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SHELLFISH POISONING FROM *CALLISTA BREVISIPHONATA* CARPENTER AND ITS CLINICAL SYMPTOMS

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Introduction

In the preceding paper¹⁾, we have reported the shellfish poisoning from *Callista Brevisiphonata* CARPENTER which occurred in the vicinity of Mori, Hokkaido, in the midsummer of 1950. According to the investigation of the poisoning, twenty six people were intoxicated among 115 consumers. (morbidity 22.5%). The incubation period was very short and the onset of symptoms began only from thirty minutes to one hour after ingestion. All patients, however, have recovered from illness within one or two days and no fatal case has been observed. The Main symptoms were the itching of the skin, flushing of the face, urticaria, oppression of the chest, epigastric and abdominal pains, dyspnea, cough, vomiting, asthmatic manifestations, hoarseness etc. Correlation between the freshness of the bivalves and the occurrence of poisoning could not be observed, even the freshest samples having potentialities of causing the food poisoning.

Since the first outbreak in 1950, Mori Health Center had prohibited the catch and marketing of the shellfish, thence further outbreaks have never occurred. In the beginning of this summer, 25th May 1952, three women and a boy ingested the shellfish out of curiosity and were all intoxicated. This outbreak has involved two interesting points; first, the former outbreak had not been due to accidental reasons (such as bacterial infections), but due to some reproducible reasons (as the poisonous principles contained originally in the fresh organisms); secondly, toxicities of the bivalves have surely the seasonal prevalences and showed the peak in spawning season.

This paper deals with the location of the poisonous principles in shellfish by oral administration to normal adults and its clinical observations. Furthermore,

skin test reaction of the shellfish allergen are made. A simple method for the discrimination of sexual organs of the bivalves are also presented.

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Experimental

1. Location of the Poisonous Principles in Shellfish.

In spite of repeated trials, the location of the shellfish poison has not been clarified by the determination method of shellfish poison after Akiba²⁾, using mice, kittens and dogs as experimental animals. Finally, we have tried the oral administration to normal individuals and have located the source of poison in the visceral organs of shellfish. As clearly shown in Table I, it indicated that the ovary is responsible for the localized organ of toxicity.

Table 1. Location of poison illustrated by oral administration to normal adults.

Patients No.	Sex & Age	Weight of organs fed orally.*	Symptoms caused.	remarks
2	24 ♀	ovary total 50g.	Feeling of paralysis (mouth, tongue) Itching of the skin. Irritation of throat and larynx. Edematous exanthema, Cough. Flushing of face. Nausea. Oppression of chest.	pulse rate.** 90/min. B. 74/min. A. recovered after. 5 hrs.
9	29 ♂	"	Feeling of paralysis (ears). Irritation of throat and larynx.	73/min. B. 74/min. A.
3	31 ♂	"	Itching of skin. (round the neck). Irritation of throat and larynx. Dyspnea. capillary dilatation.	50/min. B. 44/min. A.
2	24 ♀	Testes 33 g.	No remarkable change.	75/min. B. 74/min. A.
9	29 ♂	"	"	69/min. B. 64/min. A.
3	31 ♂	"	"	58/min. B. 52/min. A.

2	24 ♀	Digestive diverticula 75 g.	No remarkable change.	74/min. B. 72/min. A.
9	29 ♂	"	"	69/min. B. 76/min. A.

* These organs of shellfish were boiled for 5-10 minutes with small volume of starch or agar and ingested.

** Abbreviations: B Before ingestion.
A After ingestion.

2. Clinical Symptoms of Food Poisoning of the Shellfish.

For the clinical observations, the oral administration of ovary to normal adults with the cooperation of nine volunteers, was carried out. Fresh shellfish were

Table 2. Subjective symptoms of the patients.

