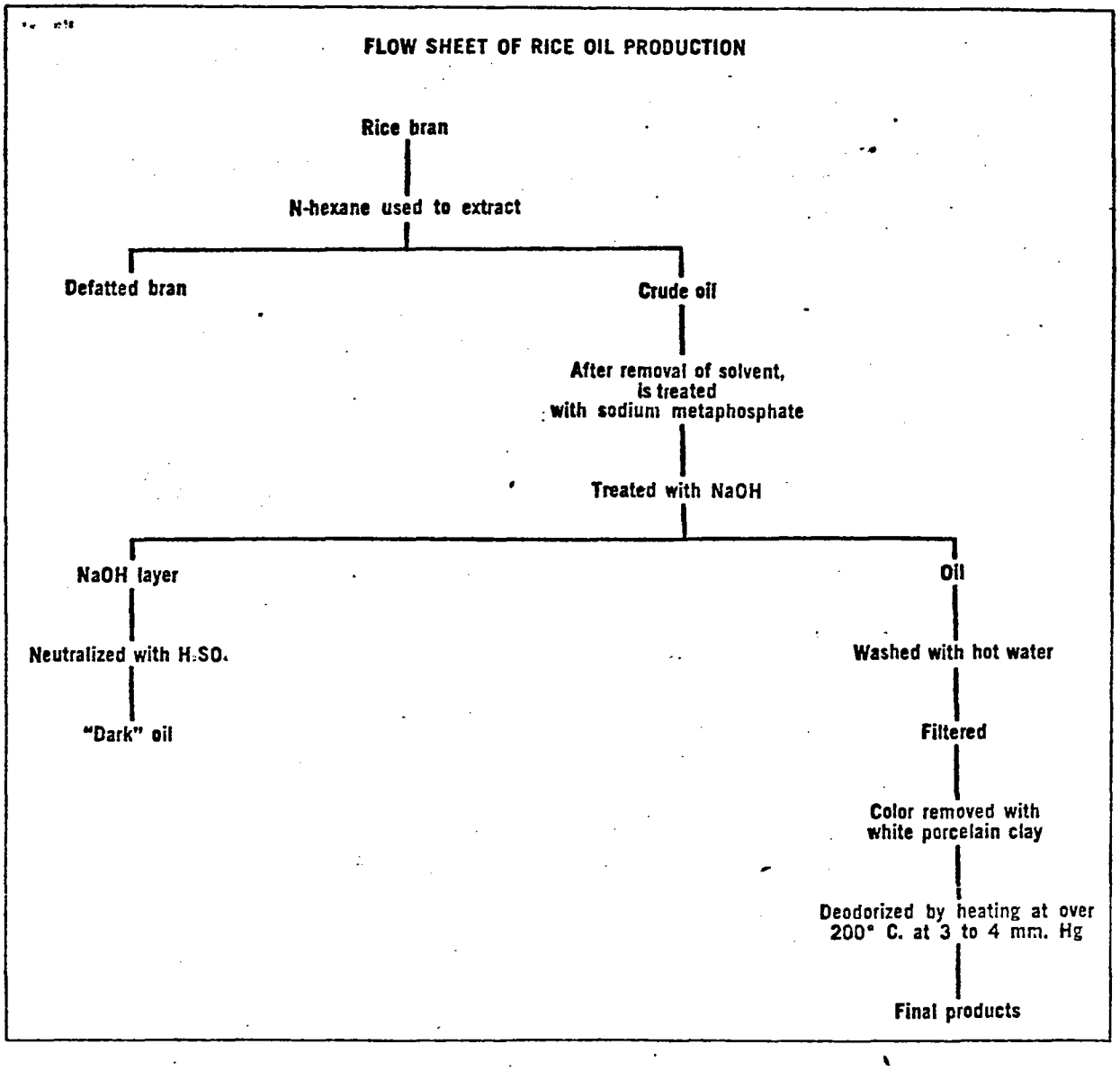

Our survey also demonstrated a high attack rate for all persons who consumed the oil. Altogether, 266 persons in 64 households had consumed canned K rice oil shipped in the period in question, and 170 had confirmed cases of Yusho. Thus, the attack rate was as high as 63.9 percent (*2*).

K Oil From Other Shipments

An additional survey seemed necessary to determine whether those persons who regularly used K rice oil but had not used any from shipments made in the period in question were free of the disease. For this purpose, a group of persons was needed who had reliable records of their health status and of their purchases of K rice oil. A group of 113 persons of 29 households living in one apartment house seemed to be appropriate subjects for this study.

