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Authors: Bunton, T. E., and Baksi, S. M.

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Cholangioma in White Perch (*Morone americana*) from the Chesapeake Bay

T. E. Bunton,[1,3] **and S. M. Baksi,**[2] [1] Division of Comparative Medicine and Department of Pathology, School of Medicine, The Johns Hopkins University, Baltimore, Maryland 21205, USA; [2] Department of Experimental Toxicology, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, Maryland 21205, USA. [3] Author to whom reprint requests should be addressed

ABSTRACT: Cholangiomas found in two of 21 wild-caught white perch (*Morone americana*) from the Chesapeake Bay are described. The two fish were part of a study investigating a condition of abnormal hepatic copper storage in this species. The tumors were superficial, solitary masses consisting of cuboidal to columnar cells in tubuloglandular arrangement. Mild to marked peribiliary inflammation and fibrosis was seen also. Environmental pollution, the condition of abnormal copper storage, peribiliary fibrosis, and/or parasites may have contributed to the development of these tumors.

Key words: Cholangioma, white perch, teleost, neoplasm, pollution, carcinogen, copper, parasite, *Morone americana*, case history.

The association between environmental pollutants and the spontaneous occurrence of neoplasms in aquatic organisms has been of increasing interest for several years due both to the potential human health risk implications and to the desire to preserve aquatic biosystems. There are a variety of factors that need to be considered when a neoplasm is detected in a wild-caught fish. When such a neoplasm is discovered, it is important to report the type of neoplasm, species of fish, location where caught, and any other factors such as parasites that

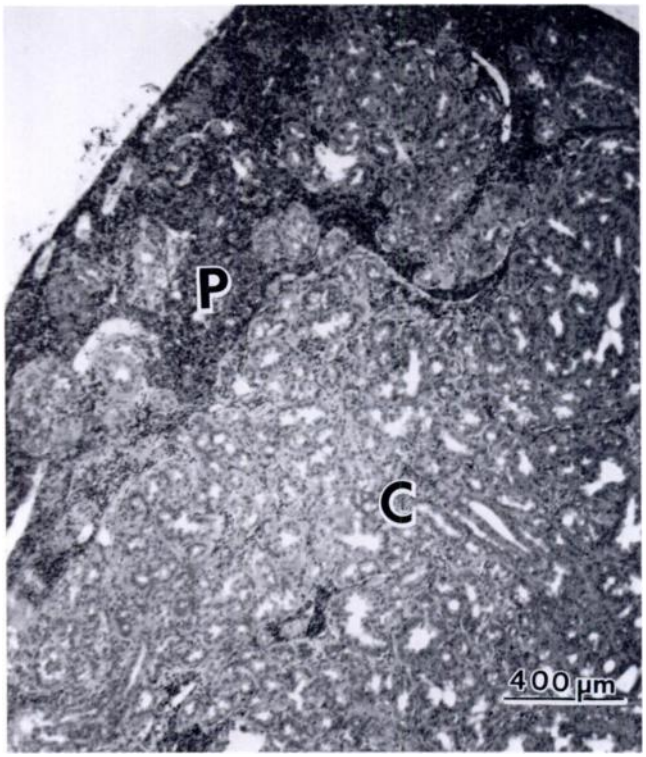

FIGURE 1. Replacement of hepatic parenchyma (P) at periphery of liver lobe by tumor cells in the white perch with cholangioma. (C). H&E.