symptoms from chief complaints.	patients No.									Morbidity	Morbidity of former outbreaks.
	1	2	3	4	5	6	7	8	9		
Thirst	-	+	-	-	-	-	-	-	-	11%	
Palpitation	-	+	-	-	-	-	-	-	-	11%	
Salivation	-	+	-	-	-	-	-	-	-	11%	
Lacrimation	-	-	-	-	-	-	-	-	-	0%	
Sweating	+	-	-	-	-	-	-	-	-	11%	
Rhinorrhoea	+	-	-	-	-	-	-	-	-	11%	
Nasal obstruction	+	+	-	-	-	-	-	-	-	22%	8%
Cough	‡	+	+	-	-	-	-	-	-	33%	32%
Expectoration	-	-	-	-	-	-	-	-	-	0%	
Dyspnea	+	+	+	-	-	-	-	-	-	33%	46%
Urticaria	‡	‡	-	-	-	-	-	-	-	22%	42%
Itching of skin.	‡	‡	‡	+	-	-	-	-	+	55	61%
Subcutaneous hemorrhage	-	-	-	-	-	-	-	-	-	0	0%
Vomiting	‡	-	-	-	-	-	-	-	-	11%	32%
Nausea	+	+	+	-	-	-	‡	-	-	44%	54%
Gurgling in abdomen.	-	+	-	-	-	-	-	-	-	11%	
Diarrhoea	+	+	-	-	-	-	-	-	-	22%	19%
Epigastralgia	+	+	-	-	-	-	‡	-	-	33%	50%
Meso- and hypogastalgia.	-	+	-	-	-	-	-	+	-	22%	42%
Chill	-	+	-	-	‡	-	-	-	-	22%	23%
Shiver	-	-	-	-	-	-	-	-	-	0	
Fever	+	+	-	-	-	-	-	-	-	22%	15%
Migraine	+	-	-	-	-	-	-	-	-	11%	27%
Vertigo	+	-	-	-	-	-	-	-	-	11%	11%
Visual disturbance	-	-	-	-	-	-	-	-	-	0	0%
Auditory disturbance	-	-	-	-	-	-	-	-	-	0	0%
Hoarseness	-	-	-	-	-	-	-	-	-	0	13%
Paralytic feeling (Body terminals)	-	‡	‡	-	-	+	+	-	+	55%	11%
Irritation of throat and larynx.	+	‡	‡	+	-	-	-	+	‡	66%	

Remarks: Patient No. 1 is the most severe case.

Patient No. 2, the susceptible case, was one of the victims in the foregoing outbreak, 25th May 1952, when she was suffered from chill, nausea, dyspnea, cough, paralytic feeling, hoarseness and itching of skin. Onset of symptoms began at 25 minutes after ingestion and recovered after 8 hours.

freed from shell and ovary was separated off therefrom by the simple discrimination method described later, cooked with some seasonings and administered 50-70 g. to the patients (hereafter these volunteers are called "patients") according to their body weight. Subjective symptoms of the patients are shown in Table 2. As for the objective symptoms, temperature, pulse, blood pressure, erythrocyte and leukocyte counts, blood sugar and protein, sugar, urobilinogen of urine were examined. Blood sugar was estimated with Erma-microsaccharimeter after Crecelius Seifert method. Protein, sugar and urobilinogen of urine were determined after sulfosalicylic acid method, Almén Nylander method and Ehrlich method respectively. These results are shown in Table 3-4 (A) (B).

The clinical histories for the patients were also inquired as in Table 5. Of nine patients examined, one severe case with positive response and one sus-

Table 3. Objective symptoms of a severe case (Patient No. 1).

Items	normal state	after ingestion
temperature	36.6°C	36.8°C
pulse	78/min.	82/min. after 30 min. 105/min. after one hour.
Blood pressure	L : 110-60 mmHg R : 110-60 "	L : 110-60 mmHg } after 40 min. R : 110-0 " } L : 105-50 " } after 1h. 45 min. R : 105-50 " }
Pupil	—	Slight dilated but not clearly. Eyes were bloodshot.
Skin (Dry or moist) and Dermographism	—	No remarkable change
Total Erythrocyte count	4,74 million	5,07 million
Total leukocyte count	6,500	11,000
Hemogram of leukocyte.		
Basophils (B)	0%	0%
Eosinophils (E)	4.5	0.5
Neutrophils (N)		
Stab nuclears (St)	4.0	1.0
Segment nuclears (S)	59.0	59.5
Lymphocyte (L)	28.0	37.0
Monocyte (M)	4.5	2.0
Other forms (Myelocyte & Juvenils)	0	0
Blood sugar	83 mg%	77 mg%
Urine Protein	Qualitatively negative.	qualitatively negative.
Sugar	"	"
Urobilinogen	±	±

Remarks: Blood was obtained from ears. Blood smears made was stained after a few minutes' drying.

pectable case were observed. Contrary to anticipation, moderately lower morbidity in this time will be attributed to the decreasing toxicity of shellfish than that of the former outbreaks, while the symptoms showed analogous manifestation.

