Annotated Bibliography: Effects of Cadmium on Fish 2009

Almeida, J. A., Y. S. Diniz, et al. (2002). "The use of the oxidative stress responses as biomarkers in Nile tilapia (Oreochromis niloticus) exposed to in vivo cadmium contamination." Environment International **27**(8): 673-679.

Water contaminants have a high potential risk for the health of populations. Protection from toxic effects of environmental water pollutants primarily involves considering the mechanism of low level toxicity and likely biological effects in organisms who live in these polluted waters. The biomarkers assessment of oxidative stress and metabolic alterations to cadmium exposure were evaluated in Nile tilapia, Oreochromis niloticus. The fish were exposed to 0.35, 0.75, 1.5, and 3.0 mg/l concentrations of Cd2+ (CdCl2) in water for 60 days. Fish that survived cadmium exposure showed a metabolic shift and a compensatory development for maintenance of the body weight gain. We observed a decreased glycogen content and decreased glucose uptake in white muscle. Lactate dehydrogenase (LDH) and creatine phosphokinase (CK) activities were also decreased, indicating that the glycolytic capacity was decreased in this tissue. No alterations were observed in total protein content in white muscle due to cadmium exposure suggesting a metabolic shift of carbohydrate metabolism to maintenance of the muscle protein reserve. There was an increase in glucose uptake, CK increased activity, and a clear increase of LDH activity in red muscle of fish with cadmium exposure. Since no alterations were observed in lipoperoxide concentration, while antioxidant enzymes glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) were changed in the liver and the red and white muscle of fish with cadmium exposure, we can conclude that oxygen free radicals are produced as a mediator of cadmium toxicity. Resistance development is related with increased activities of antioxidant enzymes, which were important in the protection against cadmium damage, inhibiting lipoperoxide formation.

Andres, S., F. Ribeyre, et al. (2000). "Interspecific comparison of cadmium and zinc contamination in the organs of four fish species along a polymetallic pollution gradient (Lot River, France)." The Science of The Total Environment **248**(1): 11-25.

The impact of cadmium (Cd) and zinc (Zn) discharges related to an old zinc ore treatment facility in the Lot River (France) was investigated in four fish species (the chub: Leusciscus cephalus, the roach: Rutilus rutilus, the perch: Perca fluviatilis and the bream: Abramis brama). The organisms were sampled in four

stations along the polymetallic contamination gradient. Cd and Zn analysis were carried out in five organs (gills, posterior intestine, liver, kidneys and skeletal muscle) in order to highlight the potential pathways of uptake, storage and elimination of metals. The results indicate a very strong Cd contamination in fish collected downstream from the metal source. The kidneys have the highest cadmium concentrations, but the gills and the intestine, as exchange organs, present the largest variations between the stations in close relation with the contamination gradient. Cd concentrations measured in the liver vary only slightly among the sampling stations. Unlike the trends observed for Cd, Zn levels in fish populations are strongly regulated and do not follow ambient Zn concentrations. The concentrations measured vary also according to fish species, for both Cd and Zn. This study shows that the trophic habits can explain the interspecific differences in Cd bioaccumulation. Zn levels observed for each species in non-contaminated populations also help to understand metal bioaccumulation patterns in polluted sites, suggesting that the determinism of interspecific differences is constitutive.

Babich, H., C. Shopsis, et al. (1986). "In vitro cytotoxicity testing of aquatic pollutants (cadmium, copper, zinc, nickel) using established fish cell lines." Ecotoxicology and Environmental Safety **11**(1): 91-99.

The cytotoxicity of cadmium toward cultured bluegill fry (BF-2) cells was determined using several assay endpoints. The concentrations of cadmium causing a 50% decrease in colony formation, cell replication, uptake of neutral red, population growth (as determined by protein analysis), and uptake of [3H]uridine and 50% detachment of cells (as determined by protein analysis) were 0.03, 0.04, 0.08, 0.09, 0.12, and 0.21 mM cadmium, respectively. The neutral red assay was used to compare the relative sensitivities of bluegill BF-2 cells and RTG-2 cells, derived from the rainbow trout, toward four metals. The concentrations of cadmium, zinc, copper, and nickel causing a 50% reduction in the uptake of neutral red were 0.08, 0.19, 0.55, and 2.0 mM, respectively, with the BF-2 cells and 0.18, 0.64, 1.45, and >> 10.0 mM, respectively, with the RTG-2 cells. The RTG-2 cells were less sensitive to the metals, in particular to nickel. The less stringent temperature requirements for growth, their greater sensitivity to pollutants, and their markedly shorter doubling time in vitro make the BF-2 cells the preferable cell line for ecotoxicity screening of aquatic pollutants.

Baldisserotto, B., M. J. Chowdhury, et al. (2005). "Effects of dietary calcium and cadmium on cadmium accumulation, calcium and cadmium uptake from the water, and their interactions in juvenile rainbow trout." Aquatic Toxicology **72**(1-2): 99-117.

The objective of this study was to examine the effects of chronically elevated dietary Ca2+ (as CaCO3), alone and in combination with elevated dietary Cd, on survival, growth, and Cd and Ca2+ accumulation in several internal compartments in juvenile rainbow trout (Oncorhynchus mykiss). In addition, effects on short-term branchial uptake and internal distribution of newly accumulated waterborne Ca2+ and Cd during acute waterborne Cd exposure (50 [mu]g/L as CdNO3 for 3 h) were monitored using radiotracers (45Ca, 65Cd).

Fish were fed with four diets: 20 mg Ca2+/g food (control), 50 mg Ca2+/g food, 300 [mu]g Cd/g food, and 50 mg Ca2+/g + 300 [mu]g Cd/g food for 30 days. There were no significant effects on growth, mortality, or total body Ca2+ accumulation. The presence of elevated Ca2+, Cd, or Ca2+ + Cd in the diet all reduced waterborne Ca2+ uptake in a short-term experiment (3 h), though the inhibitory mechanisms appeared to differ. The effects were marked after 15 days of feeding, but attenuated by 30 days, except when the diet was elevated in both Ca2+ and Cd. The presence of elevated Ca2+ in the diet had only modest influence on Cd uptake from the water during acute Cd challenges but greatly depressed Cd uptake from the diet and accumulation in most internal tissues. None of the treatment diets prevented the decreases in waterborne Ca2+ uptake and new Ca2+ accumulation in internal tissues caused by acute exposure to waterborne Cd. In conclusion, there are complex interactions between waterborne and dietary effects of Ca2+ and Cd. Elevated dietary Ca2+ protects against both dietary and waterborne Cd uptake, whereas both waterborne and dietary Cd elevations cause reduced waterborne Ca2+ uptake.

Baldisserotto, B., C. Kamunde, et al. (2004). "Acute waterborne cadmium uptake calcium in rainbow trout is reduced by dietary carbonate." Comparative Biochemistry and Physiology C-Toxicology & Pharmacology **137**(4): 363-372.

The effects of elevated dietary calcium (as CaCO3) and acute waterborne Cd exposure (50 mug/l) on whole body uptake, tissue uptake, and internal distribution of newly accumulated Cd, Ca2+, and Na+ in juvenile rainbow trout were examined. Fish were fed with three diets (mg Ca2+/g food): 20 (control), 30 and 60 for 7 days before fluxes were measured with radiotracers. The highest dietary Ca2+ elevation reduced waterborne whole body Ca2+ uptake, but did not protect against inhibition of waterborne Ca2+ uptake by waterborne Cd. Both Ca2+-supplemented diets reduced newly accumulated Ca2+ in the gills in relation to the control treatment, but did not prevent the Cd-inhibiting effect against accumulation of new Ca2+ in most compartments. Fish fed with Ca2+-supplemented diets showed markedly lower rates of whole body uptake and internalization (in some tissues) of waterborne Cd, illustrating that, while dietary Ca2+ supplementation did not protect against the impact of waterborne Cd on waterborne Ca2+ uptake, it did protect against the uptake of Cd. Waterborne Cd had no effect on Na+ fluxes, total Cl-, and in most body compartments, newly accumulated Na+ and total Na+ were also not affected. Dietary supplementation with CaCO3 had the same protective effect as demonstrated by dietary supplementation with CaCl2 in an earlier study. Thus, the reduction of waterborne Cd uptake and internalization by dietary Ca2+ was specifically due to Ca2+ and not to the anion.

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Baldisserotto, B., C. Kamunde, et al. (2004). "A protective effect of dietary calcium against acute waterborne cadmium uptake in rainbow trout." Aquatic Toxicology **67**(1): 57-73.

The present study examined the interactions between elevated dietary calcium (as ionic Ca2+ in the form of CaCl2-2H(2)O) and acute waterborne Cd exposure (50 mug/l as CdNO3 for 3 h) on whole body uptake and internal distribution of newly accumulated Cd, Ca2+, and Na+ in juvenile rainbow trout (Oncorhynchus mykiss). Fish were fed with three diets 20 (control), 30 and 60 mg Ca2+/g food: for 7 days before fluxes were measured with radiotracers over a 3 h period. The two elevated Ca2+ diets reduced the whole body uptake of both Ca2+ and Cd by >50%,and similarly reduced the internalization of both newly accumulated metals in most tissues, effects which reflect the shared branchial uptake route for Ca2+ and Cd., As the Ca2+ concentrations of the fluid phases of the stomach and intestinal contents were greatly elevated by the experimental diets, increased gastrointestinal Ca2+ uptake likely caused the down-regulation of the branchial. Ca2+ (and Cd), uptake pathway. Waterbome Na+ uptake and internal distribution were not affected. While plasma Ca2+; surged after the first two feedings of the 60 mg Ca2+/g diet, internal homeostasis was quickly restored. Total Ca2+, Na+, and Cl-, levels in tissues were not affected by diets. While dietary Ca2+ protected against waterborne Cd uptake, it did not protect against the relative inhibition of waterborne Ca2+ uptake caused by waterbome Cd. Acute exposure to 50 mug/l Cd reduced the uptake and internalization of newly accumulated Ca2+ (but not Na+) by 70% or more, regardless of diet. Since elevated dietary Ca2+ reduces waterbome Cd uptake, fish eating a Ca2+-rich invertebrate diet may be more protected against waterbome Cd toxicity in a field situation.

Barak, N. A. E. and C. F. Mason (1990). "Mercury, cadmium and lead concentrations in five species of freshwater fish from eastern England." The Science of The Total Environment **92**: 257-263.

A total of 146 samples of five species of fish were examined between March and November 1986 in four sites from the Rivers Brett and Chelmer in eastern England. Variations in heavy metals concentrations between sites and species were related mainly to size differences of fish. Mercury levels in the flesh were higher than in the liver, while cadmium and lead levels were higher in the liver.

Barhoumi, S., I. Messaoudi, et al. (2009). "Cadmium bioaccumulation in three benthic fish species, Salaria basilisca, Zosterisessor ophiocephalus and Solea vulgaris collected from the Gulf of Gabes in Tunisia." Journal of Environmental Sciences **21**(7): 980-984.

To select a marine teleost fish which can be used as a bioindicator of cadmium (Cd) pollution in the Gulf of Gabes in Tunisia, Cd concentrations in liver and gill were compared in three benthic fish species including Salaria basilisca, Zosterisessor ophiocephalus and Solea vulgaris. Fish samples were collected from three selected sites in the Gulf of Gabes, with different degrees of Cd contamination: the industrialized coast of Sfax (S1), the coast of Douar Chatt (S2) and the coast of Luza (S3). The results shows that Cd concentrations in both sediment and water collected from S1 were significantly higher ($p < 0.0001$) than those from S2 and S3. For each species, Cd concentrations, in both liver and gill, showed the decreasing order: S1 > S2 > S3. The highest concentration of Cd was detected in the liver of S. basilisca, and only S. basilisca showed bioaccumulation factors (BAF) greater than 1 in all studied sites. In S1 and S2, BAF values respect the following order: S. basilisca > Z. ophiocephalus > S. vulgaris. These results of significant bioaccumulation of Cd, in terms of hepatic concentrations and bioaccumulation factors, indicated that S. basilisca can be used as bioindicator to evaluate the evolution of Cd pollution in the Gulf of Gabes.

Beauvais, S. L., S. B. Jones, et al. (2001). "Cholinergic and Behavioral Neurotoxicity of Carbaryl and Cadmium to Larval Rainbow Trout (Oncorhynchus mykiss)." Ecotoxicology and Environmental Safety **49**(1): 84-90.

Pesticides and heavy metals are common environmental contaminants that can cause neurotoxicity to aquatic organisms, impairing reproduction and survival. Neurotoxic effects of cadmium and carbaryl exposures were estimated in larval rainbow trout (RBT; Oncorhynchus mykiss) using changes in physiological endpoints and correlations with behavioral responses. Following exposures, RBT were videotaped to assess swimming speed. Brain tissue was used to measure cholinesterase (ChE) activity, muscarinic cholinergic receptor (MChR) number, and MChR affinity. ChE activity decreased with increasing concentrations of carbaryl but not of cadmium. MChR were not affected by exposure to either carbaryl or cadmium. Swimming speed correlated with ChE activity in carbaryl-exposed RBT, but no correlation occurred in cadmium-exposed fish. Thus, carbaryl exposure resulted in neurotoxicity reflected by changes in physiological

and behavioral parameters measured, while cadmium exposure did not. Correlations between behavior and physiology provide a useful assessment of neurotoxicity.

Benoit, D. A., E. N. Leonard, et al. (1976). "TOXIC EFFECTS OF CADMIUM ON 3 GENERATIONS OF BROOK TROUT (SALVELINUS-FONTINALIS)." Transactions of the American Fisheries Society **105**(4): 550-560.

Berntssen, M. H. G., O. O. Aspholm, et al. (2001). "Tissue metallothionein, apoptosis and cell proliferation responses in Atlantic salmon (Salmo salar L.) parr fed elevated dietary cadmium." Comparative Biochemistry and Physiology C-Toxicology & Pharmacology **128**(3): 299-310.

Atlantic salmon parr were reared for 4 months on experimental diets supplemented with 0 (control), 0.5, 5, 25, 125, or 250 mg Cd kg(-1) feed to establish a threshold concentration for dietary cadmium exposure by assessing early adaptive cellular responses. At the end of the experiment, the lowest dietary Cd concentration that caused significant accumulation in the gut, kidney and muscle was 5 mg Cd kg(-1) compared to the control group. Over time, dietary Cd accumulated first in the gut (after 1 month), followed by the kidney (2 months), and later by muscle (4 months). Highest Cd accumulation (100-fold) was found in the gut. A significant increase in regulated cell death and proliferation in salmon fed 125 mg Cd kg(-1) compared to control fish appeared efficient in preventing gross histopathological damage in the intestine. The highest increase in metallothionein levels was found in the kidney, and metallothionein (MT) levels increased disproportionally to Cd accumulation at increased exposure concentrations. It was concluded that MT was not directly associated with long-term Cd accumulation. Atlantic salmon showed increased metallothionein levels in the kidney at a median effective concentration (concentration of dietary Cd giving 50% of the maximum increase in metallothionein, EC50) of 7 mg Cd kg(-1), indicating toxic exposure at this concentration.

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Atlantic salmon (Salmo salar L.) parr were reared for 4 months on experimental diets supplemented with Cd (0.5, 5, 25, 125, or 250 mg Cd kg-1) to assess the long-term energetic changes based on the digestibility and biochemical deposition of the major dietary nutrients and to evaluate a maximum tolerable dietary toxicant concentration. Growth did not differ significantly (P>0.05) from the control groups. The biochemical composition of the carcass, but not the viscera, was negatively affected by dietary Cd exposure. The significant decreases in protein, lipid, and glycogen concentrations in the carcass (P<0.05, 25 mg kg-1 compared to control groups) caused a reduction in calculated whole-body energy content in fish fed 125 mg kg-1compared to control groups. This reduction in calculated whole-body energy content was explained by a concurrent significant disturbance to the gastrointestinal function (measured as reduced digestibility). Only at the highest dietary Cd exposure (250 mg kg-1), increased metabolic costs to cope with Cd toxicity was thought to contribute significantly to the reduction in carcass energy content. The most important factor effecting calculated total energetics was nutrient digestibility. Based on the logarithmic effective median concentration for reduced calculated energy digestibility (dietary Cd concentration corresponding to 50% reduction, EC50), the maximum tolerable dietary Cd concentration is 11 mg kg-1 diet.

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Besser, J. M., C. A. Mebane, et al. (2007). "Sensitivity of mottled sculpins (Cottus bairdi) and rainbow trout (Onchorhynchus mykiss) to acute and chronic toxicity of cadmium, copper, and zinc." Environmental Toxicology and Chemistry **26**(8): 1657-1665.

Studies of fish communities of streams draining mining areas suggest that sculpins (Cottus spp.) may be more sensitive than salmonids to adverse effects of metals. We compared the toxicity of zinc, copper, and cadmium to mottled sculpin (C. bairdi) and rainbow trout (Onchorhynchus mykiss) in laboratory toxicity tests. Acute (96-h) and early life-stage chronic (21- or 28-d) toxicity tests were conducted with rainbow trout and with mottled sculpins from populations in Minnesota and Missouri, USA, in diluted well water (hardness = 100 mg/L as CaCO3). Acute and chronic toxicity of metals to newly hatched and swim-up stages of mottled sculpins differed between the two source populations. Differences between populations were greatest for copper, with chronic toxicity values (ChV = geometric mean of lowest-observed-effect concentration and no-observed-effect concentration) of 4.4 mu g/L for Missouri sculpins and 37 mu g/L for Minnesota sculpins. Cadmium toxicity followed a similar trend, but differences between sculpin populations were less marked, with ChVs of 1.1 mu g/L (Missouri) and 1.9 mu g/L (Minnesota). Conversely, zinc was more toxic to Minnesota sculpins (ChV = 75 mu g/L) than Missouri sculpins (chronic ChV = 219 mu Lg/L). Species-average acute and chronic toxicity values for mottled sculpins were similar to or lower than those for rainbow trout and indicated that mottled sculpins were among the most sensitive aquatic species to toxicity of all three metals. Our results indicate that current acute and chronic water quality criteria for cadmium, copper, and zinc adequately protect rainbow trout but may not adequately protect some populations of mottled sculpins. Proposed water quality criteria for copper based on the biotic ligand model would be protective of both sculpin populations tested.

Blechinger, S. R., R. C. Kusch, et al. (2007). "Brief embryonic cadmium exposure induces a stress response and cell death in the developing olfactory system followed by long-term olfactory deficits in juvenile zebrafish." Toxicology and Applied Pharmacology **224**(1): 72-80.

The toxic effects of cadmium and other metals have been well established. A primary target of these metals is known to be the olfactory system, and fish exposed to a number of different waterborne metals display deficiencies in

olfaction. Importantly, exposure over embryonic/larval development periods can cause deficits in chemosensory function in juvenile fish, but the specific cell types affected are unknown. We have previously characterized a transgenic zebrafish strain expressing the green fluorescent protein (eGFP) gene linked to the hsp70 gene promoter, and shown it to be a useful tool for examining cell-specific toxicity in living embryos and larvae. Here we show that the hsp70/eGFP transgene is strongly and specifically upregulated within the olfactory sensory neurons (OSNs) of transgenic zebrafish larvae following a brief 3-h exposure to water-borne cadmium. This molecular response was closely correlated to an endpoint for tissue damage within the olfactory placode, namely cell death. Furthermore, cadmium-induced olfactory cytotoxicity in zebrafish larvae gives rise to more permanent effects. Juvenile zebrafish briefly exposed to cadmium during early larval development display deficits in olfactory-dependent predator avoidance behaviors 4-6 weeks after a return to clean water. Lateral line neuromasts of exposed zebrafish larvae also activate both the endogenous hsp70 gene and the hsp70/eGFP transgene. The data reveal that even a very brief exposure period that gives rise to cell death within the developing olfactory placode results in long-term deficits in olfaction, and that hsp70/eGFP may serve as an effective indicator of sublethal cadmium exposure in sensory cells.

Block, M., A. W. Glynn, et al. (1991). "Xanthate effects on cadmium intracellular distribution in rainbow trout (Oncorhynchus mykiss) gills." Aquatic Toxicology **20**(4): 267-283.

The uptake of 109cadmium through perfused rainbow trout gills in the presence of xanthates was studied, and the subcellular distribution of cadmium in perfused gill tissue was determined. Pnenol absorption was also studied because xanthates form hydrophobic Cd complexes with a log Poctanol/water similar to that of phenol. 1. Xanthate concentrations higher than 10-5 M increased the rate of cadmium transfer through the gills and cadmium retention in gill tissue. Cadmium was present as a hydrophobic complex at this and higher xanthate concentrations. 2. A redistribution of cadmium from metallothionein to high molecular weight cadmium binding fractions occurred in the presence of 10-4 M xanthate. 3. The rate of phenol transfer across the gill epithelium was much higher than the rate of cadmium transfer regardless of whether xanthate was present. The rate of phenol transfer stabilized much faster than the rate of cadmium transfer irrespective of whether xanthate was present, indicating that different uptake mechanisms were involved. We conclude that in the presence of xanthate concentrations higher than 10-5 M cadmium is taken up as a hydrophobic Cd(xanthate)2 complex by the epithelial cells. Within the cell the complex dissociates, and the metal ion is bound to intracellular cadmium-binding ligands. The metal is probably translocated through the basolateral membrane as a free ion.

Block, M. and P. Pärt (1986). "Increased availability of cadmium to perfused rainbow trout (Salmo gairdneri, Rich.) gills in the presence of the complexing agents diethyl dithiocarbamate, ethyl xanthate and isopropyl xanthate." Aquatic Toxicology **8**(4): 295-

302.

A study was made of the cadmium transfer through and retention of metal in perfused gill tissue from rainbow trout (Salmo gairdneri) in the presence of three cadmium complexing agents; DDC (diethyl dithiocarbamate), ethyl xanthate and isopropyl xanthate. The complexes formed are non-polar. The transfer of complexed cadmium was greater than the transfer of free cadmium ion. The retention of cadmium in gill tissue was increased about ten times in the presence of each of the two xanthates. However, the retention in gill tissue was not altered by DDC. It is concluded that cadmium uptake in fish gills in the presence of complexing agents is not simply a function of complexed versus free metal. It is also heavily dependent on the type of complexing agent present.

Brodeur, J. C., C. Daniel, et al. (1998). "In vitro response to ACTH of the interrenal tissue of rainbow trout (Oncorhynchus mykiss) exposed to cadmium." Aquatic Toxicology **42**(2): 103-113.

Plasma cortisol levels and responsiveness of the interrenal tissue to ACTH were determined in rainbow trout (Oncorhynchus mykiss) subjected to acute and subchronic exposures of cadmium (Cd) in the water. Plasma cortisol levels were significantly increased after 2 days of exposure to 1 [mu]g Cd l-1. They decreased to basal levels after 7 and 14 days of exposure. They significantly increased again after 30 days of exposure. The responsiveness of the interrenal tissue to ACTH was evaluated in vitro by monitoring the secretion of cortisol after stimulation of the head kidneys with 10-7 M of ACTH for 10 min in perifusion. The responsiveness to ACTH of the interrenal tissue of fish exposed to 1 [mu]g Cd l-1 for 2, 7 and 14 days and 5 [mu]g Cd l-1 for 7 days was not significantly different from controls. On the other hand, the interrenal tissue of fish exposed to 1 [mu]g Cd l-1 for 30 days secreted significantly larger amounts of cortisol in response to ACTH compared to controls. The significance of these findings to the interrenal dysfunction previously diagnosed in fish from lakes contaminated by heavy metals is discussed.

Brown, M. W., D. G. Thomas, et al. (1986). "A comparison of the differential accumulation of cadmium in the tissues of three species of freshwater fish, Salmo gairdneri, Rutilus rutilus and Noemacheilus barbatulus." Comparative Biochemistry and Physiology Part C: Comparative Pharmacology **84**(2): 213-217.

1. 1. Roach and stone loach were exposed to cadmium dissolved in their aquarium water at 500 and 1250 [mu]g/l, respectively, and the distribution of the metal accumulated in the major body organs was determined. The pattern of distribution for each species was somewhat different and was distinct in each case from that observed previously with rainbow trout.2. 2. The total body loads of cadmium accumulated by the three species were assessed during the period of exposure and found not to correlate directly with the concentration of cadmium to which the individual species had been exposed.3. 3. An alternative comparator was devised which as the quotient of the total body cadmium accumulation ([mu]g/100g body wt) and the notional cadmium dose ([mu]g/l) x weeks was described as a fractional retention coefficient for cadmium.4. 4. The coefficient

was constant for each species at different periods of exposure to cadmium alone. The values of the coefficient for roach and stone loach were however much lower than that for rainbow trout.5. 5. When rainbow trout were preexposed to zinc (100 [mu]g/l, 5 days) before being exposed to cadmium, the fractional retention coefficient for cadmium fell to a value similar to those seen with roach and stone loach exposed to cadmium alone.6. 6. The significance of these observations in relation to the nature of the intracellular proteins to which cadmium is bound in the three species is discussed in the light of their differential susceptibility to the toxic effects of cadmium.

Brown, V., D. Shurben, et al. (1994). "Cadmium toxicity to rainbow trout Oncorhynchus mykiss walbaum and brown trout Salmo trutta L. over extended exposure periods." Ecotoxicology and Environmental Safety **29**(1): 38-46.

The toxicity of cadmium in water is well known, but there have been few reports on the long-term effects of this metal on fish at concentrations near the European inland water standard of 5 [mu]g Cd liter-1. This paper describes experiments in which adult rainbow trout Oncorhynchus mykiss and brown trout Salmo trutta were exposed to cadmium concentrations near water quality standard levels for periods of up to 90 weeks. The survival and growth of these fish were assessed, and sperm and eggs were stripped from them to conduct early-life-stage tests. Continuous exposure of rainbow trout adults to cadmium concentrations of up to 5.5 [mu]g Cd liter-1 did not affect their survival or growth. However, eggs obtained from rainbow trout exposed to 1.8 and 3.4 [mu]g Cd liter-1 failed to develop to the fry stage. Oogenesis appeared to be delayed in brown trout exposed to 9.3 and 29.1 [mu]g Cd liter-1, but the eggs and fry that were produced developed normally after fertilization. Adult brown trout suffered considerable mortality in the 29.1 [mu]g Cd liter-1 treatment, with a median period of survival of 54 weeks.

Bryan, M. D., G. J. Atchison, et al. (1995). "EFFECTS OF CADMIUM ON THE FORAGING BEHAVIOR AND GROWTH OF JUVENILE BLUEGILL, LEPOMIS-MACROCHIRUS." Canadian Journal of Fisheries and Aquatic Sciences **52**(8): 1630-1638.

Standardized test protocols for assessing chemical hazards to aquatic organisms inadequately consider behavioral effects of toxicants; yet, organisms behaving abnormally in the wild have reduced growth, reduced fitness, and high mortality. We determined the chronic effects of cadmium (0, 30, 60, 120, and 240 mu g . L(-1)) on juvenile bluegill (Lepomis macrochirus) foraging behavior and growth rates in functional response experiments, each using different sized Daphnia as prey. Bluegill consumption rate increased with prey density. Cadmium-exposed fish initially attacked fewer prey per unit of time than unexposed fish, with subsequent recovery to control-level consumption rates determined by cadmium concentration and prey size. The degree of change (over time) in the number of Daphnia attacked per 30 s was the most consistently sensitive behavioral measure of sublethal stress in exposed bluegill; the lowest observed effect concentration (LOEC) was 37.3 mu g Cd . L(-1). Effects on prey attack rates

(attacks/30 s) were inversely related to prey size; cadmium had the greatest effect on bluegill foraging on the smallest prey. Cadmium had no effect on prey capture efficiency or handling time. Growth in bluegill length and weight was reduced (P less than or equal to 0.019) by all cadmium concentrations and was a more sensitive end point than were the foraging behaviors.

Buckley, J. A., G. A. Yoshida, et al. (1985). "Toxicities of total and chelex-labile cadmium to salmon in solutions of natural water and diluted sewage with potentially different cadmium complexing capacities." Water Research **19**(12): 1549-1554.

