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CHEMOTHERAPY

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Chemotherapy is defined as the use of drugs and chemicals for the treatment of infectious disease. To be useful, the chemicals must be effective against the pathogen without significant adverse effects on the fish host.

The first successful chemical was probably salt, used as a dip treatment to reduce pathogens on external surfaces (Rucker 1972). Formalin, a commonly used parasiticide, was first used in 1909 (Schnick 1973). In the U.S., drugs and chemicals used on cultured fishes must be approved by the Food and Drug Administration. Unfortunately, the list of chemicals approved for use in U. S. fish culture is very short. Table 1 lists chemicals approved for use in fish culture.

Therapeutants seldom eradicate a disease. Successful disease control involves a careful program of fish health management that will remove infected stocks, prevent reinfection, reduce stress, and maintain optimal conditions. Therapeutants give the fish only a temporary edge over the pathogens. Unless an effective fish health management program is promptly initiated, disease will reoccur whenever stresses develop making the fish more susceptible. The best treatment of all is good animal husbandry

TABLE 1. COMPOUNDS REGISTERED FOR FISHERY USES (After Schnick, Meyer, and Van Meter, 1979)

Chemicals	Fishery Use	Comments
REGISTERED		
Antimycin	Fish toxicant- 5-10 ppb (ug/l)	Nonfood fish use only
Bayer 73	Lampricide- Rate not to exceed 2% of TFM applied; as a sampling tool, 100 lb/A(112 kg/ha)	Nonfood fish use only; restricted to use by Great Lakes Fishery Commission (GLFC), Federal. or State personnel
Calcium hypochlorite (HTH)	Disinfectant · 5-10 ppm (mg/l> for 12-24 h for control of algae and bacteria; 200 ppm (mg/l) for 1 h to sanitize	Food fish use
Casoron (dichlobenil)	Herbicide- 7-15 lb/A(7.8-16.8 kg/ha)	Nonfood fish use only
Copper (from basic carbonate)	Herbicide- 14 1b/150-250 gal water/A (15.7 kg/l, 403-2338 l/ha)	Food fish use
Copper sulfate	Algicide- Rate dependent on water chemistry; 2.3-4 ppm (mgil)	Food fish use
2,4-D	Herbicide- 6-40 lb/A(6.7-45 kg/ha)	Food fish use
Dichlone	Algicide- 0.055 ppm (mg/l)	Nonfood fish use only

Chemicals	Fishery Use	Comments
Diquat	Herbicide and algicide- 5.4 ppm (mg/l> in water for submerged weeds; 3 lb/A (3.4 kg/ha) for floating weeds	Food fish use
Endothall	Herbicide 6.8-9.5 lb/A ft (2.5-3.5) g/m3)	Food fish use
Fenac	Herbicide 15-19.5 lb/A (16.8-21.9 kg/ha)	Nonfood fish use only
Fluorescein sodium	Dye to check water flows or dilution-O. 1 ppm (mg/l)	Food fish use; exempted from registration
Furanace	Antibacterial drug for myxobacteria-0.05-0. 1 ppm (mg/l) for an indefinite period; 1.0 ppm (mg/l) for 5-10 min	Nonfood fish "se only
Lime	Pond sterilant- 1338 lb/A (1165 kg/ha) of quick lime; 1784 lb/A (2002 kg/ha) of slaked lime	Food fish use; generally regarded as safe (GRAS)
Masoten	Parasiticide for copepods- 0.25 ppm (mg/l) active ingredient	Nonfood fish "se
MS-222	Anesthetic- 15-66 ppm (mg/l) for 6-48 h for sedation; 50-330 ppm (mg/l) for l-40 min for anesthesia	Food fish use, but 21.day withdrawal after use
Potassium permanganate	Oxidizer and detoxifier- 2 ppm (mg/l)	Food fish use; exempted from registration
Rhodamine B	Dye to check water flows or dilution rates-20 ppb	Food fish use; exempted from registration

