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Control of Fish Diseases

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ABSTRACT — Severity of outbreaks of communicable diseases of fishes is influenced by environmental conditions. Therefore, beneficial results of chemotherapy depend on the specific action of drugs and the maintenance of conditions favorable to the treated fishes. This paper deals mainly with the therapeutic control of fish diseases.

RELATIONSHIP OF HOST, PATHOGEN, AND ENVIRONMENT

It is generally accepted that all outbreaks of a communicable disease are the result of interaction between the host, the pathogen, and the environment. This is particularly true in regard to fishes, which are coldblooded and utilize oxygen dissolved in water. The environment of the open sea is very stable, but in the inland waters and in fish farms extreme water temperatures, low dissolved oxygen contents, presence of fish catabolic products, and general pollution often produce stresses which contribute to outbreaks of infectious diseases. According to Seleye (1955), Pasteur, who established the role of microbial pathogens in diseases, allegedly said, "Le microbe n'est rien, le terrain est tout" (the microbe is nothing; the environment is everything).

TREATMENT AND CONTROL OF FISH DISEASES

The practical fish culturist expects the fish disease specialist to provide ironclad remedies which will work under all circumstances (Snieszko, 1975; Fryer, 1978). This is not possible because a drug is just a crutch which is used to help the host survive the infection until the pathogen is subdued and the environment improved. The outcome of treatment depends on the susceptibility of the host to any particular disease, the species, number and virulence of the pathogen, and the degree and duration of stress caused by improper environment (Endo et al., 1973). (See also section on Selected References.)

This relationship can be graphically presented by the use of sets and subsets (Kemeny et al., 1957) as is done in regard to fishes by Snieszko (1973, 1974) and Wedemeyer (1974), and in regard to dental caries by Sherp (1971). It can also be presented in the form of an algebraic equation:

$$H + P + S^2 = D$$

where: H = species and strain of the host, its age, and inherited susceptibility to any particular disease;
P = the agent causing the disease with all its variability;
S = stress of the environment; and
D = the disease which results if the components on the left side of the equation are in proper qualitative and quantitative relationship.

In this equation, the square of S is used because the stress caused by the environment increases in geometrical progression when the conditions are approaching the limits of tolerance by the host.

Administration of Drugs

Drugs are administered to fishes in a number of ways (Herman, 1970) (Table 1). In external parasitic infestations, drugs can be added to water for different lengths of time. Some antibiotics are injected intraperitoneally. For oral administration, drugs may be mixed with feed. This method is complicated by the fact that the rate of feeding is calculated as a percentage of fish weight. This percentage varies with different fishes and is strongly influenced by the age of fishes and water temperature (Halver, 1972). Therefore, it is often difficult to prepare a diet with just a single concentration of the drug.

Drugs Commonly Used

Drugs which are poorly soluble in water but easily absorbed from the lumen of the intestines are preferable. In case of intestinal parasites, drugs are selected which act in the gut. Many of the drugs used in control of diseases of fishes are the same ones used for humans and domestic animals. Recently, Japanese and German manufacturers released nitrofurans for fishes. They are soluble in water and can be used as baths or mixed with feeds. The Japanese drug is ni-furpirinol (Furanace[1]) (Anonymous, n.d.; Amend and Ross, 1970). The German product is nifurprazine which is sold in Germany as Carofur (Duefel, 1970; Shiraki et al., 1970) and is also licensed for production in Japan as Aivet. These nitrofurans are excellent in systematic infections caused by *Aeromonas punctata* and related forms, and by *Vibrio anguillarum*, and for columnaris disease, gill disease, and others. They are added to water in concentrations from 0.05 to 1 ppm depending on the duration of treatment. These drugs can be used orally with feed. They are quickly eliminated from the tissues leaving no detectable residues within 2 days. Among the older nitrofurans, furazolidone (Furoxone) is effective in oral administration. Among antibiotics most often used are oxytetracycline (Terramycin), chloramphenicol (Chloromycetin), and chlortetracycline (Aureomycin) (Herman, 1970). The latter is used chiefly as a bath for aquarium fishes.

Among the most often used sulfonamides are sulfamerazine, sulfamethazine, and sulfisoxazole (Herman, 1970). Only sulfamerazine and Terramycin are now cleared by the Food and Drug Administration (FDA) for control of certain diseases of fishes.

[1]Reference to trade names does not imply endorsement by the National Marine Fisheries Service, NOAA.

Table 1.—Chemicals used most frequently for control of infectious diseases of fishes.

