Biotoxications, Allergies, and Other Disorders

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I. Classification of Disorders Due to Consumption of Fisheries Products

From a medical viewpoint, the subject of disorders caused by eating fisheries products has been a complex, confused jumble of jargon. This has often resulted in erroneous diagnoses and a general misunderstanding of the problem at large. What are these disorders? How are they related to each other, if at all?

There are five general categories into which most illnesses caused by the eating of aquatic organisms can be classed. This classification purposely does not include contamination by radioactive substances since this topic is discussed in Chapter 18 of this volume.

A. Bacterial Food Poisonings

In this particular category are classed intoxications caused by eating aquatic organisms that have been contaminated by bacteria or their toxic products. In order to produce an intoxication, the food item must have served as a medium upon which causative bacteria were able to grow. According to this strict definition of the term, only those entities are included in which toxic products actually are formed in the food prior to eating. Typical of this category are botulism and staphylococcus food poisoning. Certain other types of infections are frequently listed in this same group but should more correctly be termed food-borne infections (see Section B), since the symptoms produced are due to the ingestion of living bacteria rather than their toxic products. Examples of the latter
type of poisoning are those caused by salmonellas and *Staphylococcus faecalis*.

There are also some minor types of bacterial food poisonings which are of a more questionable nature. A distinctive characteristic of food poisoning is the sudden illness following the ingestion of a specific meal and involving a definite food item. With the exception of botulism, a gastrointestinal upset is a characteristic feature. It should be noted that putrefaction does not necessarily result in the production of toxic products. Putrid meat, as well as fish, is eaten in many parts of the world without ill effects. The subject of bacterial food poisoning through fish is analyzed in quite some detail in Chapter 11 of this volume. Reference may also be made to Meyer (1953) and Dack (1956).

**B. Food-Borne Infections**

In this instance the food merely serves as a vehicle for the transmission of the disease agent. Theoretically, a wide variety of bacterial organisms can be conveyed in this matter. Some of the better-known diseases in which aquatic organisms have been involved are typhoid fever (*Salmonella typhosa*), paratyphoid fever (*Salmonella* spp.), bacillary dysentery (*Shigella* spp.), cholera (*Vibrio comma*), and other salmonella infections. Sanitary conditions, i.e., control of sewage pollution, methods of food preservation, and cooking, are significant factors in averting these diseases. Food-borne infections differ from food poisonings in that in the former group a lag in the appearance of disease symptoms occurs due to the incubation period required by the bacterial contaminants for building up in the body.

**C. Vectors of Parasitic Diseases**

Certain species of fresh-water fishes may serve as intermediate hosts in the transmission of such helminths affecting man as *Diphyllobothrium latum*, *Clonorchis sinensis*, *Opisthorchis felineus*, *O. viverrini*, *Heterophyes heterophyes*, and *Metagonimus yokagawai*. Fresh-water crabs and crayfish are known to transmit the lung fluke, *Paragonimus westermani*. Infections result from the ingestion of improperly cooked, raw, frozen, dried, or pickled fish (Mackie *et al.*, 1955).

**D. Allergies Produced by Fish and Shellfish**

The exact nature of the physiological mechanisms involved in allergic reactions is not entirely understood. In the case of food allergy, certain foods serve as exciting agents, termed allergens or antigens. These are specific substances that stimulate the production of correspondingly
specific antibodies in a sensitive organism. Antibodies are of two general types, those which are free and circulating in the blood stream, and those which are attached to tissue cells. The latter are termed sessile antibodies. It is the interaction of the antigen with the sessile antibodies that produces symptoms in the sensitive individual. Allergic individuals are believed to have inherited a predisposition or capacity to become sensitized. Thus, there may be produced a high degree of sensitivity in the individual, resulting in a severe reaction to the allergen or antigen. It is commonly believed that there is a release of histamine in the damaged cell. However, other substances also are believed to be involved. An individual is generally sensitive to more than one allergen. Fish and shellfish are known to serve as powerful allergens which in some persons may produce almost explosive reactions. The most common symptoms produced by fish and shellfish are urticaria, angioneurotic edema, gastrointestinal disturbances, and migraine. Less common manifestations are asthma and coryza.

