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THE HONG KONG MEDICAL ASSOCIATION

Approach to Prevention and Monitoring of Infectious Disease Complications Associated with Systemic Corticosteroid Use

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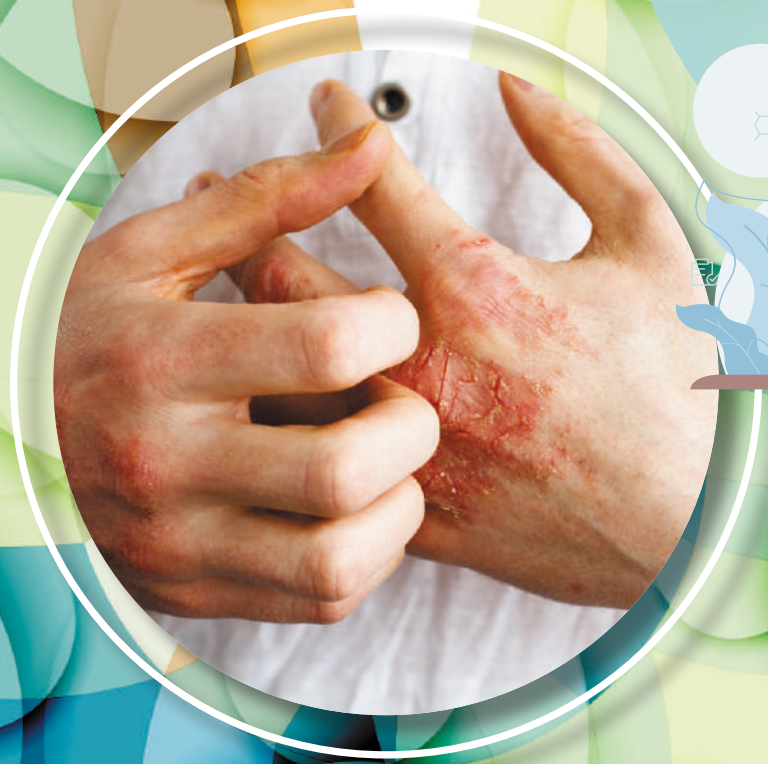
Dr SIMON, John Wingate MH



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HKMA CME Bulletin
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EDITORIAL – November 2023 Issue

Dr HO, Hung Kwong Duncan
Chief Editor, The Hong Kong Medical Association CME Bulletin

It sounds like you're enjoying the pleasant weather and the beauty of our city. It's always nice to appreciate the natural surroundings. Now, let's discuss the articles mentioned in our monthly CME Bulletin.

The Spotlight article by Dr WONG, Tin Yau Andrew and Dr SIMON, John Wingate MH seems to be an important one, considering the strict regulations imposed by the Medical Council on the use of steroids in clinical practice. It's crucial to stay updated on such guidelines and understand their implications for patient care. This article is likely to provide valuable insights and recommendations in that regard.

The case studies in Cardiology and Dermatology mentioned in the CME Bulletin also sound interesting and practical. Case studies are often an effective way to learn from real-life scenarios and enhance clinical knowledge. It would be beneficial not to miss out on these case studies, as they might offer valuable lessons or highlight important diagnostic and treatment approaches in the respective fields.

Lastly, I appreciate your well wishes for everyone's health and happiness. It's important to prioritise our well-being and enjoy the blessings we have. Taking care of ourselves allows us to make the most of life's joys and challenges.

I hope you have a wonderful time reading the articles and continue to enjoy the beautiful season in our city.

Approach to Prevention and Monitoring of Infectious Disease Complications Associated with Systemic Corticosteroid Use

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Introduction

Corticosteroids may be indicated in the management of several autoimmune, rheumatological, gastrointestinal, respiratory and hematological diseases. They are used after solid organ transplantation and after hematopoietic stem cell transplantation. Corticosteroids improve the prognosis in severe cases of COVID-19 (1).

Corticosteroids cause immunosuppression by inducing cellular immunodeficiency and increasing patient susceptibility to infections. They act by (a) impairing opsonization and phagocytic function hence increasing the risk of bacterial infections (b) impairing T-cell migration and proliferation hence increasing the risk of mycobacterial, viral and fungal infections and (c) impairing eosinophilic proliferation with increased apoptosis hence increasing the risk of parasitic infections (2).

The term 'high-dose corticosteroids' is defined as greater than 15-20mg of prednisone (or its equivalent) (PEQ) for greater than 2-4 weeks. Others define it as a dose equivalent to either ≥2 mg/kg of body weight or ≥20 mg/day of prednisone or equivalent for persons who weigh >10 kg when administered for ≥14 consecutive days. The use of 'high dose corticosteroids' is regarded as a risk factor for infection. Refer to Table 1 for equivalent conversion factors for glucocorticoid activities of different preparation of corticosteroids (3,4). It should be noted that the equivalent anti-inflammatory dose conversion applies for oral or intravenous routes of systemic corticosteroid administration only. Equivalent potency for intramuscular or intraarticular administration may vary considerably.

Numerous opportunistic infections including bacterial, mycobacterial, viral, fungal and parasitic have been reported with the use of systemic corticosteroids (Table 2). High dose and long duration of corticosteroids predispose to the development of infections and preventive measures should be assessed and implemented in all patients taking corticosteroids. This article focuses on several infections whose incidence will be reduced by the implementation of preventative recommendations.

Table 1. Comparison of systemic corticosteroid preparations (adapted from (3))

	Equivalent doses (mg)	Antiinflammatory activity relative to hydrocortisone*	Duration of action (hours)
Glucocorticoids			
Short acting			
Hydrocortisone (cortisol)	20	1	8 to 12
Cortisone acetate	25	0.8	8 to 12
Intermediate acting			
Prednisone	5	4	12 to 36
Prednisolone	5	4	12 to 36
Methylprednisolone	4	5	12 to 36
Triamcinolone	4	5	12 to 36
Long acting			
Dexamethasone	0.75	30	36 to 72
Betamethasone	0.6	30	36 to 72

Table 2. Infections associated with use of corticosteroids

Bacterial	Common organisms including *Staphylococcus aureus*, Gram negative organisms, *Nocardia* spp., mycobacteria (*M. tuberculosis* (MTB), Non-tuberculous mycobacteria (NTM) and intracellular organisms e.g. *Listeria and Salmonella* spp.
Viral	Reactivation of hepatitis B/C, herpes viruses
Fungal	*Candida spp., Aspergillus spp., Pneumocystis jirovecii*
Parasitic	*Strongyloides stercoralis* hyperactivation, *Plasmodium malariae*

Tuberculosis

In latent tuberculosis infection (LTBI) the bacteria are alive but contained by the immune system. Persons with LTBI have no apparent symptoms and are not infectious to others. Persons with LTBI may develop active tuberculosis (TB) disease if untreated. Active tuberculosis or tuberculosis disease is an illness in which tuberculosis bacteria are multiplying and attacking a part of the body, usually the lungs. A person with tuberculosis disease may be infectious and spread tuberculosis to others.

What are the severe consequence(s)?

If pulmonary TB is not treated properly, permanent lung damage can result. TB can also affect the brain, bones, spine, lymph nodes, kidneys, adrenal glands, gastrointestinal tract and other parts of the body. Untreated TB can lead to death.

Who are at risk?

Patients with LTBI who are given corticosteroids are at risk of conversion to active disease. Rhematological studies showed that patients treated with less than 15mg PEQ daily have a 2.8 fold increased risk of TB reactivation whereas patients treated with high than 15mg PEQ have a 7.7 fold increase (5). Patients treated with IV pulse-dose corticosteroids are more prone to TB reactivation (6).

How common is it?

One quarter of the global population is infected with *Mycobacterium tuberculosis*. Most infected persons are asymptomatic (LTBI) and about 5-10% of persons with LTBI progress to active TB during their lifetime (7).

How to screen?

Screening for latent TB is recommended for those who may need long term immunosuppression (for example, >= 10mg PEQ prednisone equivalent daily for >4 weeks) (8). Screening should be done with a tuberculin skin test (TST) or with a serum interferon-gamma release assay (IGRA) such as the 'QuantiFERON® Gold Plus', 'T-SPOT®TB'. Table 3 shows the advantages and disadvantages of IGRA. IGRA is generally recommended in patients with a history of Bacille Calmette-Guérin (BCG) vaccination, those with altered T-cell function (e.g. HIV/AIDS) or for those with ongoing immunosuppressive therapy.

The booster phenomenon can affect the accuracy of the baseline TST. TST may be tested negative if many years have passed since they became infected with tuberculosis. However, if this group of patients are tested again within a year of first testing, a positive reaction indicates TB infection. This is because the first test stimulates, or boosts, the ability to react to the test. This is referred to as the "booster phenomenon" and may incorrectly be interpreted as a skin test conversion (going from negative to positive). It may thus appear that these people were infected between the first and second skin tests whereas in fact the positive second reaction simply means that the person has been infected at some time in the past, and this may be many years ago. In these people active TB should be excluded and they should then be considered for LTBI treatment, particularly if they have risk factors for progression to disease.

"Two-step testing" has been developed to tell the difference between boosted reactions, reactions caused by recent infection and those who have never been infected. "Two-step testing" is especially useful for those who need to be retested periodically and should be used for the initial skin test. If the first TST result in the two-step baseline testing is positive the person is considered to be infected and should be evaluated and treated accordingly. If the first test result is negative, the TST should be repeated in 1–3 weeks. If the second test result is positive the person is considered to be infected and should be evaluated and treated accordingly. If both tests are negative the person is considered uninfected and the baseline TST should be classified as negative.

Table 3. Advantages and limitations of IGRA (8)

Advantages	Limitations
• Requires only one patient visit to conduct the test • Not subject to the biases and errors associated with TST placement and reading • Results can be available within 24 hours • Unaffected by BCG vaccine and most nontuberculous mycobacteria (NTM) • Does not cause booster phenomenon	• Blood samples must be processed within 8 to 32 hours after collection • Errors in collecting or transporting blood specimens or in running and interpreting the test can decrease the accuracy of TB blood tests • Tests may be expensive

What to do if screened positive?

If a screening test for TB is positive, the patient should be referred to an infectious disease specialist to determine whether this is LTBI or active TB. Active TB should be excluded by the medical history, physical examination, chest radiograph and sputum and urine stains/molecular testing and cultures for *M tuberculosis*. Preventive treatment for LTBI reduces the risk of developing active TB by 65% (9). Therapy for LTBI or for active TB should ideally be started at least 4 weeks before starting corticosteroids. If this is not possible then start therapy and corticosteroids at the same time.

Several antibiotics are available for the treatment of LTBI thus preventing progression to active tuberculosis. Isoniazid was the first antibiotic used to treat LTBI. However, concerns about hepatotoxicity and drug resistance resulting from low adherence with long courses of treatment have prompted recommendations for shorter courses used in combination with other medications such as rifapentine or rifampin (10).

Hepatitis B

In patients with chronic hepatitis B but without HBV viraemia immunosuppression can reactivate the hepatitis B virus (HBV). A rapid and sudden increase in HBV DNA level by 100-fold or more may occur in those with detectable HBV DNA. In those with previously undetectable viremia, HBV DNA may reappear. (11). The timing of reactivation is variable and is dependent upon host immunity and on the immunosuppressant(s) used. It can occur as early as 2 weeks after initiation of immunosuppressive therapy and may occur up to a year after the cessation of immunosuppression.

What are the severe consequence(s)?

Symptoms can vary from asymptomatic or mild with a normal or mildly abnormal increase in the transaminases to a severe hepatic flare. Severe hepatic flares can cause hepatic decompensation, liver failure and death.

Who are at risk?

The risk of reactivation of HBV is affected by the serological status and by the type, stage and duration of the immunosuppressant(s). Different international guidelines attempt to categorize the level of risk for HBV reactivation in those receiving immunosuppressants (12–14). We refer to the APASL (Asian-Pacific Association for the Study of the Liver) guidelines (12).

HBsAg positive individuals are at greater risk for HBV reactivation than those who are HBsAg negative. HBsAg negative, anti-HBc positive individuals are also at risk of HBV reactivation. A local study showed the incidence of reverting to become HBsAg positive from HBsAg negative (sero-reversion) to be 1.8% in those HBsAg negative and anti-HBc positive individuals (resolved infection) receiving steroid therapy (15).

