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Symptoms and implications of selenium toxicity in fish: the Belews Lake case example

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Abstract

Belews Lake, North Carolina was contaminated by selenium in wastewater from a coal-fired power plant during the mid-1970s. and toxic impacts to the resident fish community (20 species) were studied for over two decades. Symptoms of chronic selenium poisoning in Belews Lake fish included, (1) telangiectasia (swelling) of gill lamellae; (2) elevated lymphocytes; (3) reduced hematocrit and hemoglobin (anemia); (4) cornea1 cataracts; (5) exopthalmus (popeye); (6) pathological alterations in liver, kidney, heart, and ovary (e.g. vacuolization of parenchymal hepatocytes, intracapillary proliferative glomerulonephritis. severe pericarditis and myocarditis, necrotic and ruptured mature egg follicles); (7) reproductive failure (reduced production of viable eggs due to ovarian pathology, and post-hatch mortality due to bioaccumulation of selenium in eggs): and (8) teratogenic deformities of the spine, head, mouth, and fins. Important principles of selenium cycling and toxicity were documented in the Belews Lake studies. Selenium poisoning in fish can be 'invisible', because, the primary point of impact is the egg, which receives selenium from the female's diet (whether consumed in organic or inorganic forms), and stores it until hatching, whereupon it is metabolized by the developing fish. If concentrations in eggs are great enough (about 10 μg/g or greater) biochemical functions may be disrupted, and teratogenic deformity and death may occur. Adult fish can survive and appear healthy despite the fact that extensive reproductive failure is occurring- 19 of the 20 species in Belews Lake were eliminated as a result of this insidious mode of toxicity. Bioaccumulation in aquatic food chains causes otherwise harmless concentrations of selenium to reach toxic levels, and the selenium in contaminated sediments can be cycled into food chains for ciecades. The lessons learned from Belews Lake provide information useful for protecting aquatic ecosystems as new selenium issues emerge. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Water pollution; Coal-fired power plant; Freshwater fish; Tissue pathology; Teratogenic deformities; Environmental contaminants; Selenium

1. Introduction

One of the most extensive and prolonged cases of selenium poisoning in freshwater fish occurred at Belews Lake, North Carolina, USA (Fig. 1).

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Belews Lake was contaminated by selenium in wastewater released from a coal-fired electric generating facility. From 1974 to 1986, water was withdrawn from the lake and mixed with bottom ash from the coal burners and fly-ash collected by electrostatic precipitators. This slurry was pumped from the power plant and discharged into a 142 Ha ash basin, where suspended solids were collected by gravitational settling. Selenium-laden (150-200 μg Se per 1) return flows from the ash basin entered the west side of Belews Lake through an ash sluice water canal (Lemly, 1985).

Selenium bioaccumulated in aquatic food chains and caused severe tissue pathology and reproductive impairment in the resident fish community (Lemly, 1985; Sorensen, 1986). In late 1986, the power plant stopped discharging selenium-laden water into the lake, and a period of natural recovery began. However, monitoring studies revealed that the rate of recovery was slow-elevated selenium residues and associated biological effects in fish were still present a decade later (Lemly, 1997).

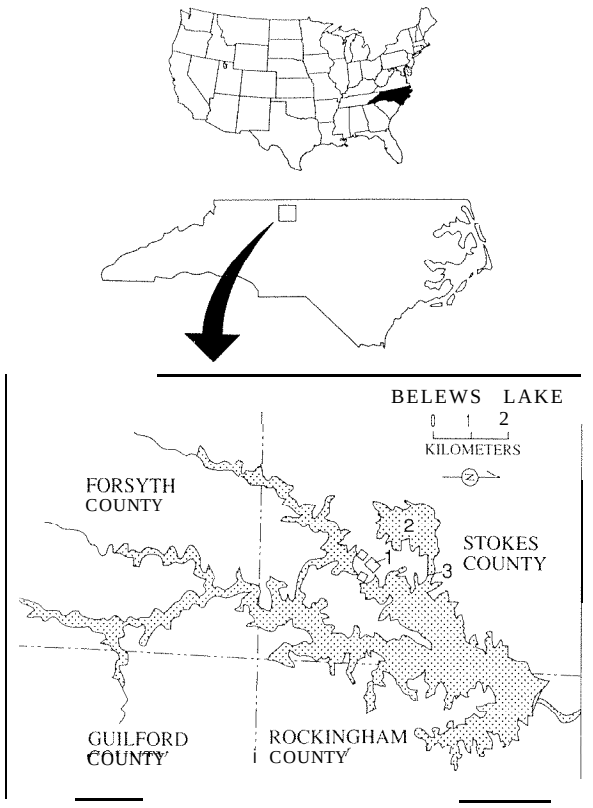

Fig. 1. Geographic location of Belews Lake, North Carolina, USA. Numbers indicate, (1) Belews Creek Steam Station (coal-fired power plant); (2) coal ash settling basin; (3) ash basin return water canal.