Group reactions to aquatic organisms are common. If a person is sensitive to one species of a phylogenetic group, he will probably be sensitive to all other members of the same general group. Hypersensitivity to all kinds of fish, however, is considered rare (Urbach and Gottlieb, 1946). Usually it is confined to one or related species. Wenderoth and Beneke (1956) report on three independent allergic groupings of fish: (1) herring-sprat; (2) hake-cod; (3) plaice-sole. It was, however, formerly considered that if someone was allergic to a bone fish, such as cod, he was most likely to react also to trout, carp, herring, sardine, etc. A person sensitive to finned fish is not necessarily bothered by mollusks or crustaceans. Extreme cases of specificity have been reported. DeBesche (1937) noted a patient reacting only to Norwegian brisling sardines. On the other hand, minute traces of fish proteins, such as fish skin used for the clearing of coffee in Norway and France (Urbach and Gottlieb, 1946, p. 306), may serve as allergens. Wenderoth (1956) established a high degree of specificity. Cases do occur, however, in which an individual is sensitive to all types of seafood. People react rather frequently to sardine and salmon; less so to cod and halibut. Positive reactions have been reported, among others, for mackerel, tuna, and sole. Although fish and shellfish frequently act as powerful allergens, they are not essentially different from most other foods in this regard. Wheat, eggs, milk, chocolate, tomatoes, legumes, and pork are common offenders. For further discussion on the subject of food allergy the reader is referred to textbooks such as those by Urbach and Gottlieb (1946) and Vaughan and Black (1954) and a recent comprehensive review by Withers and Hale (1956).
Included within this category are those disorders resulting from ingestion of a poisonous substance, a biotoxin present in the body of an otherwise edible aquatic plant or animal. Such compounds are derived from plants or animals, presumably as a result of metabolic activities. The precursors of these biotoxins, or in some instances the toxic substance itself, are believed to be derived directly through the food chain of the organism. With the single exception of scombroid poisoning (see p. 533) the degree of freshness or state of preservation of the organism has no bearing upon the production of the poison. Bacterial food poisoning, radioactive contamination, presence of parasites, and allergy are unrelated to the problem of biotoxications.

A characteristic feature of biotoxins is their apparent sporadic appearance in nature. There is no experimental evidence to indicate that so-called "poisonous species" are poisonous all the time and in every locality. Whether toxic sessile marine plants and dinoflagellates are exceptions to the foregoing statement is not known for certain. However, sporadicity is certainly characteristic of many invertebrate and vertebrate poisons.

The few poisons that are reported to occur in fresh-water fishes, such as cyclostome and barbel poison, have not been studied to any extent. Unfortunately, only five marine animal poisons, viz., paralytic shellfish poison, puffer poison, murexine, holothurin, and saurine, have been subjected to critical chemical and pharmacological evaluation. Information on sessile marine plant phytotoxins is exceedingly meager (Schwimmer and Schwimmer, 1955; Dawson et al., 1955; Habekost et al., 1955). Considerably more is known about the geographical and phylogenetic distribution of biotoxins on the basis of clinical and epidemiological reports. Although it is recognized that clinical observations are a poor substitute for basic chemical and pharmacological studies, they are, nevertheless, revealing and do provide some insight as to the occurrence of these poisons in nature. Much of the more pertinent general literature has been reviewed elsewhere by the author (Halstead, 1956).

On the basis of the scanty information available to date, it appears that most biotoxins are water-soluble substances. They are generally resistant to ordinary cooking procedures. Those that have been studied to any great extent have been found to be small-sized molecules. Many

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1 The term "poisonous," as presently used, is restricted to oral poisons, and should be differentiated from such parenteral toxins as venoms, which are an entirely different matter (see Section II, A, 2, a).
biotoxins are similar in the clinical manifestations they produce, but there is some evidence that they are chemically distinct and probably vary somewhat in their mechanism of action. The chemical literature on marine biotoxins has been reviewed by Courville et al. (1958).

1. Distribution of Biotoxins

Biotoxins can be divided into two major biological groups: *phytotoxins* and *zootoxins*. Phytotoxins are those which occur in plants. Any of the alkaloids might be cited as examples. Zootoxins are those which occur in animals. Zootoxins may be further subdivided into two general categories: *parenteral* and *oral* toxins.

