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RECENT DATA ON POSSIBLE ASSOCIATIONS OF COASTAL/ESTUARINE POLLUTION WITH FISH AND SHELLFISH DISEASES

by

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SUMMARY

The significance of environmental stress from pollutants is emerging as an important determining factor in a number of fish and shellfish diseases. This stress may take the form of direct chemical-physical damage to cell membranes or tissues, modification of biochemical reactions, buildup of facultative microbial pathogens, low environmental oxygen levels, and many others. The presence of marginal or degraded estuarine/coastal environments may be signalled by the appearance of fin erosion, "red sores", and lymphocystis in teleost fishes, by shell disease in crustaceans, and by certain neoplasms in bivalve molluscs, but a clear cause and effect relationship has not yet been demonstrated in every case.

Some circumstantial evidence for the role of environmental carcinogens in inducing neoplasms of fish and shellfish is accumulating, but at present definitive conclusions are not justified. A number of viruses have been found in crustaceans and molluscs in recent years, and the pathogenic role of two of them has been demonstrated by increasing environmental stress. It may well be that other latent virus infections of invertebrates will be identified by similar experimental methods. The multifactorial genesis of disease in marine species is becoming apparent -- involving environmental stress, facultative pathogens, resistance of hosts, and latent infections.

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INTRODUCTION

A recent review of pollution effects on fisheries (Sindermann, 1976) moved hurriedly through several examples of possible associations between coastal-estuarine environmental pollution and fish and shellfish diseases. Because the subject is worthy of careful attention, particularly in the industrialized nations where coastal pollution is a problem, a greater attempt was made to assemble and interpret available published information. The fundamental question to be answered was: "Are there examples of specific associations of pollution with diseases of resource animals?" Subsidiary questions concerned the amount and value of circumstantial or experimental evidence for such a relationship, and the effects (if any) on population size.

A number of general statements can be made, as a result of the search:

(1) A large amount of data relevant to the subject are available.

(2) Much of the evidence for an association of pollution and disease is circumstantial; but

(3) there are several instances where an association is rather clearly indicated by the data.

This paper summarizes the recent information, and conclusions drawn therefrom. It is presented hopefully as a working document, to be scrutinized and commented upon by those knowledgeable in the subject matter areas of pollution and marine diseases.

Disease is a constant concomitant of life for any species, normally removing individuals from the population continuously. Marine animals are, of course, subject to a wide spectrum of diseases of infectious or non-infectious etiology ("disease" can be defined in the broad sense as "any departure from normal structure or function of the animal" or as "the end result of interaction between a noxious stimulus and a biological system"). Disfunction and death due to the activity of infectious agents constitute the narrower, but often predominant concept of disease. Infectious diseases -- caused by viruses, bacteria, fungi, protozoa and others -- are usually prime suspects in searches for causes of mortalities, sometimes to the exclusion of other possible causes. Non-infectious diseases include such phenomena as environmentally induced skeletal anomalies,

genetic abnormalities, physiological malfunctions due to chemical environmental factors, metabolic disorders resulting from nutritional deficiencies, many forms of neoplasms, and a host of others. In many instances, it is probably the combination of an infectious agent and environmental stress that eventually causes mortality.

Infectious disease usually exists in an enzootic form, weakening or disabling individuals and rendering them more susceptible to predators or other environmental stresses. Occasionally, though, epizootics and mortalities comparable to the great plagues of the Middle Ages may sweep through animal populations. In marine species we have seen such massive epizootics at work in the great herring mortalities of the mid-1950's in the Gulf of Saint Lawrence, and the extensive oyster mortalities of the 1960's in the Middle Atlantic states. These epizootics are triggered by a complex interplay of pathogen, environment, and host population. Considering only the environmental aspects of such outbreaks, any departure from normal conditions produces a degree of stress on the population, and many contribute to an increase in prevalence of a pathogen, or of facultative invaders. Some of these environmental factors are abnormal temperature change, lack of adequate food, or overcrowding. Resistance of the host animal to the disease is of course intimately related.

Environmental stress undoubtedly exists, and has been implicated in a number of fish and shellfish diseases, but is very difficult to quantify. Even a definition of stress can be elusive. Selye (1950) defined stress as "The sum of all the physiological responses by which an animal tries to maintain or reestablish a normal metabolism in the face of a physical or chemical force." Brett (1956) defined stress as "A state produced by any environmental or other factor which extends the adaptive responses of an animal beyond the normal range, or which disturbs the normal functioning to such an extent that, in either case, the chances of survival are significantly reduced."

Human activity has introduced or has increased environmental stresses for fish in estuarine and coastal waters. We have, for instance, added pesticides and other synthetic chemicals which can, even in low concentrations, drastically affect the physiology of fish and shellfish, and with which the species may have had no previous evolutionary experience. We have added heavy organic loads, in the form of sewage sludge and effluents, which can produce anaerobic or low-oxygen environments, and which are often accompanied by other contaminants such as heavy metals, which interfere with enzymes of both fish and their food organisms.

During the past decade, several diseases and abnormalities of fish and shellfish have been described that seem associated with pollutant stresses. These can be categorized and discussed as:

1. Facultative pathogens related to contaminant stress, and the special case of stress-provoked latent infections;

2. Environmentally induced abnormalities; and

3. Genetic abnormalities associated with mutagenic and other properties of contaminants.

In the first category, a synergistic activity of chemical contaminants (or other form of pollutant stress) and an infectious agent seems to be a plausible explanation for at least some of the observed effects. In categories 2 and 3, it is sometimes difficult to determine conclusively whether environmental contaminants act directly on target tissues or biochemical pathways, or if the genetic material is first affected, with subsequent changes in structure and/or function.

During the past several years there have been signs of increasing interest in relationships between marine fish and shellfish diseases and environmental pollution. Several conferences have been held, including the 1976 "Conference on Aquatic Pollutants and Biological Effects with Emphasis on Neoplasia", held by the New York Academy of Sciences; and the 1975 Symposium on "Sublethal Effects of Pollution on Aquatic Organisms", held as part of the 13th Pacific Science Congress. Additionally, significant reviews have appeared, notably Rosenthal and Alderdice (1976) "Sublethal effects of environmental stressors, natural and pollutional, on marine fish eggs and larvae." This paper attempts to summarize the present state of our knowledge about possible associations of fish and shellfish diseases (infectious and non-infectious) and estuarine/coastal pollution. Much of the evidence for such associations is still circumstantial, and is presented as such.

DISEASE CAUSED BY FACULTATIVE PATHOGENS

Fin erosion

Probably the best known disease of fish from polluted waters is a non-specific condition known as "fin rot" or "fin erosion" (Fig. 1), a syndrome which seems rather clearly associated with degraded estuarine or coastal environments. Fin rot has been reported from the New York Bight (Mahoney et al., 1973; Ziskowski and Murchelano, 1975; Murchelano, 1975), California (Young, 1964; Southern California Coastal Water Research Project, 1973; Mearns and Sherwood, 1974).