The Belews Lake episode provides a wealth of information on environmental cycling, long-term persistence, and hazard of selenium to freshwater biota. It is an excellent case example for examining the symptoms and biological consequences of selenium toxicity. This paper utilizes that database to present a review of the pathology of selenium poisoning in fish. It also discusses the ecological lessons learned from Belews Lake and points out the need to evaluate new, emerging selenium issues that threaten aquatic habitats in the USA and elsewhere.

2. Biochemical basis of selenium toxicity

The primary manifestations of selenium toxicity are due to a simple but important flaw in the process of protein synthesis. Sulfur is a key component of proteins, and sulfur-to-sulfur linkages (ionic disulfide bonds) between strands of amino acids are necessary for protein molecules to coil into their tertiary (helix) structure which, in turn, is necessary for proper functioning of proteins, either as components of cellular structure (tissue synthesis) or as enzymes in cellular metabolism. Selenium is similar to sulfur with regard to its basic chemical and physical properties (has same valence states and forms analogs of hydrogen sulfide, thiosulfate, sulfite, and sulfate), and mammalian studies show that cells do not discriminate well between the two as proteins are being synthesized (it is assumed that the mechanistic features underlying toxicity are essentially the same for fish, since the resulting pathology and teratogenic features are the same). When present in excessive amounts, selenium is erroneously substituted for sulfur, resulting in the formation of a triselenium linkage (Se-Se-Se) or a selenotrisulfide linkage (S–Se–S), either of which prevent the formation of the necessary disulfide chemical bonds (S-S). The end result is distorted, dysfunctional enzymes and

protein molecules, which impairs normal cellular biochemistry (Canther, 1974; Stadtman, 1974; Diplock and Hoekstra, 1976; Reddy and Massaro, 1983; Sunde, 1984). Thus, while selenium is a sulfur analog in some respects, its biochemistry and potential toxicity are quite different.

These selenium-induced errors in protein biosynthesis can have several outcomes. The most well documented overt toxic symptom in fish is reproductive teratogenesis. Selenium consumed in the diet of adult fish is deposited in the eggs, where it is metabolized by larval fish after hatching. A variety of lethal and sublethal deformities can occur in the developing fish, affecting both hard and soft tissues (Lemly, 1993a). Substitution of selenium for sulfur can also impair proper formation of proteins in juvenile and adult fish, and many internal organs and tissues can develop pathological alterations that are symptomatic of chronic selenosis (Sorensen, 1986). Studies in mammals and waterfowl show that acute toxic responses may also involve tissue damage from bioreactive superoxides produced in response to high concentrations of selenium (O'Toole and Raisbeck, 1998).

3. Pathological effects in fish

3.1. Gills

The primary structure of adult teleost gills is the semi-circular gill arch, usually four pairs. Each arch contains a double row of filaments, and each filament has a row of microscopic lamellae projecting from each side (Fig. 2). The lamellae contain the blood sinusoids and capillary beds, and are covered by a thin epithelial cell layer, typically two cells thick, underlain by supporting pillar cells which maintain patency of vascular lumina. Gill lamellae are normally thin, delicate structures (Fig. 2a), which are necessary for effective gas exchange in respiration. Gills from green sunfish (*Lepomis cyanellus*) exposed to selenium contamination in Belews Lake exhibited extensively dilated blood sinusoids and swollen lamellae (telangiectasia) packed with erythrocytes (Fig. 2b; Sorensen et al., 1984). Hemorrhaging of the gill tissue often occurred in association with this condition. Selenium-induced dilation of gill lamellae causes impaired blood flow, ineffective gas exchange (reduced respiratory capacity), and metabolic stress response (increased respiratory demand and oxygen consumption) that can lead to death (Lemly, 1993b).

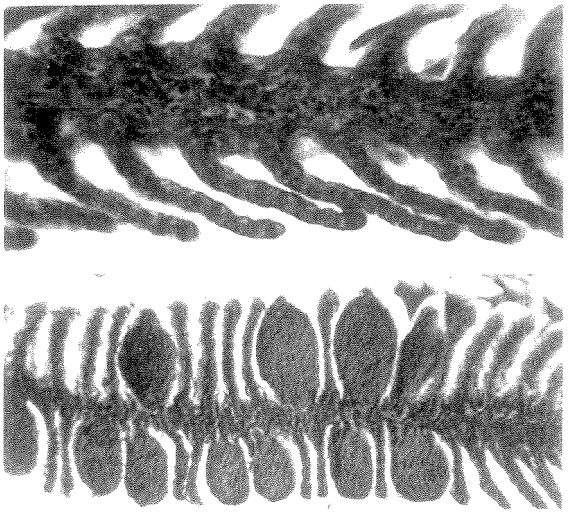

Fig. 2. Section of gill tissue from a normal green sunfish (*Lepomis cyanellus*, top, 240 ×), and a green sunfish exposed to selenium in Belews Lake (bottom, 220 ×). Secondary lamellae are uniform and well defined under normal conditions, but exposure to high selenium can cause the blood sinuses to undergo extensive swelling (telangiectasia) and become packed with erythrocytes. This reduces respiratory capacity and can lead to metabolic stress and death.