Table 4. A. General trends for the objective symptoms.

Items	Patients No.					
	1	2	3	4	5	6
Temperature	S.I.	S.I.	Doubt.	Doubt.	S.D.	Doubt.
Pulse	I. (1st) D. (2nd)	D.	S.D.	I.	D.	D.
Blood pressure	S.D. (1st) D. (2nd)	D.	S.D.	S.D.	D.	S.D.
Skin (dry or moist) & Dermographism	No remarkable change					
Erythrocyte count (I)	I. (1st) Doubt. (2nd)	Doubt.	Doubt.	D.	Doubt.	D.
Leukocyte count (2)	I. (1st)	Doubt.	Doubt.	D.	Doubt.	D.
Blood sugar	Fluctuate within the normal range					
Urine Protein sugar urobilinogen	No remarkable change qualitatively					
	S.I.	Doubt.	S.I.	I.	Doubt.	S.I.

Remarks and abbreviations :

- (1) .Fluctuate within the normal range except patient No. 1 (1st) and No. 5.
- (2) Slight leukocytosis in patient No. 1 (1st).
- I. Increasing. S.I. slightly increasing.
- D. decreasing. S.D. slightly decreasing.
- Doubt. doubtful case.

Table 4. B. Hemogram of leukocyte of patients.

Items	patients No.					
	1	2	3	4	5	6
Normal state						
B.	0%	0%	0%	1.0%	0.5%	0%
E.	4.5	2.0	4.0	2.0	11.0	1.5
St.	4.0	3.0	1.0	5.0	2.5	2.5
S.	59.0	60.0	52.0	54.0	49.0	51.5
L.	28.0	34.0	41.5	35.0	32.5	41.0
M.	4.5	1.0	1.5	2.0	4.5	3.5
Other.	0	0	0	1.0	0	0
N:L	2.25	1.9	1.3	1.7	1.6	1.3
I.R.	3.5	2.7	13.0	9.0	12.0	12.8

After ingestion						
B.	0%	0%	0%	0%	0%	0%
E	0.5	4.0	4.0	4.0	14.0	1.0
St.	3.0	3.0	2.5	3.0	4.5	3.0
S.	48.5	54.5	59.5	49.0	46.0	47.5
L.	37.5	35.0	31.0	37.0	28.0	44.5
M.	10.5	3.5	3.0	7.0	7.5	4.0
other	0	0	0	0	0	0
N:L	1.4	1.6	2.0	1.4	1.8	1.1
I.R.	14.7	9.5	3.0	12.9	12.7	13.6
	(+11.2)	(+6.8)	(-10.0)	(+3.9)	(+0.7)	(+0.8)

Remarks: Eosinophils of patient No. 5 are abnormally higher which may be a symptom of infestations by any of the worms. Owing to leukopenia (3500) and eosinophilia, she is inadequate for allergy demonstration. N:L is leuko-index.

I.R. Index of resistance = $(T-10) - (P-70)$, where T, the total leukocyte count expressed in thousands, P, neutrophilic percentage.

Table 5. Clinical records for the patients.

Items	Patients No.					
	1	2	3	4	5	6
Age	26	24	31	21	43	40
Sex	♂	♀	♂	♂	♀	♂
Body weight.	53.0kg	52.0	53.0	56.5	46.0	54.0
History of present illness.	none	none	none	none	none	none
past medical history	none	contact dermatitis from vegetable origin but not pollinosis.	none	none	none	ever afflicted from asthmatic manifestation.
1. Allergic diseases.						
2. Diseases of childhood.	measles	measles Whooping cough.	measles	measles	chicken pox	measles
3. Infectious diseases.	Sore throat Bronchitis Arthritis	Tonsillitis Typhoid fever	Tonsillitis Pleurisy Nephritis Malaria	Sore throat Tonsillitis Bronchitis Otitis media Furunculosis	Tonsillitis Influenza Nephritis Furunculosis	Sore throat Bronchitis Malaria Tonsillitis
4. parasitic diseases	round worms	none	none	round worms	round worms	round worms
5. Gastro-intestinal diseases	none	none	none	hemorrhoids	gastric distress	heart burn
6. Metabolic diseases	none	none	none	none	none	Thyroids
7. No. of pregnancy	—	none	—	—	one time	—

Social history Work	Health center office work	Health center bacteriolo- gical ex- periment	University chemical experiment	Health center bacteriolo- gical ex- periment	Health center	Health center office work
Habits	Alcohol Tobacco	Sweets	Tobacco	Alcohol Tobacco	Sweets	Alcohol Tobacco
Emotional life	Worrisome	Nervous Excitable worrisome	nervous Excitable worrisome	—	Excitable worrisome	—

Remarks: Patient No. 6 seems to be inadequate for the experiment.