The LC50 for total Cd averaged 4.8 and 8.0 [mu]g1-1 in river water and 33% sewage-treatment-plant effluent (STPE), respectively, and for Chelex-labile Cd, 3.9 and 5.6 [mu]g1-1, respectively. The LC50 values for total Cd were significantly ($P < 0.05$) different, indicating a reduction in toxicity of Cd in the presence of 33% STPE, presumably due to complexation of Cd2+. The similarity of LC50 values for Chelex-labile Cd indicates that that fraction contained toxic species of Cd at approximately the same concentration(s) in both river water and 33% STPE; it is therefore considered a better measure of Cd toxicity than total Cd. Furthermore, mortality was correlated with the concentration of Chelex-labile Cd but not with that of Chelex-nonlabile Cd. Measurements of Cd2+-complexing capacity by the Chelex method indicated that toxicity was due, at least in part, to Cd2+. Values were less than those obtained by the ion-selective-electrode method; these indicated that toxicity was due only to complexed Cd. Values from both methods were uncorrelated with LC50 values.

Burger, J. (2008). "Assessment and management of risk to wildlife from cadmium." Science of the Total Environment **389**(1): 37-45.

Cadmium, a nonessential heavy metal that comes from natural and anthropogenic sources, is a teratogen, carcinogen, and a possible mutagen. Assessment of potential risk from cadmium requires understanding environmental exposure, mainly from ingestion, although there is some local exposure through inhalation. Chronic exposure is more problematic than acute exposure for wildlife. There is evidence for bioaccumulation, particularly in freshwater organisms, but evidence for biomagnification up the food chain is inconsistent; in some bird studies, cadmium levels were higher in species that are higher on the food chain than those that are lower. Some freshwater and marine invertebrates are more adversely affected by cadmium exposure than are birds and mammals. There is very little experimental laboratory research on the effects of cadmium in amphibians, birds and reptiles, and almost no data from studies of wildlife in nature. Managing the risk from cadmium to wildlife involves assessment (including ecological risk assessment), biomonitoring, setting benchmarks of effects, regulations and enforcement, and source reduction.

Calamari, D., R. Marchetti, et al. (1980). "Influence of water hardness on cadmium toxicity to Salmo gairdneri rich." Water Research **14**(10): 1421-1426.

Acute toxicity of cadmium to Salmo gairdneri is increased by a reduction in water hardness. The role of the chemical species of the metal in the intoxication

processes in waters of different levels of hardness, is considered as well as the reasons for explaining the observed effects by biological mechanisms. The theoretical distribution of the chemical species of cadmium in water of different level of hardness (320, 80 and 20 mg CaCO3 1-1) at pH 7.2 was calculated. The results show that similar concentrations of the same form of cadmium (Cd2+) gave different levels of mortality and that similar acute toxic effects were caused by different amounts of ionic form (Cd2+). Fish acclimated at 320 mgCaCO3 1-1 but tested at 20 mg CaCO3 1-1 reacted in an intermediate way, confirming the importance of the biological hypothesis. Chloride cell proliferation in gills is a common defence response to intoxication processes. Thus the presence of a higher number of chloride cells in fish acclimated to hard water would have explained the lower sensitivity to cadmium. Fish kept in water with a wide difference in hardness and acclimated, so as to have different ionic contents in the blood, had an equal number of chloride cells in the gills. A detoxification mechanism based mainly on the increase in the number and activity of chloride cells should therefore be independent per se, of hardness and rather related to the presence of metals. On the contrary, the possibility of action by cadmium could depend upon the role of calcium in regulating gill permeability.

Carginale, V., C. Capasso, et al. (2002). "Identification of cadmium-sensitive genes in the Antarctic fish Chionodraco hamatus by messenger RNA differential display." Gene **299**(1-2): 117-124.

To investigate the ability of cadmium to affect gene transcription in fish, the messenger RNA (mRNA) differential display technique was used to analyze gene expression in the Antarctic icefish Chionodraco hamatus exposed to sublethal doses of cadmium salt. Seven DNA complementary to RNA (cDNA) bands whose steady-state levels of expression significantly changed in response to cadmium exposure were identified. The results obtained show that two groups of genes are affected by cadmium in icefish liver. The first group comprises genes that are up-regulated by the metal: in particular, a gene encoding the heat-shock protein HSP70 and another encoding a protein homologous to GP49 of Sparus aurata egg envelope. The other group comprises genes down-regulated by cadmium. These are the transferrin gene and a gene encoding a protein presenting homology to mouse T2K, a kinase having a role in the prevention of apoptosis. Three cDNAs had no homology to known gene sequences, thus suggesting that may either encode not yet identified proteins, or correspond to untranslated regions of mRNA molecules.

Carrier, R. and T. L. Beitinger (1988). "Reduction in thermal tolerance of Notropis lutrensis and Pimephales promelas exposed to cadmium." Water Research **22**(4): 511-515.

This study focused on the temperature tolerance of Notropis lutrensis and Pimephales promelas exposed to water-borne cadmium. After a 96 h LC50 (mg Cd l-1) was determined for each species, groups of fish were exposed to one of a series of sublethal cadmium concentrations (LC5, LC10 and LC20) prior to temperature tolerance measurements via the critical thermal maximum (CTM)

method. CTMs were determined on days 1, 5 and 10 of cadmium exposure. Lethal toxicity values (96 h LC50 and 95% confidence limits, mg Cd l-1) were 6.62 (6.11-7.26) for Notropis lutrensis and 3.58 (3.11-4.01) for Pimephales promelas. Both cadmium concentration and exposure time had a highly significant effect on CTMs of both species. Subsequent to 10 days of cadmium exposure, CTMs of Notropis lutrensis were 2.3-4.4°C lower than controls and 4.2-5.7°C lower than controls in Pimephales promelas. These findings suggest that exposure to cadmium at sublethal concentrations can adversely affect the ability of fish to withstand high temperature stress.

Cavas, T., N. N. Garanko, et al. (2005). "Induction of micronuclei and binuclei in blood, gill and liver cells of fishes subchronically exposed to cadmium chloride and copper sulphate." Food and Chemical Toxicology **43**(4): 569-574.

Common carp (Cyprinus carpio), Prussian carp (Carassius gibelio) and Peppered cory (Corydoras paleatus) were evaluated as target species to perform genotoxicity tests for heavy metals. Fishes were exposed to different doses of cadmium (0.005-0.1 mg/L) and copper (0.01-0.25 mg/L) for 21 days. Hexavalent chromium at a single dose of 5 mg/L was used as a positive control. Frequencies of micronuclei and binuclei were evaluated comparatively in peripheral blood erythrocytes, gill epithelial cells and liver cells. As a result it was observed that, fish species and their tissues showed differential sensitivity to the heavy metal treatment. In general, frequencies of micronucleated and binucleated cells significantly increased following the exposure for 21 days to copper, cadmium and chromium. On the other hand, gill and liver cells showed higher frequencies of micronuclei and binuclei than erythrocytes. Our results indicated the formation of micronuclei and binuclei in fish cells caused by their exposure to cadmium, copper and chromium, thus verifying results obtained earlier on mammals, which indicated that these heavy metals have cytotoxic and genotoxic effects. The suitability of the micronucleus assay in native fish species for the screening of aquatic genotoxicants is highlighted and the importance of target tissue selection in the piscine micronucleus test is emphasized.

Chandra, P. and A. R. Khuda-Bukhsh (2004). "Genotoxic effects of cadmium chloride and azadirachtin treated singly and in combination in fish." Ecotoxicology and Environmental Safety **58**(2): 194-201.

The genotoxic effects of cadmium chloride (CdCl2) and azadirachtin (Aza) were assessed singly and conjointly in a fish, Oreochromis mossambicus, with endpoints such as chromosome aberrations, abnormal red cell nuclei, abnormal sperm morphology, and protein content (both qualitative and quantitative) of selected tissues, namely, muscle, heart, eye, brain, gill, liver, spleen, and kidney. The primary objectives were, first, to examine if CdCl2, a common pollutant, and Aza, a natural product of the neem plant used extensively as an [`]ecofriendly' agent for many purposes, had any genotoxic effect of their own on nontarget aquatic organisms of economic importance; and second, if Aza could have any ameliorating effect on CdCl2-induced genotoxicity in O. mossambicus tissues. As compared with distilled water-treated controls, both CdCl2 and Aza induced

genotoxicity in O. mossambicus, the former in greater quantity than that produced by Aza. However, Cd-induced toxicity in O. mossambicus appeared to be ameliorated to some extent by Aza.

Chapman, G. A. (1978). "TOXICITIES OF CADMIUM, COPPER, AND ZINC TO 4 JUVENILE STAGES OF CHINOOK SALMON AND STEELHEAD." Transactions of the American Fisheries Society **107**(6): 841-847.

Chapman, G. A. and D. G. Stevens (1978). "ACUTELY LETHAL LEVELS OF CADMIUM, COPPER, AND ZINC TO ADULT MALE COHO SALMON AND STEELHEAD." Transactions of the American Fisheries Society **107**(6): 837-840.

Chowdhury, M. J., D. G. McDonald, et al. (2004). "Gastrointestinal uptake and fate of cadmium in rainbow trout acclimated to sublethal dietary cadmium." Aquatic Toxicology **69**(2): 149-163.

Adult rainbow trout were pre-exposed to a sublethal concentration of dietary Cd (500 mg/kg dry wt.) for 30 days to induce acclimation. A gastrointestinal dose of radiolabeled Cd (276 [mu]g/kg wet wt.) was infused into the stomach of non-acclimated and Cd-acclimated trout through a stomach catheter. Repetitive blood samples over 24 h and terminal tissue samples were taken to investigate the gastrointestinal uptake, plasma clearance kinetics, and tissue distribution of Cd. Only a small fraction of the infused dose (non-acclimated: 2.4%; Cd-acclimated: 6.6%) was internalized across the gut wall, while most was bound in the gut tissues (10-24%) or remained in the lumen (16-33%) or lost from the fish (~50%) over 24 h. Cadmium loading during pre-exposure produced a profound increase of total Cd in the blood plasma (~28-fold) and red blood cells (RBC; ~20-fold). The plasma Cd-time profiles consisted of an apparent rising (uptake) phase and a declining (clearance) phase with a maximum value of uptake in 4 h, suggesting that uptake of gastrointestinally infused Cd was very rapid. Acclimation to dietary Cd did not affect plasma Cd clearance (~0.5 ml/min), but enhanced new Cd levels in the plasma (but not in the RBC), and resulted in a longer half-life for plasma Cd. Tissue total and new Cd levels varied in different regions of the gastrointestinal tract, and overall levels in gut tissues were much greater than in non-gut tissues, reflecting the Cd exposure route. Dietary Cd, but not the infused Cd, greatly increased total Cd levels of all gut tissues in the order posterior-intestine (640-fold) > cecae (180-fold) > mid-intestine (94-fold) > stomach (53-fold) in Cd-acclimated fish relative to naïve fish. Among non-gut tissues in the Cd-acclimated fish, the great increases of total Cd levels were observed in the liver (73-fold), kidney (39-fold), carcass (35-fold), and gills (30-fold). The results provide some clear conclusions that may be useful for environmental risk assessment of dietary Cd exposure in fish.

Chowdhury, M. J., E. F. Pane, et al. (2004). "Physiological effects of dietary cadmium acclimation and waterborne cadmium challenge in rainbow trout: respiratory, ionoregulatory, and stress parameters." Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology **139**(1-3): 163-173.

A suite of respiratory, acid-base, ionoregulatory, hematological, and stress parameters were examined in adult rainbow trout (Oncorhynchus mykiss) after chronic exposure to a sublethal level of dietary Cd (500 mg/kg diet) for 45 days and during a subsequent challenge to waterborne Cd (10 [mu]g/L) for 72 h. Blood sampling via an indwelling arterial catheter revealed that dietary Cd had no major effects on blood gases, acid-base balance, and plasma ions (Ca2+, Mg2+, K+, Na+, and Cl-) in trout. The most notable effects were an increase in hematocrit (49%) and hemoglobin (74%), and a decrease in the plasma total ammonia (43%) and glucose (49%) of the dietary Cd-exposed fish relative to the nonexposed controls. Dietary Cd resulted in a 26-fold increase of plasma Cd level over 45 days (~24 ng/mL). The fish exposed to dietary Cd showed acclimation with increased protection against the effects of waterborne Cd on arterial blood PaCO2 and pH, plasma ions, and stress indices. After waterborne Cd challenge, nonacclimated fish, but not Cd-acclimated fish, exhibited respiratory acidosis. Plasma Ca2+ levels declined from the prechallenge level, but the effect was more pronounced in nonacclimated fish (44%) than in Cd-acclimated fish (14%) by 72 h. Plasma K+ was elevated only in the nonacclimated fish. Similarly, waterborne Cd caused an elevation of all four traditional stress parameters (plasma total ammonia, cortisol, glucose, and lactate) only in the nonacclimated fish. Thus, chronic exposure to dietary Cd protects rainbow trout against physiological stress caused by waterborne Cd and both dietary and waterborne Cd should be considered in determining the extent of Cd toxicity to fish.

Chowdhury, M. J. and C. M. Wood (2007). "Renal function in the freshwater rainbow trout after dietary cadmium acclimation and waterborne cadmium challenge." Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology **145**(3): 321-332.

Renal function was examined in adult rainbow trout (Oncorhynchus mykiss) after chronic exposure to a sublethal level of dietary Cd (500 mg/kg diet) for 52 d and during a subsequent challenge to waterborne Cd (10 [mu]g/L) for 72 h. Dietary Cd had no major effects on UFR (urine flow rate) and GFR (glomerular filtration rate) but caused increased renal excretion of glucose, protein, and major ions (Mg2+, Zn2+, K+, Na+, Cl- but Ca2+). However, dietary Cd did not affect any plasma ions except Na+ which was significantly elevated in the Cd-acclimated trout. Plasma glucose and ammonia levels fell by 25% and 36% respectively, but neither plasma nor urine urea was affected in Cd-acclimated fish. Dietary Cd exposure resulted in a remarkable increase of Cd load in the plasma (48-fold, ~ 22 ng/mL) and urine (60-fold, 8.9 ng/mL), but Cd excretion via the kidney was negligible on a mass-balance basis. Clearance ratio analysis indicates that all ions, Cd, and metabolites were reabsorbed strongly (58-100%) in both naïve and dietary Cd exposed fish, except ammonia which was secreted in both groups. Mg2+, Na+, Cl- and K+ reabsorption decreased significantly (3-15%) in the Cd-exposed fish relative to the control. Following waterborne Cd challenge, GFR and UFR were affected transiently, and only Mg2+ and protein excretion remained elevated with no recovery with time in Cd-acclimated trout. Urinary Ca2+ and

Zn2+ excretion rates dropped with an indication of renal compensation towards plasma declines of both ions. Cadmium challenge did not cause any notable effects on urinary excretion rates of metabolites. However, a significant decrease in Mg2+ reabsorption but an increase in total ammonia secretion was observed in the Cd-acclimated fish. The study suggests that dietary Cd acclimation involves physiological costs in terms of renal dysfunction and elevated urinary losses.

Collyard, S. A., G. T. Ankley, et al. (1994). "INFLUENCE OF AGE ON THE RELATIVE SENSITIVITY OF HYALELLA-AZTECA TO DIAZINON, ALKYLPHENOL ETHOXYLATES, COPPER, CADMIUM, AND ZINC." Archives of Environmental Contamination and Toxicology **26**(1): 110-113.

Laboratories testing Hyalella azteca use a wide range of ages (or sizes) of the amphipod in their studies. The objective of this study was to investigate age-specific differences in sensitivity of the amphipod to contaminants with varying toxic modes of action. Hyalella azteca, ranging in age from <1 to 26 d, were tested in 96-h water-only exposures with the organophosphate pesticide diazinon, a mixture of alkylphenol ethoxylates (nonionic surfactants), copper sulfate, cadmium chloride, and zinc sulfate. Overall age-specific differences in sensitivity to the five test chemicals were relatively small; 96-h LC50 values typically varied by 50% or less among the various age classes of H. azteca. When differences in sensitivity were observed, trends were apparently related to the contaminant tested rather than to the age of the amphipods, i.e., no particular age class consistently was the most sensitive to the toxicants.

Couture, P. and P. Rajender Kumar (2003). "Impairment of metabolic capacities in copper and cadmium contaminated wild yellow perch (Perca flavescens)." Aquatic Toxicology **64**(1): 107-120.

This study examined variations in resting oxygen consumption rate (ROCR), post-exercise oxygen consumption rate, relative scope for activity (RSA), liver and muscle aerobic and anaerobic capacities (using citrate synthase (CS) and lactate dehydrogenase, respectively, as indicators), and tissue biosynthetic capacities (using nucleoside diphosphate kinase (NDPK) as an indicator), in wild yellow perch from four lakes varying in copper (Cu) and cadmium (Cd) contamination. Liver Cu and Cd concentrations largely reflected environmental contamination and were positively correlated with liver protein concentrations and NDPK activities. Our results suggest that metal contamination leads to an upregulation of liver protein metabolism, presumably at least in part for the purpose of metal detoxification. In contrast, muscle NDPK activities decreased with increasing liver Cd concentrations and NDPK activities. There was a 25% decrease in ROCR for a doubling of liver Cu concentrations and a 42% decrease in RSA for a doubling of liver Cd concentrations in the range studied. Cu contamination was also associated with lower muscle CS activities. Our results support previous findings of impaired aerobic capacities in the muscle of metal-contaminated fish, and demonstrate that this impairment is also reflected in aerobic capacities of whole fish. The evidence presented suggests that mitochondria may be primary targets for inhibition by Cu, and that Cd may

reduce gill respiratory capacity. Muscle aerobic and anaerobic capacities were inversely related. This work indicates that metal exposure of wild yellow perch leads to a wide range of disturbances in metabolic capacities.

Dallinger, R., M. Egg, et al. (1997). "The role of metallothionein in cadmium accumulation of Arctic char (Salvelinus alpinus) from high alpine lakes." Aquatic Toxicology **38**(1-3): 47-66.

Cadmium, copper and zinc concentrations were measured in water and organs (gill, liver and kidney) of Arctic char (Salvelinus alpinus) from four alpine lakes in Tyrol, Austria. In comparison with control fish, concentrations of metals, especially of cadmium, were elevated in tissues of fish from low-alkalinity lakes. In contrast, low metal levels were detected in water of the alpine lakes, suggesting that the high net accumulation of metals in fish tissues might have been caused by increased availability of these metals under conditions of low alkalinity. After chromatographic purification and Reversed-Phase HPLC of tissue supernatants from lake fish, several metallothionein (MT) peaks were identified in liver and kidney. In both organs MT accounted for the sequestration of virtually all the cadmium present in the tissues, and of considerable proportions of copper and zinc. However, there were conspicuous organ-specific differences in the metal patterns of the isolated MTs. Whereas liver MT of lake fish was dominated by copper and zinc despite high amounts of cadmium in the tissue, kidney MT showed a reversed pattern with cadmium predominating at the expense of copper and zinc. At slightly elevated cadmium concentrations in the liver, sequestration of this metal was achieved by displacement of zinc from MT binding sites, whereas at higher concentrations more MT was synthesized to bind excess amounts of the metal. The concentration of (Cd,Zn)-MT in the liver was inversely correlated with lake alkalinity. Finally, significant positive correlations were observed between the age of Arctic char and hepatic concentrations of cadmium and (Cd,Zn)-MT.

Das, S. and B. B. Jana (2004). "Distribution pattern of ambient cadmium in wetland ponds distributed along an industrial complex." Chemosphere **55**(2): 175-185.

Water and sediment samples collected from 18 wetland ponds within and outside industrial areas were examined for cadmium concentration and water quality parameters during the period of January to July 1996. The Cd contents in gill, liver, mantle and shell of freshwater mussel (Lamellidens marginalis) as well as leaves and roots of water hyacinth Eichhornia those occurred in these ponds were also estimated. Cd concentration ranged from 0.006 to 0.7025 mg/l in water and from 7 to 77 [mu]g/g dw in sediments of all the ponds investigated. The amount of Cd occurring in water and sediment was much higher in concentrations in the ponds located in Captain Bheri and Mudiali farm close to industrial areas, compared to remaining ponds located outside the industrial belt. Lamellidens marginalis procured from Mudiali and Captain Bheri ponds showed regardless of size, tissue and season of collection significantly higher Cd concentration than did those from other ponds. Likewise, tissue Cd in Eichhornia collected from Mudiali pond was as high as 125-152 [mu]g/g dw in root and 21-

63 [mu]g/g dw in leaves compared to 40-108 [mu]g/g dw in root and 9-43 [mu]g/g dw in leaves in the remaining ponds. Seasonal variability of Cd was clear-cut; the concentration was relatively higher in water and sediment in all ponds during summer than during monsoon season or winter. Size-wise, smaller groups showed the highest concentrations of Cd in all tissues of Lamellidens compared with medium and large size groups. Concentration factor for all tissues of Lamellidens regardless of size and season, was inversely proportional with the ambient Cd concentrations. Concentration factor estimated for all tissues in all ponds and all seasons was in the order: liver > gill > shell > mantle. As all ponds located outside the industrial belt showed Cd concentrations ranging from 0.006 to 0.049 mg/l, it is suggested that these wetlands do not pose serious risk to the environment.

de Conto Cinier, C., M. Petit-Ramel, et al. (1999). "Kinetics of cadmium accumulation and elimination in carp Cyprinus carpio tissues." Comparative Biochemistry and Physiology Part C: Pharmacology, Toxicology and Endocrinology **122**(3): 345-352.

Carp (Cyprinus carpio) were tested for cadmium accumulation and elimination during and after a simulated pollution exposure. Fish were distributed in two 1000-l indoor concrete aquaria supplied with a continuous flow (8 l min-1) of well water. The cadmium concentration was maintained at 53 [mu]g l-1 in one aquarium and 443 [mu]g l-1 in the other aquarium for 127 days. The exposure phase was followed by a 43-day depuration period. The cadmium accumulation in liver, kidney and muscle was measured by means of ICP-MS. The data showed that cadmium exposure produces significant cadmium uptake in tissues. Cadmium concentrations increased sharply in kidney and liver, whereas the pollutant level in muscle was only significant after 106 days. After 127 days of Cd exposure (53 [mu]g l-1), the cadmium concentration in kidney was 4-fold higher than in liver and 50-fold higher than in muscle for a toxic level of 53 [mu]g l-1. At a Cd of 443 [mu]g l-1, kidney cadmium content was 2-fold higher than in liver and 100-fold higher than in muscle. In kidney and liver, the toxic concentration increased as the concentration of pollutant in water increased. During the 43 depuration days, the loss of accumulated cadmium was rapid and immediate in muscle. Conversely, no loss of cadmium was observed in kidney and liver.

de la Torre, F. R., A. Salibian, et al. (2000). "Biomarkers assessment in juvenile Cyprinus carpio exposed to waterborne cadmium." Environmental Pollution **109**(2): 277-282.

The impact of long-term exposure to waterborne cadmium (Cd) on Cyprinus carpio was evaluated through changes of selected parameters considered as biomarkers of toxicity. Fish were exposed to 1.6 mg l(-1) Cd for 14 days and then transferred to Cd-free water for 19 days. The measured parameters were gill ATPases, brain acetylcholinesterase (AchE), liver glutamate oxaloacetate (GOT) and glutamate pyruvate (GPT) transaminases, muscle water content, and protein content of liver, gills and brain. Condition factor and liver somatic index were also calculated. Branchial ATPase activities were impaired in a dissimilar way: the (Na+,K+)ATPases were inhibited by approximately 30%, while the Mg2+-ATPase

was significantly activated by 70%. Brain AchE showed no changes after Cd exposure. Both liver GOT and GPT activities were increased by the metal by 63 and 98%. Water content of the skeletal muscle showed no significant alterations. After the 19-day recovery phase, changes in the Mg2+-ATPase and GPT were reversed to values similar to controls, but the Cd exposure resulted in an irreversible alteration in GOT activity. Results indicate that the sublethal Cd concentrations are stressful to carp, particularly with reference to branchial enzymes which may disrupt the osmotic and ionic balance of the animals. (C) 2000 Elsevier Science Ltd. All rights reserved.

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De Smet, H., B. De Wachter, et al. (2001). "Dynamics of (Cd,Zn)-metallothioneins in gills, liver and kidney of common carp Cyprinus carpio during cadmium exposure." Aquatic Toxicology **52**(3-4): 269-281.

Cadmium concentrations, (Cd,Zn)-metallothionein (MT) concentrations, MT synthesis and the relative amounts of cadmium bound to (Cd,Zn)-MTs were determined in gills, liver and kidney of common carp Cyprinus carpio exposed to 0, 0.5 [mu]M (0.06 mg.l-1), 2.5 [mu]M (0.28 mg.l-1) and 7 [mu]M (0.79 mg.l-1) Cd for up to 29 days. Cadmium accumulation was in the order kidney>liver>gills. Control levels of hepatic (Cd,Zn)-MT were four times higher compared to those of gills and kidney. No increases in (Cd,Zn)-MT concentrations were observed in liver during the exposure period. In comparison with control carp, (Cd,Zn)-MT concentrations increased up to 4.5 times in kidney and two times in gills. In both these organs, (Cd,Zn)-MT concentrations were linearly related with cadmium tissue levels and with the de novo synthesis of MTs. Hepatic cadmium was almost completely bound to (Cd,Zn)-MT, while percentages of non-MT-bound

cadmium were at least 40% in gills and 25% in kidney. This corresponded with a total saturation of (Cd,Zn)-MT by cadmium in kidney and a saturation of approximately 50 and 60% in gills and liver, respectively. The final order of non-MT-bound cadmium was kidney>gills>liver. Our results indicate that cadmium exposure causes toxic effects, which cannot be correlated with the accumulated levels of the metal in tissues. Although cadmium clearly leads to the de novo synthesis of MT and higher (Cd,Zn)-MT concentrations, the role of this protein in the detoxification process is clearly organ-specific and its synthesis does not keep track with cadmium accumulation.

Dean, R. J., T. M. Shimmield, et al. (2007). "Copper, zinc and cadmium in marine cage fish farm sediments: An extensive survey." Environmental Pollution **145**(1): 84-95.

The diet of cage-farmed Atlantic salmon contains a range of trace metals, some of which have toxic properties, e.g. zinc, copper and cadmium. A survey of metal concentrations (ICP-MS analysis) in surface sediments of ca. 70 stations was carried out in both May and December 2000 around a Scottish fish farm. Additionally, at 13 stations on 2 orthogonal transects centered on the farm, sediments were analysed at 1 cm intervals to 8 cm depth. Maximum concentrations in surface sediments were 921, 805 and 3.5 [mu]g g-1 for Zn, Cu and Cd, respectively, and were found at stations near the fish farm. The calculated losses from the farm (feed input minus fish output) were 87.0%, 4.3% and 14.0% of the background-corrected inventories for Zn, Cu and Cd, respectively, indicating that for Cu and Cd at least, the feed is not the only source.

Dutta, T. K. and A. Kaviraj (2001). "Acute toxicity of cadmium to fish Labeo rohita and copepod Diaptomus forbesi pre-exposed to CaO and KMnO4." Chemosphere **42**(8): 955-958.

96-h LC50 values of cadmium (Cd) to fish Labeo rohita and the copepod Diaptomus forbesi, determined by static bioassays, were, respectively, 89.5 and 10.2 mg/l. LC50 values increased significantly when fish pre-exposed to 100-350 mg/l CaO or 0.5-1.5 mg/l KMnO4 for 4 d and the copepod to 20-70 mg/l CaO or 0.25-1.0 mg/l KMnO4 for same period. The LC50 values also increased when the pre-exposure period of CaO was increased to 12 d at concentration 100 mg/l for fish and 20 mg/l for copepod. All fish died when pre-exposed to 1.5 mg/l KMnO4 for 8 d. But LC50 values of Cd to copepod increased when pre-exposure period of 0.5 mg/l KMnO4 was increased from 4 to 8 d.

Eaton, J. G. (1973). "CHRONIC TOXICITY OF A COPPER, CADMIUM AND ZINC MIXTURE TO FATHEAD MINNOW (PIMEPHALES-PROMELAS-RAFINESQUE)." Water Research **7**(11): 1723-1736.

Farag, A. M., D. Skaar, et al. (2003). "Characterizing aquatic health using salmonid mortality, physiology, and biomass estimates in streams with elevated concentrations of arsenic, cadmium, copper, lead, and zinc in the Boulder River watershed, Montana." Transactions of the American Fisheries Society **132**(3): 450-467.

