

Meetings

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Common cutaneous infections and infestations in the elderly

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Skin is the largest organ in the body that has multiple functions. It acts as an important innate host defense against pathogens from outside world. Adaptive immune responses in skin also play an important role for host defense against various microbes. These microbes however can still invade the skin and damage our body by gaining new genetic traits, secretion of toxins or weakening of our defenses through environmental factors that help the microbes to bypass the protective function of skin. Atrophy of epidermis and dermis with reduced resistance to external injury, diminished water-binding capacity, reduced function of skin appendages, reduced vascularity and slower epidermal turnover time and healing are observations in natural skin ageing. Natural ageing of skin together with photoageing can jeopardize the skin functions making the skin of the elderly more vulnerable to infections and infestations.

A local survey for problems of feet confirmed that onychomycosis and tinea pedis were common in male & the elderly¹. Though there was no formal survey in the elder local population for identifying types of skin infection and infestations, inferences can be drawn from data of the public skin clinics. In the year 2002, the commonest skin infections/infestations found in Social Hygiene Service² were: cutaneous fungal infection (10.78% of total annual new skin diagnoses), cutaneous wart (10.4%), herpes infection (1.13%), pyoderma / cellulitis (1.1%) and scabies (0.52%).

The correct clinical diagnosis supported by microbiological confirmation for pyoderma / cellulitis will assist us to give the most appropriate treatment though the underlying causes or conditions e.g. poorly controlled diabetes mellitus must be addressed and managed. There were evidences to show that topical antibiotics were as effective and good for the elderly as the systemic antibiotics³. With topical antibiotics, there will be

fewer adverse effects and problems of drug interactions in elderly.

Herpes zoster is common in the elderly and so does its complications. The involvement of ophthalmic branch of trigeminal cranial nerve should be managed carefully because of complications from involvement of eye (uveitis, keratitis, conjunctivitis) and it is more commonly associated with postherpetic neuralgia. Postherpetic neuralgia is usually defined as pain persisting for more than 3 months after herpes zoster skin lesions have healed. In severe cases, referral to pain clinic may be necessary after counselling, supplemented with the use of tricyclic antidepressants e.g. amitriptyline and topical anaesthetics such as EMLA cream.

Cutaneous fungal infections are quite common in the elderly and most of these patients do not consult doctors for this seemingly trivial disorder. It can be confused with eczematoid eruption. Typical ringworm infection is characterised by rash with active margin, follicular accentuation and central clearing features. Tinea pedis can lead to recurrent cellulitis and erysipelas but the most persistent and diagnostically difficult problem is onychomycosis. There have been evidences to demonstrate the efficacy of newer systemic antifungals but whether these should be routinely used in the elderly depends on the probability of drug interactions, renal and liver status of the elderly. Supervision, monitoring and counselling for proper administration are most important to ensure safe use of these medications in the elderly.

Scabies, though less commonly encountered in tertiary referral centres in public skin clinic, is an important skin infestation that is commonly encountered in home for elderly and other institutions. There are newer and safer topical medications for management of scabies e.g. 5% permethrin preparation (lotion or cream) but the old formulation (5% benzyl benzoate emulsion) still works well if scabies is properly managed. Crusted scabies is a highly contagious condition that accounts for outbreaks in institutions. The treatment approach needs to be more aggressive with infection control measures. There have been many case reports for the efficacy and safety of oral ivermectin in a single dose of 200 microgram per kilogram body weight. However, it is still not a licensed medication for this condition in many parts of the world.

Other rare types of skin infestation e.g. myiasis may be encountered in our daily practice and occasionally do generate much interest in the media. It is the duty of every medical practitioner to update one's knowledge continuously in this ever-changing environment that can make many previously benign microbes more virulent and prevalent. The knowledge of preventing skin

infection and infestation together with measures to make the skin less aged and more resistant to pathogens will be invaluable advice to our clients⁴.

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The management of respiratory infections in old age homes

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The following paper focuses on nursing home-acquired pneumonia (NHAP), influenza-like illness (ILI), tuberculosis (TB) and some clinical aspects of SARS in the elderly.

