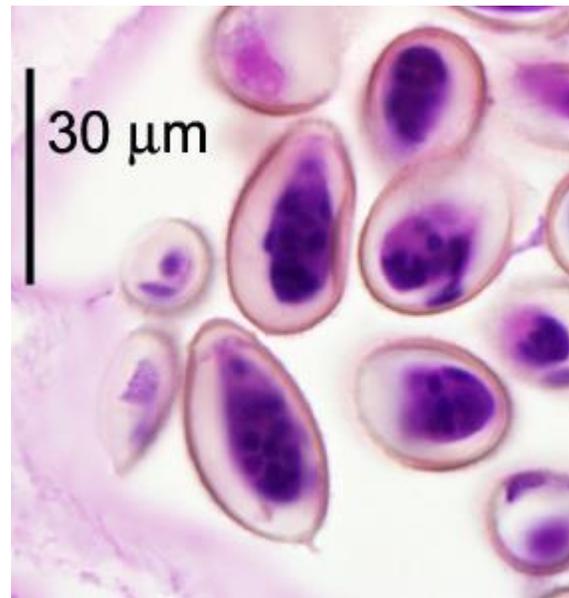
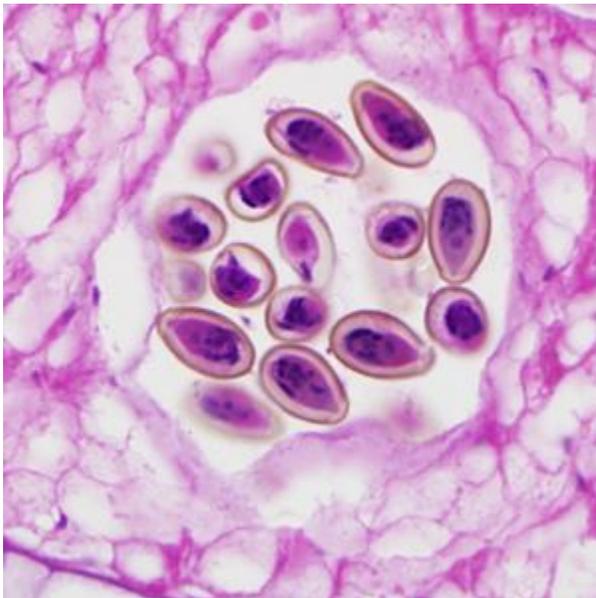
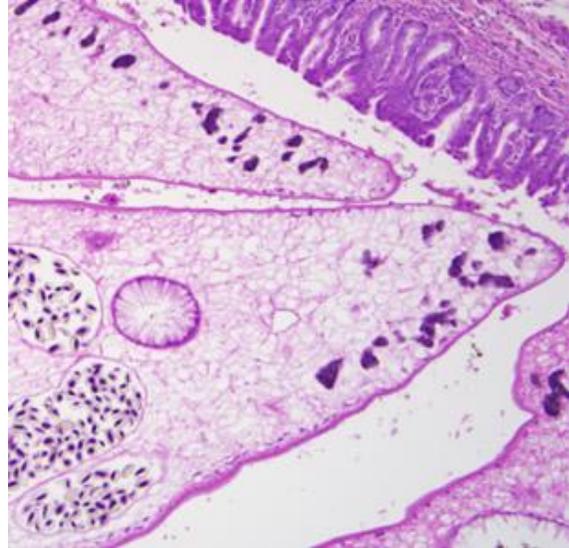
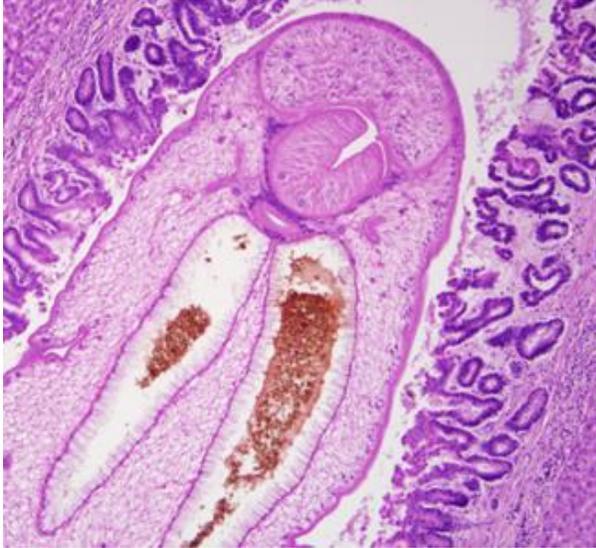


## PARASITOLOGY CASE HISTORY 12 (HISTOLOGY) (Lynne S. Garcia)

A 54-year-old man originally from Vietnam was admitted to the hospital for complaints of upper abdominal pain and liver enlargement. The bile duct was biopsied and sent to pathology for sectioning and staining. The following images were seen (H&E routine staining). Images courtesy of CDC (dpdx)

