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Scombroid Poisoning

Report of an Outbreak

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An outbreak of scombroid poisoning occurred in San Francisco in the fall of 1977. The vehicle was sashimi prepared from spoiled tuna fish. Prompt public health measures prevented further consumption of the implicated food. Laboratory studies showed the presence in the tuna of bacterial species capable of producing large amounts of histamine, a substance strongly implicated in scombroid poisoning. Chemical analysis showed that histamine is very unevenly distributed in the flesh of spoiling tuna, therefore accounting for the sometimes random occurrence of disease among people eating the same food at the same table.

THOUGH RELATIVELY RARE, scombroid poisoning has been known for many years and was first reported in 1799 in Britain.[1] In California, it once was associated primarily with smokehouses and custom canneries that process tuna caught by party boats in the southern part of the state. Reporting, spotty at first, seems to be improving. Consequently, in California, while only ten outbreaks were identified between 1927 (when records were first kept) and 1969, 13 were recorded since 1970.[2] In recent years a number of cases have resulted from the consumption of imported mahimahi (dolphinfish).[2] Since symptoms are dramatic, they seldom fail to attract attention and in the past were often ascribed to fish poisoning (ichthyosarcotoxism) or allergy. However, scombroid poisoning is clearly different from either of these.

In the fall of 1977 a classical outbreak of scombroid poisoning from commercial sources provided the opportunity to study this disease clinically and in the laboratory.

To acquaint readers with this unusual disease, this communication will describe this episode with respect to epidemiology, symptomatology, laboratory findings, etiology and public health control measures and will also discuss certain peculiarities of the disease in the light of new knowledge.

The Outbreak

In accordance with state regulations in California which make mandatory the reporting of all cases of foodborne disease (Section 2500, California Administrative Code, Title 17) and outbreaks of any type (Section 2502), the state's Infectious Disease Section was notified by the San

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Francisco Department of Public Health of an apparent outbreak of scombroid poisoning associated with several Japanese restaurants in San Francisco.

Phone notification came at 5 PM on Friday, September 16, 1977, with reports of disease in several patrons who dined at three different Japanese restaurants between September 12 and September 15. The San Francisco Department of Public Health had received its information primarily from emergency room physicians who saw many of the patients; and one call was made directly to that department by the owner of one of the restaurants involved.

On investigation 15 cases of scombroid poisoning were found. All of the persons affected had eaten sashimi (raw tuna fish) and became ill 15 to 45 minutes later. In one party of nine people who ate together, only the seven who ate sashimi became ill. In nearly all cases typical symptoms of facial flushing and headache were reported, but there were reports also of rash, swollen tongue, abdominal cramps, nausea, diarrhea, tachycardia and dizziness.

At least 11 of the people felt ill enough to seek medical attention, nine of them at hospital emergency rooms. For most, the illness lasted only a few hours but in one person who ate a large serving of approximately 10 pieces of raw tuna, acute and subacute symptoms lasted three days. As he was an articulate observer, his account is worth recording. He reported dining at one of the three Japanese restaurants on September 13; 45 minutes after eating, dizziness, abdominal discomfort, an unusual sensation ("tightness") in his face, itchy eyes and a dry, swollen feeling in his tongue developed. Abdominal discomfort steadily worsened and was followed by "violent illness" and "enormous" amount of diarrhea which began at midnight, two and a half hours after dinner. Diarrhea continued for two and a half hours, abdominal pain persisted through the night, and flatulence and weakness were present in the morning. Intermittent diarrhea, weakness and depression were experienced for the next three days; not until a full week had elapsed did this person feel normal again.

The same observer reported that of the three people who ate sashimi with him that evening, only he became violently ill, while his wife had no adverse effects whatever and a third person experienced only moderate abdominal discomfort. Five weeks previously, however, his wife became ill while he remained well after eating sashimi at the same restaurant. As we will discuss later, these events probably relate to uneven contamination of the raw tuna with agents causing scombroid poisoning.