NHAP is different from community-acquired pneumonia (CAP) in the free-dwelling elderly. The incidence of NHAP is 99-912/1000 persons per year as compared to 34/1000 for CAP. Risk factors predisposing to NHAP include poor functional status, presence of contractures, hyperextended neck, dysphagia, nasogastric feeding, advanced age, male sex, malnutrition, and the use of benzodiazepines. The pathogenesis of NHAP can be understood as anterograde aspiration of nasopharyngeal flora and retrograde aspiration of gastric contents in the face of failing host defense. In 30-50% of cases, a clear aetiological organism cannot be identified. The majority of nasogastric tube related aspirations can be a pneumonitis of chemical nature. Common pathogens isolated include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus* and *Moxarella catarrhalis*. Gram negative organisms are also implicated resulting from migration of small bowel organisms to contaminate the gastrum and colonise the oropharynx. During epidemics, viral infections becomes prevalent. Anaerobic infections

varicella four days or less before delivery or two days after (11). The recommended dose is 125 units intramuscularly after birth.

VZIG should also be given to pregnant women who are susceptible to VZV and are exposed to varicella or herpes zoster. It should be administered within 48 hours of exposure but may still be effective at 96 hours. The recommended dose is 625 units IM. The major benefit of VZIG is to diminish the severity of maternal disease. There is no evidence to confirm or refute whether administration of VZIG to the mother prevents or attenuates congenital VZV disease (11).

Vaccination

A live attenuated varicella vaccine is recommended for susceptible children under age 13 years and susceptible young adults (This is only in the USA). The seroconversion rate after vaccination is approximately 82% in adults and 91% for children. The vaccine should be given in two doses four to eight weeks apart for healthy adolescents and adults. The American Association of Pediatrics recommends that the chickenpox vaccine should be given to all healthy children between 12 months and 18 years; children between 12 months and 13 years who have not been immunized or who have not had chickenpox should receive 1 vaccination while children 13-18 years of age require 2 vaccinations 4-8 weeks apart; the vaccine has been added to the childhood immunization schedule for infants 12-28 months of age and children 11-12 years of age who have not been vaccinated previously or who have not had the disease; it is recommended to be given with the measles, mumps and rubella vaccine.

Pregnant women should not receive the vaccine due to the theoretical risk of inducing congenital disease. Non-pregnant women who received the vaccine should avoid pregnancy for at least one month thereafter (12).

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Varicella pneumonia in pregnancy is a medical emergency. The mortality rate in untreated pregnant women is in excess of 40%. Supportive care and acyclovir are the mainstays of therapy. In one retrospective review of 21 cases of varicella pneumonia in pregnant women treated with acyclovir, the mortality rate was 14%, a value lower than expected in untreated women (4).

Fetal effects of VZV

A large prospective study evaluated the fetal outcome in mothers infected with various viruses (rubella, measles, mumps and VZV); there was no increase in the incidence of spontaneous abortion with VZV (5).

Congenital varicella syndrome

The infant is born with multiple reddish pigmented areas on the thigh, hypoplastic lower limbs, clubbed feet, ocular problems (cataract, chorioretinitis, Horner syndrome, microphthalmos, nystagmus and optic atrophy), cortical atrophy, mental retardation, low birth weight and failure to thrive.

One report compared pregnancy outcome of 106 women with clinically diagnosed varicella in the first 20 weeks of pregnancy to that of 106 age-matched non-exposed controls. Congenital defects occurred in four infants born to VZV-infected women and two controls. The mean risk of embryopathy was 2.2% (6). Similar findings were noted in another series, a 2% risk of embryopathy among 351 pregnancies infected between 13 and 20 weeks, and a 0.4% risk among 472 pregnancies infected prior to 13 weeks (7).

The most recent prospective series reported only one case of congenital varicella syndrome among 231 infants of mothers infected during pregnancy. There were no documented cases of congenital varicella syndrome among infants of women with onset of the typical rash before 20 weeks of gestation; the one affected infant was born to a woman whose rash developed at 24 weeks (8).