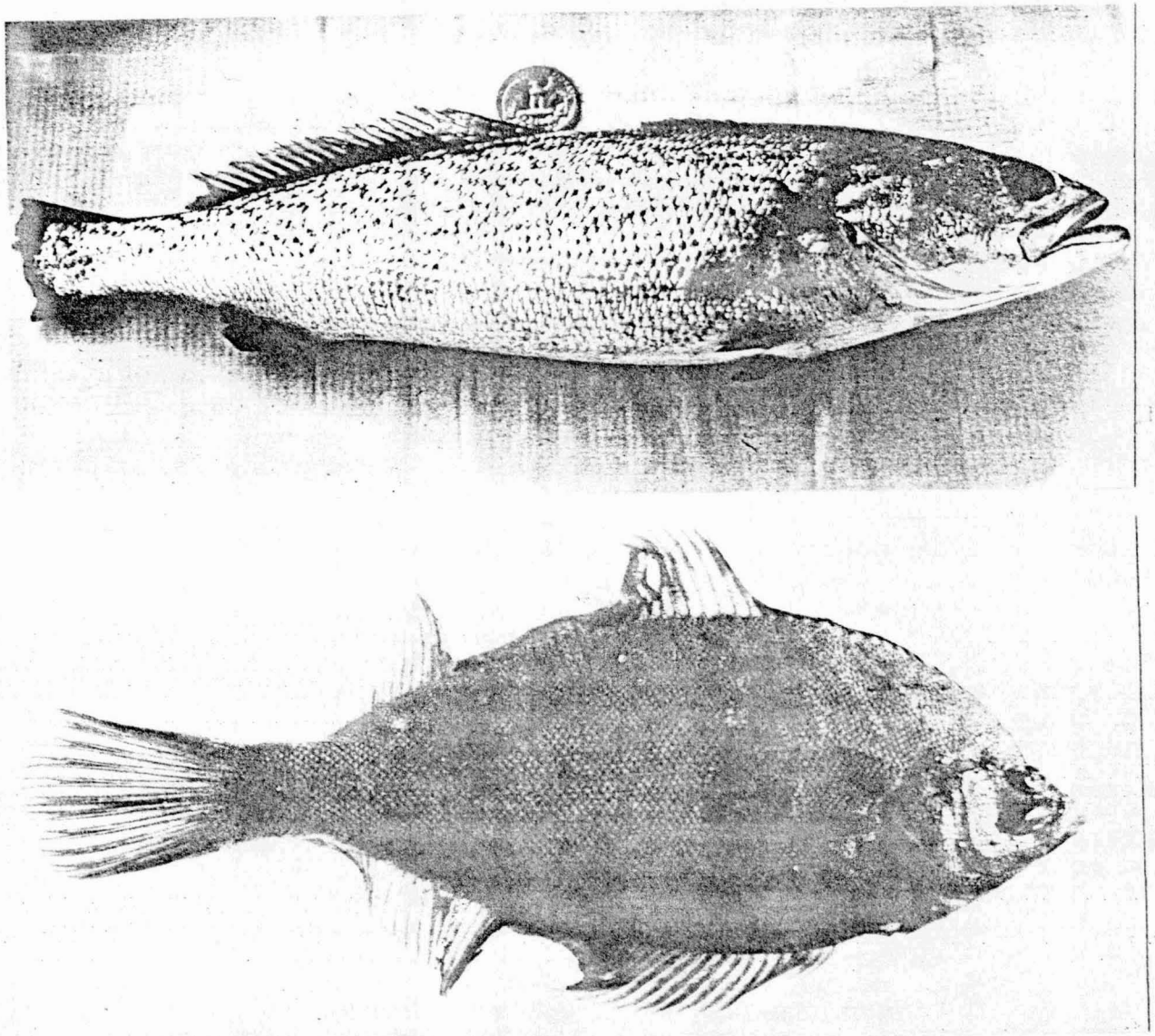

Figure 1. Fin erosion in weakfish (top) and winter flounder (bottom). (From American Littoral Soc. 1972; Mahoney et al., 1973).

Puget Sound (Wellings et al., 1976), Biscayne Bay in Florida (Sindermann, unpublished observations), Japan (Nakai et al., 1973), Escambia Bay in Florida (Couch, 1974a), and the Irish Sea (Perkins et al., 1972)

Fin rot seems to exist in at least two types: one occurring in bottom fish where damage to fins seems related to direct contact with contaminated sediments; and a second in pelagic nearshore species, characterized by predominant involvement of the caudal fin, with hemorrhagic lesions.

Recent quantitative surveys along the Middle Atlantic coast have disclosed high prevalence (up to 38 percent) of "fin rot" in samples of trawled marine fishes from the New York Bight. Thus far, 22 affected species have been found. While bacteria of the genera Vibrio, Aeromonas, and Pseudomonas were frequently isolated from abnormal fish, a definite bacterial etiology has not been determined. Fin rot disease was significantly more abundant in the New York Bight Apex, the area of greatest environmental damage, than in any comparable coastal area from Block Island to Cape Hatteras. An association between high fin rot prevalence and high coliform counts in sediments is emerging (Mahoney et al., 1973), as is an association between high fin rot prevalences and high heavy metal levels in sediments (Carmody et al., 1973). The disease signs can be produced experimentally by exposure of fish to polluted sediments.

The histopathology of fin erosion in winter flounder, Pseudopleuronectes americanus, from the New York Bight was examined by Murchelano (1975). Significant descriptive findings were epidermal hyperplasia accompanied by dermal fibrosis, hyperemia and hemorrhage. Bacterial infections were not noted, nor was pronounced inflammatory response. However, reference was made to acute fin lesions seen in summer flounder, Paralichthys dentatus, in which bacteria were readily demonstrable. The absence of pronounced inflammatory response in either species of flounder led Murchelano to suggest that the necrotic process is not primarily microbial, and that activities of a chemical irritant may be involved.

Another histopathological and bacteriological study of fin rot in winter flounder of Narragansett Bay, R. I., by Levin et al. (1972) described acute ulcerative lesions as well as fin erosion, thought to be produced by Vibrio anguillarum. Acute inflammatory response was also observed and the ulcerative phase was reproduced in fish exposed

experimentally to V. anguillarum isolates. It is possible that several poorly defined disease entities or generalized disease signs (one of which is fin erosion) may be responsible for the disparate nature of histopathological findings in this report.

Fin erosion has also been observed in striped bass overwintering in heated effluents of power plants in the Middle Atlantic States.

Fin rot, with associated mortalities, was reported by Couch (1974a) in croaker (Micropogon undulatus) and spot (Leiostomus xanthurus) from Escambia Bay, Florida. The disease syndrome and mortalities have been observed for several years during periods of high temperature and low dissolved oxygen. Escambia Bay has been polluted by the PCB, Aroclor 1254, for a number of years (Duke et al., 1970). A series of experiments at the Gulf Breeze (Florida) Environmental Research Laboratory, using the spot, Leiostomus xanthurus, resulted in experimental production of fin rot disease following exposure to 3-5 µg/l of Aroclor 1254 (Couch, 1974a). Mortalities up to 80% were reported.

Information from southern California (SCCWRP, 1973) also strongly suggests an association of fin rot with degraded habitats; relevant statements are: (p. 249) "The incidence of fin erosion was high in areas with high concentrations of waste water constituents in the sediments ...". (p. 424) "Although there is a definite association between fin erosion and waste water discharges, the causal factors are unknown." (p. 424) "Nearly half of the 72 species caught off the Palos Verdes Peninsula were affected with this syndrome" (eroded fins). It is interesting that a histopathological study of fin erosion in Dover sole, Microstomus pacificus, from the California coast (Mearns and Sherwood, 1974) produced findings very much like those of Murchelano (1975) -- hyperplasia, fibrosis, absence of inflammation, and absence of microbial infection.

Some species seem clearly more resistant to fin erosion. This was demonstrated in a recent study by Wellings et al. (1976) in a heavily polluted arm of Puget Sound. Examination of over 6000 fish of 29 species disclosed fin erosion only in starry flounder and English sole. Average incidences were 8% and 0.5% respectively. Histopathological findings were similar to those for east coast and California flatfishes -- epidermal hyperplasia, fibrosis, resorption of fin rays, and mucus cell changes.

Recent Japanese publications have mentioned fin erosion in fish from polluted bays. Nakai et al. (1973) found that as many as 60% of all stargazers (Uranoscopus japonicus) sampled from Suruga Bay had evidence of disintegration of caudal and pectoral fins. Six other species also had abnormal fins.

An increase in occurrence of fin erosion and other epidermal lesions (ulcers and lymphocystis) in flatfish from the Irish Sea since 1970 was reported by Perkins et al. (1972). Fin damage, unknown before 1970, was observed in plaice (Pleuronectes platessa), and dab (Limanda limanda). The authors pointed to ocean dumping of toxic wastes, particularly of PCB's, as a possible contributing factor, but no clear relationship with increased frequency of disease was demonstrated.

The possible role of environmental chemical contamination in the etiology of fin erosion emerges more clearly as additional studies are reported. Fish from the New York Bight, reported in studies by Mahoney et al. (1973), Murchelano (1975), and Ziskowski and Murchelano (1975), exist in a highly contaminated area, with chemicals such as heavy metals and petroleum residues in sediments far above background levels. McDermott and Sherwood (1975) found DDT to be significantly higher in fish with fin erosion, and PCB levels slightly higher in such fish than in normal individuals. Wellings et al. (1976) found abnormally high concentrations of PCB in English sole and starry flounders from the Duwamish River in Washington.

Several authors have postulated that fin erosion in flatfish may be initiated by direct contact of tissues with contaminated sediments. Mearns and Sherwood (1974), for example, suggested that toxic substances (sulfides, heavy metals, chlorinated hydrocarbons, etc.) could remove or modify the protective mucus coat and expose epithelial tissues to the chemicals. Sherwood and Bendele (1975) reported that Dover sole with fin erosion produced much less mucus than normal fish.

It seems quite likely that the "fin erosion" syndrome in fish includes chemical stress, probably acting on mucus and epithelium; stress resulting from marginal dissolved oxygen concentrations, possibly enhanced by a sulfide-rich environment; and secondary bacterial invasion in at least some instances.

A recent report by Overstreet and Howse (1976) pointed to fin erosion and other abnormalities as indicators of gradually increasing pollution stress on the Mississippi Gulf Coast. Among other disease conditions noted by Overstreet and Howse was "red sore", characterized by hemorrhagic lesions beneath scales and occasionally hyperplasia. In discussions, the authors indicated that "red sores" may now occur in many of the fish in some areas -- a striking similarity to recent observations in Biscayne Bay, Florida, where many fish of many species now exhibit the condition (Figure 2), which was unknown a decade ago (Sindermann, unpublished observations).

It seems quite likely that generalized disease signs, such as fin rot and "red sores" (and probably other epidermal lesions such as ulcerations, papillomas, and lymphocystis), are characteristic of fishes resident in degraded habitats, where environmental stresses of toxic chemicals, low dissolved oxygen, and high bacterial populations exist. The extent and nature of these external manifestations are probably variable with resistance of the particular species and the extent and nature of environmental degradation.

