Diabetes mellitus is a major risk factor for mycotic infections. The fungal infections are difficult diagnostic and therapeutic problems, serious cause of morbidity or mortality in diabetes. The particularly difficult problem makes up mycosis among hemodialysis patients with diabetes and in post-transplant diabetes after kidney transplantation. Also, the main risk factor for fungal infections is diabetes with a pre-existing kidney graft in pancreas transplant recipients. Early diagnosis and effective treatment plays an important role in proceeding to the therapy of mycotic infections.

**Oral cavity**

Diabetes mellitus is a predisposing factor of oral candidiasis (opportunistic infection caused by overgrowth of commensal of the mouth - Candida species e.g., the most prevalent *Candida albicans*), especially of pseudomembranous candidiasis (1, 2). Also non-albicans species (Pichia, Trichosporon, Geotichum) can be identified in the oral cavity of patient with poorly controlled diabetes, being prone to frequent and severe fungal infections (3, 4). The poor glycemic control is associated with a high concentration of glucose in blood and saliva which can be treated as a nutrients for fungi (4). The significant role plays promoting an exaggerated inflammatory response to the periodontal microflora (5). There is also a relationship between the presence of removable prostheses or cigarette smoking and higher rate of fungal infections by diabetics (6).

Oral candidiasis include, excepting pseudomembranous candidiasis, also: median rhomboid glossitis, athrophic glossitis, denture stomatitis and angular cheilitis (7).

The diagnosis includes examination of the mouth followed by culturing a swab from the affected area (labial and buccal mucosa, hard and soft palate, tongue periodontal tissues or oropharynx) and sensitivity testing (1, 8).

Untreated candidiasis can lead to serious, even fatal, complications or cause chronic hyperplastic candidiasis, known as candidal leukoplakia (1, 10).

It is also worth mentioning that periodontal infections can adversely affect glycemic control,
increasing serum glucose level, in people with diabetes (8).

The incidence of infections can be reduced by appropriate prophylaxis. Very important is patient education, avoiding tobacco use, proper glycemic control and oral hygiene (11). Significant is rinsing the mouth with the topical antifungal, coating the whole mucosa with the medicine and holding in the mouth for a few minutes, after removing the dentures (1). The patient should soak the denture in 0.1% hypochlorite solution or chlorhexidine solution to eliminate the fungi. White vinegar (diluted 1 : 20) can be used twice a week instead of it (12, 13).

The first line treatment is topical antifungal therapy – polyene antibiotics: nystatin and amphotericin, eventually imidazoles. Topical therapy is advised also to patients with need of systemic treatment (intolerance or resistance to local application), because of possibility of reducing dose and duration of systemic preparations, to achieve reduction of adverse effects and drug interactions. Nystatin and amphotericin are not absorbed from the gastrointestinal tract (1).

Modern medicaments – polyene antibiotics alert cell membrane permeability and azoles are inhibitors of fungal synthesizing enzymes of ergosterol (1). Recommended drugs include: nystatin, amphotericin and miconazole. First line treatment in patients without dentures is amphotericin alone (lozenges 10 mg or suspension 100 mg/mL, four times a day after meals), or if patient is wearing dentures – amphotericin with nystatin (available as ointment (100,000 U/g, oral suspension 100,000 units/mL or pastilles (100,000 IU)) or miconazoles (oral gel 20 mg/mL, after meals). The managing takes three weeks. If the therapy is ineffective, the medications should be replaced. The lozenges of amphotericin are contraindicated in diabetics because of high sugar content. For that reason also nystatin oral rinse and clotrimazole troches should be avoided by diabetes. As alternative, fluconazole (100 mg/day) and itraconazole (200 mg/day) can be prescribed (1, 12-14). In diabetic patients the modifications to insulin doses are needed for a period of oral infection to avoid infection related hyperglycemia (7). The side effects of nystatin and imidazole are: nausea, vomiting, and diarrhea. The alternative in these cases can be clotrimazole and ketoconazole, which are applied in local form. Nowadays, the most important problem is raising drug resistance. Sensitivity test results can help in choice of the most effective treatment, however, the mostly common reason of poor response to the antibiotic is non-compliance (1, 3, 7, 12).