In **high-risk** groups the incidence of HBV reactivation occurs in >10%. High risk groups include HBsAg-positive/anti-HBc–positive patients (chronic hepatitis B) receiving high dose corticosteroids (>20mg PEQ daily) for >4 weeks(12). Some guidelines (for example, Hospital Authority Hong Kong) include those taking 10-20mg prednisolone daily >4 weeks as high risk (16).

In **median (moderate)** risk groups the incidence of HBV reactivation is 1-10% and includes HBsAg-positive/anti-HBc–positive patients (chronic hepatitis B) receiving median dose corticosteroids (10-20mg PEQ daily) for >4 weeks(12). Some guidelines (e.g. Hospital Authority Hong Kong) include those HBsAg positive patients taking <10mg prednisolone daily for >4 weeks as being at moderate risk (16).

The **low-risk** group has less than a 1% risk of reactivation and includes HBsAg-negative/anti-HBc–positive patients (resolved infection) receiving high dose corticosteroids (>20mg PEQ daily) or HBsAg-positive/anti-HBc–positive patients (chronic hepatitis B) receiving less than 10mg PEQ daily(12). Some guidelines (e.g. Hospital Authority Hong Kong) regard HBsAg positive patients taking any dose of prednisolone for one week as of low risk. They also regard HBsAg negative anti-HBc patients taking any dose of steroids daily for >4 weeks as being of low risk (16).

How to screen?

Before starting immunosuppression (including corticosteroid monotherapy at a dose of PEQ>10- 20mg per day for more than 4 weeks) the patient should be screened for HBV surface antigen (HBsAg) and HBV core antibody (anti-HBc). HBV surface antibody (anti-HBs) can be checked but it is not mandatory as its presence does not eliminate the risk of HBV reactivation. In HBsAg negative and anti-HBc positive patients, the presence and titer of anti-HBs antibodies have been found to provide some protection (17). For HBsAg positive patients, serum HBV DNA should be checked and monitored.

What to do if screened positive?

Recommending preventive antiviral therapy depend upon the level of risk. All high risk and moderate risk HBsAg+ patients should be offered pre-emptive antiviral irrespective of fibrosis status. All patients with advanced fibrosis or cirrhosis should be treated with antiviral irrespective of the immunosuppressive therapy used.

Low risk HBsAg+ patients without advanced fibrosis or cirrhosis should be monitored with ALT every 3 months (Figure 1). If the ALT is ≥ 2 times above the level detected at baseline monitoring, HBsAg and HBV DNA should be measured and an antiviral should be started if either test is positive. In situations in which close monitoring is not feasible, it may be safer to administer prophylactic antiviral even when the risk of reactivation is low.

The antiviral used should have a high barrier to resistance, for example, entecavir or tenofovir (TDF or TAF))(12). Tenofovir, rather than entecavir, is preferred for patients who have previously received lamivudine. Chronic hepatitis B patients who meet treatment criteria should be offered antiviral therapy regardless of the immunosuppressant used. Even after completing immunosuppressive therapy antiviral therapy should be continued until a therapeutic endpoint is reached.

Herpes zoster

Most people when first exposed to varicella-zoster virus (VZV) will develop varicella ("chickenpox"). A few patients will get a mild, or even asymptomatic, infection not recognizable as chickenpox. In all cases after the initial VZV infection the virus lies dormant in the cranial nerve or dorsal root ganglia. In many cases it will be reactivated and present as herpes zoster ("shingles"). Reactivation may occur when host immunity declines due to old age, illness or immunosuppressants.

What are the severe consequence(s)?

A painful vesicular rash with a dermatomal distribution is the usual manifestation of herpes zoster, but in the immunocompromised a disseminated form of disease can develop with vesicles spreading beyond the affected dermatome. Encephalitis, meningitis, hepatitis, pneumonia and retinitis can also occur (18). Disseminated zoster has been reported in 10-40% of the immunocompromised (19). It has a 5 -10% mortality rate in the immunocompromised (18).

Who is at risk?

Anyone who has been previously exposed to VZV may develop herpes zoster. Age >60 years and the use of corticosteroids >7.5-10mg PEQ daily increases the incidence and severity of herpes zoster (20).

Where is it found?

It is of global distribution.

How to screen?

VZV IgG can be used as a serological marker for previous exposure to the virus. In most cases there is no need to screen. According to Hong Kong Centre for Health Protection data, over 98% of population above the age of 39 are VZV IgG positive (21).

How to prevent herpes zoster ?

On October 20, 2021, the USA Advisory Committee on Immunization Practices (ACIP) recommended 2 doses of the Recombinant zoster vaccine (RZV)("Shingrix") for the prevention of herpes zoster in adults aged ≥19 years who are, or who will be, immunodeficient or immunosuppressed because of a disease or its therapy (22). RZV is the first herpes zoster vaccine approved for use in immunocompromised persons. The old Zoster Vaccine Live (ZVL) ("Zostavax") is contraindicated in immunocompromised hosts as it is a live attenuated vaccine.

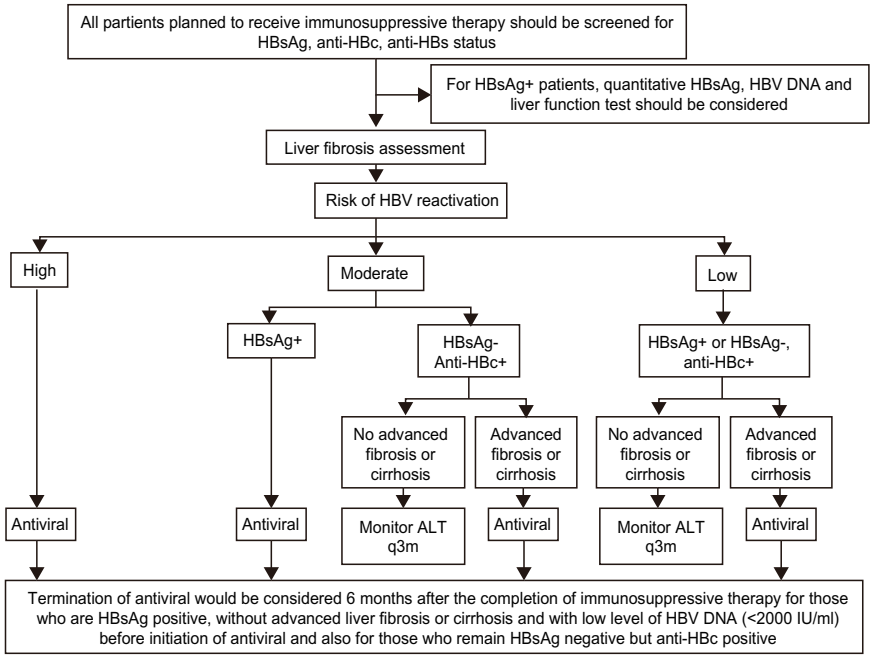

Figure 1. Algorithm for the management of hepatitis B reactivation (adapted from (12))

Two doses of RZV are needed irrespective of a past history of herpes zoster or of receipt of ZVL. The second RZV should normally be given 2 to 6 months after the first. However, for persons who are or will be immunodeficient or immunosuppressed, the second dose can be administered 1-2 months after the first. When possible, patients should be vaccinated with RZV before commencing immunosuppressive therapy which is ideally delayed for two weeks after the second dose to allow an optimal immune response to develop. Otherwise, providers should consider timing vaccination during periods of lower immunosuppression and when the disease is more stable in order to elicit a better immune response. If the second RZV dose is given sooner than 4 weeks after the first dose then another dose should be given at least 4 weeks after the dose given too early (22). RZV may be administered to patients who have previously received varicella vaccine. RZV is not a live vaccine and is not affected by any antiviral medications and these can be continued or prescribed to patients given RZV.

Pneumocystis jiroveci pneumonia (PJP)/(previously called *Pneumocystis carinii* or PCP)

Pneumocystis pneumonia (PCP) is a potentially life-threatening infection that occurs in immunocompromised individuals. Glucocorticoids usage is one of the most significant risk factors in patients without HIV. Glucocorticoids are thought to predispose to the development of PJP by suppressing cell-mediated immunity and altering lung surfactant.

What are the severe consequence(s)?

Previous studies have shown that the mortality rate of non -HIV patients with PJP was 33.3%–69.3% (23).

Who are at risk?

There are no guidelines regarding the dose and duration of corticosteroids needed to trigger PJP. Rheumatological studies suggest that the incidence of PJP is dependent on the dose of corticosteroids. In a case series of 116 consecutive patients with a first episode of PCP corticosteroids had been administered within one month of diagnosis in 91 percent. The median PEQ was 30mg per day but some patients received only PEQ of 16mg per day. The median duration of corticosteroid usage was 12 weeks but 25% had received corticosteroids for less than 8 weeks (24).

How to screen?

There is no screening method for patients prone to develop PJP after corticosteroid therapy.

What are the criteria for starting PJP prophylaxis?

PCP prophylaxis may be considered in patients who are at a higher risk for developing PJP, examples are(25)

#1. PEQ 30mg or above daily for 4 or more weeks

#2. PEQ 15-30mg daily for 8 or more weeks, either interrupted or intermittent

#3. Combination of PEQ 15-30mg daily plus cyclophosphamide (oral or IV pulses)

#4. PEQ 10mg or above daily with two or more of the followings

   a. Age >65years

   b. Coexisting lung disease, for example, COPD, lung fibrosis

   c. Use of immuno-therapeutics, for example, rituximab, anti-tumor necrosis factor

Nowadays, better therapies are often available for various condition to spare the long-term use of corticosteroids. In such cases it may not be necessary to initiate PJP prophylaxis at time of initiation of corticosteroids. Rather, one should re-evaluate the need and duration of corticosteroids use at every clinical encounter and consider PJP prophylaxis if long-term corticosteroid therapy is needed.

Which antibiotic for should be used for prophylaxis?

The first line agent is trimethoprim/sulfamethoxazole ("Septrin"/"Bactrim") 80/400mg (single strength) daily or 160/800mg (double strength) three times per week. Possible side effects include thrombocytopenia, pancytopenia (usually observed at higher dose), increased serum creatinine, hyperkalemia and rash. Alternative agents include dapsone (100mg daily) or nebulized pentamidine (300mg once monthly). Both trimethoprim/sulfamethoxazole and dapsone cannot be used in persons with G6PD deficiency. There are no formal recommendations relating to the duration of prophylaxis and we suggest prophylaxis is continued until the risk factors for the disease are no longer present. Others suggest discontinuing prophylaxis when the PEQ dose is less than 10mg per day or 5mg per day for indication #4 above (25). The effects of prolonged immunosuppression may persist after discontinuation of high-dose corticosteroids and patients should be monitored regularly after stopping corticosteroids.

Strongyloides stercoralis infection

Strongyloides stercoralis is a soil-transmitted intestinal nematode (roundworm). Humans acquire the infection via contact with contaminated soil wherein larvae penetrate the skin and then migrate to the intestine. Larvae are excreted in the feces. In addition larvae may hatch in the intestine and directly auto-inoculate the human host. This is called auto-infection and results in perpetuation of the infection for as long as the human host is alive – thus it may last for decades and is usually asymptomatic in the immunocompetent human host. Minor cutaneous (urticarial dermatitis), pulmonary (cough) and gastrointestinal (diarrhea) symptoms may be present.

What are the severe consequence(s)?

Patients with *Strongyloides stercoralis* who become immunosuppressed can develop a hyper-infection syndrome (with massive invasion of filarifom larvae into the bowel and the lungs) or disseminated disease (with the presence of worms in extra-intestinal and extra-pulmonary sites). Hyper-infection and disseminated disease can be regarded as severe strongyloidiasis. Sepsis due to Gram-negative bacteremia causing pneumonia and meningitis may occur (26). Sepsis is due to translocation of enteric bacteria by filariform larvae when they move through the bowel wall. Mortality rates are high (63%) even with adequate treatment (27).

Who are at risk?

Risk groups for acquiring strongyloidiasis include: (a) High-risk groups: people who were born or resided in, or had travelled > 6 months to, Southeast Asia, Oceania, sub-Saharan Africa, South America or the Caribbean. (b) Moderate-risk groups: Central America, Eastern Europe, Mediterranean, Mexico, Middle East, North Africa, Indian sub-continent and Asia. (c) Low-risk groups: Australia, Canada, United States or Western Europe.

