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Trichomoniasis — a review

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Introduction

Trichomoniasis is a world-wide sexually transmitted infection (STI) caused by the protozoan *Trichomonas vaginalis*. It was recently estimated that the annual incidence in the United States is five million new cases. Studies on age-specific prevalence showed an increase with age from 20 to 45 years in female patients but the situation in males appeared less precise. Treatment of trichomoniasis is needed for the many known complications including facilitation of HIV transmission. Most patients respond to a single dose of oral metronidazole. Cases resistant to treatment are uncommon but the trend appears on the increase. Knowledge of such information helps us in understanding this protozoal infection and facilitates effective control.

Microbiology

T. vaginalis, first discovered in 1836, is an amitochondrial, microaerotolerant flagellate that almost exclusively infects the human urogenital tract. Each trophozoite is pear-shaped and measures 7-23 micrometres in length (average 13 micrometres). It possesses five motile flagella arising from a blepharoplast. Four flagella project anteriorly freely while one extends backward for about two-thirds of the body length to incorporate into a moving undulating membrane. The nucleus within a porous envelope is anteriorly situated from which a long narrow axostyle projects posteriorly. The trophozoites are divided by longitudinal binary fission and there is no known true cyst stage.

Clinical features

T. vaginalis mostly infects the lower genitourinary tract of both sexes with an incubation period in women ranging from 5 to 28 days. In female, the most frequent presentation is acute or chronic vaginitis. Typical symptoms of vaginitis include vaginal discharge, soreness, itch, irritation, offensive odour and dyspareunia. Vaginal discharge varies from thin and scanty to profuse and thick. It can present in up to 70% and is often yellowish or purulent.

Trichomonal infection can also affect the bladder, urethra and paraurethral glands. Thus it can present as urinary tract infection. In one study, dysuria was observed in 29% of infected women (1). About half of the female patients could be asymptomatic, and formed a reservoir of infection (2). In pregnant women, it could be associated with adverse outcomes such as preterm delivery, premature rupture of membranes and low-birth weight babies. In men, it is one cause of non-gonococcal urethritis. The most common symptoms are dysuria and urethral discharge. The infection tends to be self-limiting and the urethral discharge is generally less profuse and purulent than that seen with gonococcal urethritis (3). In about half of the infected men the infection is asymptomatic. Other than urethritis, balanoposthitis, prostatitis, cystitis and possibly epididymo-orchitis may complicate the infection.

Trichomoniasis may be transmitted to neonates and about 2-17% of female offsprings are affected by infected mothers (3). Infection in neonates is often self-limited. After the neonatal period, nonsexually acquired infection is rare. Genital trichomoniasis in an older child raises the suspicion of sexual abuse. The disease may play a role in pelvic inflammatory disease, male and female infertility, and may also increase the risk of HIV acquisition and transmission.

Diagnosis

Diagnosis of vaginal trichomoniasis is usually done by microscopic examination of a wet smear of vaginal secretion. A drop of vaginal discharge collected from the posterior vaginal fornix is mixed with a drop of normal saline and examined immediately under dark ground microscope for the active motile protozoan. This test is quick and gives a sensitivity of 45-60% which is more sensitive than other staining methods such as Giemsa and acridine orange stains (4). In male, a wet smear is taken by gently scraping the urethra with a platinum or plastic loop. The sensitivity of detecting trichomonads by Pap smear is low compared with culture and it also carries false positivity. In a study on 268 twelve to

eighteen-year-old girls, the sensitivity of Pap smear for detecting *T. vaginalis* was only 56% against the 'gold standard' of Diamond's culture (5).

Culture remains the most sensitive (>95%) and specific test for detecting *T. vaginalis* at present and the culture medium is commercially available. Common culture media include Diamond's medium and Feinberg-Whittington medium. Locally, the Public Health Laboratory Centre uses Trichomonas Medium (*Bridson E.Y. The Oxoid Manual 8th Edition. 1998*). It is similar to the Feinberg-Whittington medium but is slightly modified by the incorporation of 0.1% w/v of agar, thereby reducing the oxygen tension allowing more prolific growth of trichomonads. Culture methods have the disadvantages of being more expensive and causing a delay in making a definitive diagnosis. If the laboratory is far away from clinic, transport medium like the Amie's gel agar can be used.

New diagnostic methods like the DNA-based and antigen-based tests using polymerase chain reaction (PCR) are currently being developed for trichomoniasis. Their results have been encouraging and may facilitate non-invasive diagnosis in men. At present, these new tests are not yet FDA approved and some are restricted to research settings. New diagnostic tests utilising PCR are likely and in need to improve the detection rate in male patients.

Treatment

The nitroimidazoles are the only recognised drugs effective for treating trichomoniasis, with a single dose of metronidazole - the standard treatment in the United States. Metronidazole resistance is uncommon. Clinically resistant *T. vaginalis* isolates usually show increased minimum lethal concentrations to metronidazole under aerobic growth conditions but not much when under anaerobic conditions (6).