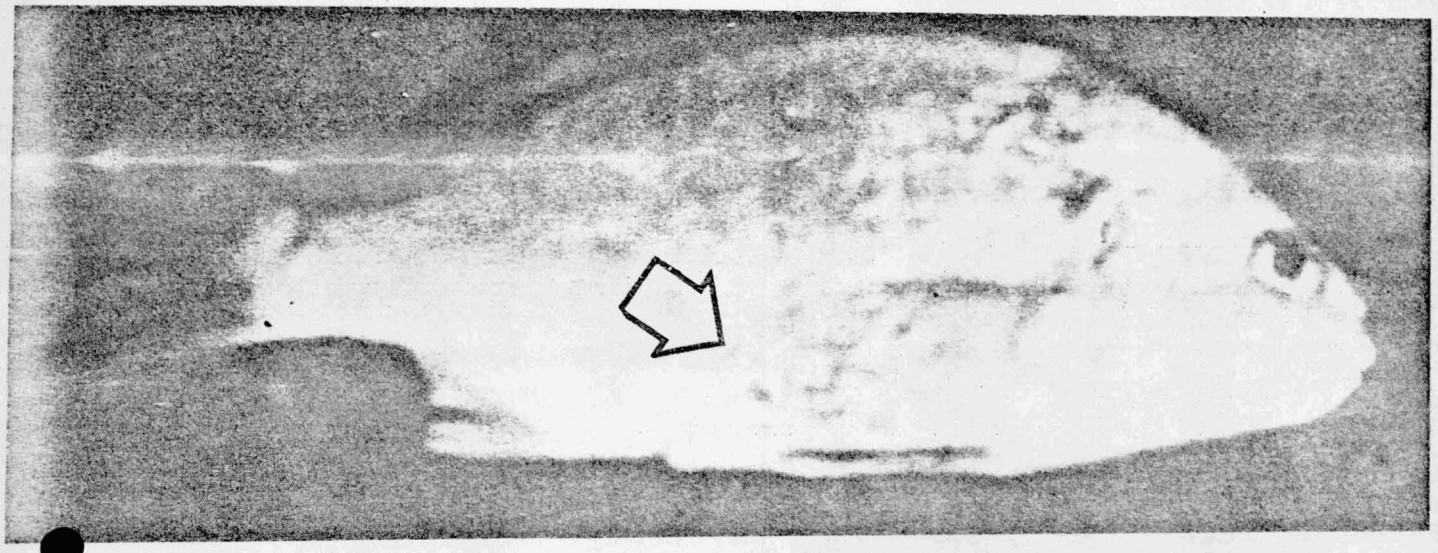

Figure 2. Hemorrhagic lesions in fish from Biscayne Bay, Florida.

Shell disease of Crustacea

Also associated with badly degraded estuarine and coastal waters is a disease condition in Crustacea commonly referred to as "shell disease" or "shell erosion."

Lobsters (Homarus americanus) and crabs (Cancer irroratus) from grossly polluted areas of the New York Bight were found to be abnormal, with appendage and gill erosion a most common sign (Young and Pearce, 1975). Skeletal erosion occurred principally on the tips of the walking legs, ventral sides of chelipeds, exoskeletal spines, on gill lamellae, and around areas of exoskeletal articulation where contaminated sediments could accumulate. Gills of crabs and lobsters sampled at the dump sites were usually clogged with detritus, possessed a dark brown coating, contained localized thickenings, and displayed areas of erosion and necrosis. Similar disease signs were produced experimentally in animals held for six weeks in aquaria containing sediments from sewage sludge dumping or dredge spoil disposal sites. Initial discrete areas of erosion became confluent, covering large areas of the exoskeleton, and often parts of appendages were lost. The chitinous covering of the gill filaments was also eroded, and often the underlying tissues became necrotic.

Dead and moribund crabs and lobsters have been reported on several occasions by divers in the New York Bight Apex, and dissolved oxygen concentrations near the bottom during the summer often approach zero (Young, 1973). Low oxygen stress, when combined with gill fouling, erosion, and necrosis, could readily lead to mortality.

In a related study, Gopalan and Young (1975) examined "shell disease" in the caridean shrimp, Crangon septemspinosa, an estuarine and coastal food chain organism on the east coast of North America -- important in the diets of bluefish, weakfish, flounders, basses, and other economic species. Examinations of samples of Crangon from the New York Bight disclosed high prevalences (up to 15%) of eroded appendages and blackened erosions of the exoskeleton. The disease condition was only rarely encountered at other collecting sites (Beaufort, N. C. and Woods Hole, Mass.). Histological examination of diseased specimens produced findings similar to those of Young and Pearce (op. cit.) with crabs and lobsters. All layers of the exoskeleton were eroded; affected portions were brittle and easily fragmented; cracking and pitting of calcified layers

occurred; and underlying tissues were often necrotic. Laboratory experiments using sea water from the highly polluted inner New York Bight resulted in appearance of the disease in 50% of individuals. Erosion was progressive, crippled individuals were cannibalized, and eroded segments of appendages did not regenerate after ecdysis. No disease signs developed in control animals held in artificial sea water.

A German study of the effects of industrial wastes (Schlotfeldt, 1972) on the shrimp, Crangon crangon, disclosed high prevalence of so-called "black spot disease", with signs very similar to those seen in Crangon septemspinosa from the New York Bight. Juvenile and adult shrimps from the Föhr Estuary had black areas of erosion on the carapace and appendages, with necrosis of underlying tissues, and frequent loss of segments of appendages. The disease condition varied in prevalence seasonally, with a peak of 8.9% in summer. Lesions persisted and worsened after ecdysis. Experimental exposure to detergent aggravated and hastened the course of the disease.

Shell disease of Crustacea has been observed in many species and under many conditions, both natural and artificial (Rosen, 1970; Sindermann, 1970). Actual shell erosion seems to involve activity of chitinoclastic bacteria, with subsequent secondary infection of underlying living tissue by facultative pathogens. Initial preparation of the exoskeletal substrate by mechanical, chemical, or microbial action probably is significant; thus high bacterial populations and the presence of contaminant chemicals in polluted environments -- as well as extensive detrital and epibiotic fouling of gills -- could combine to make shell disease a common phenomenon and a significant mortality factor in crustaceans inhabiting degraded environments.

Stress-provoked latent infections

There are at present published accounts of two viral diseases of marine invertebrates which suggest that latent infections may be provoked into patency by environmental stress. One, a baculovirus infection of pink shrimp, was first recognized in stressed laboratory populations (Couch, 1974b, 1974c). The other, a herpes-like virus infection of oysters, was discovered in a population held in a heated power plant effluent in Maine (Farley et al., 1972).

An association of disease and low-level chronic exposure to pollutant chemicals is being explored at the Gulf Breeze (Florida) Environmental Research Laboratory of the U. S. Environmental Protection Agency (Nimmo et al., 1971; Couch, 1974b). A virus disease of pink shrimp reached patent levels and caused mortalities of 50-80% in shrimps exposed to the PCB Aroclor 1254 and to the organochlorine insecticide Mirex (Couch and Nimmo, 1974; Couch, 1974c). Other experiments in which the shrimp were crowded, but not exposed to chemicals, resulted in similar enhancement of virus infections -- suggesting that environmental stress may be an important determinant of patent infections.

An association of high disease prevalence or disease enhancement in fish and shellfish sampled from thermal effluents has been made recently. Farley et al. (1972) described a lethal virus disease of oysters held in heated discharge water in Maine. The disease, which apparently existed at a low enzootic level in oysters growing at normal low environmental temperatures (12-18°C summer temperatures) seemed to proliferate in oysters at elevated temperatures (28-30°C).

A third viral infection -- lymphocystis of striped bass -- seems to have some tenuous association with heated effluents. Recent unpublished observations by staff members of the Sandy Hook (N.J.) Laboratory of the National Marine Fisheries Service, point to high prevalences of lymphocystis disease in limited samples of striped bass overwintering in the heated effluent of a Long Island generating station (Northport, N.Y.). This virus disease is considered rare in striped bass (Anonymous, 1951; Krantz, 1970), and its unusual abundance in a localized population may well be related to the abnormally high winter temperature regime in which the population exists, or to abnormal crowding. As with the oyster virus disease, the high temperatures may promote survival or transfer of the pathogen, or lower resistance of the host, resulting in grossly recognizable stages of infection. An additional area of concern about fish diseases in populations overwintering in heated effluents is that a focus of infection will be provided for incoming spring migrants.

ENVIRONMENTALLY-INDUCED ABNORMALITIES

Neoplasms (tumors)

The terms "neoplasia" and "neoplasms" -- particularly as they concern lower animals -- are difficult to define precisely. The Oxford Dictionary definition of neoplasm is "a new formation in some part of the body; a tumor." More elaborate definitions exist. Warren and Meissner (1966) defined a neoplasm as "a disturbance of growth characterized primarily by an unceasing, abnormal, and excessive proliferation of cells." Although neoplasia has been studied most in humans, the existence of tumors in fish and shellfish has been recognized for almost a century (the first oyster tumor, for example, was reported by Ryder in 1887).

