**Lecture 6.**

**Pathogenic fungi and protozoa**

**The purpose of the lecture:** To inform students about the morpho-biological characteristics of pathogenic and opportunistic fungi and protozoa, pathogenic factors, pathogenesis of diseases caused by these microorganisms, clinical signs, principles of microbiological diagnosis, treatment and prevention.

**Lecture plan:**

1. Classification of *fungi* that are pathogenic to humans.

2. Classification of mycoses: superficial mycoses (keratomycoses), skin mycoses (dermatomycoses), subcutaneous mycoses (subcutaneous) mycoses, systemic or visceral mycoses and opportunistic mycoses.

3. Morpho-biological features of the causative agents of *superficial mycoses* (tinea versicolor, black and white piedra), principles of microbiological diagnosis of the diseases they cause

4. Morpho-biological characteristics of the causative agents of *skin mycoses* (trichophytia, epdermophytia, microsporia, favus), principles of microbiological diagnosis of the diseases they cause

5. Morpho-biological characteristics of the causative agents of *subcutaneous* mycoses (sporotrichosis, chromomycosis, misetoma), principles of microbiological diagnosis of the diseases they cause

6. Morpho-biological features of the causative agents of *systemic* (visseral) mycoses (coccidioidosis, histoplasmosis, blastomycosis, paracoccidioidosis), principles of microbiological diagnosis of the diseases they cause

7. Morpho-biological characteristics of the causative agents of *opportunistic* mycoses (candidiasis, cryptococcosis, aspergillosis, mucoromycosis, pneumocystosis), the principles of microbiological diagnosis of the diseases they cause

8. The concept of mycotoxicosis

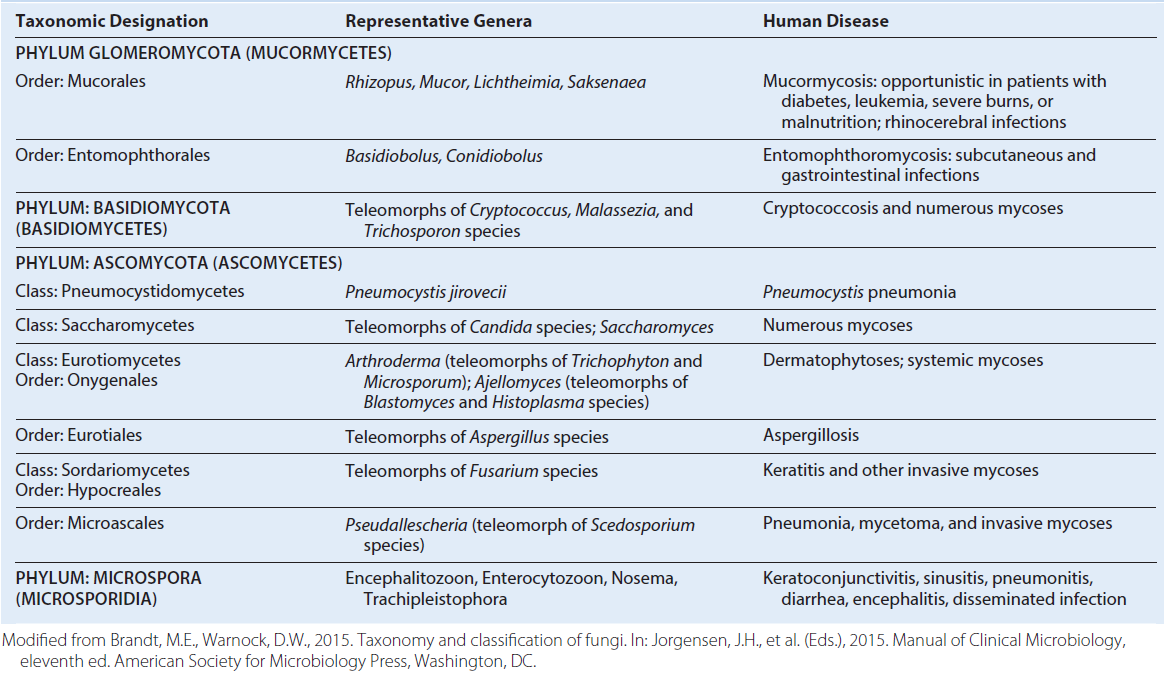
9. Causative agents and classification of *protozoan infections*

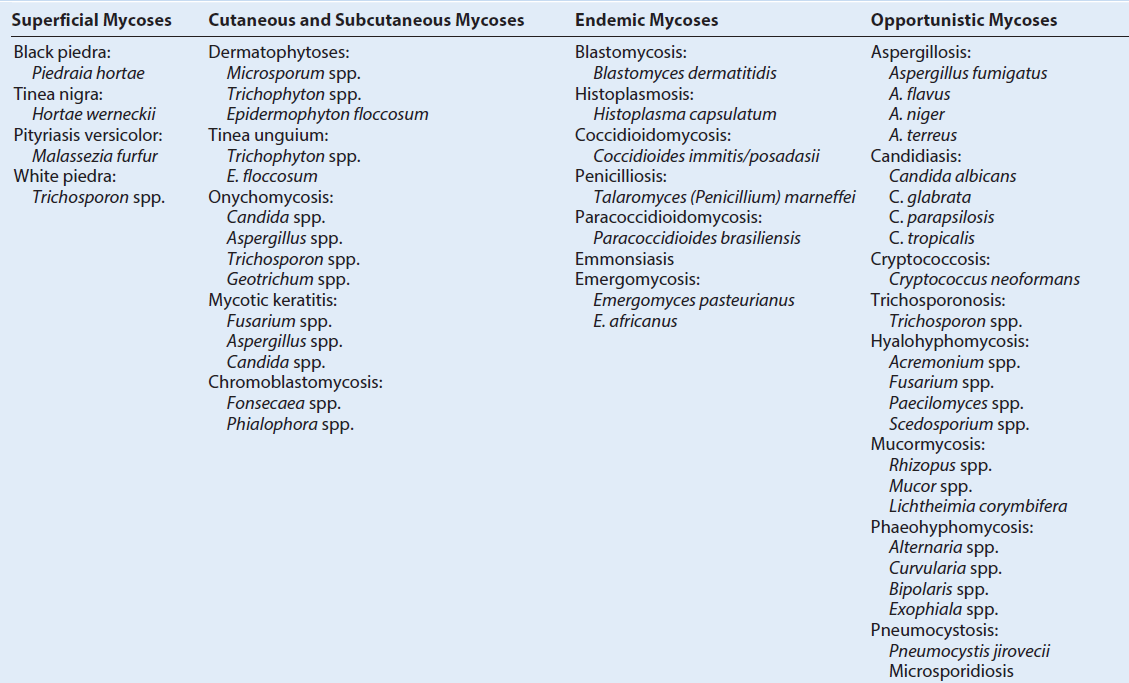
10. Morpho-biological characteristics of protozoa belonging to the type *Sarcomastigophora* (sarcodines and flagellates), principles of microbiological diagnosis of diseases caused by them (amoebiasis, giardiasis, trichomoniasis, leishmaniasis, trypanosomosis)

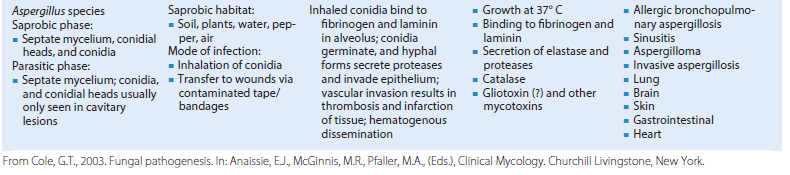
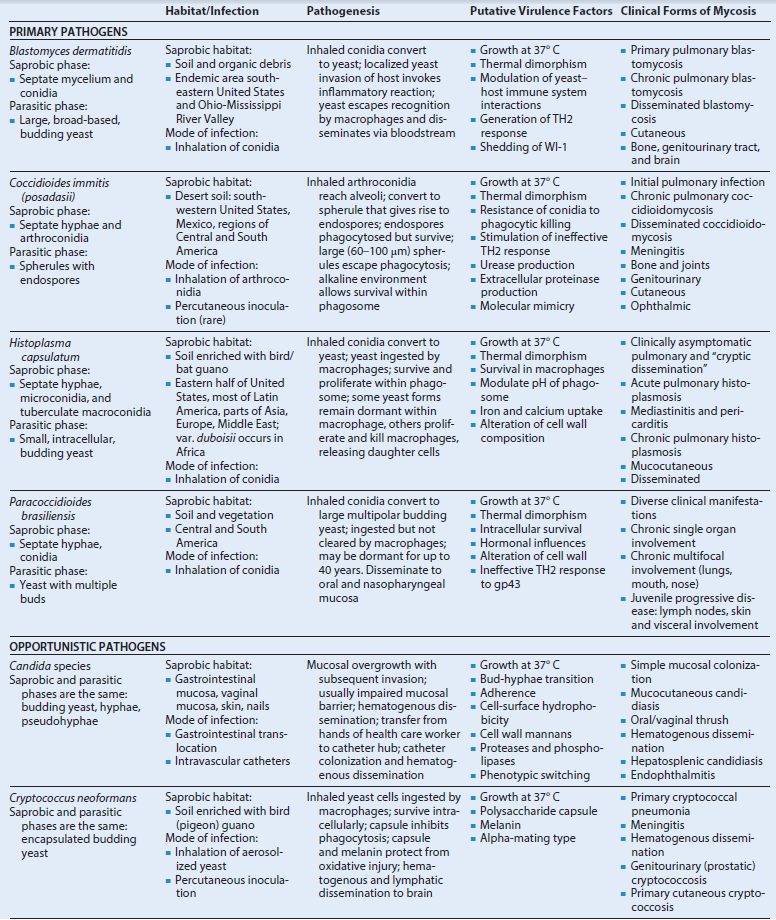
11. Morpho-biological characteristics of the primitives belonging to the type *Apicomplexa* (spores), principles of microbiological diagnosis of diseases caused by them (malaria, toxoplasmosis)

