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Message from the ***Chief Hospital Manager***

Dear Colleagues,

I have much pleasure to cheer with you, at least for now, that we are finally out of the woods with the Covid-19 pandemic. With the Omicron strain of this coronavirus being of low pathogenicity especially for those healthy vaccinated individuals, the illness it brings about is being regarded as a common viral infection like influenza or the respiratory syncytial virus. It is important that health officials and head of state of the Chinese government hold the same view. Once all the quarantine measures and hurdles affecting free human flow between Hong Kong and the rest of the world have been lifted, prospect of recovery and boom in the local economy will become a reality, not just imagination!

Now I must say that I was a bit disappointed with my Hokkaido skiing trip. The weather condition was certainly not the best – snowing day and night most of the time. Thus the skiing trails were covered with heaps of soft snow and the visibility was so bad that after hitting the slope for one day I decided to stay in the hotel during the day for the rest of our time in Niseko, reading and sipping coffee or local beer! However, I got my compensation when it came to dinner time – thanks to the hard work and meticulous itinerary prepared by our ski trip manager Ms Eva Tsoi, we had a gastronomic tour of the region sampling the best in local produce deliciously prepared by skilled chefs, some with Michelin star fame. Actually this Hokkaido trip was memorable because it was a family reunion with my two daughters who had been separated poles apart for three whole years because of the pandemic. One of them stayed in Launceston, Tasmania, while the other resided in New York City of the United States. Thus it was family affair in Sapporo for five days continuing with the gastronomic journey together with crazy shopping during the day, mostly in the labyrinth like underground part of this northernmost metropolis in Japan.

Although my ski trip was spoiled by unusual snowing condition but I considered myself lucky when I learned from the news that Japan and other countries in North America had been hit by heavy snowstorm and the big chill not seen for years. I cannot help but thinking that such extremes in climate change could be Nature's warning to the human race to go 'green' in our lift-style in order to avoid or defer as much as possible the doomsday of Global warming leading to the end of the present civilization! I may sound a bit pessimistic but all is not lost as yet. We can all do a part by conservation in energy. One can start with using less electricity in the household and workplace. Union Hospital had changed to LED lighting since 2018, thus saving tens of thousands of dollars per month in electricity bill. We are in the process of replacing all the lifts in the old hospital block and Union Court and the new one will offer 30% more in passenger movement capacity but also in electricity consumption. Extensive use of 3M Sun Control Window Film throughout the hospital and Union Court, regular maintenance or replacement of out-dated components in our air-conditioning or heat-exchange systems also help a lot in our gas and electricity consumption. Lastly but not least, the construction of our extension block on the podium floor will incorporate every currently available and applicable 'green' or 'energy saving' feature in the process.
Good-bye for now and I wish you and your family a very happy and successful Year of the Rabbit.

Yours most sincerely,

Dr. Anthony K Y Lee
Chief Hospital Manager & Medical Director

Biologics in The Management Of Chronic Rhinosinusitis

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Chronic rhinosinusitis (CRS) is a common health condition . It may be broadly defined as an inflammatory disorder of the paranasal sinuses and linings of the nasal passages that lasts 12 weeks or longer.

Studies from the United States and Europe, South America, the Caribbean, and China estimate the prevalence of CRS to be between 5 and 12 percent of the general population. The causes of CRS are not fully understood. It maybe due to the malfunction interactions between patient's characteristics (genetics) and environmental factors such as respiratory infection, immune system disorder allergic reactions, cigarette smoke or pollutants.

Symptomatology and Diagnosis

There are 4 cardinal signs and symptoms in CRS.

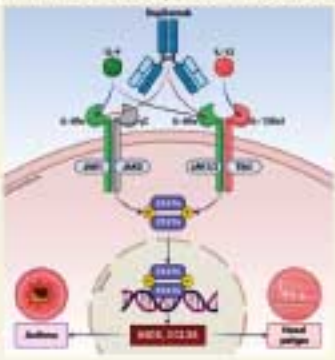
- Anterior and/or posterior nasal mucopurulent drainage
- Nasal obstruction/nasal blockage/congestion
- Facial pain, pressure, and/or fullness
- Reduction or loss of sense of smell

In children, the fourth cardinal sign/symptom is cough rather than reduction/loss of smell. Patients can also complain of non specific symptoms like fatigue, malaise, cough, sleep disturbance, ear pain or pressure, dizziness, halitosis, dental pain, dysphonia, or nasal or throat irritation.