According to the records of this group and the oil dealer who supplied them, these 113 persons had purchased canned K rice oil as a unit from one dealer and divided it among themselves fairly regularly from December 1967 to September 1968 except for the period from January to April 1968, when this bulk purchasing was not carried out. Their disease experience, particularly any skin disease that occurred during 1968, was carefully explored through interviews and, if necessary, through investigation of their medical records at hospitals. No cases of Yusho were found among

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members of this group. Thus, we demonstrated that persons who had used K rice oil regularly for more than a half year but did not use the oil from the specific shipments did not suffer from Yusho (*2*).

Retrospective Case-Control Studies

All these results suggested that Yusho was causally connected with use of the K rice oil that was shipped from K Company on February 5 and 6, 1968, or soon thereafter. Nevertheless, some other factors or agents might have been the primary or secondary cause of the epidemic. Therefore two case-control studies were done. In one, the personal backgrounds of the patients and matched controls were compared. In the other, the use of oil and fats in the households of the patients and the controls were compared.

To discover whether persons with Yusho cases and those without had different personal backgrounds, home interviews were conducted with all persons whose cases had been reported by October 31, 1968, and with healthy controls matched by age, sex, and place of residence. One hundred twenty-one patients and 121 controls (53 males and 68 females) were selected in this manner and asked 60 questions concerning their occupations, medical background, general health status, habits, customs, diet, pets, and other characteristics of their lives.

Table 6. Percent of 121 patients and 121 controls having various allergies and dietary and personal habits, based on case-control study

Items investigated	Patients	Controls
Allergic to fish	5.0	7.5
Allergic to aspirin	.0	4.2
Allergic to drugs other than aspirin	7.5	6.6
Bathing facilities at home	84.7	85.5
Bath every day	73.0	70.6
Pets at home	[1] 18.3	[1] 36.5
Floor space of house smaller than 66 square meters	66.9	66.1
Handling agricultural chemicals	2.5	6.6
Taking codliver oil	10.8	8.3
Taking vitamin pills	23.2	18.3
Taking other restorative drugs	9.1	7.5
Water supply available at home	81.3	74.7
Dining out occasionally	28.1	30.6
Taking all meals with the family	88.8	89.6
Green vegetables daily	63.1	58.9
Milk nearly every day	49.0	39.0
Butter nearly every day	22.4	24.9
Eggs nearly every day	64.7	59.8
Fried foods or tempura nearly every day	[1] 22.4	[1] 11.6
Foods prepared with oil nearly every day	45.7	35.7
Fish nearly every day	21.6	29.1
Mayonnaise nearly every day	10.8	10.8
Instant "rahmen" or Chinese noodles nearly every day	10.8	10.0

[1] $P < 0.05$.

Table 7. Distribution of 69 households with patients and 207 control households, by use of various fats or oils, based on case-control study

Fat or oil	Households with patients		Control households	
	Number	Percent	Number	Percent
Butter	35	50.7	105	50.7
Margarine	44	63.8	127	61.4
Sesame oil	21	30.5	85	41.1
Rape-seed oil	10	14.5	77	37.2
Rice-bran oil	66	95.7	64	30.9
Lard	12	17.4	38	18.4
Other oils	13	18.8	117	56.5

The patients and the controls differed significantly in respect to only two of the personal factors tested (table 6). Persons who ate fried foods or tempura nearly every day were more numerous among the patients than among the controls, while more of the controls than the patients had pets.

To compare the use of oil and fats, 69 households with Yusho patients were matched by place of residence with 207 households without such patients—three control households for each household with cases.

As to regular use of fats and oils, a distinct difference was noted between the two groups only for rice-bran oil. About 96 percent of the patients' households and 31 percent of the controls' households reportedly used rice-bran oil regularly (table 7).

When asked about the use of rice oil from the K Company, all of the households with patients affirmed its use in comparison with only 32.4 percent of the control households; 61.3 percent of the control households denied using it; the remaining 6.3 percent were uncertain. Thus, the case-control studies clearly indicated that none of the factors tested except use of K rice oil could account for the disease (*2*).

Dose-Response Relationship

To prove that a causal relationship existed, a distinct dose-response relationship needed to be demonstrated. Estimating the quantity of contaminated rice oil consumed by each patient and members of his family was not feasible. Nevertheless, if we disregarded age and sex, we could estimate roughly the average amount of oil each person had consumed by dividing the amount used in a

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household by the number of persons in it, taking into account the frequency with which these persons ate at home, but not the possible loss of oil during and after cooking, nor the varying tastes and food intake of the family members.

Dr. Masayasu Goto, a dermatologist, with no knowledge of the amount of oil used by the 146 consumers of the contaminated oil, examined these persons and then graded the cases of Yusho he diagnosed according to their clinical severity. Only later did we link the severity of the cases, as determined by the dermatologist, to the amount of contaminated oil used by the patient.

