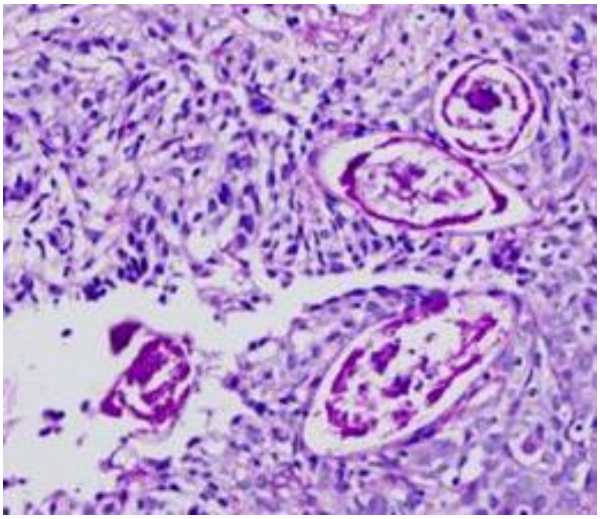
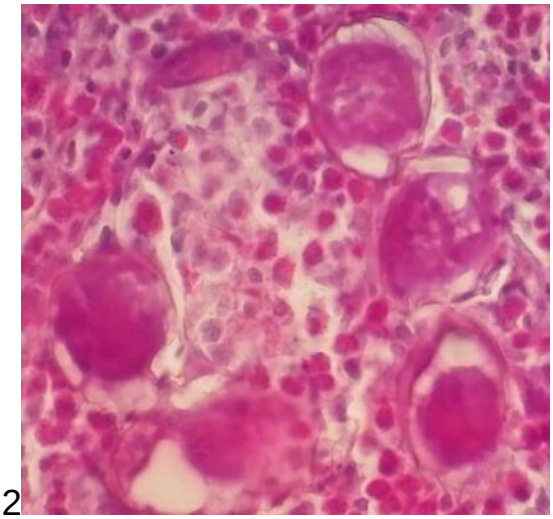
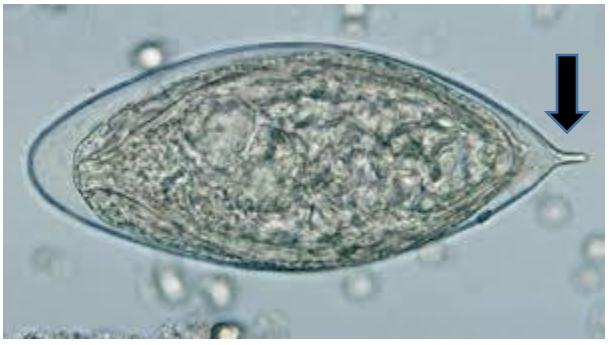
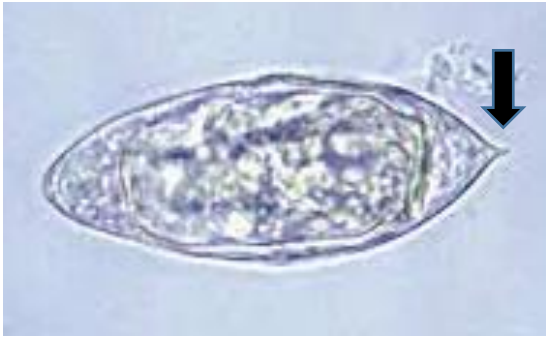
PARASITOLOGY CASE HISTORY 18 (HISTOLOGY)
(Lynne S. Garcia)

A 33-year-old man presented to the clinic with symptoms of abdominal pain and hematuria, with a suspect diagnosis of kidney stones. His history was unremarkable, other than having worked for two years in Tanzania. Appropriate biopsies were taken and stained by a routine Papanicolaou method (1, PAS) and a routine H&E stain (2, bladder mucosa) The following images were seen when the slides were reviewed:

1  2 

After the slides were screened, urine was also examined with the following images seen: Schistosoma haematobium eggs in urine; note the terminal spine (arrow).

Scroll Down for Answer and Discussion

Answer and Discussion of Histology Quiz #18

The structures are eggs of *Schistosoma haematobium*.

Life Cycle. Humans are the only significant reservoir hosts of *S. haematobium*. Fully embryonated eggs without an operculum (112 to 170 µm by 40 to 70 µm) escape from the body in the urine. The eggs are light yellowish brown and contain a conspicuous terminal spine.

The adult male worm contains minute integumentary tuberculations, smaller than those found on adult S. mansoni males. *S. haematobium* adults reside in the vesical and pelvic plexuses of the venous circulation. The adult female can contain 20 to 100 eggs in the uterus at one time. In addition to the vesical and pelvic plexuses, oviposition may occur in the rectal venules. To maintain the life cycle, the miracidium must find a suitable snail host (*Bulinus* sp.) when it is released from the egg in freshwater. The immature larval worms, after reaching the liver, may migrate via the inferior mesenteric veins to the rectal vein in order to mature. However, they most commonly migrate through the hemorrhoidal and pudendal veins to the vesical and pelvic plexuses. Within 3 months of exposure to cercariae, egg production begins.