Chemicals	Fishery Use	Comments
Rotenone	Fish toxicant- *1-5* ppm (mg/l)	Nonfood fish use only
Salt	Osmoregulatory enhancer- 0.5-l% for indefinite *period; 3%* for 10-30 min	Food fish use; GRAS
Silvex	Herbicide- Granular, *40* lb/A(45 kg/ha); liquid, 6 lb/A ft (2.2 g/m3) for submerged weeds; 8 lb/A (9 kg/ha) for emerged weeds	Nonfood fish use only
Simazine	Herbicide and algicide- 1.4-6.8 lb/A (0.5-2.5 g/m3)	Food fish use
Sulfamerazine	Antibacterial against furunculosis-10 g/l00 lb (22 g/100 kg) of fish per day for 14 days in feed	Food fish use in salmonids
Terramycin (oxytetracycliie)	Antibacterial against *Aeromonas* and *Pseudomonas*- *2.5-3.75* g/l00 lb (5.5-8.25 g/100 kg) of fish per day for 10 days in feed	Food fish use
TFM	Lampricide- l-10 ppm (mg/l), depending on water quality	Nonfood fish use only; restricted to GLFC, Federal, or State personnel
TFM: Bayer 73	Lampricide- 98 TFM: 2 Bayer 73, TFM at l-10 ppm (mg/l)	Nonfood fish use only; restricted to GLFC, Federal of State personnel
Xylene	Herbicide- 100 gal/A (935 l/ha)	Nonfood fish use only

Chemicals	Fishery Use	Comments
STATUS INDEFINITE		
Acetic acid	Parasiticide	Declared as GRAS by FDA as feed additive: not labeled for fishery use
Carbon dioxide	Anesthetic	Declared as GRAS by FDA as feed additive; not labeled for fishery use
Formalin	Parasiticide- 25 ppm (mg/l) in ponds; up to 250 ppm (mg/l) for lh in tanks and raceways	All requirements completed; final action by FDA completed
Sodium bicarbonate	Anesthetic	Declared GRAS by FDA as feed additive: not labled for fishery use

coupled with avoidance of pathogens. If an animal is given a good environment and adequate nutrition, the risk of infection by any pathogen is greatly reduced.

Drugs and chemicals are often used to correct errors in management. While this practice can be used as a stop-gap, it cannot be used to prop up poor culture programs. Sound husbandry is the best approach to disease control. Indiscriminant uses of therapeutic agents should be avoided.

Questionable practices include the continuous feeding at low levels of antibiotics in the diet as a prophylactic measure against outbreaks of bacterial disease during periods of stress, or to improve growth rates. Indiscriminant feeding of low levels of antibiotics will remove only those bacteria most sensitive to the drug and can lead to the development of drug resistant strains. Drug resistant bacteria can transmit this resistance to different species of bacteria that have never been exposed to the drug (Burrows 1973). Therefore, treatment with antibiotics is recommended only when needed, and then only at prescribed treatment levels. If a decision to use antibiotics is made, treatment should be conducted for the full time period required. Shorter treatments will also encourage the development of drug resistance and can lead to the need for elevated drug levels, and eventually, to loss of effectiveness. Information on drug resistence is provided by Shotts et al. (1976a, 1976b).

The casual use of therapeutics on a routine basis is not without possible adverse effects on the general health of the fish and is not recommended, Whenever possible, seek a positive diagnosis of any disease problem by a professional fish health specialist. Avoid "shotgun" approaches in which "hit or miss" techniques are used. Start treatment with the correct drug at the recommended level of treatment. If it is determined that a chemotherapeutant is needed, treat quickly and effectively. Users are advised to proceed with caution and to follow label directions. Recommended rates of treatment are based on the levels that researches have found to be necessary and that various fishes will tolerate. Although there is a built-in safety factor, using more than the recommended rate is not necessarily better, may be harmful, and may be illegal.

Culturists who rear anadromous fish must also exercise care when treating fingerlings at the time of smoltification. It has been shown, for example, that salmon smolts treated with diquat for bacterial gill disease just before they are released have difficulty initiating salt excretion from the gills. As a result. the smolts die when they enter salt water or may remain in the estuary and never go to sea (G.A. Wedemeyer, USFWS, Seattle, WA personal communication). Wedemeyer et al. (1980) recommend a 2-wk withdrawal from all chemotherapeutic treatments before the intended release date of smolitng salmon. Table 2 shows the effects of 12 other drugs and chemicals commonly used in fish culture on the salt pump of coho salmon smelts (Bouck and Johnson 1979).

Lastly, time requirements (identified on container labels) for clearance of drug residues from treated fish should be strictly observed. If tish are being reared for human food, sale of the carcasses may not be allowed if drug residues are found in the fish.

