Candidiasis:

Candidiasis can cause a wide spectrum of clinical syndromes, as described below. The clinical presentation can vary depending on the type of infection and the degree of immunosuppression.

Cutaneous candidiasis syndromes:

Generalized cutaneous candidiasis: This is an unusual form of cutaneous candidiasis that manifests as a diffuse eruption over the trunk, thorax, and extremities. The patient has a history of generalized pruritus, with increased severity in the genitocrural folds, anal region, axillae, hands, and feet. Physical examination reveals a widespread rash that begins as individual vesicles that spread into large confluent areas.

Intertrigo: The patient has a history of intertrigo affecting any site in which skin surfaces are in close proximity, providing a warm and moist environment. A pruritic red rash develops. Physical examination reveals a rash that begins with vesiculopustules that enlarge and rupture, causing maceration and fissuring. The area involved has a scalloped border with a white rim consisting of necrotic epidermis that surrounds the erythematous macerated base. Satellite lesions are commonly found and may coalesce and extend into larger lesions (see image below).

Erythema, maceration, and satellite pustules in the axilla, accompanied by soreness and pruritus, result in a form of intertrigo.

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Metastatic skin lesions: Characteristic skin lesions occur in approximately 10% of patients with disseminated candidiasis and candidemia. The lesions may be numerous or few and are generally described as erythematous, firm, nontender macronodular lesions with discrete borders. Biopsy specimens of these lesions demonstrate yeast cells, hyphae, or pseudohyphae, and cultures are positive for Candida species in approximately 50% of cases.

Candidafolliculitis: The infection is found predominantly in the hair follicles and, rarely, can become extensive.

Paronychia and onychomycosis: Paronychia and onychomycosis are frequently associated with immersion of the hands in water and with diabetes mellitus. The patient has a history of a painful and erythematous area around and underneath the nail and nail bed. Physical examination reveals an area of inflammation that becomes warm, glistening, tense, and erythematous and may extend extensively under the nail. It is associated with secondary nail thickening, ridging, discoloration, and occasional nail loss.

Chronic mucocutaneous candidiasis:

Chronic mucocutaneous candidiasis describes a group of Candida infections of the skin, hair, nails, and mucous membranes that tends to have a protracted and persistent course.

Most infections begin in infancy or during the first 2 decades of life; onset in people older than 30 years is rare.

Most patients survive for prolonged periods and rarely experience disseminated fungal infections. The most common cause of death is bacterial sepsis.

Chronic mucocutaneous candidiasis is frequently associated with endocrinopathies, such as the following:

Hypoparathyroidism, Addison disease, Hypothyroidism, Diabetes mellitus

Autoimmune antibodies to adrenal, thyroid, and gastric tissues (approximately 50%), Thymomas, Dental dysplasia, Polyglandular autoimmune disease,

Antibodies to melanin-producing cells.

Physical examination: Findings reveal disfiguring lesions of the face, scalp, hands, and nails. This is occasionally associated with oral thrush (see image below) and vitiligo.

White plaques are present on the buccal mucosa and the undersurface of the tongue and represent thrush. When wiped off, the plaques leave red erosive areas.

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Gastrointestinal tract candidiasis

See the list below:

Oropharyngeal candidiasis

The patient usually has a history of HIV infection, wears dentures, has diabetes mellitus, or has been exposed to broad-spectrum antibiotics or inhaled steroids. Patients are frequently asymptomatic. However, some of the symptoms may include the following:

Sore and painful mouth, Burning mouth or tongue ,Dysphagia, Whitish thick patches on the oral mucosa.

Physical examination reveals a diffuse erythema and white patches that appear on the surfaces of the buccal mucosa, throat, tongue, and gums. The following are the 4 types of oropharyngeal candidiasis (OPC):

1.Membranous candidiasis: This is one of the most common types and is characterized by creamy-white curdlike patches on the mucosal surfaces.

2.Erythematous candidiasis: This is associated with an erythematous patch on the hard and soft palates.

3.Chronic atrophic candidiasis (denture stomatitis): This type is also thought to be one of the most common forms of the disease. The presenting signs and symptoms include chronic erythema and edema of the portion of the palate that comes into contact with dentures.

4.Angular cheilitis: An inflammatory reaction, this type is characterized by soreness, erythema, and fissuring at the corners of the mouth (see image below).

5. Soreness and cracks at the lateral angles of the mouth (**angular cheilitis**) are a frequent expression of candidiasis in elderly individuals.

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Mixed: A combination of any of the above types is possible.