Abandoned tailings and mine adits are located throughout the Boulder River watershed in Montana. In this watershed, all species of fish are absent from some tributary reaches near mine sources; however, populations of brook trout Salvelinus fontitalis, rainbow trout Oncorhynchus mykiss, and cut-throat trout O. clarki are found further downstream. Multiple methods must be used to investigate the effects of metals released by past mining activity because the effects on aquatic life may range in severity, depending on the proximity of mine sources. Therefore, we used three types of effects-those on fish population levels (as measured by survival), those on biomass and density, and those at the level of the individual (as measured by increases in metallothionein, products of lipid peroxidation, and increases in concentrations of tissue metals)-to assess the aquatic health of the Boulder River watershed. Elevated concentrations of Cd, Cu, and Zn in the water column were associated with increased mortality of trout at sites located near mine waste sources. The hypertrophy (swelling), degeneration (dying), and necrosis of epithelial cells observed in the gills support our conclusion that the cause of death was related to metals in the water column. At a site further downstream (lower Cataract Creek), we observed impaired health of resident trout, as well as effects on biomass and density (measured as decreases in the kilograms of trout per hectare and the number per 300 m) and effects at the individual level, including increases in metallothionein, products of lipid peroxidation, and tissue concentrations of metals.

Felten, V., G. Charmantier, et al. (2008). "Physiological and behavioural responses of Gammarus pulex (Crustacea: Amphipoda) exposed to cadmium." Aquatic Toxicology **86**(3): 413-425.

The aim of this study was to investigate the effects of cadmium on physiological and behavioural responses in Gammarus pulex. In a first experiment, cadmium LC50s for different times were evaluated in 264 h experiment under continuous mode of exposure (LC5096h = 82.1 [mu]g L-1, LC50120h = 37.1 [mu]g L-1, LC50168h = 21.6 [mu]g L-1, LC50264h = 10.5 [mu]g L-1). In a second experiment, the physiological and behavioural responses of the amphipod exposed to cadmium (0, 7.5 and 15 [mu]g L-1) were investigated under laboratory conditions. The mortality and the whole body cadmium concentration of organisms exposed to cadmium were significantly higher than in controls. Concerning physiological responses, cadmium exposure exerted a significant decrease on osmolality and haemolymph Ca2+ concentration, but not on haemolymph Na+ and Cl- concentrations, whereas the Na+/K+-ATPase activity was significantly increased. Behavioural responses, such as feeding rate, locomotor and ventilatory activities, were significantly reduced in Cd exposed organisms. Mechanism of cadmium action and consequent energetic reallocation in favour of maintenance functions (i.e., osmoregulation) are discussed. The results of this study indicate that osmolality and locomotor activity in G. pulex could be effective ecophysiological/behavioural markers to monitor freshwater ecosystem and to assess the health of organisms.

Ferri, S. and N. Macha (1980). "Lysosokal enhancement in hepatic cells of a teleost fish

induced by cadmium." Cell Biology International Reports **4**(4): 357-363.
The toxic effects of cadmium upon the hepatic cells of a freshwater fish were studied. The experiment was developed by the addition of cadmium chloride in the water and histochemical and EM methods were performed. The results showed that acute intoxication induces an increase of lysosomal activity related to the shape, distribution as well as different functional degrees of the organelle condensation. The authors analyze the different situations whose leading alterations of lysosomal behaviour and the probable mechanisms of cadmium action.

Figueroa B, E. (2008). "Are more restrictive food cadmium standards justifiable health safety measures or opportunistic barriers to trade? An answer from economics and public health." Science of the Total Environment **389**(1): 1-9.
In the past, Cd regulations have imposed trade restrictions on foodstuffs from some developing countries seeking to access markets in the developed world and in recent years, there has been a trend towards imposing more rigorous standards. This trend seems to respond more to public and private sectors strategies in some developed countries to create disguised barriers to trade and to improve market competitiveness for their industries, than to scientifically justified health precautions (sanitary and phytosanitary measures) and/or technical barriers to trade acceptable under the Uruguay Round Agreement of the WTO. Applying more rigorous Cd standards in some developed countries will not only increase production costs in developing countries but it will also have a large impact on their economies highly dependent on international agricultural markets. In the current literature there are large uncertainties in the cause-effect relationship between current levels of Cd intakes and eventual health effects in human beings; even the risk of Cd to kidney function is under considerable debate. Recent works on the importance of zinc:Cd ratio rather than Cd levels alone to determine Cd risk factors, on the one hand, and on the declining trends of Cd level in foods and soils, on the other, also indicate a lack of scientific evidence justifying more restrictive cadmium standards. This shows that developing countries should fight for changing and making more transparent the current international structures and procedures for setting sanitary and phytosanitary measures and technical barriers to trade.

Finlayson, B. J. and K. M. Verrue (1982). "TOXICITIES OF COPPER, ZINC, AND CADMIUM MIXTURES TO JUVENILE CHINOOK SALMON." Transactions of the American Fisheries Society **111**(5): 645-650.

Förlin, L., C. Haux, et al. (1986). "Biotransformation enzyme activities and histopathology in rainbow trout, Salmo gairdneri, treated with cadmium." Aquatic Toxicology **8**(1): 51-64.
The effects of intraperitoneal administration of cadmium and exposure to cadmium in the water on rainbow trout, Salmo gairdneri, were studied. The results of intraperitoneal injection of cadmium indicate that this metal has the potential to inhibit phase I and phase II xenobiotic biotransformation activities in

the liver and kidney. The exposure to cadmium through water resulted in different responses in the liver and kidney. The marked inhibition of the glucuronidation reaction is of toxicological importance, since this may potentiate the toxic action of organic xenobiotics biotransformed through this pathway. This response in the kidney was accompanied by histopathological changes in the proximal renal tubules, which are probably associated with the plasma hypocalcaemic response observed in cadmium-poisoned fish.

Francis, P. C., W. J. Birge, et al. (1984). "Effects of cadmium-enriched sediment on fish and amphibian embryo-larval stages." Ecotoxicology and Environmental Safety **8**(4): 378-387.

Aquatic toxicity tests were conducted to evaluate the effects of cadmium-enriched sediment on embryo-larval stages of the goldfish (Carassius auratus), leopard frog (Rana pipiens), and largemouth bass (Micropterus salmoides). Natural stream sediment was collected and enriched with cadmium to nominal concentrations of 1.0, 10.0, 100, and 1000 mg/kg. Enriched sediments were placed in Pyrex dishes and covered with 350 ml of reconstituted water. Fertilized eggs were placed in the dishes and maintained through 4 days posthatching, giving a total exposure time of 6 to 7 days. For all tests the cadmium concentrations ranged from 1.1 to 76.5 [mu]g/liter in water above sediments containing 1 to 1000 mg Cd/kg, respectively. Although low frequencies of mortality were observed in all tests, goldfish, leopard frog, and bass exposed to sediments enriched to 1000 mg Cd/kg accumulated 4.61, 12.55, and 60.0 [mu]g Cd/g, respectively. No significant correlations ($P < 0.05$) were found between mortality of the goldfish and leopard frog and the cadmium concentrations in either water or sediment. However, all three species showed strong correlations (r [greater-or-equal, slanted] 0.98) between cadmium concentrations in water and tissue, sediment and tissue, and water and sediment. Tissue cadmium concentrations were related to the length of time test organisms were in direct contact with cadmium-enriched sediment.

Franklin, N. M., C. N. Glover, et al. (2005). "Calcium/cadmium interactions at uptake surfaces in rainbow trout: Waterborne versus dietary routes of exposure." Environmental Toxicology and Chemistry **24**(11): 2954-2964.

Juvenile rainbow trout (Oncorhynchus mykiss) were exposed to control, 3 mu g/L waterborne Cd, or 500 mg/kg dietary Cd in combination with either a control (20 mg/g Ca2+ as CaCO3) or elevated (60 mg/g Ca2+) Ca2+ diet for 28 d. No mortality or growth effects were observed in response to either route of Cd exposure, although fish fed Ca2+-supplemented diets exhibited minor reductions in growth within the first few days of feeding. Waterborne and dietary Cd resulted in significant Cd accumulation in most tissues, with dietary uptake being far in excess of waterborne under the exposure conditions used. The order of Cd accumulation strongly reflected the exposure pathway, being gill and kidney > liver > gut > carcass (waterborne Cd); gut > kidney > liver > gill > carcass > bone (dietary Cd). On a whole-body basis, the net retention of Cd from the diet was < 1%, indicating that the gut wall forms an important protective barrier reducing Cd

accumulation into internal tissues. Dietary Ca2+ supplementation reduced short-term whole-body uptake rates of waterborne Ca2+ and Cd by > 50% and resulted in much lower chronic accumulation of Cd (via the water and diet) in target tissues. Results suggest that Call and Cd share common pathway(s)/transport mechanism(s) in the gill and gut and that increased gastrointestinal Ca2+ uptake likely caused downregulation of branchial and gastrointestinal Call and therefore Cd uptake pathways. Because nutrient metals other than Ca2+ may also influence Cd (and other metal) uptake, new regulatory approaches to metal toxicity (e.g., biotic ligand model) require understanding of the influence of dietary status on metal accumulation.

Fu, H. and R. A. C. Lock (1990). "Pituitary response to cadmium during the early development of tilapia (Oreochromis mossambicus)." Aquatic Toxicology **16**(1): 9-18.

Immunocytochemical and morphometric methods were applied to study the response of the pituitary to 10 [mu]g Cd/l during the early development of tilapia (Oreochromis mossambicus). The affinity of prolactin (PRL) cells and adrenocorticotropic hormone (ACTH) cells for immunocytochemical staining and percentage of the pituitary volume occupied by these cells (fractional volume) were used as criteria for their activity and related to survival and to tissue Na, K, Ca and water content. Exposure of embryos to Cd led, between 144 h and 288 h after fertilization, to a higher staining intensity and a significant ($P < 0.01$) increase in fractional volume of PRL cells, indicating a higher synthesizing capacity. No such changes were observed for ACTH cells during the experimental period. Immediately after hatching a significant drop in survival ($P < 0.05$) and tissue Ca-content ($P < 0.01$) was observed in Cd-exposed larvae, followed by complete recovery around 216 h and 288 h, respectively. This recovery was concomitant with an apparent increase in the synthesizing capacity of PRL cells, suggesting a decisive role of PRL at a very early stage of development to counteract adverse effects of Cd.

Ghazaly, K. S. (1992). "HEMATOLOGICAL AND PHYSIOLOGICAL-RESPONSES TO SUBLETHAL CONCENTRATIONS OF CADMIUM IN A FRESH-WATER TELEOST, TILAPIA-ZILLII." Water Air and Soil Pollution **64**(3-4): 551-559.

Blood from Tilapia zillii exposed to three sublethal concentrations of Cd (10.62, 17.70 and 24.78 mg L-1) for 24, 48, 72 and 96 hr was analyzed to identify and evaluate changes in erythrocyte count (RBC), hematocrit (Ht), hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), erythrocyte sedimentation rate (ESR), leucocyte count (WBC), differential leucocyte counts, total protein, glucose and lactic acid. Hematological and physiological changes attributable to Cd poisoning were observed. Fish showed obvious signs of stress at 17.70 and 24.78 mg L-1 Cd. Clear time related effects of Cd on the biochemical factors were recorded. The severe stress conditions caused by Cd may be responsible for the hematological and physiological changes in blood.

Giguere, A., P. G. C. Campbell, et al. (2006). "Sub-cellular partitioning of cadmium,

copper, nickel and zinc in indigenous yellow perch (Perca flavescens) sampled along a polymetallic gradient." Aquatic Toxicology **77**(2): 178-189.

Sub-cellular metal distributions were studied in indigenous yellow perch (Perca flavescens) collected from eight lakes located along a cadmium (Cd), copper (Cu), nickel (Ni) and zinc (Zn) concentration gradient. Ambient dissolved metal concentrations were measured to evaluate exposure and total hepatic metal concentrations were determined as a measure of metal bioaccumulation. Metal partitioning among potentially metal-sensitive fractions (cytosolic enzymes, organelles) and detoxified metal fractions (metallothionein) was determined after differential centrifugation of fish liver homogenates. Major proportions of hepatic Cd and Cu were found in the heat-stable cytosolic peptides and proteins fraction (HSP), a fraction including metallothioneins, whereas the potentially metal-sensitive heat-denaturable proteins fraction (HDP) was the largest contributor to the total Ni and Zn burdens. The concentrations of Cd, Cu and Ni (but not Zn) in each sub-cellular fraction increased along the metal contamination gradient, but the relative contributions of each fraction to the total burden of each of these metals remained generally constant. For these chronically exposed fish there was no threshold exposure concentration below which binding of Cd or Ni to the heat-denaturable protein fraction did not occur. The presence of Cd and Ni in the HDP fraction, even for low chronic exposure concentrations, suggests that metal detoxification was imperfect, i.e. that P. flavescens was subject to some metal-related stress even under these conditions. (c) 2005 Elsevier B.V. All rights reserved.

Gill, T. S. and J. C. Pant (1983). "Cadmium toxicity: Inducement of changes in blood and tissue metabolites in fish." Toxicology Letters **18**(3): 195-200.

The effects of acute (24 h) and chronic (90 days) cadmium (Cd) poisoning on blood and tissue metabolite levels of a teleost, Puntius conchonius were studied. Significant hyperglycemia with an increment in liver, kidney and ovary cholesterol occurred during acute Cd poisoning. By contrast, an enduring hypoglycemia and diminished levels of tissue cholesterol manifested the chronically intoxicated fish. Both acute and chronic Cd poisoning, however, caused marked hypocholesterolemia, glycogenolysis in liver and brain, and a concomitant rise in myocardium glycogen concentration. Testes cholesterol was found to be depleted after both acute and chronic (60 days) Cd poisoning.

Gill, T. S. and J. C. Pant (1985). "Erythrocytic and leukocytic responses to cadmium poisoning in a freshwater fish, Puntius conchonius ham." Environmental Research **36**(2): 327-337.

Chronically sublethal concentrations of cadmium caused conspicuous hematological anomalies in the cyprinid fish, Puntius conchonius. Exposure to 0.63 and 0.84 mg/liter cadmium chloride (1/20 and 1/15 of 96-hr LC50) induced morphological aberrations in mature erythrocytes including cytoplasmic vacuolation, hypochromia, deterioration of cellular membrane, basophilic stippling of cytoplasm, clumping of chromatin material and extrusion of nuclei, and schistocytosis. Anomalous basophils and monocytes were also encountered

though less frequently. Decreased erythrocyte counts, hemoglobin and hematocrit values were also associated with chronic cadmium poisoning. The mean corpuscular hemoglobin and mean corpuscular volume increased (30 days) but mean corpuscular hemoglobin concentration showed no obvious change. A significant thrombocytopenia (90 days), elevated small lymphocyte and basophil populations, and a mild neutropenia were manifested in the cadmium-exposed fish. Large lymphocytes were not significantly affected.

Gill, T. S., J. C. Pant, et al. (1988). "Branchial pathogenesis in a freshwater fish, Puntius conchonius ham., chronically exposed to sublethal concentrations of cadmium." Ecotoxicology and Environmental Safety **15**(2): 153-161.

Effects of sublethal concentrations, 630 and 840 [mu]g/liter (0.05 and 0.066 fractions of the 96-hr LC50), of cadmium chloride on the gills of a freshwater fish, Puntius conchonius, were examined light microscopically during a 12-week exposure. The secondary gill lamellae showed disrupted epithelium, necrosis, accumulation of cellular debris, capillary congestion, and wilting of the pillar cell system. Hypertrophy and hyperplasia of chloride cells as well as partial or complete fusion of secondary lamellae also occurred in the Cd-exposed fish. Branchial lesions together with coagulation film anoxia are likely to result in serious respiratory distress and related tissue hypoxia.

Gill, T. S., J. C. Pant, et al. (1989). "Cadmium nephropathy in a freshwater fish, Puntius conchonius hamilton." Ecotoxicology and Environmental Safety **18**(2): 165-172.

Renal pathology was examined in a freshwater fish, Puntius conchonius, during a 12-week exposure to 500, 630, and 840 [mu]g CdCl2/liter (1/25, 1/20, and 1/15 fractions of the 96-hr TLm, respectively). Multifocal tubular epithelial degeneration including severe vacuolation and nuclear pyknosis and karyorrhexis composed the most obvious lesions. The degenerative changes were found mainly in the proximal segments, while the distal segments and the collecting tubules and ducts remained unaffected. Collapsed and shrunken glomeruli and swollen Bowman's spaces were also frequently observed. The cadmium-exposed fish appeared heavily stressed and moribund. A comparison of the renal pathology with that of other fishes and mammals and possible mechanisms of cadmium nephropathy are discussed.

Golovanova, I. L., V. V. Kuz'mina, et al. (1999). "In vitro effects of cadmium and DDVP (dichlorvos) on intestinal carbohydrase and protease activities in freshwater teleosts." Comparative Biochemistry and Physiology Part C: Pharmacology, Toxicology and Endocrinology **122**(1): 21-25.

In vitro effects of cadmium (0.5-50 mg/l) and DDVP (0.2-100 mg/l) on the total amylolytic, sucrase and protease activities of intestinal mucosa have been studied for the first time in 11 freshwater teleosts. Total amylolytic activity in burbot, crucian carp and common carp, sucrase activity in blue bream and total proteolytic activity in burbot and pike were significantly decreased by cadmium at 50 mg/l. DDVP (at 0.2 mg/l) caused a significant decrease in total proteolytic activity in pike but had no effect on either protease or carbohydrase activities in

other fish species.

Gottofrey, J., I. Björklund, et al. (1988). "Effect of sodium isopropylxanthate, potassium amylxanthate and sodium diethyldithiocarbamate on the uptake and distribution of cadmium in the brown trout (Salmo trutta)." Aquatic Toxicology **12**(2): 171-184.

Brown trout, Salmo trutta, were exposed to water containing 1 [mu]g/l of 109Cd2+, alone or with sodium isopropylxanthate, potassium amylxanthate or sodium diethyldithiocarbamate, respectively. After one week the uptake and distribution of the 109Cd2+ in the fish were examined by whole-body autoradiography and gamma spectrometry. Sodium diethyldithiocarbamate was found to enhance the uptake of the 109Cd2+ in several tissues of the fish and this effect increased with increasing concentration of the carbamate. Potassium amylxanthate induced increase in the levels of 109Cd2+ in several tissues, whereas the brain was the only tissue with increased concentration of 109Cd2+ in the presence of sodium isopropyl-xanthate. A likely mechanism for the enhanced uptake of the 109Cd2+ may be a facilitated penetration over the gill membranes of the lipophilic complexes formed between the studied compounds and the cadmium. A facilitated passage through cellular membranes may also be important for the increased uptake of the metal in other tissues. An elevated uptake of cadmium by the xanthates or the diethyldithiocarbamate may constitute an increased risk for noxious effects of the metal.

Gupta, A. K. and V. K. Rajbanshi (1991). "TOXICITY OF COPPER AND CADMIUM TO HETEROPNEUSTES-FOSSILIS (BLOCH)." Acta Hydrochimica Et Hydrobiologica **19**(3): 331-340.

Static bioassay tests were conducted to determine the acute toxic effects of copper, cadmium and their mixtures on Heteropneustes fossilis in two different seasons. Median lethal concentrations (24, 48, 72 and 96 h LC50) revealed that copper is more toxic to fish even at very low concentrations in comparison to cadmium, tested separately or in combination with cadmium. The data indicate that the level of tolerance of the fish to metallic ions tested was temperature specific. Generally, fishes were found to be more susceptible to metallic ions at higher temperatures as revealed by the threshold concentration, MATC and LC50 values. The behavioural changes of the test fishes were also observed in reference to different concentrations of the metallic ions and temperatures.

Hall, L. W., M. C. Scott, et al. (1998). "Ecological risk assessment of copper and cadmium in surface waters of Chesapeake Bay watershed." Environmental Toxicology and Chemistry **17**(6): 1172-1189.

This ecological risk assessment was designed to characterize risk of copper and cadmium exposure in the Chesapeake Bay watershed by comparing the probability distributions of environmental exposure concentrations with the probability distributions of species response data determined from laboratory studies. The overlap of these distributions was a measure of risk to aquatic life. Dissolved copper and cadmium exposure data were available from six primary data sources covering 102 stations in Is basins in the Chesapeake Bay

watershed from 1985 through 1990. Highest environmental concentrations of copper (based on 90th percentiles) were reported in the Chesapeake and Delaware (C and D) Canal, Choptank River, Middle River, and Potomac River, the lowest concentrations of copper were reported in the lower and middle mainstem Chesapeake Bay and Nanticoke River. Based on the calculation of 90th percentiles, cadmium concentrations were highest in the C and D Canal, Potomac River, Upper Chesapeake Bay, and West Chesapeake watershed. Lowest environmental concentrations of cadmium were reported in the lower and middle mainstem Chesapeake Bay and Susquehanna River. The ecological effects data used for this risk assessment were derived primarily from acute copper and cadmium laboratory toxicity tests conducted in both fresh water and salt water, chronic data were much mon limited. The 10th percentile (concentration protecting 90% of the species) for all species derived from the freshwater acute copper toxicity database was 8.3 mu g/L. For acute saltwater copper data, the 10th percentile for all species was 6.3 mu g/L copper, The acute 10th percentile for all species in the freshwater cadmium database was 5.1 mu g/L cadmium. The acute 10th percentile for all saltwater species was 31.7 mu g/L cadmium. Highest potential ecological risk from copper exposures was reported in the C and D Canal area of the northern Chesapeake Bay watershed. Relatively high potential ecological risk from copper exposure was also reported in Middle River. Moderate potential ecological risk from copper exposure was reported in selected locations in the Choptank and Potomac Rivers. Potential ecological risk from copper exposure was either low or data were insufficient to assess ecological risk in the other 14 basins. Potential ecological risk from cadmium exposures was much lower than for copper. Highest potential ecological risk from cadmium exposure was reported in the C and D Canal. Low to moderate potential ecological risk: for the most sensitive trophic group (fish) was reported in the Potomac River, upper mainstem bay, West Chesapeake watershed, Choptank River. and Chester River. In the other 12 basins, ecological risk was either judged to be low or insufficient data were available for determining risk.

Hallare, A. V., M. Schirling, et al. (2005). "Combined effects of temperature and cadmium on developmental parameters and biomarker responses in zebrafish (Danio rerio) embryos." Journal of Thermal Biology **30**(1): 7-17.

To determine the interactions between temperature and cadmium on zebrafish (Danio rerio) development.. fertilized eggs were exposed to combinations of three temperature levels (21 degreesC. 26 degreesC. and 33 degreesC) and six cadmium concentrations (0, 0.25 0.5 2.0. 5.0. and 10.0mg/L). Endpoints used included LC50 value (48h), developmental rate. mortality, heart rate. hatching success. liver histopathology, embryo abnormalities, and heat shock protein (hsp) induction. Results showed a significant acceleration in the developmental rate with increasing temperature and irrespective of the presence of cadmium. Data on LC50 and ELS-test revealed that simultaneous exposure to both cadmium ions and cold stress (21 degreesC) was highly detrimental to growing ernbryos, causing a pronounced mortality and a significant reduction in average

heart rate and embryo hatchability. In contrast. no similar reactions to cadmium were observed in pre-hatched embryos exposed to both control (26degreesC) and high temperature (33degreesC), and this can be explained by the significantly higher expression of hsp (hsp70) in embryos at these temperatures. Upon hatching, however, the larvae showed increased sensitivity to cadmium. The severity of malformations in the post-hatched larvae was in the order: hot cadmium stress>cold cadmium stress>cadmium stress alone>no stress at all. Liver histopathology as well as depletion in glycogen reserves exhibited greater severity with increasing cadmium concentration, irrespective of temperature. The present study confirms that temperature effectively confounds cadmium toxicity and needs to be considered-for the accurate prediction and assessment of cadmium-induced toxicity in fish. (C) 2004 Elsevier Ltd. All rights reserved.

Hamilton, S. J., P. M. Mehrle, et al. (1987). "CADMIUM-SATURATION TECHNIQUE FOR MEASURING METALLOTHIONEIN IN BROOK TROUT." Transactions of the American Fisheries Society **116**(4): 541-550.

Hamilton, S. J., P. M. Mehrle, et al. (1987). "EVALUATION OF METALLOTHIONEIN MEASUREMENT AS A BIOLOGICAL INDICATOR OF STRESS FROM CADMIUM IN BROOK TROUT." Transactions of the American Fisheries Society **116**(4): 551-560.

Hammock, D., C. C. Huang, et al. (2003). "The effect of humic acid on the uptake of mercury(II), cadmium(II), and zinc(II) by Chinook salmon (Oncorhynchus tshawytscha) eggs." Archives of Environmental Contamination and Toxicology **44**(1): 83-88.

The Chinook salmon (Oncorhynchus tshawytscha) is endangered or threatened in several of its ranges. The uptake of metals by Chinook salmon eggs and how humic acid (HA) affects the uptake is a subject of interest. Humic acid (0, 0.001, 0.01, and 0.05g/l) reduces the uptake of the metal ions Hg(II), Cd(II), and Zn(II), (1.0 muM) by eggs. HA is more effective in reducing the uptake of Hg than that of Cd or Zn. At [HA] = 0.001 g/L Hg uptake is reduced by 44% compared to no HA, while Cd and Zn uptakes are slightly or not reduced. Once the metals are taken up by the eggs, Hg migrates more slowly from the chorion to the yolk than either Zn or Cd. In experiments in which the metal contents of the chorion and yolk were measured at up to 24 h and five days after uptake, the order of migration was Cd > Zn > Hg. This observation is important when discussing the effects of metals on biological processes in the yolk because when Hg is taken up by eggs, a smaller percentage reaches the yolk than does Cd and Zn.

Handy, R. D. (1992). "THE ASSESSMENT OF EPISODIC METAL POLLUTION .2. THE EFFECTS OF CADMIUM AND COPPER ENRICHED DIETS ON TISSUE CONTAMINANT ANALYSIS IN RAINBOW-TROUT (ONCORHYNCHUS-MYKISS)." Archives of Environmental Contamination and Toxicology **22**(1): 82-87.

Rainbow trout, Oncorhynchus mykiss, were fed on a commercial feed enriched with either Cd or Cu for 32 days and allowed to recover on normal food for 12 days. The body burden of fish fed Cd-enriched diet increased from about 0.05 to 0.39-mu-g/g wet weight, reflected by elevation in the Cd content of gill, liver,

blood plasma, kidney, skin, mucus, and whole gut. Muscle Cd content did not alter. Most organs remained contaminated with Cd after 12 days depuration. The body burden of animals fed Cu-enriched diet increased from about 1.2 to 1.5-mu-g/g wet weight, with the gill, whole gut, blood plasma, skin, and mucus contaminated after 32 days, no changes in the liver and muscle occurred. All organs, except the gill and kidney, returned to control values after 12 days depuration. In exposed animals, 76 and 53% of the Cd or Cu body burden, respectively, were contained in the gut, unlike waterborne exposure. Differences in the body distribution of toxicants after intermittent waterborne and dietary exposure may identify the principal routes of pollutant uptake. Ratios of toxicant concentrations in gill/liver may establish the exposure status of fish, but cannot be used to differentiate dietary and waterborne contamination. Analysis of mucus may identify waterborne Cu exposure, dietary and waterborne contributions to mucus Cd content are more difficult to establish.

Hansen, J. A., P. G. Welsh, et al. (2002). "Relative Sensitivity of Bull Trout (Salvelinus Confluentus) and Rainbow Trout (Oncorhynchus Mykiss) to Acute Exposures of Cadmium and Zinc." Environmental Toxicology and Chemistry **21**(1): 67-75.

Bull trout (Salvelinus confluentus) were recently listed as threatened in the United States under the federal Endangered Species Act. Present and historical habitat of this species includes waterways that have been impacted by metals released from mining and mineral processing activities. We conducted paired bioassays with bull trout and rainbow trout (Oncorhynchus mykiss) to examine the relative sensitivity of each species to Cd and Zn independently and as a mixture. A total of 15 pairs of acute toxicity bioassays were completed to evaluate the effects of different water hardness (30 or 90 mg/L as CaCO3), pH (6.5 or 7.5), and temperature (8 or 12 degreesC) on Cd and Zn toxicity. For both species, the acute toxicity of both Cd and Zn was greater than previously observed in laboratory studies. Bull trout were about twice as tolerant of Cd and about 50% more tolerant of Zn than were rainbow trout. Higher hardness and lower pH water produced lower toxicity and slower rates of toxicity in both species. Elevated temperature significantly increased the sensitivity of bull trout to Zn but decreased the sensitivity (not significantly) of rainbow trout to Zn. At a hardness of 30 mg/L, the toxicity values (i.e., median lethal concentration; 120-h LC50) for both species were lower than the current U.S. national water quality criteria for protection of aquatic life, indicating that current national criteria may not be protective of sensitive salmonids-including the threatened bull trout-in low calcium waters.