The diagnosis of CRS is made when patients complained of 2 or more of the above cardinal signs/symptoms for more than 12 weeks. Nasoendoscopy showed generalised inflamed mucosa with mucopurulent discharge at the middle meatus or sphenoethmoidal recess. Polyp or polyploid mucosa maybe evident. CT paranasal sinus showed the sinus is lined by thickened mucosa, presence of polyp and some predisposing factors to CRS like deviated septum and concha bullosa etc.

Classification of Chronic Rhinosinusitis

The previous classification of CRS is based on the phenotypic features into CRS without nasal polyp (CRSsNP) and CRS with nasal polyp (CRSwNP). This classification does not take into account of the pathogenesis and the different inflammation endotypes. The current classification of CRS according to the European position paper on rhinosinusitis and nasal polyp 2020 (EPOS 2020) is base on the inflammatory endotypes into type 2 and non-type 2 disease. Type 2 inflammation is characterised by high IgE level and eosinophilia. So there can type 2 CRS with or without nasal polyp or non type 2 CRS with or without nasal polyp.



Current Management of Chronic Rhinosinusitis

The new classification implies a paradigm shift on the management of CRS. Current management strategies employ a combination both of medical and surgical interventions to alleviate disease burden and provide symptom control. Medical therapies target generalized inflammation and include, but are not limited to, steroid nasal sprays, oral steroids, saline rinses, and antibiotics. The advent of novel targeted biologics have shown promise in targeting a different aspect of the inflammatory pathways. The discussion below mainly focuses on the different biologics on the management of CRS.

Anti-IL-4/13

Dupilumab (Dupixent®) is an anti-IL-4 monoclonal antibody which functions by targeting the alpha chain of the IL-4Ra, the common receptor for both IL-4 and IL-13. Both IL-4 and IL-13 play a central role in the Th2 pathway and ultimately polyp formation. Dupilumab has been approved to treat severe atopic dermatitis and has shown efficacy in treating asthma. In 2019, it was the first biologic approved by the FDA for the treatment of CRSwNP. The reason for approval was based on two randomized, placebo-controlled trials, the LIBERTY-24 and LIBERTY- 52 studies. Patients in both studies showed improvement in nasal congestion, olfactory functions, pulmonary function and the CT imaging finding during the treatment course. Dupilumab greatly reduced the need for systemic steroids, improved symptoms, including olfaction, and health-related quality of life. Dupilumab treatment also reduced type 2 biomarkers in serum and nasal secretions, including total IgE. Based on the results of this trial, dupilumab was approved for use in patients with nasal polyposis. However, after the cessation of therapy, the nasal congestion symptoms and nasal polyp recurred over the follow up period. Dupilumab is currently available in UH pharmacy.

Anti-IL-5

IL-5 is a key cytokine released in the Th-2 inflammatory cascade. Release, in conjunction with IL-4 and IL-13, drives increased local production of IgE and results in eosinophilia, chemotaxis, differentiation, and activation of eosinophil survival. IL-5 is the critical factor that promotes eosinophil development and survival and therefore blockade also exhibits secondary effects via elimination of eosinophils peripherally and within tissue. IL-5 also appears to have a key role in the pathogenesis of nasal polyposis including expression of IL-5 in nasal polyps.

Mepolizumab (Nucala) is an anti-IL-5 monoclonal antibody currently under investigation as a potential therapy for nasal polyposis. Mepolizumab has been shown to reduce blood and tissue eosinophil counts and is currently approved for treatment of severe eosinophilic asthma. Bachert et al performed a randomized trial investigating the use of Mepolizumab in patients with nasal polyposis. Results showed a decreased need for surgery and improvement in nasal polyp VAS scores in the treatment group. Mepolizumab also improved olfactory function compared to placebo. Treatment led to a 10-fold reduction in eosinophil counts at week 25, which mirrored improvement in symptoms and need for surgery. Mepolizumab is currently not available in Hong Kong.