Chemical agent	Method of administration
Acetic acid, glacial	Dilute in water: 1:500 for 30-60 seconds (dip) 1:2,000 (500 ppm) as bath for 30 minutes
Acinitrazole (2-Acetamido-5-nitrothiazole)	Used for Hexamitiasis in Norway. 40 mg/kg feed for 4 days
Acriflavine (Trypaflavine)	5-10 ppm added to water from several hours to several days
Aivet (soluble powder contains 6.6% Nifurprazine HCl (same as Carofur))	See Nifurprazine
Aureomycin	See Chlortetracycline
Betadine (Iodophor containing 1.0% of iodine)	See Iodophors
Bithionol (2,2'-Thiobis) (4,6-dichlorophenol) (a French product also known as Cogla)	Orally 0.2 g/kg of fish or 2% in food. Feed for 2-3 days. For *Acanthocephala* and oral prophylaxis against *Saprolegnia*.
Brilliant green (same as Malachite green G sulfate)	See Malachite green
Bromex (Dibrom, Naled; a pesticide)	0.12 ppm added to (pond) water for indefinite time.
Buffodine	See Iodophors Buffodine is a neutral formulation of an iodophor giving nearly neutral solutions in water.
Butyl tin oxide (di-n-butyl tin oxide)	25 mg/kg body weight per day with food for 3 days.
Calcium cyanamide	Distributed on the bottom and banks of drained but wet ponds at a rate of 200 g/m^2.
Calcium oxide (quicklime)	Distributed on the bottom and banks of drained but wet ponds at a rate of 200 g/m^2.
Carbarsone oxide	Mixed with food at a rate of 0.2%. Feed for 3 days.
Carofur (a product containing 6.66% of Nifurprazine HCl.	See Nifurprazine
Chloramine—I	In water with pH 7.5-8.0, 18-20 ppm. Change 50% of water once each week if water temperature 10°C or below. At 25°C, one treatment for 2-3 days.
Chloramphenicol (Chloromycetin)	1. Orally with food 50-75 mg/kg body weight per day for 5-10 days. 2. Single intraperitoneal injection soluble form 10-30 mg/kg. 3. Added to water 10-50 ppm for indefinite time as needed.
Chlorophos	See Dylox
Chlortetracycline (Aureomycin)	10-20 ppm in water. In eel diseases in Japan it is added to feed at a rate of 10-20 mg/kg of food.
Ciodrin (Shell Petroleum product; a pesticide similar to Dipterex, Dylox, Masoten).	For control of *Lernea* in Japanese eel culture.
Cogla (D²N Cogla)	See Bithionol
Concurat (2,3,5,6 tetrahydro-6-phenylimidazo) (2, 1-b) thiazolhydrochloride)	Broad spectrum anthelminthic
Copper sulfate (Blue stone) $CuSO_4$ anhydrous $CuSO_4$ $5H_2O$ crystalline	For a 1 minute dip: 1:2,000 (500 ppm); in hard water add 1 ml glacial acetic acid /liter. 0.25-2 ppm to ponds. Quantity depends on hardness of water. Hard water requires more.
Cutrine (chelated copper compound)	Aquatic herbicide as copper sulphate but not affected by hardness of water, and somewhat less toxic to fish.
Cyzine (Enheptin-A)	20 ppm in feed for 3 days for *Hexamita*
Detrapan (in use in France)	Systemic antifungal drug, for fish after spawning: 0.25 ml/kg intramuscularly used twice every 48 hours
Devermin	0.1 g/kg of fish orally with food for control of *Cestoda*.
Diibutylin dilaurate (Butynorate, Tinostat)	250 mg/kg of fish orally or 0.3% in food
Dimeton	See Sulfamonomethoxine
Dimetridazole	0.15% mixed with food for 3 days
Dipterex	See Dylox
Diquat (patented herbicide, Ortho Co. contains 35.3% of active compound)	1-2 ppm of Diquat cation, or 8.4 ppm as purchased added to water. Treatment for 30-60 minutes. Activity much reduced in turbid water.
Dylox (Dipterex, Neguvon, Chlorophos, Trichlorfon, Foschlor, Masoten)	0.25 ppm to water in aquaria and 0.25-1.0 ppm in ponds for indefinite period
Enheptin (2-Amino-5-nitrothiazole)	0.2% in food for 3 days for *Hexamita*
Formalin (37% by weight of formaldehyde in water. Usually contains 12-15% methanol)	1:500 for 15-minute dip. 1:4,000-1:6,000 for 1 hour. 15-19 ppm to pond or aquarium water for indefinite period.
