MICROBIOLOGY

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3

Subject

Schistosomiasis – Schistosoma hematobium & Candidiasis

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Genito-Urinary System

Schistosomiasis – *Schistosoma hematobium* & Candidiasis

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SCHISTOSOMIASIS

(BLOOD FLUKE INFECTION)

Parasitology

- The schistosomes are a group of closely related flukes that inhabit the portal vascular system of a number of animals.
- Of the five species known to infect humans, three, *S. mansoni, S. haematobium,* and *S. japonicum,* are of primary importance.
- They infect individuals in Africa, the Middle East, Southeast Asia, the Caribbean and South America, and kill 1million annually.

- After mating of the adult worms in the portal vein, the conjoined couple use their suckers to ascend the mesenteric vessels against the flow of blood.
- Guided by unknown stimuli, *S. japonicum* enters the superior mesenteric vein, eventually reaching the venous radicals of the small intestine and ascending colon; *S. mansoni* and *S. haematobium* are directed to the inferior mesenteric system.

- *S. haematobium* passes through the hemorrhoidal plexus to the systemic venous system, ultimately coming to rest in the venous plexus of the bladder and other pelvic organs.
- On reaching the submucosal venules, the worms initiate oviposition. Each pair deposits 300 eggs daily for the remainder of its 4- to 35-year life span.
- Ova lying immediately adjacent to the mucosal surface rupture into the lumen of the bladder and are passed to the outside in the urine.
- The eggs measure 60 by 140 µm and possess a terminal spine.

- When the eggs are deposited in fresh water, the miracidia hatch quickly.
- On finding a snail host appropriate for their species, they invade and are transformed over 1 to 2 months into thousands of forked-tailed cercariae.
- When released from the snail, these infectious larvae swim about vigorously for a few days.
- Cercariae coming in contact with human skin during this time attach, discard their tails, and penetrate.

- During a 1- to 3-day sojourn in the skin, the resulting schistosomula enter small venules and find their way through the right side of the heart to the lung.
- After a delay of several days, the parasites enter the systemic circulation and are distributed to the gut.
- Those surviving passage through the pulmonary and intestinal capillary beds return to the portal vein, where they mature to sexually active adults over 1 to 3 months.

EPIDEMIOLOGY

- The widespread distribution and extensive morbidity of schistosomiasis makes it the single most important helminthic infection in the world today.
- The continued presence of the parasite depends on the disposal of infected human excrement into fresh water, the availability of appropriate snail hosts, and the exposure of humans to water infected with cercariae.

- Modern waste disposal and water purification facilities would break this cycle of transmission.
- Within endemic areas, there are wide variations in both infection rates and worm loads. In general, both peak in the second decade of life and then decrease with advancing age.
- Individuals who develop much heavier loads as a result of repeated infections may experience serious morbidity or mortality.

PATHOGENESIS

There are three major clinicopathologic stages in schistosomiasis.

- The first stage is initiated by the penetration and migration of the schistosomula.
- The second or intermediate stage begins with oviposition and is associated with a complex of clinical manifestations.
- The third or chronic stage is characterized by granuloma formation and scarring around retained eggs.

IMMUNITY

- The major clinicopathologic manifestations of schistosomiasis result from the host's cell mediated immune response to the presence of retained eggs.
- With time, the intensity of this reaction is muted; granulomas formed in the later stages of infection are smaller and less damaging than those formed early.
- Present evidence suggests that both suppressor T lymphocyte activity and antibody blockade are involved.

- The correlation in humans between HLA types A1 and B5 and the development of hepatosplenomegaly suggests that the extent of the immunoregulation is influenced, at least in part, by the genetic background of the host.
- As evidenced by their prolonged survival, the adult worms are remarkably well tolerated by their hosts. In part, this tolerance may be attributable to the formation of IgG4 blocking antibodies early in the course of infection.

- The prevalence and intensity of human infection begins to abate during adolescence, despite continuing exposure to infective cercariae.

CLINICAL ASPECTS

Early Stage

- Within 24 hours of penetrating the skin, a large proportion of the schistosomula die. In *S. haematobium* infections, immediate and delayed hypersensitivity to parasitic antigens results in an intensely pruritic papular skin rash that increases in severity with repeated exposures to cercariae.
- As the viable schistosomula begin their migration to the liver, the rash disappears and the patient experiences fever, headache, and abdominal pain for 1 to 2 weeks.