Source and History of the Fish

Information provided by the Los Angeles office of the Food and Drug Section, California Department of Health, disclosed that the fish was part of a 78 ton catch of yellowfin tuna taken off the coast of Mexico by a San Diego vessel. In all, 76 tons of the fish were frozen at sea in brine for canning, and 2 tons (presumably the choicer fish) were stored separately, whether on ice or in a cooler could not be determined, but in any event were not frozen in brine. These fish were destined for sale as sashimi. The 76 tons of brine frozen fish were canned and distributed under a national label, and no complaints were received about that product. The two tons of "fresh" (meaning nonfrozen) fish were picked up on Friday, September 9 at the San Diego dock, when the boat returned to port, by the refrigerated truck of the Los Angeles county wholesaler who reported that his truck did not fail to keep the temperature below 5°F. That wholesaling company cleaned and processed the fish on its San Pedro premises and reported a normal weight loss of 25 percent, leaving 3,000 pounds of salable merchandise. A San Francisco trucker picked up more than 2,000 pounds of that fish on September 9 and delivered it to four distributors (A, B, C, D) in the San Francisco Bay area. There was no indication that his refrigeration equipment was not working properly.

Investigation showed that two of the restaurants were supplied "fresh" tuna by one San Francisco fish distributor (distributor A) and the third restaurant was supplied by another San Francisco fish distributor (distributor B). It is pertinent that one of the three restaurants cited above had returned 545 pounds of that shipment back to distributor A before there were any reports of illness, simply because the fish was malodorous and decomposed. Distributor A then returned all of that fish to its wholesaler in Los Angeles County for credit. Quite independently, so did distributors B and C return fish later for the same reason. No cases of illness, however, were ever associated with fish distributed by distributor C or D.

Distributor D never returned any fish, perhaps because of that company's smaller volume of business; it bought the least of all four companies, only 280 pounds.

Of all the fish returned to the San Pedro wholesaler, only 75 pounds were discarded as spoiled while the rest was sold to a Terminal Island plant for canning.

Public Health Control Measures

In view of the potential hazard represented by the spoiled fish, the State's Infectious Disease Section requested on September 16 that an embargo be placed on the entire lot. This was done by the State Food and Drug Section and the Los Angeles County Health Department before any of the fish, raw or that which was later canned, could be sold. Samples of both the raw and canned product were analyzed at the University of California's Laboratory for Research in Food Preservation and, on the basis of the results obtained, the entire lot was destroyed.

Etiology of Scombroid Poisoning

It is important to differentiate scombroid poisoning from both so-called fish poisoning and fish allergy. Fish poisoning or ichthyosarcotoxism may result from the ingestion of certain species, mostly from tropical regions, whose flesh contains powerful toxins, although there is no evidence to indicate that so-called poisonous species are poisonous all the time or in every locality. In any case, the state of freshness of the fish has no relation to the ability of those fish to cause illness, and the symptoms produced are different from those of scombroid poisoning and much more severe. Examples of ichthyosarcotoxism are ciguatera and puffer fish poisoning.

With regard to possible allergy, the distinction is not quite so clear-cut because one of the substances that mediate allergic reactions, histamine, also seems to be involved in scombroid poisoning, per the following observations:

- The symptoms of scombroid poisoning closely resemble those of histamine effect.
- Administration of antihistamines relieves the symptoms of scombroid poisoning.
- In every incident of scombroid poisoning studied, high levels of histamine have been found in the implicated food.

Despite the seemingly crucial role of histamine, scombroid poisoning does not appear to be an allergic reaction. This is evidenced by (1) group outbreaks that may show practically 100 percent morbidity, whereas allergy to fish protein is a relatively rare occurrence; (2) observations that people who habitually eat raw fish only occasionally have signs of scombroid poisoning, and (3) the fact that histamine is present in the fish itself rather than being produced by the host as in allergy.

If histamine is the culprit, where does it come from? Because the histamine content of fresh, nondecomposed fish is well below 1 mg per dl, it becomes necessary to explain the mechanism whereby levels approaching 1,000 mg per 100 grams of flesh (1 percent) can be found in fish implicated in scombroid poisoning.