**Lower part of gastrointestinal tract**

The intestinal tract is an important reservoir for many nosocomial organisms e.g., Candida species (15). At the present time, only few studies show evidence that diabetes mellitus is a risk factor for intestinal Candida colonization (9, 16). It has been demonstrated that the frequent of colonization by moulds and yeast-like fungi in the intestine of children with diabetes mellitus is higher than in healthy children. There was a relationship between rate of colonization and HbA1c level. Other studies showed the presence of Candida albicans strains in diabetic’s stool (9).

**Skin and its appendages**

Diabetes mellitus is strongly associated with the development of fungal infections and dermatoses connected with skin manifestations. Two third of diabetic subjects have increased frequency of infections caused by Candida or dermatophytes (tinea pedis and onychomycosis) during the course of the disease process (17-20). Dermatologic problems occur more often in patients with type 2 diabetes mellitus, by whom infectious involvement of the skin is more often (autoimmune skin lesions are more common in type 1 diabetes) (21). The most frequent fungal diseases are: tinea pedis (interdigitalis), onychomycosis, candidal intertrigo and candidal vaginitis (22, 23).

Skin colonisation and the development of several skin manifestations in patients with poor glycemic control and elevated glycosylated hemoglobin, who have abnormal carbohydrate metabolism, relative insulin availability, neuron degeneration, deranged collagen production, microvascular complications and impaired wound healing, seems to be related to a multitude of skin disorders (17-19, 21, 22). In addition, the prevalence of cutaneous disease have relation to number of risk factors including age, male gender, family history of onychomycosis and intake of immunosuppressive agents (17, 20).

Candida infections can be first presenting sign of undiagnosed diabetes mellitus (6, 17). Fungal infections in diabetes can provide a portal of entry into the circulation for bacterial pathogens (17).

All infections should be mycologically proven (19).

By *Candida spp.*, the medication of choice are topical antifungal creams with nystatin, clotrimazole or econazole. If topical treatment is ineffective, oral management with fluconazole is the second line treatment (17). Very important is predicting microvascular complications. and the tight control of blood glucose (19, 21). Traditional antibiotic - griseofulvin
activity is limited to dermatophytes and is ineffective. The newer management strategy includes: itraconazole, terbinafine and fluconazole. Ketoconazole is used only in local form, because of hepatotoxicity effect. Itraconazole is administering at a dose of 200 mg/d for three months or as pulse therapy with 400 mg/d in two daily doses of 200 mg for one week per month for three or four months. Itraconazole is administering at a dose of 200 mg/d in two daily doses of 200 mg for three months or as pulse therapy with 400 mg/d for 2-12 weeks. The systemic treatment is connected with adverse effects: nausea, abdominal pain, vomiting, diarrhea, dizziness, rash and pruritus. In patients with mucormycosis, amphotericin B with debridement is used.

Patients with diabetes are at increased risk of mycological infection known as toenail onychomycosis. Gender, age and severe nail changes play role in the infections development. Onychodystrophy of several finger nails is a dermatophyte infection caused by three classes of fungi: dermatophytes (Trichophyton sp. e.g., T. galiinae (zoophilic dermatophyte) (28, 29), Fusarium solani (16)), yeast (e.g., Candida albicans) or non-dermatophyte molds (30).

Dystrophic nails look thick, brittle and discolored, often with a yellow shade. The nail plate may be separated from the nail bed (onycholysis). Characteristic is paronychial inflammation of the nail edge surrounding skin. The most severe clinical manifestation of the disease is total dystrophic onychomycosis. Nails can be very painful and make walking difficult.

Culture test of samples collected from the nail plate or subungual debris, KOH-prepared direct microscopy and histopathological examination can verify clinical suspicion of the mycological infection.