3.2. Hematology

Green sunfish from Belews Lake exhibited significantly reduced hematocrit values (packed erythrocyte volumes) as compared with fish from an uncontaminated reference lake (33 vs. 39%). but had significantly elevated numbers of lymphocytes. Thrombocytes constituted a higher percentage of total leucocytes in Belews Lake fish, but hemoblasts were less numerous than in reference fish (Sorensen et al., 1984). These shifts in hematological parameters reflect important changes in the overall health of fish. Reductions in hematocrit are associated with anemia and

lowered mean corpuscular hemoglobin concentration (MCHC; Lemly, 1993b). Reduced MCHC causes impaired respiratory capacity, because, selenium can bind to hemoglobin, rendering it incapable of carrying oxygen. A decrease in respiratory capacity can quickly lead to metabolic stress, because, the fish must expend more energy to meet respiratory demands (Lemly, 1993b). Lower numbers of hemoblasts reflects reduced erythropoiesis and delayed replacement of aging red cells in circulation, which also contributes to reduced respiratory capacity and metabolic stress (Lemly, 1993b). An elevation in lymphocytes signals a generalized immune response triggered by physiological stress and a reduced state of health.

3.3. Internal organs

3.3.1. Liver

The structural features of liver tissue from normal green sunfish consist of bilaminar arrays of hepatocytes (liver plates) separated by small blood sinusoids. Blood enters the liver from the hepatic artery and hepatic portal vein, moves between the liver plates in the sinusoids, and ultimately collects in central veins which empty into the hepatic veins. Parenchymal hepatocytes typically contain numerous mitochondria, rough endoplasmic reticulum, well developed nucleoli, and both central and peripheral chromatin islands (Sorensen, 1986). Kupffer cells, (phagocytic tissue histocytes) are rarely present in healthy individuals, and lymphocytes are not numerous. Green sunfish from Belews Lake exhibited several histopathological changes in liver tissue. Lymphocyte infiltration was apparent along with extensive vacuolization of parenchymal hepatocytes around central veins. Increased numbers of Kupffer cells were present and the central veins were distended and swollen due to loss of surrounding parenchymal cells. Cell nuclei were often deformed and pleomorphic, and numerous perisinusoidal lipid droplets (unmetabolized residues) were present (Sorensen et al., 1984). Collectively, these ultrastructural changes reflect a degeneration of tissue structure that is sufficient to significantly alter liver function. This liver pathology syndrome is characteristic of chronic selenosis in fish and other vertebrates (Sorensen, 1986).

3.3.2. Kidney

At the ultrastructure level, the kidney of normal fish is quite similar to that of humans, and is made up of glomeruli, mesangial cells, podocytes, endothelial and tubular cells, and both capillary and central veins (which collect and transport urine). Belews Lake green sunfish that had accumulated high levels of selenium showed focal intracapillary proliferative glomerulonephritis (Sorensen et al., 1984). In this condition, excessive numbers of mesangial cells are present along with an abnormally abundant matrix and periglomerular fibrosis (which can lead to a hardening of the tissue). Numerous tubular casts were present, and tubular epithelium was desquamated, vacuolated, and often destroyed (which can render the tubular system of the mesonephros incapable of functioning properly). These renal changes in Belews Lake fish were consistent with symptoms of chronic selenium poisoning in other vertebrates (Sorensen et al., 1984).

3.3.3. Heart

A clear pathological pattern occurred in the hearts of fish from Belews Lake. The pericardial spaces surrounding the heart were filled with inflammatory cells, which were not present in fish from reference locations. This condition was diagnosed as severe pericarditis. Numerous inflammatory cells were also present within the ventricular myocardial tissue, a condition known as myocarditis. The occurrence of pericarditis and myocarditis was attributed to the direct action of selenium on heart tissue, coupled with indirect effects of selenium on the kidney (induced glomerulonephritis and associated uremia; Sorensen et al., 1984).

3.3.4. Ovary

Ovaries of fish from Belews Lake contained numerous swollen, necrotic, and ruptured mature egg follicles, especially in gravid individuals. No such pathology was observed in fish from reference locations (Sorensen et al., 1984). These toxic symptoms were a primary factor contributing to

reproductive failure of fish in Belews Lake, which affected 19 species and totally altered the aquatic ecosystem for over a decade (Lemly, 1985, 1997; see Section 4).