Eighty of the 146 users of the contaminated oil were believed to have consumed, individually, less than 720 ml. (table 8). Of these 80 light users, 12 percent were not affected, 49 percent had light cases, and 39 percent had severe cases; the attack rate was 88 percent. The 45 persons who had used 720–1,440 ml. were all affected; 69 percent of this group had severe cases. A still larger proportion of the severe cases was found among the persons who had used more than 1,440 ml. of the contaminated oil; this group had an attack rate of 100 percent.

Since the clinical severity of the disease was not found to differ significantly between the sexes but differed considerably according to age, a standardization for age seemed necessary to achieve a more accurate interpretation of the observed relationship between use of the oil and the clinical severity of the disease. With the age composition of the 146 users of the oil as the standard, the factor of age was standardized for each of the three levels of oil intake. The figures, however, hardly changed from those shown in table 8. Thus a very clear dose-response relationship could be demonstrated, even though the estimates of the dose were inaccurate (*3*).

Toxic Agent

In view of all these epidemiologic observations, we concluded that K rice oil from specific shipments had caused the Yusho. Now the question arose as to why the oil was toxic. To answer this question, we of course had to rely on other approaches than epidemiology. In mid-November 1968, the chemical study subgroup discovered, mainly by gas chromatographic analysis, that the canned K rice oil shipped on February 5, 1968, portions of which had been collected from some of the patients, was contaminated with about 2,000 ppm of Kanechlor. Kanechlor is a commercial brand of polychlorinated biphenyls containing 48 percent chlorine. Skin fat collected from the patients also contained Kanechlor (*10*).

In this discovery, Prof. K. Inagami of the department of food technology, Faculty of Agriculture, Kyushu University, and his associates played a leading role. A technological inspection of the K Company plant revealed that Kanechlor was used as an agent to transfer heat to the processed oil at a reduced pressure so that odorous substances could be removed (see chart). The Kanechlor must have leaked from the heating pipe in which it was being conveyed and contaminated the oil, since small openings were discovered in the old pipe.

To discover whether only the K rice oil shipped in February 1968 was contaminated with Kanechlor, the chemical study subgroup analyzed 109 samples of the bottled K rice oil which, according to the lot numbers, had been shipped between October 1967 and October 1968. This analysis revealed that only the samples shipped on February 7, 10, 12, 15, 17, 18, and 19 and on March 11, 18, and 21, 1968, were contaminated with Kanechlor. This contamination was most marked for the oil shipped on February 7; the contamination was rapidly reduced to nil after February 10 (*10*). No analysis could be made of bottled K rice oil shipped February 5 and 6 because of the lack of samples.

Similarly, 479 random samples of bottled rice oil were analyzed for chlorine content by using the X-ray fluorescence method with a count meter from a U.S. instrument manufacturer (the Applied Research Laboratory). Again, only those samples shipped from February 7 to 10 contained a large amount of chlorine (maximum 462 ppm). None of the oils shipped in other months were contaminated with more than a trace amount of chlorine. Thus, the results of chemical analysis coincided with those achieved by epidemiologic approaches.

Other Epidemiologic Results

Babies born to patients. In late October 1968 a pregnant patient with Yusho had a stillbirth in which the fetus was unusual; the skin, nails, and gingiva were a peculiar dark brown and stained. Similar fetuses were delivered by other patients with Yusho. Since no such birth or stillbirth was known to have been reported previously in Japan, the study group investigated these occurrences with particular care. The epidemiologic study

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subgroup questioned all female patients with Yusho and all unaffected women in the households of patients with Yusho about any pregnancies and deliveries in the period from February 15, 1968, to the end of the year.

Thirteen women—10 with Yusho, two without, and one with status unspecified—had given birth to 11 live born and two stillborn infants during the specified period. (Eight of the live born infants were males and three were females; one of the stillborn infants was a female and the sex of the other was unspecified.) Among these infants and fetuses, 10 had the characteristic grayish dark-brown stained skin at birth, five the dark-colored nails and gingiva, and nine an increased eye discharge. Women with Yusho accounted for all these deliveries, except for the delivery of one of the nine babies with eye symptoms.

The high incidence of these unusual phenomena among pregnant women with Yusho strongly suggested that the phenomena were caused by ingestion of the contaminated oil. The fact that nothing unusual was seen in the women's medical histories, health conditions, or use of drugs during pregnancy also supported such an interpretation.

All these facts, together with the results of chemical assays which showed that the placenta and the subcutaneous adipose tissue of the stillborn fetuses contained components of Kanechlor, prove that babies and fetuses were affected because of the women's ingestion of this particular complex compound (*4*).