The name scombroid derives from the family Scombridae which includes mackerels, tunas and bonitos. It is this group that has caused, over the years, most scombroid poisonings. But this family does not have exclusive rights: the dolphinfish (Coryphaena hippurus) has also caused a number of outbreaks but is not at all related to the mackerel group. Even foods other than fish have caused scombroid poisoning and there is one recent report implicating a fermented cheese.[3]

It has been found, however, that all fish that cause scombroid poisoning have one thing in common: a high level of *free* histidine in their muscle tissues. All fish have this amino acid in their protein. Being part of a chain, both of the reactive end-groups of the molecule are relatively inaccessible to bacterial enzymes during spoilage. In scombroid fish and in mahimahi, however, histidine is not only present in protein but also exists, in large amounts, as the free amino acid and so is easily available for reaction.

Histidine is converted to histamine by decarboxylation. This occurs easily when the fish undergoes spoilage, because a number of bacterial types are able to produce decarboxylase.

In view of the above, it is natural that histamine levels should be the first thing studied in analyzing samples of food implicated in scombroid poisoning. Nevertheless, while we know that histamine is produced during spoilage, the actual mechanism of scombroid poisoning remains a mystery because according to current knowledge, histamine is not active when taken by mouth.[4,5] Furthermore, as a result of bacterial activity, our intestinal contents have more than enough hista-

mine to make us ill if that histamine were absorbed into the bloodstream.[4,6]

There are several possible explanations, all centering on still unidentified substances (such as "saurine"[7]) that may be formed during protein breakdown and be present in spoiled fish along with histamine. The presence of high histamine levels may merely represent a marker for the real disease-producing agent that may be there at the same time. Alternately, it is conceivable that some of these substances can facilitate the penetration of histamine through the gut or that they can somehow trigger the release of the body's own histamine, although the latter possibility appears unlikely in view of some experimental work with rats (James L. Lenney, Department of Pharmacology, University of Hawaii, oral report, Nov 22, 1977, personal communication).

Laboratory Results

Histamine levels were determined by two different methods. The University of California, San Francisco, laboratory used the fluorometric procedure of Lerke and Bell,[8] which is comparable to the current Association of Official Analytical Chemists (AOAC) procedure based on the same principle.[9] Letterman Army Institute of Research used the slightly different fluorometric procedure of Taylor and co-workers.[10]

Three separate sets of sample material were obtained. The first was collected on September 16 at one of the restaurants by the San Francisco Health Department and was split between the University of California Food Preservation Laboratory and Letterman Army Institute of Research. This sample consisted of a small amount of raw tuna scraps collected from the kitchen.

The flesh of this initial sample had a definite odor of decomposition. Six areas were sampled from the portion provided to the Food Preservation Laboratory. Analysis for histamine gave values of 565, 160, 600, 594, 516 and 325 mg per dl. A single test of the portion provided to Letterman Army Institute of Research gave a histamine content of 919 mg per dl.

The remainder of the sample at the Letterman Army Institute of Research was subjected to bacteriological analysis. The aerobic plate count (APC)[11] and presumptive coliform plate count[11] were 7.0×10^7 and 8.3×10^5 organisms per gram, respectively. The method of Guthertz and associates[12] was used for the isolation and identification

TABLE 1.—*Production of Histamine in Tuna Fish Infusion Broth by Various Bacterial Species*

Species	Log Increase in APC	Net Histamine Production (nmoles/ml)
Proteus vulgaris biotype 1	1.89	<1
Proteus vulgaris biotype 2	1.74	23
Klebsiella pneumoniae biotype 1	1.74	19,900
Klebisella pneumoniae biotype 2	1.44	<1
Citrobacter freundii	2.09	<1
Enterobacter agglomerans	1.65	31
Hafnia alvei	1.55	5
Acinetobacter calcoaceticus	1.79	<1
Proteus rettgeri	1.88	<1
Enterobacter cloacae	1.75	<1