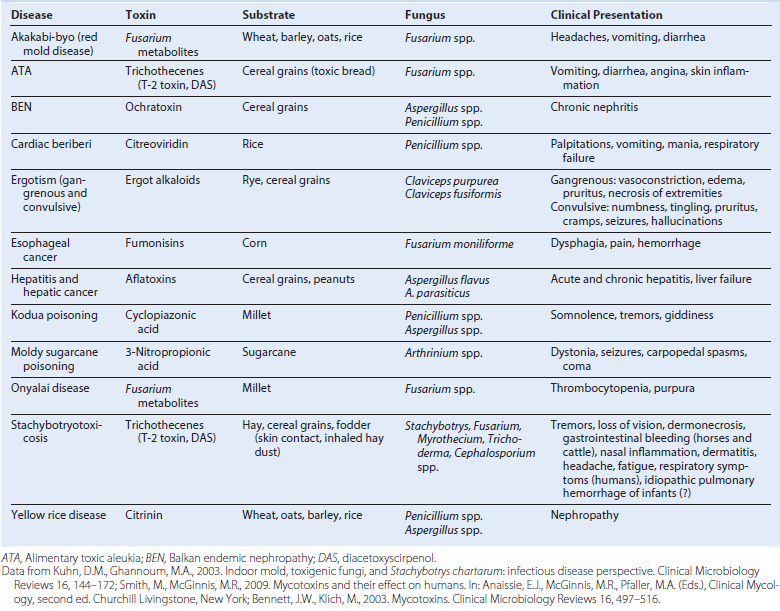
12. Morpho-biological characteristics of the protozoa belonging to the type of *Ciliophora* (ciliated), principles of microbiological diagnosis of the diseases caused by them (balantidiosis)

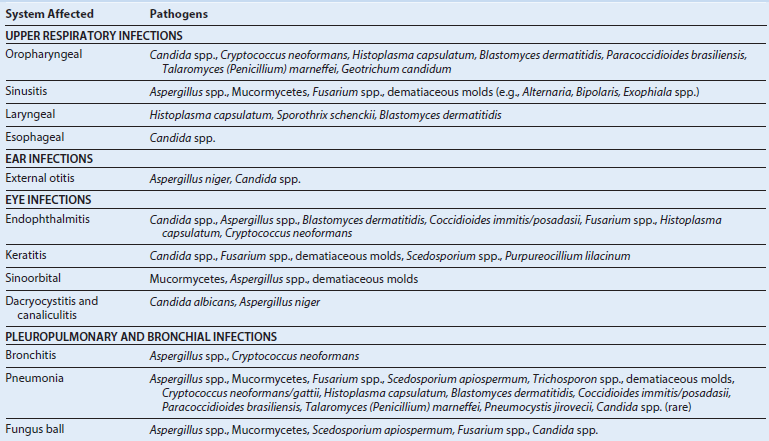
13. Morpho-biological characteristics of protozoa belonging to the *Microspora* (invasion) type, principles of microbiological diagnosis of diseases caused by them (microsporidiosis)

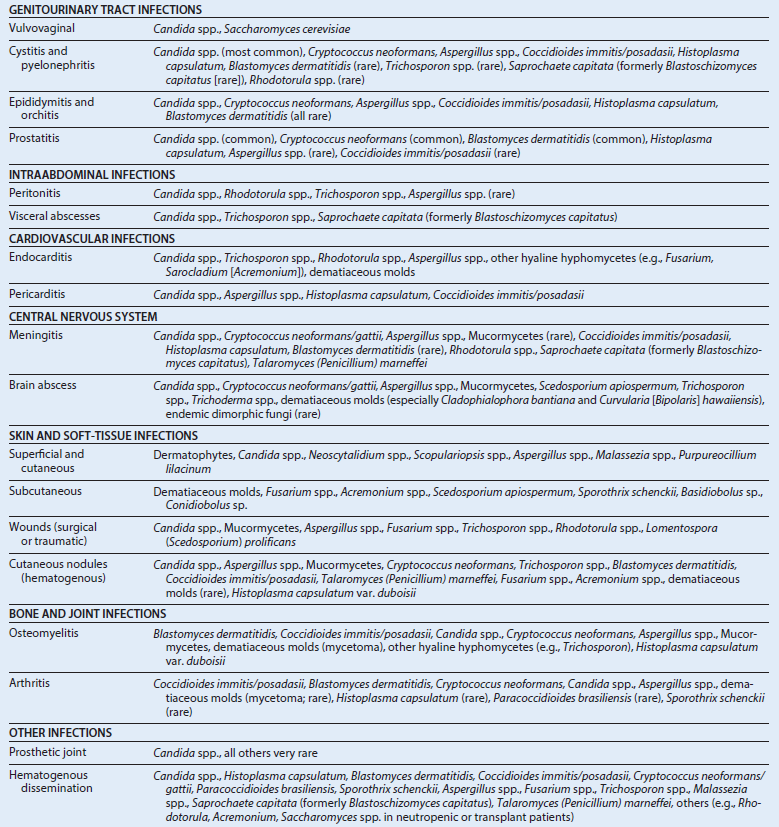
**Medically Important Fungi (Kingdom Fungi)**

**Classification of Human Mycoses and Representative Etiologic Agents**

**Characteristics of Primary and Opportunistic Fungal Pathogens**

**Mycotoxin-Related Illnesses Postulated to Affect Humans, Based on Analytic or Epidemiologic Data**

**Summary of Fungi Associated with Human Disease**



**Antifungal spectrum:** This is the range of activity of an antifungal agent against fungi. A broad-spectrum antifungal agent inhibits a wide variety of fungi, including both yeastlike fungi and molds, whereas a narrow-spectrum agent is active only against a limited number of fungi.

**Fungistatic activity:** This is the level of antifungal activity that **inhibits** the growth of an organism. This is determined in vitro by testing a standardized concentration of organisms against a series of antifungal dilutions. The lowest concentration of the drug that inhibits the growth of the organism is referred to as the **MIC.**

**Fungicidal activity:** This is the ability of an antifungal agent to **kill** an organism in vitro or in vivo. The lowest concentration of the drug that kills 99.9% of the test population is called the **MFC.**

**Antifungal combinations:** These combinations of antifungal agents may be used (1) to enhance efficacy in the treatment of a refractory fungal infection, (2) to broaden the spectrum of empiric antifungal therapy, (3) to prevent the emergence of resistant organisms, and (4) to achieve a synergistic killing effect.

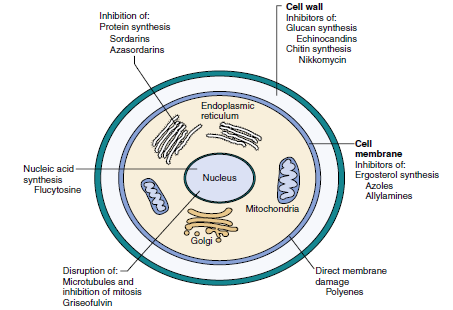
**Antifungal synergism:** These are combinations of antifungal agents that have enhanced antifungal activity when used together compared with the activity of each agent alone.

**Antifungal antagonism:** This is a combination of antifungal agents in which the activity of one of the agents interferes with the activity of the other agent.

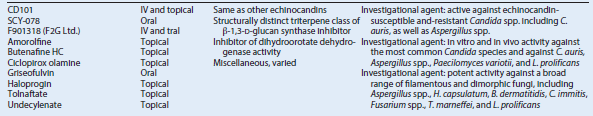
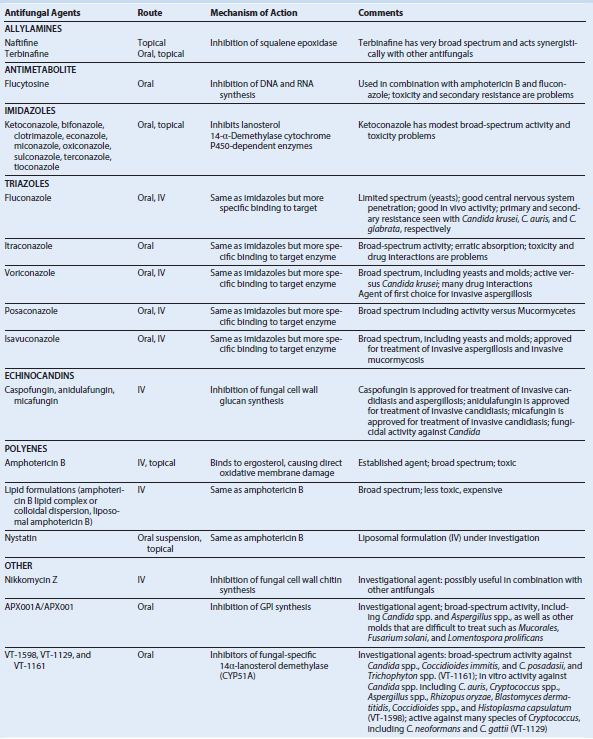
**Efflux pumps:** These are families of drug transporters that serve to actively pump antifungal agents out of the fungal cells, decreasing the amount of intracellular drug available to bind to its target.

*MFC-*Minimum fungicidal concentration; *MIC-*minimum inhibitory concentration.

**Sites of action of antifungals.**



|  |  |
| --- | --- |
|  | Metabolic pathway for the synthesis of ergosterol, showing sites of inhibition by allylamine, azole, and polyene antifungal agents. *Ac-CoA,* Acetyl-coenzyme A; *HMG-CoA,* hydroxymethyl glutaryl-coenzyme A. |

**Systemic and Topical Antifungal Agents in Use and in Development**

**DERMATOPHYTES**

**Trigger Words** Tinea, KOH preparation, ringworm, azoles, terbinafine, circular, scaling lesion with central clearing and hair loss

**Biology, Virulence, and Disease**

• Include filamentous fungi in the genera *Trichophyton, Epidermophyton,* and

*Microsporum*

• Keratinophilic and keratinolytic; able to invade and break down skin, hair, and nails

• In infections of skin, hair, and nails, only outermost keratinized layers invaded

• Various forms of dermatophytosis (tineas or “ringworm”) classified according to anatomic site or structure involved

• Clinical signs and symptoms vary

**Epidemiology**

• Classified into three categories based on natural habitat: geophilic, zoophilic, and anthropophilic

• Geophilic: live in soil, occasional pathogens of both animals and humans

• Zoophilic: parasitize hair and skin of animals but can be transmitted to humans

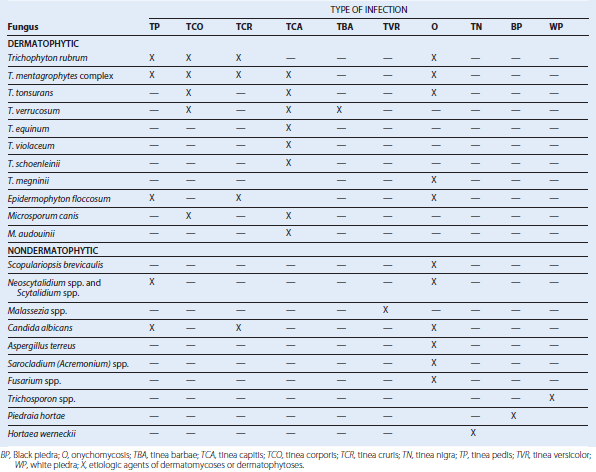
• Anthropophilic: infect humans, may be transmitted directly or indirectly from person to person