Formalin with Malachite green	In formulations of Formalin with malachite green, Formalin is used at 15 to 25 ppm and malachite green at 0.05 to 0.1 ppm. For several hours in aquaria and for indefinite period in ponds.
Fosfomicina (a Spanish antibiotic; $C_3H_7O_4P$)	For *Aeromonas* infections in fishes
Furanace (P-7138) (Ni-furpirinol); (6-hydroxymethyl-2-pyridine)	Used as bath but may be added to food. As bath: 1 ppm for 5-10 minutes; 0.05-0.1 ppm may be added for indefinite period to water. Orally for treatment: 2-4 mg/kg fish per day for 3-5 days. Orally for prophylaxis: 0.4-0.8 mg/ fish per day as long as needed.
Furazolidone (Furoxone N.F. 180 N.F. 180 Hess & Clark commerical products contain furazolidone mixed with inert materials)	On the basis of pure drug activity; 25-75 mg/kg body weight per day up to 20 days orally with food.
Furoxone	See Furazolidone
Furpyridinol (product containing 10% Furanace)	Added to water 0.3-10 ppm, as is, for 30-60 minutes. Also see Furanace.
Hyamine (Rohm & Hass Co., quaternary ammonium germicide available as crystals or as 50% solution)	1.0-2.0 ppm (on basis of 100% product) in water for 1 hour.
Iodine	In form of a Lugol solution or iodine for control of goiter and possibly corynebacterial kidney disease.
Iodophors (Betadine, Wescodyne, Bridine, etc.)	Different commercially available iodophors contain different concentration of iodine. To be used on a basis of pure iodine present in the product. Use 50-200 ppm iodine (usually 100 ppm) for disinfection of eggs for 10-15 minutes. Toxic to hatched fish. Probably also assist in control of some virus fish diseases.
Kamala	Mixed with diet at a rate of 2%. Feed to starved fish for 3 days.
Kanamycin (antibiotic also traded as Cantrex, Kamycin, Resistomycin)	50 mg/kg of fish or 25-100 mg/kg of food. Feed for a week.
Malachite green	1:15,000 in water as a dip for 10-30 seconds, 1-5 ppm in water for 1 hour; 00.5 to 2.00 ppm in ponds or aquaria for indefinite time.
Malachite green with Formalin	See Formalin
Masoten	See Dylox
Mefarol (probably similar to Hyamine)	1-2 ppm in water for 1 hour. Toxic in very soft water; less effective in hard water.
Methylene blue	1.0-3.0 ppm in water for 3-5 days.
Metronidazole (1-beta (hydroxyethyl)-2-methyl-5-nitroimidazole)	4 mg/liter of water for 3-4 days for control of protozoan ectoparasites in ornamental fishes.
Nalidixic acid (1-ethyl-1,4-dihydro-7-methyl-4-oxo-1,8-naphthyridine-3-carboxylic acid) NegGram; Wintomylon.	Similar in action to oxolinic acid. One tablet per 50 to 100 liters of water for treatment of 3-4 days duration. Infections with gram-negative bacteria.
Neguvon	See Dylox
Ni-furpirinol	See Furanace (P-7138)
Nifurprazine (HB-115) (Nitrofuran, unstable in prolonged exposure to sunlight. 1-(5 nitro-2-furyl) -2-(6-amino-3-pyridazyl) ethylene-hydrochloride) (Carofur and Aivet are water soluble formulations.)	As bath: for indefinite period 0.01-0.1 ppm. In food: 10 mg/kg of food. Feeding for 3-6 days at a time.
Nitrofurazone (5-nitro-2-furaldehyde semicarbazone)	See Furazolidone, Furoxone
Oxolinic acid (1-ethyl-1, dihydro-6, 7-methyl-enedioxy-4-oxo-3-quinoline carboxylic acid)	For control of *Aeromonas* infections. Orally 3 mg/kg fish once daily for 5 days. As bath: 1 ppm for 24 hours for columnaris disease.
Oxytetracycline (Terramycin)	50-75 mg/kg body weight per day for 10 days with food. (Law requires that it must be discontinued for 21 days before fish are killed for human consumption.)
Ozone	Is being investigated as remedy for external infection and for decontamination of water.
Potassium permanganate $KMnO_4$	1:1,000 (1,000 ppm) for a 10-40 second dip. 10 ppm up to 30 minutes, 3-5 ppm added to aquarium or pond water for indefinite time.
Potentiated sulfonamide (Sulfadimethoxine potentiated with ormetoprim)	For control of furunculosis and other systematic infections. Used with feed 50 mg /kg fish per day.

