Highlights from meeting "Seminar in Infectious Disease – Focus on paediatric infections"

Viral respiratory infections in children

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Influenza is well known to cause complications, hospitalisations and death among very young children and those with certain underlying conditions. Attack rates in healthy children range from 10% to 40%. Even in healthy children, influenza causes a wide spectrum of diseases that include lower respiratory tract disease, myositis, nervous system manifestations, Reye's syndrome and febrile seizures. We documented a higher incidence of febrile seizure associated with influenza as well as multiple seizures occurring during the same illness (1). In 2000, Neuzil et al. reported that influenza also caused a significant disease burden in children without underlying conditions in the United States, with annual excess hospitalisation for cardiopulmonary conditions of 104/10,000 (<6m), 50/ 10,000 (6-<12m), 19/10,000 (12-36m), 9/10,000 (3-<5y) and 4/10,000 (5-<15y). It accounted for 6-15 outpatient visits/100 children and 3-9 courses of antibiotics/100 children (2).

We conducted a population-based study defining influenza-related hospitalisation in children in Hong Kong (3). 8797 children < 15 years were admitted in 1998 and 1999 during the 14-week periods when influenza predominated. There were only 282 (3.2%) cases with > 1 risk factors. The adjusted rates of excess hospitalisation for acute respiratory disease that were attributable to influenza were 278.5 and 288.2 per 10,000 children less than 1 year of age in 1998 and 1999, respectively; 218.4 and 209.3 per 10,000 children 2 to less than 5 years of age; 57.3 and 20.9 per 10,000 children 5 to less than 10 years of age; and 16.4 and 8.1 per 10,000 children 10 to 15 years of age. The mean duration of hospitalisation was 3.1(±5.4) days, resulting in a total mean of 25,935 and 16,960 paediatric bed-days in 1998 and 1999, respectively. This accounted for 8.1% and 5.4% of total annual Hospital Authority paediatric bed-days and a mean annual cost of $84,677,775 and $55,374,400 for 1998 and 1999, respectively.

The human Metapneumovirus (HMPV) was first discovered in the Netherlands (4). It was subsequently identified in the nasopharyngeal aspirates from 28 children suffering from respiratory tract infection collected over the past 20 years. Twenty-seven of these children were < 5 years (thirteen < 12 months). The clinical symptoms of HMPV were thought to be similar to respiratory syncytial virus (RSV), ranging from mild respiratory problems to severe cough, bronchiolitis and pneumonia, and often accompanied by high fever, myalgia and vomiting. Some were hospitalised and needed mechanical ventilation. Seroprevalence data in the Netherlands showed that the virus has been circulating in the Netherlands at least since 1958.

HMPV was found to cause respiratory illness in the community. 9/711 swabs from patients from < 1 year to over 65 years of age with flu-like illness who attended sentinel practices in Wales and England were found to be positive (5). HMPV has been associated with severe respiratory disease and death in a young girl with acute lymphoblastic leukaemia (6). Jartti et al. found HMPV in 10 (8%) of 132 consecutive children 3 months to 16 years of age admitted with acute expiratory wheezing in Finland (7). The median age of these children was 7 months. Five of them had bronchiolitis, 4 with wheezing bronchitis and 1 with newly diagnosed asthma.

In Hong Kong, we performed a systematic sampling of children < 18 years of age admitted with acute respiratory tract infection to Queen Mary Hospital over a 13-month period (8). Detection of common respiratory viruses was done by IF and culture while HMPV was detected by RT-PCR. HMPV infected children were compared to age-matched RSV or influenza infected controls. 587 patients were studied. We found 32 (5.5%) positive for HMPV with a mean age of 31.70 ± 18.7 months. Clinical diagnoses include pneumonia (36%), asthma exacerbation (23%) and bronchiolitis (10%).

Individuals over 2 years of age in the Netherlands had higher antibody titres, suggesting boosting of antibody responses as a result of reinfection. In addition, a child in Canada had 2 different isolates in 2 consecutive winters 10 months apart. It is currently believed that most children are

infected by 5 years of age, with reinfections, possibly repeatedly, later in life.