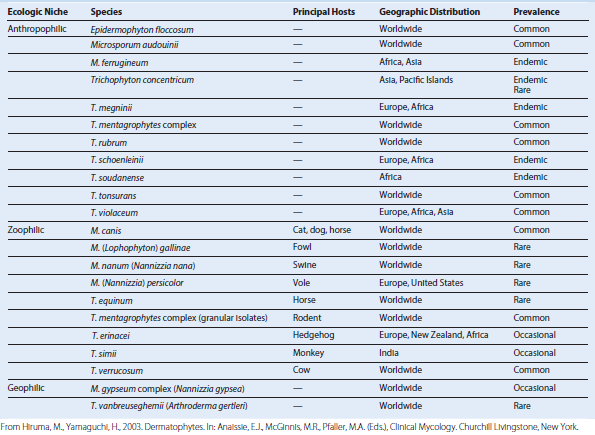
• Occur worldwide, especially in tropical and subtropical regions

**Treatment, Prevention, and Control**

• Localized infections that do not involve hair or nails may be treated effectively with topical antifungal agents (azoles, terbinafine, haloprogin)

• All others require oral therapy (griseofulvin, itraconazole, fluconazole, terbinafine)

**Common and Uncommon Agents of Superficial and Cutaneous Dermatomycoses and Dermatophytoses**

**Classification of Dermatophytes According to Ecologic Niche**

***Subcutaneous Mycoses***

**SPOROTRICHOSIS *(Sporothrix schenckii)***

**Trigger Words-**Thorn prick, rose handler’s disease, sphagnum moss, lymphocutaneous nodules

**Biology, Virulence, and Disease**

ᑏᑏ Thermally dimorphic fungus; grows as a mold at room temperature (e.g., 25° C) and as a pleomorphic yeast at 37° C and in tissue

ᑏᑏ Infection is chronic; nodular and ulcerative lesions develop along lymphatics that drain primary site of inoculation

**Epidemiology**

ᑏᑏ Sporadic, most common in warmer climates: Japan, North and South America

ᑏᑏ Outbreaks related to forest work, mining, gardening

ᑏᑏ Classic infection associated with traumatic inoculation of soil, vegetable, or organic matter contaminated with fungus

ᑏᑏ Zoonotic transmission reported in armadillo hunters and in association with infected cats

**Diagnosis**

ᑏᑏ Subcutaneous infection with lymphangitic spread

ᑏᑏDefinitive diagnosis requires culture of infected pus or tissue

ᑏᑏ In tissue, organism appears as a pleomorphic budding yeast

**Treatment, Prevention, and Control**

ᑏᑏ Classic treatment: oral potassium iodide in saturated solution

ᑏᑏ Itraconazole: safe, highly effective, treatment of choice

ᑏᑏ Alternatives: terbinafine, fluconazole, posaconazole

ᑏᑏ Local application of heat shown to be effective

**EUMYCOTIC MYCETOMA**

***(Phaeoacremonium, Curvularia, Fusarium, Madurella, Mediacopsis, Nigrograna, Trematosphaeria, Exophiala, Falciformispora, AND Scedosporium species)***

**Trigger Words-**Grains, sinus tract, dematiaceous, subcutaneous, mycetoma

**Biology, Virulence, and Disease**

ᑏᑏ Caused by a wide array of true fungi (as opposed to actinomycotic mycetomas, which are caused by bacteria)

ᑏᑏ Localized chronic granulomatous infectious process involving cutaneous and subcutaneous tissues

ᑏᑏ Painless subcutaneous nodule; increases slowly but progressively in size

ᑏᑏ Local spread may breach tissue planes, destroying muscle, fascia, and bone

ᑏᑏ Hematogenous or lymphatic spread rare

**Epidemiology**

ᑏᑏ Primarily in tropical areas with low rainfall; most common in Africa and India

ᑏᑏ Traumatic implantation into exposed body parts; foot and hand most common; back, shoulders, chest wall may also be involved

ᑏᑏ Men more often affected than women

ᑏᑏ Etiologic agent varies from country to country

ᑏᑏ Mycetomas not contagious

**Diagnosis**

ᑏᑏDemonstration of grains or granules grossly visible in draining sinus tracts; may also be seen on tissue biopsy

ᑏᑏMicroscopic examination of granules

ᑏᑏCulture usually needed for identification of organism

**Treatment, Prevention, and Control**

ᑏᑏ Usually unsuccessful; poor response to most antifungal agents

ᑏᑏ Specific antifungal therapy may slow progression: terbinafine, voriconazole, posaconazole

ᑏᑏ Local excision usually ineffective; amputation is the only definitive treatment

**ENTOMOPHTHOROMYCOSIS**

***(Conidiobolus coronatus AND Basidiobolus ranarum)***

**Trigger Words-**Entomophthoromycosis, subcutaneous, Splendore-Hoeppli, mucormycotic

**Biology, Virulence, and Disease**

ᑏᑏ Subcutaneous entomophthoromycosis caused by Mucormycetes of the order Entomophthorales: *Conidiobolus coronatus, Basidiobolus ranarum*

ᑏᑏ Chronic subcutaneous form of mucormycosis

ᑏᑏ Occurs sporadically as a result of subcutaneous implantation or inhalation of fungus present in plant debris

ᑏᑏ *B. ranarum:* infection presents with disk-shaped, rubbery, moveable masses localized to shoulder, pelvis, hips, thighs; may become quite large and ulcerate

ᑏᑏ *C. coronatus:* confined to rhinofacial area; facial deformity may be quite dramatic

ᑏᑏ Angioinvasion does not occur; dissemination or involvement of deep structures rare

**Epidemiology**

ᑏᑏ Both types seen most commonly in Africa, India

ᑏᑏ Both fungi are saprophytes present in leaf and plant debris

ᑏᑏ Rare diseases without known predisposing factors

ᑏᑏ *B. ranarum*: infection occurs after traumatic implantation of fungus into subcutaneous tissues of thighs, buttocks, trunk; occurs mainly in children; male/female ratio 3:1

ᑏᑏ *C. coronatus*: infection occurs after inhalation of fungal spores, with subsequent invasion of tissues of nasal cavity, paranasal sinuses, facial soft tissues; predominantly seen in young adults; male/female ratio 10:1

**Diagnosis**

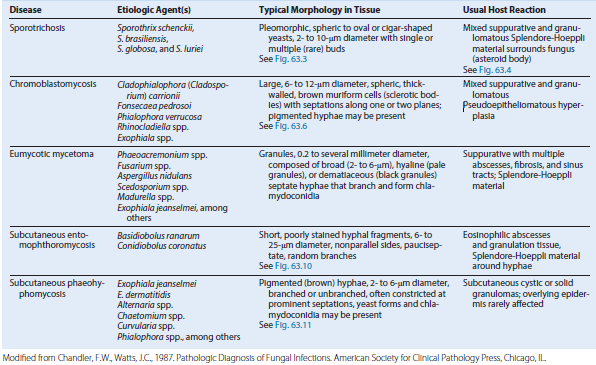
ᑏᑏClinical diagnosis usually evident based on gross physical appearance

ᑏᑏ Both types of subcutaneous entomophthoromycosis require biopsy for definitive diagnosis

**Treatment, Prevention, and Control**

ᑏᑏ Both types of infection may be treated with itraconazole; oral potassium iodide in saturated solution may be used

ᑏᑏ Facial reconstructive surgery may be necessary in the case of *C. coronatus* infection

**Common Agents of Subcutaneous Mycoses **

***SYSTEMIC MYCOSES CAUSED BY DIMORPHIC FUNGI***

**BLASTOMYCOSIS (*BLASTOMYCES DERMATITIDIS* AND *B. GILCHRISTII*)**

**Trigger Words-**Mississippi River Valley, broad-based budding yeast, healthy and immunocompromised, granuloma

**Biology, Virulence, and Disease**

ᑏᑏ Thermally dimorphic fungus: large nonencapsulated budding yeast cells in tissue and in culture at 37° C; mold colonies form in culture at 25°C

ᑏᑏUsual route of infection is inhalation of conidia

ᑏᑏ Severity of symptoms and course of disease depends on extent of exposure and immune status of exposed individual; most are asymptomatic

ᑏᑏClassic form of blastomycosis: chronic cutaneous involvement

**Epidemiology**

ᑏᑏ Ecologic niche: decaying organic matter

ᑏᑏ Area of endemicity: southeastern and southcentral states, especially bordering Ohio and Mississippi river basins; Midwest states and Canadian provinces bordering Great Lakes; and an area in New York and Canada along the St. Lawrence River

ᑏᑏ Outbreaks of infection have been associated with occupational or recreational contact with soil

**Diagnosis**

ᑏᑏMicroscopic detection of fungus in tissue or other clinical material, with confirmation by culture

ᑏᑏAntigen detection and PCR

**Treatment, Prevention, and Control**

ᑏᑏ Pulmonary blastomycosis in immunocompromised patients and those with progressive pulmonary disease should be treated

ᑏᑏ All patients with evidence of hematogenous dissemination require antifungal therapy

ᑏᑏ Lipid formulation of amphotericin B: treatment of choice for meningeal disease and other life-threatening presentations

ᑏᑏ Mild or moderate disease: itraconazole; fluconazole, posaconazole, or voriconazole may be substituted for itraconazole

**COCCIDIOIDOMYCOSIS (*COCCIDIOIDES IMMITIS* AND *C. POSADASII*)**

**Trigger Words-**Valley fever, coccidioidal granuloma, arthroconidia, spherule, skin test, precipitin test

**Biology, Virulence, and Disease**

ᑏᑏ Coccidioidomycosis caused by two indistinguishable species: *C. immitis* and *C. posadasii*

ᑏᑏ *C. immitis* is localized to California; *C.posadasii* causes most infections outside California

ᑏᑏ Disease caused by inhalation of infectious arthroconidia

ᑏᑏ Asymptomatic or subclinical, self-limited flulike illness, acute and chronic pulmonary disease, single or multisystem dissemination

ᑏᑏ Dimorphic fungi; endosporulating spherule in tissue, mold in culture at 25° C and in nature

**Epidemiology**

ᑏᑏ Endemic to U.S. southwestern desert, northern Mexico, scattered areas of Central and South America

ᑏᑏ Organism found in soil; growth in environment enhanced by bat and rodent droppings; cycles of drought/rain enhance organism dispersion

ᑏᑏ Persons ≥65 years and those with HIV infection disproportionately affected

ᑏᑏ Risk of disseminated disease highest in certain ethnic groups (Filipino, African American, Native American, Hispanic), males (9:1), women in third trimester of pregnancy, individuals with cellular immune deficiency, persons at extremes of age

**Diagnosis**

ᑏᑏHistopathologic examination of tissue or other clinical material, isolation of fungus in culture, serology

ᑏᑏHistopathologic examination that reveals endosporulating spherules in sputum, exudates, or tissue is sufficient to establish the diagnosis

ᑏᑏCulture at 25° C takes days and poses risk to laboratory workers; all work with molds should be performed in suitable biosafety cabinet