Table 1 continued on next page.

Table 1 continued.

Chemical agent	Method of administration	Chemical agent	Method of administration
Povidone-Iodine (PVP-1)	See Iodophors	Sulfamerazine (cont.)	for 14 days. (Law requires that treatment must be stopped for 21 days before fishes are killed for human consumption.)
Quinine hydrochloride or Quinine sulfate	10-15 ppm in water for indefinite time	Sulfamonomethoxine (trade name Dimeton; water soluble)	With feed as is at a rate of 100-200 mg/kg of feed. Use as needed.
Roccal (Sold as 10-50% solution of Benzalkonium chloride. Quaternary ammonia germicide—also see Hyamine)	1-2 ppm in water for 1 hour. Toxic in soft water; less effective and less toxic in hard water.	Sulfisoxazole (Gantrisin)	200 mg/kg body weight per day with food
Sodium chloride (table salt, iodized or not)	1-3% in water for 30 minutes to 2 hours only for freshwater fishes.	Terramycin	See Oxytetracycline
Sulfadimethoxine sodium (in Japan available as 10% powder)	100-200 mg calculated as pure drug per kilogram of food	Tetrafinol	For control of intestinal helminths; used with feed.
Sulfamerazine	200 mg/kg body weight per day with food	Tin oxide, di-n-butyl	See Butyl tin oxide
		Wescodyne (Iodophor containing 1.6% of iodine)	Use as explained under Iodophors

Chemoprophylaxis

With fishes, drugs are used for prevention (chemoprophylaxis) and treatment (chemotherapy). Chemoprophylaxis is very effective, particularly if applied when an outbreak of a particular disease is anticipated. Outbreaks of diseases in fish farms are greatly affected by environmental stress, and chemoprophylaxis is very effective provided the stress factor is removed before the treatment ends.

In some chronic diseases, such as corynebacterial kidney disease, timely use of chemoprophylaxis with sulfonamides may prevent, or reduce, losses very significantly. In endemic areas, fish should receive sulfamethazine or sulfamerazine with feed at a rate of about 4 g/100 kg fish per day. This treatment may be repeated daily, given several days in a week, or repeated periodically. Usually, such treatment is continued for months (Herman, 1970).

The danger of chemotherapy is in developing strains of bacteria which are resistant or contain the transferable resistance factor "R". Microorganisms isolated from imported ornamental fishes often contain a wide spectrum of transferable resistance factors (Gratzek, 1978). There is indirect evidence showing that these fish were treated with various drugs.

Prophylaxis is now applied for removal of pathogens which may be present on the surface of fish eggs. Various chemicals were used for this purpose, but recently these have been replaced by iodophors, complexes of iodine and organic chemicals. Eyed eggs are usually treated with iodophors by immersion for 15 minutes in water buffered to about pH 7.0-8.0 and containing about 100 ppm of elemental iodine present in the iodophor. It has been shown that iodophors are not only effective in control of external bacteria, but also in viral contamination (Amend and Pietsch, 1972; Nelson, 1974a).

Prophylaxis is very important in protecting incubating fish eggs from the fungus *Saprolegnia*. One of the most reliable and most widely used methods of control is the exposure of eggs (at 1- to several-day intervals) to a bath containing 2-5 ppm of malachite green (Nelson, 1974b).

Parasite Control

There is a wide selection of therapeutic agents for the control of external and intestinal parasites of fishes (Hoffman and Meyer, 1974). However, there are no treatments for systemic parasites. The intradermal parasites such as *Ichthyophthirius* and *Cryptocaryon* are very bothersome. Only their free-swimming stage is amenable to drugs. It is difficult to reach the disease-causing stage of these parasites which are buried in the skin. Observations incidental to research on potentiated sulfonamides (Bullock et al., 1974; McCarthy et al., 1974) have shown that the potentiator ormetoprim accumulates in the skin of fishes. It would be interesting to find out if it has any effect on the intradermal form of these parasites.

Early Diagnosis Important in Treatment

Chemotherapy and other treatment methods have recently been reviewed by Herman (1970) and Hoffman and Meyer (1974). Therefore, I will make only general comments here. To be effective, chemotherapy must be prompt and directed toward the specific pathogen. Therefore, correct diagnosis is of utmost importance. When diagnosis must be delayed for a day or two, it is desirable to make a tentative diagnosis immediately and start treatment because any delay may increase losses considerably. The selection of the drug may have to be modified when the final diagnosis is made and the drug's susceptibility to the pathogen is determined.

Effectiveness of Chemotherapy

In the evaluation of the effectiveness of chemotherapy, counts of mortalities are important. One must remember that reduction of mortalities may not be real but only apparent by additive counting of losses. Whenever possible, mortalities should be expressed as mortalities per day, or per period, and based on the number of fish surviving at the start of each period. This calculation is only possible if a fairly accurate number of fish is known before the disease breaks out and if accurate daily counts of losses are made.

COST OF DISEASE CONTROL OF PRIME IMPORTANCE

Realistically speaking, the monetary value of losses caused by diseases is limited. Therefore, the cost of disease control cannot exceed the value of lost fishes. It is well to keep this in mind when developing methods for control of fish diseases.

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