"Treatment Tips" by Fred P. Meyer (1968) is a useful guide for calculating dosage levels for treatments. Metric conversion tables are included.

GENERAL TREATMENT GUIDELINES

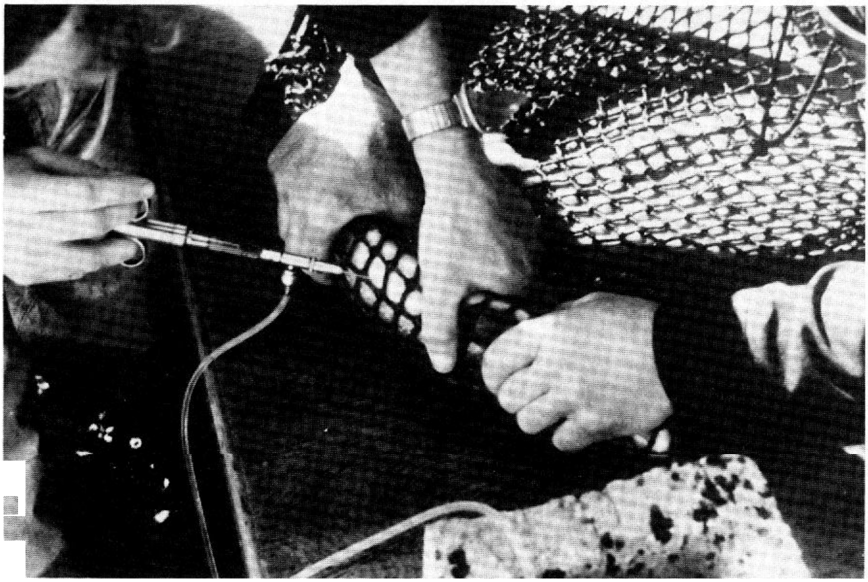
Before applying any chemotherapeutic treatment, ensure that information on chemical characteristics of the water supply is available, and ascertain how they will affect the toxicity and efficacy of the treatment. What will work at one place may not be effective elsewhere because of differences in water chemistry. Before using any chemical, be sure to test it first on a small number of sick fish. Keep in mind that healthy fish can tolerate chemical treatment more readily than sick fish and that treatment levels may need to be reduced if the fish are weak or in poor condition.

Table 2. Summary of seawater survival of coho salmon smolts following standard treatments with drugs and chemicals commonly used in fish culture (Bouck and Johnson 1979).

	Concentration of active ingredients (mg/1)	Treatment Length of daily exposure (min)	Consecutive days treatment was given	Total mortality (%) during 10d in seawater: Direct transfer into seawater following treatment	Total mortality (%) during 10d in seawater: Treatment, 4d in fresh water, then 4h acclimation to seawater
Controls	-	-	-	0	0
copper sulfate	37	20	1	100	20
Endothal	5	60	1	100	4
Formalin	167	60	1	12	0
Hyamine 1622	2	60	4	68	4
Malachite green	1	60	1	44	12
MS-222	100	100	6	1	100
Nifurpirinol	1.5	60	4	8	0
Oxytetracycline	1	60	1	20	12
Potassium permanganate	2	60	3	80	12
Quinaldine	2.5	10	1	0	0
Simazine	0.5	60	:	4	:

Poupard (1978) established a set of guidelines of things to do before, during, and after treatment. These guidelines are:

1. Ensure that rearing facilities are clean before treating. Dirty raceways or tanks may contain organic matter that will absorb part of the treatment chemical and reduce its effectiveness.
2. If the fish density is excessive, it should be reduced, if possible, prior to static treatment. Supplemental aeration should be provided, if needed.
3. During hot weather, treatments should be made during the coolest part of the day using chemicals that create the least environmental hazard or stress.
4. Starving fish l-2 d prior to treatment will reduce their oxygen consumption, will reduce ammonia production, and will increase resistance to scale loss. Never treat within 4 h after feeding.
5. Always observe fish during treatment to watch for signs of stress or unexpected toxicity.
6. Any parasitism of the gills should be treated first since such parasites may affect respiratory capability of the fish.
7. Monitor dissolved oxygen levels before and during treatment. Fish are stressed during treatment and increase their need for oxygen.
8. Before treating with a new compound or formulation or using a product for the first time on an installation, always treat a small group of fish first and watch for unexpected mortality.
9. Always check your calculations (0.1X will be ineffective; 1.0 is effective; but 10X will be fatal). If possible, have someone check your figures.
10. Keep records of all treatments, their purpose, and the results for future reference.