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Office management of urinary tract infection in children

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Urinary tract infection (UTI) is common in children. It has been estimated that 2% of boys and 8% of girls have at least 1 episode before the age of 7 years and it represents about 2% of hospital admissions. Most occur before the age of 5 years. More boys are affected in the first year.

UTI is important for its acute phase morbidities (urosepsis, convulsion) and its long-term morbidities secondary to scarring such as hypertension (5-10%) renal impairment [5-20% of end-stage renal disease (ESRD) due to chronic pyelonephritis as a result of severe renal scarring] and complications during pregnancy. And it also signifies the presence of underlying structural abnormalities (mostly vesicoureteric reflux) of the urinary tract in a large number (30-40%) of children.

Diagnosis of UTI is based on the demonstration of significant growth of bacteria in a properly collected urinary specimen. The number of colony forming unit (CFU) required for diagnosis depends on the method of urine collection. For supra-pubic tapped urine (SPTU), any growth is significant; for catheterised urine (CSU), a CFU count of > 103 - 104/ml is significant; and for midstream urine (MSU), a CFU count of single organism of > 10^5/ml is significant. Proper collection is important. False negative results may be due to improper handling or prior antibiotic treatment before culturing; and contamination can lead to false positive results. Bag urine is undesirable in the diagnosis of UTI for its very high contamination rate.

A high index of suspicion is necessary for the diagnosis of UTI. The younger the child, the more non-specific will be the clinical features (fever with no focus of infection, neonatal jaundice, failure to thrive, irritability, unwell, decreased appetite, vomiting, diarrhoea). It is also in this group of young infants that the kidneys are more prone to damage

after UTI with its subsequent long-term sequelae. Delayed diagnosis leads to delayed treatment with kidney damage and possible long-term problems. It is only in older children that UTI can present with its typical symptoms of dysuria, frequency, loin pain, and foul and turbid urine. Voiding dysfunction (urgency+/-precipitancy, frequency, infrequent voiding, urinary retention) has now been regarded to be a predisposing factors for UTI. Treatment of it can prevent recurrence of UTI and can hasten the resolution of vesicoureteric reflux (VUR) if present. It is important for us to look into it.

In suspicious case, one can save bag urine for screening with "stix" test (for leucoesterase and nitrite) and / or microscopy. Positive leucoesterase and nitrite tests have a sensitivity of 88-93% and have a specificity of 72-93% for UTI; while positive leucoesterase or nitrite or microscopy give a sensitivity of 99.8% with a lower specificity of 70%. Any positive results should be followed by a properly collected urine for culture and the child should be treated as UTI while awaiting culture result. Negative screening should also be followed by urine culturing if the suspicion of UTI is high. In urgent situation where early start of antibiotics is necessary, urine should be obtained by either SPTU or CSU for culturing. A sick child with suspected UTI should warrant hospital admission.

Antibiotic treatment is usually given for 7 to 14 days depending on clinical response. Afterwards, the child will be put on prophylactic antibiotics until imaging results are available to direct subsequent management. To prevent recurrence, the following points have to be paid attention to: a) good fluid intake to promote good urine flow; b) avoidance of constipation and subsequent possible bladder voiding dysfunction; c) in girls, cleaning after defecation in a backwards direction and avoidance of bubble bath to prevent perineal irritation; d) consideration of circumcision in boys with recurrent UTIs despite general measures and prophylactics; e) treatment of voiding dysfunction; f) double voiding in those with severe grade VUR.

Asymptomatic bacteriuria is usually caused by low-virulence bacteria with no risk of kidney damage and the eradication of it by antibiotics can result in replacement by more virulent ones with risk of kidney damage

(2). The practice of routine follow-up urine culture has been gradually falling out of favour. However, one has to be sure the bacteriuria is really asymptomatic; and this is quite difficult sometimes especially in young infants.