Circumstantial evidence associating environmental contamination with neoplasms (tumors) in fish and shellfish has accumulated from a number of studies:

(1) Russell and Kotin (1957) found 10 of 353 white croakers (Genyonemus lineatus) from Santa Monica Bay, California, with papillomas of lips and mouth. Fish were taken 2 m from an ocean outfall. No tumors were found in 1,116 croakers from non-polluted waters 70 km away.

(2) Lucke and Schlumberger (1941) described 166 catfish (Ameiurus nebulosus) with epithelomas of lips and mouth, taken from the Delaware and Schuylkill Rivers near Philadelphia. The rivers were grossly polluted. Tumors of this type may result from mechanical, infections or chemical irritation. Catfish from other areas did not have a high prevalence of tumors. The authors did not exclude the possibility that the lesions were induced by chemical carcinogens in waters. The lesions developed into epidermoid carcinomas, some of which were invasive.

(3) Cauliflower disease (epidermal papilloma) has been increasing in prevalence in the Baltic since 1957. The pattern of spread and high prevalence suggests an infectious process (viral arrays have been seen) or progressive accumulation of industrial contaminants such as fuel oil and smelter wastes (known to contain carcinogenic hydrocarbons such as benzopyrene and heavy metals such as arsenic).

(4) Halstead (1971) found in 1969 that 12% of nearly 16,000 English sole from San Francisco Bay had as many as 33 tumors per fish. Highest incidence was in the northern part of the bay where the greatest concentration of petrochemical wastes existed.

(5) Young (1964) found many small (4-6") Dover sole (Microstomus pacificus) from Santa Monica Bay with tumors. Fish above 10" long did not have tumors. Since 1956 numerous white croakers from Santa Monica and Los Angeles-Long Beach were found with papillomas of the lips, and papillomas were observed on tongue sole, cusk eels, and Pacific sand dabs. Such tumors were never seen on fish from unpolluted areas.

(6) Carlisle (1969) found "growths" frequent on white croakers and Dover sole from Santa Monica.

(7) Sindermann (unpublished data) found wart-like tumors histologically resembling fibromas in mullet from Biscayne Bay, Florida, in 1969-1970 (Figure 3). Other fibrous tumors have been reported since then by Lightner (1974) and Edwards and Overstreet (1976) in mullet from the Gulf of Mexico.

A number of Pacific flatfish species are noted for the common occurrence of epidermal papillomas. Prevalences are highest in young fish, reaching 58% in English sole, Parophrys vetulus (Stich and Acton, 1975); 55% in starry flounders, Platichthys stellatus (McArn and Wellings, 1971); 15% in flathead sole, Hippoglossoides elassodon (Miller and Wellings, 1971); and over 40% in sand sole, Psettichthys melanostictus (Nigrelli et al., 1965). A relationship of high frequencies of such papillomas with coastal pollution is still uncertain. Stich et al. (1976a) state (p. 1998) "There seems to be a higher skin tumor frequency among English sole inhabiting areas of urban contamination (Vancouver) than among fish populations in regions remote from human activities ...".

In an extension of this study, Stich et al. (1976b) reported prevalences of skin neoplasms in one-year-old English sole from 20 to 70% in samples taken near eight cities on the Pacific coast, while prevalences did not exceed 0.1% in several samples taken on the British Columbia coast more distant from cities. However, Oishi et al. (1976) examining prevalences of similar epidermal papillomas in flatfish from relatively unpolluted waters of northern Japan felt that a

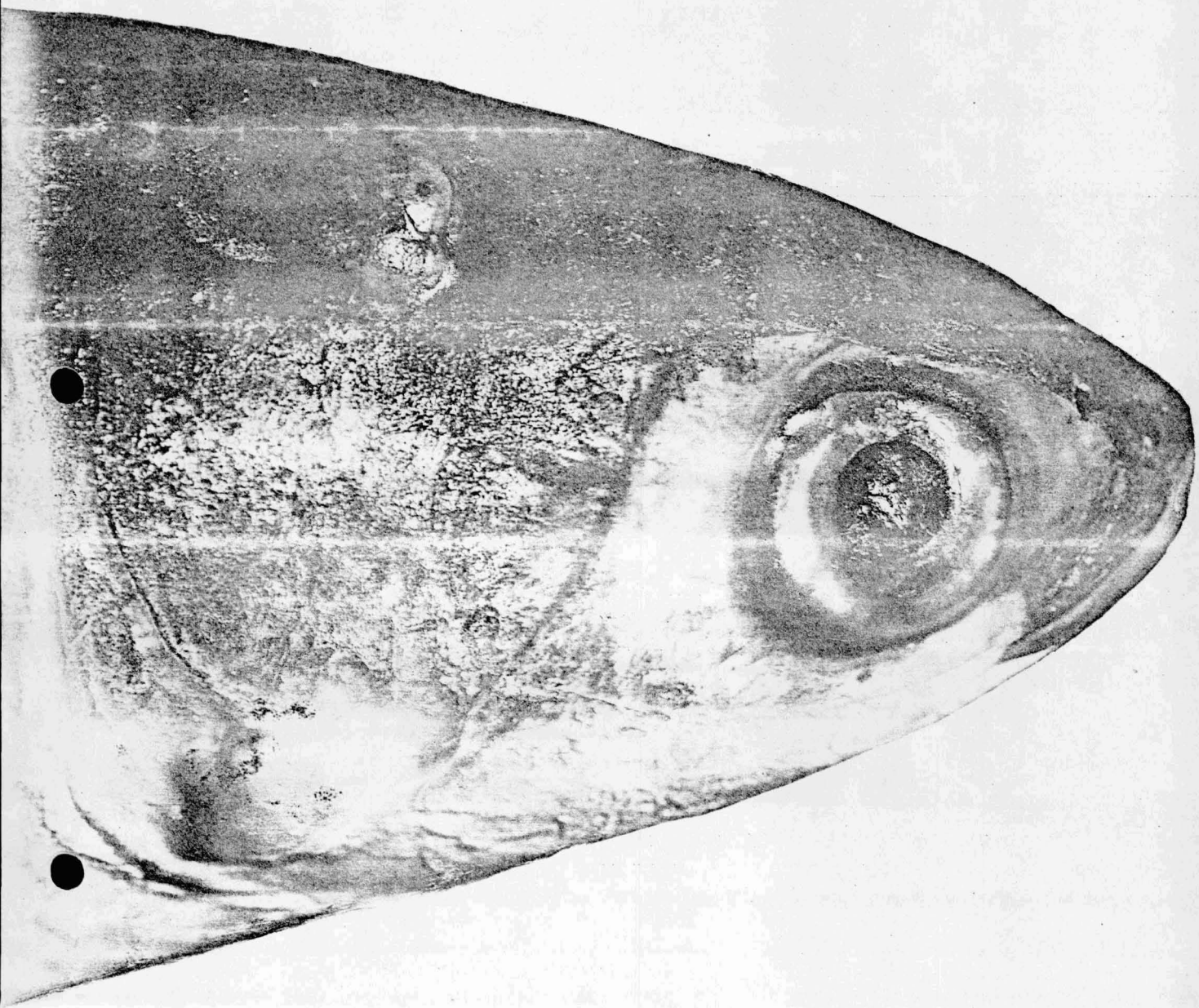

Figure 3. Wart-like fibrous tumors in mullet from Biscayne Bay, Florida.

possible association existed between high tumor occurrence (up to 20% in certain samples) and parasitization of the flesh by nematode, Philometra mariae -- but then they suggested that the involvement of naturally occurring chemical contaminants as well as man-made pollutants must be considered in the etiology of flatfish neoplasms.

The etiology of skin tumors in English sole from the Pacific coast of North America was reviewed in a recent paper by Angell et al. (1975) -- with the conclusion that the cause is unknown, and may be multifactorial. No conclusive role of an environmental carcinogen has been demonstrated, there seem to be subpopulation differences in disease prevalences, and electron microscopy has disclosed the presence of virus-like particles in cells of papillomatous fish (but attempts to isolate a viral agent have been unsuccessful). Angell et al. do admit, though, that "given the pervasiveness of certain pollutants, experimental evidence and further field studies will be necessary to clarify the relationship between tumorous flatfishes and pollution."

A recent study of neoplasms in the Atlantic hagfish, Myxine glutinosa, by Falkmer and Rappe (1976) suggested a possible relationship of PCB contamination and tumor prevalence. During a five-year (1972-1976) study in Gullmar Fjord, Sweden, neoplasm prevalences -- particularly hepatomas -- decreased from 5.8% to 0.6%. PCB levels in livers of hagfish were appreciable (5 ppm), but the use of PCB was prohibited in 1971. Liver PCB levels in hagfish caught inside the fjord were five times higher than in those caught outside.