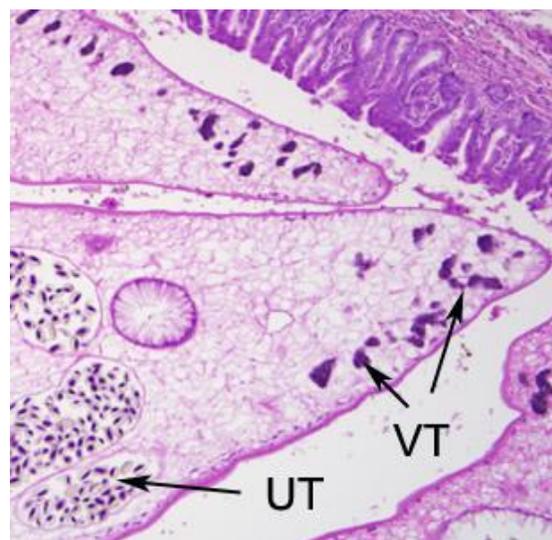
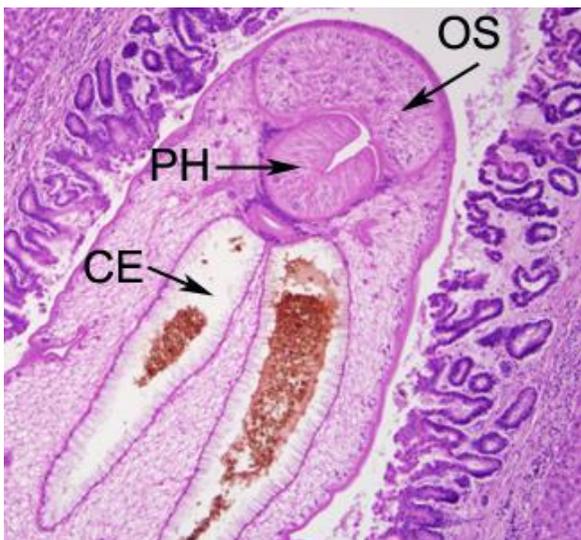
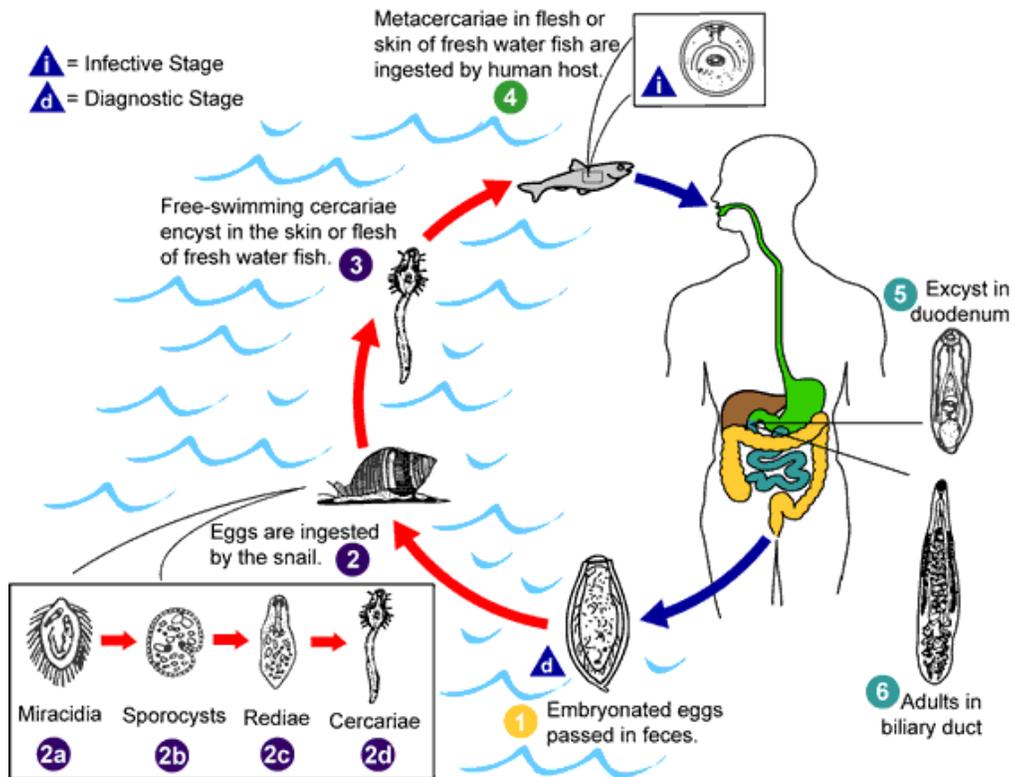


- Based on these images, what is your diagnosis?