Clinical risk factors include the use of immunosuppressant drugs (particularly corticosteroids), human T-cell leukemia virus type 1 infection, organ transplantation and hematological malignancies. Corticosteroids can provoke hyper-infection. In one study 83% of 133 patients had previously been treated with corticosteroids, with a median dose of prednisone of 40mg per day. The median time from corticosteroid initiation to the onset of hyper-infection was 42 days (28) Cases have occurred within 5 days of administration of prednisone at a dose of 20mg or following a single dose of dexamethasone or locally injected corticosteroids. The strongyloides hyper-infection syndrome appears to be independent of the dose, duration or route of corticosteroid administration (29). One of the authors of this paper (JS) saw several cases of severe strongyloidiasis at a military hospital in London in soldiers who had survived Japanese POW (Prisoner-of-War) camps in SE Asia during WWII and then retired to live in UK many years previously. As they became old they developed diseases requiring corticosteroids and several of these patients developed severe Strongyloidiasis and died.

How common is it?

It was estimated that 10-40% of the populations in tropical and subtropical regions may be infected (30) It is endemic in parts of Southeast Asia, Central America and sub-Saharan Africa. Hyper-infection or disseminated infection occurs in 1.5-2.5% of patients with strongyloidiasis (31).

How to screen?

There is no clear data on the dosage or duration of corticosteroid that may trigger severe strongyloidiasis. Some recommend screening when starting corticosteroids at a dose of 10-15mg PEQ daily for 4 or more weeks (25). Serological testing is the most sensitive method for diagnosing strongyloidiasis with a sensitivity of 83-95% and is the diagnostic test of choice. The sensitivity of stool microscopy is poor and in up to 70% of cases a single stool sample fails to identify larvae because of intermittent shedding and a low larval burden. However, if 7 serial samples are examined, the diagnostic yield improves to >95%. In immunocompromised patients, the sensitivity of serology is lower and drops from 96% to 43% (32). Possibly stool examination may give a higher diagnostic yield in the immunosuppressed as the larval burden may be higher in the immunosuppressed than in the immunocompetent. In the immunocompromised screening should involve both serologic and stool testing (33).

What to do if screened positive?

If screened positive, patients should be treated with ivermectin 200ug/kg per day orally for 1-2 days. It is considered a safe treatment but is contraindicated in persons with *Loa loa* infection, pregnancy and in those children who weigh <15 kg. Ivermectin is contraindicated in *Loa loa* which should be excluded in persons born in or with prolonged residence in, countries of the rainforest area of central Africa by a daytime blood film examination for microfilariae. If Strongyloidiasis screening is not readily available and corticosteroid therapy urgently needs to be started then presumptive ivermectin can be given to high-risk groups such as those from high incidence areas who have walked barefoot in the soil.

Plasmodium malariae infection

Plasmodium malariae has been found in blood films after the use of corticosteroids for membranoproliferative glomerulonephritis and other conditions (34–36). *P. malariae* is associated with immune complex mediated glomerular disease, resulting in nephrotic syndrome. In many cases it was not found before the use of corticosteroids, possibly because of very low level parasitemia (37). *P. malariae* is often diagnosed after immunosuppression because immunosuppression allows the proliferation of *P. malariae*, sometimes to high levels (36). Thrombocytopenia may occur before the parasites appear on a blood smear and may be a clue to the diagnosis. *P. malariae* may cause lifelong asymptomatic infection and should be considered in any patient presenting with thrombocytopenia after corticosteroid use even in non-endemic areas – as they may have a past history of travel to, or residence in, an endemic area. (37).

Vaccination considerations

Immunization with inactivated vaccines can be given not less than **two** weeks before starting high-dose corticosteroids (see Introduction for definition) are initiated. Immunization with live vaccines can be given not less than **four** weeks before starting high-dose corticosteroids. If the vaccines cannot be given before then live-virus vaccination should be deferred for at least 1 month after discontinuing high-dose corticosteroids. Killed or inactivated vaccines and toxoids may be given but the response to such vaccines cannot be predicted (38).

Summary

Corticosteroids are commonly used to treat many medical diseases and their use is associated with an increased risk of infections. Appropriate laboratory screening, antimicrobial prophylaxis, vaccinations and patient education diminishes the risk of infections. Clinicians should do a thorough risk assessment and implement necessary preventive measures before prescribing corticosteroids.

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Q&A Assessment Questions

Complete Spotlight, **1 CME Point** will be awarded for at least five correct answers

Answer these on page 16 or make an online submission at: www.hkma.org.

Please indicate whether the following statements are true or false.

1. Patients who are HBsAg negative, anti-HBc positive and anti-HBs positive are not susceptible to reactivation of HBV when put on high dose corticosteroids.
2. One has to rule out the possibility of *Plasmodium malariae* infection in patients presenting with fever of unknown origin with thrombocytopenia after given corticosteroids.
3. In immunocompromised hosts, a negative IgG to *Strongyloides stercoralis* can exclude the possibility of hyper-infection after corticosteroids.
4. PJP prophylaxis should be started right away when patients are given corticosteroids irrespective of intended duration to protect the patients.
5. For persons who are or will be immunodeficient or immunosuppressed, the second dose of recombinant zoster vaccine can be administered 1-2 months after the first.
6. Tuberculin skin test (TST) can be falsely negative in someone who had been infected with TB long time ago.
7. HBsAg negative patients are not at risk of HBV reactivation as they are not carriers.
8. Bacterial sepsis are more common in patients given long term corticosteroids.
9. A hydrocortisone dosage of 100mg per day is equivalent to 20mg Prednisolone per day in terms of anti-inflammatory activity.
10. Live-virus vaccination should be deferred for at least 1 month after discontinuing high-dose corticosteroids.

Answer to October 2023

Spotlight – On Becoming A Competent Family Doctor

1. T 2. F 3. T 4. T 5. T 6. T 7. T 8. T 9. T 10. F

The content of the November 2023 Cardiology Series is provided by:
Dr HO, Ka Hei Carmen
MBChB (CUHK), FHKAM (Medicine), Specialist in Cardiology
Dr SUNG, Jonathan Gabriel
MBChB, FHKAM (Medicine), FRCP (Glasg), Specialist in Cardiology
十一月臨床心臟科個案研究之內容承蒙**何嘉希醫生**及**宋司灝醫生**提供。

Complete Cardiology case,
0.5 CME POINT will be awarded for
at least 2 correct answers in total

A 50-Year-Old Lady Complained of Exertional Dyspnea for One Week

A 50-year-old lady, with good past health, sought medical attention due to exertional dyspnea for one week. She also complained of orthopnea and bilateral lower limb edema. Physical examination showed no pallor or cyanosis. Blood pressure 140/90 mmHg, heart rate 90 bpm and SaO2 94% on room air. Jugular venous pressure was elevated. Chest examination revealed bilateral basal crepitation. Cardiovascular examination showed pansystolic murmur at apex.

Blood test showed hemoglobin 14g/dL (Ref: 11.6-15.5), creatinine 120 μmol/L (Ref: 50-98), urea 15 mmol/L (Ref: 3.5-7.2), sodium 133 mmol/L (Ref: 136-145), albumin 36g/L (Ref: 32-46), bilirubin 33 μmol/L (Ref: 3-21), ALP 140 U/L (Ref: 53-141), ALT 40 U/L (Ref: ≤34).

Q&A Please answer ALL questions

Answer these on page 16 or make an online submission at: www.hkma.org.

1. **What is the most likely diagnosis based on the above history, physical examination and investigation?**
   a) Nephrotic syndrome
   b) Liver cirrhosis
   c) Congestive heart failure
   d) Severe aortic stenosis
   e) Pulmonary fibrosis

   She was put on intravenous furosemide and symptoms markedly improved. Echocardiogram showed left ventricular ejection fraction was 38%. There was also severe functional mitral regurgitation.

2. **Which of the following is not an appropriate medical treatment in this case?**
   a) Beta-blocker
   b) Calcium channel blocker
   c) Sodium-glucose cotransporter 2 inhibitor
   d) Angiotensin receptor-neprilysin inhibitor
   e) Mineralocorticoid antagonist

   She was put on guideline-directed medical therapy and returned to clinic 4 months later for review after optimisation of medications. Although her symptoms markedly improved when compared to index consultation, she still had dyspnea when walking upslope. Echocardiogram showed persistent severely impaired LV systolic function with LVEF 35% and moderate mitral regurgitation. An electrocardiogram was performed:

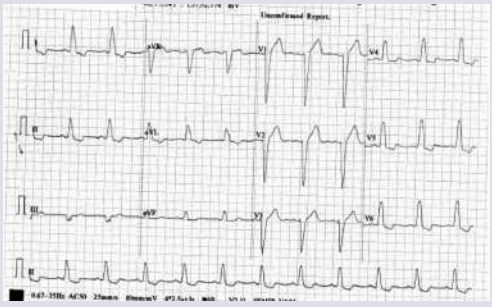

Figure 1

3. **What would be the most appropriate next step of treatment for this lady?**
   a) Step up diuretic for symptoms control
   b) Add ivabradine
   c) Add digoxin
   d) Cardiac resynchronisation therapy
   e) Add hydralazine-isosorbide dinitrate

Cardiology October Answers

Discussion:

Here was a case of Brugada syndrome that was diagnosed after presentation with VF cardiac arrest. The diagnosis was made after a normal coronary angiogram, echocardiogram demonstrating no structural and valvular heart disease and a confirmatory old ECG demonstrating a type 1 Brugada ECG pattern.

There are 3 types of repolarization patterns in the ECG that are associated with Brugada syndrome. Types 2 and 3 Brugada ECG pattern are not diagnostic and merely only suggest the syndrome may be present. To diagnose Brugada syndrome one must demonstrate both 1) a type 1 Brugada ECG pattern and 2) clinical criteria that support the diagnosis. The clinical criteria fall into 3 categories: either family history, arrhythmia-related symptoms (history of syncope, seizures etc) or documented ventricular arrhythmias. Patients with a type 1 Brugada ECG pattern but absence of any clinical symptoms are described as having an "Idiopathic Brugada ECG pattern". Patients with Brugada syndrome may have a normal ECG with the type 1 ECG pattern unmasked by fever, alcohol, large meals or drugs. Placing the right precordial leads at progressively higher intercostal spaces can sometimes produce a more definitive ECG pattern due to the right ventricular outflow tract being located at different anatomical spaces between individuals.

Answers: 1. C 2. A 3. C

Individuals with Brugada syndrome who have survived an aborted cardiac arrest or have documented sustained ventricular tachycardia should be treated with an implantable cardioverter defibrillator (ICD). Pharmacological therapy (with Quinidine) and catheter ablation have roles to help reduce the occurrence of ventricular arrhythmias but only an ICD has evidence to reduce the risk of sudden cardiac death.

The content of the October 2023 Cardiology Series is provided by:
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MBBS(HK), MRCP(UK), FHKCP, FHKAM(Med), Specialist in Cardiology
Dr Karl CHAN
MBBS(HK), MRCP(UK), FHKCP, FHKAM(Med), Specialist in Cardiology
十月臨床心臟科個案研究之內容承蒙**張玲玲醫生**及**陳斯暑醫生**提供

香港醫生網
The Hong Kong Doctors Homepage

www.hkdoctors.org

This web site is developed and maintained by the Hong Kong Medical Association for all registered Hong Kong doctors to house their Internet practice homepage. The format complies with the Internet Guidelines which was proposed by the Hong Kong Medical Association and adopted by the Medical Council of Hong Kong.

We consider a practice homepage as a signboard or an entry in the telephone directory. It contains essential information about the doctor including his specialty and how to get to him. This facilitates members of the public to communicate with their doctors.

This website is open to all registered doctors in Hong Kong. For practice page design and upload, please contact the Hong Kong Medical Association Secretariat.