Esophageal candidiasis

The patient's history usually includes chemotherapy, the use of broad-spectrum antibiotics or inhaled steroids, the presence of HIV infection or hematologic or solid-organ malignancy. Patients may be asymptomatic or may have one or more of the following symptoms:

Normal oral mucosa (>50% of patients)

Dysphagia ,Odynophagia ,Retrosternal pain ,Epigastric pain ,Nausea and vomiting

Nonesophageal gastrointestinal candidiasis

The patient usually has a history of neoplastic disease of the gastrointestinal tract. The esophagus is the most commonly infected site, followed by the stomach. Less commonly, patients have chronic gastric ulcerations, gastric perforations, or malignant gastric ulcers with concomitant candidal infection. The small bowel is the third most common site of infection (20%). The frequency of candidal infection in the small bowel is the same as in the large bowel. Approximately 15% of patients develop systemic candidiasis.

Physical examination findings vary depending on the site of infection. The diagnosis, however, cannot be made solely on culture results because approximately 20%-25% of the population is colonized by Candida. The following symptoms may be present:

Epigastric pain ,Nausea and vomiting ,Abdominal pain ,Fever and chills
Abdominal mass (in some cases), Respiratory tract candidiasis

The respiratory tract is frequently colonized with Candida species, especially in hospitalized patients. Approximately 20%-25% of ambulatory patients are colonized with Candida species.

Laryngeal candidiasis: This is an uncommon form of invasive candidiasis that sometimes results in disseminated infection. It is primarily seen in patients with underlying hematologic or oncologic malignancies. The patient may present with a sore throat and hoarseness. The physical examination findings are generally unremarkable, and the diagnosis is frequently made with direct or indirect laryngoscopy.

Candida tracheobronchitis: This is also an uncommon form of invasive candidiasis. Most patients with Candida tracheobronchitis are HIV-positive or are severely immunocompromised. Most patients with Candida tracheobronchitis report fever, productive cough, and shortness of breath. Physical examination reveals dyspnea and scattered rhonchi. The diagnosis is generally made with bronchoscopy.

Candida pneumonia: This rarely develops alone and is associated with disseminated candidiasis in rare cases. The most common form of infection is multiple lung abscesses due to the hematogenous dissemination of Candida species. The high degree of Candida colonization in the respiratory tract greatly complicates the diagnosis of Candida pneumonia. The history reveals risk factors similar to those of disseminated candidiasis, along with reports of shortness of breath, cough, and respiratory distress. Physical examination reveals fever, dyspnea, and variable breath sounds, ranging from clear to rhonchi or scattered rales.

Genitourinary tract candidiasis:

Vulvovaginal candidiasis (VVC): This is the second most common cause of vaginitis. The patient's history includes vulvar pruritus, vaginal discharge, dysuria, and dyspareunia. Approximately 10% of women experience repeated attacks of VVC without precipitating risk factors. Physical examination findings include a vagina and labia that are usually erythematous, a thick curdlike discharge, and a normal cervix upon speculum examination.

Candida balanitis: Patients report penile pruritus along with whitish patches on the penis. Candida balanitis is acquired through direct sexual contact with a partner who has VVC. Physical examination initially reveals vesicles on the penis that later develop into patches of whitish exudate. The rash occasionally spreads to the thighs, gluteal folds, buttocks, and scrotum .

Dry, red, superficially scaly, pruritic macules and patches on the penis represent candidal balanitis.

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Candida cystitis: Many patients are asymptomatic. However, bladder invasion may result in frequency, urgency, dysuria, hematuria, and suprapubic pain. Candida cystitis may or may not be associated with the use of a Foley catheter. Physical examination may reveal suprapubic pain; other findings are unremarkable.

Asymptomatic candiduria: Most catheterized patients with persistent candiduria are asymptomatic, similar to noncatheterized patients. Most patients with

candiduria have easily identifiable risk factors for Candida colonization. Thus, invasive disease is difficult to differentiate from colonization based solely on culture results because approximately 5%-10% of all urine cultures are positive for Candida.

Ascending pyelonephritis: The use of stents and indwelling devices, along with the presence of diabetes, is the major predisposing risk factor in ascending infection. Most patient report flank pain, abdominal cramps, nausea, vomiting, fever, chills and hematuria. Physical examination reveals abdominal pain, costovertebral-angle tenderness, and fever.

Fungal balls: This is due to the accumulation of fungal material in the renal pelvis. The condition may produce intermittent urinary tract obstruction with subsequent anuria and ensuing renal insufficiency.