The role of environmental chemical factors in induction of neoplasms in shellfish is even less clear than for fishes, but there is some limited suggestive information. Yevich and associates (Barry and Yevich, 1975; Yevich and Barszcz, 1976a, 1976b) have for a number of years examined the occurrence of neoplastic growths in soft clams, Mya arenaria, in relation to petroleum contamination. Gonadal and hematopoietic neoplasms were observed in animals collected from two chronically contaminated sites on the Maine coast, with prevalences up to 29% in certain samples. The authors state that "no tumors similar to those described from the petroleum contaminated area have been encountered in animals collected from any other area." They described the scope of their study as "several thousand animals from all coastal areas of the United States." Additional samples of clams from a number of other coastal locations are needed, as is a more precise description of the neoplastic condition.

It is interesting that a counterpart study of soft-shell clams from Rhode Island and Massachusetts (Brown et al., 1976) reported occurrences of neoplasia, apparently of hematopoietic origin, in up to 26%, with the highest frequency in samples from a 1975 oil spill area near Bourne, Mass.

Other types of cellular abnormalities have been reported from soft-shell clams. In earlier studies by Yevich and associates (Barry et al., 1971) atypical epidermal hyperplasia in gills and kidney was reported in up to 40% of clams sampled near Providence, R. I. Lesions occurred more frequently in large animals, and seasonal changes were not observed. Lower prevalences were found in limited samples from Maine, Maryland, and California. Unlike the oil spill studies, no association with environmental factors was made by the authors.

Yevich and associates (Yevich and Barry, 1969; Barry and Yevich, 1972) have also described gonadal neoplasms in quahogs, Mercenaria mercenaria, from Narragansett Bay, R. I. Samples collected in 1968, 1969, and 1970 had tumor frequencies of 0.2%, 2.3% and 2.7% respectively.

Epizootic neoplasms with a possible environmental etiology were reported from several molluscan species of Yaquina Bay, Oregon (Farley, 1969; Farley and Sparks, 1970; Mix et al., 1976). Blue mussels, Mytilus edulis; native oysters, Ostrea lurida; and two species of Macoma were affected, and winter mortalities were associated with the disease. Neoplasms have not been found in bivalve molluscs sampled elsewhere on the Oregon coast (Mix et al., 1976).

In another study (Christensen et al., 1974) similar epizootic neoplasms (up to 10% prevalence) were found in a localized population of the clam Macoma balthica from a tributary of Chesapeake Bay. The neoplasms were invasive and systemic, with initial foci in the gill epithelia. Holding experiments indicated that the disease was usually fatal. The authors suggest, but do not demonstrate, an environmental contaminant etiology, possibly associated with bottom detritus. Other bivalve mollusks in Chesapeake Bay contain neoplasms. Oysters, Crassostrea virginica, were found with hematopoietic neoplasms (Couch, 1969; Farley, 1969; Frierman and Harshbarger, 1974). Individual oysters have been reported to contain other types of neoplasms (Couch, 1970).

Skeletal Anomalies

Skeletal anomalies -- particularly those of the spinal column -- are commonly observed in fish, and are the subject of an extensive literature (see Hickey, 1972, for a recent summary).

Such anomalies may be genetic, resulting from mutations or recombinations; epigenetic, acquired during embryonic development; or post-embryonic, acquired during larval development, at metamorphosis, or during juvenile development. Spinal flexures and compressions, as well as vertebral fusions have been observed in many teleost species, as have head and fin abnormalities. Evidence exists for a hereditary basis for some skeletal anomalies (Gordon, 1954, Rosenthal and Rosenthal, 1950), but other evidence points to effects of environmental factors such as temperature, salinity, dissolved oxygen, radiation, dietary deficiencies and toxic chemicals. For example, increased percentages of abnormal embryos and larvae of Atlantic herring, Clupea harengus, resulted from exposure to sulfuric acid waste water (Kinne and Rosenthal, 1967) and to algicide 2,4- and 2,5 dinitrophenol (Rosenthal and Stelzer, 1970).

Recently, increased prevalences of skeletal deformities and anomalies -- considered to be pollution-associated -- have been recognized in a few fish species from southern California and Japan. In studies carried out in California, skeletal deformities occurred with greater frequency in samples from areas with significant pollutant stress (Valentine and Bridges, 1969; Valentine, Soulé and Samollow, 1973). Exposure of fry to very low concentrations of DDT ($\leq$ 1 ppb) produced significant anomalies in fin rays (Valentine and Soulé, 1973).

Probably the most convincing evidence for environmental influences on induction of abnormalities in marine fish is that presented by Valentine (1975). Examining samples of barred sand bass, Paralabrax nebulifer, from the southern California and Baja California coasts, Valentine found significantly higher prevalences of skeletal anomalies -- particularly gill raker deformities -- in fish from the California coast (Los Angeles and San Diego). The anomalies increased in frequency and severity with increasing size of the fish and an association with disturbed calcium metabolism was suggested. The author pointed to the high chlorinated hydrocarbon and heavy metal levels which characterize the California coastal area (Schmidt et al., 1971; Galloway, 1972), but emphasized that a causal relationship with increased prevalence of anomalies had not been established.

However, Valentine's suggestion of a possible causal relationship between high environmental levels of chlorinated hydrocarbons and heavy metals -- both of which are known to interfere with calcium metabolism -- and skeletal anomalies in fish seems reasonable, in view of experimental evidence from a wide range of vertebrates (Galloway, 1972; Peakall and Lincer, 1970; Pichirallo, 1971; McCaull, 1971; Ferm and Carpenter, 1967; Fimbreite et al., 1970; Lehner and Egbert, 1969).

Valentine (1975) referred briefly to additional observations on two other Pacific coastal species -- California grunion, Leuresthes tenuis, and barred surf perch, Amphistichus argenteus -- in which gill raker anomalies increased in frequency with age, and were virtually restricted to samples from southern California. This finding in three species reduces the likelihood that frequency differences could be attributable to inherited subpopulation differences in one of the three species studied.

While the deformed gill rakers were the most prevalent anomalies observed in southern California barred sand bass by Valentine, other abnormalities (pugheadedness, cranial asymmetries, deformed vertebrae, and fin anomalies) occurred, and were associated directly in frequency and severity with gill raker deformity.

There is some evidence from studies of a few other fish species for an involvement of environmental stress in the occurrence of skeletal anomalies. Gabriel (1944) noted anomalies in vertebrae of Fundulus heteroclitus due to temperature changes, and Mottley (1937) found anomalies in vertebral number of trout due to temperature (and possibly oxygen). Hubbs (1959) found high prevalences of vertebral abnormalities in Gambusia affinis from Texas warm springs, and concluded that the elevated environmental temperature was responsible.

Several reports from Japan refer to high and increasing occurrences of skeletal anomalies in fish. Komada (1974) observed increasing numbers of malformed sweetfish, Plecoglossus altivelis, in rivers and culture farms, and Matsusato (1974) found similar skeletal anomalies in a number of coastal species.

GENETIC ABNORMALITIES

The mutagenic properties of a number of chemical contaminants including heavy metals and pesticides have been demonstrated in experimental studies with terrestrial animals (Longwell, 1975). Fish eggs can be vulnerable to contaminant effects from the body burden of the parent female and from exposure to contaminants in surface water and/or sediments (depending on where in the water column spawning and development occur). Sperm cells are sensitive to contaminants, and eggs are especially sensitive during meiosis and early cleavage stages. Furthermore, chemical mutagens can reduce the rate of cell division, and can damage the spindle apparatus. Pelagic eggs may be most severely damaged, since the surface film of the ocean has been found to contain high concentrations of contaminants such as petroleum components, halogenated hydrocarbons and heavy metals (MacIntyre, 1974).

Some experimental evidence is available. Fish larvae incubated in cadmium-polluted water accumulated the metal (Westernhagen et al., 1974, Rosenthal and Sperling, 1974), and eggs incubated in as little as 1 ppm cadmium produced low percentages of viable larvae (Westernhagen et al., 1975). Some relevant experimental research on radionuclide-induced mutagenesis (AEC-TR-7299, 1972; Ivanov, 1967, Romashov and Belyayeva, 1966) has disclosed that many fish embryos with severe chromosomal damage died during the transition from blastula to gastrula. Abnormal post-gastrula embryos contained higher numbers of chromosomal aberrations than normal embryos, and the abnormal embryos had high mortality just before hatching. However, even the normal-appearing embryos with radiation exposure (and consequent genetic disturbances) had low viability and high mortality at hatching and subsequent to hatching.

Recently, Longwell (1976a, 1976b) reported high prevalences of chromosomal anomalies in Atlantic mackerel (Scomber scombrus) eggs and embryos in certain samples taken from the New York Bight in 1974. All degrees of chromosomal damage were found, including failure to align at the metaphase plate, incomplete spindle formation, translocation bridges, chromosomal "stickiness", losses of portions of chromosomes and "pulverization." Eggs with at least one chromosome or mitotic abnormality varied from 13 to 79%. Higher percentages seemed associated generally with degrees of environmental degradation. In addition to chromosomal anomalies, one station (the one with highest prevalence of anomalies) was also characterized by significant (26%) egg mortality.