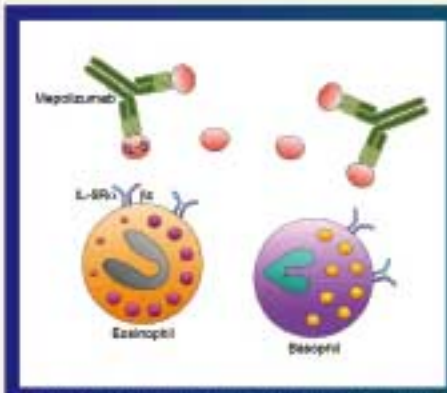
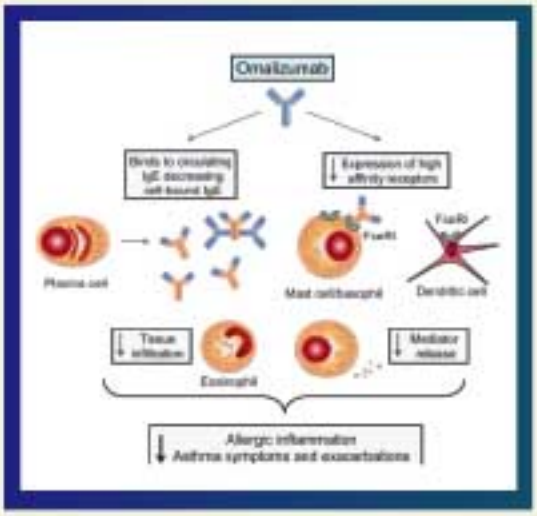


Figure 2 Mechanism of action of mepolizumab. Mepolizumab binds with high affinity to IL-5, thus preventing its interaction with the IL-5 receptor exceptor expressed by eosinophils and, to a lesser extent, also by basophils.
Abbreviation: IL-5, interleukin-5.

Anti-IgE

Omalizumab is an anti-IgE monoclonal antibody that binds to the Fc receptor on a multitude of different inflammatory cells including mast cells and basophils. It functions to reduce total serum levels of IgE and downstream effects of IgE mediated release of inflammatory cytokines. It is marketed under the trade name of Xolair and was originally FDA approved for use for the treatment of moderate to severe persistent allergic asthma in people 6 years of age or older whose asthma symptoms are not controlled by inhaled corticosteroids, and for chronic idiopathic urticaria in people 12 years of age and older. It is given via a subcutaneous injection every 2–4 weeks with dose determined by serum total IgE and body weight. Its role in CRSwNP was based on literature suggesting a pathophysiologic mechanism related to local intranasal IgE production that leads to an inflammatory cascade.

Further clinical evidence for its efficacy in CRSwNP was originally assessed in a double blinded placebo- controlled trial by Gevaert et al and demonstrated a reduction in total endoscopic nasal polyp score (NPS), improved pre and post treatment computed tomography (CT) scores, improved nasal peak inspiratory flow, as well as symptoms related to allergy and asthma quality of life measures. No change in smell function was found. More recent evidence from Phase III clinical trials, Polyps I and II has demonstrated efficacy in treatment of CRSwNP and in December of 2020 FDA granted approval for Omalizumab for treatment of adults with refractory CRSwNP.



Role of Surgery In The Era Of Biologics

While biologics show some promising result in the management of CRSwNP, it still cannot replace surgery as the preferred management strategy. Biologics is costly and the long term effect has not been validated. There is report of recurrence of the nasal polyps after cessations of treatment. A sufficient endoscopic sinus surgery (ESS) has been shown to improve medical management and quality of life. Many authors still suggested that medical management including nasal steroid spray, antihistamines, normal saline nasal douching is the first line treatment. ESS is indicated after failure of medical treatment. Biologics remains the adjuvant treatment when there is recurrent disease.

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Procedural Sedation For Children Difficult Airway

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Case Description

X is a 2 year old boy, weighing 12 kg, diagnosed with Mucopolysaccharidosis (MPS) type IV, requiring procedural sedation for an MRI scan with contrast for C-spine. On examination, he had typical features of MPS including coarse facial features, enlarged tongue, and difficult IV access. EMLA cream was applied to both dorsi of hand 45 minutes before the start of appointment. 3mcg/kg Dexmedetomidine was then given nasally by the anesthesiologist, via a mucosal atomizer 30 minutes before the appointment. X was monitored continuously by pulse oximetry and sedation level with the University of Michigan Sedation Score (UMSS). After 30 minutes, he was deeply sedated with UMSS 3. Intravenous access was obtained, and Dexmedetomidine was given intravenously for the duration of the MRI at 1.5mcg/kg/hr. Throughout the procedure, 2L/min Oxygen was given via nasal cannula with capnography monitoring; SpO2, Blood pressure and ECG were also monitored. Other than bradycardia of heart rate 65, vital signs were all normal throughout the procedure. Dexmedetomidine was stopped 5 minutes before the end of the procedure. X woke up 20 minutes after the procedure. He was able to tolerate fluids at 1 hour and was deemed fit to be discharged home after 2 hours.