3.4. Eyes

One of the less well known symptoms of selenium poisoning in fish is the occurrence of selenium-induced cataracts. This condition can affect both the lens and cornea, and has been induced experimentally in mammals by dietary exposure to selenite (Shearer et al., 1987). Fish from Belews Lake sometimes had cornea1 cataracts on their eyes (Fig. 3); none were found in fish from reference lakes. Cataracts were present in up to 8.1% of fish examined in surveys conducted during 1975–1982, which was the period of maximum selenium concentrations in fish. By 1992, selenium residues had fallen in fish, commensurate with reduced selenium inputs to Belews Lake, and the prevalence of cataracts had also fallen, to about 1% (Lemly, 1993a).

Another abnormality of the eyes that is associated with selenium poisoning in fish is a condition known as edema-induced exopthalmus, or protruding eyeballs. One of the general physiological responses of fish to high levels of selenium is edema, which is the accumulation of fluid in the body cavity and head (Ellis et al., 1937). The fluid

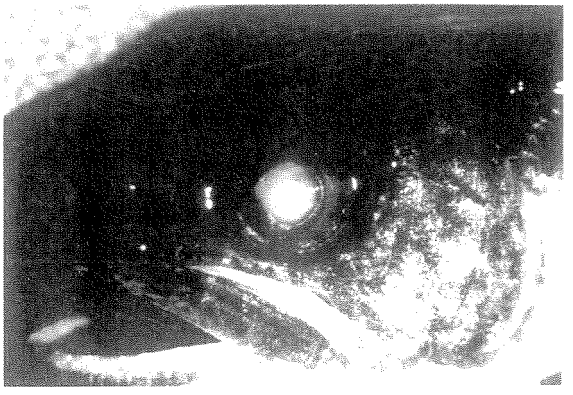

Fig. 3. Corneal cataract in the eye of a juvenile largemouth bass (*Micropterus salmoides*) from Belews Lake. During the peak period of selenium contamination (1975–1985), up to 8.1% of the fish community was afflicted with cataracts.

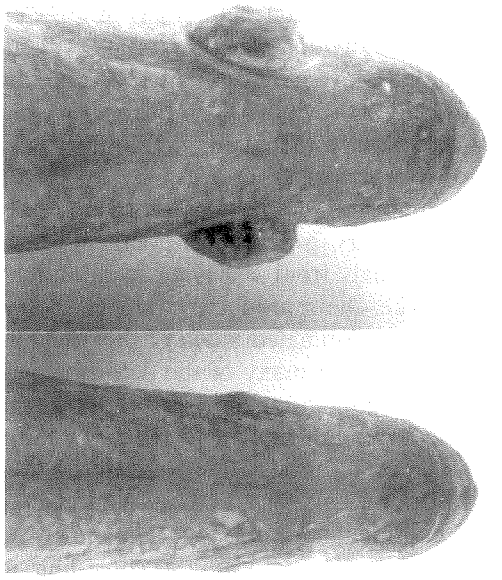

Fig. 4. Exposure to high levels of selenium can cause fluid to build up and create pressure inside the head, leading to exopthalmus (protruding eyeballs), shown here in this juvenile white crappie (*Pomoxis annularis*) from Belews Lake (top), (bottom individual is normal).

results from tissue damage, specifically an upset in cell permeability as a consequence of distorted selenoproteins in the membrane structure that causes internal organs to become 'leaky'. The excess fluid can create pressure sufficient to swell the abdomen and force the eyes to protrude from their sockets (Fig. 4). Blood may be present in the fluid, resulting in noticeable hemorrhaging around the eyes. Up to 21% of some fish species in Belews Lake exhibited exopthalmus, with the greatest prevalence occurring in crappie, *Pomoxis* spp. (Lemly, 1993a).

3.5. Teratogenic deformities

Developmental malformations are among the most conspicuous and diagnostic symptoms of chronic selenium poisoning in fish. Terata are permanent biomarkers of toxicity, and can be used to reliably identify and evaluate impacts of selenium on fish populations (Lemly, 1997). De-

formities in fish that affect feeding or respiration can be lethal shortly after hatching (Fig. 5). Consequently, few individuals bearing terata will survive to join the juvenile population. Terata that are not directly lethal, but which distort the spine and fins, can reduce the swimming ability of fish and lead to increased susceptibility to predation-an important indirect cause of mortality. These two factors generally prevent most deformed individuals from surviving to adulthood. In Belews Lake, the reproductive impacts on piscivorous species eliminated much of the predation pressure and allowed many of the deformed individuals of non-piscivorous species to persist into the juvenile and adult life stages (Lemly, 1985).