3. Skin Tests of Shellfish Allergens.

For the preparation of liquid allergen, the allergic excitants of ovary, testes and digestive diverticula were extracted with the following Coca & Milford buffer.

Original solutions of buffer after Coca & Milford.

1st. solution KH_2PO_4 3.63 g
 $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ 14.31 g
 NaCl 50.0 g
 Distilled water 1000 ml.

2nd. solution 4% phenol.

Equal volume of the 1st and 2nd solutions were mixed to which four times of its volume of distilled water was added. This resultant solution is the extracting fluid (pH 7.0) for allergen. The allergic excitants of each organ were

Table 6. Skin tests of shellfish allergen by intracutaneous injection.

Age & sex of patients	Source of allergen*	classification of the reaction			
		after 20 min	after 1 hour	after 10 hours	
31 ♂	(1)	P: 40×20 mm R: 50×50	P: 40×20 mm R: 50×40	W: 3×3 mm R: 0	markedly positive
	(2)	W: 15×10 R: 30×30	W: 15×15 R: 20×17	W: 3×3 R: 0	slightly positive
	(3)	P: 40×25 R: 60×50	P: 45×20 R: 50×45	W: 3×3 R: 0	markedly positive
	(4)	W: 5×5 R: 10×10	W: 5×5 R: 0	W: 3×3 R: 0	negative
29 ♂	(1)	W: 15×10 R: 40×30	W: 17×16 R: 30×25	I: 5×5 R: 22×20	moderately positive
	(2)	W: 8×7 R: 0	W: 10×9 R: 0	W: 0 R: 0	negative
	(3)	W: 10×10 R: 35×25	W: 14×12 R: 30×25	I: 19×14 R: 25×19	moderately positive
	(4)	W: 5×5 R: 15×15	W: 5×5 R: 3×3	W: 0 R: 3×3	negative

24 ♀	(1)	W : 15×10 R : 30×25	W : 14×14 R : 19×19	I : 3×3 R : 0	slightly positive
	(2)	W : 15×10 R : 20×20	W : 7×7 R : 12×12	I : 4×5 R : 0	Doubtful
	(3)	P : 18×14 R : 45×40	P : 25×25 R : 35×30	W : 0 R : 70×40	markedly positive
	(4)	W : 15×8 R : 10×18	W : 6×6 R : 0	W : 15×12 R : 0	negative

Remarks & abbreviations : (1) Digestive diverticula. (2) Testes. (3) Ovary.
(4) Control. W : Wheal. P : Pseudopodia or papule.
I : Induration.

extracted with this solution and packed in ampules and stored in ice box. A small amount (0.05 ml) of the liquid allergen was injected by a tuberculin syringe into the inner forearm of the skin intracutaneously.

The reading of the reaction obtained at 20 minutes, 1 hour, and 10 hours after injection. For the reading of reactions, the Cooke's classification was adopted. Markedly positive reaction of the ovary agreed with the results of oral administration and this reaction lasted moderately for longer period, leaving characteristic wheals. The results obtained is given in Table 6.