Discussion

This above case is chosen for discussion as children with MPS have classically been identified with difficult airway, hence challenging to provide sedation for, especially in remote non-operating areas. Most sedative agents have respiratory depressive effects, while most healthy children can tolerate it safely, they may be deemed unsafe for children with a marginal airway. Moreover, some drugs, such as Chloral hydrate, have a prolonged half-life and may re-sedate children, rendering it less safe to discharge children with difficult airway or prone to airway obstruction on the same day.[1]

Dexmedetomidine (Precedex) was chosen as a sole sedative agent in this case study, due to its safety profile of minimal clinically significant respiratory depression. Dexmedetomidine is a selective alpha-2 adrenoreceptor agonist with anxiolytic, sedative and analgesic properties. It is believed to produce sedation mimicking natural sleep by acting on the alpha 2 adrenergic receptors in locus coeruleus in the central nervous system. Even though Dexmedetomidine is considered 'off-label' use in paediatrics, it has been extensively studied and proved beneficial in sedation and perioperative setting for the pediatric population, and has been adopted by many international centers in their paediatrics sedation protocol. It can be administered intranasally, intravenously, intramuscularly and intrathecally. Intranasal administration in the paediatric population is often welcomed as it is less anxiety provoking and less invasive. Moreover, intranasal Dexmedetomidine is less irritative than intranasal midazolam. Studies show successful sedation with intranasal Dexmedetomidine ranging from 2mcg/kg to 4mcg/kg, with decreasing requirement for additional rescue dose for doses above 3mcg/kg. One study using intranasal Dexmedetomidine at 3mcg/kg quoted 92% success rate in initiation of sedation. Time-to-peak ranges between 30-45 minutes with faster onset time but somewhat prolonged recovery time to usual activities with higher doses (>3mcg/kg).[2,3,4]

In short, non-invasive procedures that do not require an IV access (e.g. plain MRI scans, transthoracic echocardiography, electroencephalography etc.), intranasal Dexmedetomidine alone may suffice for providing sedation for the procedure. While desaturation is rarely observed in studies, a decrease in heart rate of 20% from baseline is often observed with Dexmedetomidine sedation, significant hypotension (>20% from baseline) requiring intervention is very rarely required.[2]

Even though Dexmedetomidine has a reassuring safety profile, a thorough pre-sedation assessment of the airway and respiratory system, as well as stand-by age-appropriate airway equipment and experienced personnel is always warranted for conducting a safe remote site sedation for children with potential difficult airway. In the case of MPS, screening for obstructive sleep apnea, cervical spine instability in view of the associated odontoid hypoplasia, and any cardiovascular comorbidities such as hypertrophic cardiomyopathy, valvular and conduction abnormalities must be conducted. [4] If cervical spine instability is suspected, finding a comfortable position for the child before sedation is paramount to minimize inadvertent mispositioning after sedation, leading to cord compression. Even though MPS has been traditionally associated with difficult intubation and difficult facemask ventilation, modern technologies utilizing video laryngoscopy-guided intubation and laryngeal masks as airway rescue have improved the rates of successful intubation and ventilation respectively. [5] Such important airway adjuncts must be present in providing sedation for these children with high risk of airway and respiratory difficulties.

In conclusion, sedative medication with less respiratory depression safety profile such as Dexmedetomidine can be utilized safely in providing sedation for children with difficult airway. Nevertheless, thorough assessment of the airway, continuous monitoring of vitals especially capnography, as well as standby preparation for airway rescue remains paramount in conducting safe sedation in remote areas.