Untreated fusarial onychomycosis leads to serious consequences. Vascular insufficiency, impaired wound healing, and compromised immunologic state predispose to secondary fungal and bacterial infections (paronychia, cellulitis) (29). Diabetic patients with peripheral neuropathy and sharp edged nails are more likely to cause abrasion injuries, what affect in decreased quality of life and is a risk factor for other foot disorders and limb amputation (17, 29, 30). Erosion of the nail bed and hyponychium can progress osteomyelitis of underlying bone (30).

For diabetic patients possible managing options are: topical therapy, systemic therapy, combination therapy, and nail removal. Well tolerated and effective are oral antifungal agents: itraconazole and terbinafine in treating onychomycosis caused by dermatophytes and traconazole by molds infections. The systemic treating can cause side effects and drug interactions, especially in diabetic patients. Griseofungin (500-1000 mg daily) has a lot of disadvantages: narrow spectrum, poor efficacy, inconsistent bioavailability and significant adverse effects. The newer drug are: itraconazole (200 mg twice daily for 1 week each month, duration: 12 weeks) and terbinafine (250 mg, duration: 12 weeks). They can be used in continuous or pulse therapy. The possible adverse effects are: gastrointestinal disturbances, dizziness, skin rash, pruritis, and headache. The agents may cause drug interactions (they are competitive inhibitors of the cytochrome P-450 3A4 isozyme).(17, 29-31, 34)

According to some authors fluconazole (150-300 mg weekly, duration: 6-18 months) can be effective in therapy of onychomycosis caused by dermatophytes and molds (17, 29-31). In case, when oral medications are contraindicated, the topical therapy (ciclopirox 8% solution) is available, well tolerated and effective treatment option, with a good penetration of the nail matrix. The adverse event is mild erythema. The medicine should be applied once daily for up to 6 months.

**Diabetic foot**

Fungal foot infection (FFI) is diabetic dermopathy which includes the most frequent mycological infections in the form of both tinea pedis (skin infection) and onychomycosis (nail infection) (35, 36). FFI occurs in one-thirds of patients (37) and increases the risk of developing diabetic foot syndrome - a major reason of disability and mortality in diabetic subjects, particularly men (29, 34, 35, 38). The most common pathogens are: yeast and dermatophytes and the most frequent dermatophyte is Trichophyton rubrum (39, 40).

Food disorders (non healing ulcers and other lesions) appears to be secondary to multiple factors, including diabetes-induced impairments in circulation and peripheral neuropathy, retinopathy, obesity and duration of diabetes. This situation, together with poor nail grooming, serve as an entry portal for infectious organisms (29, 34, 37, 39, 40).
Sharp, infected nails can injure or even pierce the skin. Fissures in the plantar or interdigital skin can become an entry side for bacteria, especially cellulitis infection (39, 41). Diabetics with FFI demonstrate decreases of bodily pain, impairment of mental health, self-esteem and social functioning, enhancing patients quality of life and often leading to social isolation (34, 38). Sometimes, it can be difficult to note and recognize foot disorders because of decrease of sensation what can result in deep infection. The potential implication is a higher rate of gangrene, diabetic ulcers and an increased incidence of lower extremity amputation (35, 39, 41, 42).

Clinical symptoms of onychomycosis include onycholysis, hyperkeratosis, brittleness, paronychial inflammation, and color change (29).

The diagnosis should be confirmed by fungal culturing, direct microscopy or histopathologic examination (29, 34, 38).

Regression and recurrence of illness is characterized for treatment of fungal infections. To improve the efficacy of management there is a need of appropriate antifungal therapy containing the use of oral antifungal agents, topical therapy and mechanical intervention. Griseofulvin is connected with number of adverse effects and modest efficacy. More effective and safe are itraconazole, terbinafine and fluconazole (29, 34, 36, 38). Preferred and effective is topical therapy (ciclopirox) characterized by lower potential for adverse effects and drug interactions but also by poor penetration and minimal efficacy. But in the cases, when lunula is already affected, the topical therapy is not sufficient and systemic agents must be prescribed. The therapy can be improved by using a combination of topical and systemic agents (29, 36, 37). The significant role plays also prevention through inspection, hygiene, appropriate foot wear, skin care with creams or lotions containing 10% urea (39).