The CDC recommended regimen for treating trichomoniasis is metronidazole 2 g orally given in a single dose. The cure rate is about 90-95%. An alternative regimen is metronidazole 500 mg bd for 7 days. If treatment fails, the patient should be re-treated with metronidazole 500 mg bd for 7 days. If this fails again, the patient should be treated with 2-g metronidazole once a day for 3-5 days. The treatment regimen for trichomoniasis in the Social Hygiene Service is similar to that recommended by the CDC. Either metronidazole or tinidazole, a second generation nitroimidazole in a single 2 g oral dose is given, or metronidazole 400 mg bd orally for 5-7 days is used if the single dose fails (7). Test for cure should be undertaken for infection documented by wet smear or culture. Tinidazole is a second generation nitroimidazole with activity against protozoa and anaerobic bacteria. A 2 g dose of tinidazole is equivalent to a 2 g dose of metronidazole. Tinidazole has a plasma elimination half-life twice that of metronidazole and it penetrates better into male reproductive tissues than metronidazole. For all cases where initial metronidazole treatments fail, poor drug compliance and re-infection from an untreated and usually asymptomatic male sexual partner should be excluded. Possibility of metronidazole inactivation by vaginal bacteria can be covered by either a course of amoxicillin 250 mg tds or erythromycin 250 mg qid for 5-7 days given before or concurrent with re-treatment with metronidazole.

Side effects for metronidazole include nausea, vomiting, metallic taste, and gastrointestinal upset, and are usually self limiting. Patients taking metronidazole should not take alcohol during treatment and at least 48 hours afterwards due to disulfiram-like reaction. Metronidazole should be avoided in the first trimester of pregnancy and during lactation. Local clotrimazole pessaries can be used for symptomatic relief during this period. After the first trimester, systemic metronidazole treatment would ultimately be needed for eradicating the infection. Tinidazole is not recommended in pregnancy and lactation, or in patients with blood dyscrasia or active neurological disorders.

Trichomoniasis is a prevalent STI. All sexual contacts should be traced and treated irrespective of presence or absence of symptoms. The patients and their sex partners should be screened for co-existent STIs and HIV infection.

Conclusion

Trichomoniasis is the most prevalent STI in the world but it is curable and most cases can be cured with a single dose or short course of nitroimidazole drugs. Local incidence and prevalence rates are

lacking and public and private collaborative surveillance studies are helpful to explore the local epidemiology of this STI. Treatment of sexual partners irrespective of symptoms should be done and all patients and their sexual partners should be screened for other STIs including HIV infection. It is important to note that in most male and many female patients, the infection is asymptomatic and they serve as a reservoir for infection. The development of inexpensive or affordable, rapid, sensitive and specific diagnostic tests is therefore needed not only to improve detection, but also to enhance our knowledge of the epidemiology, risk factors and clinical manifestations of trichomoniasis.

References

1. Schneider H, Coetzee DJ, Fehler HG, Bellingan A, Dangor Y, Radebe F, et al. Screening for sexually transmitted diseases in rural South African women. Sex Transm Infect. 1998;74 Suppl 1:S147-52.
2. Draper D, Parker R, Patterson E, Jones W, Beutz M, French J, et al. Detection of Trichomonas vaginalis in pregnant women with the InPouch TV culture system. J Clin Microbiol. 1993;31:1016-8.
3. Krieger JN. Epidemiology and clinical manifestations of urogenital Trichomoniasis in men. In: Honigberg BM, ed. Trichomonads parasitic in humans. New York; Springer-Verlag:1990:235-45.
4. Lossick JG, Kent HL. Trichomoniasis: trends in diagnosis and management. Am J Obstet Gynecol. 1991;165:1217-22.
5. Thomason JL, Gelbart SM, Sobun JF, Schulien MB, Hamilton PR. Comparison of four methods to detect Trichomonas vaginalis. J Clin Microbiol. 1988;26:1869-70.
6. Muller M, Lossick JG, Gorrell TE. In vitro susceptibility of Trichomonas vaginalis to metronidazole and treatment outcome in vaginal trichomoniasis.
   Sex Transm Dis. 1988;15:17-24.
7. Recommendations in case management of sexually transmitted infections in Hong Kong 2002. In: Lo KK, Chong LY, Tang YM, Ho KM, ed. Handbook of Dermatology and Venereology: 2003: 546-7.

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Antifungal therapy in critically ill patients

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Fungal infections represent a major cause of morbidity and mortality among compromised patients. The mortality rates have remained high despite the availability of effective antifungal drugs. The reported figures are 30-40% for systemic candidiasis and 50-90% for systemic aspergillosis. The incidence quoted is still an underestimate and the diagnosis is frequently made at post mortem examinations. A study on the mortality due to invasive fungal infections in the US from 1980 to1997 showed that the rate for candidiasis was between 0.3 to 0.5 per 1000, and the rate for aspergillosis had climbed to a peak of 0.4 per 1000 (1).