The risk of congenital varicella syndrome appears to be small, around 0.4 to 2%.

Neonatal varicella

The mortality rate is up to 25%. Fatality rate is significantly increased when symptoms of maternal infection occur less than 5 days prior to delivery to 2 days after delivery.

The clinical picture is variable. Fever may develop within the first day of life followed by vesicular eruption. In mild cases, the lesions heal within seven to ten days, however, in disseminated disease, visceral involvement may ensue.

Administration of varicella-zoster immune globulin (VZIG) within one day of life to infants born to women with active varicella infection at delivery may ameliorate neonatal disease (Depending on different guidelines, VZIG should be administered to the infant as soon as possible for cases of maternal infection with onset around 1 week before to 1 week after delivery.).

Diagnosis

The diagnosis of varicella is usually made clinically. The virus may be visualized under electron microscopy in vesicular fluids, although it could not be differentiated from other herpes viruses. Direct antigen detection using the immunofluorescence test on cells from vesicle bases may also confirm the diagnosis. VZV may be cultured from vesicular fluid. Serological tests may help document acute infection in confusing cases or indicate immunity. Ig M antibody may be detected as soon as three days after VZV symptoms appear and Ig G may be detected as early as seven days after varicella symptoms.

Prenatal diagnosis of fetal varicella infection is possible. Ultrasonography can detect limb abnormalities in affected fetuses. Fetal blood has been obtained via percutaneous blood sampling for VZV antibody or DNA on blood or amniotic fluid (9,10)

Prevention – 2 modalities

Varicella-zoster immune globulin

It is recommended that VZIG should be administered to neonates whose mothers develop

however are rare. The practice of routine anaerobic coverage with metronidazole is questionable. Elderly people with NHAP complain less of dyspnoea, pleuritic pain, chills or cough. Residents of old age homes however may present with deterioration of general condition or delirium. A poorly verbalized history often results in inadequate documentation and assessment. However, taking note of the time of clinical onset, association with feeding schedules, posture during feeding and characteristics of previous episodes will guide subsequent management and prevention. NHAP can largely be managed in the residential setting, and is associated with lower mortality and preservation of functional status. Recognition of clinical severity is important. A respiratory rate of greater than 30/min, pulse 120/min, and altered mental status are associated with increased mortality, and this group would warrant hospitalisation. Guidelines for treatment of NHAP on site are available. An oral antibiotic should be chosen such as amoxicillin with clavulanate, a 2nd or 3rd generation cephalosporin or a respiratory quinolone. If clinical condition requires, parenteral antibiotics can be administered intramuscularly and preferably on a daily basis. One such option is ceftriaxone. If retrograde aspiration of milk products is highly suspected, nasogastric feeding should be suspended and the fever observed for spontaneous defervescence in 24 hours before considering antibiotics. Hydration can be maintained by subcutaneous fluids. Such practice in a residential setting need to be developed. NHAP can be reduced with annual influenza vaccination, attention to oral hygiene, proper posturing during and after feeding, control of reflux, reducing the use of acid lowering agents, and restraints either chemical or physical. The medical advisor to the old age home should be vigilant during a community epidemic to help identify the earliest sign of an outbreak of viral infections in the old age home.

Influenza in the elderly can be lethal but preventable. Attack rates in long term care facilities are 20-40%, with mortality of 15-30%. Most deaths occur in aged persons above 65yrs old. 10% of infected elderly people may require more intensive care. Mortality is related to pneumonia and exacerbation of cardiopulmonary diseases, especially in persons with underlying metabolic and renal comorbidities, and immuno-suppressed states. A low rate of staff and residential client vaccination, large homes, closed wards, common dining areas and poor ventilation are also risks factors for an institutional outbreak. Yearly vaccination of residents and staff 4-6 weeks before an epidemic reduces hospitalisation rates, mortality,