Urogenital system

Candida microorganisms are responsible for vulvovaginal candidosis (VVC) (even 25% of vulvovaginal infections). Predominant yeast are Candida albicans, Candida glabrata and Candida tropicalis (43, 44). The incidence of infection affects 70-75% of women. The prevalence is higher in the sexually active, young women (44-46). Women with uncontrolled, severe type 2 diabetes are more prone to be infected (45, 47-49). Antibiotic use, hyperglycemia, diabetes type and HbA1c level are recognized as a cause of VVC (48, 50, 51).

Women carry candida organisms in the vagina without symptoms or signs of vaginitis, because of balance between pathological effects and vaginal defense factors (45, 52). To the source of infection belongs: intestinal reservoir, sexual transmission and vaginal relapse (persisting) (45).

Identification of the type of infection and classification of its degree of severity can assist in the selection of appropriate therapy. Microscopic examination of vaginal secretion and culturing confirm the diagnosis. There is a possibility of use of PCR detection test. In women and adolescent girls with recurrent VVC is a glucose tolerance test recommended (45, 53, 54).

VVC can be asymptomatic or can clinically manifest with: acute pruritus, cottage-cheese-like vaginal discharge, vaginal soreness, irritation, vulvar burning, dyspareunia, external dysuria, slight odor, erythema and swelling of the labia and vulva (45).

There is the need for effective antifungal treatment with topical azoles or oral ones e.g., itraconazole, miconazole, clotrimazole, butoconazole or fluconazole (44, 45, 53). Oral drugs are more frequently associated with systemic toxicity and drug interactions (55). The response to single dose of fluconazole is reduced by diabetics (53). Important is also restricting dietary intake of sugar (45). In otherwise healthy women, treatment with an antifungal is not advised (45, 48).

Itraconazole has good efficacy and safety with C. albicans and other Candida species. Acute vulvovaginitis can be treated by using itraconazole (capsules 400 mg, single-dose: 200 mg in the morning and 200 mg in the evening) (44). In the case of limited response, the managing should be prolonged to 5-7 days. The common side effect is burning sensation (45).

In recurrent vulvovaginal candidosis the induction course of azole (ketocanazole 100 mg daily, clotrimazole 500 mg in suppositories, fluconazole 150 mg daily) is continued to the time, when patient is asymptomatic and culture negative. It can take 7-14 days. The self-diagnosis and the early initiation of empiric topical therapy (500 mg clotrimazole intravaginally). Beside of side effects (gastrointestinal, hepatotoxicity of ketoconazole), the drug interaction with hypoglycemic agents can be essential in diabetic population (45, 55).

Only 33% of diabetic women with vulvovaginitis candidiasis achieve the success in treating with fluconazole (single dose 150 mg). It is associated with high prevalence of C. glabrata in diabetic population (43, 45, 56). Relatively good efficacy follows boric acid (vaginal suppositories, 600 mg daily, duration: 7-14 days). It is well-tolerated. Possible adverse events are: burning sensation and
vestibular erythema. The action way of boracic acid is unknown, but presumably it destroys the cell wall of fungi (43, 46, 49). If there is no response to boric acid, the use of 17% flucytosine or fluconazole with amphotericin B (topical intervaginal cream, duration: 2 weeks) is successful. But the treatment should be not too long because of possibility of resistance. Intravaginal use of flucytosine don’t show side effects in comparison with oral or parenteral form (gastrointestinal and bone marrow toxicity) (43, 45).

Rosenstock et al. reported that diabetic patients achieve better glycemic control with low rate of hypoglycemia, after adding canagliflozin (inhibitor of subtype 2 sodium-glucose transport protein, which increases urinary glucose excretion) to metformin therapy. The disadvantage of canagliflozin is higher rate of genital infections (57). The treatment cause the higher incidence of vulvovaginal adverse events in diabetic females (58). The other study showed that there is no influence on urinary tract infections (59).