***Scroll Down for Answer and Discussion***

## Answer and Discussion of Histology Quiz #12

This was a case of clonorchiasis caused by the liver fluke *Clonorchis sinensis*. However, based on the images and clinical presentation, it was impossible to distinguish between *C. sinensis* and *Opisthorchis* spp; thus opisthorchiasis would have been acceptable as an alternative diagnosis. Key morphologic features can be seen below:





OS = oral sucker, PH = thick, muscular pharynx, CE = branching intestinal cecum, UT = uterus filled with eggs, VT = vitelline glands, OP = operculum at one end of the egg, KN = abopercular knob at the other end of the egg. Note the adult fluke – slender shape to get into the bile duct. Also note the egg (approximately 30 microns, one of the smallest helminth eggs found in humans).

**Life Cycle.** The definitive hosts of *C. sinensis* are humans, dogs, hogs, cats, martens, badgers, mink, weasels, and rats. Adult worms deposit eggs in the bile ducts, and the eggs are discharged with the bile fluid into the feces and passed out into the environment. The adult worm is a small trematode with an elliptical shape and an average length of 10 to 25 mm. The trematode is a true hermaphrodite (both sexes in the same worm) and has a life span of 20 to 25 years, which explains the persistent infection for a long duration.

**Clinical Disease.** Most patients with mild infections of fewer than 100 flukes have few symptoms, which may include general malaise, abdominal discomfort, and diarrhea. In 10 to 40% of patients, peripheral eosinophilia occurs with fluctuating obstructive jaundice. Moderate infections with fewer than 1,000 worms include symptoms of fever and chills, fatigue, anorexia, diarrhea, weight loss, discomfort, and abdominal distention. In severe disease with up to 20,000 flukes, an additional symptom may include acute right upper quadrant pain. In the late stage of severe cases, jaundice, diarrhea, portal hypertension, hepatosplenomegaly, ascites, and edema can occur.

In general, the complications of clonorchiasis are the result of biliary obstruction. As the worms mature in the distal bile ducts, an inflammatory response is seen in the biliary epithelium. The extent of pathologic changes is

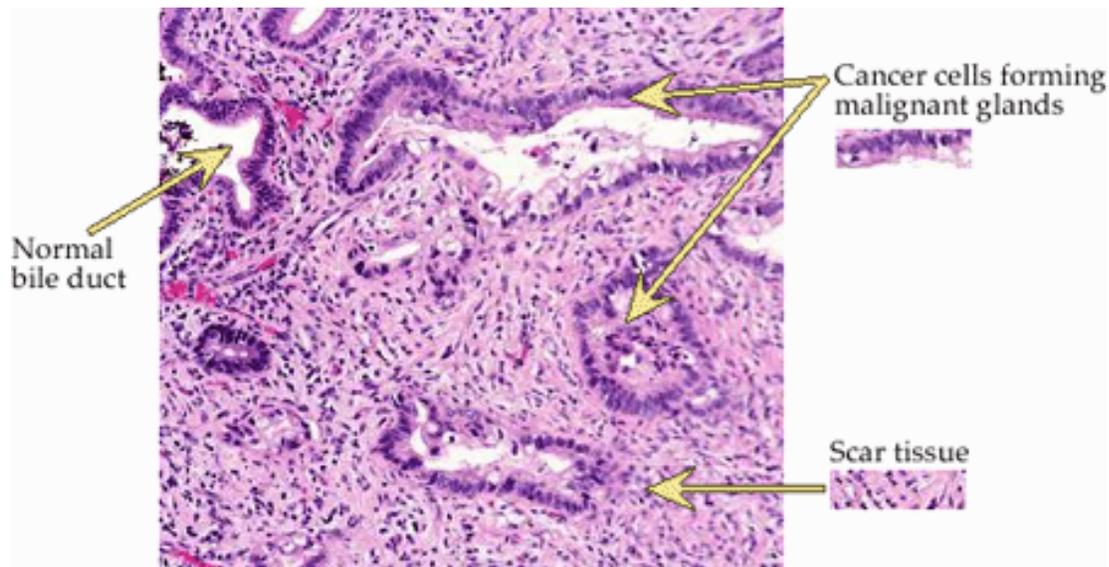
related to the intensity and duration of infection. The lesions are confined mainly to the biliary system and are the result of mechanical irritation and toxins produced by the worms. In light infections, there appears to be little or no change in liver parenchyma, whereas heavy infections cause thickening and localized dilations of the bile ducts with hyperplasia of the mucinous glands. As a result, the biliary tract may become obstructed, causing bile retention, infiltration of lymphocytes and eosinophils, and fibrosis. The adenomatous changes may persist for many years in patients with light infections. The infections have been associated with obstructive jaundice, which may be aggravated by biliary stones and liver abscesses. Patients who have had the disease for a long time show liver enlargement with some degree of functional impairment that is secondary to biliary obstruction.