由香港醫學會成立並管理的《香港醫生網》，是一個收錄本港註冊西醫執業網頁的網站。內容是根據由香港醫學會擬訂並獲香港醫務委員會批准使用的互聯網指引內的規定格式刊載。

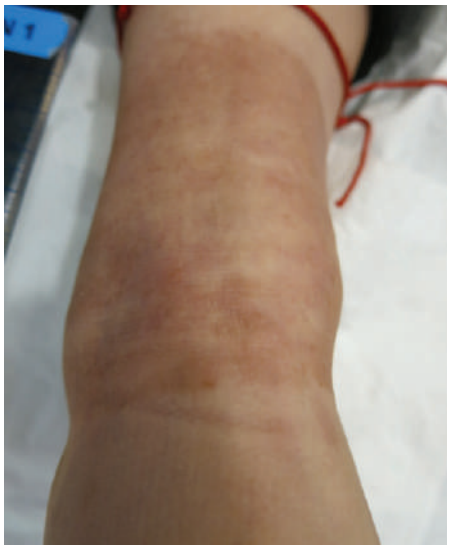
醫生的「執業網頁」性質與電話索引內刊載的資料相近。目的是提供與醫生執業有關的基本資料，例如註冊專科及聯絡方法等，方便市民接觸個別醫生。

任何香港註冊西醫都可以參加《香港醫生網》。關於網頁版面安排及上載之詳情，請與香港醫學會秘書處聯絡為荷。

Dermatology Series for November 2023 is provided by:
Dr CHAN, Hau Ngai Kingsley, Dr TANG, Yuk Ming William, Dr LEUNG, Wai Yiu, Dr KWAN, Chi Keung, Dr NG, Shun Chin, Dr CHENG, Hok Fai and Dr KOH, Chiu Choi
Specialists in Dermatology & Venereology
十一月皮膚科個案研究之內容承蒙**陳厚毅醫生、鄧旭明醫生、梁偉耀醫生、關志強醫生、吳順展醫生、鄭學輝醫生**及**許招財醫生**提供。

Complete Dermatology case,
0.5 CME POINT will be awarded for at least 3 correct answers in total

A 24-Year-Old Woman Presents with Itchy Rash



A 24-year-old woman with good past health complained of a very itchy rash on her left leg. She suffered from a left leg sprain 1 week ago. She took paracetamol, NSAID, and applied a skin patch with herbal oil daily prescribed by her bone-setter. The rash appeared a few days after commencing the treatment. She had no fever nor systemic symptoms.

Q&A Please answer ALL questions

Answer these on page 16 or make an online submission at: www.hkma.org.

1. Which of the following is the most likely diagnosis?

A. Sun burn
B. Erysipelas
C. Contact dermatitis
D. Urticaria
E. Drug eruption

2. What is the likely culprit of this condition?

A. NSAID
B. Streptococci
C. Paracetamol
D. Insect bite
E. Herbal oil patch

3. Which of the following is a proper investigation for this patient?

A. Blood culture
B. Wound swab
C. Skin biopsy
D. Skin patch test
E. Skin prick test

4. What is the underlying pathological mechanism of this condition?

A. Infection
B. Type IV hypersensitivity
C. Autoimmune
D. Photosensitivity
E. Type I hypersensitivity

5. Which of the following is NOT the proper management?

A. Emollient
B. Oral antihistamine
C. Gentle cleanser
D. Topical steroid
E. Oral antibiotic

Dermatology October Answers

1. E

There is background facial erythema with telangiectasia over face without other area involved. No acniform papules/comedone was noted. No feature of lupus erythematous, dermatomyositis, contact dermatitis, acne vulgaris, seborrheic dermatitis, carcinoid syndrome was found. It is clinically rosacea. Diagnosis of rosacea usually can be made clinically without laboratory investigation.

2. E

It is clinically erythemato-telangiectatic rosacea. Rosacea is a common disorder in middle -aged people over 30 years old. Cutaneous finding includes central face erythema, telangiectasia, papules, pustules and phymatous change (e.g., rhinophyma). Ocular involvement occurs occasionally. Pathogensis hypothesis includes vascular dysfunction/ hypersensitivity, abnormal immune/inflammatory reaction to microorganism e.g., demodex mites, genetic factor, ultraviolet light exposure. Subtype- based classification includes erythemato-telangiectatic, papulopustular, phymatous, ocular rosacea (e.g., blepharitis, keratitis, conjunctivitis, anterior uveitis). Phenotype- based classification was also used which include diagnostic phenotypes (centrofacial erythema, phymatous changes), major phenotypes (papules and pustules, flushing, telangiectasia, ocular features, secondary phenotypes (burning, edema, dry skin)

3. E

Precipitating factors include sun exposure, exposure to extreme temperature, alcohol, spicy food, exercise, emotion (e.g., anger), drug (e.g., vasodilator).

4. E

Management includes avoidance of precipitating factor, sun protection, gentle skin care, frequent skin moisturization and avoid irritating topical product. Treatment of erythemato-telangiectatic type rosacea includes pulsed dye laser, topical brimonidine. Treatment of papulopustular type include topical metronidazole, topical ivermectin, topical azelaic acid, topical retinoid, topical antimicrobial, oral antibiotic (e.g., doxycycline), low-dose isotretinoin. Treatment of phymatous type include nasal debulking by laser/surgery. Treatment of ocular type include ocular lubrication, lid hygiene, and refer to ophthalmology team for further advice.

Dermatology Series for October 2023 is provided by:
Dr KOH, Chiu Choi, Dr TANG, Yuk Ming William, Dr CHAN, Hau Ngai Kingsley, Dr LEUNG, Wai Yiu, Dr KWAN, Chi Keung, Dr NG, Shun Chin and **Dr CHENG, Hok Fai**
Specialists in Dermatology & Venereology
十月皮膚科個案研究之內容承蒙**許招財醫生、鄧旭明醫生、陳厚毅醫生、梁偉耀醫生、關志強醫生、吳順展醫生**及**鄭學輝醫生**提供。

Name

HKMA Membership No.

HKID No. - xxx(x)

Signature:

Contact Tel No.:

Answer Sheet

November 2023

ANSWER SHEET

Please answer ALL questions and write the answers in the space provided.

SPOTlight

Complete Spotlight, 1 CME point will be awarded for **at least 5** correct answers

1	2	3	4	5	6	7	8	9	10

Cardiology

Complete Cardiology, 0.5 CME point will be awarded for **at least two** correct answers

1	2	3

Dermatology

Complete Dermatology, 0.5 CME point will be awarded for **at least three** correct answers

1	2	3	4	5

A maximum of 20 points can be awarded for self-study per year and no upper limit of CME points for attending CME lectures

Please return the completed answer sheet to the HKMA Secretariat (email: cme@hkma.org or Fax: 2865 0943) on or before 15 December 2023 for documentation.

If you want to complete the exercise online, please scan the below QR code and you are NOT required to return the answer sheet by fax/email.

CME Self-Studies Series

You can register the CME Lectures and finish the CME Self-Studies Series within the webpage (https://www.thkma.org/cme/continuous_medical_education/).

Don't wait! Please register and create your own account through https://www.thkma.org/members/register.phpc (*1st time register account is limited on desktop ONLY*) to experience our new Members Portal.

Please scan the QR code below to access the latest CME Self-Studies Series online.

HKMA CME Lecture Policy and Procedure

Lecture in Physical Attendance Mode

1. Unless otherwise specified, registrations are accepted from HKMA Members or Medical Practitioners in Hong Kong ONLY. Non-Medical Practitioners will not be served.
2. Prior registration is strictly required.
3. Registration is basically on a first-come-first-served basis except for district-based lectures that registration priorities will be given to doctors practicing in the related districts.
4. No walk-in will be accepted. Attendance without registration will not be recognized and no CME point(s) will be awarded. (*Please refer to the policy of "Non-registrants at CME Lecture in Physical Attendance Mode")
5. HKMA Members and Medical Practitioners intending to register for CME lectures must complete the online registration form at https://www.thkma.org/cme/continuous_medical_education/and return to HKMA Secretariat before deadline.
6. Confirmation emails will be sent out by the HKMA Secretariat to successful registrants before each lecture. Please ensure that registration is confirmed before coming to CME lecture.
7. Successful registrants must attend the lecture in real-time and sign in person the attendance form(s) for obtaining the CME point(s).
8. Successful registrants can only attend ONE lecture at a time regardless of which CME providers. Only 1 Lecture will be counted if the doctor watches multiple CME Lectures conducted at the same time.

Non-registrants at CME Lecture in Physical Attendance Mode

1. Basically, all CME lectures require prior registration and entertain no non-registrant. But under exceptional circumstances that non-registrants come to CME lecture without prior registration, a non-registrant fee will be charged.
2. If under such exceptional circumstances, non-registrants must produce proof of personal identity together with MCHK registration for verification by the on-site HKMA staff.
3. Non-registrants must settle the exact amount of the non-registrant fees in cash or cheque before accessing the lecture. Electronic payment is not accepted, and no change will be provided.
4. The non-registration fees schedule is shown below:

	HKMA Premises	Venues outside HKMA Premises
HKMA Member	HK$150 per person	HK$300 per person
Non-HKMA Member	HK$300 per person	HK$600 per person

5. Any non-registrants in breach of the above policy will have to bear full legal responsibilities. The HKMA serves rights to take action against non-registrants for loss incurred for the non-observance.
6. This policy takes effect from 1 June 2023.

Lecture in Online (via ZOOM)

1. Registration is open to HKMA Members or Medical Practitioners in Hong Kong ONLY. Non-Medical Practitioners will not be served.
2. Prior registration is strictly required.
3. Registration is basically on a first-come-first-served basis.
4. No walk-in will be accepted. Attendance without registration will not be recognized and no CME point(s) will be awarded.
5. Please complete the online registration form at https://www.thkma.org/cme/continuous_medical_education/ and return to HKMA Secretariat before deadline.
6. Confirmation / notification emails will be sent out by the HKMA Secretariat to successful registrants 1 day and 1 hour before each lecture. Please ensure that registration is confirmed before attending the CME lecture online.
7. CME accreditation will apply to both specialist and non-specialist doctor for each lecture. If the CME accreditation is for non-specialist doctors only, there will be a notice showing in the registration form.
8. CME point(s) will be awarded to successful registrants after attending the lecture and completing the quiz with at least 50% correct answers.
9. Successful registrants must watch the lecture in real-time and complete the online quiz within the designated time after the lecture. Late submission of the quiz will not be accepted.
10. Successful registrants can only attend ONE lecture at a time regardless of which CME providers. Only 1 Lecture will be counted if the doctor watches multiple CME Lectures conducted at the same time.
11. Successful registrants may install ZOOM app/launcher system to join the lecture online.
12. Wi-Fi connection is recommended on your mobile device or computer while watching the lecture via ZOOM. Unstable internet connection may cause interruption to the broadcasting.
13. In case of technical issue and broadcast interruption, please be patient while the HKMA Secretariat works on fixing the problem; the video should resume in a few minutes.

Lecture in Hybrid Format (Online + Physical Attendance)

1. Registration policy applies the same statements as above.
2. Please ensure that registration is confirmed before attending the lecture.

General lecture policy

1. Doctor should sign for own CME.
2. Registration will cease when Q & A Session starts.
3. No recording unless permission is granted by the HKMA.
4. If doctor has attended CME Lecture in physical attendance and CME online at the same point of time, only CME Point(s) for the Lecture in physical attendance would be counted.
5. The HKMA will investigate when non-compliance at CME Session is reported, further action will be considered to ensure all CME activities are properly held.

Typhoon/Black Rainstorm/Extreme Conditions Policy

When Tropical Storm Warning Signal No. 8 (or above) or the Black Rainstorm signal or Extreme Conditions Warning Signal is hoisted within 3 hours of the commencement time, the relevant CME function will be cancelled. (i.e. CME starting at 2:00 pm will be cancelled if the warning signal is hoisted or in force any time between 11:00 am and 2:00 pm).

The function will proceed as scheduled if the signal is lowered three hours before the commencement time. (i.e. CME starting at 2:00 pm will proceed if the warning signal is lowered at 11:00 am, but will be cancelled even if it is lowered at 11:01 am).

When Tropical Storm Warning Signal No. 8 (or above) or Black Rainstorm signal or Extreme Conditions Warning Signal is hoisted after CME commencement, announcement will be made depending on the conditions as to whether the CME will be terminated earlier or be conducted until the end of the session.

The above are general guidelines only. Individuals should decide on their CME attendance according to their own transportation and work/home location considerations to ensure personal safety.

Contact

For enquiries, please contact the CME Department of the HKMA Secretariat at 2527-8452 or cme@hkma.org.