4. A Simple Method for the Discrimination of Sexual Organs of Shellfish.

The poisonous principles of the shellfish was found to be located in ovary,

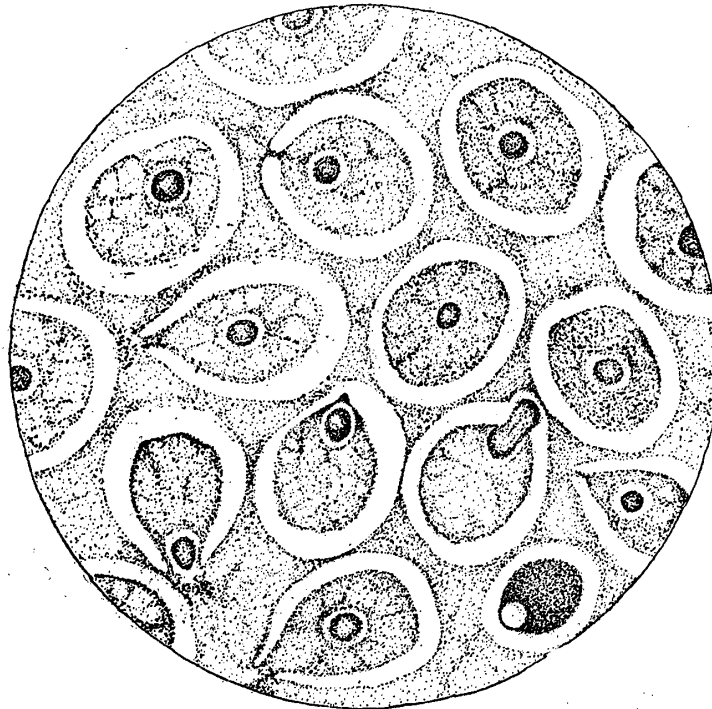


Fig. 1. Ova of *Callista brevisiphonata* Carpenter. (×500)

therefore, the consumers must distinguish toxic female shellfish from nontoxic male. The authors found a simple discrimination method of sexuality of shellfish which may be convenient for the consumers to avoid food poisoning without special knowledge and instrument.

The technique is as follows ; Take the minute amount of white or yellowish colored gonad with knife and smear it on a thin glass plate. If the shellfish is female, one will find white granular particles of ova. The size of ova is larger than sperm and is enriched with fatty substances, so it looks hydrophobic when smeared on glass plate. (Fig. 1). Whereas in male, the smears look like milky paste.

Discussion

The reasons why all consumers of the shellfish are not always patients chiefly depend upon the fact that the poisonous principles are localized in ovary alone, while the consumers ingest both male and female shellfish at random and that, even in female shellfish, the toxicity have also seasonal variations. Furthermore, individual difference of tolerance to the potent allergic substance may have a concern in this variable occurrence.

According to Tuft (3), clinical manifestations of food allergy may be grouped into : (1) respiratory, (2) gastro-intestinal, (3) cutaneous, (4) neurologic, and (5) miscellaneous. Judging from the subjective symptoms in Table 2, the clinical manifestations of this poisoning indicate complex symptoms of these food allergy. When the onset of symptoms is acute and typical in nature, the following changes can be observed ; slight increase in temperature, moderate increase of pulse, erythrocyte and leukocyte count, and decrease in blood pressure. The latter is probably due to capillary dilatation. In case of patient No. I, onset of symptoms began at 50 minutes after ingestion. At first he began to complain the itching of skin which was followed by irritation of throat and larynx, cough, flushing of face, developing urticaria from upper part of the body to the lower, nausea, vomiting, vertigo etc.

As soon as clinical observations were accomplished, he was injected 20 mg of antihistaminic drugs (Dimethylaminoethylbenzhydylether hydrochloride) hypodermally and recovered from illness after few hours without ill prognosis. As for the changes of differential count of leukocyte, total count increase in acute, decrease in eosinophils and neutrophils, and corresponding increase in lymphocytes and monocytes were observed. Generally speaking, decrease in leuko-index and monocytosis are of clinical interest, indicating the moderate stronger in their tolerance for such causations.

The clinical significance of markedly positive skin reaction of ovary allergen in Table 6 is not easy to interpret, but it is clear that this poisoning is surely

allergic food poisoning and, though unexplained, some relationship between the allergen and poisonous principles does exist. Cooking as a rule has little effect upon such sea food allergen.

Summary

1. The poisonous substance of a lamellibranchiata, *Callista Brevisiphonata* CARPENTER was located in ovary. Removal of ovary will prevent the consumers from poisoning.
2. Clinical symptoms were discussed in detail as the results of oral administration to normal individuals, illustrating in Table 2-4 (B).
3. Clinical symptoms and markedly positive skin reaction proved that the shellfish poisoning is surely of allergic nature.
4. For the detoxication of this poisoning, it is recommended to use anti-histaminic drugs to the patients.
5. A simple discrimination method of sexual organs was described.

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