ᑏᑏ Serology (antigen and antibody) may be useful for initial screening, confirmation, or prognostic evaluation

**Treatment, Prevention, and Control**

ᑏᑏ Most individuals with primary infection do not require therapy

ᑏᑏ For those with concurrent risk factors or a more severe presentation: lipid formulation of amphotericin B followed by an oral azole as maintenance therapy (severe disease)

ᑏᑏ Chronic cavitary pulmonary disease: azole for at least 1 year

ᑏᑏ Nonmeningeal extrapulmonary disseminated infections: oral azole

ᑏᑏ Meningeal coccidioidomycosis: fluconazole; itraconazole, posaconazole or voriconazole are secondary choices

**HISTOPLASMOSIS (*HISTOPLASMA CAPSULATUM*)**

**Trigger Words-**Intracellular yeasts, bird and bat droppings, chicken coop, caves, guano, granulomas

**Biology, Virulence, and Disease**

ᑏᑏ Histoplasmosis caused by two varieties of *H. capsulatum*

ᑏᑏ *H. capsulatum* var. *capsulatum:* causes pulmonary and disseminated infections

ᑏᑏ *H. capsulatum* var. *duboisii:* causes predominantly skin and bone lesions

ᑏᑏ Disease caused by inhalation of infectiousmicroconidia

ᑏᑏ Severity of symptoms and course of disease depend on extent of exposure and immune status of infected individual; most are asymptomatic, self-limited; flulike illness also occurs

ᑏᑏ Thermally dimorphic fungus: hyaline mold in nature and in culture at 25° C, budding yeast in tissue (intracellular) and in culture at 37° C

**Epidemiology**

ᑏᑏ *H. capsulatum* var. *capsulatum:* localized to Ohio and Mississippi river valleys; occurs throughout Mexico and Central and South America

ᑏᑏ *H. capsulatum* var. *duboisii:* confined to tropical Africa (e.g., Gabon, Uganda, Kenya)

ᑏᑏ Found in soil with high nitrogen content (e.g., areas contaminated with bird or bat droppings)

ᑏᑏ Outbreaks of disease have been associated with exposure to bird roosts, caves, and decaying buildings or urban renewal projects involving excavation and demolition

ᑏᑏ Immunocompromised individuals and children most prone to develop symptomatic disease

ᑏᑏ Reactivation of disease and dissemination common among immunosuppressed individuals, especially those with AIDS

**Diagnosis**

ᑏᑏDirect microscopy, culture of clinical material, serology (antigen and antibody), β-D-glucan, and PCR have been useful

ᑏᑏ Yeast phase of organism can be detected in sputum, bronchoalveolar lavage fluid, peripheral blood films, bone marrow, and tissue stained with Giemsa, GMS, or PAS stains

ᑏᑏCultures should be handled in a biosafety cabinet

ᑏᑏ Serologic diagnosis includes tests for antibody and antigen

**Treatment, Prevention, and Control**

ᑏᑏ Severe acute infections: lipid formulation of amphotericin B followed by oral itraconazole

ᑏᑏ Chronic pulmonary histoplasmosis: lipid formulation of amphotericin B followed by itraconazole

ᑏᑏ Disseminated infection: lipid formulation of amphotericin B followed by itraconazole

**PARACOCCIDIOIDOMYCOSIS (*PARACOCCIDIOIDES BRASILIENSIS* AND *P. LUTZII*)**

**Trigger Words-**Pilot’s wheel, South American blastomycosis, ulcer, multiple buds

**Biology, Virulence, and Disease**

* Thermally dimorphic fungus: slowly growing mold phase in nature and at 25° C, yeast phase (variable sized with single or multiple buds) in tissue and in culture at 37° C
* Usual route of infection is inhalation or possible traumatic inoculation of conidia or hyphal fragments
* Paracoccidioidomycosis may be subclinical or progressive with acute or chronic pulmonary forms or acute, subacute, or chronic disseminated forms

**Epidemiology**

* Endemic throughout Latin America, areas of high humidity, rich vegetation, moderate temperatures, acid soil
* Ecologic niche not well established
* Overt disease uncommon among children and adolescents; in adults, disease more common in men aged 30 to 50 years
* Most patients with clinically apparent disease live in rural areas and have close contact with soil
* No reports of epidemics or person-toperson transmission

**Diagnosis**

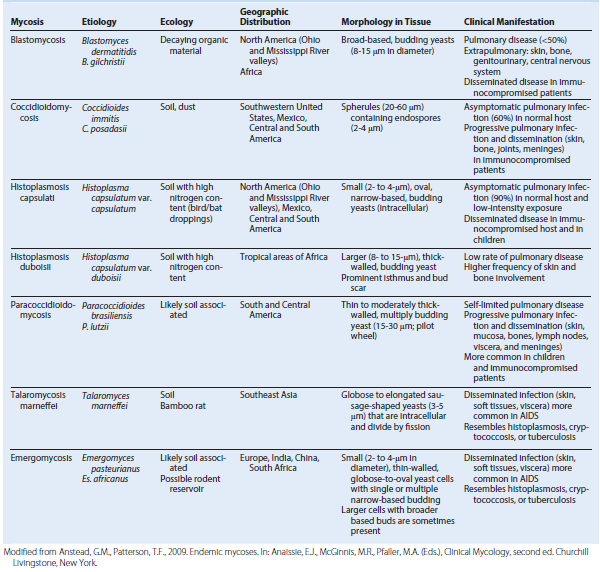
ᑏᑏDemonstration of characteristic yeastforms on microscopic examination of clinical material: oval to round with double refractile walls and single or multiple buds; “pilot-wheel” morphology

ᑏᑏMay be isolated in culture and should be handled in a biosafety cabinet

ᑏᑏ Serology testing may help in suggesting diagnosis, evaluating response to therapy

**Treatment, Prevention, and Control**

* Itraconazole: treatment of choice for most forms of disease
* More severe or refractory forms: lipid formulation of amphotericin B followed by either itraconazole or sulfonamide therapy

**Characteristics of Endemic Dimorphic Mycoses **

***OPPORTUNISTIC MYCOSES***

**CANDIDIASIS**

**Trigger Words-***Candida,* pseudohyphae, endogenous, exogenous, yeast, immunocompromised, vaginal thrush, oropharyngeal

**Biology, Virulence, and Disease**

ᑏᑏ Opportunistic yeasts causing infections ranging from superficial mucosal and cutaneous disease to hematogenously disseminated, often fatal, infections

ᑏᑏ Vast majority of infections are caused by five major species: *Candida albicans, C. glabrata, C. parapsilosis, C. tropicalis,* and *C. krusei*

ᑏᑏ Morphology ranges from budding yeasts to pseudohyphae and true hyphae

ᑏᑏ Reproduction is by formation of blastoconidia (buds)

ᑏᑏ Most important group of opportunistic fungal pathogens

ᑏᑏ May be community acquired (mucosal infections) or hospital associated (invasive disease)

**Epidemiology**

ᑏᑏ *Candida* spp. are known colonizers of humans and other warm-blooded animals

ᑏᑏ Primary site of colonization is the GI tract; commensals in the vagina, urethra, skin, and nails

ᑏᑏ Most infections are endogenous, involving normally commensal host flora

ᑏᑏ Exogenous transmission in hospitals also occurs

ᑏᑏ *C. albicans* predominates in most types of infection

ᑏᑏ Consequences of *Candida* BSIs are severe; risk factors include hematologic malignancies and neutropenia, abdominal surgery, prematurity in infants, and age >70 years

**Diagnosis**

ᑏᑏClinical appearance, direct microscopic examination, and culture

ᑏᑏHematogenously disseminated infections and candidemia difficult to diagnose on clinical grounds alone

ᑏᑏ Laboratory diagnosis involves procurement of appropriate clinical material, followed by direct microscopic examination; culture; and (increasingly) application of molecular, antigenic, and proteomic analysis

**Treatment, Prevention, and Control**

ᑏᑏ Mucosal and cutaneous infection: topical and systemically active antifungal agents include azoles (itraconazole, fluconazole, miconazole, and many others), polyenes (amphotericin B and nystatin)

ᑏᑏ Invasive candidiasis and candidemia: oral or intravenous administration depending on antifungal agent and severity of disease and/or immunosuppression; azoles (fluconazole, voriconazole, posaconazole, isavuconazole), echinocandins (anidulafungin, caspofungin, micafungin), amphotericin B formulations (deoxycholate and lipid formulations), flucytosine

**CRYPTOCOCCOSIS**

**Trigger Words-**Capsule, budding yeast, CNS, neurotropic, India ink, antigen, AIDS

**Biology, Virulence, and Disease**

ᑏᑏ Systemic mycosis caused by the fungi *Cryptococcus neoformans* and *C. gattii*

ᑏᑏ *C. neoformans* includes capsular serotypes A, D, and AD; var. *grubii* (serotype A) and var. neoformans (serotype D)

ᑏᑏ *C. gattii* includes serotypes B and C

ᑏᑏ Spherical to oval, encapsulated, yeastlike organisms that replicate by budding

ᑏᑏ Both species may cause pulmonary, hematogenously disseminated, and CNS disease

**Epidemiology**

ᑏᑏ Usually acquired by inhaling aerosolized cells of *C. neoformans* and *C. gattii*

ᑏᑏ Both species pathogenic for immunocompetent individuals

ᑏᑏ *C. neoformans*: most often encountered as opportunistic pathogen; found worldwide in soil contaminated with avian excreta

ᑏᑏ *C. gattii*: found in tropical and subtropical climates in association with eucalyptus trees; the focus in the Pacific Northwest has been associated with Douglas fir trees

ᑏᑏ Disease is similar, although *C. gattii* infection tends to occur in immunocompetent individuals and has a lower associated mortality

ᑏᑏ Incidence has progressively declined since early 1990s because of widespread use of fluconazole and successful treatment of HIV infection with antiviral drugs

**Diagnosis**

ᑏᑏMay present as pneumonic process or (more commonly) as CNS infection

ᑏᑏDiagnosis may be made by culture of blood, CSF, or other clinical material

ᑏᑏMicroscopic examination of CSF may reveal characteristic encapsulated budding yeast cells

ᑏᑏCryptococcal meningitis: diagnosis by detection of polysaccharide antigen in serum or CSF

**Treatment, Prevention, and Control**

ᑏᑏ Cryptococcal meningitis and other disseminated forms universally fatal if left untreated

ᑏᑏ Antifungal therapy: amphotericin B (deoxycholate or lipid formulation) plus flucytosine followed by maintenance/consolidation therapy with fluconazole (preferred) or itraconazole

ᑏᑏ Effective management of CNS pressure and IRIS crucial to successful management of cryptococcal meningitis