Respiratory Syncytial Virus Infection in Older Adults

Dr. TSO, Raymond
LMCHK, DABIM, DABIM (Pulmonary D),
Specialist in Respiratory Medicine

Tracking RSV transmission through the seasons

Respiratory Syncytial Virus (RSV) infection has been a recurring theme of public health management. Despite virulence in vulnerable groups, its disease burden was often overlooked as mild symptoms in otherwise healthy adults.[1-3] Dedicated care is direly needed to address poor subgroup prognosis of RSV infection.[4]

RSV was transmitted via inhalation of droplets or contact with respiratory secretions of infected ones, who were typically contagious for 3-8 days.[5] Older adults may shed the virus for a longer duration, and on average, the basic reproduction number (R_0) was around 3.[6,7] Therefore, RSV could spread readily within households.[8]

The seasonality of RSV epidemics varied with hemispheres and zones.[9,10] In Hong Kong (HK), two annual peaks were observed, from early March to mid-April or mid-July to mid-September.[11] The trend lagged behind influenza season and lasted longer. However, COVID-19 mitigation measures have disrupted RSV seasonality, with a triple pandemic of RSV, influenza and SARS-CoV-2 infections during the 2022-23 season.[12,13] The out-of-season RSV infection outbreaks post-pandemic were foreseeable.[12,14]

Risk assessment for RSV infection

Age was a major risk factor for RSV infection.[1-3]While virtually all children would be infected by 2 years old, adults aged ≥60 years were at high risk of severe complications.[1-3,15] Local studies found that nursing home residents were involved in 19.7% of RSV-associated hospitalizations, having relatively higher RSV influenza-like illness rates than actual influenza attacks.[16,17] Alternatively, adults with certain comorbidities or weak immune status were also at increased risk of RSV infection.[2,3,18] According to a prospective study in New York State, RSV-associated hospitalization rates increased with age, asthma, coronary artery disease (CAD), congestive heart failure (CHF), asthma, COPD and diabetes.[2]

Disease burden beyond RSV infection

The disease burden of RSV infections also varied with regions.[4,11] Local research reported that male children <5 years and elderly ≥65 years shared similar mean mortality rates (39 per 1,000,000 persons-year).[11] The respective trend was different for female, in which elderly had higher mean mortality rate than children (53 vs. 18 per 1,000,000 persons-year).[11] In the local ranking, RSV was the second killer among hospitalized elderly due to respiratory infection, reaching 20.1% among elderly ≥65 years.[11] Whereas in the US, the incidence of RSV-associated hospitalizations and mortality was substantially higher in older adults than children.[4]

According to a retrospective cohort study in HK, the sample of adult RSV patients at the mean age of 75 Consisted of 80.4% having ≥1 complications.[19] These included lower respiratory conditions (pneumonia, acute bronchitis, exacerbation of chronic obstructive pulmonary disease (COPD) or asthma) and cardiovascular conditions (exacerbation of heart failure, atrial fibrillation, acute coronary or cerebrovascular events).[19] As a result, 67.9% required supplemental oxygen; on average, survivors were hospitalized for as long as 12 days.[19] In fact, many reported health outcomes of RSV infections in HK and the US were numerically more severe than those of influenza infections.[19,20] Statistical significance was reached for more RSV-associated lower respiratory complications and supplemental oxygen therapy or ventilatory support in HK.[19]

An exemplary case for RSV surveillance

A local RSV case of diagnostic importance was shared.[20] The case referred to an elderly male (aged 72) under chronic steroid therapy for COPD.[20] He was admitted for pneumonia leading to type I respiratory failure, and Non-Invasive Ventilation (NIV) was required.[20] Given the patient history, his condition was initially managed as an exacerbation episode of bacterial infective COPD, but treatment response with steroids and antibiotics was poor. Subsequent Polymerase Chain Reaction (PCR) assay revealed RSV in the respiratory sample, and he was treated accordingly.[20] Nevertheless, the diagnostic setback resulted in a prolonged Intensive Care Unit (ICU) stay.[20] This highlighted the significance of incorporating the RSV test for elderly refractory to typical treatments.

The case also illustrated nuances of arriving at RSV diagnosis. Since symptoms of RSV infection were non-specific and might be indistinguishable from those of other respiratory infections, laboratory testing was necessary to confirm diagnosis.[21] Yet, RSV testing and options as diagnosis were not routinely considered for adults with influenza-like illness.[22] As a result, RSV infections were under-diagnosed and under-recognized.[22]

Meanwhile, there is currently no specific treatment for adult RSV infections.[22] Supportive care was the mainstay of therapy for acute infection.[23] With the advent of immunotherapy research, multiple candidate drugs are now in different phases of clinical trials.[24] Leading the race is two US market-approved recombinant RSV vaccines (Recombinant Respiratory Syncytial Virus Pre-Fusion F Protein Adjuvanted with AS01E and Respiratory Syncytial Virus Vaccine (bivalent, recombinant)), together with two monoclonal antibodies (nirsevimab and palivizumab).[24-26]

Landmark trial for recombinant RSV vaccine

AReSVi-006 was an ongoing international phase III trial evaluating the use of RSVPreF3 OA vaccine in preventing RSV-associated lower respiratory tract disease (LRTD) for adults aged ≥60.[27] 24,966 participants were randomly assigned in 1:1 ratio to receive one dose of RSVPreF3 OA or placebo before RSV season 2021-22.[27] Following season 1, the treatment group was re-randomized again to receive one dose of RSVPreF3 OA or placebo.[28] The three groups would be followed for two seasons, recording the efficacy of preventing RSV infections. [28]

LRTD was defined as suffering from ≥2 lower respiratory symptoms/signs (including ≥1 sign) or ≥3 lower respiratory symptoms lasting for ≥24 hours.[28] Demographic characteristics were balanced between study groups.[27]

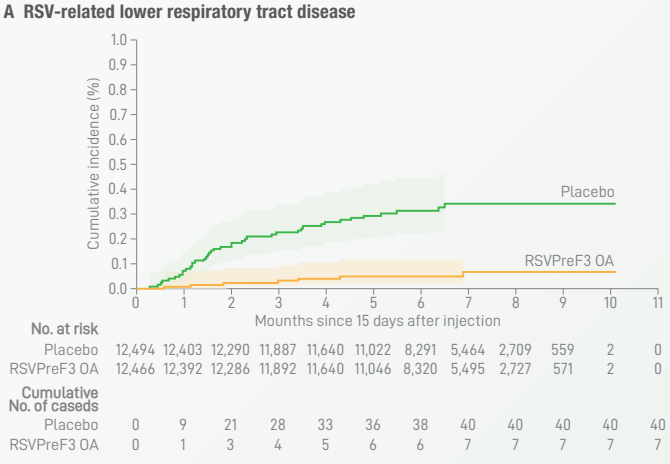


Figure 1. Cumulative incidence of RSV-related LRTD over time since day 15 post-assignment. Shaded areas indicate 96.95% CI.[27]

Guaranteed performance of RSV vaccine irrespective of subgroup

Subgroup analysis indicated that vaccine efficacy was maintained in severe RSV-LRTD (efficacy 94.1%; 95% CI: 62.4-99.9) and systemic RSV-ARI (efficacy 71.7%; 95% CI: 56.2-82.3).[27] Efficacy in RSV-LRTD was especially evident for adults aged 70-79 (efficacy 93.8%; 95% CI: 60.2-99.9).[27] In addition, efficacy was observed in vulnerable populations, including the pre-frail group (efficacy 92.9%; 95% CI: 53.4-99.8) and the group with ≥1 pre-existing comorbidity predisposing for severe RSV disease (efficacy 94.6%; 95% CI: 65.9-99.9).[27] Vaccine efficacy was also consistent across LRTD caused by RSV subtype A (efficacy 84.6%; 95% CI: 32.1-98.3) and subtype B (efficacy 80.9%; 95% CI: 49.4-94.3).[27]

The secondary endpoint was further vaccine efficacy over two seasons under the above assignment.[28] From disclosed data of 2022/23 meetings of the Advisory Committee on Immunization Practices (ACIP) at the Centers for Disease Control and Prevention (CDC), it was reported that a single dose of RSVPreF3 OA could sustain efficacy over two seasons (efficacy 67.2%; 95% CI: 48.2-80.0).[28] However, revaccination after one season did not confer additional efficacy benefit over the same interval (efficacy 67.1%; 95% CI: 48.1-80.0).[28] In other words, vaccine response could extend beyond seasons, and the optimal timing of revaccination remains to be determined.[28]

Efficacy aside, RSVPreF3 also has an acceptable safety profile in AReSVi-006.[27] Within four days of vaccination, most solicited adverse events (AE) were transient (mean duration of 1-2 days) and mild-to-moderate.[27] The most frequent local AE was pain (60.9%; 95% CI: 57.5-64.1), while that of systemic AE was fatigue (33.6%; 95% CI: 30.4-36.8).[27] Grade 3 AEs were rare.[27] Similar trends were observed for unsolicited AEs up to 30 days post-injection and severe AE or potential immune-mediated disease (pIMD) up to 6 months after injection.[27]

Conclusion

RSV infection was potentially life-threatening for older adults with immunocompromising comorbidities.[2,3,15,18] In lack of routine diagnosis and RSV-specific therapy, prevention would be the most suitable response.[22] RSVPreF3 OA vaccine has demonstrated high and consistent efficacy against full spectrum of RSV disease, regardless of RSV subgroups.[29] Its immunogenicity was robust and persistent, without interference with co-administered influenza vaccines.[29] It was also well-tolerated.[29]

Guidelines were updated in light of promising vaccine trial outcomes.[30,31] The US CDC ACIP recommended that adults aged ≥60 receive a single dose of RSV vaccine, whereas the UK Joined Committee on Vaccination and Immunisation (JCVI) favoured a routine vaccination program for those aged ≥75.[30,31] As the RSV vaccine was approved by US Food and Drug Administration (FDA), UK Medicines and Healthcare products Regulatory Agency (MHRA) and European Commission, RSVPreF3 OA would be a reliable addition to the local RSV management repertoire.[25,32,33]

Disclaimer: The above editorial is for medical education purposes supported by GlaxoSmithKline Limited.

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香港醫學會
THE HONG KONG MEDICAL ASSOCIATION

The HKMA CME Live Lecture in November 2023

CME LIVE
zoom LIVE

All lectures start at 2:00-3:00 p.m.

	Date	Organiser and Topic	Speaker	CME Points	CME Accreditation from Colleges (Pending) #
1.	27 November (Mon)	**The Hong Kong Medical Association** The Role of Probiotics in the Treatment of NAFLD and Metabolic Disease *Sponsor: G-NiiB, Genie Biome Limited*	**Dr CHAN, Nor Norman** *Specialist in Endocrinology, Diabetes & Metabolism*	1	Yes
2.	28 November (Tue)	**The Hong Kong Medical Association** 1. Updates on Colorectal Cancer Screening 2. Multitarget FIT-DNA Technology as the Latest Colorectal Cancer Screening Option in Hong Kong *Sponsor: Prenetics Limited*	**1.Dr LAM, Yuk Fai Frank** *Specialist in Gastroenterology & Hepatology* **2.Dr MA, Wu Po Mike** *Chief R&D Officer, Prenetics, Ltd.*	1	Yes
3.	29 November (Wed)	**The HKMA District Health Network (Central, Western & Southern)** Diagnosis and Management of Common Skin Infections in Primary Care *No Sponsor*	**Dr HO, King Man** *Hon. Clinical Associate Professor, Department of Medicine, The University of Hong Kong*	1	Yes

Physical Attendance Mode

	Date	Organiser and Topic	Speaker	CME Points	CME Accreditation from Colleges (Pending)
1.	30 November (Thu) 2:00-3:00pm	**The HKMA District Health Network (Hong Kong East)** Changing Paradigms in Hyperlipidemia Management: What are the Available Evidence in CV Risk Reduction and Long Term Safety? *Sponsor: Amgen Hong Kong Limited*	**Dr CHEUNG, Chi Yeung** *Specialist in Cardiology*	1	Yes

HKMA CME Bulletin
Monthly Self-Study Series
Call for Articles

Since its publication, the HKMA CME Bulletin has become one of the most popular CME readings for doctors. This monthly publication has been serving more than 10,000 readers each month through practical case studies and picture quizzes. To enrich its content, we are inviting articles from experts of different specialties. Interested contributors may refer to the General Guidance below. Other formats are also welcome.

For further information, please contact **CME Dept. at 2527 8452 or by email at cme@hkma.org.**

General Guidance for Authors

Intended Readers	:	General Practitioners
Length of Article	:	Approximately 8-10 A-4 pages in 12-pt fonts in single line spacing, or around 1,500-2,000 words.
Review Questions	:	Include 10 self-assessment questions in true-or-false format. (It is recommended that analysis and answers to most questions be covered in the article.)
Language	:	English
Highlights	:	It is preferable that key messages in each paragraph/section be highlighted in bold types.
Key Lessons	:	Recommended to include, if possible, a key message in point-from at the end of the article.
Others	:	List of full name(s) of author(s), with qualifications and current appointment quoted, plus a digital photograph of each author.
Deadline	:	All manuscripts for publication of the month should reach the Editor before the 1st of the previous month.