Parenteral toxins, i.e., animal venoms, are poisons introduced into the victim by means of a stinging or biting device. Animal venoms are to be found in numerous animal groups such as coelenterates, annelids, echinoderms, arthropods, fish, reptiles, and mammals. In fish, the venomous stings are generally situated on the dorsal fin, gill covers, or other fin spines. Venomous fish carrying specific poisons, termed ichthyoacanthotoxins, secreted by special venom glands, occur in most seas of the world. However, few food fishes are venomous, and in those species that are, their venomous properties have no adverse effects upon the edibility of the flesh, although their venomous stings may constitute a hazardous deterrent to their commercial use. The weever, *Trachinus draco*, which is an extremely venomous species, is usually processed in commercial filleting plants where the fillets are cut from the fish for the fresh-fish markets along the Atlantic coast of Europe. Many of the catfishes are venomous, but in most instances are not poisonous to eat. See Fish and Cobb (1954) and Halstead (1959) for further information on venomous fishes.

Oral toxins are poisons which are ingested. From the viewpoint of aquatic resources and food economy, there are two groups of primary importance—poisonous mollusks and fishes. However, it should be pointed out that oral zootoxins are widely distributed throughout the entire animal kingdom.

2. Poisonous Mollusks

There are two currently recognized main types of intoxications resulting from the eating of mollusks, namely, (1) paralytic shellfish poisoning, and (2) venerupin poisoning. There is a third type, termed cephalopod poisoning, which appears to be due to a pathogenic microorganism, but thus far all microbiological analyses have failed to reveal the etiological agent. There has recently appeared a fourth type of shellfish
intoxication in Japan, termed Minamata disease, which is believed to be caused by a contaminating metallic compound of some type.

a. Paralytic Shellfish Poisoning

This disease has been recognized on the American continent since at least 1793, when it was first reported from Vancouver Island. Since then, numerous other cases have been described from the west coast of North America ranging from Alaska to the Gulf of California (Meyer, 1953). Medcalf et al. (1947), Needler (1949), and Tennant et al. (1955) have cited a series of outbreaks along the east coast of Canada. More than a hundred cases of shellfish poisoning have been known to occur in South Africa, New Zealand, Belgium, Germany, France, England, and Ireland (Meyer et al., 1928; Koch, 1940, Sapeika, 1948; von Bonde, 1948).

For many years, the primary cause of paralytic shellfish poisoning was unknown. It has now been demonstrated that the poison is derived from toxic dinoflagellates ingested by shellfish, which in turn are eaten by man (Sommer and Meyer, 1937; Koch, 1939; Needler, 1949). The dinoflagellate species Gonyaulax catenella, G. tamarensis, and Pyrodinum phoneus have been definitely incriminated, and still other species are suspected of serving as primary sources of the poison.

Some of the species of shellfish more commonly involved in human intoxications are the following:

| California mussel (Mytilus californianus) | Northern horse mussel (Volvella modiolus) |
| Common (black) mussel (Mytilus edulis) | Solid surf clam (Spisula solidissima) |
| Soft-shell clam (Mya arenaria) | Atlantic jackknife clam (Ensis directus) |
| Smooth Washington clam [syn. (Alaska) butterclams] (Saxidomus giganteus syn. S. nuttali) | Sea scallop (Pecten grandis) |
| Razor clams (Siliqua patula) | Common cockle (Cardium edule) |
| White mussel (Donax serra) | Edible oyster (Ostrea edulis) |
| | Atlantic deep-sea scallop (Placopecten magellanicus) |

A comprehensive review of most aspects of paralytic shellfish poisoning is by McFarren et al. (1957).

(1) Clinical Characteristics

The initial symptoms consist of a tingling or burning sensation of the lips, gums, tongue, and face, which gradually progress to the neck, arms, fingertips, legs, and toes. The paresthesias later change to a sensation of numbness. Voluntary movements become progressively worse. Other symptoms consist of weakness, dizziness, malaise, prostration, headache, salivation, incoherence of speech, intense thirst, dysphagia, anuria, and muscle pains. Gastrointestinal symptoms are variable and secondary to the neurological disturbances. In the terminal stages, the
victim becomes progressively worse, finally developing muscular twitchings, convulsions, paralysis, and death by respiratory failure. The case fatality rate is about 8.5%.

The principal action of the poison is on the central and peripheral nervous systems, affecting respiratory and vasomotor centers, and neuromuscular junctions, cutaneous tactile endings, and muscle spindles. On this basis, one can consider it a neuromuscular poison, similar to curare, but having a more generalized effect (Kelloway, 1935; Fingerman et al., 1953).

There is no specific treatment or antidote for paralytic shellfish poisoning. The gastrointestinal tract should be evacuated as rapidly as possible. Diuretics are indicated. Artificial respiration may be required.