A firm diagnosis of UTI is important for after diagnosis the child may be subjected to a battery of invasive and costly investigations to reveal underlying urological abnormalities and to assess the degree and extent of renal injury. The extent of investigations will be dependent on the age and sex of the child and the severity of clinical manifestations (and the availability of the investigatory tool). In general, upper tract (kidneys) can be assessed with ultrasound examination and the lower tract (bladder) by micturating cystourethrogram or isotopic voiding cystogram, and kidney damage by DMSA scan. VUR is the commonest abnormality identified and has the tendency to resolve with time even for severe grade VUR. Those with renal scar should have long-term follow-up for possible complications.

In conclusion, UTI in children is common and important. A firm diagnosis by a properly collected urine culture is necessary. The child should be treated for at least 7 days, and be investigated and managed accordingly afterwards.

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Sexually transmitted and lifestyle associated infections in adolescents

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Introduction

Adolescence is the time period in a person's life when he or she develops from childhood to adulthood. It is a stage of rapid metamorphosis in one's value system and hence behavioural pattern. It is an opportunity for one to regain and master his/her locus of control. The adolescents explore and experiment in the perplexing world however, exposing themselves to hazards that are not familiar to them.

Peer recognition and intimacy that can be mis-judged as experience in drug and sex, is something pursued by most adolescents. Fuelled by the uncensored flood of information via the internet, the value and behaviour of the adolescents will be modelled in a way that is conducive of health hazard of various kinds. Sexually transmitted infections (STIs) and HIV among others are the notorious examples of lifestyle-associated diseases.

Trends of sexually transmitted infections and sexual behaviours among local adolescents

Comprehensive data is not available concerning STIs in Hong Kong. Data collected by the Government Social Hygiene Service (GSHS) can be used to highlight some of the recent local trend. From 1991 to 2000, new cases of all types of STIs increased from 12446 to 28541 in Social Hygiene Clinics (SHCs) attendees along with an increase from 394 to 976 for adolescents (1). Adolescents constitute less than 5% of the total new STI cases. It can be inferred that chlamydial infection is the commonest genital tract infection among the adolescents (2, 3, 4).

According to the Hong Kong Family Association Sexuality Survey conducted in 2001 (courtesy of Dr Shum PY), 8.7% and 5.2% of male and female F3-F7 students reported sexual experience. These rates were 1.2% and 0.2% respectively in 1991. The mean age of sexual debut was

18.2 years. Sixty-one percent of 18-27 years old respondents claimed that they had premarital sex from 15 to 19 years of age. Among young female aged 18 to 27 years of age, 14% had ever been pregnant. It can be concluded that the local young people have early sexual exposures and a substantial number of them do not use birth control (including condom) while having premarital sex. These indicate their vulnerability to STIs. Given the fact that many of these unplanned pregnancies will end with abortion, both legal and illegal, they will put themselves at additional risk of genital tract infection.

The trend in sexual behaviours of the local young people can be accounted for by the following factors: local taboo in sex and sex education not keeping in pace with the development of the young people, flooding of pornographic information fuelled by the internet, increased mobility for recreational purposes and the recent hyperendemicity of substance abuse among the young people.

Substance abuse among young adolescents in Hong Kong

According to the 2000 Survey of Drug Use among Students commissioned by the Action Committee against Narcotics conducted by Lau (courtesy of Dr Lau TF), a high percentage of current and ever users of alcohol, tobacco, heroin and psychoactive substances were observed. An increasing trend was noted as compared to findings in 1992 and 1996. In 2000, 30.2%, 0.9% and 2.1% of the respondents claimed that they were current users of alcohol, heroin and psychoactive substances respectively. The number of ever users was even higher and 79.7%, 2.6% and 4.1% claimed that they were ever users of this substance respectively. For the current psychoactive substances users, 35% used at least once per week while 57% at least once every fortnight. Of the ever psychoactive substances users, 29.8% admitted that they had sexual intercourse after drug use. It can be envisaged that the chance of unprotected sex and with multiple concomitant partners might be high. In addition, the number of these young people who engaged in injecting drug use and commercial sex (in exchange of money for drug) could not be under-estimated (5). These behavioural patterns facilitate the transmission of STIs and blood borne infections including HIV.