While the *Candida* and *Aspergillus* species are the aetiological agents for the majority of invasive fungal infections, the mechanism of disease is different for each of them. As a result of chemotherapy injury to the gastrointestinal tract mucosa, and selection of *Candida* species from the commensal flora by antibiotics, local infection by these organisms is established. This is followed by translocation of the *Candida* across the mucosa into the blood stream, leading to systemic infection. On the other hand, *Aspergillus* species are found in the environment and can easily go into the bronchial tree by the inhalation route. Any breach in the immune barrier of the respiratory tract will facilitate the invasion of *Aspergillus* species into the blood stream through the respiratory mucosa, resulting in systemic disease.

The following discussion will concentrate mainly on candidiasis with reference to other fungi when appropriate. *Candida* species are now the fourth most common nosocomial pathogens isolated from the blood stream. The highest incidence is found in burn/trauma units and surgical intensive care units. It is important to identify the *Candida* species because of the different sensitivity of the organisms to antifungal therapy and association with specific disease state. *C. albicans* is more common in HIV/AIDS and surgical patients. *C. glabrata* is partially resistant to most antifungal agents. *C. parapsilosis* infection is usually catheter related. *C tropicalis* and *C. krusei* are commonly found in the neutropenic state. Both *C. guillermondi* and *C. lusitaniae* are resistant to amphotericin B. *C. dubliniensis* is isolated from HIV/AIDS patients in > 90% of cases. The diagnosis of systemic candidiasis is difficult owing to the non-specific manifestations, insensitive tests and low incidence of positive culture (40-60%), which is even less if prior antifungal treatment has been given. In order to make the clinical diagnosis, clinicians should have a high index of suspicion in the setting of appropriate risk factors and unresponsiveness of fever to broad spectrum antibiotics. The low yield of blood cultures in systemic candidiasis is related to the intermittent shedding of *Candidia* from abscesses into the blood stream, growth inhibition of *Candida* in blood cultures, rapid adherence of *Candida* to host tissues via receptor-ligands with removal by the reticulo-endothelial system, and high false negative rate. The incidence of fungaemia in deep invasive candidiasis varies from 8.3% in hepatosplenic candidiasis to 28% in single visceral organ involvement and 58% in multi-organ candidiasis (2,3).

The risk factors of systemic candidiasis include intravenous catheters (3x risk), malignancy, broad spectrum antimicrobials, total parenteral nutrition (2x risk), surgery (primarily GI), diabetes mellitus, burns/trauma, transplantation (BMT, liver) and haemodialysis (18x risk). Using haematological malignancy as an example (4), high risk groups for invasive fungal infection, especially candidiasis, are found to be patients with neutrophils < 0.1×10^9/L for more than 3 weeks, colonized by *Candida tropicalis*, undergoing allogeneic unrelated or mismatched donor BMT, suffering from graft-versus-host disease, having neutropenia < 0.5×10^9/L for more than 5 weeks, on corticosteroids > 1 mg/kg and neutrophils < 1×10^9/L for more than 1 week, on corticosteroids > 2 mg/kg for more than 2 weeks, on high dose of cytosine arabinoside and on fludarabine (relationship not definite). In neutropenic cancer patients with invasive candidiasis, the most common clinical characteristics are broad-spectrum antibiotics in previous 2 weeks, chemotherapy within previous 30 days and central venous catheter in place at the time of positive blood culture ($\geq$ 90% of patients). For non-neutropenic cancer patients, only the previous first and third features are more common ($\geq$ 80% of patients)

The manifestations of systemic candidiasis are protean. The clinical picture may resemble that of bacteraemia. The severity can range from low grade fever to septic shock. The usual presentation is fever unresponsive to 3-5 days of antimicrobials in association with 2 or more risk factors and evidence of Candida colonization. Clinically, the patients may have macronodular skin lesions (10%), endophthalmitis (from < 10% to 30-40%), sudden onset of fever, tachycardia, tachypnoea and hypotension. However, none of these manifestations are characteristic of systemic candidiasis.

The essence of the management of candidaemia or candidiasis is removal of the focus of infection, removal or decrease of immunosuppression and early antifungal therapy. The catheter is suspected in candidaemia of non-cancer patients. After chemotherapy, the catheter is less important and microabscesses of visceral organs become a more prominent factor. Up to 15% of candidaemia have obvious sources like the urinary tract or abscesses instead of the catheter. On the whole, the catheter is still the most common cause of candidaemia with a mortality of 30-40 %. Diagnostic techniques are insensitive. Because of the potential morbidity and mortality plus the risk of delayed complications and end organ infection, the minimally toxic and efficacious agent, fluconazole, is frequently used for early treatment. In one study, it was shown that removal of the catheter plus amphotericin B or removal of catheter alone had better outcome than amphotericin B alone.