All articles submitted for publication are subject to review and editing by the CME Bulletin & Online Editorial Board.

The HKMA CME Live Lecture in December 2023

All lectures start at 2:00-3:00 p.m.

	Date	Organiser and Topic	Speaker	CME Points	CME Accreditation from Colleges (Pending) #
1.	4 December 2023 (Mon)	**The Hong Kong Medical Association** Triple Inhalation Therapy in Severe Asthma *Sponsor: GlaxoSmithKline Limited*	**Dr WONG, Wing Ching** *Specialist in Respiratory Medicine*	1	Yes
2.	8 December 2023 (Fri)	**The Hong Kong Medical Association** What's New in Hypertension Management? *Sponsor: Synmosa Biopharma (HK) Co. Ltd*	**Dr AU, Shek Yin Stanley** *Specialist in Cardiology*	1	Yes
3.	11 December 2023 (Mon)	**The Hong Kong Medical Association** Antiplatelet Therapy in 2023: From Guidelines to Clinical Practice *Sponsor: Sanofi Hong Kong Limited*	**Dr LAU, Chun Leung** *Specialist in Cardiology*	1	Yes
4.	15 December 2023 (Fri)	**The Hong Kong Medical Association** Understanding Therapeutic Index and Improving Allergic Rhinitis Management *Sponsor: GlaxoSmithKline Limited*	**Dr CHAN, YAP** *Specialist in Otorhinolaryngology*	1	Yes
5.	21 December 2023 (Thu)	**The Hong Kong Medical Association** Updates in Management of Lipid Disorders *Sponsor: Abbott Laboratories Limited*	**Dr NG, Lok Hang Canice** *Specialist in Cardiology*	1	Yes

Physical Attendance Mode

Points to note for CME Lecture with Physical Attendance Mode:

1. **Enrolment for CME lecture with physical attendance mode will be given to HKMA Members or Medical Practitioners in Hong Kong ONLY.**
2. **On behalf of the policy for lecture with physical attendance mode, please refer to P. 17 for more details.**

	Date	Organiser and Topic	Speaker	CME Points	CME Accreditation from Colleges (Pending)
1.	1 December (Fri) 2:00-3:00pm	**The HKMA District Health Network (Kowloon West)** Navigating the Landscape: Advances in Prostate Cancer Diagnosis and Treatment Venue: Greater China Club, Unit A, 10/F, D2 Place ONE, 9 Cheung Yee Street, Lai Chi Kok, Kowloon *Sponsor: Janssen, a division of Johnson & Johnson (HK) Ltd.*	**Dr LAM, Yiu Chung Thomas** *Specialist in Urology*	1	Yes
2.	20 December (Wed) 2:00-3:00pm	**The HKMA District Health Network (Central, Western & Southern)** Lipid Management in High-risk Patients - What Else From LDL Reduction? Venue: The HKMA Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong *Sponsor: Sanofi Hong Kong Limited*	**Dr LUK, Ngai Hong** *Specialist in Cardiology*	1	Yes

Please register through https://forms.gle/qiwmsPVbiKo8DibQA or scan the QR code if you are interested to attend. For enquiry, please contact the Secretariat at 2527 8285.

Accreditation from various colleges pending, for specialists, please complete the quiz online within two hours after the lecture with at least 50% correct for CME/CPD points. For lecture without "Yes", CME Accreditation is for Non-Specialists Only. Non-Specialists doctors must complete lecture quiz (10 Q&A) and answer questions within two hours after the lecture with at least 50% correct.

香港醫學會
THE HONG KONG MEDICAL ASSOCIATION

The Hong Kong Medical Association
District Health Network (Tai Po) CME Lecture

zoom LIVE

Tuesday, 12 December 2023

PROGRAMME	
2:00 – 2:45 p.m.	**Alcoholism, How Much Do You Drink and How Much Do You Know?** **Dr CHAN, Pierre** *Vice President, The Hong Kong Medical Association* *Specialist in Gastroenterology and Hepatology*
2:45 – 3:00 p.m.	**Q&A Session**

Format & Venue : **Hybrid; ZOOM/Jade Garden (Tai Po Mega Mall), Shop 136-150, 1/F, Zone B, Tai Po Mega Mall, 8 &10 On Pong Road, Tai Po**

Fee : **Free-of-charge**

Capacity : **The Capacity for physical attendance is 48. Registration for both physical attendance and virtual format are strictly required on a first-come, first served basis.**

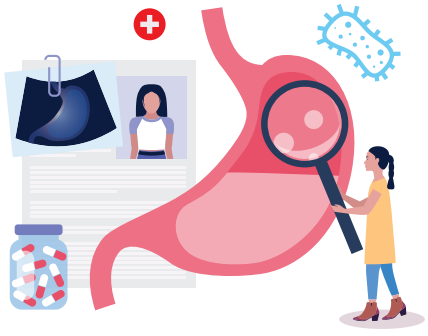
Registration Deadline : **Monday, 4 December 2023**

Registration : **Please register through https://forms.gle/XFShe6iLSjnkJGED8 or scan the QR code if you are interested to attend.**

CME Accreditation : **For Non-specialist Doctors: 1 CME point #**
Accreditation for Specialist Doctors: Yes #

 # Accreditation from various colleges are pending. For specialists who attended online, please completed the quiz online within two hours after the lecture with at least 50% correct for CME/CPD points. Non-Specialists doctors who attended online must also complete lecture quiz (10 Q &A) within two hours after the lecture with at least 50% correct.

Enquiry : **Please contact the HKMA CME Department at 2527 8452 or email to cme@hkma.org.**



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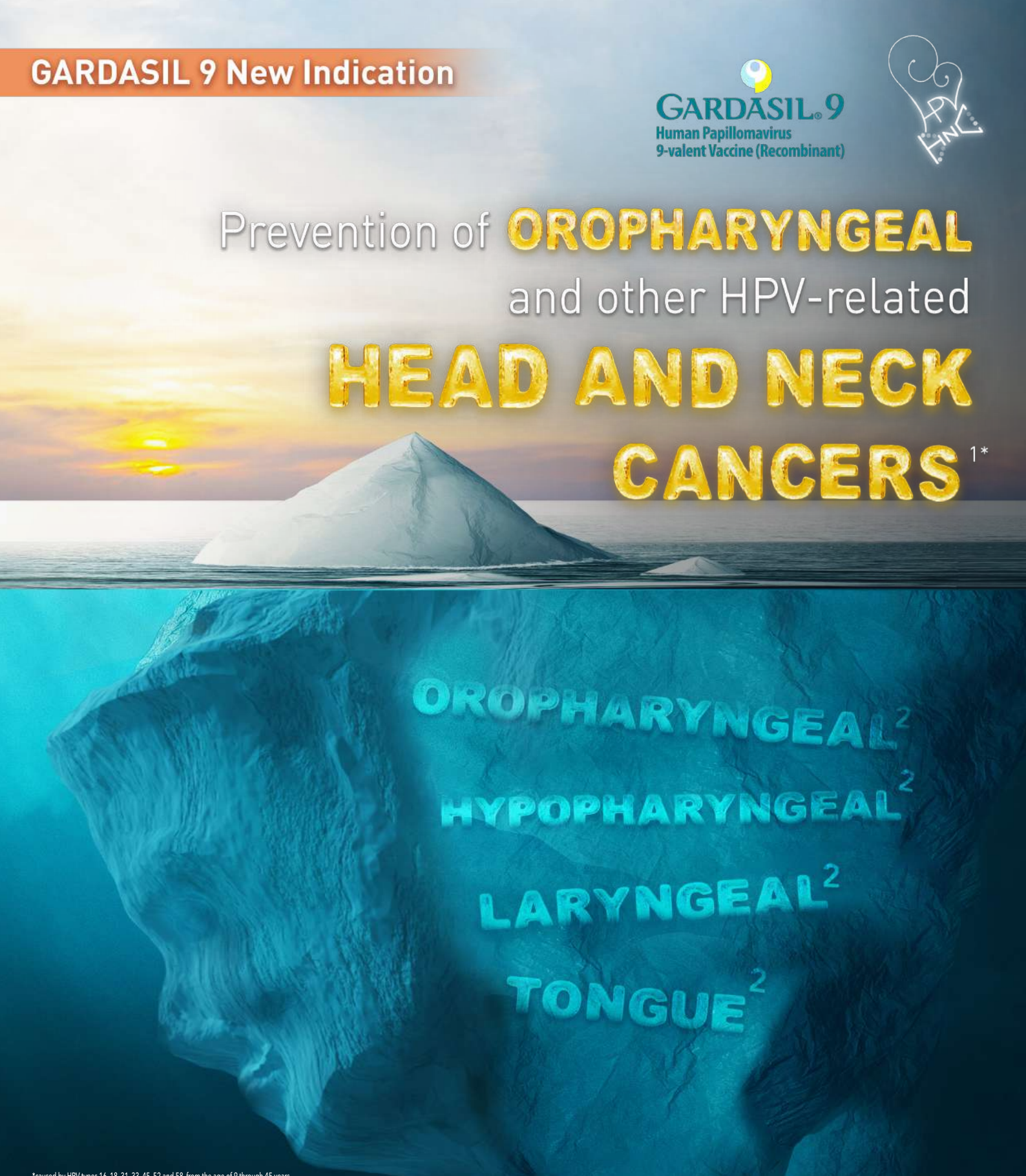


*caused by HPV types 16, 18, 31, 33, 45, 52 and 58, from the age of 9 through 45 years

References: 1. Hong Kong Product Circular (GARDASIL® 9 MSD) **2.** Centers for Disease Control and Prevention. Head and Neck Cancers. https://www.cdc.gov/cancer/headneck/index.htm Accessed on: April 13, 2023.

Selected Safety Information Indications: GARDASIL® 9 is indicated for active immunisation of individuals from the age of 9 years against the following HPV diseases: Premalignant lesions and cancers affecting the cervix, vulva, vagina and anus caused by vaccine HPV types. Genital warts (Condyloma acuminata) caused by specific HPV types. GARDASIL® 9 is indicated for active immunisation of individuals from the age of 9 through 45 years against the following HPV diseases: Cancers affecting the oropharynx and other head and neck sites caused by HPV types 16, 18, 31, 33, 45, 52, and 58. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients. Individuals with hypersensitivity after previous administration of GARDASIL® 9 or Gardasil should not receive GARDASIL® 9. **Precautions:** The decision to vaccinate an individual should take into account the risk for previous HPV exposure and potential benefit from vaccination. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine. Vaccinees should be observed for approximately 15 minutes after vaccination. It is important that procedures are in place to avoid injury from fainting. Vaccination should be postponed in individuals suffering from an acute severe febrile illness. However, the presence of a minor infection, such as a mild upper respiratory tract infection or low-grade fever, is not a contraindication for immunisation. As with any vaccine, vaccination with GARDASIL® 9 may not result in protection in all vaccine recipients. The vaccine will only protect against diseases that are caused by HPV types targeted by the vaccine. Therefore, appropriate precautions against sexually transmitted diseases should continue to be used. The vaccine is for prophylactic use only and has no effect on active HPV infections or established clinical disease. The vaccine has not been shown to have a therapeutic effect. The vaccine is therefore not indicated for treatment of cervical, vulvar, vaginal, anal, oropharyngeal and other head and neck cancers, high-grade cervical, vulvar, vaginal and anal dysplastic lesions or genital warts. It is also not intended to prevent progression of other established HPV-related lesions. GARDASIL® 9 does not prevent lesions due to a vaccine HPV type in individuals infected with that HPV type at the time of vaccination. Vaccination is not a substitute for routine cervical screening. Routine cervical screening remains critically important and should follow local recommendations. There are no data on the use of GARDASIL® 9 in individuals with impaired immune responsiveness. Safety and immunogenicity of a qHPV vaccine have been assessed in individuals aged from 7 to 12 years who are known to be infected with human immunodeficiency virus (HIV). Individuals with impaired immune responsiveness, due to either the use of potent immunosuppressive therapy, a genetic defect, Human Immunodeficiency Virus (HIV) infection, or other causes, may not respond to the vaccine. This vaccine should be given with caution to individuals with thrombocytopaenia or any coagulation disorder because bleeding may occur following an intramuscular administration in these individuals. There are no safety, immunogenicity or efficacy data to support interchangeability of GARDASIL® 9 with bivalent or quadrivalent HPV vaccines. **Adverse events:** The most common adverse reactions observed with GARDASIL® 9 were injection-site adverse reactions and headache. These adverse reactions usually were mild or moderate in intensity. Very common (≥1/10) or common (≥1/100 to <1/10) side effects include headache, injection site pain, swelling or erythema, dizziness, nausea, pyrexia, fatigue, injection site pruritus or bruising, etc. For detailed adverse events, please consult the full prescribing information. **Before prescribing, please consult the full prescribing information.**

MSD

MERCK SHARP & DOHME (ASIA) LTD.
27/F Lee Garden Two, 28 Yun Ping Road, Causeway Bay, Hong Kong.
TEL: (852) 3971 2800 FAX: (852) 2834 0756

CME Hybrid

HKMA-HKSH CME Programme 2023-2024

zoom LIVE

Time : 1:00 – 2:00pm Lunch
2:00 – 2:45pm Lecture
2:45 – 3:00pm Q&A

Format & Venue : Hybrid; ZOOM/The Hong Kong Medical Association Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong

Fee : Free-of-charge

Capacity : The capacity for physical attendance is 40. Registration for both physical attendance and virtual format are strictly required on a first-come, first-served basis.