Several types of teratogenic deformities were evident in Belews Lake fish, and many individuals exhibited multiple malformations. The most overt terata were spinal deformities consisting of kyphosis, lordosis, and scoliosis (Figs. 6-S). Less obvious but no less common were terata involving the mouth and fins (Fig. 9; Lemly, 1993a). The prevalence of deformities varied among species and between years, reaching a high of 70% in green sunfish during 1982. There was a close parallel between levels of selenium in fish tissues and frequency of deformities. Terata became more common as selenium increased from 1975 to 1982, peaked in 1982, and decreased in frequency

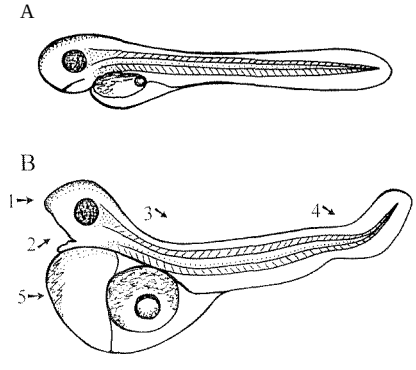

Fig. 5. Typical appearance of larval fish at about 2–4 days after hatching. (A) Normal larvae with yolk absorption nearing completion and straight, developing spine, (B) Abnormal development due to selenium-induced terata, (1) deformed, pointed head; (2) deformed, gaping lower jaw; (3) kyphosis (curvature of the thoracic region of the spine); (4) lordosis (concave curvature of the lumbar and/or caudal region of the spine). Other symptoms of selenium poisoning that usually accompany terata include (5) edema (swollen, fluid-filled abdomen) and delayed yolk absorption.

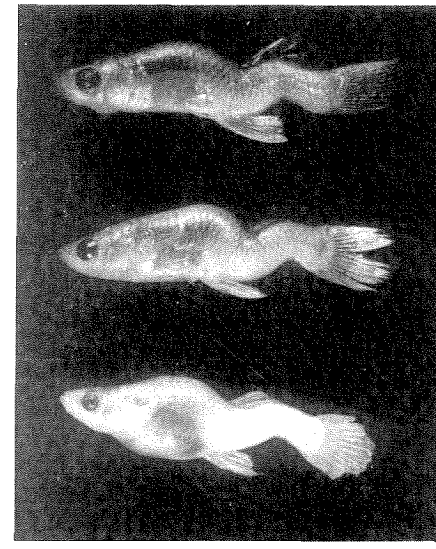

Fig. 6. One of the most common and outwardly visible teratogenic effects of selenium in Belews Lake fish was dorso-ventral spinal deformities (kyphosis and lordosis), shown here in mosquitofish (*Gambusia affinis*).

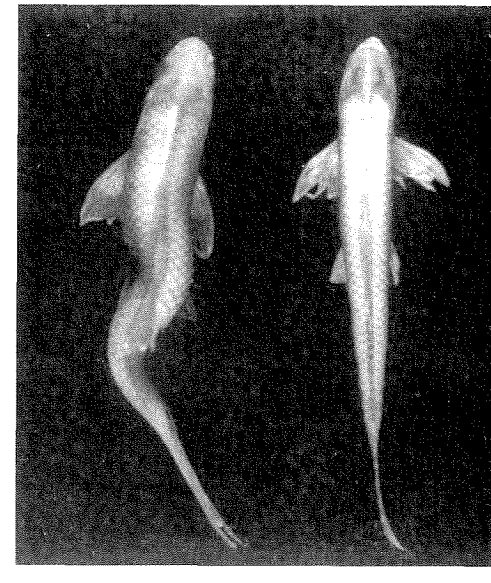

Fig. 7. Lateral curvature of the spine (scoliosis, left individual) in a red shiner (*Notropis lutrensis*), caused by exposure to elevated selenium in Belews Lake. Individual on right is normal.

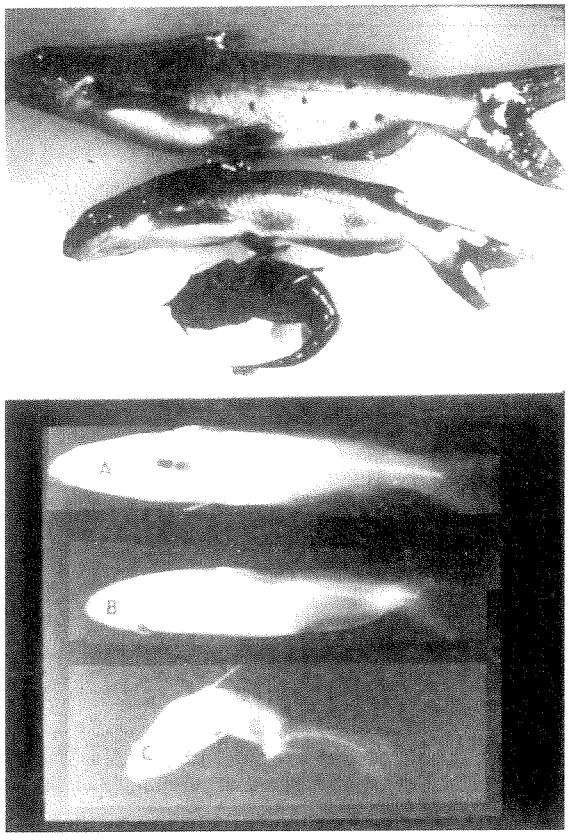

Fig. 8. Outward appearance and X-ray image of selenium-induced terata in channel cattish (*Ictalurus punctatus*) from Belews Lake. (A, Normal: 13. mild spinal deformity (kyphosis and lordosis); C, severe deformities (kyphosis and scoliosis).

following the cessation of selenium inputs to the lake in 1986 (Lemly, 1993a). In 1996, selenium residues had fallen by 85 95% from their 1982 high, and the prevalence of deformities was 6% or less (Lemly, 1997). An overall relationship between tissue selenium burdens and incidence of deformities in the Belews Lake fish community is shown in Fig. 10 (Lemly, 1993a, 1997). Belews Lake was the first site to provide conclusive evidence that exposure to elevated selenium causes teratogenic deformities in natural populations of freshwater fish.