Hepatosplenic candidiasis (chronic systemic candidiasis):

Hepatosplenic candidiasis is a form of systemic candidiasis in patients with an underlying hematologic malignancy and neutropenia and develops during the recovery phase of a neutropenic episode. The patient's history includes the following:

Fever unresponsive to broad-spectrum antimicrobials ,Right upper quadrant pain Abdominal pain and distension, Jaundice (rare).

Physical examination findings include right upper quadrant tenderness and hepatosplenomegaly (< 40%).

Systemic candidiasis:

Systemic candidiasis can be divided into 2 primary syndromes: candidemia and disseminated candidiasis (organ infection by Candida species). Deep organ infections due to Candida species are generally observed as part of the disseminated candidiasis syndromes and may involve one or more organs.

Candidemia:

Candida species are currently the fourth most commonly isolated organism in blood cultures, and Candida infection is generally considered a nosocomial infection. [12, 13] The patient's history commonly reveals the following:

Several days of fever that is unresponsive to broad-spectrum antimicrobials; frequently the only marker of infection

Prolonged intravenous catheterization

A history of several key risk factors (see Pathophysiology)

Possibly associated with multiorgan infection

Physical examination results may include the following:

Fever

Macronodular skin lesions (approximately 10%)

Candidal endophthalmitis (approximately 10%-28%)

Occasionally, septic shock (hypotension, tachycardia, tachypnea)

Other causes of candidemia without invasive disease include the following:

Intravascular catheter-related candidiasis: This entity usually responds promptly to catheter removal and antifungal treatment.

Suppurative thrombophlebitis: This is associated with prolonged central venous catheterization. Suppurative thrombophlebitis manifests as fever and persistent candidemia despite appropriate antifungal therapy and catheter removal. Sepsis and septic shock may develop.

Endocarditis: The frequency of endocarditis has recently increased. [14] Candida species, primarily C albicans and Candidaparapsilosis (>60% of cases), are the most common cause of fungal endocarditis. The aortic and mitral valves are most commonly involved. The endocarditis may be exogenous (due to direct inoculation during surgery) or endogenous (due to hematogenous dissemination

during bloodstream invasion. Candida endocarditis is associated with 4 main risk factors, including intravenous heroin use (frequently associated with C parapsilosis infection), chemotherapy, prosthetic valves (approximately 50%), and prolonged use of central venous catheters. The physical examination reveals a broad range of manifestations, including feverunresponsive to antimicrobials, hypotension, shock, new or changing murmurs, and large septic emboli to major organs, a characteristic of fungal endocarditis.

Disseminated candidiasis: This is frequently associated with multiple deep organ infections or may involve single organ infection. Unfortunately, blood cultures are negative in up to 40%-60% of patients with disseminated candidiasis. The history of a patient with presumptive disseminated candidiasis reveals a fever unresponsive to broad-spectrum antimicrobials and negative results from blood culture. Physical examination reveals fever (may be the only symptom) with an unknown source and associated sepsis and septic shock.

Candidaendophthalmitis: The two primary forms of Candida endophthalmitis are the exogenous form and the endogenous form. Exogenous endophthalmitis is associated with either accidental or iatrogenic (postoperative) injury of the eye and inoculation of the organism from the environment. Endogenous endophthalmitis results from hematogenous seeding of the eye. It has been found in 10%-28% of patients with documented candidemia. Recently, newer studies have shown a decreasing incidence of Candida endophthalmitis, possibly due to an increased awareness of this complication and the initiation of early or empirical antifungal therapy. [15] It is important to note that hematogenous candidal endophthalmitis is a marker of disseminated candidiasis.

The patient's history reveals a broad range of manifestations, including the following:.

Eye injury, Ophthalmic surgery, Underlying risk factors for candidemia

Asymptomatic and detected upon physical examination; Ocular pain, Photophobia ,Scotomas ,Floaters.

Physical examination reveals fever.

Funduscopic examination reveals early pinhead-sized off-white lesions in the posterior vitreous with distinct margins and minimal vitreous haze. Classic lesions are large and off-white, similar to a cotton-ball, with indistinct borders covered by an underlying haze. Lesions are 3-dimensional and extend into the vitreous off the chorioretinal surface. They may be single or multiple.

Renal candidiasis:

This is frequently a consequence of candidemia or disseminated candidiasis. The patient's history includes fever that is unresponsive to broad-spectrum antimicrobials. Frequently, patients are asymptomatic and lack symptoms referable to the kidney.

Physical examination findings are generally unremarkable, and the diagnosis is made with a urinalysis and with a renal biopsy. Otherwise, this condition is commonly diagnosed at autopsy.