(2) Preventive Measures

There should be strict adherence to local quarantine regulations in those areas where they have been established. At the present time, quarantine measures are established on the basis of toxicological surveys of the shellfish beds. This technique is inadequate and should be revised. Waiting for shellfish to develop a sufficiently high titer of poison is not satisfactory public health control. In at least one instance, there was a severe outbreak in the populace because public health sampling techniques failed to reveal a bed of shellfish containing lethal titers of poison. The shellfish were eaten and 32 persons intoxicated before sampling techniques indicated that a quarantine should have been established. Greater attention should be directed to fluctuations in the causative toxic dinoflagellate population along coastal areas where shellfish poisoning is known to be a problem.

Poisonous shellfish cannot be detected by their appearance, smell, or by discoloration of a silver object, and various other home detection methods. Safe testing requires laboratory procedures involving the use of mice or other laboratory animals. Ordinary cooking procedures do lower the toxin content, but not sufficiently for safe eating. The digestive organs, or dark meat, gills, and in some species, the siphons, contain the greatest concentration of the poison. The musculature or white meat is generally safe to eat. The bouillon or broth in which shellfish have been cooked can be extremely dangerous, since the poison is water-soluble.

(3) Seasonal Fluctuation of Toxic Dinoflagellates

The period when toxicity levels are highest varies somewhat according to geographical location. The dangerous period along the Pacific Coast of North America is from May through October. The Alaska clam,
Saxidomus giganteus, maintains dangerous toxicity levels throughout the year. The most dangerous period along the east coast of Canada is during July through September. Occasionally there is some fluctuation in these cycles, and that is when difficulty is encountered. Most of the European and South African outbreaks take place during May through October.

(4) Control of Toxic Shellfish Canning

In the United States, toxicity standards for the amount of allowable poison in shellfish utilized for commercial processing are controlled largely by the Shellfish Sanitation Section of the United States Public Health Service. In Canada, shellfish toxicity controls are managed by the Department of Fisheries. Both countries require the toxicity level to be less than 400 mouse units per 100 g. of whole fresh, frozen, or canned shellfish. Minced or chopped clams, which are considered to be subject to less variation, are permitted to have a higher toxicity level, but must not exceed 2000 mouse units per 100 g. of contents. About 70% of the poison is destroyed during the commercial canning procedure. Research is currently in progress in an attempt to standardize bioassay techniques using purified paralytic shellfish poison as a reference standard (McFarren et al., 1956). Additional controls are maintained by establishing quarantine, and thereby designating the time and place in which shellfish may be commercially taken.

(5) Testing Methods for Paralytic Shellfish Poison

Various methods have been used, but the following is the one generally accepted by most public health agencies. The shellfish are shucked, washed, drained, and then minced in a meat grinder. A 100-g. portion of the ground meat is added to 100 ml. of 0.1 N HCl and boiled gently for 5 min. with continuous stirring. After cooling, the mixture is adjusted to pH 4.0 or 4.5 with the use of 0.1 N NaOH or 5 N HCl, and then made up to 200 ml. with distilled water. A clear supernatant liquid is obtained by settling or centrifugation. A 1-ml. sample of the supernatant fluid is injected into each of 3 Swiss Webster white mice. A mouse unit is defined as the amount of poison present in a crude extract of 1 ml. necessary to produce a mean death time of 10 to 20 min. using 3 mice. The number of mouse units corresponding to various death times is determined by using tables based on Sommer and Meyer's (1937) graph. In order to obtain the toxicity per 100 g. of meat, it is necessary to multiply the number of mouse units contained in 1 ml. by 200, the combined volume of 100 g. of meat plus 100 ml. of dilute acid (McFarren et al., 1956). Recently, this bioassay method, after minor modifications, has been adopted as official after extensive testing (McFarren, 1959).
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(6) Chemistry

The exact nature of the poison has not been completely defined. Its toxicity is said to surpass any other known alkaloid. The toxin is dialyzable and has a specific rotation value of 130 degrees ± 5. It is soluble in methanol, hot ethanol, aqueous acetone, glacial acetic acid, and acidified water, but is insoluble in ether, chloroform, and the hydrocarbon solvents. For a more complete review of the chemistry of paralytic shellfish poison, see Schantz et al. (1957), Mold et al. (1957), and Courville et al. (1958).