Local service provision to adolescents with STIs

Sexual health and health problem related to substance abuse should be explored proactively by the caring physicians. A non-judgmental and caring attitude is crucial. Confidentiality should be respected in the appropriate settings. The general principles in the management of STIs in adolescents are not much different from the adults. Apart from drug treatment, counseling on safer sex practice and prompt medical advice seeking should be re-emphasized. The caring physicians should also keep an inventory of medical expertise and social resources relevant to caring of the adolescents. The Government SHCs provide walk-in service for clients with STIs. Registration fee and referral are not required under the current policy. The Youth Health Care Centres of the Hong Kong Family Association also provide one-stop service concerning sexual health to the young people, however, adopting a cost recovery policy. The Accident and Emergency Department of Kwong Wah Hospital runs a crisis clinic for those victims of sexual abuse/assault. Doctors can also access to the Social Hygiene Service recommendations on medical treatment of the common STIs in Hong Kong in the website: http://www.aids.gov.hk; basic information on commonly asked questions in human sexuality is available in the local website: dsonline.com.hk; and leaflet on STI/HIV and substance abuse is available in the Red Ribbon Centre of DH. The input from the primary care physicians and other related health workers is invaluable in enhancing the sexual health of the youngsters of the local community (6).

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Case report
Septic arthritis complicating chickenpox infection in a 6 months old baby

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A previously healthy 6-month-old girl was hospitalised with a 7-day history of chickenpox and persistent fever. The maximum temperature was up to 39"C. General practitioner was consulted one day prior to admission, and symptomatic treatment was given. Acute left ankle swelling with local redness noticed the day before admission, and the infant refused to bear weight.

On examination, her general condition was good, despite a fever of 38.7°C. The vesicular rash was mostly scabbed. One infected chickenpox lesion was noticed on the left buttock. Her left hip and left knee were in flexed position when she was held to bear weight. Mild swelling, erythema, local tenderness and increased temperature and hotness were found over the dorsal and medial aspects of the ankle joint. Passive movement caused pain and the range of movement was decreased at her left ankle.

Plain radiograph of left ankle showed only soft tissue swelling. Full blood count showed a WBC of 9.5 x IO^L, with normal haemoglobin and platelet count. The working diagnosis was chickenpox complicated by septic arthritis. Intravenous ampicillin and cloxacillin were commenced. Orthopaedic surgeon was consulted and conservative treatment was advised.

On the second day, fever came down. However, the joint swelling, erythema and hotness persisted around the joint. Reports of the initial laboratory investigations further clarified and the clinical suspicion: C-reactive protein was up to 51.1 mg/dL. Gram stain of the initial blood culture revealed Gram-positive cocci in clusters.

Emergency left ankle joint aspiration performed under fluoroscopy yielded 1 - 2 ml of turbid fluid, and was followed by formal arthrotomy.

Joint fluid was drained and sent for culture. The joint space was thoroughly irrigated.

Staphylococcus aureus, which was sensitive to cloxacillin was subsequently recovered from the blood culture. Joint fluid culture revealed no organism. Erythema and swelling of the left ankle gradually subsided with continued intravenous cloxacillin. She started to have weight bearing of the left lower limb at the end of the second week. Antibiotic was switched to oral flucloxacillin after 2 weeks. Serum for bactericidal titer against the Staphylococcus aureus isolated showed a peak of 128 and trough of 32, confirming the adequate treatment with oral antibiotics. The girl was discharged 3 weeks after admission, when she attained full weight bearing of the left lower limb with normal range of movement of the left ankle. A total of 4 weeks of antibiotic therapy was given. Follow-up examination revealed no permanent sequelae or disability.

Discussion

Septic arthritis is a less known complication of varicella. There are only a few anecdotal reports in the literature. Septic arthritis per se is infrequently seen in children nowadays and often not managed by paediatricians.

In retrospect, the case could have been managed more aggressively with early diagnostic joint aspiration and timely surgical intervention in addition to antibiotic therapy. The following is a brief review of the condition in children.