The techniques developed by Longwell permitted examination of historical collections of eggs and embryos for chromosomal damage. A limited collection from the same geographic area (New York Bight) in 1966 disclosed a lower incidence of cytogenetic abnormalities than that found in the 1974 collection.

Samples examined to date from normal and degraded waters are still insufficient (as Longwell points out) to make definitive statements about the relationship of pollutants and extent of damage to genetic material, but the data presented so far are highly suggestive of such a relationship. Because of the implications of these findings in survival and abundance of economic marine species, it is particularly important that this area of research be pursued vigorously. It may well be that a new and significant mortality factor for estuarine and coastal populations -- increased genetic damage -- may have been introduced with increasing chemical pollution.

CONCLUSIONS

In considering pollution-associated diseases of fish and shellfish, a number of conclusions seem warranted:

(1) The significance of environmental stress from pollutants is emerging as an important determining factor in a number of fish and shellfish diseases. This may take the form of direct chemical-physical damage to cell membranes or tissues, modification of biochemical reactions, buildup of facultative microbial pathogens, low environmental oxygen levels, and many others.

(2) Some circumstantial evidence for the role of environmental carcinogens in inducing neoplasms of fish and shellfish is accumulating, but at present definitive conclusions are not justified.

(3) The multifactorial genesis of disease in marine species is becoming apparent -- involving environmental stress, facultative pathogens, resistance of hosts, and latent infections.

(4) The presence of marginal or degraded estuarine/coastal environments may be signalled by the appearance of fin erosion, "red sores", and lymphocystis in teleost fishes, by shell disease in crustaceans, and by certain neoplasms in bivalve molluscs, but a clear cause and effect relationship has not yet been demonstrated in every case.

(5) A number of viruses have been found in crustaceans and molluscs in recent years, and the pathogenic role of two of them has been demonstrated by increasing environmental stress. It may well be that other latent virus infections of invertebrates will be identified by similar experimental methods.

REFERENCES

AEC-TR-7299. Marine radioecology. 1972. (Distributed by NTIS, U.S. Dept. Commerce, Springfield, Va.

American Littoral Society. 1972. Special newsletter alert -- fin rot. Amer. Littor. Soc., Highlands, N.J., Aug. 1972, 4 pp.

Angell, C. L., B. S. Miller and S. R. Wellings. 1975. Epizootiology of tumors in a population of juvenile English sole (Parophrys vetulus) from Puget Sound, Washington. J. Fish. Res. Bd. Can. 32: 1723-1732.

Anonymous. 1951. Diseased stripers in Connecticut are safe to eat. Salt Water Sportsman. June 22, p. 1.

Barry, M. M. and P. P. Yevich. 1972. Incidence of gonadal cancer in the quahog. Oncology 26: 87-96.

Barry, M. and P. Yevich. 1975. The ecological, chemical, and histopathological evaluation of an oil spill site. Part III. Histopathological studies. Mar. Poll. Bull. 6: 171-173.

Barry, M. M., P. P. Yevich and N. H. Thayer. 1971. Atypical hyperplasia in the soft shell clam. J. Invert. Pathol. 17: 17-27.

Brett, J. R. 1956. Some principles in the thermal requirements of fishes. Quart. Rev. Biol. 31: 75-87.

Brown, R. S., R. E. Wolke and S. B. Saila. 1976. A preliminary report on neoplasia in feral populations of the soft-shell clam, Mya arenaria: prevalance, histopathology and diagnosis. Proc. First Internat. Colloq. Invert. Pathol., Kingston, Ontario, Canada, pp. 151-159.

Carlisle, J. G. Jr. 1969. Results of a six-year trawl study in an area of heavy waste discharge: Santa Monica Bay, California. Calif. Fish. Game 55(1): 26-46.

Carmody, D., J. Pearce and W. Yasso. 1973. The distribution of five heavy metals in the sediments of New York Bight. Mar. Poll. Bull. 4: 132-135.

Christensen, D. J., C. A. Farley and F. G. Kern. 1974. Epizootic neoplasms in the clam Macoma balthica (L.) from Chesapeake Bay. J. Nat. Cancer Inst. 52: 1739-1749.

Cooper, R. C. and C. A. Keller. 1969. Epizootiology of papillomas in English sole, Parophrys vetulus. Nat. Cancer Inst. Monogr. 31: 173-85.

Couch, J. 1969. An unusual lesion in the mantle of the American oyster (Crassostrea virginica). Nat. Cancer Inst. Monogr. 31: 557-562.

Couch, J. 1970. Sarcoma-like disease in a single specimen of the American oyster. In: Bibl. haemat. no. 36, ed. R. M. Dutcher, p. 647, Kager, Basel/München/Paris/ New York.

Couch, J. 1974a. Free and occluded virus, similar to Baculovirus, in hepatopancreas of pink shrimp. Nature, 247: 229-231.

Couch, J. 1974b. An enzootic nuclear polyhedrosis virus of pink shrimp. I. Ultrastructure, prevalence and enhancement. J. of Invert. Patho. 24: 311-331.

Couch, J. 1974c. Histopathologic effects of pesticides and related chemicals on the livers of fishes. In: The Pathology of Fishes. University of Wisconsin Press.

Couch, J. 1974d. Possible activation of enhancement of latent Baculovirus infections in penaeid shrimp. In: Neoplasms in Aquatic Animals. Prog. Exp. Tumor Res., F. Homburger (ed.), vol. 21, S. Karger: Basel, München, Paris, New York.

Couch, J. and Nimmo, D. 1974a. Ultrastructural studies of shrimp exposed to the pollutant chemical, polychlorinated biphenyl (Aroclor 1254). Bull. of Pharmacol. and Environm. Pathologists, 11: 17-20.

Couch, J. and Nimmo, D. 1974b. Detection of interactions between natural pathogens and pollutants in aquatic animals. In: Proc. Symposium on Diseases of Aquatic Animals, LSU-Sea Grant 75-5, pp. 261-268.

Dahlberg, M. D. 1970. Frequencies of abnormalities in Georgia estuarine fishes. Trans. Amer. Fish. Soc. 99: 95-97.

Dawe, C. J. and Harshbarger, J. C. (eds.). 1969. Neoplasms and related disorders of invertebrate and lower animals. Natl. Cancer Inst. Monogr. 31, 772 pp.

Dawson, C. E. 1964. A bibliography of anomalies of fishes. Gulf Res. Rept. 1(6): 308-399.

Dawson, C. E. 1966. A bibliography of anomalies of fishes. Supplement 1. Gulf Res. Rept. 2(2): 169-176.

Dawson, C. E. 1971. A bibliography of anomalies of fishes. Supplement 2. Gulf Res. Rept. 3(2): 215-239.

Duke, T. W., J. I. Lowe and A. J. Wilson,Jr. 1970. A polychlorinated biphenyl (Aroclor 1254) in the water sediment, and biota of Escambia Bay, Florida. Bull. Envir. Contam. and Toxicol. 5: 171-180.

Dunn, B. P. and H. F. Stich. 1976. Monitoring procedures for chemical carcinogens in coastal waters. J. Fish. Res. Bd. Can. 33: 2040-2046.

Edwards, R. H. and R. M. Overstreet. 1976. Mesenchymal tumors of some estuarine fishes of the northern Gulf of Mexico. I. subcutaneous tumors, probably fibrosarcomas, in the striped mullet, Mugil cephalus. Bull. Mar. Sci. 26(1): 33-40.

Falkmer, S. and C. Rappe. 1976. Hepatomas and other neoplasms in a primitive vertebrate, the Atlantic hagfish (Myxine glutinosa). Conference on Aquatic Pollutants and Biological Effects with Emphasis on Neoplasia. N. Y. Acad. Sci. (1976), Abstract No. 24.

Farley, C. A. 1969a. Probable neoplastic disease of the hematopoietic system in oysters, Crassostrea virginica and Crassostrea gigas. Natl. Cancer Inst. Monogr. 31: 541-555.

Farley, C. A. 1969b. Sarcomatoid proliferative disease in a wild population of blue mussels (Mytilus edulis). J. Natl. Cancer Inst. 43: 509-516.

Farley, C. A. and Sparks, A. K. 1970. Proliferative disease of hemocytes, endothelial cells and connective tissue cells in molluscs. In: Comparative Leukemia Research 1969, Bibl. Haemat., No. 36, R. M. Dutcher (ed.), pp. 610-617, S. Karger: Basel, München, Paris, New York.

Farley, C. A., W. G. Banfield, G. Kasnic,Jr. and W. S. Foster. 1972. Oyster herpes-type virus. Science 178: 759-760.

Ferm, V. H. and Carpenter, S. J. 1967. Developmental malformation from the administration of lead salts. Exp. Mol. Pathol. 7: 208.