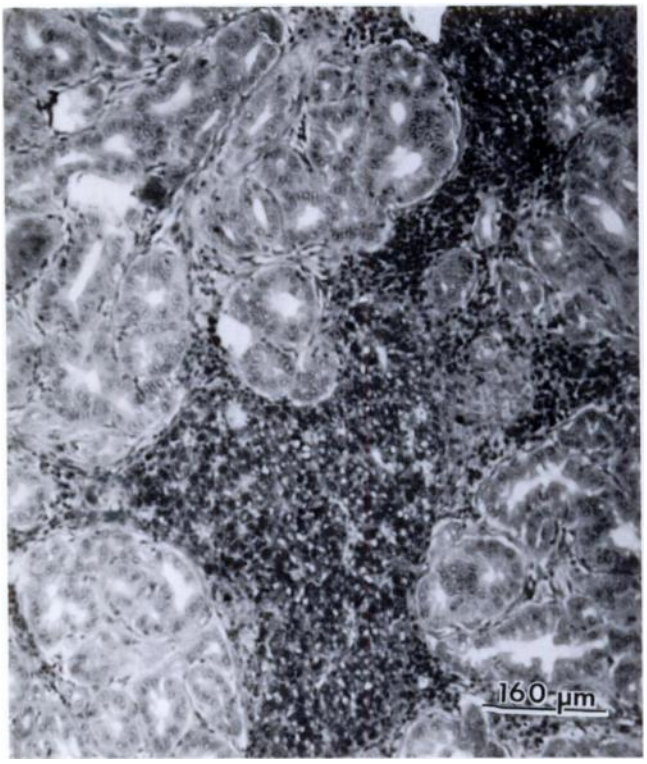

FIGURE 2. Higher magnification from Figure 1 showing nonencapsulated encroachment of tumor cells into hepatocytes. H&E.

could function in tumorigenesis. This will allow for expansion of the database on fish neoplasms and may result in a greater understanding of tumor biology in aquatic species.

Two of 21 wild-caught white perch (*Morone americana*) from various regions of the Chesapeake Bay (39°33′N to 39°8′S, 76°4′E to 76°24′W) were diagnosed as having cholangioma. They were part of a study investigating a condition of abnormal hepatic copper storage in this species (Bunton et al., 1987). The two fish measured approximately 18.0 and 20.0 cm, and were caught from Cedar Point, Maryland (39°15′N, 76°24′W). Sections of liver were placed in Bouins fixative and routinely processed for paraffin embedment. Sections were stained with hematoxylin and eosin, and rubeanic acid for copper (Uzman, 1956).

Both solitary tumors were superficially located on the periphery of liver lobes and were visible through the capsule as pale, slightly raised 0.5-cm masses sharply defined from the liver parenchyma. Both had similar histology, and were well demarcated but nonencapsulated proliferations of cuboidal to columnar cells arranged in closely approximated tubuloglandular structures separated by a fine fibrovascular stroma (Figs. 1, 2). The cells were in single rows, and had oval vesicular nuclei with prominent nucleoli (Fig. 3). Mitotic figures were less than one per high power field. In both fish, there were changes associated with copper storage including prominent melanomacrophage centers and parenchymal cytoplasmic granules as described (Bunton et al., 1987). In one fish there was marked peribiliary fibrosis, with a moderate mononuclear peribiliary infiltrate. In the second fish there was mild peribiliary fibrosis and portal inflammation was mild.

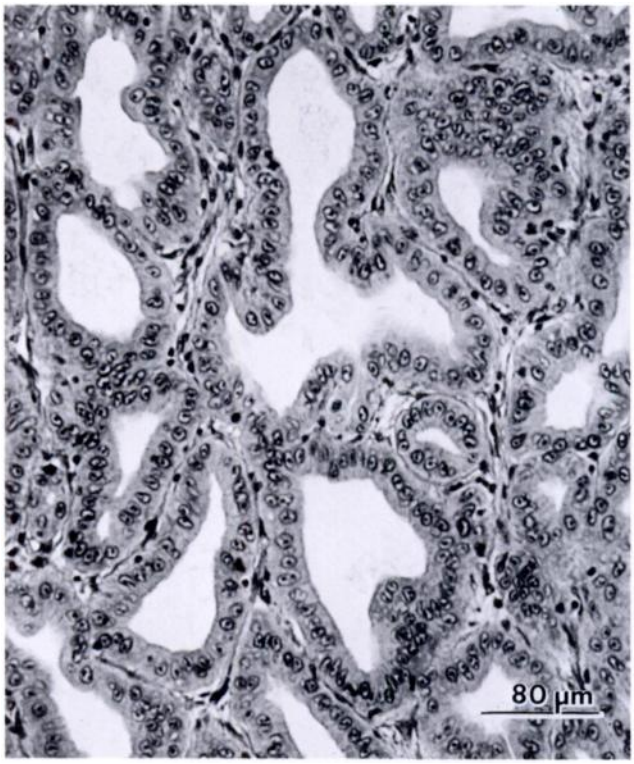

FIGURE 3. Tubuloglandular arrangement of columnar tumor cells from a cholangioma in the white perch. H&E.

Rodlet cells were a prominent feature in bile duct epithelium (Fig. 4) but were not observed in either tumor mass. Tumor cells stained negatively for copper and metastases were not observed.