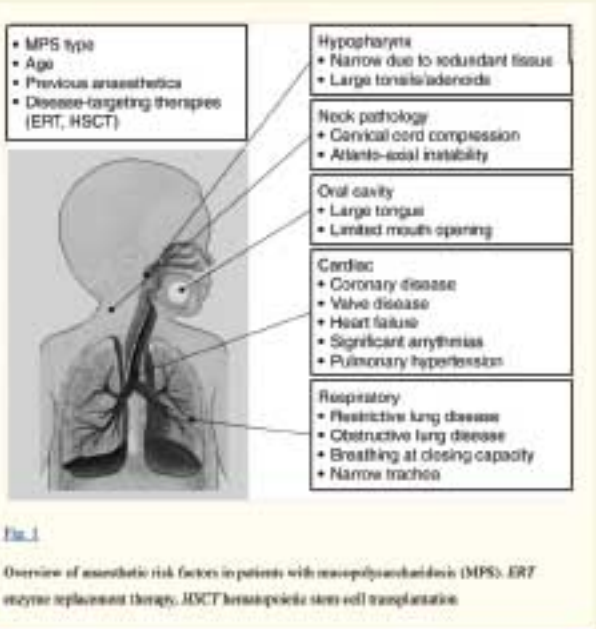

Fig. 1

Overview of anesthetic risk factors in patients with mucopolysaccharidosis (MPS). *ERT* enzyme replacement therapy, *HSCT* hematopoietic stem cell transplantation

Table taken from reference [5].

Example of mucosal atomizer used for intranasal administration

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Trends of Cultured Pathogens

The Most Frequently Isolated Pathogens from Urine Cultures during September to December 2022

Most Common Pathogens Isolated	*Escherichia coli*	
Period	Sep to Dec 2022	May to Aug 2022
Number of Isolates per Admission (Total number of Urine Cultures)	224 (2104) (including 48 ESBL & 1 CPE)	236 (2338) (Include 48 ESBL 20.3%)
Isolation Rate	10.6%↑	10.1%↓
Antibiotics	**Non-susceptible Rate**	
Amoxicillin/Clavulanic Acid	26%↑	11%
Ampicillin	71%↑	66%
Ampicillin/Sulbactam	60%↑	55%
Cefazolin (Oral)	27%↑	24%
Ceftriaxone/Cephalosporins 3G	23%↑	22%
Cefuroxime (Oral)	32%↑	27%
Cefuroxime (Parenteral)	25%↑	23%
Ciprofloxacin*	55%↑	45%
Ertapenem	0.4%↑	0%
Gentamicin	24%↑	23%
Imipenem	0.4%↑	0%
Levofloxacin*	70%↑	59%
Nitrofurantoin	3%↑	2%
Trimethoprim/Sulfamethoxazole	35%↓	37%

*Non-susceptible Rate of Levofloxacin & Ciprofloxacin is increased as the criteria for the interpretation of Susceptibility on Levofloxacin & Ciprofloxacin were changed on 1st April 2020.

The Most Frequently Isolated Pathogens from Respiratory Secretion Cultures during September to December 2022

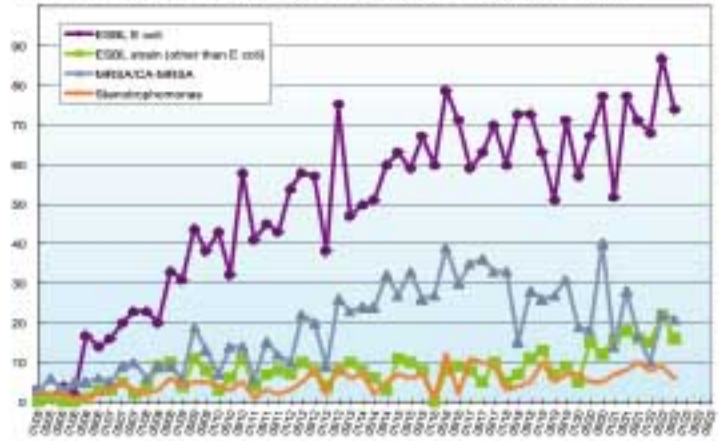
Period	Sep to Dec 2022		May to Aug 2022	
No of Requests	259		261	
Pathogens	Number of Isolates	Isolation Rate	Number of Isolates	Isolation Rate
Pseudomonas aeruginosa	21	8.1%↓	28	10.7%
Staphylococcus aureus	17 (Including 1 MRSA 5.9%)	6.5%↓	32 (Including 4 MRSA 12.5%)	12.3%
Klebsiella pneumoniae	14	5.4%↓	15 (Include 1 ESBL *Kleb.*)	5.7%
Escherichia coli	11	4.2%↑	4	1.5%

The Most Frequently Isolated Pathogens From Genital Cultures During September to December 2022