Antibiotics and biologics can be administered to large fish through the use of an automatic syringe (U.S. Fish and Wildl. Serv.)

TREATMENT IN THE DIET

If available, commercial feed with antibiotic additives is cheap and easy to use. Medicated feed stores well and can be used in place of the regular diet.

If commercially medicated feed is not available, medicated feed can be prepared on site. Antibiotics, such as oxytetracycline (Terramycin), which are water soluble may leach out of the feed unless preventive steps are taken. It is best to suspend such drugs in oil when preparing medicated feed (cod liver oil seems to have better palatability than soy bean or corn oils, but any of these will do). The daily ration of feed can then be coated with the oil/antibiotic mixture while the pellets are tumbled in a small cement mixer.

Once treatment has been started, keep rigidly to the recommended dose and treatment schedule. Do not try to save money stopping treatment when mortalities stop, by using lesser amounts, or by treating for shorter periods (Johnson 1971).

LOCALIZED APPLICATIONS

EXTERNAL

Localized skin applications are feasible only for broodstock and other valuable fish. Herwig (1979) recommends that the drug used should be relatively insoluble in water, act on contact, and either be denser than water or so adhesive that the fish can't rub it off.

INTERNAL

For small numbers of valuable fish, injections of antibiotics can be used but may be very expensive and labor intensive.

Intraperitoneal injection are superior to subcutaneous or intramuscular injections. If possible, the fish should be immobilized by holding it in the web of a large mesh net. If struggling causes scale losses or injury, or if the fish are simply too large to handle, it may be best to anesthetize the animals. Both MS-222 (tricaine methanesulfonate) and carbon dioxide have been used with success for this purpose. Injections of drugs require small syringes and use a 20 to 26 gauge needle depending on the size of the fish. Insert the needle through the body wall just posterior to the pelvic girdle at a shallow angle until resistance suddenly ceases. Avoid puncturing the intestine or gonads by inserting the needle too far (Herwig 1979).

BATH/DIP TREATMENTS

Dipping the fish involves a short bath treatment with a duration varying from only a few seconds to 5 min, depending on the chemical and concentration used. Leitritz and Lewis (1976) recommend the use of wood tubs but plastic avoids possible chemical reactions between galvanized metal and treatment chemicals, which may be toxic to the fish.

Dip treatments are often used on broodstock. They are effective but can be highly stressful. After treatment, the fish should be rinsed in clean water before they are returned to the holding facility to avoid transfer of chemical to the tank (Poupard 1978). Treated fish should be placed in water that is free of parasites or pathogens (Leitritz and Lewis 1976).

SHORT BATHS

For treatments up to 1 h, when fish are held in facilities where fresh water is available and adequate oxygen levels can be maintained, short baths are useful because high concentrations of chemicals can be used. Extreme care is required to avoid chemical overdoses or overly long contact times.

INDEFINITE TREATMENTS

This method is suitable only for treating ponds. Low concentrations of chemical are used and allowed to dissipate in the pond. Treatments may have adverse effects on the biota or on dissolved oxygen levels. The degradation of formalin uses 1 ppm oxygen for each 5 ppm formalin as it decomposes. Formalin is also algicidal and can lead to depressed dissolved oxygen levels due to loss of photosynthetic activity and cellular decay. Pond applications require a boat and motor. A boat bailer can be used to pump the chemical into the water.

FLUSH TREATMENTS

In treatments of this type, a measured amount of concentrated chemical is added at the inlet and allowed to flush through a pond or raceway. Amounts of chemical used must be accurately determined for your hatchery. Lowering the water level in the holding unit can be used to reduce the amount of chemical needed and also facilitates rapid dilution of the treatment when fresh water is added to restore normal levels (Poupard 1978). This technique is also useful when using indefinite treatments in ponds (see above).

CONSTANT FLOW

In constant flow treatments. the chemical is metered into the water inflow at a constant rate to maintain a given concentration for a given period of time. This treatment method requires accuracy and is expensive in terms of the amount of chemical needed. The method requires no special attention to oxygen or ammonia levels, since the water flow remains unchanged. Application equipment may vary from a controlled drip bottle to a 135 liter (30 gal.) plastic garbage can with a siphon, depending on the amount of chemical required.

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