Registration Deadline : Monday, 27 November 2023

Registration : [If you have already registered for this CME Programme, you are already registered for the whole Programme. You will receive the notification email 1 day and 1 hour before each lecture. Therefore, you are not advised to register the Programme repeatedly.]

Please register through https://forms.gle/vR61p9L8pffZLQ9SA or scan the QR code if you are interested to attend.

CME Accreditation : For Non-specialist Doctors: 1 CME point for each lecture #
Accreditation for Specialist Doctors: Yes #

\# *Accreditation from various colleges are pending. For specialists who attended online, please completed the quiz online within two hours after the lecture with at least 50% correct for CME/CPD points. Non-Specialists doctors who attended online must also complete lecture quiz (10 Q&A) within two hours after the lecture with at least 50% correct.*

Enquiry : Please contact the HKMA CME Department at 2527 8452 or email to cme@hkma.org.

Date (Tuesday)	Topic	Speaker
5 December 2023	Advances in Proton Therapy for Cancer Treatment	Dr CHANG, Tien Yee Amy *Specialist in Clinical Oncology*
2 January 2024	Novel Diagnostics & Therapeutics in Allergy Practice	Dr HO, Hok Kung Marco *Specialist in Paediatric Immunology, Allergy and Infectious Diseases*
6 February 2024	Updates in Interventional Endoscopy	Dr TEOH, Yuen Bun Anthony *Specialist in General Surgery*
5 March 2024 to 3 September 2024	The remaining lectures shall be announced in coming CME Bulletin issues.	

香港醫學會
THE HONG KONG MEDICAL ASSOCIATION

HKMA-CUHK Medical Centre CME Programme 2023

香港中文大學醫院 CUHK Medical Centre
Pioneering Solutions in Healthcare 開拓醫護新領域

zoom LIVE

Time : 1:00 – 2:00pm Lunch
2:00 – 2:45pm Lecture
2:45 – 3:00pm Q&A

Format & Venue : Hybrid; ZOOM/The Hong Kong Medical Association Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong

Fee : Free-of-charge

Capacity : The capacity for physical attendance is 40. Registration for both physical attendance and virtual format are strictly required on a first-come, first-served basis.

Registration Deadline : Friday, 1 December 2023

Registration : [If you have already registered for this CME Programme, you are already registered for the whole Programme. You will receive the notification email 1 day and 1 hour before each lecture. Therefore, you are not advised to register the Programme repeatedly.]

Please register through https://forms.gle/5azipM5jaxmfdqjg6 or scan the QR code if you are interested to attend.

CME Accreditation : For Non-specialist Doctors: 1 CME point #
Accreditation for Specialist Doctors: Yes #

\# *Accreditation from various colleges are pending. For specialists who attended online, please completed the quiz online within two hours after the lecture with at least 50% correct for CME/CPD points. Non-Specialists doctors who attended online must also complete lecture quiz (10 Q&A) within two hours after the lecture with at least 50% correct.*

Enquiry : Please contact the HKMA CME Department at 2527 8452 or email to cme@hkma.org.

Date (Wednesday)	Theme	Topic	Speaker
13 December	Women's Health	Breast Health and Breast Surgery	Dr CHAN, Ho Yan Yolanda *Specialist in General Surgery*

香港醫學會
THE HONG KONG MEDICAL ASSOCIATION

HKMA-HKSTP CME Programme 2023

HKSTP

zoom LIVE

Time : 1:00 – 2:00pm Lunch
2:00 – 2:45pm Lecture
2:45 – 3:00pm Q&A

Format & Venue : Hybrid; ZOOM/The Hong Kong Medical Association Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong

Fee : Free-of-charge

Capacity : The capacity for physical attendance is 40. Registration for both physical attendance and virtual format are strictly required on a first-come, first-served basis.

Registration Deadline : Thursday, 30 November 2023

Registration : [If you have already registered for this CME Programme, you are already registered for the whole Programme. You will receive the notification email 1 day and 1 hour before each lecture. Therefore, you are not advised to register the Programme repeatedly.]

Please register through
https://forms.gle/AMe1QGz6ymVzg3ft7
or scan the QR code if you are interested to attend.

CME Accreditation : For Non-specialist Doctors: 1 CME point for each lecture #
Accreditation for Specialist Doctors: Yes #

\# *Accreditation from various colleges are pending. For specialists who attended online, please completed the quiz online within two hours after the lecture with at least 50% correct for CME/CPD points. Non-Specialists doctors who attended online must also complete lecture quiz (10 Q&A) within two hours after the lecture with at least 50% correct.*

Enquiry : Please contact the HKMA CME Department at 2527 8452 or email to cme@hkma.org.

Date (All Thursday)	Theme	Topic	Speaker
7 December 2023 (Remark: Rescheduled from 23 November 2023)	Series 4: Cancerous Disease Diagnosis + Treatment/ Rehabilitation Solution	DNA Methylation and Its Role in Health and Disease: Implications for Early Prediction, Prevention and Intervention	Dr Moshe SZYF *Founder, HKG Epitherapeutics; Professor, Department of Pharmacology & Therapeutics, McGill University, Canada*
14 December 2023		Optimising the Molecular Diagnostics Strategy and Subject Recruitment Rate in Clinical Trials	Dr YU, Chi Shing Allen *Co-Founder and CTO, Codex Genetics Limited*
25 January 2024 to 29 February 2024		The remaining lectures shall be announced in coming CME Bulletin issues.	

香港醫學會
THE HONG KONG MEDICAL ASSOCIATION

HKMA-GHK CME Programme 2023

Gleneagles Hospital HONG KONG 港怡醫院

zoom LIVE

Time : 1:00 – 2:00pm Lunch
2:00 – 2:45pm Lecture
2:45 – 3:00pm Q&A

Format & Venue : Hybrid; ZOOM/The Hong Kong Medical Association Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong

Fee : Free-of-charge

Capacity : The capacity for physical attendance is 40. Registration for both physical attendance and virtual format are strictly required on a first-come, first-served basis.

Registration Deadline : Friday, 8 December 2023

Registration : [If you have already registered for this CME Programme, you are already registered for the whole Programme. You will receive the notification email 1 day and 1 hour before each lecture. Therefore, you are not advised to register the Programme repeatedly.]

Please register through
https://forms.gle/sutCWaBkf4Ky8w9HA
or scan the QR code if you are interested to attend.

CME Accreditation : For Non-specialist Doctors: 1 CME point #
Accreditation for Specialist Doctors: Yes #

\# *Accreditation from various colleges are pending. For specialists who attended online, please completed the quiz online within two hours after the lecture with at least 50% correct for CME/CPD points. Non-Specialists doctors who attended online must also complete lecture quiz (10 Q&A) within two hours after the lecture with at least 50% correct.*

Enquiry : Please contact the HKMA CME Department at 2527 8452 or email to cme@hkma.org.

Date (Tuesday)	Topic	Speaker
19 December	Topic in Ophthalmology	Dr CHAN, Jonathan Cheuk Hung *Specialist in Ophthalmology*

The Hong Kong Medical Association

Dr HO, Wan Sze Wency giving a CME lecture on 11 October 2023

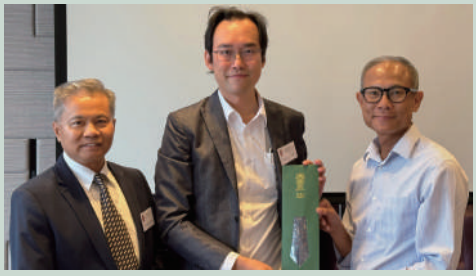
Dr NG, Kei Yan giving a CME lecture on 17 October 2023

Dr POON, Yick Kwan Vincent giving a CME Live lecture on 24 October 2023

Dr YE, Bin giving a CME lecture on 26 October 2023

The HKMA District Health Network – Central Coordination Committee

CME lecture of the HKMA District Health Network (Kowloon East)



Moderator Dr MA, Ping Kwan Danny (Left) and Dr AU, KA KUI Gary (Right) presenting a souvenir to Speaker Dr CHEUNG, Sai Wah (Middle) on 5 October 2023

CME lecture of the HKMA District Health Network (Shatin)

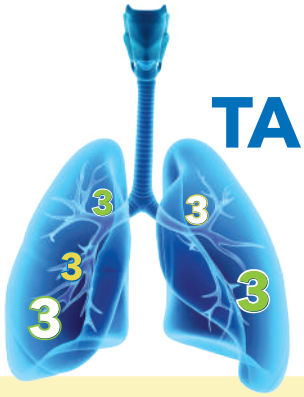
Moderator Dr MAK, Siu King (Left) presenting a souvenir to Speaker Dr LI, Siu Lung Steven (Right) on 18 October 2023

CME lecture of the HKMA District Health Network (Kowloon City)

The HKMA District Health Network Central Coordinator Dr YEUNG, Hip Wo Victor (Left) presenting a souvenir to Speaker Dr WONG, Cheuk Lik (Right) on 20 October 2023

Vaxneuvance®
Pneumococcal 15-valent
Conjugate Vaccine

MSD | 瞄準肺



TARGET OUR BURDEN

NEW Pneumococcal Conjugate Vaccine since 2011[2]

Vaxneuvance® (PCV15) was **SUPERIOR**[a] to PCV13 for shared Serotype 3[1]

SEROTYPE 3 is the **NO.1 Burden** of IPD[b] in Hong Kong[3]

INFANTS

When compared to PCV13, Vaxneuvance® induced

73%

increases IgG GMC against **SEROTYPE 3**,

which was selected as one of the immunogenicity outcomes in phase 3 clinical trial[4,5]

(GMC ratio = 1.73, 95% CI 1.61, 1.87) p<0.001
Superiority criteria: lower bound of the 2-sided 95 % CI for the IgG GMC ratio (V114/PCV13) >1.2

ADULTS

When compared to PCV13, Vaxneuvance® induced

~60%

increases IgG GMC against **SEROTYPE 3**,

which was selected as one of the immunogenicity outcomes in phase 3 clinical trial[1]

GMT Ratio: 1.60 (95% CI: 1.38-1.85)

Vaxneuvance® (PCV15) was noninferior[1a,4a] to PCV13 for all 13 shared serotype[1,4]

Vaxneuvance® (PCV15) was **SUPERIOR**[1a,4c] to PCV13 for **unique serotypes 22F and 33F**[1,4]

[1a] in terms of OPA GMTs (according to a Phase 3 trial), [b] IPD: invasive pneumococcal disease, [4a] In terms of IgG response rates (proportion of participants meeting the serotype-specific IgG threshold value of ≥ 0.35μg/ml) at 30 days PD3 and IgG GMCs at 30 days PD4. (Non-inferiority criteria: for IgG response rates, the lower bound of the 2-sided 95 % CI for the between-group differences > -10 percentage points; for IgG GMCs, the lower bound of the 2-sided 95 % CI for the V114/PCV13 GMC ratios > 0.5), [4c] In terms of IgG response rates at 30 days PD3 and IgG GMCs at 30 days PD3 and 30 days PD4 (superiority criteria: for IgG response rates and IgG GMCs, the lower bound of the 2-sided 95 % CI for the between-group differences > 10 percentage points and > 2.0, respectively)