Hansen, J. A., P. G. Welsh, et al. (2002). "The effects of long-term cadmium exposure on the growth and survival of juvenile bull trout (Salvelinus confluentus)." Aquatic Toxicology **58**(3-4): 165-174.

Bull trout (Salvelinus confluentus) have been listed recently as threatened in the United States under the federal Endangered Species Act. This species currently resides, or historically resided, in several waterways that either are impacted or are under threat of impact from metals mining activities. We conducted a 55-day

sub-chronic (i.e. sublethal) cadmium (Cd) exposure in water at 30 mg l-1 (as CaCO3) hardness, pH 7.5, and 8 °C. Exposures were conducted using six replicate exposure tanks for each of the six treatments (five Cd concentrations and one control). Measured Cd concentrations were <0.013 (control), 0.052, 0.089, 0.197, 0.383, and 0.786 [mu]g Cd l-1. Exposure to 0.786 [mu]g Cd l-1 caused increased mortality (37%) and reduced growth (28% reduction in weight change) in fish exposed for 55 days. All Cd exposure concentrations caused significant whole body accumulation of Cd compared with controls. Our results indicate that even though fish are significantly accumulating Cd in each non-control treatment, growth reductions in bull trout occurred only at Cd concentrations that also caused significant mortality. The Cd concentration that reduced growth and survival in this long-term exposure (0.786 [mu]g Cd l-1) is greater than the recently-revised US federal aquatic life criteria (ALC) value for the corresponding hardness concentration (ALC=0.62 [mu]g Cd l-1 for acute effects and 0.11 [mu]g Cd l-1 for chronic effects).

Harper, D. D., A. M. Farag, et al. (2008). "Effects of acclimation on the toxicity of stream water contaminated with zinc and cadmium to juvenile cutthroat trout." Archives of Environmental Contamination and Toxicology **54**(4): 697-704.

We investigated the influence of acclimation on results of in situ bioassays with cutthroat trout in metal-contaminated streams. Cutthroat trout (Oncorhynchus clarki) were held for 21 days (1) in live containers at a reference or "clean" site having dissolved metals near detection limits (0.01 mu g/L cadmium [Cd] and 2.8 mu g/L zinc [Zn]; hardness 32 mg/L as CaCO3) and (2) at a site in a mining-impacted watershed having moderately increased metals (0.07 mu g/L Cd and 38 to 40 mu g/L Zn; hardness 50 mg/L as CaCO3). The 96-hour survival of each treatment group was then tested in situ at five sites from September 5 to 9, 2002, and each group exhibited a range of metal concentrations (0.44 to 39 mu g/L arsenic [As], 0.01 to 2.2 mu g/L Cd, and 0.49 to 856 mu g/L Zn). Survival was 100% at three sites for both treatments. However, a higher percentage of metal-acclimated fish survived at the site with the second highest concentrations of Cd and Zn (0.90 and 238 mu g/L, respectively) compared with fish acclimated at the reference site (100% vs. 55%, respectively). Survival was 65% for acclimated fish and 0% for metal-naive fish at the site with the largest metal concentrations (2.2 mu g/L Cd and 856 mu g/L Zn). Water collected from the site with the largest concentrations of dissolved metals (on October 30, 2002) was used in a laboratory serial dilution to determine 96-hour LC50 values. The 96-hour LC50 estimates of naive fish during the in situ and laboratory experiments were similar (0.60 mu g Cd/L and 226 mu g Zn/L for in situ and 0.64 mu g Cd/L and 201 mu g Zn/L for laboratory serial dilutions). However, mortality of naive cutthroat trout tested under laboratory conditions was more rapid in dilutions of 100%, 75%, and 38% site water than in situ experiments.

Haux, C. and Å. Larsson (1984). "Long-term sublethal physiological effects on rainbow trout, Salmo gairdneri, during exposure to cadmium and after subsequent recovery." Aquatic Toxicology **5**(2): 129-142.

The effects on hematology, blood plasma ion balance and carbohydrate metabolism were studied in rainbow trout, Salmo gairdneri, kept in brackish water, and after 18 and 30 wk of exposure to sublethal levels of cadmium (10 and 100 [mu]g Cd/liter), after 25 and 57 wk of subsequent recovery in clean water. Cadmium exposure caused anemia, hypocalcemia and hypermagnesemia. These effects have previously been observed in fish during shorter periods of exposure, but disappeared in the present study within 25 wk of recovery. This suggests that it is the presence of free cadmium ions during the exposure that is responsible for most of the hematological and biochemical effects. Contrary to these findings, the hyperglycemia, that was present during the exposure, persisted throughout the recovery period. Further evidence for a disturbed carbohydrate metabolism after cessation of the exposure was indicated by a dose-dependent decrease in muscle glycogen content after 25 wk of recovery, and by a dose-dependent increase in liver glycogen content after 57 wk of recovery. These effects on the carbohydrate metabolism could be mediated via the selective uptake of cadmium ions in the pancreas and an inhibitory effect on the insulin secretion, thus resulting in an abnormal endocrine control of the metabolism. Analyses of cadmium revealed a dose-dependent accumulation of cadmium in the muscle, that had reached equilibrium after 18 wk of exposure, while a continuing and dose-dependent accumulation was found in the liver throughout the exposure. The levels attained in the liver were about 100 times higher than in the muscle. The slow elimination from liver and kidney suggest a biological half-life for cadmium of more than 1 yr in these tissues. A close positive correlation was found between cadmium levels in liver and in kidney (r = 0.90) in fish after 57 wk of recovery.

Hollis, L., J. C. McGeer, et al. (1999). "Cadmium accumulation, gill Cd binding, acclimation, and physiological effects during long term sublethal Cd exposure in rainbow trout." Aquatic Toxicology **46**(2): 101-119.

Juvenile rainbow trout, on 3% of body weight daily ration, were exposed to 0 (control), 3, and 10 mu g l(-1) Cd (as Cd(NO3)(2). 4H(2)O) in moderately hard (140 mg l(-1) as CaCO3), alkaline (95 mg l(-1) as CaCO3, pH 8.0) water for 30 days. Particular attention focused on acclimation, and on whether a gill surface binding model, originally developed in dilute softwater, could be applied in this water quality to fish chronically exposed to Cd. Only the higher Cd concentration caused mortality (30%, in the first few days). The costs of acclimation, if any, in our study were subtle since no significant effects of chronic Cd exposure were seen in growth rate, swimming performance (stamina and U-Crit), routine O-2 consumption, or whole body ion levels. Substantial acclimation occurred in both exposure groups, manifested as 11- to 13-fold increases in 96-h LC50 values. In water quality regulations, which are based on toxicity tests with non-acclimated fish only, this remarkable protective effect of acclimation is not taken into account. Cd accumulated in a time- and concentration-dependent fashion to 60-120 x (gills), 8-20 x (liver), 2-7 x (carcass), and 5-12 x (whole bodies) control levels by 30 days. Chronically accumulated gill Cd could not be removed by ethylenediaminetetraacetic acid (EDTA) challenge. These gill Cd concentrations

were 20- to 40-fold greater than levels predicted by the gill-binding model to cause mortality during acute exposure. In short-term gill Cd-binding experiments (up to 70 mu g l(-1) exposures for 3 h), gill Cd burden increased as predicted in control fish, but was not detectable against the high background concentrations in acclimated fish. In light of these results, Cd uptake/turnover tests were performed using radioactive Cd-109 to improve sensitivity. With this approach, a small saturable binding component was seen, but could not be related to toxic response in acclimated fish. Acclimated trout internalized less Cd-109 than control fish, but interpretation was complicated by the possibility of radioisotopic exchange and specific activity dilution in the large 'cold' Cd pool on the gills. We conclude that gill Cd burden is not predictive of mortality in acclimated fish, that the present gill modelling approach does not work in acclimated fish, and that longer term Cd-109 turnover studies are needed for this purpose. (C) 1999 Elsevier Science B.V. All rights reserved.

Hollis, L., L. Muench, et al. (1997). "Influence of dissolved organic matter on copper binding, and calcium on cadmium binding, by gills of rainbow trout." Journal of Fish Biology **50**(4): 703-720.

Complexation of Cu by 5 mg C l(-1) dissolved organic matter (DOM) from a marsh kept Cu from binding to gills of small rainbow trout Oncorhynchus mykiss in 9-day exposures to 0.5 mu m Cu in soft water. The protective effect of DOM occurs because the formation of Cu-DOM complexes reduces the amount of free Cu in the water, so the disruptive effects of Cu on ionoregulation, such as inhibited Na uptake, cannot develop. The Cu-DOM complexes themselves do not bind to the gills. Calcium (1100 mu M) reduced the accumulation of Cd by trout gills in short, 2-h exposures through competition for gill binding sites but not over longer, 7-day exposures to 0.14 mu M Cd. However, the protective effect of Ca against Cd toxicity persisted throughout the longer experiment, likely due to the decrease in the electrochemical gradient for diffusive loss of Ca from the fish to the water. Rainbow trout and fathead minnows Pimephales promelas accumulated Cu and Cd on their gills in a similar manner; thus, binding constants for metal-gill interactions determined for one species of fish can be generalized to other fish species. When literature binding constants determined for fathead minnows were applied to our studies with rainbow trout, computer modelling of Cu-gill and Cu-DOM interactions simulated our results well. In contrast Cd-gill and Ca-gill modelling predicted the initial competitive effect of Ca against Cd accumulation by trout gills, but did not predict the longer-term accumulation of Cd by trout gills. (C) 1997 The Fisheries Society of thr British Isles.

Honda, R. T., M. Fernandes-de-Castilho, et al. (2008). "Cadmium-induced disruption of environmental exploration and chemical communication in matrinxã, Brycon amazonicus." Aquatic Toxicology **89**(3): 204-206.

The effects of cadmium exposure on both environment exploration and behavioral responses induced by alarm substance in matrinxã (Brycon amazonicus), a fish species endemic to the Amazon basin, were investigated. Fish exposed to 9.04 ± 0.07 [mu]g/L waterborne cadmium for 96 h followed by

24 h depuration period in clean water, were video-recorded for 15 min, followed by immediate introduction of conspecific skin extract to the tank and a new 30 min period of fish video-recording. Cd-exposed matrinxã showed a significantly lowered locomotor activity (t-test t12 = 2.7; p = 0.025) and spatial distribution (t-test t12 = 2.4; p = 0.03) relative to the unexposed control fish prior to the alarm substance introduction, and did not present any significant reaction when the skin extract was introduced. The control fish, in opposite, showed a higher level of activity and spatial distribution prior the skin extract contact and significantly decreased their response after the chemical stimulus (locomotion--repeated-measure ANOVA F1,11 = 5.6; p = 0.04; spatial distribution F1,11 = 19.4; p = 0.001). In conclusion, exposure to a low level of cadmium affects both the environment exploration performance and the conspecific chemical communication in matrinxã. If the reduced environmental exploration performance of Cd-exposed fish is an adjustment to the compromised chemical communication or an independent effect of cadmium is the next step to be investigated.

Huang, Z. Y., Q. Zhang, et al. (2007). "Bioaccumulation of metals and induction of metallothioneins in selected tissues of common carp (Cyprinus carpio L.) co-exposed to cadmium, mercury and lead." Applied Organometallic Chemistry **21**(2): 101-107.

The concentrations of mercury (Hg), cadmium (Cd) and lead (Pb) at various exposure periods were determined in the gill, kidney, liver and muscle of common carp (Cyprinus carpio L.) co-exposed to 1.0 mu g ml(-1) each of Cd2+, Hg2+ and Pb2+ for up to 10 days. Metallothionein fractions (MTs) in these organs were characterized using the hyphenated technique of size-exclusion chromatography (SEC) and inductively coupled plasma mass spectrometry (ICP-MS). After 10 days of exposure, maximum toxic metal concentrations of Hg, Cd and Pb were 10.7 (gill), 0.145 (kidney) and 0.112 mu g g(dry weight)(-1) (gill), respectively. The pattern of accumulation of Hg and Pb was in the order gill > kidney > liver > muscle. In the case of Cd, accumulation was in the order kidney > gill > liver > muscle. Cd and Hg binding MTs were significantly induced in the gill, kidney and liver of all the exposure groups in comparison with the control group ($p < 0.05$), and the amounts of them increased with the longer exposure time. Despite the higher intracellular Hg concentration and the stronger Hg-SH binding affinity, the amount of Cd-binding MTs was much higher than that of Hg-binding MTs. The results indicate that NIT synthesis in these organs was clearly metal-specific. MTs in gill may be used as a bio-marker to detect the metal pollution caused by Hg and Cd. Zinc and copper binding MTs in the organs of the exposed fish were also increased. This may be due to the MTs' important role in the homeostatic regulation of essential metals and their protective role against the acute toxicity of non-essential metals. Even though there was considerable accumulation of lead in the organs of the exposed fish, Pb-binding MT synthesis was non-significant. Copyright (c) 2006 John Wiley & Sons, Ltd.

Hutchinson, T. H. and M. J. Manning (1996). "Effect of in vivo cadmium exposure on the respiratory burst of Marine Fish (Limanda limanda L.) phagocytes." Marine

Environmental Research **41**(4): 327-342.

Following the in vivo exposure of dab (Limanda limanda L.) to cadmium chloride, kidney phagocytes were collected and their respiratory burst measured in vitro using chemiluminescence. Fish were exposed to mean measured concentrations of 1.3, 2.7 and 5.5 mg Cd litre-1 (as total cadmium ion) for a total of nine weeks, followed by a three week depuration period in clean sea water. Compared with control fish, the respiratory burst of kidney phagocytes from dab sampled after six weeks was significantly reduced in the 2.7 and 5.5 mg Cd litre-1 treatments (Steel's test, $p < 0.05$). Significant reductions were observed in the respiratory burst of phagocytes from all cadmium exposed fish compared with control fish after nine weeks (Steel's test, $p < 0.05$). After a further three week depuration period in clean sea water, the respiratory burst of phagocytes from fish previously exposed to 1.3 and 2.7 mg Cd litre-1 were still significantly less than in the control group (Steel's test, $p < 0.05$). Muscle tissue cadmium concentrations were also analysed, although there was no clear relationship between the muscle total cadmium levels and kidney phagocyte chemiluminescence. The results are discussed with respect to the possible mechanism(s) of cadmium immunotoxicity in dab and recommendations made for future work.

Hutchinson, T. H., T. D. Williams, et al. (1994). "Toxicity of cadmium, hexavalent chromium and copper to marine fish larvae (Cyprinodon variegatus) and copepods (Tisbe battagliai)." Marine Environmental Research **38**(4): 275-290.

For comparative purposes, the toxicity of cadmium, hexavalent chromium and copper to marine fish larvae (Cyprinodon variegatus) and copepods (Tisbe battagliai) has been evaluated. Toxicity to fish larvae was measured in terms of survival and growth over 7 days, whilst toxicity to copepods was assessed in terms of survival and reproduction after 8 days exposure. For fish larvae, 96 h LC50 values (based on mean measured concentrations of total metal ion) were 1.23 mg Cd/litre, 31.6 mg Cr6+/litre and >0.22 mg Cu/litre. Subchronic values (SChVs) for larval fish survival and growth after 7 days were 0.75 mg Cd/litre, 24.0 mg Cr6+/litre and 0.16 mg Cu/litre. For copepod nauplii and adults, 96 h LC50 values were as follows: 0.46 mg Cd/litre and 0.34 mg Cd/litre, respectively; 1.60 Cr6+/litre, and 5.9 mg Cr6+/litre respectively; and 0.064 mg Cu/litre and 0.088 mg Cu/litre, respectively. SChVs for naupliar survival and adult survival or reproduction after 8 days were 0.024 mg Cd/litre, 0.42 mg Cr6+/litre and 0.008 mg Cu/litre.

Hutchinson, T. H., T. D. Williams, et al. (1994). "TOXICITY OF CADMIUM, HEXAVALENT CHROMIUM AND COPPER TO MARINE FISH LARVAE (CYPRINODON-VARIEGATUS) AND COPEPODS (TISBE BATTAGLIAI)." Marine Environmental Research **38**(4): 275-290.

For comparative purposes, the toxicity of cadmium, hexavalent chromium and copper to marine fish larvae (Cyprinodon variegatus) and copepods (Tisbe battagliai) has been evaluated. Toxicity to fish larvae was measured in terms of survival and growth over 7 days, whilst toxicity to copepods was assessed in tel ms of survival and reproduction after 8 days exposure. For fish larvae, 96 h

LC(50) values (based on mean measured concentrations of total metal ion) were 1.23 mg Cd/litre, 31.6 mg Cr6+/litre and >0.22 mg Cu/litre. Subchronic values (SChVs) for larval fish survival and growth after 7 days were 0.75 mg Cd/litre, 24.0 mg Cr6+/litre and 0.16 mg Cu/litre. For copepod nauplii and adults, 96 h LC(50) values were as follows. 0.46 mg Cd/litre and 0.34 mg Cd/litre, respectively, 1.60 Cr6+/litre, and 5.9 mg Cr6+/litre respectively; and 0.064 mg Cu/litre and 0.088 mg Cu/litre, respectively. SChVs foR naupliar survival and adult survival or reproduction after 8 days were 0.024 mg Cd/litre, 0.42 mg Cr6+/litre and 0.008 mg Cu/litre.

James, V. A. and T. Wigham (1986). "The effects of cadmium on prolactin cell activity and plasma cortisol levels in the rainbow trout (Salmo gairdneri)." Aquatic Toxicology **8**(4): 273-280.

Treatment of rainbow trout with cadmium by intraperitoneal injection (4.4 and 7.7 mg·kg-1), exposure in tank water (0.5, 1 and 10 mg·l-1) or incubation of trout pituitary glands in medium containing cadmium (50 mg·l-1) had no consistent effect on prolactin cell activity. Exposure of trout to 0.05 and 0.1 mg·l-1 of cadmium in the tank water produced time-dependent changes in plasma cortisol levels which may reflect the alarm, resistance and exhaustion stages in the response of the fish to the cadmium.

John, J., E. T. Gjessing, et al. (1987). "Influence of aquatic humus and pH on the uptake and depuration of cadmium by the atlantic salmon (Salmo Salar L.)." Science of the Total Environment **62**: 253-265.

Uptake and release of cadmium by Atlantic salmon at the concentrations near the background values for fresh water have been studied using cadmium labelled with Cd-109. Cumulation constant and biological half-time of release were established for different concentrations of humus and values of pH. The uptake is strongly dependent on the concentration of humus, showing a pronounced maximum at a DOC concentration of ?.7 mg/1. Release of cadmium is relatively slow, the biological half-time exceeds one year in the water without humic substances. Calculated bioconcentration factors range from 130 to several thousands, which may explain the wide differences of bioconcentration factor reported for natural systems. A general equation enabling calculation of bioconcentration factors for various conditions has been derived. An attempt is done to discuss the results from the point of view of physico-chemical forms of cadmium in respective waters. The amount of cadmium adsorbed on the surface of the fish was proved to be insignificant when compared with total concentration of cadmium bioaccumulated in the fish.

Jones, I., P. Kille, et al. (2001). "Cadmium delays growth hormone expression during rainbow trout development." Journal of Fish Biology **59**(4): 1015-1022.

Growth hormone (GH) mRNAs were first detected in rainbow trout Oncorhynchus mykiss during organogenesis (stage 29) within a control group while Gli expression in cadmium exposed embryos was not detected until a later organogenic period (stage 31). GH transcripts were subsequently detected at all

further developmental stages analysed within both treatment groups. These included hatching (stage 32), larval development (stages 33, 34, 35 and 36) and first feeding (stage 37). These results confirm that the GH axis is functional during early rainbow trout development and demonstrate an in vivo endocrine disrupting capacity at the molecular level for cadmium in teleosts. This is of particular relevance to freshwater habitats as heavy metal induced endocrine disruption may be a contributing factor in the decline of salmonid populations. (C) 2001 The Fisheries Society of the British Isles.

Kamunde, C. (2009). "Early subcellular partitioning of cadmium in gill and liver of rainbow trout (Oncorhynchus mykiss) following low-to-near-lethal waterborne cadmium exposure." Aquatic Toxicology **91**(4): 291-301.

Non-essential metals such as cadmium (Cd) accumulated in animal cells are envisaged to partition into potentially metal-sensitive compartments when detoxification capacity is exceeded. An understanding of intracellular metal partitioning is therefore important in delineation of the toxicologically relevant metal fraction for accurate tissue residue-based assessment of toxicity. In the present study, the early intracellular Cd accumulation was studied to test the prediction that it conforms to the spillover model of metal toxicity. Juvenile rainbow trout (10-15 g) were exposed for 96 h to three doses of cadmium (5, 25 and 50 [mu]g/l) and a control (nominal 0 [mu]g/l Cd) in hard water followed by measurement of the changes in intracellular Cd concentrations in the gill and liver, and carcass calcium (Ca) levels. There were dose-dependent increases in Cd concentration in both organs but the accumulation pattern over time was linear in the liver and biphasic in the gill. The Cd accumulation was associated with carcass Ca loss after 48 h. Comparatively, the gill accumulated 2-4× more Cd than the liver and generally the subcellular compartments reflected the organ-level patterns of accumulation. For the gill the rank of Cd accumulation in subcellular fractions was: heat-stable proteins (HSP) > heat-labile proteins (HLP) > nuclei > microsomes-lysosomes (ML) >= mitochondria > resistant fraction while for the liver it was
HSP > HLP > ML > mitochondria > nuclei > resistant fraction. Contrary to the spillover hypothesis there was no exposure concentration or internal accumulation at which Cd was not found in potentially metal-sensitive compartments. The proportion of Cd bound to the metabolically active pool (MAP) increased while that bound to the metabolically detoxified pool (MDP) decreased in gills of Cd-exposed fish but remained unchanged in the liver. Because the Cd concentration increased in all subcellular compartments while their contribution to the total increased, decreased or remained unchanged following Cd exposure, use of percentage data to infer spillover requires caution.

Kargin, F. and H. Y. Cogun (1999). "Metal interactions during accumulation and elimination of zinc and cadmium in tissues of the freshwater fish Tilapia nilotica." Bulletin of Environmental Contamination and Toxicology **63**(4): 511-519.

Kim, S.-G., J.-H. Jee, et al. (2004). "Cadmium accumulation and elimination in tissues of

juvenile olive flounder, Paralichthys olivaceus after sub-chronic cadmium exposure." Environmental Pollution **127**(1): 117-123.

Experiments were carried out to investigate the accumulation and elimination of cadmium (Cd) in tissues (gill, intestine, kidney, liver and muscle) of juvenile olive flounder, Paralichthys olivaceus, exposed to sub-chronic concentrations (0, 10, 50, 100 [mu]g l-1) of Cd. Cd exposure resulted in an increased Cd accumulation in tissues of flounder with exposure periods and concentration, and Cd accumulation in gill and liver increased linearly with the exposure time. At 20 days of Cd exposure, the order of Cd accumulation in organs was gill > intestine > liver > kidney > muscle and after 30 days of exposure, those were intestine > gill > liver > kidney > muscle. An inverse relationship was observed between the accumulation factor (AF) and the exposure level, but AF showed an increase with exposure time. During the depuration periods, Cd concentration in the gill, intestine and liver decreased immediately following the end of the exposure periods. No significant difference was found Cd in concentration in the kidney and muscle during depuration periods. The order of Cd elimination rate in organs were decreased intestine > liver > gill during depuration periods.

Klinck, J. S., W. W. Green, et al. (2007). "Branchial cadmium and copper binding and intestinal cadmium uptake in wild yellow perch (Perca flavescens) from clean and metal-contaminated lakes." Aquatic Toxicology **84**(2): 198-207.

Branchial binding kinetics and gastro-intestinal uptake of copper and cadmium where examined in yellow perch (Perca flavescens) from a metal-contaminated lake (Hannah Lake, Sudbury, Ontario, Canada) and an uncontaminated lake (James Lake, North Bay, Ontario, Canada). An in vivo approach was taken for gill binding comparisons while an in vitro gut binding assay was employed for gastro-intestinal tract (GIT) uptake analysis. By investigating metal uptake at the gill and the gut we cover the two main routes of metal entry into fish. Comparisons of water and sediment chemistries, metal burdens in benthic invertebrate, and metal burdens in the livers of perch from the two study lakes clearly show that yellow perch from Hannah L. are chronically exposed to a highly metal-contaminated environment compared to a reference lake. We found that metal-contaminated yellow perch showed no significant difference in gill Cd binding compared to reference fish, but they did show significant decreases in new Cd binding and absorption in their GITs. The results show that gill Cd binding may involve low-capacity, high-affinity binding sites, while gastro-intestinal Cd uptake involves binding sites that are high-capacity, low-affinity. From this we infer that Cd may be more critically controlled at the gut rather than gills. Significant differences in branchial Cu binding (increased binding) were observed in metal-contaminated yellow perch. We suggest that chronic waterborne exposure to Cu (and/or other metals) may be the dominant influence in gill Cu binding rather than chronic exposure to high Cu diets. We give supporting evidence that Cd is taken up in the GIT, at least in part, by a similar pathway as Ca2+, principally that elevated dietary Ca2+ reduces Cd binding and uptake. Overall our study reveals that metal pre-exposure via water and diet can alter uptake kinetics of Cu and Cd at the gill and/or the gut.

Klinck, J. S., T. Y. T. Ng, et al. (2009). "Cadmium accumulation and in vitro analysis of calcium and cadmium transport functions in the gastro-intestinal tract of trout following chronic dietary cadmium and calcium feeding." Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology **150**(3): 349-360.

Juvenile rainbow trout (Oncorhynchus mykiss) were fed diets made from Lumbriculus variegatus containing environmentally relevant concentrations of Cd (~ 0.2 and 12 [mu]g g- 1 dry wt) and/or Ca (1, 10, 20 and 60 mg g- 1 dry wt) for 4 weeks. Ten fish per treatment were removed weekly for tissue metal burden analysis. In all portions of the gastro-intestinal tract (GIT) (stomach, anterior, mid, and posterior intestine), chronic exposure to elevated dietary Ca decreased Cd tissue accumulation to varying degrees. At week five, the GITs of the remaining fish were subjected to an in vitro gut sac technique. Pre-exposure to the different treatments affected unidirectional uptake and binding rates of Cd and Ca in different manners, dependent on the specific GIT section. Ca and Cd uptake rates were highly correlated within all sections of the GIT, and the loosely binding rate of Cd to the GIT surfaces predicted the rate of new Cd absorption. Overall, this study indicates that elevated dietary Ca is protective against Cd uptake from an environmentally relevant diet, and that Ca and Cd uptake may occur through both common and separate pathways in the GIT.

Kraemer, L. D., P. G. C. Campbell, et al. (2008). "Modeling cadmium accumulation in indigenous yellow perch (Perca flavescens)." Canadian Journal of Fisheries and Aquatic Sciences **65**(8): 1623-1634.

We used field data from transplantation and caging Studies With juvenile yellow perch (Perca flavescens) to test a kinetic bioaccumulation model for cadmium (Cd). The model, which considers both dietary and aqueous sources of Cd, was first used to predict the dynamics of Cd accumulation in perch exposed to high ambient Cd for 70 days. Model simulations for hepatic Cd agreed well with the observed time course of Cd accumulation in (lie liver, but for the gills and gut, the predicted accumulations after 70 days were about three times higher than the observed values, suggesting that these latter organs can alter their ability to take Lip and (or) eliminate Cd. The model was also used to predict steady-state Cd concentrations in the gills, gut, and liver of perch living in lakes along a Cd gradient. Agreement between predicted and observed steady-state Cd concentrations was reasonable in lakes with low to moderate Cd concentrations, but in lakes with high dissolved Cd (>1.5 nmol.L-1), the model overestimated Cd accumulation, particularly in the gills and gut. These results suggest that kinetic bioaccumulation models may better apply to some organs than to others. Because metal-induced toxicity is normally organ-specific, their application in a risk assessment context should be undertaken with caution.

Krause, P. R. and R. N. Bray (1994). "Transport of cadmium and zinc to rocky reef communities in feces of the blacksmith (Chromis punctipinnis), a planktivorous fish." Marine Environmental Research **38**(1): 33-42.

The blacksmith (Chromis punctipinnis), an abundant planktivorous reef fish off

southern California, releases fecal material as it forages in the water column during the day and shelters in reefs at night. This behavior results in direct transportation of cadmium and zinc to reef communities. Cadmium and zinc concentrations, measured in fish feces after digestion in weak hydrochloric acid to better assess metal levels potentially available to detritivores, averaged 24·2 [mu]g cadmium and 368 [mu]g zinc g-1 dry weight of feces. Concentrations of both metals varied significantly among the five sampling dates. Fresh feces spiked with 109Cd and 65Zn adsorbed additional metals for 9 and 6 h, respectively, but the increase was negligible (<0·1%). The total amount of weak-acid-leachable cadmium and zinc egested by sheltering blacksmiths is approximately 4·4 [mu]g and 66·8 [mu]g m-2 night-1, respectively, and may represent more cadmium and almost as much zinc as is transported by the passive settlement of particulate material from the water column. This transport mechanism between planktonic and benthic communities via feces of reef fishes is probably widespread in temperate and tropical seas.