duration of illness and exacerbation of cardiovascular morbidity; although efficacy of vaccination may be as low as 30-40% in elderly in preventing influenza infection. Clinical features of influenza include a spiking temperature of 38°C or above and constitutional manifestations of chills, headache, malaise, sore throat or dry cough. In Hong Kong, influenza A activity is expected to commence in January and peak in February to March. Another smaller peak may recur in July to August. The first cases should be confirmed with rapid diagnostic tests. An institutional outbreak is defined as occurrence of 2-3 cases within 2-3 days. Infected clients should be started on a neuraminidase inhibitor or M2 channel inhibitor within 48 hours. Ill clients should be cohorted for 5-7 days. During a large scale outbreak, other residential clients should receive chemoprophylaxis throughout the epidemic irrespective of vaccination status, which can prevent 60-80% of illness. All new staff and clients should be vaccinated and receive 2 weeks of chemoprophylaxis. Contacts and movements should be reduced among clients and visitations should be stopped.

A respiratory syncytial virus (RSV) outbreak can parallel that of influenza. RSV outbreaks are less explosive than influenza, but can cause severe disease in the frail elderly and the immunocompromised or persons with underlying cardiopulmonary diseases. Management is supportive with oxygen and bronchodilators. A vaccine is not available. Rapid test and viral culture are useful for diagnosis if respiratory tract aspirates are obtained early during the clinical course. The diagnosis could also be confirmed by serology. Clinically, RSV is associated with more rhinorrhoea and wheezing, whereas Influenza has more systemic and gastrointestinal symptoms and a higher spike of fever. Infection control measures for RSV follow that of influenza.

Tuberculosis continues to be a threat to the health of the community of Hong Kong. The ageing population and the high past tuberculosis burden increase the prevalence of TB in the elderly probably through reactivation of latent disease in a host with failing immunity. Residents of old age home in a highly dependent state pose diagnostic and management challenges. Conventional investigations may fail to reveal positive microbiological or histological evidence of TB infection. Treatment of TB in the frail elderly should start with a mild regime e.g. isoniazid and ethambutol, adding other drugs when an initial response is observed. Frail elderly are prone to complications from multi-drug regimes at the start.

Challenges in the diagnosis of SARS in the frail elderly lie in the modified presentation, uncertainty in exposure, apparently prolonged incubation, masking by underlying comorbidities, over-diagnosis during an epidemic, and a high mortality of 75% in patients aged 75 years and above. The lengthened incubation may be due to presentation or clinical diagnosis made only at phase 2 in the 2nd week of disease. The masked or subclinical first phase renders the infected elderly a silent shedder of the virus. SARS intensifies the inflammatory cascade which overwhelms the compensatory mechanisms resulting in mortality. Death can also be related to exacerbations of comorbidities and complications from treatment interventions. Being largely nosocomial in nature, prevention of SARS in the elderly should take a community approach in offering medical treatment for most medical conditions e.g. NHAP, gout, mild to moderate COPD and heart failure etc., in order to reduce unnecessary admissions to a hospital. During an epidemic, the infection control loop is closed with proper cohorting of residential clients discharged from hospitals.

RNA interference in viral infections

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Introduction

RNA interference (RNAi) is also known as RNA silencing or posttranscriptional gene silencing. It is a process that responds to double-stranded RNA by silencing gene expression in a sequence specific manner. The exogenous double-stranded RNA acts as a guide to target and destroy the specific cellular or viral RNAs. The phenomenon of RNAi was first discovered in the nematode worm *Caenorhabditis elegans* as a response to double-stranded RNA. The process is conserved in a diverse variety of organisms like plants, *Neurospora* and *Drosophila spp* and mammals. Plants responded to RNA viruses by targeting viral RNAs for destruction. RNAi is one of the antiviral mechanisms in plants.

Mechanism of post-transcription gene silencing

RNAi is mediated by small interfering RNAs (siRNAs) that are produced from long dsRNA of exogenous or endogenous origin by an endonuclease of the ribonuclease-III type which is called the dicer enzyme. The dsRNAs are converted into smaller fragments with 21-25 nucleotides in length by the dicer enzyme. A nuclease complex called RNA-induced silencing complex (RISC) is formed with these siRNAs and other domains. The sequence of the siRNAs acts as a guide for the targeting destruction of the mRNA inside the cells. The mRNA complementary to the siRNAs will be cleaved by this complex and cannot be translated into functional proteins.