Safety Result: Adults: The majority of participants experienced at least 1 adverse event (67.9% after V114 and 58.2% after PCV13). The most frequently reported AEs (>5% of participants in either group) were the solicited events of injection-site pain, injection-site erythema, injection-site swelling, arthralgia, fatigue, headache, and myalgia.[1]
Children: The majority of participants experienced at least 1 adverse event (93.8% after V114 and 92.4% after PCV13). The overall proportions of participants with injection-site, systemic, vaccine-related, and serious AEs were generally comparable between treatment groups. The most common AEs were those solicited in the trial, with the 3 most frequently reported AEs being irritability, somnolence, and injection-site pain.[4]

Adults: Adults ≥ 50 Years old; CI: confidence interval; GMT: geometric mean titers; Infants: Healthy infants; IPD: invasive pneumococcal disease; OPA: opsonophagocytic activity; PCV13: 13-valent pneumococcal conjugate vaccine; PCV15: 15-valent pneumococcal conjugate vaccine

Study design: This was a phase 3, randomized, double-blind, active comparator- controlled study to evaluate the safety, tolerability, and immunogenicity of VAXNEUVANCE compared to PCV13 in healthy pneumococcal-vaccine naïve adults 50 years of age or older (Protocol V114-019). The study was conducted from June 2019 through March 2020 at 30 sites. The study enrolled 1,202 participants randomized in a 1:1 ratio to receive a single dose of Vaxneuvance (n=602) or PCV13 (n=600). Randomization was stratified by participant age at enrollment. The primary immunogenicity objectives were to compare Vaxneuvance to PCV13 for noninferiority of immune responses at 30 days postvaccination for shared serotypes (noninferiority met when lower bound of the 2 sided 95% CI of the OPA GMT ratio >0.5) and superiority of immune response at 30 days postvaccination for serotypes unique to Vaxneuvance (superiority met when lower bound of the 2-sided 95% CI of the OPA GMT ratio >2, and the lower bound of the 2-sided 95% CI of the difference between the proportions of participants with a ≥ 4-fold rise >0.1). The secondary immunogenicity objective was to assess superiority of immune response for serotype 3 at 30 days postvaccination (superiority met when lower bound of the 2-sided 95% CI of the OPA GMT ratio >1.2, and the lower bound of the 2-sided 95% CI of the difference between the proportions of participants with a ≥4-fold rise >0).[1]

This study was a phase 3, randomized, active comparator-controlled, double-blind study to evaluate the safety, tolerability, and immunogenicity of a 4-dose regimen of Vaxneuvance in healthy infants (protocol V114-029). It was conducted from June 2019 to May 2021. The study enrolled 1720 participants randomized in a 1:1 ratio to receive a 4-dose vaccination regimen of Vaxneuvance (n=858) or PCV13 (n=856). Primary immunogenicity objectives were to compare Vaxneuvance to PCV13 for non-inferiority for all serotypes using anti-PnPs serotype-specific IgG response rates (proportion of participants meeting the serotype-specific IgG threshold value of ≥0.35 Ig/ml) at 30 days PD3 and IgG geometric mean concentrations (GMCs) at 30 days PD3 and 30 days PD4. Serotypes 22F and 33F were compared to the lowest response rate or IgG GMC for any of the 13 shared serotypes among recipients of PCV13, excluding serotype 3. For IgG GMCs, the lower bound of the 2-sided 95% CI for the Vaxneuvance/ PCV13 GMC ratios needed to be >0.5 to meet non-inferiority criteria. Secondary objectives were to compare Vaxneuvance to PCV13 for superiority for IgG against serotypes 3, 22F, and 33F using anti-PnPs serotype-specific IgG response rates at 30 days PD3 and IgG GMCs at 30 days PD3 and 30 days PD4. For IgG response rates and IgG GMCs to serotypes 22F and 33F, the lower bound of the 2-sided 95% CI for the between-group differences needed to be >10 percentage points and >2.0, respectively, to meet superiority criteria. For shared serotype 3, superiority based on IgG response rates and IgG GMCs was demonstrated if the lower bound of the 2-sided 95% CI for the between-group was >0 percentage points and >1.2, respectively.[4]

References: 1. Platt HL *et al; Vaccine* 2022; 40(1):162-172. doi: 10.1016/j.vaccine.2021.08.049 2. Centre for Health Protection. Scientific Committee on Vaccine Preventable Diseases. Updated Recommendations on the Use of 13-valent Pneumococcal Conjugate Vaccine in Childhood Immunisation Programme; 2019. Adopted from: https://www.chp.gov.hk/files/pdf/updated_ recommendation_on_the_use_of_pcv3_in_hkcip_march2019_accessibility.pdf. Accessed on Nov 17, 2022. 3. Centre for Health Protection. Communicable Diseases Watch. *IPD* (2015-2021). 4. Lupinacci R *et al; Vaccine* 2023;41(5):1142-1152. doi: 10.1016/j. vaccine.2022.12.054. 5. Hong Kong Product Circular, Vaxneuvance, MSD.

Vaxneuvance Selected Safety Information: Indications: • Vaxneuvance is indicated for active immunisation for the prevention of invasive disease, pneumonia and acute otitis media caused by *Streptococcus pneumoniae* in infants, children and adolescents from 6 weeks to less than 18 years of age • Vaxneuvance is indicated for active immunisation for the prevention of invasive disease and pneumonia caused by *Streptococcus pneumoniae* in individuals 18 years of age and older. • The use of Vaxneuvance should be in accordance with official recommendations. **Contraindications:** Hypersensitivity to the active substances, to any of the excipients, or to any diphtheria toxoid-containing vaccine. **Precautions:** • In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. • Vaxneuvance must not be administered intravascularly. • As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine. Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination. • As with other intramuscular injections, the vaccine should be given with caution to individuals receiving anticoagulant therapy, or to those with thrombocytopenia or any coagulation disorder such as haemophilia. Bleeding or bruising may occur following an intramuscular administration in these individuals. • The potential risk of apnoea and the need for respiratory monitoring for 48-72 hours should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination generally should not be withheld or delayed. • Immunocompromised individuals, whether due to the use of immuno-suppressive therapy, a genetic defect, HIV infection, or other causes, may have reduced antibody response to active immunisation. • Safety and immunogenicity data for Vaxneuvance are available for individuals living with HIV infection. Safety and immunogenicity data for Vaxneuvance are not available for individuals in other specific immunocompromised groups (e.g., haematopoietic stem cell transplant) and vaccination should be considered on an individual basis. • As with any vaccine, vaccination with Vaxneuvance may not protect all vaccine recipients. Vaxneuvance will only protect against *Streptococcus pneumoniae* serotypes included in the vaccine. • This medicinal product contains less than 1 mmol sodium (23 milligrams) per dose, i.e. essentially 'sodium-free'. **Adverse events:** The most frequently reported adverse reactions following vaccination with Vaxneuvance were solicited. The most frequent adverse reactions were pyrexia, injection-site pain, fatigue, myalgia, headache, injection-site swelling, injection-site erythema and arthralgia. The majority of solicited adverse reactions were mild (based on intensity or size) and of short duration (≤ 3 days); severe reactions (defined as being extremely distressed or unable to do usual activities or size > 7.6 cm) occurred in ≤4.5% of children and adolescents; severe reactions (defined as an event that prevents normal daily activity or size > 10 cm) occurred in ≤1.5% of adults across the clinical program. • Older adults reported fewer adverse reactions than younger adults. • For detailed side effects, please consult the full prescribing information.
Before prescribing, please consult the full prescribing information.

MSD

Merck Sharp & Dohme (Asia) Ltd.
27/F, Lee Garden Two, 28 Yun Ping Road, Causeway Bay, Hong Kong.
Tel: (852) 3971 2800 Fax: (852) 2834 0756
Website: www.msd.com.hk

HK-PVC-00061 Jun/2023

CME Calendar

November 2023

27 November (Mon)
2:00-3:00 p.m.
The Hong Kong Medical Association
The Role of Probiotics in the Treatment of NAFLD and Metabolic Disease
HKMA CME Live Lecture
HKMA CME Dept. – Tel: 2527 8452

28 November (Tue)
2:00-3:00 p.m.
The Hong Kong Medical Association
1. Updates on Colorectal Cancer Screening
2. Multitarget FIT-DNA Technology as the Latest Colorectal Cancer Screening Option in Hong Kong
HKMA CME Live Lecture
HKMA CME Dept. – Tel: 2527 8452

29 November (Wed)
2:00-3:00 p.m.
The HKMA District Health Network (Central, Western and Southern)
Diagnosis and Management of Common Skin Infections in Primary Care
HKMA CME Live Lecture
HKMA District Health Network Dept. – Tel: 2861 1979

30 November (Thu)
2:00-3:00 p.m.
The HKMA District Health Network (Hong Kong East)
Changing Paradigms in Hyperlipidemia Management: What are the Available Evidence in CV Risk Reduction and Long Term Safety?
HKMA CME Physical Lecture
HKMA District Health Network Dept. – Tel: 2861 1979

December 2023

1 December (Fri)
2:00-3:00 p.m.
The HKMA District Health Network (Kowloon West)
Navigating the Landscape: Advances in Prostate Cancer Diagnosis and Treatment
HKMA CME Physical Lecture
HKMA District Health Network Dept. – Tel: 2861 1979

4 December (Mon)
2:00-3:00 p.m.
The Hong Kong Medical Association
Triple Inhalation Therapy in Severe Asthma
HKMA CME Live Lecture
HKMA CME Dept. – Tel: 2527 8452

5 December (Tue)
2:00-3:00 p.m.
The Hong Kong Medical Association and the Hong Kong Sanatorium & Hospital
Advances in Proton Therapy for Cancer Treatment
HKMA CME Hybrid Lecture
HKMA CME Dept. – Tel: 2527 8452

7 December (Thu)
2:00-3:00p.m.
The Hong Kong Medical Association and the Hong Kong Science and Technology Park
DNA Methylation and Its Role in Health and Disease: Implications for Early Prediction, Prevention and Intervention
HKMA CME Hybrid Lecture
HKMA CME Dept. – Tel: 2527 8452

8 December (Fri)
2:00-3:00 p.m.
The Hong Kong Medical Association
What's New in Hypertension Management
What's New in Hypertension Management
HKMA CME Live Lecture
HKMA CME Dept. – Tel: 2527 8452

11 December (Mon)
2:00-3:00 p.m.
The Hong Kong Medical Association
Antiplatelet Therapy in 2023: From Guidelines to Clinical Practice
HKMA CME Live Lecture
HKMA CME Dept. – Tel: 2527 8452

12 December (Tue)
2:00-3:00 p.m.
The HKMA District Health Network (Tai Po)
Alcoholism, How Much Do You Drink and How Much Do You Know?
HKMA CME hybrid Lecture
HKMA District Health Network Dept. – Tel: 2861 1979

13 December (Wed)
2:00-3:00 p.m.
The Hong Kong Medical Association and the CUHK Medical Centre
Breast Health and Breast Surgery
HKMA CME Hybrid Lecture
HKMA CME Dept. – Tel: 2527 8452

14 December (Thu)
2:00-3:00 p.m.
The Hong Kong Medical Association and the Hong Kong Science and Technology Park
Optimising the Molecular Diagnostics Strategy and Subject Recruitment Rate in Clinical Trials
HKMA CME Hybrid Lecture
HKMA CME Dept. – Tel: 2527 8452

15 December (Fri)
2:00-3:00 p.m.
The Hong Kong Medical Association
Understanding Therapeutic Index and Improving Allergic Rhinitis Management
HKMA CME Live Lecture
HKMA CME Dept. – Tel: 2527 8452

19 December (Tue)
2:00-3:00 p.m.
The Hong Kong Medical Association and the Gleneagles Hong Kong Hospital
Topic on Ophthalmology
HKMA CME Hybrid Lecture
HKMA CME Dept. – Tel: 2527 8452

20 December (Wed)
2:00-3:00 p.m.
The HKMA District Health Network (Central, Western & Southern)
Lipid Management in High-risk Patients – What Else From LDL Reduction?
HKMA CME Physical Lecture
HKMA District Health Network Dept. – Tel: 2861 1979

21 December (Thu)
2:00-3:00 p.m.
The Hong Kong Medical Association
Updates in Management of Lipid Disorders
HKMA CME Live Lecture
HKMA CME Dept. – Tel: 2527 8452