The white perch from the Chesapeake Bay has been shown to exhibit an age-related progressive accumulation of copper in the liver (Bunton et al., 1987). Hepatocellular carcinoma has been reported in copper storage disease (Wilson's disease) in man, but not at the same high frequency as other causes of cirrhosis (Shikata, 1976). The relationship of cholangioma or cholangiocarcinoma to Wilson's disease is not known. In fish the size of those in this report, fibrotic changes were observed in the liver which were not seen to the same degree in smaller fish. Cholangiocarcinoma has been associated with chronic cholangitis with fibrosis (Shikata, 1976), but in one of these fish, fibrosis was not a major feature, and the masses appeared to be benign. The superficial and peripheral locations were similar to bile duct adenomas in man (Peters, 1986), which are usually incidental findings. Thus, the correlation between copper levels, fibrosis and the tumors in these fish is not clear.

A number of carcinogenic agents have been shown to experimentally produce cholangioma and cholangiocarcinoma in fish, including diethylnitrosamine (Stanton, 1965), o-aminoazotoluene (Pliss and Khudoley, 1975), N-2-fluorenylacetamide (Pliss and Khudoley, 1975), dichlorodiphenyltrichloroethane (Hendricks et al., 1984) and methylazoxymethanol acetate (Aoko and Matsudaira, 1984). In addition, cholangioma (Dawe et al., 1964) and cholangiocarcinoma (Malins et al., 1985a, b) have been reported in various fish from waters polluted with a variety of toxic chemicals. The levels and types of pollu-

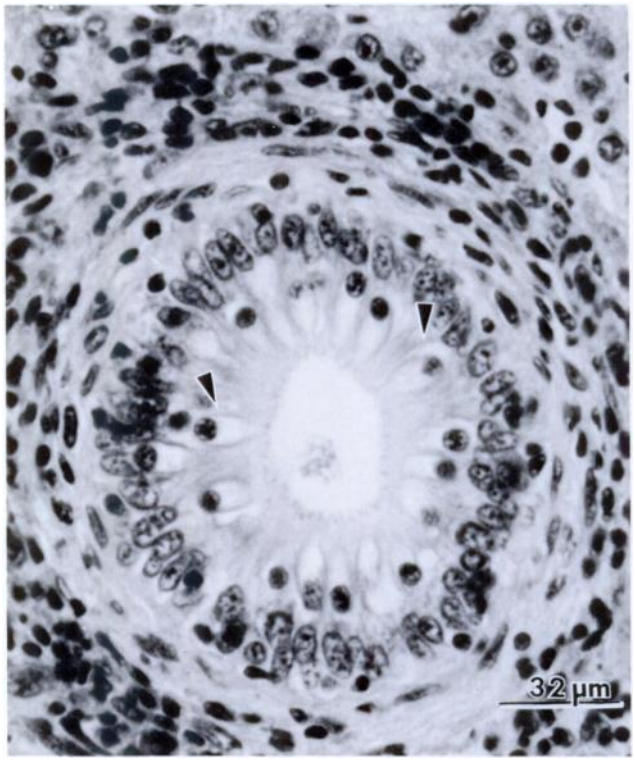

FIGURE 4. Bile duct surrounded by mononuclear inflammatory cells and rodlet cells (arrows) from a white perch with cholangioma. H&E.

tants in the waters from which the two fish in the present study were caught are not known, but pollutants may have played a role in the development of the tumors.

Two species of parasitic Digenea, *Clonorchis sinensis* (Shikata, 1976) and *Opisthorchis viverrini* (Kurathong et al., 1985) have been associated with cholangiocarcinoma in man, but they were not seen histologically in these two fish. Unidentified trematodes were observed in livers of other white perch and may have been a tumorigenic factor. A peculiar cell or organism found in both normal and neoplastic bile duct epithelium in white suckers (*Catostomus commersoni*) caught from Deep Creek Lake, Maryland (Dawe et al., 1964) was suggested as a possible etiologic factor of tumor development. These structures have alternatively been called parasites (*Rhabdospora thelohani*) (Mayberry et al., 1979; Bielek and Veihberger, 1983) or normal secretory rodlet cells (Leino, 1974) and have been observed in various organs in fish. They were observed with great frequency in most bile duct epithelium of the white perch examined including the two in this report, but were not observed in the tumor masses. Since the cells were seen in normal white perch bile duct epithelium with no inflammatory reaction and may be normal structures, their role in tumorigenesis remains obscure.

It was not possible to attribute one specific etiologic factor to the development of cholangioma in these white perch. They may have developed due to a combination of innate and environmental conditions.

Representative paraffin embedded tissue blocks of the tumor described in this study have been deposited in the Registry of Comparative Pathology (Armed Forces Institute of Pathology, Washington, D.C. 20306, USA; Accession number 2144311).

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