Potential applications of RNAi in infectious diseases

siRNAs can clear viral infections without causing any visible harm to the infected cells. In our knowledge of immunology, clearance of virus from the mammalian host requires destruction of the infected cells, either by the action of the immune system or by apoptosis induced by the virus. But in the use of RNAi, it was observed that the reduction and even clearance of viral genomes can be achieved in the absence of significant cytopathology. It was reported that siRNA can effectively clear poliovirus from infected HeLa cells and also clearing of Hepatitis C replicons in cell culture. For some chronic viral infection like hepatitis B, hepatitis C and HIV, RNAi shed a light on the possibility of clearing the viral genome from the infected cells. The treatments for these infections at the moment are not without side effects. Although there are still a lot of problems and obstacles that need to be solved before it can be applied to human body, this new modality of treatment may hopefully be applicable to maintaining human health in the near future.

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Chickenpox in Pregnancy

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Rarely, varicella causes problems in pregnancy for the mother and her unborn child. The incidence of varicella is estimated to be 1 to 5 cases per 10,000 pregnancies (1). The low incidence is largely related to immunity due to prior infection.

Varicella (chickenpox) and herpes zoster (shingles) are caused by varicella-zoster virus (VZV), which is a member of the herpes virus family. VZV is a double-stranded, linear DNA virus encoding about 75 proteins and possessing a lipid-containing envelope with glycoprotein spikes. The virus is distributed worldwide.

Varicella

Varicella is usually transmitted by infected secretions harboured in the nasopharyngeal mucosa by droplets onto the conjunctival or nasal/oral mucosa. Other mechanisms include direct contact with vesicular fluids that contain virus and airborne spread of the virus.

Viral replication is started in regional lymph nodes and tonsils or possibly ductal tissue of salivary glands. It continues for four to six days. The virus then spreads to internal organs. After continued replication in these organs, VZV is again released into the bloodstream and invades cutaneous tissue resulting in the VZV exanthema by day 14.

Primary varicella generally confers lifelong immunity, although there are reported cases of re-infection. Varicella developed during pregnancy in four exposed women despite pre-infection sera showing seropositivity for VZV (2).

Herpes zoster

VZV remains latent in the dorsal root ganglia and may be reactivated. The reactivation is often associated with impaired cell-mediated immunity.

In utero infection

The exact mechanism of in utero VZV infection is unknown. It is postulated that maternal viraemia precedes placental infection and subsequent fetal infection. Placental pathology includes granulomas and acute placentitis.

The site of VZV replication in the fetus is unclear. It has been suggested that the fetus develops chickenpox in utero followed by resolution and subsequent infection of the dorsal root ganglia. This results in cell destruction of nerve tissue which may account for limb denervation changes seen in the congenital varicella syndrome.

Clinical features

The incubation period of chickenpox is 10 to 21 days. Many patients experience a prodrome of fever, malaise and myalgia one to four days prior to the onset of rash. A vesicular rash of the superficial dermis may erupt involving the trunk, face, oropharynx and scalp. Several crops of vesicles may erupt every two to three days lasting six to ten days.

Varicella pneumonia

Varicella pneumonia is seen in up to 20% of adult chickenpox cases. Retrospective studies suggest that varicella pneumonia may be more severe, although not more frequent, in pregnant compared to non-pregnant women. A case-control study of 18 pregnant women with varicella pneumonia and 72 pregnant controls with varicella but no pneumonia, found that smoking and the occurrence of 100 or more skin lesions were risk factors for the development of pneumonia (3).

The predominant clinical features of varicella pneumonia in pregnancy are cough, dyspnoea, fever and tachypnoea. Pneumonia usually develops within one week of the rash. The clinical course is unpredictable and may rapidly progress to hypoxia and respiratory failure. The chest x-ray findings include a diffuse or military/nodular infiltrative pattern in peribronchial distribution involving both lungs.