**ASPERGILLOSIS**

**Trigger Words-**Septate branching hyphae, hypersensitivity pneumonitis, angioinvasive, aspergilloma, conidia

**Biology, Virulence, and Disease**

ᑏᑏ Broad spectrum of diseases caused by filamentous fungi (molds) of genus *Aspergillus*

ᑏᑏ Exposure to spores in environment may cause allergic reactions in hypersensitized hosts or destructive, invasive, pulmonary, and disseminated disease in highly immunocompromised hosts

ᑏᑏ Vast majority of infections caused by *A.fumigatus* (most common), *A. flavus, A.niger*, and *A. terreus*

ᑏᑏ Hyaline molds that produce vast amounts of spores (conidia) that serve as infectious propagules on inhalation by host

ᑏᑏ Invasive aspergillosis marked by angioinvasion and tissue destruction caused by infarction

ᑏᑏ Hematogenous dissemination of infection to extrapulmonary sites (most commonly brain, heart, kidneys, GI tract, liver, spleen)

common because of angioinvasive nature of fungus

**Epidemiology**

ᑏᑏ *Aspergillus* spp. common worldwide; conidia ubiquitous in air, soil, decaying matter

ᑏᑏ Within hospital environment, *Aspergillus* spp. may be found in air, showerheads, water storage tanks, potted plants

ᑏᑏ Conidia (spores) constantly being inhaled; respiratory tract most frequent and important portal of entry

ᑏᑏ Host reaction, associated pathologic findings, and outcome of infection depend more on host factors than virulence or pathogenesis of individual species

**Diagnosis**

ᑏᑏ Serologic, culture, histopathologic, molecular, biochemical, and antigenic methods supplemented by imaging studies

**Treatment, Prevention, and Control**

ᑏᑏ Treatment usually involves administration of corticosteroids coupled with pulmonary toilet

ᑏᑏ Treatment of chronic pulmonary aspergillosis may involve steroids and long-term antifungal therapy, usually with an azole antifungal agent

ᑏᑏ Prophylaxis of high-risk (neutropenic) patients usually accomplished by administration of a mold-active azole (itraconazole, posaconazole, voriconazole)

ᑏᑏ Specific antifungal therapy of invasive aspergillosis usually involves administration of voriconazole or a lipid formulation of amphotericin B; isavuconazole has recently been cleared by the U.S. Food and Drug Administration for treatment of invasive aspergillosis

ᑏᑏ Efforts to decrease immunosuppression and/or reconstitute host immune defenses important, as is surgical resection of infected tissue if possible

ᑏᑏ Resection of aspergillomas only considered in instances of severe hemoptysis

*BSI,* Bloodstream infections; *CNS,* central nervous system; *CSF,* cerebrospinal fluid; *GI,* gastrointestinal; *IRIS,* immune reconstitution inflammatory syndrome.

**Agents of Opportunistic Mycoses**

|  |  |
| --- | --- |
| ***Candida* spp.**  *C. albicans*  *C. glabrata*  *C. parapsilosis*  *C. tropicalis*  *C. krusei*  *C. lusitaniae*  *C. guilliermondii*  *C. dubliniensis*  *C. rugosa*  *C. auris* | **Microsporidia Aspergillus *spp.***  *A. fumigatus*  *A. flavus*  *A. niger*  *A. versicolor*  *A. terreus* |
| ***Cryptococcus Neoformans* and Other Opportunistic Yeastlike Fungi**  *C. neoformans/gattii*  *Malassezia* spp.  *Trichosporon* spp.  *Rhodotorula* spp.  Saprochaete capitata | **Mucormycetes**  *Rhizopus* spp.  *Mucor* spp.  *Rhizomucor* spp.  *Lichtheimia corymbifera*  *Cunninghamella* spp. |
| **Other Hyaline Molds**  *Fusarium* spp.  *Sarocladium* spp.  *Paecilomyces* spp.  *Purpureocillium lilacinum*  *Trichoderma* spp.  *Scopulariopsis* spp. | **Dematiaceous Molds**  *Alternaria* spp.  *Bipolaris* spp.  *Cladophialophora* spp.  *Curvularia* spp.  *Exophiala* spp.  *Exserohilum* spp.  *Lomentospora prolificans*  *Scedosporium* spp.  *Wangiella* spp. |
|  | ***Pneumocystis jirovecii*** |

**SPECTRUM OF DISEASES CAUSED BY ASPERGILLUS SPECIES**

**Allergic Reactions-**Nasal cavity, Paranasal sinuses, Lower respiratory tract

**Colonization-**Obstructed paranasal sinuses, Bronchi, Preformed pulmonary cavities

**Superficial Cutaneous Infections-**Wounds, Catheter sites

**Limited Invasive Infections-**Bronchi, Pulmonary parenchyma, Mildly immunodeficient patients

**Frankly Invasive Pulmonary Infection-**Severely immunodeficient patients,

Systemic dissemination, Death

***Fungal and Fungal-Like Infections of Unusual or Uncertain Etiology***

**CHLORELLOSIS**

**Trigger Words-**Chloroplasts, green lesions, water exposure, alga

**Biology, Virulence, and Disease**

ᑏᑏ Infection of humans and animals caused by a unicellular green alga of genus *Chlorella*

ᑏᑏ *Chlorella:* unicellular, ovoid, spherical or polygonal, reproduce by endosporulation

ᑏᑏ Fresh lesions in liver, lymph nodes, cutaneous tissue are green on gross examination; smears reveal organisms that contain green refractile granules (chloroplasts)

ᑏᑏ A single human infection reported thus far; most infections occur in sheep and cattle

**Epidemiology**

ᑏᑏ A single human infection in Nebraska; resulted from exposure of a surgical wound to river water

ᑏᑏ Infections in domestic and wild animals range from lymph node and deep organ involvement to cutaneous and subcutaneous lesions, presumably related to exposure to water containing the organism

**Diagnosis**

ᑏᑏ*Chlorella* spp. infections diagnosed by culture and histopathologic examination of infected tissue

ᑏᑏOn culture, colonies are bright green

ᑏᑏWet mounts of wound exudate or touch preparations of infected tissue reveal ovoid, endosporulating cells with characteristic green cytoplasmic granules

ᑏᑏ In tissue, cells stain with GMS and PAS but not H&E stains

**Treatment, Prevention, and Control**

ᑏᑏ Repeat debridement, irrigation with Dakin solution, gauze packing and removal for drainage and granulation

ᑏᑏ Amphotericin B therapy combined with administration of tetracycline may be useful

**LACAZIOSIS**

**Trigger Words-**Cutaneous trauma, soil, vegetation, water, dolphins, cutaneous nodules, tropical

**Biology, Virulence, and Disease**

ᑏᑏ Chronic fungal skin infection caused by *Lacazia loboi*

ᑏᑏ *L. loboi:* ascomycete fungus, reproduces by sequential budding, forms chains of spherical to oval cells connected by narrow tubelike bridges

ᑏᑏ Slowly developing cutaneous nodules of varying size and shape

ᑏᑏ Nodular keloid-like lesions most common; occur on the face, ears, arms, legs, feet

ᑏᑏ Lesions increase in size and number over a period of 40 to 50 years

ᑏᑏ Most patients asymptomatic; no systemic manifestations of disease

**Epidemiology**

ᑏᑏ Human disease endemic in tropical regions of Central and South America

ᑏᑏ *L. loboi* considered a saprophyte of soil and vegetation

ᑏᑏ Mode of infection: cutaneous trauma; occurs in individuals involved in farming and jungle clearing

ᑏᑏ Lacaziosis occurs in both marine and fresh water dolphins, suggesting an aquatic reservoir

**Diagnosis**

ᑏᑏ Based on demonstrating yeast cells in lesion exudate or tissue sections

ᑏᑏ Biopsy reveals a dispersed granulomatous infiltrate and numerous fungal forms in dermis and subcutaneous tissue

**Treatment, Prevention, and Control**

ᑏᑏ Surgical excision of localized lesions

ᑏᑏ Does not respond to antifungal therapy

**RHINOSPORIDIOSIS**

**Trigger Words-**Polypoid lesions, oropharynx, sporangium, trophocyte, endoconidia, granulomatous

**Biology, Virulence, and Disease**

ᑏᑏ Granulomatous disease of humans and animals caused by *Rhinosporidium seeberi*

ᑏᑏ Characterized by development of nasopharyngeal and ocular conjunctival polyps

ᑏᑏ Two developmental forms seen in tissue: a large spherical form (sporangia) and a smaller trophic form

**Epidemiology**

ᑏᑏ≈90% of all known cases of rhinosporidiosis occur in India and Sri Lanka

ᑏᑏ Natural habitat unknown

ᑏᑏ Occurs primarily in men aged 20 to 40

ᑏᑏ Appears to be associated with both rural and aquatic environments

ᑏᑏ No evidence rhinosporidiosis is contagious

**Diagnosis**

ᑏᑏHistopathologic examination of affected tissues; distinctive appearance of trophocytes and sporangia in routine H&Estained