CNS infections due to Candida species:

CNS infections due to Candida species are rare and difficult to diagnose. The two primary forms of infection include the exogenous infection and the endogenous infection. The exogenous infection results from postoperative infection, trauma, lumbar puncture, or shunt placement. The endogenous infection results from hematogenous dissemination and thus involves the brain parenchyma and is associated with multiple small abscesses (eg, disseminated candidiasis).

As with other organ infections due to Candida species, patients usually have underlying risk factors for disseminated candidiasis. CNS infections due to Candida species are frequently found in patients hospitalized for long periods in ICUs. The spectrum of this disease includes the following:

Meningitis ,Granulomatous vasculitis, Diffuse cerebritis with microabscesses

Mycotic aneurysms ,Fever unresponsive to broad-spectrum antimicrobials Mental status changes.

Physical examination reveals the following:

Fever ,Nuchal rigidity ,Confusion, Coma, Candida arthritis, osteomyelitis, costochondritis, and myositis

Candidal musculoskeletal infections were once uncommon; recently, they have become much more common, possibly due to the increased frequency of candidemia and disseminated candidiasis. The most common sites of involvement continue to be the knee and the vertebral column. The pattern of involvement is similar to the pattern observed in bacterial infections. The infection may be divided into exogenous or endogenous forms. The exogenous infection is due to the direct inoculation of the organisms, such as postoperative infection or trauma. Affected sites include the following:

Ribs and leg bones (patients < 20 y)

Vertebral column and paraspinal abscess (adulthood)

Flat bones (any age group)

Sternum - Generally observed postoperatively after cardiac surgery

The patient is frequently asymptomatic, and the history reveals risk factors typical of disseminated candidiasis, as well as pain localized over the affected site. The physical examination findings are frequently unremarkable but may reveal tenderness over the involved area, erythema, and bone deformity, occasionally in association with a draining fistulous tract.

Arthritis: Candida arthritis is generally a complication of disseminated candidiasis but may be caused by trauma or direct inoculation due to surgery or steroid injections. Most cases are acute and begin as a suppurative synovitis. A high percentage of cases progress to osteomyelitis. In addition, Candida arthritis after joint replacement is not uncommon.

Osteomyelitis: Candida osteomyelitis originates either exogenously or endogenously. The exogenous infection is due to direct inoculation of the organisms via routes such as postoperative infection, trauma, or steroid injections. The endogenous form is a complication of candidemia or disseminated candidiasis. In most cases due to hematogenous seeding, the vertebral disks are involved and frequently progress to discitis with contiguous extension into the vertebrae body. Other bones affected include the wrist, femur, scapula, and proximal humerus.

Costochondritis: This is an uncommon form of infection and also has two modes of infection. Candida costochondritis is usually due to hematogenous infection spread or direct inoculation during surgery (median sternotomy). Costochondritis is frequently associated with pain localized over the involved area.

Myositis: Candida myositis is uncommon but is frequently associated with disseminated candidiasis. Most patients are neutropenic and report muscular pain.

Myocarditis-pericarditis: This infection is usually due to direct hematogenous spread in association with candidemia and is rarely due to the direct extension from the sternum or the esophagus. Myocarditis-pericarditis occurs as diffuse abscesses scattered throughout the myocardium surrounded by normal cardiac tissue. In patients with disseminated candidiasis, the rate of Candida myocarditis-pericarditis has been documented as high as 50%. The patient history reveals serious complications in 10-20% of cases without valvular disease. Physical examination reveals fever, hypotension, shock, tachycardia, and new murmurs or rubs (or recent changes in previously detected murmurs).

Candida peritonitis :

The patient history frequently reveals an association with gastrointestinal tract surgery, viscous perforation, or peritoneal dialysis. Candida peritonitis tends to remain localized, disseminating into the bloodstream in only 15% of cases. The range of manifestations is broad and includes fever and chills, abdominal pain and cramping, nausea, vomiting, and constipation. The isolation of Candida

species from the peritoneal fluid in surgical patients needs to be carefully evaluated.

Physical examination may reveal the following:

Fever, Abdominal distention, Abdominal pain, Absent bowel sounds ,Rebound tenderness, Localized mass

Candidasplenic abscess and hypersplenism: Both are manifestations of disseminated candidiasis and are usually simultaneously associated with liver involvement. Manifestations of hypersplenism are common (see Hepatosplenic candidiasis).

Candida cholecystitis: This is uncommon and is generally associated with bacterial cholangitis and ascending cholangitis. In general, Candida cholecystitis is diagnosed at the time of surgery when a culture is