Specific fungal infections

Mucormycosis, considering to be the most invasive fungal infection, shows increased number of saprophytic members of the Mucorales. There is significant link between initiated airborne infection of upper and lower respiratory tract and the clinical development of sinusitis, rhinocerebral mucormycosis, pulmonary infection or even liver and brain mucormycosis. Its incidence is closely correlated to diabetic ketoacidosis, neutropenia, protein-calorie malnutrition, and iron overload (60-62). The disease can be fatal (61).

Clinical manifestations include: facial pain or headache and fever. In orbital form orbital cellulosis, extraocular muscle paresis, periorbital edema, proptosis, chemosis and blindness are commonly found and in cerebral form the common signs are: formation of abscesses and necrosis of the frontal lobes. Black, necrotic eschar can be found on the palate or in the nasal mucosa (21, 60). Facial numbness is frequent and results from infarctions of sensory nerves such as branches of the fifth cranial nerve (21).

The diagnosis contain: culturing, histological examination and MRI (60, 61).

Mucormy cosis should be treated aggressively by surgical debridement (often repeated every day) combined with administration of intravenous amphotericin B (1 mg/kg daily, 1.5 mg/kg daily by incidence of aggressive infection and 0.8-1 mg/kg daily after stabilization of health state). The common adverse event is nephrotoxicity. In resistant patients and in cases of nephrotoxicity amphotericin B lipid complex (3 mg/kg daily) should be prescribed. Efficiency of azoles (itraconazole, fluconazole) is not documented. The protocols with additional regimen of rifampicin or tetracycline aren’t recommended because of lack of study. Diabetic ketoacidosis should by immediately corrected (60, 61).

Diabetic individuals are more likely to be infected with angio-invasive, saprophytic opportunistic fungal zygomatoses. By diabetics the rhinocerebral form is especially of high prevalence. The lung and cutaneous involvement are less frequent. The incidence of mucormycosis is decreasing (65).

Predisposing factors include: phagocytic dysfunction due to neutrophenia, ketoacidosis, neutrophil dysfunction during diabetes and low serum pH, which reduce the activity of inflammatory response against Rhizopus (63).

The episode of sinusitis not responding to short-term antibacterial therapy should be considered as a zygomatosis. Characteristic for infected tissues is necrosis (63). If the disease concerns lungs, characteristic are: acute pneumonia, fever, cough and pleural pain (64).

Pathological examination and culturing should be performed to obtain appropriate diagnosis (63, 64).

The mortality of diabetic patients with zygomycosis is 44%. Aggressive surgical treatment can decrease death rate. Management strategies includes high-dose amphotericin B (5-6 mg/kg daily) or posaconasole. Posaconasole has low efficiency, high risk of drug interactions and must be given peroral. These are the reasons, why it shouldn’t be prescribed as first-line therapy. New antifungal drugs are not active against zygomatosis. There is also need to control glycemia and acidosis (63). Statins show the activity against a range of Zygomycetes molds (65).

Coccidiodomycosis is a fungal infection caused by Coccidoides species. The relation of coccidiodomycosis and glycemia is significant, and that’s why this infection affects patients with diabetes mellitus. The measurement of serum glucose in persons with coccidiodomycosis is recommended to identify patients with increased risk of severe, complicated infection. The symptoms of infection disappear spontaneously without medical treatment (66).

Futhermore, high-risk diabetic patients are considered to represent predisposing factors, such as suppression of neutrophil activity, for aspergillosis: cerebral, sino-orbital and pulmonary (67-70).
**Fungemia**

The occurrence of the invasive candidiasis like candidemia, representing high mortality rate and the need of long treatment, has been increasing recently (71, 72). It is a common medical condition in patients with immunosuppressive therapy for organ transplantation, chemotherapy for malignancy or after surgery treatment. Candidemia incidence is statistically correlated with hyperglycemia. Severe hyperglycemia is considered as important risk factor of serious consequences: increased morbidity, worst clinical course, longer hospital stay, late complications and mortality (71, 73-77). This invasive mucositis is due to opportunistic fungal pathogens: yeasts (e.g., *Candida albicans*), molds (e.g., *Aspergillus fumigates*) and a broad list of other fungi. In diabetic population non-albicans Candida is prominent cause of candidemia. Up to 30% of all patients with candidemia are diabetic individuals (78, 79).