APC = aerobic plate count

of aerobic Gram-negative organisms. Two biotypes each of Proteus vulgaris and Klebsiella pneumoniae were isolated along with single biotypes of Citrobacter freundii, Enterobacter agglomerans, Hafnia alvei, Acinetobacter calcoaceticus, Proteus rettgeri and Enterobacter cloacae. These bacterial strains were examined for their ability to produce histamine in a tuna fish infusion broth (TFIB) prepared as follows: fresh tuna muscle was homogenized with 2 volumes (w/v) of water, steamed at 100°C for one hour, filtered through paper, supplemented with 1 percent glucose, and sterilized at 120°C for 15 minutes. Then, 70 ml of TFIB was inoculated with 2 ml of an 18-hour trypticase-soy broth-histidine culture of each of the isolated organisms, and incubated for seven hours in a shaking incubator at 32°C. The growth and net histamine production by these bacterial strains after the seven hour incubation in TFIB are shown in Table 1.

The results indicate that one particular strain of K. pneumoniae could have been responsible for the high levels of histamine encountered in the tuna. Bacteriological studies of material from previous outbreaks had shown Proteus morganii to be the most active histamine producer[13,14] and, to our knowledge, had never implicated K. pneumoniae.

A second set of specimens was collected by the State Food and Drug Section at the San Pedro wholesaling company, after the fish had been returned there from San Francisco, and these specimens were examined at the university laboratory. One sample consisted of a half cross section of a fish, approximately 25 cm by 15 cm, and 15 cm thick, taken at the level of the gut cavity. There were two other smaller pieces whose average histamine content was determined

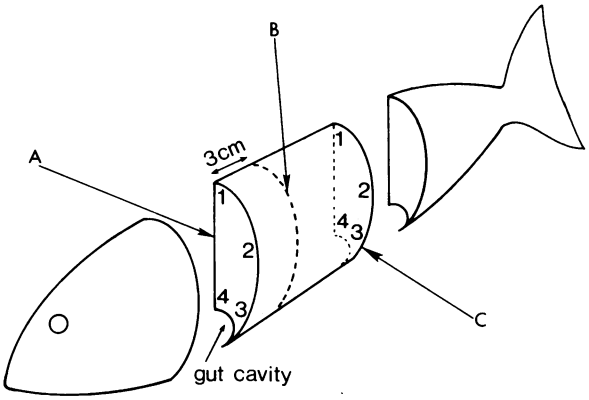

Figure 1.—Schematic representation of tuna fish section from which samples were taken for analysis of histamine (see text). Results are shown in Table 2.

to be 821 and 716 mg per dl, respectively. Of special interest, however, was the large piece since it allowed us to study the distribution of histamine in the fish flesh.

Three specimens, approximately 10 grams each, were taken along the periphery of the fish, about 2 cm under the skin starting at the dorsal fin and proceeding ventrally (Figure 1). A fourth specimen was taken next to the gut cavity. This sampling pattern was carried out in three planes: the anterior surface (A), a plane 3 cm caudad to it (B) and the posterior surface of the section (C). In each plane the sampling areas were spaced about 8 cm from each other. In the case of plane B a double amount of flesh was cut out and split into two pieces which were analyzed separately. This was done to assess the variability in histamine levels over very small distances. Consequently, two values are shown in the corresponding column of Table 2.

In that the maximum analytical error of the method is 10 percent, it can be concluded from these results that the distribution of histamine in spoiling tuna is quite uneven, varying more than fourfold over a distance of 3 cm (location 4, columns A and B) and almost threefold in contiguous areas (location 1, column B). Furthermore, the concentration of histamine seems to be higher near the gut cavity.

The final set of samples received by the university laboratory consisted of product canned from the same lot of tuna. Of 24 cans examined, half had histamine values above 10 mg per dl, ranging up to 113. Accordingly, and as indicated previously, the lot was destroyed.