A colorimetric test for the determination of shellfish poison has been developed. This test depends on the selective absorption and elution of the poison from a trichloroacetic acid extract of clam meat on a specific ion-exchange resin. The eluate is submitted to a probe of identity by applying the Jaffe test (McFarren et al., 1958), later modified to suit this purpose still better (McFarren et al., 1959).

b. VENERUPIN POISONING

This is an unusual form of shellfish poisoning, which so far has been restricted to certain brackish-water areas of the Shizuoka prefecture in Japan. Three species of shellfish have been incriminated thus far, namely, the Japanese oyster (Crassostrea gigas), Japanese dosinia (Dosinia japonica), and asari (Tapes [formerly called Venerupis] semidecussata). Poisonings have occurred only during the period from January to April. The primary cause and nature of the poison are not known. No relationship between plankton and shellfish has been found. Bacteriological tests for human pathogens have been essentially negative. The poison is concentrated primarily in the hepatic organ of the shellfish.

The incubation period is usually within 24 to 48 hr. The initial symptoms consist of gastrointestinal upset, headache, and malaise. Various types of bleeding disturbances are generally noted. The poison appears to be organotropic, affecting largely the liver (Akiba, 1943, 1949; Akiba and Hattori, 1949; Hashimoto et al., 1950; Hashimoto and Migita, 1950; Hattori and Akiba, 1952).

Several efforts have been made to obtain the causative agent in a chemically pure form. In attempts to use treatment with benzoic acid, the typical venerupin was lost, and in its place a muscarine-like poison appeared (Migita et al., 1956).

c. CEPHALOPOD POISONING

A large series of intoxications of unknown etiology has been reported from eating fresh squid (Ommastrephes sloani pacificus), and octopus (Octopus vulgaris, O. dofleini), in the Niigata, Yamagata, and Nagano prefectures of Japan. Gastrointestinal upset is the predominant manifesta-
tion. Most of the victims recover within 48 hr. The case fatality rate is less than 1%. All poisonings have taken place from June to November. Bacteriological tests and chemical examination for the presence of amines have thus far been negative (Kawabata et al., 1957).

d. **Minamata Disease**

This is a little-known type of neurological disorder resulting from the ingestion of fish or shellfish taken from Minamata Bay, Kyushu, Japan. The disease was first reported in 1953. The exact cause of the intoxication is not known, but it is believed to be due to a chemical contaminant in the water which is ingested by marine organisms and retained in their bodies (McAlpine and Araki, 1958; Kitamura et al., 1957). The poison seems to affect principally the central nervous system, causing cellular degeneration in the granular layer of the cerebellum, basal ganglia, hypothalamus, midbrain, and cortex, and other pathological effects. Clinically, the disease is described as a severe toxic encephalopathy characterized by symptoms of numbness, slurred speech, ataxia, deafness, disturbances of vision, hypersalivation, emotional lability, tremors, choreiform or athetosic movements, hemiballismus, etc. In most instances, cerebellar signs seem to dominate the picture. A number of fatalities have occurred.

### 3. Poisonous Fishes

A wide variety of illnesses caused by the eating of fishes has been reported in the medical literature over the past two hundred years. A general lack of understanding regarding the nature of these intoxications has resulted in much confusion regarding the terminology used to describe these disorders. Therefore, the following classification has been developed with the hope of clarifying the matter. The system is admittedly an artificial one, based upon clinical manifestations and the source of the poison. Present knowledge regarding the chemical and pharmacological properties of these poisons is as yet too meager to permit a more definitive classification. Additional information relating to some of these categories is available in reviews by Fish and Cobb (1954), Mills (1956), Anonymous (1957), and Halstead (1958).

a. **IchthyoSarcotoxism**

This general category includes intoxications caused by eating the flesh of poisonous fishes, i.e. musculature, viscera, skin, etc. This particular category of fish poisoning is characterized by the variety of places in the body of the fish in which the poison may be found. In other words, ichthyoSarcotoxins are not restricted to any particular organ of the fish body. Included within this category are a variety of specific types of ichthyoSarcotoxism. They are as follows.
(1) Lamprey and Hagfish Poisoning

The slime and flesh of certain lampreys and hagfishes are reported to produce a gastrointestinal upset. No neurotoxic symptoms have been reported. The nature of the poison is unknown.

(2) Elasmobranch Poisoning

The flesh of some sharks and rays is dangerous to eat. Tropical sharks and one such species from the Arctic (Somniosus microcephalus—the Greenland shark) are especially dangerous. Several deaths have been reported from eating the livers. Gastrointestinal symptoms usually predominate in mild cases, but neurotoxic symptoms are most pronounced in severe cases. The nature of the poison is unknown.