The most commonly involved joints in paediatric cases of septic arthritis are knees (41%), hips (23%), ankles (14%) and elbows (12%). 94% of cases have monoarticular involvement (l). Fever, pain, hotness and swelling of joint in the absence of a history of trauma should lead to clinical suspicion. However, these typical signs and symptoms may be completely absent in young infants and neonates (2).

Early diagnosis is the single most important factor in determining the outcome of septic arthritis (3, 4).

ESR is increased in 90% of cases (1, 5), including young infants (6), and often to high levels. White cell count is raised in 30 to 60% of cases and a left shift may be seen in up to 2/3 of the patients (2, 6). Blood culture is positive in about 40% of the cases (2), and the yield is of course affected by prior antibiotic therapy.

Diagnostic needle aspiration of the joint is of paramount importance. It should be done before starting antibiotics. Gram stain alone may confirm the diagnosis in 30 to 50% of cases (7). This is especially important if blood and joint aspirate cultures are negative as a result of prior antibiotic therapy. It also provides guidance for initial antibiotic selection. Synovial fluid culture is positive in 80% of established septic arthritis (2). Total synovial white cell counts range from 25,000 to 250,000 cells/mm (3). The diagnosis of sepsis is highly probable if the total synovial white cell count exceeds 50,000/mm3, of which > 90% are polymorphs (8).

The destructive effect of the infected synovial fluid in septic arthritis on articular cartilage has been shown by different studies (9, 10). An animal study demonstrated that glycosaminoglycan and collagen depletion began within 8 hours of infection and could only be prevented by pretreating experimental rabbits with antibiotics prior to the injection of bacteria 11). This points out the fact that in addition to antibiotics, which control the infection, direct interventions such as drainage and lavage are needed to prevent damage to the cartilage. Multiple aspirations, arthroscopy, and arthrotomy have all been used with reported success in case series. Direct antibiotic instillation into the joint may cause a chemical synovitis and has no additional beneficial effect on treatment.

It cannot be overemphasised that antibiotic therapy should only be initiated after synovial fluid and blood culture are saved. As mentioned above, Gram stain of the synovial fluid provides a guide to the initial choice of antibiotics. However, if it is not informative, empirical therapy should target the most likely organisms according to the patient's age. The most common organisms in infants are Staphylococcus aureus, followed by Group B Streptococcus and Haemophilus influenzae (1).

Cefuroxime is a good choice to cover the above 3 organisms (13).

In children over 1 year, Staphylococcus aureus and streptococci are the most common (1). Oxacillin, cloxacillin, flucloxacillin, nafcillin or clindamycin are appropriate. Penicillin G can be given instead if Streptococcus or susceptible Pneumococcus is subsequently isolated (13). For gonococcal arthritis, which is most common in adolescents, ceftriaxone is the initial choice. Penicillin can only be given if the isolated organism is susceptible (13). There is no definite data on the required duration of antibiotic therapy for uncomplicated septic arthritis. Older textbooks commonly recommend a minimum of 4 to 6 weeks. More recent references suggest a shorter course of treatment, e.g. 2 weeks for uncomplicated H. influenzae, streptococci or Gram-negative cocci; 3 weeks for Staphylococcus or Gram-negative bacilli other than H. influenzae (12); and 7 to 10 days for gonococcal arthritis with intravenous ceftriaxone (13).

Once the patient is receiving oral antibiotics, serum bactericidal titer (SBT) must be monitored to ensure adequate drug levels to effect cure. The SBT should be at least 8 for Staphylococcus aureus. For highly susceptible bacteria, such as pneumococci and Group A Streptococci, titers are usually greater than 32(14). The commonest complication of chickenpox is still secondary bacterial skin and skin structure infection. However, a high index of suspicion for septic arthritis should be maintained if the apparent cellulitis or overlying skin infection across a joint is associated with limitation of joint movement or weight bearing. With early diagnosis and timely combined medical and surgical interventions, the prognosis is favourable.

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