tissue is diagnostic

ᑏᑏ *R. seeberi* has not been grown in culture

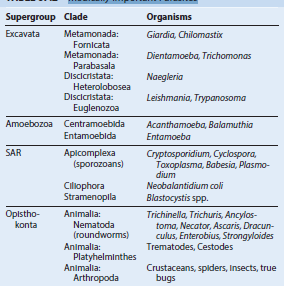
**Treatment, Prevention, and Control**

ᑏᑏ Only effective form of treatment is surgical excision of lesions

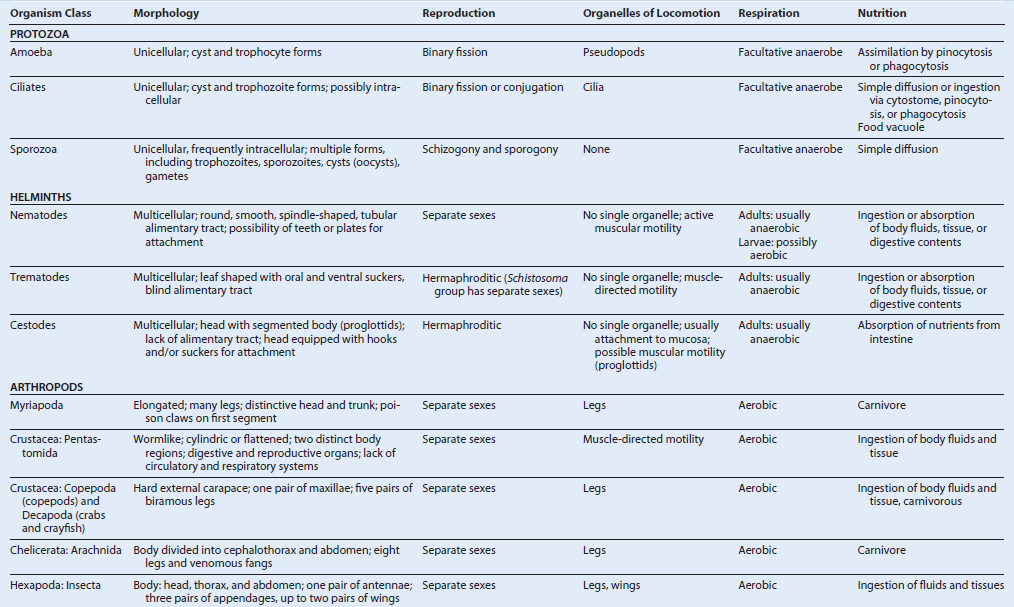
ᑏᑏ Recurrences common

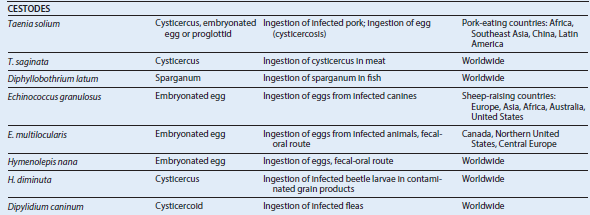
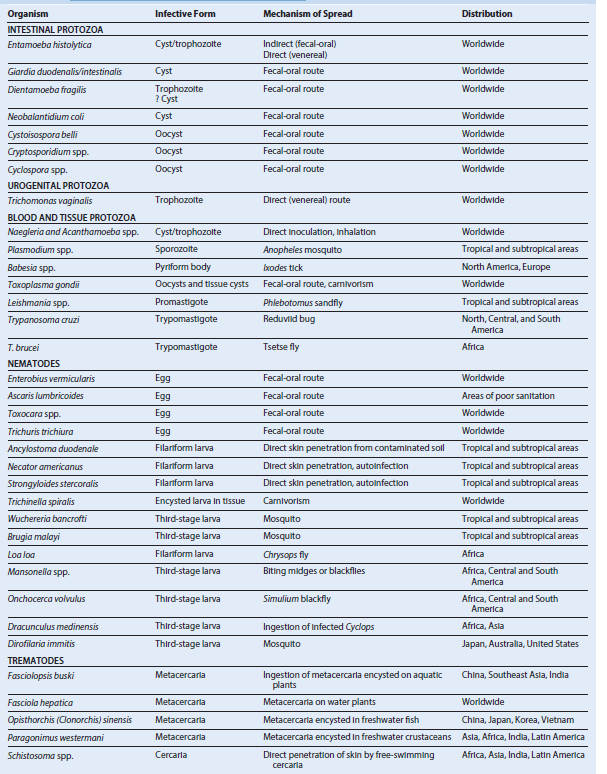
**ESTIMATED DISEASE BURDEN OF PARASITIC INFECTIONS**

Medically Important Parasites

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**Biologic, Morphologic, and Physiologic Characteristics of Pathogenic Parasites**

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**Transmission and Distribution of Pathogenic Parasites **

**Factors Associated with Parasite Pathogenicity**

Infective dose and exposure

Penetration of anatomic barriers

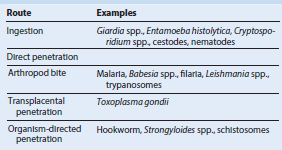
Attachment

Replication

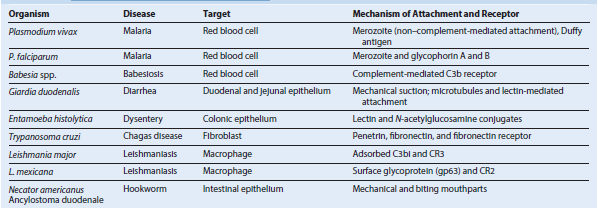
Cell and tissue damage

Disruption, evasion, and inactivation of host defenses

**Parasite Ports of Entry**

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**Examples of Parasitic Adherence Mechanisms**

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**Some Pathologic Mechanisms in Parasitic Diseases**

**TOXIC PARASITE PRODUCTS**

Hydrolytic enzymes, proteinases, collagenase, elastase - Schistosomes (cercariae), *Strongyloides* spp., hookworm, *Entamoeba histolytica*,

African trypanosomes, *Plasmodium falciparum*

Amebic ionophore - *E. histolytica*

Endotoxins - African trypanosomes, *P. falciparum*

Indole catabolites - Trypanosomes

**MECHANICAL TISSUE DAMAGE**

Blockage of internal organs - *Ascaris* spp., tapeworms, schistosomes, filaria

Pressure atrophy - *Echinococcus* spp., *Cysticercus* spp.

Migration through tissue - Helminthic larvae

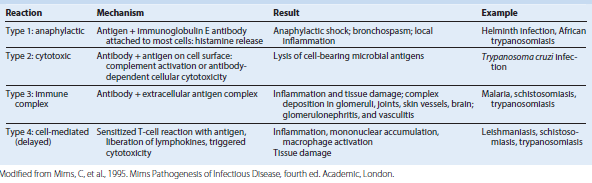
**IMMUNOPATHOLOGY**

Hypersensitivity

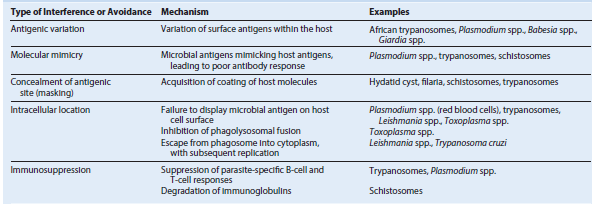
Autoimmunity

Protein-losing enteropathies - Hookworm, tapeworm, *Giardia* spp., *Strongyloides* spp.

Metaplastic changes - *Opisthorchis* spp. (liver flukes), schistosomes

**Immunopathologic Reactions to Parasitic Disease** ****

**Microbial Interference with or Avoidance of Immune Defenses**

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**SUMMARY OF PARASITES ASSOCIATED WITH HUMAN DISEASE**

**BLOOD**

Malaria - *Plasmodium falciparum, P. knowlesi, P. malariae, P. ovale, P. vivax*

Babesiosis - *Babesia* spp.

Filariasis - *Wuchereria bancrofti, Brugia malayi, Mansonella* spp., *Loa loa*

**BONE MARROW**

Leishmaniasis - *Leishmania donovani, L. tropica*

**CENTRAL NERVOUS SYSTEM**

Meningoencephalitis - *Naegleria fowleri, Trypanosoma brucei gambiense, T. b. rhodesiense, T. cruzi, Toxoplasma gondii*

Granulomatous encephalitis - *Acanthamoeba* spp., *Balamuthia mandrillaris*

Mass lesion, Brain abscess - *T. gondii, Taenia solium, Schistosoma japonicum, Acanthamoeba* spp*., B. mandrillaris*

Eosinophilic meningitis, Cerebral malaria - *Angiostrongylus cantonensis, Toxocara* spp., *Baylisascaris* (neural larva migrans), *P. falciparum*

Cerebral paragonimiasis - *Paragonimus westermani*

**EYE**

Keratitis - *Acanthamoeba spp., Onchocerca volvulus*

Chorioretinitis, Conjunctivitis - *T. gondii, O. volvulus, L. loa*

Ocular cysticercosis (mass lesion) - *T. solium*

Toxocariasis - *Toxocara* spp. (ocular larva migrans; mimics retinoblastoma)

**TRACT**

Anal pruritus - *Enterobius vermicularis*

Colitis - *Entamoeba histolytica, Neobalantidium coli*

Diarrhea/dysentery - *E. histolytica, Giardia duodenalis (intestinalis), Cryptosporidium parvum, Cyclospora cayetanensis, Cystoisospora belli, Schistosoma mansoni, Strongyloides stercoralis, Trichuris trichiura*

Toxic megacolon - *T. cruzi*

Obstruction, Perforation - *Ascaris lumbricoides, Fasciolopsis buski*

Rectal prolapse - *T. trichiura*

**LIVER, SPLEEN**

Abscess - *E. histolytica, Fasciola hepatica*

Hepatitis - *T. gondii*

Biliary obstruction - *A. lumbricoides, F. hepatica, Opisthorchis (Clonorchis) sinensis*

Cirrhosis/hepatosplenomegaly - *L. donovani, L. tropica, Toxocara canis and T. cati* (visceral larva migrans), *S. mansoni, S. japonicum*

Mass lesions - *T. solium, Echinococcus granulosus, E. multilocularis*

**GENITOURINARY**

Vaginitis/urethritis - *Trichomonas vaginalis, E. vermicularis*

Renal failure - *Plasmodium* spp., *L. donovani*

Cystitis/hematuria - *S. haematobium, P. falciparum* (blackwater fever)

**HEART**

Myocarditis - *T. gondii, T. cruzi*

Megacardia/complete heart block - *T. cruzi*

**LUNG**

Abscess - *E. histolytica, P. westermani*

Nodule/mass - *Dirofilaria immitis, E. granulosus, E. multilocularis*

Pneumonitis - *A. lumbricoides, S. stercoralis, Toxocara* spp., *P. westermani, T.gondii, Ancylostoma brasiliense*

**LYMPHATICS**

Lymphedema - *W. bancrofti, B. malayi,* other filaria

Lymphadenopathy *T. gondii,* trypanosomes

**MUSCLE**

Generalized myositis *Trichinella spiralis, Sarcocystis lindemanni, Toxocara* spp.

Myocarditis *T. spiralis, T. cruzi, Toxocara* spp.

**SKIN AND SUBCUTANEOUS TISSUE**

Ulcerative lesion - *Leishmania* spp., *Dracunculus medinensis*

Nodule/swellings - *O. volvulus, L. loa, T. cruzi, Acanthamoeba* spp., *Toxocara* spp.

