

without cirrhosis revealed significant risk factors for HCC as follows: age (over 40 yrs old, $p=0.009$), male ($p=0.011$), AFP (>20 ng/mL, $p=0.011$), severe liver parenchymal echopattern in ultrasonography ($p=0.0002$) and heavy alcoholics ($p=0.0428$). Based on these factors, the establishment of screening program for HCC is in the pipeline.

Concurrent Session 14 – Fungal Infection

I-67 Fungal infections – Insights from the bench-side

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Invasive fungal infections have always been a life-threatening disease for immunocompromised patients. Traditionally, the microbiology laboratory often offers little help in the diagnosis and treatment of these patients. However, with the advent of molecular and chemical diagnostic methods, and the standardization of susceptibility testing, more insights can now be shed. Molecular techniques generally detect the presence of the highly conserved region of the fungal organisms. Its success has been variable, and standardization of methods has been slow in progress. Chemical detection methods such as mannan, galactomannan has received renewed interest. The application of beta-D-glucan detection in the clinical settings has raised further enthusiasm not only in its high sensitivity, but also potentially as a monitoring marker for disease progress and treatment response. Disc diffusion susceptibility testing has allowed certain azole agents to be readily tested in the laboratory. Although the susceptibility of most *Candida* species can be predicted from its speciation, the availability of susceptibility surveillance programme allows monitoring of resistance pattern. The advent of echinocandins further improves the clinical outcomes. Its selective toxicity is a much needed contribute in the treatment of these fatal diseases. With further clinical trials and animal models, understanding of this class of anti-fungal agent should widen its clinical application.

I-68 Invasive fungal infections in Asia-Pacific region

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Invasive fungal infection has emerged as an important nosocomial infection, especially in critically ill patients. An increasing incidence of candidemia became apparent from the 1980 to the end of the 1990's followed by relative stability. The incidence of candidemia in intensive care units (ICUs) is 5 to 10-fold that in overall hospitals, and more than 100-fold greater than in the general population in Asia-Pacific region. The crude mortality rate of patients with candidemia is in the range of 35–60%, however, ICU patients with candidemia had a higher mortality rate than non-ICU patients. The crude mortality with invasive aspergillosis is more than 60%, particularly in patients with hematological malignancy and transplant patients. *Candida albicans* remains the predominant cause of invasive candidiasis in more than 50% of all cases. *C. tropicalis*, *C. glabrata* and *C. parapsilosis* are the three most common non-*albicans Candida* species causing invasive candidiasis. The above four *Candida* species account for more than 90% of invasive candidiasis. Overall, invasive non-*albicans Candida* isolates remained highly susceptible to fluconazole

(>90% susceptible) over the past two decades. However, the susceptible rate of *C. glabrata* to fluconazole varied widely from 22 to 72% and the resistant rate ranged from 2 to 16% in Asian countries. Analysis of the fluconazole susceptibilities of 204 bloodstream *C. glabrata* isolates revealed a rapid shift from susceptible (64% in 1999 to 2001 to 19% in 2007) to susceptible-dose dependent (27% in 1999 to 2001 and 75% in 2007) in Taiwan. Periodic surveillance is needed to monitor antifungal resistance because reduced fluconazole susceptibility in non-*albicans Candida* is not an uncommon trend. Echinocandins continue to exhibit excellent in vitro fungicidal activities against all *Candida* isolates and are promising agents for the treatment of patients with invasive candidiasis, particularly in ICU patients.

I-69 Genotype distribution of *Candida albicans* in China

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Candida albicans is the most common opportunistic fungal pathogen of humans. It causes from benign infections such as oral and vaginal candidiasis to fatal, systematic infections in immunocompromised or critically ill patients. The genotype distributions of *C. albicans* strains with different sources were investigated using single-strand conformation polymorphism and GeneScan analyses of a microsatellite locus called CAI. The *C. albicans* strains from various extragenital sites, those from vaginas of asymptomatic women, and those causing vulvovaginal candidosis (VVC) of women and balanoposthitis of men, were employed. Genetic similarity of representative strains with the same and different CAI genotypes were examined by sequence analysis of housekeeping genes *CaADP1*, *CaSYA1* and *CaVPS13*. The CAI genotypes of independent *C. albicans* strains from extragenital sites were mostly of individual specificity. In contrast, strains associated with VVC were mainly concentrated to a few dominant genotypes, with two CAI genotypes being the most common. The enrichment trend of the dominant genotypes of *C. albicans* strains correlated positively with the severity of VVC. A similar biased genotype distribution pattern of *C. albicans* strains associated with balanoposthitis was also revealed. The genetic similarity of strains with the dominant genotypes associated with both VVC and balanoposthitis was confirmed by sequence analysis of the three genes. The results suggest the existence of vaginopathic *C. albicans* strains with enhanced virulence and tropism for the vagina, and the high possibility of sexual transmission of genital *C. albicans* infection. Identification of specific genotypes that correlate with severity of VVC is certainly of diagnostic and therapeutic significance.

I-70 Non-culture diagnosis of fungal infection

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In recent years, as the growing number of immunocompromised hosts, there is an obviously increasing of opportunistic fungal infections. *Candida* infection is the commonest one especially Candidemia could lead to a high mortality. Other non-*Candida* yeasts infections are emerging, such as *Trichosporon* spp. infection. In BMT patients and other immunocompromised patients, invasive aspergillosis has been one of the major causes of death. How to improve the early and specific diagnosis level of fungal infection, especially the invasive fungal infection, is a big challenge

to the clinical mycologists. There is an urgent need to develop the new diagnosis procedures such as the non-culture methods though the detection of the fungal antigen and nuclear acid. The application of 1,3- β -D-Glucan (G-test) and Glactomann (GM test) as well as the PCR related procedures will be discussed in this presentation. In future, multi-centered prospective study is still needed to the better evaluation of these methods.