Intermediate Stage

- One to two months after primary exposure, patients with severe infections may experience the onset of an acute febrile illness that bears a striking resemblance to serum sickness. The onset of oviposition leads to a state of relative antigen excess, the formation of soluble immune complexes, and the deposition of these in the tissues of the host. In addition to the fever and chills, patients experience cough, urticaria, arthralgia, lymphadenopathy, splenomegaly, abdominal pain, and diarrhea.

❑Chronic Stage

- Approximately one half of all deposited eggs reach the lumen of the bowel or bladder and are shed from the body. Those retained induce inflammation and scarring, initiating the final and most morbid phase of schistosomiasis.
- Soluble antigens excreted by the eggs stimulate the formation of T lymphocyte–mediated eosinophilic granulomas. Early in the infection, the inflammatory response is vigorous, producing lesions more than 100-fold larger than the inciting egg itself.

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- Inflammatory and fibrotic reactions to retained eggs cause chronic disease, the severity of tissue damage is directly related to the total number of eggs retained.
- In *S. haematobium* infection, the bladder mucosa becomes thickened, papillated, and ulcerated. Hematuria and dysuria result; repeated hemorrhages produce anemia. In severe infections the muscular layers of the bladder are involved, with loss of bladder capacity and contractibility. Progressive obstruction leads to renal failure and uremia. Bladder carcinoma is frequently seen.

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DIAGNOSIS

- Definitive diagnosis requires the recovery of the characteristic eggs in urine, or biopsy specimens.
- In *S. haematobium* infections, eggs are most numerous in urine samples obtained at midday. When examination of the sediment yields negative results, eggs may sometimes be recovered by filtering the urine through a membrane filter.

- Cystoscopy with biopsy of the bladder mucosa may be required for the diagnosis of mild infection.
- Conventional serologic tests detect circulating antibodies with sensitivities exceeding 90% but cannot distinguish active from inactive infection.

TREATMENT

- No specific therapy is available for treatment of schistosomal dermatitis. Antihistamines and corticosteroids may be helpful in ameliorating their more severe manifestations.
- Several antihelmintic agents may be used. Praziquantel, which is active against all three species of schistosomes, is the agent of choice, although there is increased resistance to this single-dose oral agent in mass therapy programs.

PREVENTION

- It has proved both difficult and expensive to control this deadly disease.
- Programs aimed at interrupting transmission of the parasite by the provision of pure water supplies and the sanitary disposal of human excreta are often beyond the economic reach of the nations most seriously affected.
- Similarly, measures to deny snails access to newly irrigated lands are expensive.

- Chemical molluscicides have been shown effective in limited trials.
- Mass therapy of the infected human population has, until recently, been severely limited by the toxicity of effective agents.
- Currently, there is intense interest in developing a vaccine suitable for human use. A vaccine made from irradiated *S. bovis* cercariae, developed for cattle, appears to confer a significant degree of protection against infection.

Candida albicans

- *C. albicans* grows in multiple morphologic forms, most often as a yeast with budding by formation of blastoconidia. *C. albic*ans is also able to form hyphae triggered by changes in conditions such as temperature, pH, and available nutrients.
- When observed in their initial stages when still attached to the yeast cell, these hyphae look like sprouts and are called germ tubes.

- Other elongated forms with restrictions at intervals are called pseudohyphae because they lack the parallel walls and septation of the true hyphae.
- Chlamydoconidia develop from hyphae in culture under certain cultural conditions.
- The *C. albicans* cell wall is made up of a mixture of the polysaccharides mannan, glucan, and chitin alone or in complexes with protein. The exact composition of the cell wall and surface components varies under different growth and morphologic conditions.

CANDIDIASIS

- Candidiasis occurs in localized and disseminated forms.
- Localized disease is seen as erythema and white plaques in moist skin folds (diaper rash) or on mucosal surfaces (oral thrush). It may also cause the itching and thick white discharge of vulvovaginitis.
- Deep tissue and disseminated disease are limited almost exclusively to the immuno-compromised. Diffuse pneumonia and urinary tract involvement are especially common.