TABLE 2.—*Mg per dl of Histamine in Various Anatomical Locations of a Spoiled Tuna Fish*

	Plane		
*Location**	*A*	*B*	*C*
1	48	15, 43	15
2	4	4.0, 5.7	7
3	26	73, 139	11
4	124	656, 659	314

*See Figure 1.

Discussion

Several factors are important to our understanding of scombroid poisoning. First, it is a consequence of spoilage that occurs at fairly high temperatures. For many years a close relationship has been recognized between tuna being held at elevated temperatures, such as on decks of party boats in Southern California, and episodes of scombroid poisoning. Conversely, tuna that has been allowed to spoil at temperatures below 10°C has never, to our knowledge, been implicated in scombroid poisoning and has not contained histamine levels above 25 mg per dl.

Few bacteriologic studies, of the kind presented in this paper, are available in the literature. However, the types of bacteria that have been found in connection with this type of spoilage belong almost exclusively to the enteric group, where the optimum growth temperature is around 37°C (98°F) with a maximum at about 43°C (109°F). This is compatible with recently obtained preliminary data showing that under controlled spoilage conditions, the highest levels of histamine are obtained in tuna held between 95 and 100°F (Helmer A. Frank, Department of Food Science, University of Hawaii, oral report, Aug 14, 1978, personal communication). Those very conditions are commonly encountered during commercial tuna fishing operations.

While tuna seining is usually done in tropical waters at about 80°F, the body temperatures of these metabolically active fish may be as much as 15° higher. As soon as the purse is tightened, the fish die of asphyxiation and decomposition begins.

Normally the fish are transferred into cold brine and frozen before any gross damage can occur but any factor that prevents or delays cooling will notably increase the likelihood of histamine production. Examples are mechanical or refrigeration breakdowns, unusually large fish and overloading of storage wells.

In the present outbreak we have no evidence of undue delays in bringing the fish on board but we do know that the fish set aside for the "raw fish" trade were large and that they were not placed in the cooling brine. Whether they were put on ice or in a refrigerator, the rate of cooling must necessarily have been considerably slower, affording ample opportunity for bacterial proliferation during the first 18 hours or so.

Another remarkable aspect was that some of the fish that caused illness, and which was later found to contain very high levels of histamine, was judged acceptable by several persons who would have been expected to be discriminating, namely people in charge of sashimi preparation in at least one Japanese restaurant, as well as their patrons. Likewise, the large section of raw fish examined by one of us (P.A.L.) had only a very mild "off-odor," yet a high level of histamine.

Similar observations are well documented in the literature[15,16] and are consistent with our knowledge about the bacteriology of fish spoilage. Specifically, histamine-producing bacteria do not seem to be true spoilage bacteria in the sense that they do not necessarily give rise to the offensive odors that we associate with spoilage. While the two types may coexist in any given fish environment, this is not always the case; there are numerous cases on record at the university laboratory of spoiled tuna low in histamine and, conversely, of seemingly acceptable fish with very high histamine levels.

Also important is the observation that histamine levels vary tremendously over very short distances in the same cut of flesh. This explains why not everyone sharing the same poorly-preserved fish need suffer illness and also why in the investigation of consumer complaints, it is important to obtain for analysis a portion of the food that was actually eaten as well as that which is available in the restaurant's refrigerator.

The episode just described illustrates the importance of prompt reporting by physicians of any cases of food poisoning of which they may become aware, since it enables public health authorities to launch immediate control measures and thereby prevent exposure of additional persons. Moreover, in most states such reporting is required by regulations for just that purpose. Indeed, failure to report a reportable disease was among the charges in the disciplinary action taken by the Board of Medical Quality Assurance in 1978 against a Bay Area physician.

For further information on scombroid poisoning the reader is referred to the excellent review by Hudson and Brown.[17]

Addendum

At the 1978 annual meeting of the American Society for Microbiology, Drs. Donald A. Corlett, Mark B. Jeffrey and Charles F. Niven, Jr., of the Del Monte Research Center in Walnut Creek, California, reported on the isolation of strains of Klebsiella pneumoniae that were able to produce high levels of histamine from raw mackerel gut and from mahi-mahi fillets.

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