The majority of the babies were small for their periods of gestation. As they grew older, their stained skin gradually faded. Postnatal growth curves for the affected babies were found to be similar in shape to the national standards when both sexes combined were compared. When only males were compared, the curves for the affected male infants were plainly lower than the national standard curves. A clear comparison between the curves for girls could not be made because of the limited number of female infants who were affected by Yusho.

The amount of contaminated rice oil that nine of the 13 mothers consumed during pregnancy was estimated to be 0.3 to 2.6 liters. No distinct dose-effect relationship could be demonstrated between oil consumption and the babies' symptoms because of the limited number of cases available for analysis. Nor could evidence be obtained in regard to any possible physical and mental retardation of the babies (*4*).

Growth of affected children. To discover whether Yusho disturbs children's growth, the affected school children, 23 boys and 19 girls, were compared in 1967, 1968, and 1969 with 719 healthy children matched in height and body weight. The gain in height or in body weight which each sick child showed before the poisoning, namely from 1967 to 1968, and the gain after the poisoning, from 1968 to 1969, were compared with the distribution of the corresponding gains seen in the corresponding control group.

The gains of the affected boys in both height and weight decreased significantly after the poisoning, while the affected girls showed no definite change in this respect. Because of the limited number of cases available for analysis, no significant relationship could be found between the clinical severity of the cases and the decrease in gains in height and weight.

Discussion

This unfortunate episode of rice oil poisoning taught us some important lessons. In the food industries of many countries, no effective administrative control and supervision is apparently exercised over the use of toxic substances like Kanechlor. These products do not contaminate the final products in normal operations, but they do when the operation is accidentally disturbed or carelessly conducted. In contrast to the case with food additives, too little care has been exercised to avoid the hidden risks in the use of such substances. A greatly increased effort is needed to improve this situation.

The polychlorinated biphenyls seem to be particularly hazardous in this respect because their use is still increasing in many industries, including food industries. If these substances are absorbed by the body, they will easily accumulate, gradually reaching a level high enough to exert adverse effects, since they have an extremely slow rate of metabolization or excretion. Many patients with Yusho are still tortured by the disease even after more than 2 years of treatment. A 1971 report has indicated that the subcutaneous fat of the patients still contains a large amount of polychlorinated biphenyls although their dermal conditions are slowly improving (*12*).

Recently, also, it has been demonstrated that wide environmental pollution with polychlorinated biphenyls is quietly growing in many countries (*11*). To prevent another epidemic of Yusho,

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which will break out on a global scale if the pollution worsens, radical efforts are urgently needed.

Our success in identifying the cause of the epidemic seems to have been due to many factors: (*a*) common epidemiologic principles were honestly followed, (*b*) local health departments and the patients themselves cooperated fully, (*c*) the causal agent was not multiple, but single, (*d*) contamination of the oil with Kanechlor was temporary and marked, (*e*) the latent period of the epidemic was several months, and the epidemic was relatively short, (*f*) Yusho had characteristic symptoms, allowing easy differentiation from other diseases, (*g*) some of the oil used by the patients, along with the original containers, were still available, and (*h*) some persons who bought the oil as a group had contracted the disease. All these factors facilitated our study.

Epidemiologic study of an illness or of adverse effects which were more chronic, less peculiar, which progressed less noticeably than Yusho, and were caused by multiple agents would present greater difficulties.

We need to develop more sensitive and more efficient epidemiologic methods. We must, moreover, exert constant efforts to make our epidemiologic information more accurate, quantitatively and qualitatively, by using the methodology of other disciplines when it seems necessary for our purposes.

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KURATSUNE, MASANORI (Kyushu University), YOSHIMURA, TAKESUMI, MATSUZAKA, JUNICHI, and YAMAGUCHI, ATSUKO: *Yusho, a poisoning caused by rice oil contaminated with polychlorinated biphenyls. HSMHA Health Reports, Vol. 86, December 1971, pp. 1083–1091.*

A peculiar skin disease, Yusho, was observed in residents of Fukuoka-Ken, Japan, in October 1968, which later spread over the western part of the country. By use of basic epidemiologic methods, the cause of the disease was shown to be a specific brand of rice oil that had become contaminated with a heat transfer agent during processing. This agent, Kanechlor, is a complex mixture of polychlorinated biphenyls.

Women who consumed the contaminated oil delivered babies or fetuses with peculiar dark-brown stained skin, nails, and gingiva. The poisoning significantly decreased the growth of the boys who were affected, while the girls who were affected showed no such change. Many of the persons who contracted the disease are still tortured by it even 2 or more years later, despite all possible treatment methods.

In view of the slow recovery from the poisoning and the increasing pollution of the environment with these compounds on a global scale, radical efforts must be made to avoid the hidden risks of contamination.

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