4. Ecological implications

4.1. Insidious mode of toxicity

Selenium poisoning in fish can be 'invisible', because, the primary point of impact is the egg, which receives selenium from the female's diet and stores it until hatching, whereupon teratogenic deformity and death may occur. Adult fish can survive and appear healthy despite the fact that massive reproductive failure is occurring (Lemly, 1985; Coyle et al., 1993). Consequently, fish populations can decline or even disappear over the course of a few years for no apparent reason—unless one is cognizant of selenium's insidious mode of toxicity. In Belews Lake, fish populations disappeared over the course of 4 years (1974–1977), and by the time biologists documented

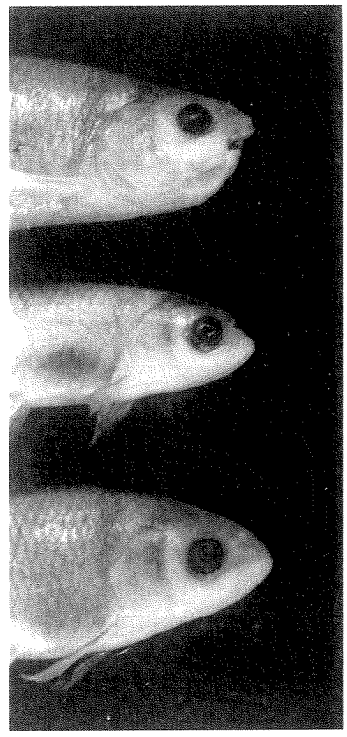

Fig. 9. Other teratogenic effects of selenium in Belews Lake fish, shown here in red shiners (*Notropis lutrensis*), included deformed mouth and jaws (top), and deformed upper head and vestigial pectoral tins (middle). Individual on bottom is normal.

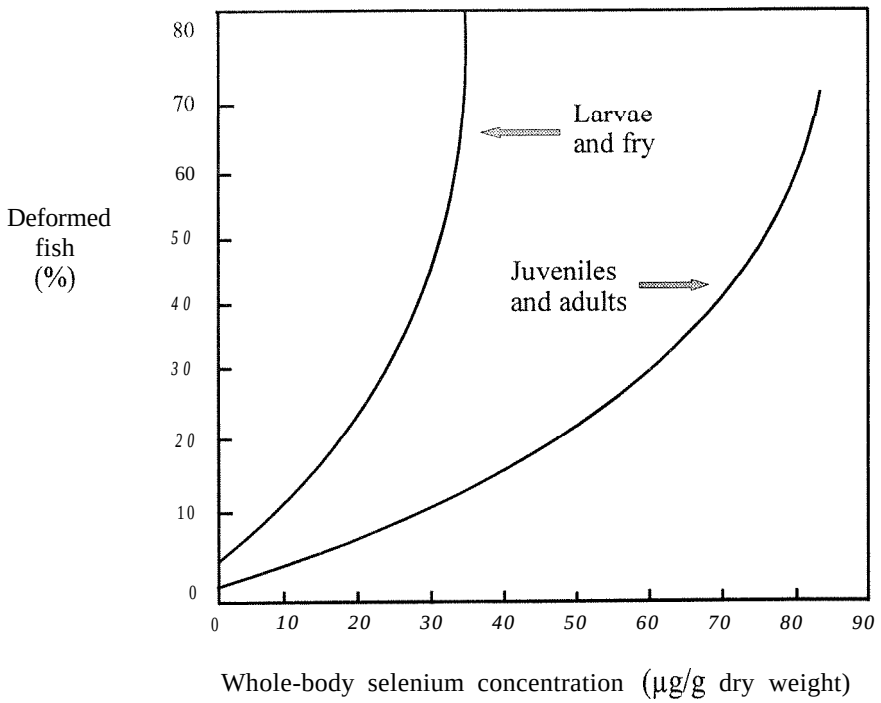

Fig. IO. Relationship between whole-body concentrations of selenium and prevalence of tcratogenic deformities in the fish community of Belews Lake, NC, during the period 1975 1996. Lines represent the best fit exponential function (cubic model, r^2 = 0.881) for plots of data from all fish species combined.

changes in population structure associated with elevated selenium (Cumbie and Van Horn, 1978), it was far too late to prevent the fishery from collapsing.