Clinical Disease. Urogenital Disease. Light infections with urinary schistosomiasis usually produce no symptoms; however, in early disease there may be dysuria and hematuria due to cystitis from deposited eggs. Depending on the worm burden, symptoms may include dysuria, frequency, and terminal or total hematuria. Hematuria is so common that in some areas of endemic infection this phenomenon was considered to be analogous to menarche in girls. Symptoms are usually not seen for 3 to 6 months and may take a year or more to develop. Physical examination is usually normal, but urinalysis may reveal many red blood cells and a few white blood cells on microscopic examination; reagent strip results may indicate hematuria and proteinuria. Chronic disease may lead to major diseases, including obstructive uropathy, chronic bacteriuria, **bladder carcinoma**, and bladder calcification.

Eggs are most highly concentrated in the tissues of the bladder and lower ureter. As the eggs become trapped in the tissues, granulomas and pseudoabscesses form, leading to fibrosis and ulceration. With extensive fibrosis, the bladder loses its contractility. The urethra frequently is occluded

because of hyperplasia, polyp formation, and discharge of purulent debris plugs from the bladder. The ureters are also frequently involved, and obstruction can cause urine reflux, hydronephrosis, retrograde infections, and renal failure. Heavy infections in males may involve the penis, resulting in elephantiasis due to blockage of the scrotal lymphatics by egg deposition. Detection of *S. haematobium* eggs in 43% of semen samples with increased levels of eosinophil cationic protein suggests that the male genital organs are frequently affected.

Bladder Carcinoma. Carcinoma of the bladder has been frequently noted in patients infected with *S. haematobium*. Many factors have been suggested as agents promoting schistosome-associated bladder cancer. N-Nitroso compounds in association with secondary bacterial infections of the urinary tract may contribute to the high prevalence of bladder cancer. Bladder cancer is the most prevalent cancer in Egyptians. Many of the tumors involve the posterior wall of the bladder and are noted to occur more frequently in males than in females. The extent of *S. haematobium* infection plays a significant role in the induction of different types of carcinoma, since squamous cell carcinoma (**see figure 1 above**) is usually associated with moderate and/or high worm burdens while transitional cell carcinoma occurs more frequently in areas associated with lighter parasite loads. The predominance of squamous cell carcinoma in urinary bladder tissues in patients with schistosomiasis is probably due to continuous exposure to the larger quantities of carcinogens (N-nitroso compounds) in urine in patients with the disease.

Another factor that may play a major role in bladder carcinogenesis is continuous physical irritation and inflammation produced by Schistosoma eggs in the bladder mucosa.

Diagnosis. Diagnostic Procedures. *S. haematobium* eggs are usually detected in the urine, although in heavy infections they may also be found in the stools. The terminal hematuria portion of the urine specimen may contain numerous eggs trapped in the mucus and pus. Peak egg excretion occurs between noon and 3 p.m. Samples collected during this time, or during a 24-h urine collection without preservatives, may be used for examination. Urine can be examined under a microscope after sedimentation or centrifugation. It is important to use saline and not water for the concentration procedures; this will avoid premature hatching of the eggs. Nuclepore filtration is an excellent method for the concentration of eggs in urine. Some data indicate that egg output in urine is an accurate method of confirming the diagnosis and shows less day-to-day variation than in ELISA detection of schistosome circulating antigens in urine

Epidemiology. *S. haematobium* infections occur in Africa, Asia Minor, Cyprus, the islands off the African east coast, and southern Portugal; there is a focus of endemic infection in India. Humans appear to be the only important reservoir hosts, although naturally infected monkeys, baboons, and chimpanzees have been found. The intermediate snail host, *Bulinus* sp., can survive in the mud when the water dries up. The snails retain their infectivity and resume shedding cercariae when the rainy season begins. In some areas, cercariae are found in areas where infected snails are absent, and sometimes cercariae are absent in the presence of infected snails.

Data suggest that fewer than 1 in 100 contacts result in infection and less than 1 in 1,000 result in egg output. This suggests that there may be substantial attrition of invading cercariae even in naïve individuals.

In many areas of endemic infection, awareness of urinary schistosomiasis and its symptom of blood in the urine is high, but specific knowledge about the parasite, its vector, and the interaction between them in the life cycle is lacking. Activities that require behavior and attitude modification can be identified and encouraged as components in the control of schistosomiasis.

References:

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2. **Cassell A., Yunusa B., Jalloh M.**, et al. Nonmuscle invasive bladder cancer: a review of the current trend in Africa. World Journal of Oncology. 2019;10(3):123–131. doi: 10.14740/wjon1210

3. **Honeycutt J., Hammam O., Fu C.-L., Hsieh M. H.** Controversies and challenges in research on urogenital schistosomiasis-associated bladder cancer. *Trends in Parasitology*. 2014;30(7):324–332. doi: 10.1016/j.pt.2014.05.004.

4. **Bray F., Ferlay J., Soerjomataram I., Siegel R. L., Torre L. A., Jemal A.** Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*. 2018;68(6):394–424. doi: 10.3322/caac.21492.