Catheter-related candidiasis is only part of the spectrum of systemic candidiasis, and in a wider sense, of systemic fungal infection. Management of invasive fungal disease should be viewed from a more general perspective. In fact, antifungal strategies have been developed basing on disease likelihood and type of treatment that can be used. The disease categories (% chance of proven disease) have been classified as: remote (0-4%), possible (5-15%), probable (15-35%) and proven. The treatment employed is called prophylaxis for remote (high risk host factors), empirical for possible (persistent fever and mucositis), pre-emptive for probable (clinical features and mycological evidence) and specific for proven (tissue evidence). Applying these principles, fluconazole 800 mg QD for 14-21 days has been used for empirical therapy of *Candida* in non-neutropenic hosts. Amphotericin B 1.0 mg /kg/day alone or the combination of amphotericin B or fluconazole with caspofungin can be used if the patient is on fluconazole prophylaxis, or colonized by *C. krusei* or *C. glabrata*. For neutropenic hosts, those who have had fluconazole prophylaxis will receive amphotericin B 0.7-1.0 mg/kg /day, or lipid formulations of amphotericin B 3-5 mg/ kg/day, or combination of amphotericin B and fluconazole or caspofungin. Those who have had no prophylaxis can be given fluconazole 800 mg /day. For this group, alternatives include amphotericin B plus fluconazole or adding caspofungin to either of these drugs. The rationale of using early pre-emptive therapy for Candida again rests on the difficulty in diagnosis and high mortality rate of systemic candidiasis. Pre-emptive therapy will be used if the patient's temperature remains > 38.3°C for 72 hours, has received broad spectrum antimicrobials for 96 hours, has no obvious source of fever and is colonized by *Candida* species in 2 or more sites. In specific therapy for *Candida*, fluconazole 800 mg followed by 400 mg QD IV or PO is considered equivalent to amphotericin B. Alternatively, amphotericin B at 0.7 mg/kg/day or lipid formulations of amphotericin B at 5 mg/kg/day is just as effective. If the *Candida* species is *C. glabrata*, fluconazole has to be increased to 800 mg QD (IV or PO) and amphotericin B has to be stepped up to 0.7-1.0 mg/kg/day. Overall speaking, current antifungal therapy for systemic candidiasis relies on high clinical suspicion and early treatment in high risk patients (5). The future directions will likely be increased use of lipid formulations of amphotericin B, host immune response augmentation by G-CSF, GM-CSF and interferon, combination therapy and new antifungals.

The combination of amphotericin B and 5-flucytosine has proven to be effective for *Cryptococcus* but to have doubtful potency for *Candida*. Other possible combinations in studies include amphotericin plus fluconazole, fluconazole plus 5-flucytosine, fluconaziole plus terbinafine, caspofungin plus amphotericin B, caspofungin plus fluconazole or itraconazole, caspofungin plus voriconazole or posaconazole. Nevertheless, antagonism has been found in the 2-drug combination of amphotericin B plus itraconazole or other azoles like ketoconazole, voriconazole and possibly posaconazole.

The new generation of antifungal agents is the hope for the future. These include new azoles like voriconazole, posaconazole and ravuconazole. They are potent and specific inhibitors of the synthesis of fungal sterol, which is a vital component of fungal cell membrane. The other group is the echinocandins, which include caspofungin, micafungin and anidulafungin. They inhibit the synthesis of

β-(1,3)-D-glucan, which is a critical component of fungal cell wall. Voriconazole and caspofungin are now available for general use and they have been strong competitors to become the leader in the field of antifungal therapy. The investigational agents posaconazole and ravuconazole have antifungal spectra similar to that of voriconazole. It is of interest that ravuconazole has a long half -life of about 1 week.

Voriconazole has inhibitive effect on *Candida, Aspergillus* and *Penicillium* species, and on moulds like *Fusarium* and *Scedosporium* species (amphotericin B resistant). It is fungistatic against *Candida* species and *Cryptococcus neoformans*, and fungicidal against *Aspergillus* species. On the other hand, caspofungin has a spectrum largely limited to *Candida* and *Aspergillus* species. It is fungicidal against *Canduida* species but has no action on *Cryotpcoccus neoformans*. It should not be used for filamentous moulds like *Mucor*, *Fusarium*, *Rhyzopus* etc.

Voriconazole, thus, has a wider spectrum than caspofungin. Both oral and IV formulations are available. It has dose-related transient visual disturbance in 30% and rash in 5% of patients in trials. Photosensitivity also occurs. The risk of hepatotoxicity is 10%, which is the least among azoles. The IV formulation should be avoided in renal failure due to accumulation of the cyclodextrin excipient. It has many drug interactions as a result of its being both the substrate and inhibitor of the cytochrome P450 system. Caspofungin, in contrast, has a narrower spectrum of activity. Only the IV formulation is available. Side effects are few and the more common ones include fever and histamine-mediated reactions like rash, pruritus and bronchospasm. There is some risk of hepatotoxicity but it is low. No change in dosage is necessary in renal failure. Caspofungin is unlikely to have drug interactions. However, its level is increased by cyclosporine.