Lacroix, A. and A. Hontela (2006). "Role of calcium channels in cadmium-induced disruption of cortisol synthesis in rainbow trout (Oncorhynchus mykiss)." Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology **144**(2): 141-147.

The mechanisms of toxicity of cadmium (Cd2+) in adrenal steroidogenesis were investigated in vitro in adrenocortical cells of rainbow trout (Oncorhynchus mykiss). Toxicity of Cd2+ was increased in absence of extracellular Ca2+, but was prevented in Ca2+-supplemented medium. Pretreatment of cells with BAY K8644 (BAY), an agonist of voltage-dependent calcium channels, increased the Cd2+-mediated inhibition of ACTH-stimulated secretion but not pregnenolone (PREG)-stimulated secretion. Nicardipine, an antagonist of voltage-dependent calcium channels, also increased the inhibition of adrenocorticotropic hormone (ACTH)-stimulated secretion by Cd2+. These results suggest that opening of voltage-dependent calcium channels with BAY may allow Cd2+ entry at the same time as calcium, thus increasing toxicity of Cd2+, however voltage-dependent calcium channels may not be the only way of entry into adrenocortical cells. The influx of Cd2+, measured as intracellular Cd2+ using Fluo-3 in PREG-stimulated adrenocortical cells, was significantly enhanced by the stimulation. These results suggest that the deleterious effect of Cd2+ on cortisol steroidogenesis may be enhanced when the endocrine stress response is triggered.

Lange, A., O. Ausseil, et al. (2002). "Alterations of tissue glutathione levels and metallothionein mRNA in rainbow trout during single and combined exposure to cadmium and zinc." Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology **131**(3): 231-243.

The objective of this study was to assess the effects of Cd and Zn exposure of rainbow trout (Oncorhynchus mykiss) on (a) hepatic glutathione (GSH) levels; and (b) hepatic and branchial metallothionein (MT) mRNA expression. Juvenile rainbow trout were exposed to waterborne Cd (nominal concentrations: 1.5 or 10 [mu]g Cd l-1), Zn (150 or 1000 [mu]g Zn l-1) or Cd/Zn mixtures (1.5 [mu]g Cd l-1 with 200 [mu]g Zn l-1 or 10 [mu]g Cd l-1 with 1000 [mu]g Zn l-1). After 14 and 28

days of treatment, hepatic concentrations of total glutathione, oxidized glutathione (GSSG) and cysteine were determined by means of fluorometric high performance liquid chromatography (HPLC). Branchial and hepatic expression of MT mRNA was measured by means of semi-quantitative RT-PCR. Exposure of trout to Zn did not result in significantly elevated tissue levels of Zn, whereas Cd accumulation factors changed significantly with time and concentration. Despite of the absence of Zn accumulation, hepatic GSH but not MT mRNA levels were significantly altered in Zn-exposed fish. Cd, on the contrary, affected mainly the MT response but not GSH. Also tissue specific differences in the regulation of the two thiol pools were expressed. The thiol response after exposure to metal mixtures could not be explained by simple addition of the effects of the individual metals. The results indicate that cellular thiol pools show different reaction patterns with respect to specific metals and metal mixtures. Under conditions of long-term, low dose metal exposure, the function of GSH appears to go beyond that of a transitory, first line defense.

Lourdes, M. and A. Cuvinaralar (1994). "SURVIVAL AND HEAVY-METAL ACCUMULATION OF 2 OREOCHROMIS-NILOTICUS (L) STRAINS EXPOSED TO MIXTURES OF ZINC, CADMIUM AND MERCURY." Science of the Total Environment **148**(1): 31-38.

Two Nile tilapia strains of Oreochromis niloticus (L.) (Cichlidae, Teleostei) fingerlings were exposed to mixtures of zinc, cadmium and mercury. The two strains used were Chitralada or NIFI (originally from the National Inland Fisheries Institute, Thailand) and CLSU (from the Freshwater Aquaculture Center of the Central Luzon State University, The Philippines). Short-term (10 days) exposure to a metal mixture of 5 mg l-1 zinc (Zn), 0.5 mg l-1 cadmium (Cd) and 0.02 mg l-1 mercury (Hg) gave significantly higher survival percentage in the NIFI strain compared with the CLSU strain. Similar exposure conditions using larger and older fingerlings of the two strains also showed a slightly higher survival percentage in the NIFI strain but the difference was not significant. Prolonged exposure of the fingerlings to a lower concentration of the metal mixture (1.0 mg l-1 Zn, 0.1 mg l-1 Cd, 0.01 mg l-1 Hg) also resulted in similar survival percentages between the two strains at the end of the 60 days run. Whole body accumulation of Zn was significantly higher in CLSU than in NIFI after 14-day exposure to the low concentration metal mixture. There was no significant difference in the accumulation of Cd and Hg between the two strains. Of the three metals, Hg had the highest bioaccumulation factor (BF) which was approximately 900-1000, followed by Cd with 255-280 and Zn with 180-195 times the nominal concentration in the water. Concentration of Cd and Hg in fish tissues increased with exposure period while the concentration of Zn was maintained in NIFI and decreased in CLSU between the 6th and 14th day of exposure, suggesting that Zn (an essential element) accumulation maybe regulated by both strains.

Lundebye, A. K., M. H. G. Berntssen, et al. (1999). "Biochemical and physiological responses in Atlantic salmon (Salmo salar) following dietary exposure to copper and

cadmium." Marine Pollution Bulletin **39**(1-12): 137-144.

Three experiments were conducted with Atlantic salmon (Salmo salar) to assess the effects of dietary exposure to copper and cadmium. The results presented here provide an overview, details of each experiment will be published in full elsewhere. In the first experiment, salmon parr exposed for four weeks to 35 and 700 mg Cu kg(-1) diet had significantly elevated intestinal copper concentrations, cell proliferation (PCNA) and apoptosis rates compared to control fish. No differences were observed in gib or plasma copper concentrations among the groups, In contrast to the controls, the Cu exposed groups did not grow significantly during the exposure period. The second experiment (three months exposure) was conducted to assess the effects of dietary copper (control, 35, 500, 700, 900 or 1750 mg Cu kg(-1) diet) on growth and feed utilization in salmon fingerlings, Growth was significantly reduced after three months exposure to dietary Cu concentrations above 500 mg kg-l. Similarly, copper body burdens were significantly higher in fish exposed to elevated dietary copper concentrations (above 35 mg Cu kg(-1) diet). In the third experiment, salmon parr were exposed to one of six dietary cadmium concentrations (0, 0.5, 5, 25, 125 or 250 mg Cd kg(-1) diet) for four months. Cadmium accumulated in the liver > intestine > gills of exposed fish. Rates of apoptosis and cell proliferation in the intestine increased following exposure to dietary cadmium. Exposure to elevated concentrations of dietary cadmium had no effect on growth in salmon parr. Results from these studies indicate that cellular biomarkers have potential as early warning signs of negative effects on the overall fitness of an organism.

Marion, M. and F. Denizeau (1983). "Rainbow trout and human cells in culture for the evaluation of the toxicity of aquatic pollutants: A study with cadmium." Aquatic Toxicology **3**(4): 329-343.

Rainbow trout (RTG-2) and human skin epithelial cells (NCTC 2544) were tested as bioassay organisms for the evaluation of the toxicity of aquatic pollutants. Cadmium (Cd) was used as a representative model compound. The cell lines were grown as monolayers at 15 (RTG-2) and 37°C (NCTC 2544) in minimal essential medium supplemented with 10% fetal bovine serum (FBS). RTG-2 and NCTC 2544 cells were exposed to 100 ppb and 2.4 ppm Cd. Exposure to Cd was maintained for a period of time sufficient for an inoculum of 105 cells (RTG-2) or 5 × 104 cells (NCTC 2544) to reach confluence in the controls in a 60-mm Petri dish: 20 days for RTG-2 and 9 days for NCTC 2544. Every 2 days (RTG-2) or every day (NCTC 2544) the medium was renewed and 3 Petri dishes were used in each group for the determination of the following parameters: total protein, total DNA, total RNA content and the incorporation of [3H]thymidine in DNA and [14C]uridine in RNA. The cytotoxicity of Cd was apparent only when the serum concentration in the medium was reduced. With 1% FBS in the medium Cd induced a dramatic inhibition in the increase of total protein DNA and RNA content of RTG-2 cells. At 2.4 ppm, these effects were seen as early as 5 days (protein and RNA) after Cd was added to the cultures. The incorporation of labelled precursors was equally much lower in the treated samples (2.4 ppm)

compared to the controls. At 100 ppb, only the incorporation of [14C]uridine in RNA was affected; the effect was seen after 10 days of exposure and persisted until the end of the experiment. NCTC 2544 cells appeared to be more sensitive to cadmium than RTG-2 cells. At 2.4 ppm, as seen with trout cells, a severe depression in all the parameters was observed. However, at 100 ppm, contrasting with RTG-2 cells, significant differences were measured at least on 4 parameters (protein, DNA, RNA and [14C] incorporation). The data are compared to those previously obtained with lead using a similar system. The results are also analysed in the light of the available in vivo data in an attempt to establish a correlation between in vitro and in vivo responses. This is considered as an important step in the process of validation of the present bioassay system.

Mason, C. F. (1987). "A survey of mercury, lead and cadmium in muscle of British freshwater fish." Chemosphere **16**(4): 901-906.

Analyses of mercury, lead and cadmium in muscle of 221 fish, mainly eel and roach, from 67 sites in Great Britain are presented. Concentrations of metals in a significant number of fish were above recommended standards for human consumption.

Matsuo, A. Y. O., C. M. Wood, et al. (2005). "Effects of copper and cadmium on ion transport and gill metal binding in the Amazonian teleost tambaqui (Colossoma macropomum) in extremely soft water." Aquatic Toxicology **74**(4): 351-364.

Metal toxicity in fish is expected to be most severe in soft waters because of the low availability of cations (particularly Ca2+) to out-compete the metal forms for binding sites on the gills. Natural waters in the Amazon basin are typically soft due to regional geochemistry, but few studies have focused on metal toxicity in fish native to the basin. We assessed the ionoregulatory effects of waterborne copper (Cu) and cadmium (Cd) on tambaqui (Colossoma macropomum) in extremely soft water (10 [mu]mol l-1 Ca2+). Tambaqui had a very high tolerance to Cu (50-400 [mu]g l-1), as indicated by a complete lack of inhibition of Na+ uptake and an ability to gradually recover over 6 h from elevated diffusive Na+ losses caused by Cu. The insensitivity of active Na+ influx to Cu further supports the notion that Amazonian fish may have a unique Na+ transport system. Addition of 5-10 mg C l-1 of dissolved organic matter (DOM) did not prevent initial (0-3 h) negative Na+ balance in tambaqui exposed to Cu. Exposure to 40 mg C l-1 DOM prevented Na+ losses in tambaqui even at 400 [mu]g l-1 Cu, probably because most Cu was complexed to DOM. Tambaqui exposed to waterborne Cd (10-80 [mu]g l-1) experienced an average of 42% inhibition in whole body Ca2+ uptake relative to controls within 3 h of exposure to the metal. Inhibition of Ca2+ uptake increased over time and, at 24 h, Ca2+ uptake was suppressed by 51% and 91% in fish exposed to 10 and 80 [mu]g l-1 Cd, respectively. Previous acclimation of fish to either elevated [Ca2+] or elevated [DOM] proved to be very effective in protecting against acute short-term metal accumulation at the gills of tambaqui in soft water (in the absence of the protective agent during metal exposure), suggesting a conditioning effect on gill metal binding physiology.

Matz, C. J., R. G. Treble, et al. (2007). "Accumulation and elimination of cadmium in larval stage zebrafish following acute exposure." Ecotoxicology and Environmental Safety **66**(1): 44-48.

A number of recent studies have examined the impact of acute cadmium exposure on early zebrafish development at the morphological, cellular, and molecular levels. However, no information on the accumulation and elimination of cadmium during early life stages of zebrafish development has been available. Here we have quantified cadmium accumulation in larval zebrafish (Danio rerio) by graphite furnace atomic absorption spectroscopy following short-term acute exposure and recovery periods. Zebrafish (80 h postfertilization) were exposed to various concentrations of cadmium (0.2, 1.0, 5.0, 25, 125 [mu]M) for 3 h. Cadmium accumulation in larvae increased with exposure concentration. After exposure at 5.0, 25, and 125 [mu]M cadmium, the fish were allowed to recover in freshwater for 0, 12, or 24 h. Cadmium content did not show a statistically significant decrease over the recovery period when exposed to 5.0 or 25 [mu]M cadmium, whereas significant losses over the recovery period were observed following 125 [mu]M exposure. These results suggest that the larval zebrafish decrease total cadmium body burden only following relatively high short-term acutely toxic exposures.

Mazet, A., G. Keck, et al. (2005). "Concentrations of PCBs, organochlorine pesticides and heavy metals (lead, cadmium, and copper) in fish from the Drôme river: Potential effects on otters (Lutra lutra)." Chemosphere **61**(6): 810-816.

In this study samples of ten species of fish were analyzed for concentrations of organochlorine pesticides, PCBs and heavy metals (Pb, Cd, and Cu). Fish were captured using electric fishing on ten sites along the Drôme river (Rhône-Alpes region). Quantitative determination of the organochlorine and PCBs compounds was performed by gas chromatography-electron-capture detection (GC-ECD). The concentrations of heavy metals were determined by atomic absorption spectrophotometry. Samples contained detectable concentrations of lindane, PCBs, and heavy metals but at concentrations below the maximum residue limit (MRL). Non-parametric statistical analysis was performed to distinguish groups of sites with different levels of contamination. PCBs concentrations increased along the river with four groups of sites significantly different from each other. Cadmium concentrations were below the MRL. Lead contamination showed two groups significantly different and a repartition similar to PCBs. Copper contamination was correlated with the localization of vineyards. We assessed the potential effects of contamination the otter (Lutra lutra). The concentrations of all pollutants analyzed in fish sampled in this study are lower than the threshold values described in literature. The Drôme river is relatively unpolluted river, and the establishment of otter populations should not be affected by pollution.

McCahon, C. P. and D. Pascoe (1988). "Increased sensitivity to cadmium of the freshwater amphipod Gammarus pulex (L.) during the reproductive period." Aquatic Toxicology **13**(3): 183-193.

Six stages in the embryonic development of Gammarus pulex and the hatching process are described. The toxicity of cadmium to sexually mature males, and females carrying eggs at each stage of development was determined. The 48-h LC50 value for sexually mature males was 1.9 times greater than for females carrying eggs at stages 2-6 or embryos, whilst it was 12.8 times greater than females not carrying eggs or brooding unfertilized or stage 1 eggs. The difference in female tolerance is independent of both the developmental stage or number of eggs carried but is associated with the moult cycle. Results are discussed in relation to the importance of designing toxicity tests and the establishment of water quality standards.

McCoy, C. P., T. M. Ohara, et al. (1995). "LIVER AND KIDNEY CONCENTRATIONS OF ZINC, COPPER AND CADMIUM IN CHANNEL CATFISH (ICTALURUS-PUNCTATUS) - VARIATIONS DUE TO SIZE, SEASON AND HEALTH-STATUS." Veterinary and Human Toxicology **37**(1): 11-15.

Significant differences in liver and kidney concentrations of zinc (Zn), copper (Cu) and cadmium (Cd) were detected in normal Mississippi farm-raised channel catfish (Ictalurus punctatus) collected at different times of the year. These seasonal differences were not solely due to variation in fish size. Comparing the concentration of each metal in liver vs kidney indicated that Cd was lower in liver for all seasons studied, Cu was higher in liver for all seasons studied, and Zn was higher in the liver in the winter-killed (winter mortality syndrome) and the spring fish groups. Metal concentration was associated with body weight, as indicated by significant Pearson correlation coefficients for kidney Cd (all seasons and fall), liver Cu (summer), liver Zn (all seasons and winter), and kidney Zn (all seasons and winter). The adjusted means were not dramatically changed as compared to the raw data. Differences were noted when seasonal values obtained from normal fish were compared to tissues of moribund fish afflicted with winter mortality syndrome. Zinc was reduced in liver and kidney of these moribund fish.

Meador, J. P., D. W. Ernest, et al. (2005). "A comparison of the non-essential elements cadmium, mercury, and lead found in fish and sediment from Alaska and California." Science of the Total Environment **339**(1-3): 189-205.

Concentrations of three non-essential elements (cadmium (Cd), mercury (Hg), and lead (Pb)) were determined in sediment and fish from several locations in Alaska (AK) and California (CA) and used to examine differences in bioaccumulation within and between geographic locations. We analyzed tissue (liver, muscle, gill, and stomach contents) from white croaker (Genyonemus lineatus) and English sole (Pleuronectes vetulus) in California and flathead sole (Hippoglossoides elassodon) in Alaska, in addition to several species of invertebrates (mercury only). As found in previous work on arsenic (As) [Meador et al., 2004], Cd in fish liver exhibited a negative correlation with sediment concentrations. No such correlations were found for Hg and Pb when fish liver and sediment were compared; however, these metals did exhibit a positive relationship between liver and organic carbon normalized sediment

concentrations, but only for the CA sites. Sediment concentrations of Hg at the AK sites were lower than those for the CA sites; however, AK invertebrates generally bioaccumulated more Hg than CA invertebrates. Conversely, Hg bioaccumulation was higher in CA fish. Even though ratios of total metal/acid volatile sulfides (AVS) in sediment were one to two orders of magnitude higher for the AK sites, bioaccumulation of these elements was much higher in fish from the CA sites. Bioaccumulation factors ([liver]/[sediment]) (BAFs) were highest at relatively clean sites (Bodega Bay and Monterey), indicating that elements were more bioavailable at these sites than from more contaminated locations. The observation of high BAFs for As in fish from Alaska and low BAFs for the California fish, but reversed for Cd, Hg, and Pb in this study, implies that differences in fish species are less important than the unique geochemical features at each site that control bioavailability and bioaccumulation and the potential sources for each element. Additionally, these data were also used to examine the metal depletion hypothesis, which describes the inverse relationship between elements and organic contaminants documented in some monitoring studies. Our results suggest that the enhanced bioavailability of the metals at some uncontaminated sites is the main determinant for the inverse correlation between metal and organic contaminants in tissue.

Mebane, C. A., D. P. Hennessy, et al. (2008). "Developing acute-to-chronic toxicity ratios for lead, cadmium, and zinc using rainbow trout, a mayfly, and a midge." Water Air and Soil Pollution **188**(1-4): 41-66.

In order to estimate acute-to-chronic toxicity ratios (ACRs) relevant to a coldwater stream community, we exposed rainbow trout (Oncorhynchus mykiss) to cadmium (Cd), lead (Pb), and zinc (Zn) in 96-h acute and 60+ day early-life stage (ELS) exposures. We also tested the acute and sublethal responses of a mayfly (Baetis tricaudatus) and a midge (Chironomus dilutus, formerly C. tentans) with Pb. We examine the statistical interpretation of test endpoints and the acute-to-chronic ratio concept. Increasing the number of control replicates by 2 to 3x decreased the minimum detectable differences by almost half. Pb ACR estimates mostly increased with increasing acute resistance of the organisms (rainbow trout ACRs <approximate to mayfly < Chironomus). The choice of test endpoint and statistical analysis influenced ACR estimates by up to a factor of four. When calculated using the geometric means of the no- and lowest-observed effect concentrations, ACRs with rainbow trout and Cd were 0.6 and 0.95; Zn about 1.0; and for Pb 3.3 and 11. The comparable Pb ACRs for the mayfly and Chironomus were 5.2 and 51 respectively. Our rainbow trout ACRs with Pb were about 5-20x lower than earlier reports with salmonids. We suggest discounting previous ACR results that used larger and older fish in their acute tests.

Melgar, M. J., M. Perez, et al. (1997). "Accumulation profiles in rainbow trout (Oncorhynchus mykiss) after short-term exposure to cadmium." Journal of Environmental Science and Health Part a-Environmental Science and Engineering & Toxic and Hazardous Substance Control **32**(3): 621-631.

Cadmium accumulation and its effect were examined in several organs of

rainbow trout (Oncorynchus mykiss). Groups of 20 trouts were exposed for a three-week period at different subacute oral doses of Cl2Cd (0.01, 0.025 and 0.05 mu g Cd/mL, respectively). Cadmium uptake and storage were weekly studied in some soft tissues: kidney, liver, gills, muscle and brain. Cadmium determination was carried out using the Atomic Absorption Spectroscopy technique (AAS) with graphite furnace. After 21 days of exposure, cadmium concentrations increased significantly in all studied tissues, except in muscle and brain. The most important cadmium exposure effect was on the kidney.

Mount, D. R., A. K. Barth, et al. (1994). "DIETARY AND WATERBORNE EXPOSURE OF RAINBOW-TROUT (ONCORHYNCHUS-MYKISS) TO COPPER, CADMIUM, LEAD AND ZINC USING A LIVE DIET." Environmental Toxicology and Chemistry **13**(12): 2031-2041.

In two 60-d exposures, rainbow trout fry were fed brine shrimp (Artemia sp.) enriched with Cu, Cd, Pb, and Zn both individually and as a mixture combined with As. Dietary concentrations fed to trout were selected based on metal concentrations measured in invertebrates collected from the Clark Fork River (CFR), Montana. In addition to dietary exposure, treatments also included simultaneous exposure to a mixture of waterborne metals at sublethal concentrations. Fish in all treatments showed increased tissue metal concentrations from water and/or dietary exposure. Despite these accumulations, trout showed no effects on survival or growth from dietary concentrations as high as 55 mu g Cd/g dry weight, 170 mu g Pb/g dry weight, or 1,500 mu g Zn/g dry weight (corrected for depuration). Dietary Cu concentrations up to 350 mu g Cu/g dry weight did not reduce survival or growth. Fish fed Cu concentrations higher than those typical of CFR invertebrates (660 and 800 mu g Cu/g dry weight; corrected for depuration) showed about 30% mortality with no effect on growth; waterborne Cu released from Artemia may have contributed to this mortality. Trout exposed to diets with a mixture of Cu, Cd, Pb, Zn, and As dose to that measured in CFR invertebrates showed tower weight than did control fish after 35 d, but this difference was no longer present after 60 d.

Murad, A. and A. H. Houston (1988). "Leucocytes and leucopoietic capacity in goldfish, Carassius auratus, exposed to sublethal levels of cadmium." Aquatic Toxicology **13**(2): 141-154.

By comparison with animals in essentially cadmium-free water (< 2 [mu]g Cd2+/l) goldfish exposed for 3 wk to 90, 270 and 445 [mu]g Cd2+/l (5, 15 and 25% 240-h LC50) exhibited significant reductions in total leucocyte counts. These were the result of decreases in lymphocyte and thrombocyte numbers. Mitogenic response to administered PHA as well as sharp decreases in blast cell numbers suggested that lympho- and thrombopenia reflect, in part at least, decreased proliferative capacity. By contrast, neutrophil, cosinophil and basophil numbers increased in cadmium-intoxicated fish. Cadmium apparently reduced PHA-related changes in granulocyte abundances.

Muramoto, S. (1981). "Vertebral column damage and decrease of calcium concentration

in fish exposed experimentally to cadmium." Environmental Pollution Series A, Ecological and Biological **24**(2): 125-133.

The variations of the Ca, P, Mg and Cd concentrations in the bodies of deformed and normal fish exposed for long periods to water containing low chemical concentrations of Cd were determined. The vertebrae of the fish were then examined by X-ray photography and the mechanism of the development of malformation caused by the loss of Ca from the bones was studied. Deformed fish appeared on the 47th, 85th and 73rd days after Cd exposure in water containing 0·01, 0·05 and 0·1 ppm of Cd, respectively. Due to exposure to the Cd-containing water, the Cd content of the fish increased, whereas the Ca and P contents in the vertebrae tended to decrease. Cavitation of the bone metabolism and contracted adhesion of articulations and strain at the costal apices due to pressure were observed. The percentage of ash weight/dry weight in the bones was also reduced in the deformed fish.

Murphy, C. A., K. A. Rose, et al. "Modeling vitellogenesis in female fish exposed to environmental stressors: predicting the effects of endocrine disturbance due to exposure to a PCB mixture and cadmium." Reproductive Toxicology **19**(3): 395-409.

A wide variety of chemical and physical environmental stressors have been shown to alter the reproductive processes in fish by interfering with endocrine function. Most endocrine indicators or biomarkers are static measures from dynamic hormonally-mediated processes, and often do not directly relate to reproductive endpoints of ecological significance. Adequate production of the yolk precursor protein, vitellogenin, is critical for the survival and normal development of the sensitive egg and yolk-sac larval fish life stages. We developed a model that simulates vitellogenesis in a mature female sciaenid fish. The model simulates the major biochemical reactions over a 6-month period from the secretion of gonadotropin (GtH) into the blood to the production of vitellogenin. We simulated the effects of two endocrine disrupting chemicals (EDCs) that have different actions on vitellogenin production: a PCB mixture and cadmium. Predicted changes in steroid concentrations and cumulative vitellogenin production compared favorably with changes reported in laboratory experiments. Simulations illustrate the potential utility of our model for interpreting reproductive endocrine biomarkers measured in fish collected from degraded environments.

Niyogi, S., P. Couture, et al. (2004). "Acute cadmium biotic ligand model characteristics of laboratory-reared and wild yellow perch (Perca flavescens) relative to rainbow trout (Oncorhynchus mykiss)." Canadian Journal of Fisheries and Aquatic Sciences **61**(6): 942-953.

This study evaluated the >400-fold tolerance to acute waterborne Cd of a metal-tolerant fish, yellow perch (YP, Perca flavescens), relative to a sensitive model fish, rainbow trout (RBT, Oncorhynchus mykiss), from the perspective of the acute Cd biotic ligand model (BLM). Three-hour gill binding characteristics for Cd and its competitor, Ca, in both species exhibited only small quantitative differences, but gill Cd accumulations at 3 h and 24 h, which were associated

with 50% lethality at 96 h (3- and 24-h LA50s), were 52- to 60-fold higher in YP relative to RBT. However, the acute Cd BLM cannot be extended from RBT to YP by simple adjustments of LA50 values because unlike RBT, in YP, LA50s (3 and 24 h) were 26- to 47-fold greater than the capacity of the characterized set of Cd-binding sites. Moreover, 3-h gill Ca and Cd binding characteristics in wild YP, collected from one clean (Geneva) and two metal-contaminated softwater lakes (Hannah and Whitson) around Sudbury region, northern Ontario, revealed that chronic waterborne factors like hardness and Cd preexposure can influence both Cd and Ca binding in fish gills and could have major implications for the future refinement of the acute Cd BLM approach.

Niyogi, S., R. Kent, et al. (2008). "Effects of water chemistry variables on gill binding and acute toxicity of cadmium in rainbow trout (Oncorhynchus mykiss): A biotic ligand model (BLM) approach." Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology **148**(4): 305-314.

This study investigated the short-term (3 h) cadmium binding characteristics of the gills, as well as the influence of various water chemistry variables [calcium, magnesium, sodium, pH, alkalinity and dissolved organic carbon (DOC)] on short-term gill accumulation and acute toxicity of cadmium in juvenile freshwater rainbow trout. The cadmium binding pattern revealed two types of cadmium binding sites in the gill: (i) saturable high affinity sites operating at a low range of waterborne cadmium concentration, and (ii) non-saturable low affinity sites operating at a higher range of cadmium concentration. Among the water chemistry variables tested, only calcium and DOC significantly reduced both gill accumulation and toxicity of cadmium. Interestingly, alkalinity (15-90 mg L- 1 as CaCO3) did not influence the gill cadmium accumulation but a significant increase in toxicity was recorded at a higher alkalinity level (90 mg L- 1). Affinity constants (log K) for binding of competing cations (Cd2+ and Ca2+) to the biotic ligand and for binding of Cd2+ to DOC were derived separately from the 3 h gill binding tests and the 96 h toxicity tests. In general, the values agreed well, indicating that both tests targeted the same population of high affinity binding sites, which are likely Ca2+ uptake sites on the gills. These parameters were then incorporated into a geochemical speciation model (MINEQL+) to develop a biotic ligand model for predicting acute toxicity of cadmium in trout. The model predictions exhibited a good fit with the measured toxicity data except for high alkalinity and pH.