[I-71] Systemic mycoses of local importance

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Penicillium marneffe was first isolated from the visceral organs of bamboo rats in Vietnam in 1956. It is considered as an endemic pathogen of the Southeast Asia and South China. Sporadic case reports were cases living in or having travelled to these regions. It can affect both apparent normal hosts and immunocompromised hosts such as lymphoma. In the AIDS era, outburst of cases was reported from the North of Thailand. Between 1991- 1996, there were 1,020 cases diagnosed in Chiangmai University Hospital, all were HIV-infected people. Hence, this infection is considered an AIDS-defining illness in this part of the world.

Penicilliosis marneffe was also reported in AIDS cases in Manipur State in West India. Transmission is most likely via inhalation of infective spores in the environment. Roles of bamboo rats remain unclear. Clinical features of disseminated infection include prolonged fever (98%), anemia (75%), weight loss (70%), cutaneous lesions (70%), lymphadenopathy (52%), hepatomegaly (45%), lung involvement (35%), splenomegaly (14%), and osteolytic lesions (4%). Diagnosis can easily be made quickly by demonstrating intra- and extracellular yeasts, 3–5 micron in size, some elongated with septum centrally, on Wright's stain of the skin-scraping. Peripheral blood smear, bone marrow smear, lymphnode touch-prep are also helpful in making diagnosis. Confirmation by culture requires more time. Treatment should be started with Amphotericin B (0.6 mg/kg/d) for 2 weeks, followed by itraconazole (200 mg bid) for another 10 weeks. Secondary prophylaxis should be given to prevent relapse until immune recovery with HAART.

Another unique mycosis in this region is **pythiosis**, the infection caused by *Pythium insidiosum*. The most recognized form with high morbidity and mortality is arteritis, presenting with symptoms and signs of arterial insufficiency: intermittent claudication, chronic ischemic ulcers or limb gangrene, mainly of lower limbs. Pathologically, the infection spread along the arterial vessel wall, causing destruction, thrombosis, or aneurysmal dilatation, in the ascending fashion towards aorta. False aneurysm is observed. Aortic rupture is ultimately fatal outcome. Almost all patients have hemoglobinopathy/thalassemic syndrome and expose to this organisms in the environment such as rice field. Treatment of this entity is still problematic since it is not a true fungus and the response to the available antifungal agents is unsatisfactory. Some successful treatment reported includes the combination of itraconazole and terbinafine, and immunotherapy with *Pythium* Vaccine developed by Dr. Mendoza. Amputation of the affected limb is usually unavoidable. Ocular form is also devastating. It progresses from corneal ulcer, invading deeper into the globe resulting in endophthalmitis, nonresponsive to any topical antifungal agents. Evisceration or enucleation is the usual outcome. Considering its habitat in the tropic, it is likely that pythiosis is under- recognized in the Southeast Asia region, and

physicians should be aware of this infection and manage early to reduce the morbidity and mortality.

Concurrent Session 15 – HIV/AIDS Treatment – Never Simple

[I-72] The changes and distributions status of opportunistic infections during 6 months after HAART initiation

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Background: It is well known that OIs are the main causes of HIV/AIDS patients' hospitalizations and deaths. With the different immune system status, the OIs spectrum is different. With the introductions of HAART, the incidence and mortality of OIs will be declined greatly. But as we know, the impaired immune system function will be reconstituted after HAART of 3–6 months at least. The OIs still have chance to happen during the first 6 months after HAART initiation. During the first 6 months, not only the side effects of the ARV drugs but also IRIS will make the diagnosis of OIs difficult.

Objective: To explore the changes and distributions status of Opportunistic Infections during 6 months after HAART initiation.

Methods: To research retrospectively and prospectively with the uniform CRF. The contents of the CRF include the data below: subject number, the date of the HAART initiation, gender, age, ARV regimen, OI status during 3 months before HAART, and 2 weeks, 2 weeks to 3 months, 3–6 months after HAART respectively, and CD4 cell counts changes of baseline, 3 months and 6 months of treatments.

Results: 93 patients had the symptom of fever during 3 months before treatments among 192 patients. The incidence of fever is 48.44%. 39 cases had the symptom of diarrhea (20.31%). 46 patients had TB (35.9%); the baseline CD4 cell count is 91/ μ l; after 2 weeks treatment, the fever incidence rate is 35.9%, 3.65% is new onset. The incidence rate of respiratory system disease is 29.69% (57 cases). 56.1% cases are TB. Among them only 3 cases are newly diagnosed or infected with TB. The incidences of oral thrush (12.5%) and herpes zoster (14.6%) are relatively high. The respiratory system symptom incidence rate is 2.08% at the week 2–month 3 of treatments, oral thrush (1.56%) and herpes zoster (1.56%). And there is no new TB case; there are still the cases of fever and lung disease. But the rate is very low; The CD4 cell count increased 111/ μ l after 6 months treatments.

Conclusions: Fever is the most common sign of the AIDS patient. The incidence of fever will be reduced greatly as the HAART continues ($P < 0.05$). And whether a patients has a fever is related with his fever status before the treatment. Swallow difficulty and pain become less ($P < 0.05$). TB, oral thrush, lung disease and herpes zoster have been reduced significantly ($P < 0.05$). The diarrhea becomes less but the difference is not significant ($P > 0.05$). Perhaps, it is because that the diarrhea is related with not only the OI but also the side effects of drugs and non-specific inflammations. We can not make the right judgements on the neuro system features and vision changes.