(3) Chimaeroid Poisoning

Some of the chimaeras or ratfishes have been incriminated as containing a neurotoxin. No clinical data are available, and the chemical nature of the poison is unknown. The viscera of these fishes are believed to be especially dangerous.

(4) Moray Eel Poisoning

Some of the larger moray eels, particularly of the genus Gymnothorax, inhabiting tropical reefs, may contain a violent neurotoxic substance. Intoxications are manifested by motor paralysis and convulsions predominating in severe cases. A variety of other symptoms such as gastrointestinal upset, paresthesias, and motor incoordination may also be present. The relationship of this poison, if any, to the ciguatera type of fish poisoning is not known. Moray eel poisoning resembles ciguatera quite closely, but the symptoms are almost consistently more severe, and the mortality rate higher. Whether this represents a greater concentration of the poison or a chemical difference is not known.

(5) Ciguatera

More than 300 species of marine fishes distributed throughout the orders Isospondyli, Apodes, Mesichthyes, and Acanthopterygii have been incriminated in human intoxications. Some of the varieties involved are: sea bass, jack, barracuda, snapper, wrasse, parrot fish, and surgeon fish. The barracuda poison was recently studied by Hashimoto (1956). The disease is most common in tropical areas (Arcisz, 1950). Both gastrointestinal and neurological disturbances are present, but paresthesias, extreme weakness, joint aches, muscle pains, and disturbances in temperature sensation dominate the clinical picture. The case fatality rate is less than 10%.

This is an extremely treacherous form of fish poisoning. Without a
single known exception, the fishes producing this form of poisoning are edible in some areas, but toxic in others. Moreover, the toxicity in some regions seems to shift from time to time. Ciguatera constitutes a serious economic and public health threat to the future development of shore fisheries in tropical regions.

Tentatively Randall (1958), in an extensive review of available data, suggested that ciguatera might be explained by the transfer via fishes of a toxin produced by certain blue-green algae. The Soviet scientist Vinberg (1954) explains the mysterious Baltic Sea Haff disease on a similar basis, although the symptoms in this case do not coincide with those for ciguatera. Haff disease also occurs in Swedish and Russian lakes, after luxuriant blooms of blue-green algae.

Information concerning the physical and chemical characteristics of ciguatera toxin is extremely meager. Based on the examination of only very crude preparations, the poison is soluble in such solvents as methanol, ethanol, acetone, ether, chloroform, carbon tetrachloride, hexane, petroleum ether, benzene, and ethyl acetate. It is insoluble in water and dilute aqueous solutions of sodium hydroxide and hydrochloric acid. These solubility data indicate that ciguatera toxin is lipoid in nature but probably is not a phospholipid, and that the molecule evidently contains no acidic or alkaline functional groups. The toxin is heat-stable and shows a measure of sensitivity to oxygen. The poison is generally not destroyed by ordinary cooking procedures.

(6) Puffer Poisoning

The most violent form of fish poisoning is produced by tetraodontoid fishes, namely puffers (Tetraodon spp.), sharp-nosed puffers, ocean sunfishes, and porcupinefishes (Diodon spp.). The majority of the human intoxications are due to puffers of the families Lagocephalidae and Tetraodontidae. Gastrointestinal upset may be present, but is not significant. The neurological disturbances develop rapidly, and are generally violent, consisting of parasthesias, motor paralysis, convulsions, and death by respiratory failure. The case fatality rate is about 60%. If the victim survives the first 24 hr., the prognosis is good.

The empirical formula and structure of puffer poison have not been fully established. Two forms of the poison have been recognized. The more potent form favors the formula C_{12}H_{17}O_{10}N_{3}, whereas the less potent form is said to be C_{11}H_{19}O_{8}N_{3}. This poison has been studied to a greater extent than any other type of ichthyosarcotoxin. A more complete review of the chemical nature of tetraodontotoxin or puffer poison has been presented by Courville and associates (1958). Indian cases of tetraodontid fish poisonings were studied by Jones (1956).
Scombroid Poisoning