EPIDEMIOLOGY

- *C. albicans* is a common member of the oropharyngeal, gastrointestinal, and female genital flora. Infections are endogenous except in cases of direct mucosal contact with lesions in others (eg, through sexual intercourse). Although *C. albicans* is a common cause of nosocomial infections, the fungi are also derived more frequently from the patient's own flora. Invasive procedures and indwelling devices may provide portal of entry, and the number of *Candida* may be enhanced by the use of antibacterial agents.

PATHOGENESIS

- Because *C. albicans* is regularly present on mucosal surfaces, disease implies a change in the organism, the host, or both.
- Shift from yeast to hyphae is associated with enhanced pathogenic potential of *C. albicans* (invasion). This switch is controlled in vitro by the manipulation of environmental conditions.
- *C. albicans* hyphae have the capacity to form strong attachments to human epithelial cells, mediated by a surface mannoproteins; hyphal wall protein (Hwp1) found only on surface of germ tubes and hyphae & extracellular matrix.

- Hyphae also secrete proteinases and phospholipases that are able to digest epithelial cells and facilitate invasion.
- *C. albicans* has protein surface receptors that bind the C3 component of complement in an antiopsonic manner.
- Antimicrobics and immunosuppression increase risk of local and invasive infection.
- Mechanical disruptions of the mucosa (indwelling devices) may enhance the invasion process by exposing *Candida* binding sites in the ECM. Diabetes mellitus also predisposes to *C. albicans* infection.

IMMUNITY

- Both humoral immunity and cell-mediated immunity are important in defense against *Candida* infections.
- Opsonized yeast forms are killed by PMNs, the naturally occurring antimannan IgG is able to activate the classical complement pathway and facilitate the alternate pathway.
- Hyphal forms are too large to be ingested by PMNs, but they can still kill fungi by attaching to the hyphae and discharging metabolites generated by the oxidative metabolic burst.

- A deficit in neutrophils or neutrophilic function is the most common correlate of serious *C. albicans* infection.
- Compromised CMI is associated with progressive infection.
- *Candida* cell wall mannan has been shown to play an immunoregulatory function by downregulating cell-mediated immune responses.
- Balance between TH1- and TH2- mediated cytokine responses is necessary to enhance resistance against infection & chronic disease respectively.

CANDIDIASIS

CLINICAL ASPECTS

MANIFESTATIONS

- Superficial invasion of the m. membranes produces a usually painless, white, cheesy plaque called thrush that is loosely adherent to the mucosal surface.
- Vaginal candidiasis, produces a thick, curd-like discharge and itching of the vulva. Vaginitis may be recurrent.
- Skin infections occur in crural folds and other areas in which wet, macerated skin surfaces are opposed.

- Chronic mucocutaneous candidiasis is associated with specific T-cell defects.
- Inflammatory patches similar to thrush may develop in the esophagus and intestine with or without associated oral candidiasis.
- Urinary tract infections are ascending or hematogenous may produce cystitis, pyelonephritis, abscesses, or expanding fungus ball lesions in the renal pelvis.
- Endophthalmitis appears as white cotton on the retina. Endophthalmitis and infections of other eye structures can lead to blindness.

DIAGNOSIS

- KOH and Gram smears of superficial lesions show budding yeast and hyphae.
- Cultures from specimens such as sputum run the risk of contamination from the normal flora or a superficial mucous membrane lesion. Lung involvement requires a direct aspirate, biopsy, or bronchoalveolar lavage.
- Deep organ involvement is difficult to prove without a direct aspirate or biopsy. Even +ve blood cultures are interpreted with caution. Endocarditis may require arterial cultures.
- Immunodiagnostic procedures are not routine.

TREATMENT

- *C. albicans* is usually susceptible to nystatin, amphotericin B, flucytosine, and the azoles.
- Topical nystatin or azoles generally used for the treatment of superficial lesions. Measures to decrease moisture and chronic trauma are important adjuncts in treating skin infections.
- Deeper infections may resolve spontaneously with elimination or control of predisposing conditions, as an infected catheter or control of diabetes. Amphotericin B, flucytosine, and azoles for invasive disease