Norey, C. G., M. W. Brown, et al. (1990). "A comparison of the accumulation, tissue distribution and secretion of cadmium in different species of freshwater fish." Comparative Biochemistry and Physiology Part C: Comparative Pharmacology **96**(1): 181-184.

1. Rainbow trout and stone loach were exposed to cadmium in their aquarium water and the fractional retention coefficient for the metal ([[mu]g Cd/100g body wt]/([[mu]g Cd/l) × weeks]) was measured in both species under different conditions of water hardness. 2. The significant differences that distinguish the Cd-sensitive (rainbow trout) from the Cd-tolerant species (stone loach) were

maintained. 3. Rainbow trout and stone loach were exposed to cadmium in their aquarium water for a minimum of 63 days. Following their transfer into cadmium-free water, elimination of the metal from both species of fish was monitored for up to 132 and 170 days, respectively, and found to be minimal. 4. The distribution of cadmium within the three major cadmium-sequestering organs (liver, kidney and gills) of the rainbow trout and stone loach did not not change significantly during the period of their maintenance in cadmium-free water. 5. A comparison of the tissue distribution of cadmium in rainbow trout and stone loach during early stages of exposure to the metal at 3 [mu]g/l in their aquarium water under identical conditions indicated that the gill was the primary organ of accumulation in rainbow trout, whereas liver and kidney together were more important in the stone loach. 6. The significance of these observations in relation to the differential susceptibilities of freshwater fish species to the toxic effects of cadmium is discussed.

Norey, C. G., A. Cryer, et al. (1990). "A comparison of cadmium-induced metallothionein gene expression and Me2+ distribution in the tissues of cadmiumsensitive (rainbow trout; Salmo gairdneri) and tolerant (stone loach; Noemacheilus barbatulus) species of freshwater fish." Comparative Biochemistry and Physiology Part C: Comparative Pharmacology **97**(2): 221-225.

1. The accumulation of cadmium in the liver, kidney and gills of rainbow trout and stone loach was measured during exposure of the fish to the metal at 3 smg/l in their aquarium water. The pattern of accumulation of the toxic metal in the individual organs was different between the two species. 2. The tissue concentrations of metallothionein-specific mRNA and metallothionein protein were also determined in these organs from the same fish. In rainbow trout, the induction of metallothionein gene expression resulted in a gradual increase in metallothionein concentration in gill over the course of the experiment whereas increases in metallothionein in the liver and kidney were detected only at the later time points of analysis (beyond 19 weeks). By contrast, in the same tissues from stone loach, relatively minor changes were quantified in specific mRNA and metallothionein concentrations. 3. Throughout the experimental period, tissue concentrations of zinc and copper were determined in the liver, kidney and gills of the rainbow trout and stone loach. Subtle decreases were observed in the zinc concentration of gills in rainbow trout and substantial increases were observed in the hepatic copper concentrations in both species at the later time points of analysis. 4. The ability of cadmium to induce metallothionein gene expression and its subsequent ability to compete for the sequestration sites on the newly-synthesized protein is discussed with regard to the relative levels of cadmium, zinc and copper in the organs studied and differing regimes of cadmium administration.

Odzak, N. and T. Zvonaric (1995). "Cadmium and lead uptake from food by the fish Dicentrarchus labrax." Water Science and Technology **32**(9-10): 49-55.

Cadmium and lead uptake from the fish food in liver and muscle tissue of sea bass Dicentrarchus labrax were investigated experimentally. The conditions as

close as possible to those in natural environment were ensured by this experiment. The sea bass was exposed to elevated concentrations of Cd (5.36, 38.5 and 485 mg kg-1) and Pb (2.58, 25.1 and 238 mg kg-1) in fish food. In fish exposed to these concentrations, a linear metal concentration increase (in liver and muscle tissue) was established during the experiment However, liver and muscle tissue respond differently during metal uptake. Although at the end of the experiment (62 days) Cd concentration was much higher in the liver of exposed fish, bioaccumulation in the muscle tissue was faster. Quite an opposite trend was recorded for lead bioaccumulation. Bioaccumulation of Pb in the liver was faster than in muscle tissue. The results of this experiment confirmed that the liver, as a central organ of metabolic processes, may be a measure of an actual Cd and Pb load of an organism.

Olsson, P. E., P. Kling, et al. (1995). "INTERACTION OF CADMIUM AND ESTRADIOL-17-BETA ON METALLOTHIONEIN AND VITELLOGENIN SYNTHESIS IN RAINBOW-TROUT (ONCORHYNCHUS-MYKISS)." Biochemical Journal **307**: 197-203.

The induction of metallothionein and vitellogenin synthesis in rainbow trout liver was studied after injection of oestradiol-17 beta alone or in combination with cadmium or zinc. Intraperitoneal injection of oestradiol-17 beta increased the liver somatic index, with subsequent induction of vitellogenin synthesis. Oestradiol-17 beta did not induce metallothionein synthesis. Injection of cadmium induced the synthesis of metallothionein mRNA and metallothionein. Injection of oestradiol-17 beta in combination with cadmium resulted in inhibition of transcription and translation of both vitellogenin and metallothionein. Chromatography of liver cytosols revealed that cadmium, when co-injected with oestradiol-17 beta, did not bind to metallothionein but would initially bind to high-molecular-mass (HM(r)) cytosolic proteins. In fish injected with cadmium in combination with oestradiol-17 beta, cadmium was gradually redistributed from HM(r) proteins to metallothionein. This resulted in induction of metallothionein synthesis and in binding of most of the cadmium to metallothionein. Induction of vitellogenin mRNA was observed 15 days after injection, as cadmium was being redistributed to newly synthesized metallothionein. These findings indicate that cadmium inhibits the transcription of vitellogenin. The binding of cadmium to these non-metallothionein proteins represses the induction of metallothionein and results in increased toxicity of the metal. Preinduction of metallothionein by zinc injections resulted in decreased cadmium sensitivity of the fish and a decrease in the repression of vitellogenin mRNA. Furthermore, a role for metallothionein in the detoxification of cadmium is indicated by the induction of vitellogenin synthesis that occurs once metallothionein has begun sequestering cadmium.

Olsson, P.-E. and P. Kille (1997). "Functional comparison of the metal-regulated transcriptional control regions of metallothionein genes from cadmium-sensitive and tolerant fish species." Biochimica et Biophysica Acta (BBA) - Gene Structure and Expression **1350**(3): 325-334.

The promoter region of teleost metallothioneins (MTs) contains multiple metal-responsive elements (MREs) organized in proximal and distal clusters which

together mediate gene induction by heavy metals. This arrangement of MREs is found both in cadmium-sensitive species, such as the rainbow trout, and in cadmium-tolerant species such as the pike and the stone loach. On comparison of the putative regulatory elements identified within the 5'-flanking region of these genes the major differences are that the number of MREs differ between the different species and that, while both the stone loach and rainbow trout MT genes contain TATA boxes, the pike MT gene has a TTTA box. In order to investigate if the metal sensitivity of a species is correlated to the regulatory potential of the putative MT detoxification system the promoter regions of MT genes from all three species were assessed for their ability to enhance transcription in response to the heavy metals Zn, Cd and Cu. The polymerase chain reaction was used to produce nested deletion sets of each prornoter region and these were cloned into the mammalian expression vector pGL-2 upstream of the firefly luciferase gene. The inducibility of the different constructs in response to heavy metal challenge was tested in two cell lines, one fish cell line (homologous to rainbow trout and heterologous to the two other species), the rainbow trout hepatoma, RTH-149, cell line and one cell line that was heterologous to all studied species, the human hepatoblastoma; HepG2, cell line. Maximum inducibility of each gene was achieved with constructs containing both the proximal and the distal MRE clusters. Both the rainbow trout and the stone loach MT genes showed inducibility of comparable amplitude whilst the pike MT gene on the other hand was less inducible, partly due to fewer MREs and partly due to the TTTA box. These data indicate that more than one mechanism is responsible for the differences in cadmium sensitivity of these three teleost species. Although MT is the main heavy-metal detoxifying system in most vertebrates and appears to be contributing to the differences seen between rainbow trout and pike, the present study shows that the relative sensitivity of these species is not primarily due to MT.

Oronsaye, J. A. O. (1987). "The uptake and loss of dissolved cadmium by the stickleback, Gasterosteus aculeatus L." Ecotoxicology and Environmental Safety **14**(1): 88-96.

The whole-body uptake of cadmium by the three-spined stickleback (Gasterosteus aculeatus) has been measured after exposure of fish to 2.5 and 5.0 mg Cd2+/liter hard water and equal amounts of 2.0 mg Cd2+ plus 2 mg Zn2+/liter and 4.0 mg Cd2+ plus 4.0 mg Zn2+/liter hard water, respectively. Fish absorbed and retained cadmium while the uptake and accumulation of zinc was depressed. The loss of absorbed cadmium was quicker in fish previously exposed to cadmium plus zinc solutions used together. This phenomenon is discussed in relation to the ability of fish to excrete absorbed cadmium.

Palace, V. P. and J. F. Klaverkamp (1993). "Variation of hepatic enzymes in three species of freshwater fish from precambrian shield lakes and the effect of cadmium exposure." Comparative Biochemistry and Physiology Part C: Comparative Pharmacology **104**(1): 147-154.

1. Variation of three antioxidant enzymes, Superoxide dismutase (SOD), catalase

(CAT) and glutathione peroxidase (GPx), and effects of Cd exposure in a whole lake experiment on these enzymes were investigated in liver from three freshwater fish species, (Pearl Dace (Semotilus margarita), White Sucker (Catostomus commersoni) and Lake Charr (Salvelinus namaycush)). 2. Enzymatic activity varied significantly between different lakes in geographical proximity. 3. Other than GPx activity, which was lower in Lake Charr, activities of the three enzymes were not different between the three fish species. 4. Seasonal variation was observed in both CAT and SOD activities. 5. Cd exposure resulted in increased liver concentrations of the metal, but metallothionein protein did not significantly increase. 6. SOD activity in liver of fish exposed to Cd was consistently higher than in liver of fish from reference lakes.

Palus, J., K. Rydzynski, et al. (2003). "Genotoxic effects of occupational exposure to lead and cadmium." Mutation Research/Genetic Toxicology and Environmental Mutagenesis **540**(1): 19-28.

This study was designed to assess genotoxic damage in somatic cells of workers in a Polish battery plant after high-level occupational exposure to lead (Pb) and cadmium (Cd), by use of the following techniques: the micronucleus (MN) assay, combined with in situ fluorescence hybridization (FISH) with pan-centromeric probes, analysis of sister chromatid exchanges (SCEs), and the comet assay. Blood samples from 44 workers exposed to lead, 22 exposed to cadmium, and 52 unexposed persons were used for SCE and MN analysis with 5'-bromodeoxyuridine (BrdU) or cytokinesis block, respectively. In parallel, the comet assay was performed with blood samples from the same persons for detection of DNA damage, including single-strand breaks (SSB) and alkali-labile sites (ALS). In workers exposed mostly to lead, blood Pb concentrations ranged from 282 to 655 [mu]g/l, while the range in the controls was from 17 to 180 [mu]g/l. Cd concentration in lead-exposed workers fell in the same range as for the controls. In workers exposed mainly to cadmium, blood Cd levels varied from 5.4 to 30.8 [mu]g/l, with respective values for controls within the range of 0.2-5.7 [mu]g/l. Pb concentrations were similar as for the controls. The incidence of MN in peripheral lymphocytes from workers exposed to Pb and Cd was over twice as high as in the controls ($P<0.01$). Using a combination of conventional scoring of MN and FISH with pan-centromeric probes, we assessed that this increase may have been due to clastogenic as well as aneugenic effects. In Cd- and Pb-exposed workers, the frequency of SCEs as well as the incidence of leukocytes with DNA fragmentation in lymphocytes were slightly, but significantly increased ($P<0.05$) as compared with controls. After a 3 h incubation of the cells to allow for DNA repair, a clear decrease was found in the level of DNA damage in the controls as well as in the exposed workers. No significant influence of smoking on genotoxic damage could be detected in metal-exposed cohorts. Our findings indicate that lead and cadmium induce clastogenic as well as aneugenic effects in peripheral lymphocytes, indicating a potential health risk for working populations with significant exposures to these heavy metals.

Pärt, P., O. Svanberg, et al. (1985). "The availability of cadmium to perfused rainbow

trout gills in different water qualities." Water Research **19**(4): 427-434.

The uptake of cadmium in perfused gills from rainbow trout (Salmo gairdneri, Rich.) in different water qualities has been studied. In the naturally hard alkaline Uppsala tap water, the calcium concentration was the dominating factor controlling the cadmium transfer through the gills. A strong inverse relationship was measured between the external Ca2+ concentration up to 3 mmol l-1 (< 120 mg Ca2+ l-1), and the Cd transfer. A higher Ca2+ concentration (10 mmol l-1) did not further affect the transfer. Magnesium decreased the transfer, but only at concentrations 4 to 5 times as high as calcium. At a constant Ca2+/Mg2+ hardness, the transfer was a function of the free cadmium ion activity (Cd2+). Ca2+ and Mg2+ selectively reduced the transfer by a biological mechanism, probably by changing the permeability of the gill epithelium. Cd transfer was not dependent on pH in the range pH 5-7. A lower transfer at pH 7.6 was related to a lower Cd2+ activity, probably due to the formation of non-available bicarbonate/carbonate complexes. Cd transfer decreased in the presence of 121 mmol l-1 NaCl (0.7% salinity). This decrease was not caused by the altered osmotic gradient over the gills. The transfer was proportional to the Cd2+ activity. CdCl+ and CdCl2 were not available for the gills. The retention of Cd in perfused gill tissue was proportional to the Cd2+ activity in all water qualities tested. Tissue accumulation of Cd was not sensitive to external Ca and Mg and in this respect different from the transfer.

Pelgrom, S., L. P. M. Lamers, et al. (1994). "INTERACTIONS BETWEEN COPPER AND CADMIUM DURING SINGLE AND COMBINED EXPOSURE IN JUVENILE TILAPIA OREOCHROMIS-MOSSAMBICUS - INFLUENCE OF FEEDING CONDITION ON WHOLE-BODY METAL ACCUMULATION AND THE EFFECT OF THE METALS ON TISSUE WATER AND ION CONTENT." Aquatic Toxicology **30**(2): 117-135.

Juvenile tilapia (Oreochromis mossambicus) were exposed for 96 h to ranges of sublethal concentrations of Cu or Cd, under both fed and non-fed conditions. Exposure to one metal (Cu or Cd) not only resulted in an increased whole body content of the metal exposed to, but also influenced the concentration of the other metal present in the fish. Furthermore, the total amount of Cu and Cd accumulated during exposure to heavy metals was influenced by the nutritional state of the fish. Besides exposure to either Cu or Cd, fish were also exposed to mixtures of Cu and Cd. Results indicated that accumulation during Cu/Cd co-exposure cannot be predicted by simple addition of the effects of single metal exposures. Obviously, complex interaction mechanisms are involved, as was concluded e.g. from the significantly decreased whole body Cd-content of Cu/Cd-co-exposed fish compared to the Cd-content of Cd-exposed fish. This phenomenon was observed in both fed and non-fed fish. Because ionic homeostasis is known to be affected by heavy metals, in this study also whole body water, calcium and sodium content in Cu and/or Cd-exposed fish were determined. The results indicate that also with respect to these parameters the two metals interact. The effects on water and ion appear to be dissociated. The data reveal previously unrecognized effects of interaction of the metals on whole body metal content, water and ion regulation.

Pelgrom, S. M. G. J., L. P. M. Lamers, et al. (1994). "Interactions between copper and cadmium during single and combined exposure in juvenile tilapia Oreochromis mossambicus: Influence of feeding condition on whole body metal accumulation and the effect of the metals on tissue water and ion content." Aquatic Toxicology **30**(2): 117-135.

Juvenile tilapia (Oreochromis mossambicus) were exposed for 96 h to ranges of sublethal concentrations of Cu or Cd, under both fed and non-fed conditions. Exposure to one metal (Cu or Cd) not only resulted in an increased whole body content of the metal exposed to, but also influenced the concentration of the other metal present in the fish. Furthermore, the total amount of Cu and Cd accumulated during exposure to heavy metals was influenced by the nutritional state of the fish. Besides exposure to either Cu or Cd, fish were also exposed to mixtures of Cu and Cd. Results indicated that accumulation during Cu/Cd co-exposure cannot be predicted by simple addition of the effects of single metal exposures. Obviously, complex interaction mechanisms are involved, as was concluded e.g. from the significantly decreased whole body Cd-content of Cu/Cd-co-exposed fish compared to the Cd-content of Cd-exposed fish. This phenomenon was observed in both fed and non-fed fish. Because ionic homeostasis is known to be affected by heavy metals, in this study also whole body water, calcium and sodium content in Cu and/or Cd-exposed fish were determined. The results indicate that also with respect to these parameters the two metals interact. The effects on water and ion appear to be dissociated. The data reveal previously unrecognized effects of interaction of the metals on whole body metal content, water and ion regulation.

Pelgrom, S. M. G. J., L. P. M. Lamers, et al. (1995). "Interactions between copper and cadmium modify metal organ distribution in mature tilapia, Oreochromis mossambicus." Environmental Pollution **90**(3): 415-423.

Sexually mature female tilapia were exposed to sublethal concentrations of waterborne Cu and/or Cd over 6 days, and subsequent body concentrations of these metals were determined in several organs. The results show that the distribution of Cu and Cd was metal and organ specific. This is demonstrated, for example, by the observation that in tilapia, Cu exposure did not result in Cu accumulation in the liver, whereas in the intestinal wall, notably high concentrations of Cu and Cd were measured in metal exposed fish. In addition to single metal exposed fish, we also determined Cu and Cd body distribution in Cu---Cd co-exposed fish. The observed interactions in metal accumulation were most pronounced in the organs of fish exposed to low, environmentally realistic, metal concentrations.

Pierron, F., M. Baudrimont, et al. (2008). "Cadmium uptake by the European eel: Trophic transfer in field and experimental investigations." Ecotoxicology and Environmental Safety **70**(1): 10-19.

Due to its status of threatened species and being heavily contaminated by metals, the European eel (Anguilla anguilla) was selected to investigate cadmium contamination levels of fish settled along a historically cadmium-contaminated

hydrosystem, the Garonne-Gironde continuum (France), according to its various location sites and fish length. Results have shown an important site effect on cadmium concentrations in liver but not in gills, highlighting the possible predominance of the trophic exposure route. Subsequently, uncontaminated eels were experimentally exposed to cadmium by water uptake and/or trophic route(s). Eels were fed with different preys: white shrimps collected in an unpolluted area in the Gironde estuary, and cadmium-enriched shrimps. Data obtained tend to show that the use of cadmium-enriched food during experimental investigations triggers an underestimation of the metal trophic transfer rate. These two complementary approaches provide some elements to suggest that the trophic route plays an important role in cadmium contamination of wild eels.

Planelló, R., J. L. Martínez-Guitarte, et al. (2007). "Ribosomal genes as early targets of cadmium-induced toxicity in Chironomus riparius larvae." Science of the Total Environment **373**(1): 113-121.

Cadmium is a widespread environmental pollutant that causes severe impacts in organisms. Although the effects of cadmium on aquatic insects have been studied in terms of their toxicity and changes in developmental parameters, little is known about its molecular and genetic effects. We have investigated the alterations in the pattern of gene expression provoked by acute exposure to cadmium in Chironomus riparius Mg. (Diptera, Chironomidae), a sentinel organism widely used in aquatic toxicity testing. The early cytotoxic effects were evaluated using immunocytochemistry and specific fluorescent probes in fourth instar larvae after 12 h of 10 mM cadmium treatments; under these conditions no significant effect on larvae mortality was detected until after 36 h of exposure. The changes in the pattern of gene expression were analysed by means of DNA/RNA hybrid antibodies in the polytene chromosomes from salivary gland cells. A decrease in the activity of the nucleolus is especially remarkable, accompanied by a significant reduction in size and the modification in nucleolar architecture, as shown by FISH. The inhibition of rDNA transcription was further evaluated by Northern blot analysis, which showed a marked decrease in the level of preribosomal rRNA (54% 45S 12 h). However, the BR genes, whose products are the giant polypeptides that constitute the silk-like secretion for constructing housing tubes, remain active. Simultaneously, decondensation and activation take place at some chromosomal regions, especially at the centromeres. The changes observed in the pattern of gene expression do not resemble those found after heat shock or other cell stressors. These data provide the first evidence that cadmium interacts with ribosomal genes and results in a drastic impairment of the functional activity of the nucleolus, an essential organelle for cellular survival. Therefore, the depletion of ribosomes would be a long-term effect of Cd-induced cellular damage. These findings may have important implications for understanding the adverse biological effects of cadmium and its toxic mechanism, as yet not clearly defined, and provide a sensitive biomarker of cadmium exposure.

Playle, R. C., D. G. Dixon, et al. (1993). "COPPER AND CADMIUM-BINDING TO FISH GILLS - ESTIMATES OF METAL GILL STABILITY-CONSTANTS AND MODELING OF METAL ACCUMULATION." Canadian Journal of Fisheries and Aquatic Sciences **50**(12): 2678-2687.

Fathead minnows (Pimephales promelas) were exposed to 17 mug Cu . L-1 or 6 mug Cd . L-1 in synthetic soft water in the presence of competing ligands. Measured gill metal concentrations correlated with free metal ion concentrations, not with total metal. Langmuir isotherms were used to calculate conditional metal-gill equilibrium constants and the number of binding sites for each metal. Log K(Cu-gill) was estimated to be 7.4 and the number of Cu binding sites on a set of gills (70 mg, wet weight) was approximately 2 x 10(-8) mol (approximately 30 nmol . g wet weight-1). Log K(Cd-gill) was approximately 8.6, and the number of Cd binding sites on minnow gills was approximately 2 x 10(-10) mol (approximately 2 nmol . g wet weight-1). Stability constants for H+ and Ca interactions at metal-gill binding sites and for metal interactions with dissolved organic carbon (DOC) were estimated using these metal-gill constants. All stability constants were entered into the MINEQL+ aquatic chemistry program, to predict metal accumulation on fish gills using metal, DOC, and Ca concentrations, and water pH. Calculated metal accumulation on gills correlated well with measured gill metal concentrations and with LC50 values. Our approach of inserting biological data into an aquatic chemistry program is useful for modelling and predicting metal accumulation on gills and therefore toxicity to fish.

Playle, R. C., D. G. Dixon, et al. (1993). "COPPER AND CADMIUM-BINDING TO FISH GILLS - MODIFICATION BY DISSOLVED ORGANIC-CARBON AND SYNTHETIC LIGANDS." Canadian Journal of Fisheries and Aquatic Sciences **50**(12): 2667-2677.

Adult fathead minnows (Pimephales promelas) were exposed to 17 mug Cu . L-1 or 6 mug Cd . L-1 for 2 to 3 h in synthetic softwater solutions at pH 6.2 containing either naturally-occurring, freeze-dried dissolved organic carbon (DOC) or synthetic ligands such as EDTA. After exposures, gills were assayed for bound Cu or Cd. As a first approximation, lake of origin or molecular size fraction of DOC did not influence Cu binding to gills, while DOC concentration did. DOC concentrations greater-than-or-equal-to4.8 mg . L-1 prevented Cu from accumulating on fathead gills. At the relatively low concentrations used, neither Cu nor Cd interfered with binding of the other metal on gills, suggesting different gill binding sites. Cadmium accumulation on gills was more sensitive to increased concentrations of Ca and H+ than was Cu. Surprisingly, Cd bound to gills to the same or greater extent than did Cu: for synthetic ligands, Cd binds less well than Cu. This result corroborates previously published observations that Cd, unlike Cu, is taken up at gills through high affinity Ca channels. Accumulation of Cd on fish gills was never associated with C-14-labelled EDTA or C-14-citrate, indicating that free metal interacts with the gill while metal-ligand complexes usually do not.

Pratap, H. B. and S. E. Wendelaar Bonga (1993). "Effect of ambient and dietary

cadmium on pavement cells, chloride cells, and Na+/K+-ATPase activity in the gills of the freshwater teleost Oreochromis mossambicus at normal and high calcium levels in the ambient water." Aquatic Toxicology **26**(1-2): 133-149.

The effects of cadmium on the gills of the African freshwater cichlid Oreochromis mossambicus in water with normal and relatively high calcium concentrations were studied for periods up to 35 days. The exposure was either through the ambient water or via the diet. Changes in the ultrastructure of the gill epithelium upon exposure to cadmium in the ambient water indicated degeneration of pavement cells and chloride cells, and acceleration in the turnover of the chloride cells. Studies of the Na+/K+-ATPase activity of the gills indicated that a transient increase in the total number of chloride cells was not associated with an increase, but rather a decrease of the total ion-exchange capacity of the chloride cells. Macrophages, lymphocytes, rodlet cells and neutrophilic granulocytes infiltrated the filament epithelium. Recovery of the gills was observed after 35 days. Dietary cadmium caused similar, although delayed, effects. High water calcium concentration reduced the impact of water-borne cadmium, but had no ameliorating effect on dietary cadmium. The data indicate that the disturbance of ion regulation in fish caused by sublethal levels of dietary cadmium is the result of effects of the metals on the gills rather than on the kidney.

Ramesh, M. (2006). "Studies on the impact of heavy metal cadmium on certain enzymes in a freshwater teleost fish, Cyprinus carpio." Toxicology Letters **164**(Supplement 1): S157-S157.

Ranaldi, M. M. and M. M. Gagnon "Accumulation of cadmium in the otoliths and tissues of juvenile pink snapper (Pagrus auratus Forster) following dietary and waterborne exposure." Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology **In Press, Corrected Proof**.

Laboratory experiments were conducted to examine if incorporation of Cd into the otoliths of juvenile pink snapper (Pagrus auratus Forster) was related to levels in the food or water. In the first experiment, fish were fed a regular diet (control group) or a Cd-contaminated diet (500 mg Cd kg- 1 or 1500 mg Cd kg- 1) for 35 days. In the second experiment, fish were exposed to waterborne Cd concentrations of <0.002 µg L- 1 (control), 50 µg L- 1, 100 µg L- 1 and 150 µg L- 1 for 35 days. The sagittal otoliths were analysed using laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS). Juvenile fish exposed to higher concentrations of waterborne or dietary Cd showed increased Cd levels in their otoliths. This study clearly demonstrated that both aqueous and dietary Cd exposures can result in Cd incorporation into the otoliths of pink snapper.

Rangsayatorn, N., M. Kruatrachue, et al. (2004). "Ultrastructural changes in various organs of the fish Puntius gonionotus fed cadmium-enriched cyanobacteria." Environmental Toxicology **19**(6): 585-593.

The accumulation and toxicity of cadmium in Puntius gonionotus fish that consumed the cyanobacterium Spirulina platensis contaminated with cadmium were studied. Fish were fed cadmium-contaminated cells for 4 weeks, after which

cadmium accumulation in various organs was determined. The highest cadmium content was found in the kidney (56.0 mug Cd/g wet weight). Cadmium was not detected in the gill during the entire 4 weeks of cadmium feeding. Histopathological alteration of cells was observed in the gill, kidney, and liver. The results showed that dietary cadmium caused hypertrophy and edema of gill filaments. Coagulative necrosis and karyolysis of the nucleus were observed in the kidney. Vacuoles and hyaline droplets had accumulated in the epithelial cells of the proximal tubule. In the liver vacuolation of the cytoplasm, infiltration of macrophages, and focal necrosis were found. The ultrastructural changes that occurred in the cells of different organs were similar. These included a proliferation of vacuoles and lysosomes, formation of myelin bodies, degranulation, vesiculation, and dilation of rough endoplasmic reticulum, as well as swelling of mitochondria with loss of cristae. (C) 2004 Wiley Periodicals, Inc.

Rathore, H. S., P. K. Sanghvi, et al. (1979). "Toxicity of cadmium chloride and lead nitrate to Chironomus tentans larvae." Environmental Pollution (1970) **18**(3): 173-177.

Chironomid larvae form an important link in aquatic food chains. Effluents from textile and pulp mills contain cadmium and lead salts which are dangerous to chironomid larvae, an important fish food. Toxicities of cadmium chloride and lead nitrate were studied under experimental conditions and the mean survival time and LD100 values were calculated. Results suggest that following poisoning by CdCl2 the total protein contents of the chironomid larvae decrease. This may diminish the nutritive value of these larvae as fish food. Qualitative analysis of larvae following exposure to CdCl2 and Pb(NO3)2 showed that these heavy metals were taken up by the chironomids.