On rare occasions, scombroid fishes, i.e., tuna, skipjack, bonito, and mackerel, may cause ciguatera, but more frequently they cause an entirely different form of intoxication. This is the only known type of fish poisoning in which bacteria are directly concerned with the production of the poison. When scombroid fishes are kept at room temperature, a toxic, “histamine-like” substance is developed within the musculature of the fish. This substance is believed by Geiger (1944a, b; 1948) and Geiger et al. (1944) to be produced by a decarboxylation of histidine through the activity of bacteria. He has shown that the “histamine” content of the flesh of the Pacific mackerel, Pneumatophorus diego, increases from 0.09 mg. per 100 g. of tissue to about 95 mg. per 100 g. when kept at room temperature (20–25°C.) for about 10 hr. More recently, the chemistry of the substance has been studied by Kawabata et al. (1955), who claim that this is not histamine, but rather a closely related substance which they have termed “saurine” (see further Chapter 9 for discussion of histamine in fish).

Clinically, scombroid poisoning produces symptoms resembling those of a severe allergy or histamine intoxication. Initial symptoms are frequently a “sharp or peppery taste,” followed by headache, dizziness, abdominal pain, burning of the throat, difficulty in swallowing, thirst, and gastrointestinal upset. A severe urticarial eruption may develop, covering the entire body and accompanied by severe itching. Death due to suffocation and shock has been reported. However, the acute symptoms are generally transient, seldom lasting more than 12 hr. Antihistaminic agents are said to give effective relief.

Gempylid Diarrhea

Some of the fishes of the family Gempylidae, the escolars, contain an oil within their flesh and bone marrow which has a pronounced purgative effect when ingested. Diarrhea develops rapidly, and is said to be without cramping or pain. Since there are no other untoward effects, ingestion of the oil can hardly be considered as an intoxication in the usual sense of the word.

b. Ichthyoötoxism

Ichthyoötoxism is a general term used to designate intoxications resulting from the ingestion of the roe of fishes. The poison is believed to be restricted to the gonads. Most of the fish causing this form of intoxication are fresh-water species, members of the groups Acipenseroidae, Subholostei, and Ostariophysi. Most of the reported intoxications have
occurred in Europe and Asia from eating fresh-water bream \((Abramis)\), barbel \((Barbus)\), and fine-scaled carp \((Schizothorax)\) (Phisalix, 1922). Only one marine species has been incriminated to date—a cabezon \((Scorpaenichthys marmoratus)\) (Hubbs and Wick, 1951).

Symptoms consist of gastrointestinal upset, chest pain, dryness of the mouth, intense thirst, and ringing of the ears. In severe cases there may be muscular cramps, convulsions, coma, and death. Most victims recover within a period of 5 days.

There is a definite relationship between gonadal development and toxicity. Ichthyoötoxic fishes are most dangerous to eat during the reproductive period of the year.

There is little or no information available regarding the chemical nature of ichthyoötoxins.

c. ICHTHYOHEMOTOXISM

This is a general term used to designate intoxications resulting from the ingestion of fresh fish blood. Ichthyohemotoxism is exceedingly rare, and among the least known of zoointoxications. The most frequent cause of these poisonings has been the drinking of raw eel blood from members of the genera \(Muraena\) and \(Anguilla\). Cooking and contact with gastric juices destroy the poison in most instances. Injection of ichthyohemotoxins into laboratory animals results in convulsions and death. Such disturbances as gastroenteritis, paresthesias, paralysis, and death have been reported in human beings. Raw eel blood placed on the tongue or in the eye is said to result in a severe inflammatory response (Camus and Gley, 1898; Steindorf, 1914). This is denied by Bandt (1952-1953).

II. Skin Disorders in the Fish Industry

Skin infections are among the chief occupational hazards of the fishing industry. Because of the nature of their work and certain adverse operational conditions, fishermen and fish handlers encounter a variety of skin irritants which are of minor concern to other occupations. Schwartz and Tabershaw (1945) have conveniently classified these dermatological conditions into several categories, as follows:

1. \textit{Abrasions, lacerations, and fissures}. These are the most commonly contracted skin lesions. They are generally the result of handling fish spines, fishing gear, and other sharp objects.

2. \textit{Secondary infections}. These infections are generally caused by staphylococci and streptococci. The constant irritation of oilskins rubbing against the skin results in a contamination and breaking-down of the skin.

3. \textit{Bites and stings}. Injuries of this type may be caused by a variety
of invertebrates and fishes that are handled during the course of fishing. Serious inflammatory conditions may result from fish stings, even though the fish may not be a venomous species (Fisher 1956; Halstead 1959). Jellyfish stings can be very painful, and a few species may cause death.