4.2. Bioaccumulation and reproductive failure

Selenium bioaccumulated in the aquatic food chains of Belews Lake and caused severe reproductive failure in fish (Cumbie and Van Horn, 1978; Lemly, 1985). Concentrations of selenium in the lake water averaged IO µg/l (uncontaminated reference locations had selenium concentrations < l µg/l), but were accumulated from 519 times (periphyton) to 3975 times (visceral tissue of fish) in the biota. The pattern and degree of accumulation were essentially complete within 2 years after the initial operation of the power plant, and persisted throughout the period of selenium discharge into the lake (1974-1985). Highest concentrations of selenium were found in fish, followed by benthic macroinvertebrates, plankton, and periphyton. The planktonic and detrital food pathways exposed fish to potential dietary concentrations of selenium that were some 770 and 510– 1395 times the waterborne exposure, respectively.

Of the 20 species of fish originally present in Belews Lake, 19 were effectively rendered sterile, because of reproductive failure. Some persisted as adults for a few years, but eventually all 19 were eliminated. Only one of the original resident species, the seieniurn-tolerant mosquitofish (*Gambusia affinis* Baird and Girard) survived relatively unaffected, along with two introduced cyprinids. The fishery was decimated without massive fish kills, because of the subtle, yet lethal mechanism

by which selenium impacts can occur. The severe toxic impacts in Belews Lake took place even though concentrations of waterborne selenium were only IO-20 times those in nearby uncontaminated reservoirs; the flora and fauna contained about 10–50 times as much selenium.

4.3. Persistence of impacts

In response to concerns about the fishery problems in Belews Lake the electric utility company switched to a dry-ash handling system that disposed the waste in a landfill rather than a wet-basin. By late 1986, selenium-laden wastewater no longer entered the lake (NCDNRCD, 1986), and in subsequent years a stocking program was successful in re-establishing adult populations of sport fish (e.g. centrarchids such as largemouth bass *Micropterus salmoides* Lacepede, and bluegill *Lepomis macrochirus* Rafinesque). Follow-up studies were conducted in 1996 to assess recovery of the ecosystem in Belews Lake (Lemly, 1997). Selenium concentrations and associated impacts to fish were measured and compared with pre-1986 conditions to determine how much change occurred during the decade since selenium inputs stopped. Findings were also examined using a hazard assessment protocol (Lemly, 1995) to determine if ecosystem-level hazards to fish and aquatic birds had changed as well. Results showed that waterborne selenium fell from a peak of 20 μg/l before 1986, to < 1 μg/l in 1996; concentrations in biota were 85–95% lower in 1996. Hazard ratings indicated that high hazard existed prior to 1986 and that moderate hazard was still present in 1996, primarily due to selenium in the sediment-detrital food pathway. Concentrations of selenium in sediments fell by about 65–75% during the period but remained sufficiently elevated (1-4 μg/g) to contaminate benthic food organisms of fish and aquatic birds. Field evidence confirmed the validity of the high hazard ratings. Developmental abnormalities in young fish persisted in 1996, indicating that selenium-induced teratogenesis and reproductive impairment were still occurring. Moreover, the concentrations of selenium in benthic food organisms were sufficient to cause mortality in young bluegill and other centrarchids, because of Winter Stress Syndrome, which is a substantial (up to 33%) increase in the sensitivity of fish to selenium during cold weather (Lemly, 1993b, 1996).At the ecosystem level, recovery in Belews Lake was very slow, with impacts on fish reproduction evident 10 years after the input of selenium stopped (Lemly, 1997). The low inflow of water and long retention time (volume replacement time about 1500 days), combined with low productivity (oligotrophic), tend to reduce natural flushing and enhance recycling of selenium within the reservoir. Projections indicate that several more decades may be necessary for the ecosystem to fully recover (Lemly, 1997). The latent effects occurred, because, selenium persisted in sediments, where it was mobilized through the food chain gradually, yet continually, and accumulated to toxic levels in fish eggs. Impacts to reproduction persisted even though adult populations were re-established through a stocking program.

5. Conclusions

The findings from Belews Lake serve as clear evidence of how selenium can rapidly, yet insidiously, impact fish populations. Moreover, this case example demonstrates that selenium can accumulate and be biologically magnified to toxic levels when waterborne concentrations are only 5– 10 μg/l. This information was instrumental in the US Environmental Protection Agency's decision to lower the US national water quality criterion for selenium from 35 to 5 μg/l (USEPA, 1987).

In the United States, anthropogenic disturbances have greatly increased the likelihood that aquatic ecosystems will experience elevated selenium. From the 1960s through the 1980s, two disturbances stood apart as the major human-related causes of selenium mobilization on a regional and national scale. These were, (1) combustion of fossil fuels; and (2) agricultural irrigation of seleniferous soils in arid and semi-arid regions (Lemly, 1985; Lemly et al., 1993c).