Proliferation of fungi in deep tissues and organs is associated with disruption of this barrier due to peripheral vascular disease, neuropathy, insulin injections, surgery, or insertion of intravascular catheter (78).

Diagnosis depends upon clinical suspicion, isolating and identification of the infecting pathogens by culturing and histopathology (72, 74).

For patients from high risk groups prophylactic antifungal therapy and strict glycemia control are extremely important (78). Recommended, first-line treatment is administration of amphotericin B. Undergoing surgical debridement and eradicating therapy with alternative antifungal agents is preferred in case of nonsusceptible to standard azole or polyene therapy (72).

*C. glabrata* infections demonstrate a high rate of fluconazole resistance. In such cases, the results can be greatly improved by using of amphotericin B or flucytosine. The most proper management for opportunistic yeast-like fungi (e.g., *Trichosporon spp.*) is amphotericin B, fluconazole or both of them. In infections caused by *Geotrichum* or *Rhodotorula*, amphotericin B, flucytosine or fluconazole are mainly used (72, 74).

The recent study have shown the benefit from anidulafungin treatment of candidemia or invasive candidiosis in critically ill patients with fluconazole resistance (200 mg on the first day and than 100 mg daily, duration: 10-42 days, intravenous) (80).

**Mycosis among hemodialysis patients with diabetes**

Hemodialysis patients and diabetics are both at increased risk of developing onychomycosis. Dialysis duration and presence of diabetes mellitus are independent predisposing factors. The uremic patients with hemodialysis suffer more often from dystrophic nail changes and onychomycosis. Nail diseases in this disease affect 71.4% of patients. The most frequent occurring change is half and half nails. Absence of lunula is also common. Secondary to hypochromic anemia or chronic renal failure brittle nails are observed. The prevalence of it is also increased among immunocompromised patients like diabetics (81, 82). Patients with continuous ambulatory peritoneal dialysis with previous bacterial peritonitis and antibiotic management demonstrate an increased propensity to develop fungal peritonitis (83).

There is a pressing need to take care of hemodialysis, diabetic patients nails and foot. Hemodialysis diabetics should be especially carefully examined for onychomycosis, because of dangerous, serious implications such as erysipelas or amputation (81).

**Post-transplant diabetes after kidney transplantation**

Systemic infectious diseases are the important cause of morbidity and mortality in renal transplant recipients. Systemic fungal infections occurs in 1-14% after kidney transplantation and the incidence of invasive fungal infections is informed even to 1.5%. Recipients are especially prone to Candida spp. (fungemia, catheter and urinary tract), *Aspergillus* spp. (lungs and central nervous system), *Cryptococcus neoformans* (lungs and central nervous system) and Zygomatosis infections as a consequence of immunosuppressive therapy. Patients with anti-rejection therapy or/and diabetes mellitus are showing an increased propensity to develop fungal infection (84-88). Also skin infections (e.g., candidal infections, dermatomycoses, onychomycoses) take place more frequently by renal transplant recipients, especially prone were diabetics (89). Early diagnosis combined with appropriate therapy may prevent local spread and potential systemic dissemination (84, 87, 90).

New onset diabetes after transplantation (NODAT), called also post-transplant diabetes mellitus (PTDM) has a high incidence after kidney transplantation. Risk factors of PTDM are immunosuppression scheme (high doses of tacrolimus and corticosteroi), age, ethnicity, overweight, obesity, hepatitis C infection and cytomegalovirus infection. The prevalence of this complication after solid organ transplant is evaluated from 2 to 53%, and after kidney transplantation 4-25%. PDFA is an independent predictor associated with serious com-
complications like infections, cardiovascular disease, chronic transplant dysfunction and worst graft survival (91-94).

Diagnostic procedures include conventional fungal laboratory diagnosis, enzymatic activity tests, serologic tests, molecular diagnosis of samples from recipients who are highly predisposed to mycotic infections (84, 95).