4. "Red feed" dermatitis. This lesion is the result of handling mackerel or herring, during the period from June to September, which have been feeding on a reddish-orange crustacean, largely *Calanus* species. Handling this "red feed," together with gastric juices from the digestive tract of the fish, results in swelling, redness, and numerous superficial skin ulcerations. The lesions are found chiefly on the palms and along the sides of the fingers. Such "red feed" accelerates the proteolytic breakdown of the gastric wall, which explains the simultaneous ready appearance of gastric juices.

5. *Scombroid dermatitis*. The skin of scombroid fishes, tuna, skipjack, bonito, etc., contains a substance which is considered to be a primary irritant. Spoiled fish are said to be more irritating than unspoiled ones. Anyone working with ungloved hands with scombroid fishes for any length of time may develop this form of dermatitis.

6. *Erysipeloid*. This is an infective dermatitis due to an infection with *Erysipelothrix rhusiopathiae*, which also causes swine erysipelas. Most of the infections are localized on the hand, but may appear elsewhere on the body, and can lead to septicemia. This disease is most frequently contracted from handling gurry or the remains of any fish that have undergone putrefactive changes. A special study of this human and Dicks (1949) from Australia. Oppenheimer (1953) brought evidence disease spread by marine fishes and crustaceans has been made by Sheard that this organism grows well in a sea-water medium, which might indicate it could be a potential human pathogen of the sea, as such not requiring fish or related forms as conveyors. The pathogen also occurs in fresh water and, consequently, harasses fishermen in lakes and rivers. Several such cases were reported by Bandt (1952-1953).

7. *Skin cancer*. Persons exposed to an excessive amount of sunlight are apt to develop skin cancers. Exposure to tar over extended periods of time appears to be an additional contributing factor.

8. *Allergy*. Fish oils are a common cause of allergic skin manifestations in some individuals.

The treatment of skin lesions is varied and frequently complicated and is generally a matter which should be treated by the physician. Cleanliness, protection of the hands with rubber or plastic gloves, and protection from chronic irritants will do much to prevent skin disorders in the fishing industry.
III. Medical and Economic Significance of Poisonous Aquatic Resources

The medical importance of poisonous aquatic organisms has been continually pointed up whenever and wherever they have been encountered by man. Military troops dependent upon the availability of local fisheries supplies have frequently been harassed by the problem. The French, Russian, Japanese, and American navies have published manuals dealing with the dangers of these organisms. Ichthyotoxism has been a problem in Russia and elsewhere in Europe for many decades (Phisalix, 1922; Pawlowsky, 1927). Puffer poisoning in Japan has accounted for as much as 44% of all the fatal food intoxications (Halstead, 1958). Poisonous fishes may contribute to the overfishing of one area and the underdevelopment of the shore fisheries of another because of their presence. This is somewhat the situation at present in the Line and Hawaiian Islands (Halstead, 1957).

Biotoxicological surveys of the shore fishes of some of the islands of the tropical Pacific show the incidence of poisonous fishes to range from 29 to 75% (Halstead, 1958). Although the practical toxicity potential of these fishes is considerably less than the figures cited, it is, nevertheless, sufficiently high to be of practical importance when considered from the over-all viewpoint of commercial development and public health regulations. The monetary damage to the fisheries industry resulting from mass outbreaks of biotoxications can hardly be computed, dollarwise. As time goes on and human population pressures continue to exert their influence toward developing new fishing grounds and a broadened spectrum of fisheries products, it becomes urgent that more serious attention be given to this area of research by both public health and fisheries scientists.

A positive, and probably in the long run a more important, aspect of the problem is the latent potentialities of aquatic biotoxins as a new source of chemical and therapeutic agents. Many of these compounds possess powerful pharmacological properties which, for the most part, have not been evaluated as to their possible medicinal and industrial uses. Certainly the ocean with its myriads of plants and animals offers a vast, almost unexplored reservoir of little-known chemical agents that may some day contribute greatly to the cure of some of mankind's worst ills.

Finally, aquatic biotoxicology offers a great number of unsolved, complex biological and chemical riddles which constitute an intriguing challenge to research. This is an area of marine biology which so far has been largely ignored. It presumably will continue to remain in its present undeveloped state until teams of researchers consisting of ecolo-
gists, systematists, epidemiologists, chemists, pharmacologists, zoologists, and algologists are given the opportunities of interdisciplinary cross-fertilization and adequate budgetary support.

REFERENCES