Fimbreite, N., Fyfe, R. W. and J. A. Keith. 1970. Mercury contamination of Canadian prairie seed-eaters and their avian predators. Can. Field Natur. 84: 269.

Frierman, E. M. 1976. Occurrence of hematopoietic neoplasms in Virginia oysters (Crassostrea virginica). Mar. Fish. Rev. 38(10): 34-36.

Gabriel, M. L. 1944. Factors affecting the number and form of vertebrae in Fundulus heteroclitus. J. Exp. Zool. 95: 105.

Galloway, J. N. 1972. Man's alteration of the natural geochemical cycle of selected trace metals. Ph.D. thesis, Univ. Calif., San Diego.

Gopalan, U. K. and J. S. Young. 1975. Incidence of shell disease in shrimps in the New York Bight. Mar. Poll. Bull. 6: 149-153.

Gordon, M. 1954. The genetics of fish diseases. Trans. Amer. Fish. Soc. 83: 229-240.

Halstead, B. W. 1971. Toxicity of marine organisms caused by pollutants. F.A.O. Tech. Conf. on Marine Pollution and its effects on Living Resources and Fishing. Doc. MP/70/R-6, 21 pp.

Harshbarger, J. C. 1974. Activities Report (of the) Registry of Tumors in Lower Animals 1965-1973. Smithsonian Institution, Washington, D. C. 141 pp.

Hickey, C. R. Jr. 1972. Common abnormalities in fishes, their causes and effects. N. Y. Ocean Sci. Lab. Tech. Rept. No. 0013, 20 pp.

Hubbs, C. 1959. High incidence of vertebral deformities in two natural populations of fishes inhabiting warm springs. Ecology 40: 154.

Ivanov, V. N. 1967. Effects of radioactive substances on the embryonic development of fish. In: Problems of Biological Oceanography. p. 185 in AEC-TR-6940.

Kimura, I., T. Sugiyama and Y. Ito. 1967. Papillomatous growth in sole from Wakasa Bay area. Proc. Soc. Exp. Biol. Med. 125: 175-177.

Kinne, O. 1963. The effects of temperature and salinity on marine and brackish water animals. I. Temperature. 301-340. In Barnes, H. (ed.), Oceanography and Marine Biology, Vol. I, George, Allen and Unwin, Ltd., London.

Kinne, O. and H. Rosenthal. 1967. Effects of water pollutants on fertilization, embryonic development and larvae of the herring, Clupea harengus. Marine Biology. 1: 65-83.

Klontz, G. W. and R. A. Bendele. 1973. Histopathological analysis of fin erosion in southern California marine fishes. Southern Calif. Coastal Water Res. Proj., El Segundo, Calif., Rep. TM203: 8 p.

Komada, N. 1974. Studies on abnormality of bones in anomalous "Ayu", Plecoglossus altivelis. Fish. Pathol. 8: 127-135 (In Japanese, English Abstract).

Krantz, G. 1970. Lymphocystis in striped bass, Roccus saxatilis, in Chesapeake Bay. Chesapeake Sci. 11: 137-139.

Kroger, R. L. and Guthrie, J. F. 1971. Incidence of crooked vertebral columns in juvenile Atlantic menhaden, Brevoortia tyrannus. Chesapeake Sci. 12: 276.

Lehner, P. N. and Egbert, A. 1969. Dieldrin and eggshell thickness in ducks. Nature (London) 224: 1218.

Levin, M. A., R. E. Wolke and V. J. Cabelli. 1972. Vibrio anguillarum as a cause of disease in winter flounder, Pseudopleuronectes americanus). Can. J. Microbiol. 18: 1585-1592.

Lightner, D. V. 1974. Case reports of ossifying fibromata in the striped mullet. J. Wildl. Dis. 10(4): 317-320.

Longwell, A. C. 1975. Mutagenicity of marine pollutants as it could be affecting inshore and offshore marine fisheries. Middle Atlantic Coastal Fisheries Center, Natl. Mar. Fish. Ser., Inf. Rept. No. 79, 72 pp.

Longwell, A. C. 1976a. Chromosome mutagenesis in developing mackerel eggs sampled from the New York Bight. ASLO Spec. Sympos. 2: 337-339 (Abstract).

Longwell, A. C. 1976b. Chromosome mutagenesis in developing mackerel eggs sampled from the New York Bight. NOAA Tech. Memo. ERL-MESA-7, 61 pp.

Lucké, B. and H. Schlumberger. 1941. Transplantable epitheliomas of the lip and mouth of catfish. J. Exp. Med. 74: 397-408.

MacIntyre, F. 1974. The top millimeter of the ocean. Sci. Amer. 203: 62.

Mahoney, J. B., F. H. Midlige and D. G. Deuel. 1973. A fin rot disease of marine and euryhaline fishes in the New York Bight. Trans. Am. Fish. Soc. 102: 596-605.

McArn, G. E. and S. R. Wellings. 1971. A comparison of skin tumors in three species of flounders. J. Fish. Res. Board Can. 28: 1241-1251.

McArn, G. E., R. G. Chuinard, B. C. Miller, R. E. Brooks and S. R. Wellings. Pathology of skin tumors found on English sole and starry flounder from Puget Sound, Washington. J. Natl. Cancer Inst. 41: 299-242.

McCaull, J. 1971. Building a shorter life. Environment (St. Louis) 13: 2.

McDermott, D. J. and J. Sherwood. 1975. Annual report. Dep. Fish. Mar. Fish Program. Coastal Water Res. Proj., El Segundo, Calif., p. 37.

Mearns, A. J. and M. Sherwood. 1974. Environmental aspects of fin erosion and tumors in Southern California Dover sole. Trans. Am. Fish. Soc. 103: 799-810.

Miller, B. S. and S. R. Wellings. 1971. Epizootiology of tumors on flathead sole (Hippoglossoides elassodon) in East Sound, Orcas Island, Washington. Trans. Am. Fish. Soc. 100: 247-266.

Mix, M. C., R. T. Riley, H. J. Pribble and S. P. Tomasovic. 1976. Neoplastic disease in marine animals in estuarine waters from Oregon with emphasis on research conducted on proliferative disorders of Yaquina Bay bivalve molluscs. Conference on Aquatic Pollutants and Biological Effects with Emphasis on Neoplasia, N. Y. Acad. Sci. (1976), Abstract No. 25.

Mottley, C. McC. 1937. The number of vertebrae in trout (Salmo). J. Biol. Board Can. 3: 169.

Murchelano, R. A. 1975. The histopathology of fin rot disease in winter flounder from the New York Bight. J. Wildl. Dis. 11: 263-268.

Nakai, Z., M. Kosaka, S. Kudoh, A. Nagai, F. Hayashida, T. Kubota, M. Ogura, T. Mizutani and I. Uotani. 1973. Summary report on marine biological studies of Suruga Bay accomplished by Tokai University 1964-72. J. Fac. Mar. Sci. Tech. Tokai Univ., 10th Anniv. Commem. Vol. pp. 63-118.

Nigrelli, R. F., K. S. Ketchen and G. D. Ruggieri. 1965. Studies on virus diseases of fishes. Epizootiology of epithelial tumors in the skin of flatfishes of the Pacific coast, with special reference to the sand sole (Psettichthys melanostictus) from northern Hecate Strait, British Columbia, Canada. Zoologica 50(3): 115-122.

Nimmo, D. R., R. R. Blackman, A. J. Wilson Jr., and J. Forester. 1971. Toxicity and distribution of Aroclor (R) 1254 in the pink shrimp, Penaeus duorarum. Mar. Biol. 11: 191-197.

Nimmo, D., Hansen, D., Couch, J., Cooley, N., Parrish, P. and Lowe, J. 1975. Toxicity of Aroclor (R) 1254 and its physiological activity in several estuarine organisms. Archives of Envir. Contam. and Toxicol. 3: 22-39.

Oishi, K., F. Yamazaki and T. Harada. 1976. Epidermal papillomas of flatfish in the coastal waters of Hokkaido, Japan. J. Fish. Res. Bd. Can. 33: 2011-2017.

Oppenheimer, C. 1958. A bacterium causing tail rot in the Norwegian codfish. Pub. Inst. Mar. Sci. Univ. Texas 5: 160-164.

Overstreet, R. M. and H. D. Howse. 1976. Some parasites and diseases of estuarine fishes in polluted habitats of Mississippi. Conference on Aquatic Pollutants and Biological Effects with Emphasis on Neoplasia. N. Y. Acad. Sci. (1976). Abstract No. 29.

Pauley, G. B. 1969. A critical review of neoplasia and tumor-like lesions in mollusks. Natl. Cancer Inst. Monogr. 31: 509-539.

Peakall, D. B. and Lincer, J. L. 1970. Polychlorinated biphenyls, another long-life widespread chemical in the environment. BioScience 20: 958.

Pearce, J. B. 1972. The effects of solid waste disposal in the New York Bight. In: Marine Pollution and Sea Life, ed. Ruivo, M., pp. 404-411, London: Fishing News (Books).

