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*"Lessons Learned from Fish on Prozac and Other Adventures in Urban Waters."*

More people now live in cities than ever before. Historically, human populations thrived near rivers and their mouths at coastlines, but with urban expansion the footprints of metropolitan areas extend throughout watersheds and ultimately encompass smaller order tributaries. Such population densities dictate the need for new water supplies and reclamation infrastructure, which results in effluent discharges to these headwater streams, dramatically modifying instream hydrology, particularly in regions where ephemeral streams are normative. When effluent-dominated and dependent instream flows become critical arteries for beneficial water reuse, as increasingly is observed in areas experiencing climate changes and rapid population growth, an urban water cycle is realized. Over a decade has passed since our research group initially reported several adverse effects of Prozac (fluoxetine) to aquatic organisms commonly employed for developing environmental quality criteria, evaluating whole effluent toxicity, and monitoring ambient toxicity of surface waters and sediments. Our subsequent observation of fluoxetine, sertraline (Zoloft) and their active metabolites (norfluoxetine and desmethylsertraline, respectively) accumulating in muscle, liver and brain tissues of three different fish species from an effluent-dominated stream was termed "Fish on Prozac." Here I briefly review some scientific lessons learned from our study of urban aquatic systems. Using probabilistic hazard assessment and fish plasma modeling approaches, selective serotonin reuptake inhibitors and tricyclic antidepressants are predicted to result in therapeutic hazard to fish (internal fish plasma level equaling mammalian therapeutic dose) when exposed to water (inhalational) at or below 1 µg/L, a common trigger value for environmental assessments. Though many questions remain unanswered, studies of antidepressants in urbanizing aquatic systems have provided, and will continue to develop, an advanced understanding of environmental hazards and risks from pharmaceuticals and other contaminants.