During the 1990s, other issues have emerged as potentially important factors in the mobilization and bioaccumulation of hazardous concentrations of selenium, including, (1) phosphate mining; (2) use of constructed wetlands to treat selenium-laden wastewater; (3) accumulation of animal waste at livestock feedlots and intensive rearing facilities; and (4) landfill disposal of ash from coal-fired power **plants.** These new selenium threats may be sufficient to cause widespread, unforseen impacts on fish populations (Lemly, 1999). Lessons learned from Belews Lake regarding the mode, rate, and persistence of selenium toxicity provide a foundation for protecting aquatic ecosystems as new selenium issues emerge in the USA and elsewhere.

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References

Coyle, J.J.. Buckler, D.R.. Ingersoll, C.G.. Fairchild. J.F., May. T.W.. 1993. Effects of dietary selenium on the reproductive success of bluegills (*Lepomis macrochirus*). Environmental Toxicology and Chemistry 12, 55 I 565.

Cumbie, P.M., Van Horn, S.L., 1978. Selenium accumulation associated with fish mortality and reproductive failure. Proceedings of the Annual Conference of the Southeastern Association of Fish and Wildlife Agencies 32, 612 624.

Diplock, A.T., Hoekstra, W.G., 1976. Metabolic aspects of selenium action and toxicity. CRC Critical Reviews in Toxicology 5, 271 329.

Ellis. M.M., Motley. H.L., Ellis. M.D., Jones, R.O.. 1937. Selenium poisoning in fishes. Proceedings of the Society of Experimental Biology and Medicine 36, 519 522.

Ganther, H.E., 1974. Biochemistry of selenium. In: Zingaro, R.A., Cooper, W.C. (Eds.), Selenium. Van Nostrand Reinhold. New York, NY. pp. 546 614.

Lemly. A.D., 1985. Toxicology of selenium in a freshwater reservoir: implications for environmental hazard evaluation and safety. Ecotoxicology and Environmental Safety IO, 314 338.

Lemly, A.D., Finger, S.E., Nelson, M.K., 1993. Sources and impacts of irrigation drainwater contaminants in arid wetlands. Environmental Toxicology and Chemistry. 12, 2265 2279.

Lemly, A.D., 1993a. Teratogenic effects of selenium in natural populations of freshwater fish. Ecotoxicology and Environmental Safety 26, 181 -204.

Lemly, A.D., 1993b. Metabolic stress during winter increases the toxicity of selenium to fish. Aquatic Toxicology 27, 133 158.

Lemly, A.D., 1995. A protocol for aquatic hazard assessment of selenium. Ecotoxicology and Environmental Safety. 32, 280 288.

Lemly, A.D., 1996. Winter Stress Syndrome: An important consideration for hazard assessment of aquatic pollutants. Ecotoxicology and Environmental Safety. 34, 223 227.

Lemly, A.D., 1997. Ecosystem recovery following selenium contamination in a freshwater reservoir. Ecotoxicology and Environmental Safety 36, 275 –281.

Lemly, A.D., 1999. Selenium impacts on fish: an insidious time bomb. Human and Ecological Risk Assessment 5. 1139–1151.

NCDNRCD (North Carolina Department of Natural Resources and Community Development), 1986. North Carolina Water Quality Standards Documentation: the freshwater chemistry and toxicity of selenium with an emphasis on its effects in North Carolina. Report number 86-02. NCDNRCD. Raleigh, NC, USA.

O'Toole, D.. Rnisbeck, M.F., 1998. Magic numbers, elusive lesions: comparative pathology and toxicology of selenosis in waterfowl and mammalian species. In: Frankenberger, W.T. Jr, Engberg, R.A. (Eds.), Environmental Chemistry of Selenium. Marcel Dckker, New York, USA, pp. 355 395.

Reddy, C.C., Massaro, E.J., 1983. Biochemistry of selenium: an overview. Fundamental and Applied Toxicology 3, 431 436.

Shearer. T.R.. David, L.L., Anderson, R.S., 1987. Selenite cataract: a review. Current Eye Research 6, 289 300.

Sorensen, E.M.B., 1986. The effects of selenium on freshwater teleosts. In: Hodgson, E. (Ed.). Reviews in Environmental Toxicology 2. Elscvier, New York, NY, USA, pp. 59-116.

Sorensen, E.M.B., Cumbie, P.M., Bauer, T.L., Bell, J.S., Harlan, C.W.. 1984. Histopathological, hematological, condition-factor, and organ weight changes associated with

selenium accumulation in fish from Belews Lake, North Carolina. Archives of Environmental Contamination and Toxicology 13, 153 162.

Stadtman, T.C., 1974. Selenium biochemistry. Science 183, 915–922.

Sunde, R.A., 1984. The biochemistry of selenoproteins. Journal of the American Organic Chemistry Society 61, 1891 1900.

USEPA (US Environmental Protection Agency), 1987. Ambient Water Quality Criteria for Selenium 1987. EPA-440/S-87-006. USEPA, Office of Water Regulations and Standards. Washington. DC, USA.