Strength (A-D) and quality (I-III) of evidence have been utilized in the recommendations for the use of voriconazole and caspofungin (6). Voriconazole is the initial treatment of choice for proven or suspected acute invasive aspergillosis in immunocompromised patients (AI). It is also used in non-neutropenic patients with candidaemia or invasive candidiasis and those with fluconazole-resistant organisms (CIII). Caspofungin is recommended for neutropenic patients with PUO and high risk of invasive mould infection (AI). It has been given in neutropenic patients with candidaemia or invasive candidiasis (BI). It can serve as an alternative for suspected or proven invasive aspergillosis (BII). In a recent paper, caspofungin has been found to be as effective as and generally better tolerated than liposomal amphotericin B when given as empirical antifungal therapy in patients with persistent fever and neutropenia (7).
In conclusion, invasive fungal diseases, exemplified by deep-seated candidiasis and aspergillosis, have become the most fatal infections in immunocompromised hosts. Fluconazole and amphotericin B have all along been the pillars of drug treatment. The relatively low efficacy of the former and adverse side effects of the latter have fuelled the development of a new range of more potent and safer agents. They appear to have a promising role in antifungal therapy of the future.

References

1. McNeil MM, Nash SL, Hajjeh RA, et al. Trends in mortality due to invasive mycotic diseases in the United States, 1980-1997. *Clinical Infectious Diseases* 2001; 33: 641-7
2. Berenguer J, Buck M, Witebsky F, Stock F, Pizzo PA, Walsh TJ. Lysis-centrifugation blood cultures in the detection of tissue-proven invasive candidiasis. Disseminated versus single-organ infection. *Diagnostic Microbiology & Infectious Disease* 1993; 17:103-9
3. Thaler M, Pastakia B, Shawker TH, O'Leary T, Pizzo PA. Hepatic candidiasis in cancer patients: the evolving picture of the syndrome. *Annals of Internal Medicine* 1988; 108: 88-100
4. Prentice HG, Kibbler CC, Prentice AG. Towards a targeted, risk-based, antifungal strategy in neutropenic patients. *British Journal of Haematology* 2000; 110: 273-84
5. Pappas PG, Rex JH, Sobel JD, et al Infectious Diseases Society of America. Guidelines for

treatment of candidiasis. *Clinical Infectious Diseases* 2004; 38: 161-89

6. Slavin MA, Szer J, Grigg AP, et al. Guidelines for the use of antifungal agents in the treatment of invasive Candida and mould infections. *Internal Medicine Journal* 2004; 34: 192-200
7. Walsh TJ, Teppler H, Donowitz GR, et al. Caspofungin versus liposomal amphotericin B for empirical antifungal therapy in patients with persistent fever and neutropenia. *New England Journal of Medicine* 2004; 351: 1391-402

Laribacter hongkongensis gastroenteritis — an update

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Laribacter hongkongensis, a novel genus and species, was first discovered in Hong Kong in 2001 from the blood and empyema pus of a 54-year old Chinese man with alcoholic cirrhosis and bacteraemic empyema thoracis.[1] It is a facultative anaerobic, motile, non-sporulating, Gram-negative, S-shaped bacillus. It grows on sheep blood agar as non-hemolytic, gray colonies of 1 mm in diameter after 24 hours of incubation at 37°C in ambient air. Growth also occurs on MacConkey agar, at 25°C and 42°C, but not at 4°C, 44°C, and 50°C. It can grow in 1%, 2%, but not 3%, 4%, or 5% NaCl. No enhancement of growth is observed in 5% CO_2. It is catalase, cytochrome oxidase, urease and arginine dihydrolase positive, and it reduces nitrate. It does not ferment, oxidize, or assimilate any sugar tested. Phylogenetically, it belongs to the *Neisseriaceae* family of the β-subclass of *Proteobacteria*.

After the discovery of *L. hongkongensis*, intensive efforts were made to find its disease association. As the patient's underlying liver cirrhosis and ascites suggested that the gastrointestinal tract might be a possible primary site of infection, *L. hongkongensis* was intensively sought in faecal specimens of patients with gastroenteritis. During a period of two months, *L. hongkongensis* was discovered, on charcoal cefoperazone deoxycholate agar (CCDA), in three of our patients with community-acquired gastroenteritis.[2] A similar finding was also observed in three other patients in Switzerland.[2] Pulsed-field gel electrophoresis (PFGE) of the *Spe*I digested genomic DNA of the six isolates and that of the type strain revealed that the seven isolates were genotypically unrelated strains. The isolation of *L. hongkongensis* from patients in both Asia and Europe suggested that the bacterium is likely to be of global importance. Curved Gram-negative bacilli isolated from CCDA and grown in aerobic environment without CO_2 should not be discarded as non-pathogens.