**Cholangiocarcinoma.** Liver flukes play a major role in East Asia, while exposure to chemical compounds, such as naphthenic acids, has been postulated as a source of the rate increase in Western countries. *C. sinensis* has been linked to neoplasms of the bile duct and to cholangiocarcinoma, which is most frequently observed in areas where clonorchiasis is endemic. Cholangiocarcinoma is a malignant tumor that arises from the bile duct epithelium and is the second most prevalent liver cancer after hepatocellular carcinoma. The tumor usually occurs in patients 60 to 80 years of age and rarely in patients younger than 40 years. There appears to be no direct link between infection and carcinoma, although one of the first steps in malignant transformation may be induced by the biliary tract hyperplasia caused by the worms. Therefore, identification of patients with deteriorating liver function prior to the development of cholangiocarcinoma remains an important goal in the management of PSC, particularly in areas where *C. sinensis* infection is endemic.

Cholangiocarcinoma, also known as bile duct cancer, is a form of cancer that is composed of mutated epithelial cells (or cells showing characteristics of epithelial differentiation) that originate in the bile ducts which drain bile from the liver into the small intestine. Other biliary tract cancers include gallbladder cancer and cancer of the ampulla of Vater. Cholangiocarcinoma is a relatively rare neoplasm that is classified as an adenocarcinoma (a cancer that forms glands or secretes significant amounts of mucins). It has an annual incidence rate of 1–2 cases per 100,000 in the Western world, but rates of cholangiocarcinoma have been rising worldwide over the past few decades.

More than 80% of all cancers of the gallbladder and bile ducts are carcinomas: tumors that arise in the epithelium (or surface lining). These cases are most often seen in the Far East and include *Clonorchis sinensis*

(most prevalent in Japan, Korea, and Vietnam) and *Opisthorchis viverrini* (most prevalent in Thailand, Laos, and Malaysia). Clonorchis is acquired when humans eat fresh water fish that harbor the infective stage. The cysts develop into flukes (flatworms) in the human intestine, and ascend from the duodenum (the first part of the intestine) into the common bile duct where they mature.



**Aquaculture.** Aquaculture of freshwater fish has increased dramatically and now accounts for 45.1% of the total aquaculture production. The production of grass carp, an important species that serves as an intermediate host for food-borne trematodes, has increased from >10,000 tons in 1950 to >3 million tons in 2002. Growth of this industry must be monitored for potential problems related to an increased incidence of disease in which infection is transmitted through the ingestion of raw or poorly cooked fish. Freshwater fish aquaculture has increased from an annual production of 136,000 tons in 1952 to 16.6 million tons 50 years later in China, the Republic of Korea, and Vietnam. Most (97.6%, 16.2 million tons) of this fish is produced in China. The farmed fish population has increased 100-fold globally in 60 years: from 320,000 tons in 1950, aquaculture fish production reached 32,000,000 tons in 2007. It is estimated that by 2030, at least half of the globally consumed fish will come from aquaculture farming. In one study of fish farms in Vietnam, the prevalence of fish-borne zoonotic trematodes in fish increased by 11 percentage points during a one-year culture period. It was also emphasized that the young fish were already highly infected when stocked into the grow-out systems.

**Prevention.** The life cycle can be broken and infection can be prevented in humans by thorough cooking of all freshwater fish. However, cultural habits regarding the ingestion of raw freshwater fish are difficult to change.

**References:**

1. **Garcia, LS**, 2016. *Diagnostic Medical Parasitology*, 6th Ed., ASM Press, Washington, DC.
2. **Keiser, J., and J. Utzinger.** 2005. Emerging foodborne trematodiasis. *Emerg. Infect. Dis.* 11:1507–1514.
3. **Choi, B. I., J. K. Han, S. T. Hong, and K. H Lee.** 2004. Clonorchiasis and cholangiocarcinoma: etiologic relationship and imaging diagnosis. *Clin. Microbiol. Rev.* 17:540–552.
4. **Al-Bahrani, R, Y Abuetabh, N Zeitouni, C Sergi.** 2013. Cholangiocarcinoma: risk factors, environmental influences and oncogenesis. *Ann Clin Lab Sci* 43:195-210.
5. **Qian, MB, YD Chen, S Liang, GJ Yang, XN Zhou.** 2012. The global epidemiology of clonorchiasis and its relation with cholangiocarcinoma. *Infect Dis Poverty* 2012; 1:4.
6. **Keiser J, J Utzinger.** 2009. Food-Borne Trematodiasis. *Clin Microbiol Rev.* 22:466–483.