Rash/vesicles - T*. gondii, A. brasiliense,* other migrating worms, schistosomes (cercarial dermatitis)

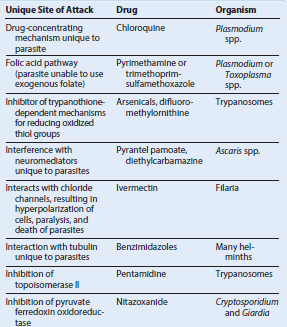
**SYSTEMIC**

General dissemination and multiple organ dysfunction - *P. falciparum, T. gondii, L. donovani, T. cruzi, Toxocara* spp., *S. stercoralis, T. spiralis*

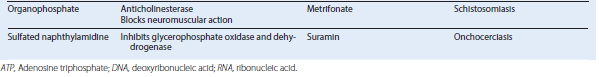
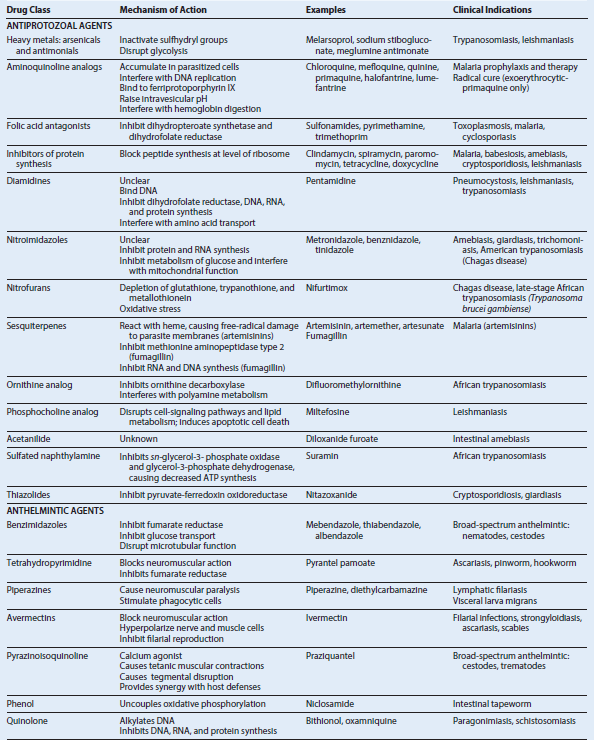
Iron deficiency, anemia Hookworms- *(A. duodenale, Necator americanus)*

Megaloblastic anemia (vitamin B12 deficiency) - *Diphyllobothrium latum*

**Chemotherapeutic Strategies Exploit Differences between Parasite and Host**

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Mechanisms of Action and Clinical Indications for the Major Antiparasitic Agents

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***INTESTINAL AND UROGENITAL PROTOZOA***

**AMEBAE (AMOEBOZOA)**

**Trigger Words-**Protozoa, amebae, trophozoite, cyst, intestinal amebiasis, extraintestinal amebiasis, hepatic amebiasis, flask-shaped ulcer, *Entamoeba*

**Biology, Virulence, and Disease**

• Primitive unicellular organisms with a simple two-stage life cycle

• Motility accomplished by extension of a pseudopod (false foot)

• Most amebae found in humans are commensal organisms

• Human pathogens: *Entamoeba histolytica* (most important), *E.polecki*

**Epidemiology**

• *E. histolytica* has worldwide distribution, with highest incidence in tropical and subtropical regions

• As many as 50% of the population in some areas are infected (average prevalence, 10% to 15%); U.S. prevalence is 4% to 5%

• Many carriers asymptomatic; pass cysts in stool (reservoir)

• Main source of food and water contamination is asymptomatic carrier who passes cysts

**Diagnosis**

• Microscopic examination of stool allows identification of cysts and trophozoites of *E. histolytica*

• Must differentiate from nonpathogenic and commensal species of amebae

• Specific serologic tests can confirm diagnosis

• Examination of stool samples may be negative in extraintestinal amebiasis

• Newer diagnostic approaches: fecal antigen, PCR, DNA probe

**Treatment, Prevention, and Control**

• Acute amebiasis treated with metronidazole, followed by iodoquinol, diloxanide furoate, or paromomycin

• Carrier state may be eradicated with iodoquinol, diloxanide furoate, or paromomycin

• Elimination of cycle of infection requires introduction of adequate sanitation measures, education about routes of transmission, chlorination, and filtration of water supplies

• Travelers to developing countries should avoid consumption of water (including ice cubes), avoid unpeeled fruits and raw vegetables, boil water, and thoroughly clean fruits and vegetables before consumption

**CILIATES (METAMONADA [FORMERLY FLAGELLATES])**

**Trigger Words-**Giardiasis, trichomoniasis, worm egg, contaminated stream, stool antigen test, cilia, wet mount, diarrhea, IgA deficiency

**Biology, Virulence, and Disease**

• Clinically important Metamonada: *Giardia duodenalis (lamblia/intestinalis), Dientamoeba fragilis, Trichomonas vaginalis*

• *G. duodenalis* life cycle has both cyst and trophozoite stages; *D. fragilis* has a trophozoite stage (cyst stage in mice); *T. vaginalis* has only a trophozoite stage

• Most flagellates move by lashing of cilia that pull organism through fluid environments

• Infection with *G. duodenalis* initiated by ingestion of cysts; asymptomatic carriage (50% of infected individuals); symptomatic disease ranges from mild diarrhea to a severe malabsorption syndrome

• Most infections with *D. fragilis* asymptomatic

• *T. vaginalis* causes urogenital infections

• Diseases produced by Metamonada result from mechanical irritation, inflammation of gastrointestinal and genitourinary (*Trichomonas*) mucosa

**Epidemiology**

• *G. duodenalis* has a worldwide distribution

• Giardiasis acquired by fecal-oral route

• Risk factors for giardiasis: poor sanitary conditions, travel to known endemic areas, consumption of inadequately treated water, day-care centers, oral-anal sexual practices

• *D. fragilis* has a worldwide distribution; transmission by fecal-oral and oral-anal routes

• *T. vaginalis* has a worldwide distribution; transmission primarily by sexual intercourse

**Diagnosis**

• *Giardia* may be detected by microscopic examination of fecal samples or duodenal aspirates

• Detection of *Giardia* fecal antigen by enzyme immunoassay, immunofluorescent microscopy

• Infection with *D. fragilis* diagnosed by microscopic examination of fecal specimens

• Trichomoniasis: microscopic examination of vaginal or urethral discharge

**Treatment, Prevention, and Control**

• Drug of choice for treatment of giardiasis (both symptomatic patients and carriers): metronidazole or nitazoxanide; alternatives: furazolidone, tinidazole, paromomycin, albendazole, quinacrine

• Prevention and control of giardiasis involves avoidance of contaminated water and food

• No consensus on best approach for treating *D. fragilis* infections; infection can be avoided by adequate sanitary conditions

• Drug of choice for trichomoniasis is metronidazole; personal hygiene, avoidance of shared toilet articles and clothing, and safe sexual practices are important preventive actions

**CILIATES (CILIOPHORA)**

**Trigger Words -** Macronucleus, pig feces, cytostome, cilia, intestinal ulceration

**Biology, Virulence, and Disease**

• Protozoan organisms whose locomotion involves coordinated movement of rows of hairlike structures (cilia)

• *Neobalantidium coli:* only Ciliophora parasite of humans

• *N. coli* has a funnel-like primitive mouth called a cytostome, a large and small nucleus involved in reproduction, food vacuoles, and two contractile vacuoles

• Disease produced by *N. coli* is similar to amebiasis; symptoms include abdominal pain, tenderness, tenesmus, nausea, anorexia, watery stools with blood and pus, ulceration of intestinal mucosa; extraintestinal infection very rare

**Epidemiology**

• *N. coli* distributed worldwide; swine and monkeys most important reservoirs

• Infections transmitted by fecal-oral route

• Outbreaks associated with contamination of water supplies with pig feces

• Person-to person spread has been implicated in outbreaks

• Risk factors include contact with swine and substandard hygienic conditions

**Diagnosis**

• Microscopic examination of feces for trophozoites and cysts

**Treatment, Prevention, and Control**

• Drug of choice is tetracycline; iodoquinol and metronidazole are alternatives

• Important preventive measures: personal hygiene, maintenance of sanitary conditions, careful monitoring of pig feces

**SPOROZOA**

**Trigger Words-**Coccidia, oocyst, chronic diarrhea, acid-fast, fecal antigen, waterborne transmission, contaminated fruits and vegetables

**Biology, Virulence, and Disease**

• Sporozoa constitute a very large group of protozoa called Apicomplexa or Coccidia

• All sporozoans demonstrate typical characteristics: asexual (schizogony) and sexual (gametogony) reproduction; share alternative hosts

• Intestinal sporozoan: *Cystoisospora belli, Sarcocystis spp., Cryptosporidium spp., Cyclospora cayetanensis*

• *C. belli:* coccidian parasite of intestinal epithelium; causes malabsorption syndrome

• *Sarcocystis* spp. can be detected in stool samples; nausea, abdominal pain, and diarrhea after ingestion of infected meat; muscular infections can occur if sporocysts ingested

• *Cryptosporidium* spp. cause intestinal disease, usually self-limited enterocolitis characterized by watery diarrhea without blood

• *Cyclospora:* illness self-limited in immunocompetent hosts, prolonged in HIV infected individuals

**Epidemiology**

• *Cystoisospora* organisms distributed worldwide; disease frequent in patients with AIDS; infection reported with increasing frequency in both healthy and immunocompromised patients

• *Sarcocystis* spp. are isolated from pigs and cattle

• *Cryptosporidium* spp. are distributed worldwide

• *C. hominis* and *C. parvum* cause most human infections; *C. ubiquitum* and *C. felis* are emerging human pathogens

• *Cyclospora:* worldwide distribution; infection acquired through contaminated water; outbreaks correlated with consumption of contaminated fruits and vegetables

**Diagnosis**

• *C. belli* infection best diagnosed by careful examination of concentrated stool sediment

• *Sarcocystis* spp. sporocysts may be detected in human stool specimens

• *Cryptosporidium* spp. may be detected in unconcentrated stool specimens from immunocompromised patients with diarrhea

• Diagnosis of cyclosporiasis is based on microscopic detection of oocysts in stool

• Both *Cryptosporidium* and *Cyclospora* infections may be diagnosed by PCR

**Treatment, Prevention, and Control**

• *C. belli:* treatment of choice is trimethoprim-sulfamethoxazole; prevention and control effected by maintaining personal hygiene and sanitation, avoiding oral-anal sexual contact

• No known treatment for intestinal or muscular sarcocystosis in humans

• No broadly effective therapy has been developed for managing *Cryptosporidium* infections in immunocompromised patients; nitazoxanide is approved by the FDA for the treatment of cryptosporidiosis in nonimmunocompromised individuals older than 12 months

• Cyclosporiasis has been treated with modest success using trimethoprim sulfamethoxazole

***BLOOD AND TISSUE PROTOZOA***

***PLASMODIUM***

**Trigger Words-**Malaria, quotidian, tertian, quartan, blackwater fever, cerebral malaria, benign tertian, malignant tertian, multiple ring forms, gametocytes, *Anopheles* mosquito, tropics and subtropics, prophylaxis

**Biology, Virulence, and Disease**

• Plasmodia: coccidian or sporozoan parasites of RBCs

• Five species that infect humans share a common life cycle

• Routes of acquisition: mosquito, transfusion, needle sharing, congenital

• *P. falciparum* produces daily (quotidian) chills and fever with nausea, vomiting, diarrhea progressing to tertian (36 to 48 hours) periodicity with fulminating disease (malignant tertian); no persistent liver stage

• *P. knowlesi* produces daily (quotidian) fever, chills, headache, rigors, abdominal pain, cough (severe symptoms in 7% of cases; respiratory distress and hepatorenal failure); no persistent liver stage

• *P. vivax* causes “benign tertian malaria” with paroxysms of fever and chills every 48 hours; a spectrum of severe, life-threatening syndromes similar to that with *P. falciparum* may be seen; a liver stage may cause relapses and recrudescence’s