Richards, J. G., B. K. Burnison, et al. (1999). "Natural and commercial dissolved organic matter protects against the physiological effects of a combined cadmium and copper exposure on rainbow trout (Oncorhynchus mykiss)." Canadian Journal of Fisheries and Aquatic Sciences **56**(3): 407-418.

Environmentally realistic concentrations of a natural dissolved organic matter (DOM) (8 mg C/L as dissolved organic carbon (DOC)) protected against the acute respiratory and ionoregulatory effects of 0.2 mu M Cd and 0.8 mu M Cu on rainbow trout (Oncorhynchus mykiss). The protection afforded by low natural DOC was the same as that afforded by similar or higher concentrations of commercial DOG. Trout exposed to the metals alone experienced large decreases in arterial Pot, increases in arterial P-CO2, increases in blood lactate, decreases in plasma concentrations of Cl, and developed pronounced haemoconcentration. There were no deleterious effects of 31 mg C/L commercial DOC on any measured aspect of trout physiology except for an increase in plasma Cl, which was probably due to elevated aqueous Cl concentrations associated with the DOM addition. No concentration of DOC used in the present study prevented Cd from being bound by trout gills, and some of these fish showed hypocalcemia; however, Cu was kept off the gills of trout exposed to metals plus DOM. Computer modelling using metal-gill binding constants simulated well the accumulation of Cd and the lack of Cu accumulation by trout

gills in the presence of DOM.

Risso-de Faverney, C., A. Devaux, et al. (2001). "Cadmium induces apoptosis and genotoxicity in rainbow trout hepatocytes through generation of reactive oxygene species." Aquatic Toxicology **53**(1): 65-76.

Cadmium poses a serious environmental threat in aquatic ecosystems but the mechanisms of its toxicity remain unclear. The purpose of this work was first to determine whether cadmium induced apoptosis in trout hepatocytes, second to determine whether or not reactive oxygen species (ROS) were involved in cadmium-induced apoptosis and genotoxicity. Hepatocytes exposed to increasing cadmium concentrations (in the range of 1-10 [mu]M) showed a molecular hallmark of apoptosis which is the fragmentation of the nuclear DNA into oligonucleosomal-length fragments, resulting from an activation of endogenous endonucleases and recognized as a [`]DNA ladder' on conventional agarose gel electrophoresis. Exposure of hepatocytes to cadmium led clearly to the DEVD-dependent protease activation, acting upstream from the endonucleases and considered as central mediators of apoptosis. DNA strand breaks in cadmium-treated trout hepatocytes was assessed using the comet assay, a rapid and sensitive single-cell gel electrophoresis technique used to detect DNA primary damage in individual cells. Simultaneous treatment of trout hepatocytes with cadmium and the nitroxide radical TEMPO used as a ROS scavenger, reduced significantly DNA fragmentation, DEVD-related protease activity and DNA strand breaks formation. These results lead to a working hypothesis that cadmium-induced apoptosis and DNA strand breaks in trout hepatocytes are partially triggered by the generation of ROS. Additional studies are required for proposing a mechanistic model of cadmium-induced apoptosis and genotoxicity in trout liver cells, in underlying the balance between DNA damage and cellular defence systems in fish.

Risso-de Faverney, C., N. Orsini, et al. (2004). "Cadmium-induced apoptosis through the mitochondrial pathway in rainbow trout hepatocytes: involvement of oxidative stress." Aquatic Toxicology **69**(3): 247-258.

Cadmium (Cd) induces oxidative stress and apoptosis in trout hepatocytes. We therefore investigated the involvement of the mitochondrial pathway in the initiation of apoptosis and the possible role of oxidative stress in that process. This study demonstrates that hepatocyte exposure to Cd (2, 5 and 10 [mu]M) triggers significant caspase-3, but also caspase-8 and -9 activation in a dose-dependent manner. Western-blot analysis of hepatocyte mitochondrial and cytosolic fractions revealed that cytochrome c (Cyt c) was released in the cytosol in a dose-dependent manner, whereas the pro-apoptotic protein Bax was redistributed to mitochondria after 24 and 48 h exposure. We also found that the expression of anti-apoptotic protein Bcl-xL, known to be regulated under mild oxidative stress to protect cells from apoptosis, did not change after 3 and 6 h exposure to Cd, then increased after 24 and 48 h exposure to 10 [mu]M Cd. In the second part of this work, two antioxidant agents, 2,2,6,6-tetramethylpiperidinyl-1-oxyl (TEMPO) (100 [mu]M) and N-acetylcysteine (NAC,

100 [mu]M) were used to determine the involvement of reactive oxygen species (ROS) in Cd-induced apoptosis. Simultaneously exposing trout hepatocytes to Cd and TEMPO or NAC significantly reduced caspase-3 activation after 48 h and had a suppressive effect on caspase-8 and -9 also, mostly after 24 h. Lastly, the presence of either one of these antioxidants in the treatment medium also attenuated Cd-induced Cyt c release in cytosol and the level of Bax in the mitochondria after 24 and 48 h, while high Bcl-xL expression was observed. Taken together, these data clearly evidenced the key role of mitochondria in the cascade of events leading to trout hepatocyte apoptosis in response to Cd and the relationship that exists between oxidative stress and cell death.

Rombough, P. J. and E. T. Garside (1982). "CADMIUM TOXICITY AND ACCUMULATION IN EGGS AND ALEVINS OF ATLANTIC SALMON SALMO-SALAR." Canadian Journal of Zoology-Revue Canadienne De Zoologie **60**(8): 2006-2014.

Rose, W. L., R. M. Nisbet, et al. (2006). "Using an integrated approach to link biomarker responses and physiological stress to growth impairment of cadmium-exposed larval topsmelt." Aquatic Toxicology **80**(3): 298-308.

In this study, we used an integrated approach to determine whether key biochemical, cellular, and physiological responses were related to growth impairment of cadmium (Cd)-exposed larval topsmelt (Atherinops affinis). Food intake (Artemia franciscana nauplii), oxygen consumption rates, apoptotic DNA fragmentation (TUNEL assay), and metallothionein (MT)-like protein levels, were separately measured in relation to growth of larval topsmelt aqueously exposed to sublethal doses of Cd for 14 days. Cadmium accumulation and concentrations of abundant metals were also evaluated in a subset of fish. Fish in the highest Cd treatments (50 and 100 ppb Cd) were smaller in final mean weight and length, and consumed fewer A. franciscana nauplii than control fish. Food intake was positively correlated with final weight of larval topsmelt in Cd and control treatments; food intake increased as final weight of the fish increased. Oxygen consumption rates were positively correlated with Cd concentration and mean oxygen consumption rates were inversely correlated with final mean weight of topsmelt; the smallest fish were found in the highest Cd treatment and were respiring at higher rates than control fish. Apoptotic DNA fragmentation was concentration-dependent and was associated with diminished growth. Apoptotic DNA fragmentation was elevated in the gill of fish exposed to 50ppbCd, and in the gut, gill, and liver of fish exposed to 100 ppb Cd. Metallothionein (MT)-like protein levels in fish from 100 ppb Cd treatments were significantly higher than those in other treatments. Oxygen consumption rates may have increased as a compensatory response to Cd exposure. However, it is likely that the energy produced was allocated to an increased metabolic demand due to apoptosis, NIT synthesis, and changes in ion regulation. This diversion of energy expenditures could contribute to growth impairment of Cd-exposed fish. (c) 2006 Elsevier B.V. All rights reserved.

Saiki, M. K., D. T. Castleberry, et al. (1995). "Copper, Cadmium, and Zinc

Concentrations in Aquatic Food-Chains From the Upper Sacramento River (California) and Selected Tributaries." Archives of Environmental Contamination and Toxicology **29**(4): 484-491.

Metals enter the Upper Sacramento River above Redding, California, primarily through Spring Creek, a tributary that receives acid-mine drainage from a US EPA Super-fund site known locally as Iron Mountain Mine. Waterweed (Elodea canadensis) and aquatic insects (midge larvae, Chironomidae; and mayfly nymphs, Ephemeroptera) from the Sacramento River downstream from Spring Creek contained much higher concentrations of copper (Cu), cadmium (Cd), and zinc (Zn) than did similar taxa from nearby reference tributaries not exposed to acid-mine drainage. Aquatic insects from the Sacramento River contained especially high maximum concentrations of Cu (200 mg/kg dry weight in midge larvae), Cd (23 mg/kg dry weight in mayfly nymphs), and Zn (1,700 mg/kg dry weight in mayfly nymphs). Although not always statistically significant, whole-body concentrations of Cu, Cd, and Zn in fishes (threespine stickleback, Gasterosteus aculeatus; Sacramento sucker, Catostomus occidentalis; Sacramento squaw-fish, Ptychocheilus grandis; and chinook salmon, Oncorhynchus tshawytasch) from the Sacramento River were generally higher than in fishes from the reference tributaries.

Saiki, M. K., B. A. Martin, et al. (2001). "Copper, cadmium, and zinc concentrations in juvenile chinook salmon and selected fish-forage organisms (aquatic insects) in the upper Sacramento River, California." Water Air and Soil Pollution **132**(1-2): 127-139.

This study assessed the downstream extent and severity of copper (Cu), cadmium (Cd), and zinc (Zn) contamination from acid mine drainage on juvenile chinook salmon (Oncorhynchus tshawytscha) and aquatic insects over a roughly 270-km reach of the Sacramento River below Keswick Reservoir. During April-May 1998, salmon were collected from four sites in the river and from a fish hatchery that receives water from Battle Creek. Salmon from river sites were examined for gut contents to document their consumption of various invertebrate taxa, whereas salmon from river sites and the hatchery were used for metal determinations. Midge (Chironomidae) and caddisfly (Trichoptera) larvae and mayfly (Ephemeroptera) nymphs were collected for metal determinations during April-June from river sites and from Battle and Butte creeks. The fish hatchery and Battle and Butte creeks served as reference sites because they had no history of receiving mine drainage. Salmon consumed mostly midge larvae and pupae (44.0%, damp-dry biomass), caddisfly larvae (18.9%), Cladocera (5.8%), and mayfly nymphs (5.7%). These results demonstrated that insects selected for metal determinations were important as fish forage. Dry-weight concentrations of Cu, Cd, and Zn were generally far higher in salmon and insects from the river than from reference sites. Within the river, high metal concentrations persisted as far downstream as South Meridian (the lowermost sampling site). Maximum concentrations of Cd (30.7 mug g(-1)) and Zn (1230 mug g(-1)), but not Cu (87.4 mug g(-1)), in insects exceeded amounts that other investigators reported as toxic when fed for prolonged periods to juvenile salmonids.

Sarnowski, P. and M. Witeska (2008). "The Effects of Copper and Cadmium in Single Exposure or Co-Exposure on Growth of Common Carp (Cyprinus Carpio L.) Larvae." Polish Journal of Environmental Studies **17**(5): 791-796.

The effects of copper and cadmium in single or co-exposure (each at the concentration of 0.2 mgxdm(-3), and in mixture -0.1 mgxdm(-3)) on growth of common carp larvae (in terms of body length and perimeter area) during the first 30 days post hatching were evaluated. Body length increased in a similar rate during the entire experimental period, while the increase of body perimeter area became faster after the shift into exogenous feeding, and then during swim bladder inflation. Copper was more toxic to the fish comparing cadmium or a mixture of both metals which indicates a possible antagonism of cadmium against copper toxicity. Body perimeter area was a more sensitive indicator of heavy metal intoxication compared to body length, and may be Used as an approximation of body mass for very small fish that cannot he accurately weighed alive.

Sastry, K. V. and P. K. Gupta (1979). "The effect of cadmium on the digestive system of the teleost fish, Heteropneustes fossilis." Environmental Research **19**(2): 221-230.

The effect of a sublethal concentration (6.8 mg/liter) of cadmium chloride on the histological structure and enzyme activities of the different parts of the alimentary tract and liver of a teleost fish, Heteropneustes fossilis, has been studied after exposure for 30 days. Liver and intestine were structurally as well as functionally the most affected portions. In the liver, connective tissue damage, liver cord disarray, enlargement and vacuolation of hepatocytes, degeneration of nuclei, accumulation of lipid, and focal necrosis were the most conspicuous changes. The erosion of mucous epithelium was noted in the stomach. In the intestine flattening and degeneration of the villi occurred and the mucus-secreting goblet cells showed hyperactivity. Three phosphatases studied showed significant inhibition in activity in the liver and intestine. An elevation in pepsin activity was recorded in the stomach but trypsin showed inhibition in the intestine. Marked inhibition was also noted in the activities of aminotripeptidase and glycylglycine dipeptidase. The results point out that cadmium produces structural damage in the digestive system and decreases the digestive efficiency by inhibiting the activity of a number of enzymes.

Sastry, K. V. and S. Subhadra (1984). "Effect of cadmium and zinc on intestinal absorption of xylose and tryptophan in the fresh water teleost fish." Chemosphere **13**(8): 889-898.

The effect of cadmium and of zinc on the rate of uptake of a pentose sugar xylose and an aminoacid tryptophan by the intestine of a teleost fish, was studied under two experimental conditions. In the first, four concentrations of cadmium or zinc (1.0 mM, 0.1 mM, 0.01 mM and 0.001 mM) mixed with the nutrient solution were filled in the intestinal sacs, and the rate of absorption was recorded after 1 h at 23°C. In the second experiment fish were exposed by bath to a sublethal concentration of cadmium (0.26 mg/1) or zinc (4 mg/1) for 15 and 30 days and the rate of absorption of the two nutrients was measured. The activity of intestinal

Na+, K+ activated adenosine triphosphatase was also assayed. The two heavy metals at all the four concentrations decreased the rate of intestinal transport of nutrients. Increase in the concentration of each of the heavy metals decreased the uptake of nutrients, but the decreases were not linear. The rate of intestinal absorption of the two nutrients was also reduced by exposure of fish to the heavy metals . The activity of Na+, K+ ATPase decreased with all four concentrations of cadmium and zinc and was diminished in fish exposed for 15 and 30 days. Of the two heavy metals, cadmium was more effective in reducing the rate of transport of xylose and tryptophan.

Scherer, E., R. E. McNicol, et al. (1997). "Impairment of lake trout foraging by chronic exposure to cadmium: a black-box experiment." Aquatic Toxicology **37**(1): 1-7.

The foraging success of lake trout (Salvelinus namaycush) on fingerling rainbow trout (Oncorhynchus mykiss) was evaluated after both species were exposed to 0.5 and 5 [mu]g Cd l-1 for 8-9 months (up to 277 days). Predation of rainbow fingerlings by lake trout was measured by daily counts of remaining prey in tanks where groups of exposed and unexposed prey fish were presented to exposed and unexposed predators. Using this measure, exposed prey presented to unexposed predators showed slight, but no significant increases in vulnerability to predation. Significant dose-dependent decreases of foraging rates were observed when exposed lake trout were presented with unexposed prey. Of four lake trout tissues sampled, posterior kidney had the highest cadmium concentration reaching 2.5 [mu]g g-1 after 9 months exposure to 5.0 [mu]g Cd l-1. Thyroid follicle epithelial cell height (a measure of thyroid functional state) was significantly decreased at both 6 and 9 months exposure to 5 [mu]g Cd l-1. Results underline a low response threshold for cadmium-caused behavioral changes, determined in a simple, efficient experimental design.

Schwartz, M. L., P. J. Curtis, et al. (2004). "Influence of natural organic matter source on acute copper, lead, and cadmium toxicity to rainbow trout (Oncorhynchus mykiss)." Environmental Toxicology and Chemistry **23**(12): 2889-2899.

Natural organic matter (NOM) was concentrated from various sites across Canada using a portable reverse-osmosis unit to obtain a range of NOM types, from mainly allochthonous (terrestrially derived) to mainly autochthonous (aquatically derived) NOM. The addition of NOM to Cu exposures in ion-poor water always decreased Cu toxicity to rainbow trout (Oncorhynchus inykiss, similar to1 g) over a 96-h period, and the degree of protection varied with respect to NOM source. A good correlation was found between the specific absorbance coefficient (SAC) and time to reach 50% mortality (LT50; $p < 0.001$), indicating that more optically dark, allochthonous-like NOM decreases Cu toxicity better than does optically light, more autochthonous-like NOM. A similar, good relationship between NOM source and Pb toxicity was seen ($p < 0.001$), once confounding effects of Ca binding to NOM were accounted for. No significant relationship between Cd toxicity and NOM optical quality was seen ($p = 0.082$), and in toxicity tests with Cd the presence of some of the NOM sources increased Cd toxicity compared to Cd-only controls. Specific absorbance coefficients were

used as a proxy measurement of NOM aromaticity in our study, and fluorescence indices were run on some NOM samples to obtain percent aromaticity for each sample. A good correlation was found between SAC and percent aromaticity, indicating that the simple SAC measurement is a reasonable indication of NOM aromaticity and of metal binding by NOM.

Scott Jackson, C., J. Sneddon, et al. (2003). "Use of flame atomic absorption spectrometry and the effect of water chemistry for the study of the bioaccumulation of cadmium in Menidia beryllina (cope), the tidewater silverside." Microchemical Journal **75**(1): 23-28.

In laboratory controlled experiments using Menidia beryllina, the Tidewater Silverside (fish), it was shown that the salinity of the water affects accumulation of cadmium. The concentration of cadmium was determined using a previously described flame atomic absorption spectrometric method. In general, the higher the salinity, the less cadmium is accumulated in fish. At low or no salinity, higher concentrations of cadmium are found in fish. Elimination of cadmium occurred at a faster rate in fish exposed to higher levels of salinity. It is proposed that the low bioaccumulation of cadmium in high saline waters was due to competition between the free Cd2+ ion, Ca2+, and Cl- ion preventing Cd2+ from entering fish.

Sherman, R. E., S. P. Gloss, et al. (1987). "A comparison of toxicity tests conducted in the laboratory and in experimental ponds using cadmium and the fathead minnow (Pimephales promelas)." Water Research **21**(3): 317-323.

Acute toxicity tests were conducted in the laboratory with fathead minnows (Pimephales promelas) to determine the 96-h LC50 of cadmium under three conditions: (1) in laboratory water, (2) in water from experimental ponds, and (3) in pond water underlain by sediment. Cadmium was then applied at doses equivalent to the estimated LC50 values to 0.07-ha ponds containing caged fathead minnows. A cadmium ion selective electrode, ultrafiltration, and equilibrium calculations were used to determine cadmium speciation, and several water quality characteristics were measured to correlate differences in mortality between test systems (laboratory and field) with observed differences in water quality. The LC50 estimates (mg l-1) for the bioassays were 4.39 for the laboratory water, 3.52 for the pond water with sediment, and 2.91 for the pond water. Concentrations of Cd2+ decreased and those of cadmium in the particulate (> 1.2 [mu]m) and 300,000 mol. wt (0.018-1.2 [mu]m) fractions increased over the 96-h; cadmium in these fractions was believed to consist of colloidal sized CdCO3 precipitates. Concentrations of Cd2+ decreased at different rates between test systems, regulated by the degree of CdCO3(s) supersaturation which in turn depended on pH and total metal concentrations. Differences in toxicity in the laboratory tests were attributed to differences in water hardness and Cd2+ concentrations. Mortality of fathead minnows was low (0-10%) during the 96-h test period in the ponds due to the higher pH, which produced supersaturated conditions resulting in the rapid formation of nontoxic CdCO3 precipitates and a more rapid decrease in Cd2+ concentrations as

compared to the laboratory bioassays.

Sjöbeck, M.-L., C. Haux, et al. (1984). "Biochemical and hematological studies on perch, Perca fluviatilis, from the cadmium-contaminated river Emån." Ecotoxicology and Environmental Safety **8**(3): 303-312.

In a field investigation, biochemical and hematological parameters were measured in perch, Perca fluviatilis, living in the cadmium-contaminated river Emån in the southeast of Sweden. The number of lymphocytes was 45-100% higher in perch from the contaminated area than in the reference perch, indicating a stimulated immune defense. In addition, the cadmium-loaded fish suffered from a slight anemia and a disturbed carbohydrate metabolism and blood plasma ion composition. The observed effects suggest that cadmium affects fish in the environment similar to what has been observed in laboratory studies. However, the weaker response may imply that the perch in the field situation have been adapted and thus acquired an increased resistance to cadmium.

Sloman, K. A., G. R. Scott, et al. (2003). "Cadmium affects the social behaviour of rainbow trout, Oncorhynchus mykiss." Aquatic Toxicology **65**(2): 171-185.

The present study investigated both the effects of cadmium on the social interactions of rainbow trout and the differential accumulation of waterborne cadmium among social ranks of fish. Fish exposed to waterborne cadmium concentrations of 2 [mu]g l-1 for 24 h, followed by a 1, 2 or 3 day depuration period in clean water, had a decreased ability to compete with non-exposed fish. However, the competitive ability of exposed fish given a 5 day depuration period was not significantly impaired. Cadmium accumulated in the olfactory apparatus of fish exposed to waterborne cadmium for 24 h and decreased significantly only after 5 days depuration in clean water. Among groups of ten fish held in stream tanks, where all fish were exposed to cadmium, there were significant effects on social behaviour and growth rate. Dominance hierarchies formed faster among fish exposed to cadmium than among control fish, and overall growth rates were higher in the cadmium treatment. In groups of ten fish, social status also affected tissue accumulation of cadmium during waterborne exposure, with dominant fish accumulating more cadmium at the gill. In conclusion, exposure to low levels of cadmium, affects the social behaviour of fish, in part due to accumulation in the olfactory apparatus, and dominant fish accumulate more gill cadmium than subordinates during chronic waterborne exposure.

Soares, S. S., H. Martins, et al. (2008). "Vanadium and cadmium in vivo effects in teleost cardiac muscle: Metal accumulation and oxidative stress markers." Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology **147**(2): 168-178.

Several biological studies associate vanadium and cadmium with the production of reactive oxygen species (ROS), leading to lipid peroxidation and antioxidant enzymes alterations. The present study aims to analyse and compare the oxidative stress responses induced by an acute intravenous exposure (1 and 7 days) to a sub-lethal concentration (5 mM) of two vanadium solutions,

containing different vanadate n-oligomers (n = 1-5 or n = 10), and a cadmium solution on the cardiac muscle of the marine teleost Halobatrachus didactylus (Lusitanian toadfish). It was observed that vanadium is mainly accumulated in mitochondria (1.33 ± 0.26 [mu]M), primarily when this element was administrated as decameric vanadate, than when administrated as metavanadate (432 ± 294 nM), while the highest content of cadmium was found in cytosol (365 ±231 nM). Indeed, decavanadate solution promotes stronger increases in mitochondrial antioxidant enzymes activities (catalase: + 120%; superoxide dismutase: + 140%) than metavanadate solution. On contrary, cadmium increases cytosolic catalase (+ 111%) and glutathione peroxidases (+ 50%) activities. It is also observed that vanadate oligomers induce in vitro prooxidant effects in toadfish heart, with stronger effects induced by metavanadate solution. In summary, vanadate and cadmium are differently accumulated in blood and cardiac subcellular fractions and induced different responses in enzymatic antioxidant defence mechanisms. In the present study, it is described for the first time the effects of equal doses of two different metals intravenously injected in the same fish species and upon the same exposure period allowing to understand the mechanisms of vanadate and cadmium toxicity in fish cardiac muscle.

Srivastava, A. K. and S. Mishra (1979). "Blood dyscrasia in a teleost fish, Colisa fasciatus, associated with cadmium poisoning." Journal of Comparative Pathology **89**(4): 609-613.

Exposure of a freshwater teleost, Colisa fasciatus to a sub-lethal concentration (100 mg per 1) of cadmium, as cadmium sulphate induced lymphocytosis and anaemia, with simultaneous regeneration of red blood cells, at 90 h post treatment. The 96 h LC50 value, determined concurrently by static bioassay, for the metal was 126 mg per 1. The treatment also evoked thrombocytosis with concomitant hypercoagulability of whole-blood. These results are compared with heavy metal poisoning in this and in other fish, and with cadmiosis in man.

Stubblefield, W. A., B. L. Steadman, et al. (1999). "Acclimation-induced changes in the toxicity of zinc and cadmium to rainbow trout." Environmental Toxicology and Chemistry **18**(12): 2875-2881.

Adults and juvenile rainbow trout exposed for 21 d to sublethal levels of zinc or cadmium exhibited significant changes in their respective incipient lethal levels (ILL). Acclimation resulted in exposure-dependent changes in both tolerance (ILL concentration) and resistance (time to ILL) in both size classes of fish for each metal. The ILLs for adult rainbow trout exposed to zinc increased from 695 mu g/L at 131 h for nonacclimated fish to 2,025 mu/L at 168 h for fish previously exposed to 0.5 ILL (324 mu g/L zinc). The ILLs for cadmium-exposed fish increased from 6 mu g/L at 187 h for nonacclimated fish to 122 mu g/L at 266 h for Fish acclimated to 0.5 ILL (10.2 mu g/L cadmium). Similar, although somewhat less dramatic, acclimation responses were observed for juveniles with both zinc and cadmium. Juveniles were found to be approximately three times less sensitive to the toxic effects of the metals than were adult fish.

Sunila, I. (1986). "Chronic histopathological effects of short-term copper and cadmium exposure on the gill of the mussel, Mytilus edulis." Journal of Invertebrate Pathology **47**(2): 125-142.

Mussels, Mytilus edulis, were exposed to elevated concentrations of copper (0.1, 0.2, 0.4, and 0.8 mg/liter) and cadmium (1, 2, 4, and 8 mg/liter) in aquaria. After the 24 hr exposure they were put in cages submerged in the sea. Samples from the gills were taken over a period of 1 year for histopathological analysis. Acute changes occurring were the swelling of the endothelial cells and the detachment of the abfrontal cells in the copper-exposed gills, and the dilatation of the branchial veins in the cadmium-exposed gills. The gills were invaded by granulocytes, indicating an inflammatory reaction. After 1 year, cavities were formed under the proximal ends of the postlateral cells in the copper- and cadmium-exposed mussels. Copper-exposed mussels had low gills with folded edges. Forty-four percent of the copper-exposed gills had structural deformities caused by the fusion of the gill filaments. The abnormalities were of the following types: fusion of frontal parts of the filaments, fusion of abfrontal parts of the filaments, or interlamellar fusion of the abfrontal parts of the filaments of opposite lamella.

Suresh, A., B. Sivaramakrishna, et al. (1993). "PATTERNS OF CADMIUM ACCUMULATION IN THE ORGANS OF FRY AND FINGERLINGS OF FRESH-WATER FISH CYPRINUS-CARPIO FOLLOWING CADMIUM EXPOSURE." Chemosphere **26**(5): 945-953.

Cadmium concentration was determined by AAS in the gill and muscle of fry, and gill, kidney, liver and muscle of fingerlings of the freshwater fish Cyprinus carpio after Days 1, 2, 3 and 4 of exposures to lethal and Days 1, 7, 15 and 30 of exposures to sublethal concentrations of cadmium. Both the percentage and rate of accumulation were increased with the exposure time under lethal concentrations and the degree of accumulation among the organs was in the order: gill > muscle of fry; gill > kidney > muscle > liver of fingerlings. In sublethal concentrations though a significant amount of cadmium accumulation was recorded in the organs of fry and fingerlings, the rate of accumulation significantly declined with the exposure time and the degree of accumulation among the organs was in the order: gill > muscle of fry; liver > gill > kidney > muscle of fingerlings. Further, the percentage/rate of metal accumulation was greater in the organs of fry than in those of fingerlings exposed to lethal concentration eventhough the ambient cadmium concentration was substantially less for fry than fingerlings; whereas the reverse was observed in sublethal concentration. Possible reasons for the dependence of accumulation on the factors such as ambient medium concentration, duration of exposure and size of the animal are discussed.

Suresh, A., B. Sivaramakrishna, et al. (1993). "Patterns of cadmium accumulation in the organs of fry and fingerlings of freshwater fish following cadmium exposure." Chemosphere **26**(5): 945-953.