To better characterize its role in infectious diarrhoea, we developed a new selective medium, cefoperazone MacConkey agar (CMA) containing 32 μg/ml cefoperazone, for primary isolation of *L. hongkongensis* from stool.[3] The performance of CMA on the quantitative recovery of *L. hongkongensis* and suppression of standard aerobic enteric bacteria was superior to MacConkey agar, CCDA and CCDA with 8 μg/ml cefoperazone. CMA supported the growth of *L. hongkongensis* as easily recognized, lactose-negative colonies at 37°C after incubation in ambient air for 24 hours.

Using this selective medium, we carried out a prospective study to determine the association of *L. hongkongensis* with gastroenteritis, the risk factors associated with *Laribacter* gastroenteritis and the source of *L. hongkongensis.*[4] Faecal samples from patients with community-acquired gastroenteritis and controls were cultured for *L. hongkongensis*. A case-control study and targeted food surveillance were performed to identify the potential source of *L. hongkongensis*. During a four-month period, *L.*

hongkongensis was recovered from 17 out of 3788 patients with community-acquired gastroenteritis, but none of 1894 controls (P<0.005). *Laribacter* gastroenteritis was associated with recent history of travel (59% vs 6% in controls, P<0.001), fish consumption (94% vs 56% in controls, P<0.01), and minced freshwater fish meat consumption (29% vs 3% in controls, P<0.05). Twenty-seven additional *L. hongkongensis* isolates were recovered from intestinal samples in 25% of freshwater fish (29% of mud carp, 59% of grass carp, 53% of bighead carp, and 6% of large-mouth bass) and 15% of minced freshwater fish meat from retail markets in Hong Kong. *L. hongkongensis* of the same PFGE pattern and ribotype was recovered from a patient and minced freshwater fish meat from the retail market where he had recently purchased minced freshwater fish meat for cooking. This particular combination of PFGE pattern and ribotype was not seen in any other isolates. Based on the results of this study, we conclude that *L. hongkongensis* is associated with community-acquired gastroenteritis and traveller's diarrhoea. Freshwater fish is the source of *Laribacter* gastroenteritis. Careful handling of fish, proper cooking of the fish and related products, and prevention of cross-contamination at the processing, food preparation, and service steps are crucial in preventing infections associated with *L. hongkongensis.*

References

1. Yuen KY, Woo PCY, Teng JLL, Leung KW, Wong MKM and Lau SKP. Laribacter hongkongensis gen. nov., sp. nov., a novel Gram-negative bacterium isolated from a cirrhotic patient with bacteraemia and empyema. J Clin Microbiol 2001; 39:4227-4232.
2. Woo PCY, Kuhnert P, Burnens AP, Teng JLL, Lau SKP, Que TL, Yau HH Yau and Yuen KY. Laribacter hongkongensis: a potential cause of infectious diarrhea. Diagn Microbiol Infect Dis 2003; 47:551-556.
3. Lau SKP, Woo PCY, Hui WT, Li MWS, Teng JLL, Que TL, Yung RWH, Luk WK, Lai RWM and Yuen KY. Use of cefoperazone MacConkey agar for selective isolation of Laribacter hongkongensis. J Clin Microbiol 2003; 41:4839-4841.
4. Woo PCY, Lau SKP, Teng JLL, Que TL, Yung RWH, Luk WK, Lai RWM, Hui WT, Wong SSY, Yau HH and Yuen KY. Association of Laribacter hongkongensis in community-acquired gastroenteritis with travel and eating fish: a multicentre case-control study. Lancet 2004; 363:1941-1947.

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Walsh TJ, Teppler H, Donowitz GR et al. Caspofungin versus liposomal amphotericin B for empirical antifungal therapy in patients with persistent fever and neutropenia. N Engl J Med. 2004; 351: 1391-402.
Klastersky J. Antifungal therapy in patients with fever and neutropenia--more rational and less empirical? N Engl J Med. 2004; 351: 1445-7.

The empirical use of broad-spectrum antibiotics, in combination with antifungal coverage has been the standard of care for managing patients with persistent fever and neutropenia, especially among those with cancer undergoing chemotherapy or receiving bone marrow transplantations. However, there has been some controversy as to the best antifungal agent to use under these circumstances. In a recently completed, multinational, randomised double-blind trial published in the New England Journal of Medicine, researchers set out to compare the use of caspofungin (Cancidas®) and liposomal amphotericin B in such patients. A total of 1095 patients were enrolled, and the study was partially sponsored by drug company. The primary study endpoint was a favourable response, as defined by a number of clinical criteria: successful treatment of baseline fungal infections; absence of breakthrough fungal infection; survival for 7 days after completion of therapy; resolution of fever; and no premature discontinuation of assigned treatment, either due to drug toxicity or lack of efficacy. Analysis of the primary endpoint showed that favourable responses were obtained in 33.9% and 33.7% of caspofungin and liposomal amphotericin B recipients respectively. Caspofungin was found to be superior to liposomal amphotericin B with respect to the following criteria: treatment of baseline infections, survival to 7-day follow-up, and discontinuation of study medication. No significant differences were seen between the two agents in rates of resolution of fever during neutropenia or documented breakthrough fungal infections.