• *P. ovale* causes benign tertian malaria similar to that of *P. vivax* with both relapses and recrudescence

• *P. malariae* has a long (18 to 40 days) incubation period and causes a moderate to severe disease with a 72-hour (quartan or malarial malaria) periodicity; no persistent liver stage

**Epidemiology**

• Infection with *Plasmodium* spp. Accounts for 216 million episodes with approximately 500,000 deaths annually, 90% of which are in Africa

• Vector is the *Anopheles* mosquito, which is widely distributed in tropical, subtropical, and temperate regions

• *P. falciparum:* occurs almost exclusively in tropical and subtropical regions

• *P. knowlesi:* infects Old World Monkeys, and increasingly humans, in Malaysia and neighboring countries throughout Southeast Asia

• *P. vivax:* widest geographic distribution (tropics, subtropics, temperate regions); 80% of cases occur in South America and Southeast Asia

• *P. ovale:* distributed primarily in tropical Africa; also found in Asia and South America

• *P. malariae:* occurs in same tropical and subtropical areas as other malarial parasites but less prevalent

**Diagnosis**

• Most widely used method: detection of parasites in thick and thin blood filmsstained with Giemsa or Wright stain

• Antigen detection using an RDT; used in both the field and diagnostic laboratories as an adjunct to microscopic examination of blood films

**Treatment, Prevention, and Control**

• Treatment of malaria is based on history regarding travel to endemic areas, prompt clinical review and differential diagnosis, accurate and rapid laboratory work, and correct use of antimalarial drugs

• Chloroquine or parenteral quinine is drug of choice for susceptible strains of *Plasmodium;* widespread resistance to chloroquine seen with *P. falciparum* and *P. vivax*

• Chemoprophylaxis with chloroquine, doxycycline, Malarone, or mefloquine coupled with avoiding mosquito bites (netting, insect repellents, clothing) required for prevention

• Elimination of mosquito breeding places

***BABESIA***

**Trigger Words-***Babesia,* zoonosis, ticks, tetrad forms, splenectomy, intracellular, RBC

**Biology, Virulence, and Disease**

• Intracellular sporozoan parasites, morphologically resemble plasmodia

• Zoonosis infecting a variety of animals

• *Babesia microti:* usual cause of babesiosis in United States; transmitted by *Ixodes* ticks

• Incubation period of 1 to 4 weeks

• Symptoms: general malaise, fever without periodicity, headache, chills, sweating, fatigue, weakness • Hemolytic anemia coupled with renal failure can occur

• Splenectomy or functional asplenia, immunosuppression, HIV infection, advanced age increase susceptibility to infections and more severe disease

**Epidemiology**

• >70 different species of *Babesia* found in Africa, Asia, Europe, North America

• *Ixodes dammini:* tick vector along U.S. northeastern seaboard

• Natural reservoir hosts: field mice, voles, other small rodents

• Disease may be severe in HIV-infected individuals

• *B. microti* increasingly transmitted by blood transfusions

**Diagnosis**

• Examination of blood smears is diagnostic method of choice

• Serologic tests and PCR also used to diagnose babesiosis

**Treatment, Prevention, and Control**

• Treatment of choice for mild to moderate illness: combination of atovaquone and azithromycin

• Treatment for severe disease: clindamycin, quinine, exchange transfusion

• Protective clothing, insect repellents can minimize tick exposure

• Prompt removal of ticks can be protective

***TOXOPLASMA GONDII***

**Trigger Words-**Cat feces, raw meat, lymphadenitis, CNS lesion, encephalomyelitis, cat litter, congenital infection, AIDS

**Biology, Virulence, and Disease**

• Typical coccidian intracellular parasite found in a wide variety of animals, including birds and humans

• Essential reservoir host: common house cat and other felines

• Most *T. gondii* infections asymptomatic

• Symptoms occur when parasite moves from blood to tissues; include fever, chills, headaches, myalgia, lymphadenitis, fatigue

• Chronic disease marked by hepatitis, encephalomyelitis, and myocarditis

• Chorioretinitis may lead to blindness

• Congenital infection has serious sequelae

• Reactivation of cerebral toxoplasmosis is a major cause of encephalitis in patients with AIDS

**Epidemiology**

• Human infections ubiquitous

• Infection from ingestion of improperly cooked meat from intermediate-host animals or ingestion of infective oocysts from contaminated cat feces

• Transplacental infection can occur during pregnancy

• Rate of severe infection affected by patient’s immune status

• Illness in immunocompromised host believed to be caused by reactivation of previously latent infection rather than new exposure to organism

**Diagnosis**

• Increasing antibody titers documented inserially collected blood specimens

• Panel of tests (TSP) is used to determine recent versus past acquisition of infection

• Diagnosis of *Toxoplasma* encephalitis usually involves imaging study of brain

• Microscopy, serologic, and moleculartechniques may be required for definitive diagnosis

**Treatment, Prevention, and Control**

• Treatment of choice: initial high-dose regimen of pyrimethamine plus sulfadiazine followed by lower doses of both drugs indefinitely (AIDS patients and other immunocompromised patients)

• Clindamycin or spiramycin may be used in first trimester of pregnancy

• High-risk patients may be considered for prophylaxis

• Additional preventive measures: avoid consumption and handling of raw or undercooked meat, avoid exposure to cat feces

***LEISHMANIA***

**Trigger Words-**Kala-azar, Dumdum fever, cutaneous and mucocutaneous disease, visceral leishmaniasis, sand fly, post–kala-azar dermal leishmaniasis

**Biology, Virulence, and Disease**

• *Leishmania:* obligate intracellular parasites transmitted from animal to human or human to human by bites from infected female sand fly

• Many different species can infect humans, producing a variety of diseases (cutaneous, diffuse cutaneous, mucocutaneous, visceral)

• Clinical syndromes depend on species involved; most common species: cutaneous *(L. tropica),* mucocutaneous *(L. braziliensis),* visceral *(L. donovani, L. infantum),* post–kala-azar dermal leishmaniasis *(L. donovani)*

**Epidemiology**

• Natural reservoirs: rodents, possums, anteaters, sloths, dogs, cats

• Infection may be transmitted by animalvector- human or human-vector-human cycle, by direct contact with infected lesion, or mechanically by flies

• Mucocutaneous leishmaniasis most often occurs in Bolivia, Brazil, Peru; cutaneous leishmaniasis much more widespread throughout Middle East and in focal areas of South America

• Visceral leishmaniasis (kala-azar, Dumdum fever): ≈50,000 cases per year, 90% localized to Bangladesh, Brazil, India, Nepal, Sudan

**Diagnosis**

• Diagnosis of visceral, cutaneous, or mucocutaneous leishmaniasis made on clinical grounds in endemic areas

• Definitive diagnosis depends on detecting amastigotes in clinical samples or promastigotes in culture; molecular techniques have been used for diagnosis, prognosis, and species identification

**Treatment, Prevention, and Control**

• Drug of choice for all forms of leishmaniasis is the pentavalent antimonial compound sodium stibogluconate (Pentostam)

• Fluconazole and miltefosine efficacious in cutaneous disease

• Stibogluconate remains drug of choice for mucocutaneous leishmaniasis

• Prevention involves prompt treatment of human infections and control of reservoir hosts, along with vector control

**TRYPANOSOMES**

**Trigger Words-**Sleeping sickness, tsetse fly, reduviid bugs, chagoma, Romaña sign, megaesophagus, Winterbottom sign, Chagas disease

**Biology, Virulence, and Disease**

• *Trypanosoma*, a hemoflagellate, causes two distinctly different forms of disease: African trypanosomiasis and American trypanosomiasis

• African trypanosomiasis (sleeping sickness): chronic disease of several years’ duration, transmitted by tsetse flies, fatal without treatment

• American trypanosomiasis (Chagas disease): asymptomatic, acute, or chronic forms, transmitted by reduviid bugs

**Epidemiology**

• *T. brucei gambiense* limited to tropical West and Central Africa, correlating to range of tsetse fly vector

• *T. b. rhodesiense* found in East Africa, especially cattle-raising countries

• Domestic and wild game animals act as reservoir hosts for *T. b. rhodesiense*

• *T. cruzi* occurs widely in both reduviid bugs and a wide variety of reservoir animals in North, Central, and South America

• Because of the chronic nature of infection, screening of solid organ and blood donors for Chagas disease has become important

**Diagnosis**

• Agents of sleeping sickness can be demonstrated in blood films, aspirations from lymph nodes, and concentrated spinal fluid

• *T. cruzi* can be demonstrated in blood films early in acute stage of disease

**Treatment, Prevention, and Control**

• Suramin: drug of choice for treating acute blood and lymphatic stages of both Gambian and Rhodesian forms of sleeping sickness; pentamidine is an alternative

• Melarsoprol: drug of choice for CNS disease

• Effective control measures: integrated approach to reduce human reservoir of infection, use of fly traps and insecticide

• Drugs of choice for treatment of Chagas disease: benznidazole and nifurtimox

• Vector control important: insecticide, eradication of nests, construction of homes to prevent nesting of bugs

***CNS,* Central nervous system; *PCR,* polymerase chain reaction; *RBC,* red blood cell; *RDT,* rapid diagnostic test; TSP, *T. gondii* serologic profile.**

**MEDICALLY IMPORTANT BLOOD AND TISSUE PROTOZOA**

*Plasmodium* species

*Babesia* species

*Toxoplasma* species

*Sarcocystis* species

*Acanthamoeba* species

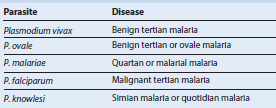
*Balamuthia* species

*Naegleria* species

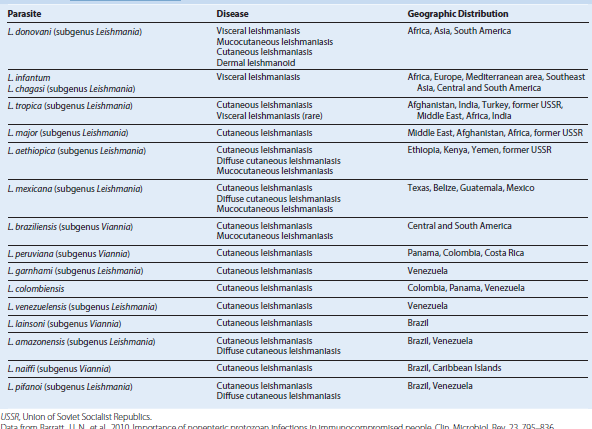
*Leishmania* species

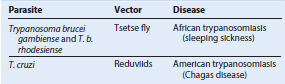
*Trypanosoma* species

**Human Malarial Parasites**

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**Leishmaniasis in Humans**

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**Trypanosoma Species Responsible for Human Diseases**