The prophylaxis of fungal infections in renal transplant recipients isn’t recommended. The widely used fluconazole prophylaxis is associated with negative selection of resistant strains. The empirical treatment should be administer in the event of invasive fungal infection clinical suspicion. The drugs of choice are: amphotericin B, lisosomal amphotericin B, itraconazole, voriconazole, posaconazole or caspofungin. After the results of microbiologic examination are known, the choice of proper management should be arranged individually and depends on sensitivity examination, minimal inhibitory concentration and clinical state of the patient. The high rate of drug resistance is observed, especially to azole agents (fluconazole). The use of echinocandins can be considered (84, 85).

Pancreas transplant recipients

Patients after solid organ transplantation, including simultaneous pancreas-kidney transplantation (SPK) which improves long-term survival of insulin-dependent diabetes mellitus, are predisposed to develop fungal infection. The most frequent pathogens responsible for colonization and infection are: Candida and Cryptococcus neoformans. That is one of most frequent causes of prolonged hospitalization, higher morbidity and mortality rate. To minimize the risk of this important complication, fluconazole (C. albicans), voriconazole (non-albicans species), fluconazole or amphotericin B (e.g., mucormycosis) can be used. The removal of the transplanted organ may be necessary if antifungal treatment is unsuccessful (96-99). The use of amphotericin B causes adverse events (renal and bone marrow toxicity), which could be reduced with antihistamine and anti-inflammatory prophylaxis. Saline administration or use of lipid form of amphotericin B can reduce renal toxicity. Using of amphotericin B combined with cyclosporine can lead to acute renal failure. The interaction with the P450 enzyme system must be considered by fluconazole (100, 101).

Morbidity and mortality in pancreas transplant recipients remain high mainly owing of infection, especially fungal one with 6-38% rate. Causes connected with fungal transmission are undetectable or link to the donor organ or bloodstream, but donor-related transmission occurs infrequently. Most of infections occur up to six months after surgery. Bladder drainage, accumulation of pancreatic fluid in the peritoneal cavity, vascular graft thrombosis, preoperative peritoneal dialysis, pancreatitis after reperfusion, retransplantation, preexisting renal graft and use of immunossupression, type and duration of diabetes mellitus are factors which predispose transplant patients to developing fungal diseases. The most frequent are: predominating Candida (risk rate > 45%), Aspergillus and Coccomidoidomycosis or more rare Mucormycosis. The typical infection are: superficial, deep wound, intraabdominal or urinary tract infection, peritonitis or fungemia. This complications impact significantly risk of graft loss (the function continued in only 22%, graft pancreatectomy takes place in > 78% and mortality rate is 20%) (99-108).

The proper diagnostic tools are: culture and serology examination, antigen detection, nucleic acid detection, antibody detection, histopathology and radiology (100). Transplant donors control would reduce the risk of infection transmission (109).

To eradicate fungi and increase graft survival amphotericin B and azoles (fluconazole = 4 weeks) are recommended (95, 102, 104). In high risk groups prophylaxis with fluconazole should be considered. It has been reported to be effective and well tolerated. The difficulties due to nonalbicans Candida species, which can be fluconazole resistant, are possible. In this cases other azoles, lipid form of amphotericin B or echinocandins should be prescribed (102, 107, 110).

CONCLUSION

Particular attention must be given to patients with diabetes mellitus because of high incidence of fungal infections in this population. Also the diabetic patients during hemodialysis and after pancreas or kidney transplantation are more prone to fungal infections. The prevalence of mycosis in diabetics is a serious mortality cause. The problem may be minimalized by proper use of prophylaxis and regular communication with patient. The restricted sensitivity to popular agents, e.g., fluconazole, should be always considered. To avoid treatment-resistance every case of mycosis must be precisely diagnosed. The acquaintance with fungi strain, its drug sensitivity and minimal inhibitory concentration can allow to arrange the best agent, dose and length of management and greatly improve the success in treatment.
Statement

The authors declare that there is no conflict of interest.

REFERENCES


Received: 04.09.2012