Pichirallo, J. 1971. PCB's: Leaks of toxic substances raises issue of effects, regulation. Science (Wash., D. C.) 1973: 899.

Perkins, E. J., Gilchrist, J. R. S. and Abbott, O. J. 1972. Incidence of epidermal lesions in fish of the north-east Irish Sea, 1971. Nature, 238, 101-103.

Rentchnick, P. (ed.). 1976. Neoplasms in aquatic animals as indicators of environmental carcinogens. UICC (Union Int. Cancer) Bull. 14(2): 4-5.

Romashov, D. D. and V. N. Belyayeva. 1966. Retention of radiation lesions to chromosomes in fish embryogenesis. Genetika 4: 3.

Rosen, B. 1970. Shell disease of aquatic crustaceans. pp. 409-415. In: Snieszko, S. F. (ed.). A Symposium on diseases of fishes and shellfishes. Amer. Fish. Soc., Spec. Pub. No. 5. 526 pp.

Rosenthal, H. and D. F. Alderdice. 1976. Sublethal effects of environmental stressors, natural and pollutional, on marine fish eggs and larvae. J. Fish. Res. Bd. Can. 33: 2047-2065.

Rosenthal, H. L. and R. S. Rosenthal. 1950. Lordosis, a mutation in the guppy. J. of Heredity. 41: 217-218.

Rosenthal, H. and K.-R. Sperling. 1974. Effects of cadmium on development and survival of herring eggs. p. 383-396. In: J. H. S. Blaxter (ed.). The early life history of fish. Springer-Verlag, Berlin.

Rosenthal, H. and R. Stelzer. 1970. Wirkungen von 2,4- und 2,5 dinitrophenol auf die Embryonalentwicklung des Herings. Marine Biol. 5: 325-336.

Russell, F. E. and Kotin, P. 1957. Squamous Papilloma in the White Croaker. J. Natl. Cancer Inst., 18(6): 857-861.

Ryder, J. A. 1887. On a tumor in the oyster. Proc. Acad. Nat. Sci. Phila. 44: 25-27.

Schlotfeldt, H.-J. 1972. Jahreszeitliche Abhängigkeit der "Schwarzfleckenkrankheit" bei der Garnele, Crangon crangon L. Ber. dt. wiss. Kommn. Meeresforsch. 22: 397-399.

Schmidt, T. T., Risebrough, R. W. and Gress, R. 1971. Input of polychlorinated biphenyls into California coastal waters from urban sewage outfalls. Bull. Environ. Contam. Toxicol. 6: 235.

Selye, H. 1952. The story of the adaptation syndrome. Acta. Inc., Montreal, Que. 255 p.

Sherwood, M. J. and R. A. Bendele. 1975. Mucous production in Dover sole. Annual report. Coastal Water Res. Proj., El Segundo, Calif. p. 51.

Sindermann, C. J. 1976. Effects of coastal pollution on fish and fisheries -- with particular reference to the New York Bight. pp. 281-301. In: Gross, M. G. (ed.) Middle Atlantic continental shelf and the New York Bight. Amer. Soc. Limnol. Oceanog., Spec. Sympos. Vol. 2, 441 pp.

Sindermann, C. J. 1970. Principal Diseases of Marine Fish and Shellfish. Academic Press, New York and London.

Southern California Coastal Water Research Project. 1973. The ecology of the Southern California Bight: Implications for water quality management. Ref. No. SCCWRP TR 104, El Segundo, Calif.

Stich, H. F. and A. B. Acton. 1975. The possible use of fish tumors in monitoring for carcinogens in the marine environment. Exp. Tumor Res. 20. (In press).

Stich, H. F., A. B. Acton and C. R. Forrester. 1976a. Fish tumors and sublethal effects of pollutants. J. Fish. Res. Board Can. 33: 1993-2001.

Stich, H. F., A. B. Acton, K. Oishi, F. Yamazaki, T. Harada and H. G. Moser. 1976b. Systematic collaborative studies on neoplasms in marine animals as related to the environment. Conference on Aquatic Pollutants and Biological Effects with Emphasis on Neoplasia. N. Y. Acad. Sci. (1976). Abstract No. 26.

Valentine, D. W. 1975. Skeletal anomalies in marine teleosts. pp. 695-718. In: Ribelin, W. E. and G. Migaki (eds.). The Pathology of Fishes. U. Wisc. Press, 1004 pp.

Valentine, D. W. and K. W. Bridges. 1969. High incidence of deformities in the serranid fish Paralabrax nebulifer from southern California. Copeia 1969(3): 637-8.

Valentine, D. W. and M. Soulé. 1973. Effect of p,p'-DDT on developmental stability of pectoral fin rays in the grunion, Leuresthes tenuis. Fish. Bull. 71: 921-926.

Valentine, D. W., Soulé, M. E. and Samollow, P. 1973. Asymmetry: A possible indicator of environmental stress. U. S. Nat. Mar. Fish. Bull. 71: 357.

Warren, S. and W. A. Meissner. 1966. Pathology. Vol. 1, Chap. 16. In: Anderson, W. A. (ed.). C. V. Mosby, St. Louis.

Wellings, S. R. 1969. Environmental aspects of neoplasia in fishes. p. 3-22. In: O. W. Neuhaus and J. E. Halver (ed.). Fish in research. Atademic Press, Inc., New York, N. Y.

Wellings, S. R. 1969. Neoplasia and primitive vertebrate phylogeny: Echinoderms, prevertebrates and fishes - A review. Nat. Cancer Inst. Monogr. 31: 59-128.

Wellings, S. R. and R. G. Chuinard. 1964. Epidermal papillomas with virus-like particles in flathead sole, Hippoglossoides elassodon. Science 146: 932-4.

Wellings, S. R. and R. A. Cooper. 1967. Ultrastructural studies of normal skin and epidermal papillomas of the flathead sole, Hippoglossoides elassodon. Z. Zellforsch. 78: 370.

Wellings, S. R., R. G. Chuinard and M. Bens. 1965. A comparative study of skin neoplasms in four species of pleuronectid fishes. Ann. N. Y. Acad. Sci. 126: 479-501.

Wellings, S. R., R. G. Chuinard, R. T. Gourley and R. A. Cooper. 1964. Epidermal papillomas in the flathead sole, Hippoglossoides elassodon, with notes on the occurrence of similar neoplasms in other pleuronectids. J. Nat. Cancer Inst. 33: 991-1004.

Wellings, S. R., R. G. Chuinard and M. Bens. 1965. A comparative study of skin neoplasms in four species of pleuronectid fishes. Annals N. Y. Academy of Sci. 126(1): 479-501.

Wellings, S. R., C. E. Alpers, B. B. McCain and B. S. Miller. 1976. Fin erosion disease of starry flounder (Platichthys stellatus) and English sole (Parophrys vetulus) in the estuary of the Duwamish River, Seattle, Washington. J. Fish. Res. Bd. Can. 33: 2577-2586.

Wells, N. A. and C. E. Zobell. 1934. Acromobacter ichthyodermis, n. sp. the etiological agent of an infectious dermatitis of certain marine fishes. Proc. Nat. Acad. Sci. 20: 123-6.

Westernhagen, H. von and V. Dethlefsen. 1975. Combined effects of cadmium and salinity on development and survival of flounder eggs. J. Mar. Biol. Assoc. U. K. 55: 945-957.

Westernhagen, H. von, V. Dethlefsen and H. Rosenthal. 1975. Combined effects of cadmium and salinity on development and survival of gar pike eggs. Helgol. Wiss. Meeresunters. 27: 268-282.

Westernhagen, H. von, H. Rosenthal and K.-R. Sperling. 1974. Combined effects of cadmium and salinity on development and survival of herring eggs. Helgol. Wiss. Meeresunters. 26: 416-433.

Yevich, P. P. and M. M. Barry. 1969. Ovarian tumors in the quahog. J. Invert. Pathol. 14: 266-267.

Yevich, P. P. and C. A. Barszcz. 1976a. Gonadal and hematopoetic neoplasms in Mya arenaria. Marine Fish. Rev. 38(10): 42-43.

Yevich, P. P. and C. A. Barszcz. 1976b. Marine animal neoplasms associated with oil pollution. Conference on Aquatic Pollutants and Biological Effects with Emphasis on Neoplasia, N. Y. Acad. Sci., (1976). Abstract No. 28.

Young, P. H. 1964. Some effects of sewer effluent on marine life. Calif. Fish Game 50(1): 33-41.

Young, J. S. 1973. A marine kill in New Jersey coastal waters. Mar. Poll. Bull. 4(5): 70.

Young, J. S. and J. B. Pearce. 1975. Shell disease in crabs and lobsters from New York Bight. Mar. Poll. Bull. 6: 101-105.

Ziskowski, J. and R. Murchelano. 1975. Fin erosion in winter flounder, (Pseudopleuronectes americanus) from the New York Bight. Mar. Poll. Bull. 6: 26-28.

Zobell, C. E. and N. A. Wells. 1934. An infectious dermititis of certain marine fishes. J. Infect. Dis. 65: 299-305.