Points to note: The results from this major study lend support to the empiric use of caspofungin as a less toxic alternative to liposomal amphotericin B in patients with neutropenic fever. Further trials comparing the use of caspofungin and voriconazole (another agent with proven efficacy in this situation), as well as a means to determine patient subgroups who are most likely to benefit from empirical antifungal therapy, are now issues which should be addressed in future studies.

Liaw YF, Sung JJ, Chow WC, et al. for the Cirrhosis Asian Lamivudine Multicentre Study Group. Lamivudine for patients with chronic hepatitis B and advanced liver disease. N Engl J Med. 2004; 351: 1521-31.

Worldwide and especially in Asia region, chronic hepatitis B is the cause of approximately 1.2 million deaths per year, primarily due to the occurrence of hepatic decompensation and hepatocellular carcinoma in affected patients. Lamivudine, a nucleoside analogue, is able to suppress hepatitis B virus (HBV) replication and improves hepatic fibrosis and liver function in patients with chronic hepatitis B. However, its effect on HBV-related advanced fibrosis and cirrhosis is unclear. Now, in an industry-supported, prospective, randomised double-blind trial conducted at 41 Asian and Pacific sites and recently published in the New England Journal of Medicine, researchers have evaluated the efficacy of lamivudine in patients with chronic hepatitis B and advanced liver disease. Participants were randomised to receive either oral lamivudine (100 mg daily; n=436) or placebo (n=215). At the second interim analysis, the study was prematurely stopped because the results met the predefined criteria for efficacy. At that point, after a median treatment duration of over 30 months, 7.8% of lamivudine recipients and 17.7% of placebo recipients showed overall disease progression, which was a statistically significant difference (*P*=0.001); 3.4% of lamivudine versus 8.8% of placebo recipients had worsening of their Child-Pugh scores, indicating deterioration in hepatic function (*P*=0.02); and hepatocellular carcinoma developed in 3.9% of lamivudine versus 7.4% of placebo recipients (*P*=0.047). HBV genotypic resistance in the form of YMDD mutation developed in 48.6% of lamivudine and 5.1% of placebo recipients. Among lamivudine recipients, Child-Pugh scores increased in 6.7% of those harbouring YMDD mutants, whereas less than 1% of those without YMDD mutants experienced

such an increase. Overall serious adverse events occurred in 12.4% of lamivudine recipients versus 17.7% of placebo recipients.

Points to note: This study demonstrates that long-term lamivudine therapy significantly reduces the incidence of hepatic decompensation and the risk for hepatocellular carcinoma in patients with advanced liver disease due to chronic hepatitis B. The development of HBV YMDD mutations in nearly 50% of the lamivudine-treated patients is a cause for concern; it remains to be seen whether these favourable results could be seen with the use of adefovir, an agent approved for treatment of chronic hepatitis B which appears to induce resistance much less frequently as compared to lamivudine. Of note, there is some preliminary evidence to suggest that combining lamivudine and adefovir might enhance treatment efficacy and reduce emergence of viral resistance.

Correspondence

Dear Editor,

In the June 2004 issue of our Society's Newsletter it is written “Lateral neck radiograph & flexible fibreoptic laryngoscopy are most helpful in making a diagnosis.” whereas in *Respiratory Medicine* edited by Gibson & Geddes, Chapter 35 under “Epiglottitis” it is written “On no account should the traditional X-ray of the neck be performed as putting the child in the position to obtain good quality radiograph has a high risk of inducing complete obstruction”.

I would be very grateful for your comments.

Regards,

Dr. Y. C. Chan, Consultant i/c, TB & Chest Unit, TWGHs Wong Tai Sin Hospital

Reply from Author, Owen T. Y. Tsang, Infectious Disease Control Training Centre, Hospital Authority

Dear Editor,

We are delighted to receive Dr Chan’s comment. In response, we have the following feedback:

We agree with Dr Chan that putting an irritated child under an X-ray machine to look for possible epiglottitis is dangerous.

We acknowledge the fact that use of lateral XR of the neck for the diagnosis of epiglottitis is controversial because:

1. Bansal A, Miskoff J, Lis RJ. Otolaryngologic critical care. Critical Care Clinics 2003;19:55-72 — point out that: “Thickening of the epiglottis is the classic radiographic finding and is present on 73% to 86% of lateral neck radiographs. The fact that supraglottitis can present with little epiglottic edema may contribute to this finding. To provide a more quantifiable evaluation of the lateral neck radiograph, Nezmek et al proposed comparing the width of the epiglottis to the anterior posterior width of the 4th cervical vertebral body. In patients without significant degeneration of the boney anatomy, this ratio should not be greater than 0.33. With this diagnostic threshold, a sensitivity of 96% and specificity of 100% for the diagnosis of acute epiglottitis was found in a retrospective review of 27 patients…..” but he also pointed out that “Because the lateral neck radiograph has sensitivity as low as 75%, laryngoscopy should be used to evaluate patients with a clinical suspicion of acute epiglottitis but with a negative neck radiograph….”
2. Frantz TD, Rasgon BM, Quesenberry CP Jr. Acute epiglottitis in adults. Analysis of 129 cases. JAMA. 1994 Nov 2;272(17):1358-60.----point out in the discussion that “lateral neck soft-tissue roentgenograms can demonstrate swelling of the supraglottitic region and are useful if laryngoscopy cannot be performed….”
3. Ames WA, Ward VM, Tranter RM, Street M. Adult epiglottitis: an under-recognized, life-threatening condition. Br J Anaesth. 2000 Nov;85(5):795-7. ---point out that “Otherwise, once the **airway is deemed safe**, a lateral, soft tissue radiograph may show a thickening of the epiglottitis…. Ducic and colleagues have proposed the “vallecula sign” to improve the diagnostic accuracy of soft tissue radiographs…”
4. Stroud RH & Friedman NR. An Update on Inflammatory Disorders of the Pediatric Airway: Epiglottitis, Croup, and Tracheitis. Am J Otolaryngol 2001;22:268-275.-----also point out that “When the diagnosis is in question and the child has no symptoms of airway compromise, radiographic examination can confirm the diagnosis and rule out foreign body, retropharyngeal abscess, or croup, all of which are included in the differential diagnosis. The lateral soft tissue neck film is the single most useful study.” Although we may not totally agree with it, we think that such XR can give the clinician more information once a patient presented with only mild SOB and sore throat.

5. A local study by Dr CH Chung. Acute epiglottitis presenting as the sensation of a foreign body in the throat. HKMJ 2000;6:322-4 — also think that " diagnosis can usually be established by lateral soft-tissue radiography of the neck" **BUT** "Indirect, direct, or flexible fibreoptic laryngoscopy are the most accurate investigations, and they are not associated with any complications."

We do not intend to say that lateral RX is the only modality of investigation. Instead we say "Lateral neck radiography **and** flexible fiberoptic laryngoscopy are most helpful in making a diagnosis." In fact, one would not send an acutely dyspnic or distressed patient for an XR without securing his or her airway. Our sentence is only a general statement without taking into consideration of many scenarios. We have to apologize for any misinterpretations that come up.

Regards,

Dr. Owen Tsang

Feedback from Dr. Y. C. Chan

Dear Editor,

Thank you very much indeed for the reply. The Society Newsletter is a high quality publication which I always recommend to my colleagues. The reason for me writing to you is, as Dr Tsang seems also to agree in the last paragraph of his reply, that the casual reader of the newsletter may not be alerted to the possible complication of performing this very useful investigation in the dyspnoeic child.

Best regards,

YC Chan

Meetings	
1-5 Dec 2004 Bangkok, Thailand	**9th Western Pacific Congress on Chemotherapy and Infectious Diseases (9th WPCCID) "Regional Infectious Disease Problems of Global Concern"** Western Pacific Society of Chemotherapy Contact: Pediatric Infectious Disease Society of Thailand Royal Golden Jubilee Building, Floor 9 Soi Soonvijai, New Petchburi Road Huaykwang, Bangkapi, Bangkok 10320, Thailand Phone: + 662 716-6534 Fax.: +662 716-6535 Web: www.wpccid2004.org www.idthai.org/wpccid2004
9-11 Dec 2004 Seattle, USA	20th Annual Infectious Diseases Conference **Tel: +1 425 262 3690** **Fax: +1 425 261 3695** **E-mail: jeri.sackett@providence.org**
5 March 2005 Hong Kong	**9th Annual Scientific Meeting** **Hong Kong Society for Infectious Diseases** Time : 2pm-9pm Venue: Theatre 2, Hong Kong Convention and Exhibition Centre Web: www.hksid.org
24-25 March 2005 Carlton Crest Singapore	Improving Patient Safety: Preventing Healthcare associated Infections Seminar Australian Resource Centre for Healthcare Innovations Contact: ARCHI National Office Phone: +61 2 4924 0900 E-mail: admin@archi.net
2 - 5 April 2005 Copenhagen, Denmark	**15th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID)** *European Society of Clinical Microbiology and Infectious Diseases* Contact: AKM Congress Service Phon: +41 61 686 77 11 Fax: +41 61 686 77 88 Email: info@akm.ch Web: www.escmid.org
9-13 April 2005 Busselton W. A. Australia	**Annual Scientific Meeting** **Australasian Society for Infectious Diseases** Contact: Dart Associates PO Box 781, Lane Cove, Australia 2066 Phone: +61 2 9418 9396 Fax: +61 2 9418 9398 E-mail: dartconv@mpx.com.au Web: www.racp.edu.au/asid
15-18 June 2006 Lisbon, Portugal	**12th International Congress on Infectious Diseases** Contact: International Society for Infectious Diseases 181 Longwood Avenue Boston MA 02115, USA Phone: 617-277-0551 Fax: 617-731-1541 Web: http://www.isid.org