Cadmium concentration was determined by AAS in the gill and muscle of fry, and gill, kidney, liver and muscle of fingerlings of the freshwater fish after Days 1, 2, 3 and 4 of exposures to lethal and Days 1, 7, 15 and 30 of exposures to sublethal concentrations of cadmium. Both the percentage and rate of accumulation were increased with the exposure time under lethal concentrations and the degree of accumulation among the organs was in the order: gill > muscle of fry; gill > kidney > muscle > liver of fingerlings. In sublethal concentrations though a significant amount of cadmium accumulation was recorded in the organs of fry and fingerlings, the rate of accumulation significantly declined with the exposure time and the degree of accumulation among the organs was in the order: gill > muscle of fry; liver > gill > kidney > muscle of fingerlings. Further, the percentage/rate of metal accumulation was greater in the organs of fry than in those of fingerlings exposed to lethal concentration eventhough the ambient cadmium concentration was substantially less for fry than fingerlings; whereas the reverse was observed in sublethal concentration. Possible reasons for the dependence of accumulation on the factors such as ambient medium concentration, duration of exposure and size of the animal are discussed.

Suresh, A., B. Sivaramakrishna, et al. (1995). "Cadmium induced changes in ion levels and ATPase activities in the muscle of the fry and fingerlings of the freshwater fish." Chemosphere **30**(2): 367-375.

Levels of sodium, potassium and calcium ions and the activities of Na+---K+, Mg2+ and Ca2+ ATPases were estimated in the muscle of the fry and fingerlings of an economically important edible freshwater fish, , at 1,2,3 and 4 days on exposure to the lethal, 4.3 mg/L and 17.1 mg/L respectively for the fry and fingerlings,and 1,7,15 and 30 days on exposure to sublethal, 0.86 mg/L and 3.42 mg/L, concentrations of cadmium. All the ion levels and ATPase activities progressively decreased over time of exposure, in the order day 1 < 2 < 3 < 4, in the muscle of both fry and fingerlings on exposure to lethal concentrations; the magnitude of decrease was higher in the fry than the fingerlings. In sublethal concentrations, an initial decrease in these parameters of the fry was noticed at day 1, but on further exposure they increased over control, however, the order was day 7 > 15 > 30 in sodium ions and Na+---K+ and Mg2+ ATPase activities and 7 < 15 > 30 in potassium and calcium ions and Ca2+ ATPase activity. In fingerlings, all the parameters decreased at days 1 and 7 (day 1 < 7) but increased at days 15 and 30 (day 15 < 30). All these changes in iono-regulatory pattern of the fish were discussed in the light of available literature.

Szczerbik, P., T. Mikolajczyk, et al. (2006). "Influence of long-term exposure to dietary cadmium on growth, maturation and reproduction of goldfish (subspecies: Prussian carp Carassius auratus gibelio B.)." Aquatic Toxicology **77**(2): 126-135.

The influence of long-term exposure of goldfish to dietary cadmium (Cd) on its accumulation in tissues, growth, ovarian development, luteinizing hormone (LH) secretion and a response to hormonal stimulation of spawning were evaluated. The study was conducted on four groups of females for the period of 3 years, from the age of 10 weeks to second spawning. Four doses of Cd were applied in

the feed: 0 (control group), 0.1, 1 and 10 mg Cd g(-1) of feed (wet weight). The highest dose of Cd (10 mg g(-1)) inhibited growth and caused several behavioural effects. In contrast, lower dose of Cd (1 mg g(-1)) stimulated fish growth. The doses of Cd from 0.1 to 1 mg Cd g(-1) did not influence ovarian development. The gonado-somatic index (GSI) and histological analysis of ovaries showed no differences in ovarian development between the control group and the groups receiving these doses of Cd. However, in the group receiving the highest Cd dose, GSI decreased. This was associated with persistent, long-lasting elevation of plasma LH levels. Ovulation did not occur in this group. Injections of salmon GnRH-analogue (sGnRHa) alone or with domperidone (a dopamine receptor antagonist) in sexually mature fish caused an increase of LH levels in all groups, although in the group fed with the highest Cd dose the effect was weaker than in the other groups. After the first spawning season, a negative effect of lower Cd doses (0.1 and 1 mg Cd g(-1)) on ovarian recrudescence (rebuilding of ovaries) and on the response to the consecutive hormonal stimulation of spawning was observed (lower number of ovulating females). There was a significantly higher content of Cd in the livers of fish than in their muscles. The results of hormonal stimulation of spawning and histological analysis of ovaries suggest that in goldfish cadmium acts mainly at the level of ovary rather than on the pituitary gland. We suppose that in the natural environment cadmium present in the feed can play an important role in the accumulation of this element in fish tissues and can influence vital physiological processes. (c) 2005 Elsevier B.V. All rights reserved.

Tao, S., C. Liu, et al. (2000). "Uptake of Cadmium Adsorbed on Particulates by Gills of Goldfish (Carassius auratus)." Ecotoxicology and Environmental Safety **47**(3): 306-313.

Goldfish (Carassius auratus) were exposed to mixtures of constant dissolved cadmium (0.01 mg/L) and cadmium adsorbed on gibbsite particles at concentrations of 0, 0.025, 0.050, 0.075, and 0.100 mg/L. The gills of the fish were excised after a 5-day exposure experiment and both cadmium and aluminum in the gills were measured. The gills were also examined with a light microscope for surface adherence of the particles after the exposure. The evidence collected demonstrated that the concentration of cadmium in the gills increased with increased concentration of particulate cadmium during the exposure while the dissolved cadmium remained constant. The ratio of cadmium to aluminum in the gills was apparently higher than that in the solution, indicating the stripping and translocation of cadmium from the particles. A multistep uptake process is proposed and the bioavailability of particulate cadmium to fish gills is discussed.

Thompson, J. and J. Bannigan (2008). "Cadmium: Toxic effects on the reproductive system and the embryo." Reproductive Toxicology **25**(3): 304-315.

The heavy metal cadmium (Cd) is a pollutant associated with several modern industrial processes. Cd is absorbed in significant quantities from cigarette smoke, and is known to have numerous undesirable effects on health in both experimental animals and humans, targeting the kidneys, liver and vascular

systems in particular. However, a wide spectrum of deleterious effects on the reproductive tissues and the developing embryo has also been described. In the testis, changes due to disruption of the blood-testis barrier and oxidative stress have been noted, with onset of widespread necrosis at higher dosage exposures. Incorporation of Cd into the chromatin of the developing gamete has also been demonstrated. Ovarian Cd concentration increases with age, and has been associated with failure of progression of oocyte development from primary to secondary stage, and failure to ovulate. A further mechanism by which ovulation could be rendered ineffective is by failure of pick-up of the oocyte by the tubal cilia due to suboptimal expansion of the oocyte-cumulus complex and mis-expression of cell adhesion molecules. Retardation of trophoblastic outgrowth and development, placental necrosis and suppression of steroid biosynthesis, and altered handling of nutrient metals by the placenta all contribute to implantation delay and possible early pregnancy loss. Cd has been shown to accumulate in embryos from the four-cell stage onwards, and higher dosage exposure inhibits progression to the blastocyst stage, and can cause degeneration and decompaction in blastocysts following formation, with apoptosis and breakdown in cell adhesion. Following implantation, exposure of experimental animals to oral or parenteral Cd causes a wide range of abnormalities in the embryo, depending on the stage of exposure and dose given. Craniofacial, neurological, cardiovascular, gastrointestinal, genitourinary, and limb anomalies have all been described in placentates, with axial abnormalities and defects in somite structure noted in fish and ventral body wall defect and vertebral malformation occurring in the chick. In this paper, we examine the mechanisms by which Cd can affect reproductive health, and consider the use of micronutrients in prevention of these problems.

Tort, L., B. Kargacin, et al. (1996). "The effect of cadmium exposure and stress on plasma cortisol, metallothionein levels and oxidative status in rainbow trout (Oncorhynchus mykiss) liver." Comparative Biochemistry and Physiology Part C: Comparative Pharmacology and Toxicology **114**(1): 29-34.

Selected variables related to the stress response in mammals, such as cortisol, metallothionein (MT), glutathione (GSH) and lipid peroxidation measured as thiobarbituric acid-reactants (TBARs) were evaluated in rainbow trout in order to establish whether chemical stress by cadmium exposure or physical stress by handling cause a significant response and comparable effects between stressors. The results obtained show about three times higher levels of liver MT in fish exposed to cadmium as compared to controls and twice as high after stress, whereas plasma cortisol levels increased significantly both after stress and cadmium exposure. This indicates that both MT and cortisol were sensitive indexes to stress in this species. In contrast, liver cytosolic GSH was affected only by cadmium treatment and liver TBARs remained unaffected.

Tort, L. and L.-H. Madsen (1991). "The effects of the heavy metals cadmium and zinc on the contraction of ventricular fibres in fish." Comparative Biochemistry and Physiology Part C: Comparative Pharmacology **99**(3): 353-356.

1. The force-frequency relationship has been determined in strips of ventricular fibres of sea bass and dogfish after treatment with several concentrations of cadmium and zinc. 2. At increasing metal concentrations a reduction of twitch force is observed in the heart fibres, the reduction being similar in the two species for each metal. 3. Cadmium shows a more powerful effect since comparable reduction is obtained at 10 times lower concentration. 4. The removal of metal concentrations in previously-treated strips does not allow the initial force to recover. 5. The results are discussed in relation to the consequences of metal exposure on the heart function and the repercussion on fish performance.

van Dyk, J. C., G. M. Pieterse, et al. (2007). "Histological changes in the liver of Oreochromis mossambicus (Cichlidae) after exposure to cadmium and zinc." Ecotoxicology and Environmental Safety **66**(3): 432-440.

The toxic effects, of two heavy metals, cadmium (Cd) and zinc (Zn), on the histology of the liver of the southern African freshwater fish Oreochromis mossambicus, were investigated. The goal was to identify whether metal concentrations and exposure period influence the degree and nature of histological changes in the liver of exposed fish. Selected fish were exposed to a mixture of 5% concentrations of the LC50 of cadmium and zinc and to a mixture of 10% concentrations of the LC50 of cadmium and zinc, over both short- and long-term exposure periods. Similar histological changes occurred in the livers of specimens exposed to both 5% and 10% concentrations, indicating a definite toxic response to both the metal concentrations. These histological changes included hyalinization, hepatocyte vacuolation, cellular swelling, and congestion of blood vessels. The intensity of these histological changes was, however, influenced by the extent of the exposure period.

Van Hoof, F. and M. Van San (1981). "Analysis of copper, zinc, cadmium and chromium in fish tissues. A tool for detecting metal caused fish kills." Chemosphere **10**(10): 1127-1135.

In order to find the causative agent in frequently occuring fish kills in a Belgian river a series of toxicity tests has been conducted in which rudd (Scardinius erythrophtalmus) were exposed to acute lethal and subacute non lethal concentrations of copper, chromium, cadmium and zinc. The concentrations of these metals in gills, opercle, kidney, liver and muscle were measured. Metal levels in gills were the most valuable indicator of acute lethal exposure. This information was compared with levels found in rudd from a surface water storage reservoir and from the river Meuse. Fish collected after fish kills in the river Meuse were analysed. In one case copper could be identified as one of the toxicants concerned by fish tissue analysis. Metal levels in fish tissues can give valuable additional information concerning the cause of kills provided that background information is available about metal levels in water and normal tissue levels.

Versteeg, D. J. and J. P. Giesy (1986). "The histological and biochemical effects of

cadmium exposure in the bluegill sunfish (Lepomis macrochirus)." Ecotoxicology and Environmental Safety **11**(1): 31-43.

Cadmium effects on the bluegill sunfish (Lepomis macrochirus) were assessed histologically and biochemically and the effects were compared with effects on the ecologically relevant parameters of growth and survival. Growth and survival were monitored and tissues were removed for histopathological assessment of toxicant effects in a 163-day chronic exposure. The biochemical effects of cadmium were determined in a 32-day subchronic exposure. Exposure of fish to cadmium in hard water (363 mg Cd/liter) caused significant reductions in growth at 3.9 and 12.7 mg Cd/liter. Mortality was significantly increased over controls at 12.7 mg Cd/liter. Histopathological lesions were observed in gill tissue from fish exposed to 3.9 and 12.7 mg Cd/liter at all times during the chronic exposure. No histopathological lesions were observed in any internal organ during this exposure. In a 32-day subchronic exposure, cadmium caused significant increases in serum acid phosphatase and N-acetyl-[beta]--glucosaminidase activities. Serum aspartate and alanine transaminase and lactate dehydrogenase activities were not increased by cadmium exposure. Liver lysosomal membranes were destabilized by cadmium exposure. This indicates an alteration in lysosome function. The utility of biochemical and histological procedures for estimating safe concentrations of environmental pollutants are discussed.

Voegborlo, R. B., A. M. El-Methnani, et al. (1999). "Mercury, cadmium and lead content of canned tuna fish." Food Chemistry **67**(4): 341-345.

Mercury levels in canned tuna fish were determined by cold vapour atomic absorption spectrophotometry while cadmium and lead levels were determined by flame atomic absorption spectrophotometry. The metal contents in the samples, expressed in [mu]g g-1 wet weight, varied from 0.20 to 0.66 with an average value of 0.29 for mercury, from 0.09 to 0.32 with an average value of 0.18 for cadmium and from 0.18 to 0.40 with an average value of 0.28 for lead. The results of this study indicate that tuna fish from the Mediterranean coast of Libya have concentrations well below the permissible levels for these toxic metals. Their contribution to the body burden can therefore be considered negligible.

Wennberg, M., T. Lundh, et al. (2006). "Time trends in burdens of cadmium, lead, and mercury in the population of northern Sweden." Environmental Research **100**(3): 330-338.

The time trends of exposure to heavy metals are not adequately known. This is a worldwide problem with regard to the basis for preventive actions and evaluation of their effects. This study addresses time trends for the three toxic elements cadmium (Cd), mercury (Hg), and lead (Pb). Concentrations in erythrocytes (Ery) were determined in a subsample of the population-based MONICA surveys from 1990, 1994, and 1999 in a total of 600 men and women aged 25-74 years. The study took place in the two northernmost counties in Sweden. To assess the effect of changes in the environment, adjustments were made for life-style factors that are determinants of exposure. Annual decreases of 5-6% were seen for Ery-

Pb levels (adjusted for age and changes in alcohol intake) and Ery-Hg levels (adjusted for age and changes in fish intake). Ery-Cd levels (adjusted for age) showed a similar significant decrease in smoking men. It is concluded that for Pb and maybe also Hg the actions against pollution during recent decades have caused a rapid decrease of exposure; for Hg the decreased use of dental amalgam may also have had an influence. For Cd, the decline in Ery-Cd was seen only in smokers, indicating that Cd exposure from tobacco has decreased, while other environmental sources of Cd have not changed significantly. To further improve the health status in Sweden, it is important to decrease the pollution of Cd, and actions against smoking in the community are important.

Wicklund Glynn, A., L. Andersson, et al. (1992). "Cadmium turnover in minnows, Phoxinus phoxinus, FED 109Cd-labeled Daphnia magna." Chemosphere **24**(3): 359-368.

Minnows, Phoxinus phoxinus, were individually fed with cadmium-containing Daphnia magna (2/d) for 30 days. The fish were then given a 3-d dose of 109Cd-labeled D. magna (2/d). Thereafter, during continuous feeding with D. magna, the retention, redistribution and elimination of the tracer was studied for 47 days. After the 3-d 109Cd exposure, the whole body retained 5.6% and the intestine 5% of the dose. Only 0.6% of the dose was present in the rest of the body. The intestine lost 99.8% of the retained tracer during the 47-d elimination period, whereas 96.2% was eliminated from the fish. The 109Cd content in the liver and kidney increased 2 to 4 times during the same period, and at day 47 the organs had accumulated 0.04% and 0.12% of the administered dose, respectively. A theoretical comparison of the relative contribution of the two routes for Cd uptake (gills-intestine) to Cd accumulation in the liver and kidney was made. It indicated that uptake through the gills dominates in Cd-uncontaminated waters, whereas the uptake from food may dominate in Cd-contaminated waters.

Woodworth, J., A. S. A. Evans, et al. (1983). "The production of cadmium-binding protein in three species of freshwater fish." Toxicology Letters **15**(4): 289-295.

Cadmium-binding protein (Cd-BP) was detected in the liver and kidney of stoneloach, Noemacheilus barbatulus, roach, Rutilus rutilus and rainbow trout, Salmo gairdneri which had been dosed i.p. with 1 mg cadmium (Cd)/kg body weight 168 h previously. The cadmium content ([mu]g Cd/g wet weight tissue) was much lower in the liver and kidney of trout than in stoneloach and roach, but there was no clear relationship between the amount of Cd-BP detected and the reported sensitivity of each species to cadmium.

Woodworth, J. and D. Pascoe (1983). "Induction of cadmium-binding protein in the three-spined stickleback." Aquatic Toxicology **3**(2): 141-148.

Three-spined sticklebacks (Gasterosteus aculeatus L.) were dosed with cadmium either by natural exposure (0, 0.1 or 1.0 mg Cd·l-1) or by injection (0 or 5 [mu]g Cd·g-1 body weight). Analysis of the particle-free supernatant of liver homogenates (Sephadex G-75 chromatography) from each treatment group showed that sticklebacks exposed to cadmium by either means were capable of

binding the metal to a protein (cadmium-binding protein or Cd-BP) which was not detected in large quantities in control fish. Some characteristics of the Cd-BP and its possible role are discussed.

Wu, S. M., Y. C. Ho, et al. (2007). "Effects of Ca2+ or Na+ on metallothionein expression in tilapia larvae (Oreochromis mossambicus) exposed to cadmium or copper." Archives of Environmental Contamination and Toxicology **52**(2): 229-234.
The objectives of this study were to try to determine the reasons of the external Ca2+ and Na+ enhancement of Cd2+ and Cu2+ resistance in fish. Tilapia larvae at 3 days posthatch were exposed to (A) 0 (control), 40 mu g/L Cd2+, 40 mu g/L Cd2+ + 2 mM Ca2+ (Cd/hyper-Ca), and 2 mM Ca2+ or (B) 0 (control), 75 mu g/L Cu2+, 75 mu g/L Cu2+ + 0.52 mM Na+ (Cu/hyper-Na), and 0.52 mM Na+. After 48 hours, results indicated that (1) Cd/hyper-Ca and Cu/hyper-Na treatments showed decreased growth inhibition induced by the metals; (2) metal accumulation in Cd/hyper-Ca-treated larvae was lower compared with those exposed only to Cd; and (3) metallothionein (MT) expression was significantly higher in Cu/hyper-Na-treated larvae than in the group treated with Cu only. Taking all of this into account, either supplementary Ca2(+) or Na+ in ambient water may help fish to maintain Ca2(+) or Na+ homeostasis, which could decrease metal accumulation and its detrimental effects. Consequently, the fish increase MT expression and retard the growth inhibition caused by metals.

Yilmaz, M., A. Gül, et al. (2004). "Investigation of acute toxicity and the effect of cadmium chloride (CdCl2 · H2O) metal salt on behavior of the guppy (Poecilia reticulata)." Chemosphere **56**(4): 375-380.
In this study 96-h LC50 value of cadmium chloride (CdCl2 · H2O), a metal salt widely used in industry, was determined for the guppy (Poecilia reticulata, Pallas, 1859). The experiments were planned in four series of a total of 440 guppies employing the static test method of acute toxicity. 10 fish were placed in each replicate of each dose. The experiments were performed as four replicates, and behavioral changes in the guppy were determined for each cadmium chloride metal salt concentration. The data obtained were statistically evaluated by the use of EPA computer program based on Finney's Probit Analysis Method and a 96-h LC50 value for P. reticulata was found to be 30.4 mg/l in a static bioassay test system. This value was estimated to be 30.6 mg/l with Behrens-Karber's method. The two methods were in good agreement. 95% lower and upper confidence limits for the LC50 were 29.3 and 31.7 mg/l, respectively. The water temperature was kept between 21 and 23 °C. The behavioral changes observed in fish were, swimming in imbalanced manner, capsizing, attaching to the surface, difficulty in breathing and gathering around the ventilation filter.

Yorulmazlar, E. and A. Gul (2003). "Investigation of acute toxicity of cadmium sulfate (CdSO4 center dot H2O) and behavioral changes of grass carp (Ctenopharyngodon idellus Val., 1844)." Chemosphere **53**(8): 1005-1010.
This study attempts to determine the 96-h LC50 Values of CdSO4 . H2O, a metal salt widely used in industry, for grass carp (Ctenopharyngodon idellus Val.,

1844). The study was carried out in two stages with 120 grass carp individuals using statistic method of aquatic toxicity. In addition, the behavioral changes of grass carp at different CdSO4 . H2O concentrations were determined. The results were evaluated using probit analysis method and the LC50 value for grass carp species was calculated as 9.42 mg/l. (C) 2003 Elsevier Ltd. All rights reserved.

Yudkovski, Y., A. Rogowska-Wrzesinska, et al. (2008). "Quantitative immunochemical evaluation of fish metallothionein upon exposure to cadmium." Marine Environmental Research **65**(5): 427-436.

Efficient implementation of an environmental biomarker requires multi-annual comparability over a wide geographical range. The present study improved the comparability of a quantitative competitive metallothionein (MT) enzyme-linked-immuno-sorbent-assay (ELISA) in the sentinel fish Lithognathus mormyrus by introducing to the assay recombinant MT and beta-actin standards. Commercial antibodies for cod MT and mammalian actin were implemented. In addition, a sensitive anti L. mormyrus MT antibody was produced, adequate only for solid phase immunochemical assays. Cadmium was applied to the fish through injection and feeding to serve as a testing platform of the ELISA. The results demonstrated high potential protective capacity of the liver against toxic levels of transition metals through increasing MT levels. MT transcript levels were evaluated also from fish sampled at polluted and relatively clean natural sites, indicating applicability of MT as biomarker of exposure to a multi-factorial pollution, in comparison to its low revealed sensitivity to controlled cadmium exposure.

Zaroogian, G., S. Anderson, et al. (1992). "INDIVIDUAL AND COMBINED CYTOTOXIC EFFECTS OF CADMIUM, COPPER, AND NICKEL ON BROWN CELLS OF MERCENARIA-MERCENARIA." Ecotoxicology and Environmental Safety **24**(3): 328-337.

Zettergren, L. D., C. A. Conrad, et al. (1991). "Immunochemical and immunohistochemical studies of cadmium associated proteins in Rana tadpoles." Toxicology Letters **59**(1-3): 221-228.

Previous observations suggested that Rana tadpoles treated with aqueous cadmium (Cd) accumulate Cd in their liver and mesonephros. In order to study the response to Cd in these tissues we (a) exposed tadpoles in mid-limb bud stages to sublethal quantities of Cd, (b) isolated Cd-associated protein (CAP) from a liver cytosol fraction, (c) prepared a heterologous rabbit antiserum against glutaraldehyde-treated CAP (G-CAP), (d) used the rabbit anti-G-CAP antiserum in order to assess the tissue distribution of CAP in Cd-treated and untreated tadpoles, and (e) assessed species crossreactivities of our anti-G-CAP with CAPs and metallothioneins (MTs) isolated from Cd-treated vertebrate liver cytosol fractions. We found that (a) CAP was present in higher quantities in liver cytosol obtained from Cd-treated tadpoles compared to liver cytosol obtained from untreated control tadpoles, (b) indirect immunofluorescent analysis revealed

that CAP was localized in liver hepatocytes and kidney tubule epithelial cells in Cd-treated tadpoles, and (c) the anti-G-CAP crossreacted with rodent and fish CAP. These observations suggest that the developing liver and mesonephros are involved in responses to toxic metals and that our anti G-CAP antiserum may be used to gauge exposure to environmental Cd.

Zhang, L. and W.-X. Wang (2007). "Gastrointestinal uptake of cadmium and zinc by a marine teleost Acanthopagrus schlegeli." Aquatic Toxicology **85**(2): 143-153.

Gastrointestinal metal uptake represents a potential route for metal bioaccumulation in marine fish. Drinking of seawater for osmoregulation causes constant waterborne exposure of the gastrointestinal tract. Tissue specific Cd and Zn accumulation and distribution were investigated in juvenile black sea bream (Acanthopagrus schlegeli) exposed to waterborne Cd (5.7 nM) and Zn (2.6 nM) for 4 h-7 days. The intestine accumulated a large portion of the Cd (43-58%) and Zn (18-28%), and had the highest Cd (>1.0 nmol g-1) and Zn (>1.8 nmol g-1) concentrations of all body fractions, suggesting that the intestines were the major uptake sites for these waterborne metals. Among all the segments of the gastrointestinal tract, the anterior intestine played the most important role in Cd and Zn uptake. A gastrointestinal injection assay was conducted to distinguish waterborne metal uptake by the intestines and the gills. The intestine contained over 90% of the Cd in the body after depuration for 3-7 days, suggesting that little waterborne Cd entered the rest of the body through the intestine, and that Cd may exert its toxic effects on the gastrointestinal system. In contrast, intestine retained less than 20% of the total Zn after depuration, suggesting that Zn tended to be transported from the intestine to the internal tissues via the cardiovascular system. The uptake kinetics of waterborne Cd and Zn by the intestines and the gills were determined as a first-order and saturated pattern, respectively, over a wide range of ambient metal concentrations (6.2 nM-4.5 [mu]M for Cd, and 13 nM-15 [mu]M for Zn). An in vitro intestinal perfusion assay investigated the effects of intestinal metal composition and drinking rate on uptake. The presence of EDTA significantly reduced intestinal Zn uptake to 11%, while cysteine improved it by 59%. The intestinal Cd and Zn uptake rates were unaffected by the perfusion rate.

Zhang, L. and W.-X. Wang (2007). "Waterborne cadmium and zinc uptake in a euryhaline teleost Acanthopagrus schlegeli acclimated to different salinities." Aquatic Toxicology **84**(2): 173-181.

Metal uptake and toxicity in marine fish are usually much lower than those in freshwater fish, but the underlying mechanisms remain unclear. In this study, we investigated Cd and Zn uptake by the euryhaline black sea bream (Acanthopagrus schlegeli) over a salinity range from 0 to 35 psu. Cd and Zn uptake increased as salinity decreased. The gills were the most sensitive organs in response to salinity change, and played a more important role in Cd and Zn uptake at a lower salinity. Cd and Zn uptake in the viscera contributed to 34-36% of the overall accumulation at full salinity (35 psu), but decreased to 13-16% in freshwater despite the increase of uptake rate. Water permeability, drinking, and

major ion uptake (Ca) in the fish at different salinities were also concurrently examined. The overall water uptake was comparable, whereas the drinking rate decreased at lowered salinities. In contrast, the Ca uptake increased significantly with decreasing salinity. The responses of Cd and Zn uptake to salinity challenge were correlated with the Ca uptake, suggesting that they may be taken up through the Ca uptake pathway. At a constant salinity, Cd and Zn uptake increased with reducing Ca concentration, indicating the competitive effect of Ca on metal uptake. Ca channel blockers (verapamil and lanthanum) significantly reduced the uptake of Cd, Zn, and Ca when the fish were acclimated in freshwater, but had no impact on their uptake in marine water. Furthermore, the chloride cell number in the gills could not explain the lower Cd and Zn uptake in seawater. Our results indicated that both ambient physicochemical factors and the physiological responses of fish resulted in difference of metal uptake in marine and freshwater environments.

Zhu, J.-Y., H.-Q. Huang, et al. (2006). "Acute toxicity profile of cadmium revealed by proteomics in brain tissue of Paralichthys olivaceus: Potential role of transferrin in cadmium toxicity." Aquatic Toxicology **78**(2): 127-135.

An analytical approach using two-dimensional polyacrylamide gel electrophoresis (2D-PAGE) separated proteins from the brain tissue of the fish Paralichthys olivaceus. Approximately 600 protein spots were detected from the brain sample when applying 600 [mu]g protein to a 2D-PAGE gel in the pH range 3.5-10.0. Compared to a control sample, significant changes of 24 protein spots were observed in the fish tissue exposed to acute toxicity of seawater cadmium (SCAT) at 10 ppm for 24 h. Among these spots, nine were down-regulated, nine were up-regulated, two showed high expression, and four showed low expression. The collected spots were identified by peptide mass fingerprinting (PMF) and database search, and they were further classified by LOCtree, a hierarchical system of support vector machines which predict their sub-cellular localization. The amount of transferrin expression in brain cells decreased linearly with the increase of SCAT concentration in seawater. Among the 24 proteins identified on a 2D-PAGE gel, 9 demonstrated a synchronous response to acute cadmium, suggesting that they might represent a biomarker profile. Based on their variable levels and trends on the 2D-PAGE gel this protein (likely to be transferrin) suggesting they might be utilized as biomarkers to investigate cadmium pollution levels in seawater and halobios survival, as well as to evaluate the degree of risk of human fatalities. The results indicate that the application of multiple biomarkers has an advantage over a single biomarker for monitoring levels of environmental contamination.