Most Common Pathogens Isolated	*Group B Streptococci*		*Candida albicans*		*Yeast (Candida albicans excluded)*	
Period	Sep to Dec 2022	May to Aug 2022	Sep to Dec 2022	May to Aug 2022	Sep to Dec 2022	May to Aug 2022
Number of Isolates per Admission (Total number of Genital Cultures)	151 (799)	162 (816)	112 (799)	92 (816)	52 (799)	40 (816)
Isolation Rate	18.9%↓	19.8%	14.0%↑	11.3%	6.5%↑	4.9%
Antibiotics	**Non-susceptible Rate**					
Cefotaxime	0.0%	0.0%				
Clindamycin	54.3%↓	67.9%				
Levofloxacin	12.6%↓	15.4%				
Penicillin	0.0%	0.0%				
Vancomycin	0.0%	0.0%				

[1]Suspectible to penicillin can be considered susceptible to ampicillin, amoxicillin, amoxicillin/clavulanic acid, ampicillin/sulbactam, cefaclor, cefazolin, cefdinir, cefepime, cefprozil, cefotaxime, ceftriaxone, cefuroxime, cefpodoxime, ceftizoxime, cephalothin, cephapirin, imipenem, loracarbef, and meropenem.

Trend of ESBL, MRSA & *Stenotrophomonas* isolated from all specimen types by every four months



	ESBL *E coli*	ESBL strain (other than *E coli*)	MRSA/ CA-MRSA	*Stenotrophomonas*
Sep-Dec 16	71	9	30	2
Jan-Apr 17	59	8	35	11
May-Aug 17	63	5	36	10
Sep-Dec 17	70	10	33	9
Jan-Apr 18	60	5	33	3
May-Aug 18	73	7	15	4
Sep-Dec 18	73	11	28	5
Jan-Apr 19	63	13	26	10
May-Aug 19	51	7	27	5
Sep-Dec 19	71	9	31	7
Jan-Apr 20	57	5	19	7
May-Aug 20	67	15	18	5
Sep-Dec 20	77	12	40	5
Jan-Apr 21	52	16	14	7
May-Aug 21	77	18	28	8
Sep-Dec 21	71	16	17	10
Jan-Apr 22	68	15	10	8
May-Aug 22	67	22	22	9
Sep-Dec 22	74	16	21	8

Antibiotics non-susceptible profile of commonly isolated bacterial pathogen at Union Hospital 2022

Pathogens	*Acinetobacter sp.*	*Enterobacter sp.*	*Escherichia coli*	*Enterococcus sp. (1)*	*Haemophilus influenzae*	*Klebsiella sp.*	*Proteus sp.*	*Pseudomonas aeruginosa*	*Staphylococcus aureus*	*Salmonella sp.*	*Group B Streptococci*
Antibiotics / Count	45 + 1 CRAB	57	737 + 225 ESBL + 2 CPE	228	13	296 + 40 ESBL + 4 CPE	115 + 10 ESBL	177	339 + 135 MRSA + 25 CA-MRSA	346	591
Amikacin								1.1%			
Amoxicillin											
Amoxicillin/Clavulanic Acid		100%	19.5%		0.0%	31.8%	35.2%				
Ampicillin			69.2%	2.2%	46.2%	100%	49.6%			74.0%	
Ampicillin/Sulbactam	15.8%		57.1%			28.6%	25.0%				
Cefazolin/Cephalosporins 1G		100%	32.9%			44.4%	26.4%				
Cefepime								3.4%			
Cefotaxime					0.0%						0%
Ceftriaxone/Cephalosporins 3G		23.6%	24.7%		7.7%	17.4%	8.0%			9.2%	
Ceftriaxone (meningitis)											
Ceftriaxone (non-meningitis)											
Ceftazidime/Cephalosporins 3G	24.4%				0.0%			3.4%			
Cefuroxime (Oral)			33.5%		7.7%	20.8%	17.6%				
Cefuroxime (Parenteral)			26.7%			20.1%	17.6%				
Ciprofloxacin	13.0%	15.8%	49.3%			23.5%	21.0%	15.3%			
Clarithromycin					15.4%						
Clindamycin											53.2%
Erythromycin				84.6%					23.4%		
Ertapenem		3.6%	0.2%			1%	2.4%				
Gentamicin	2.2%	3.5%	24.1%			6.2%	19.2%	4.0%	3.8%		
Gentamicin (High Conc)											
Imipenem		0.0%	0.2%			1.2%	6.4%				
Levofloxacin		11.5%	64.5%	18.7%	0.0%	25.0%	21.6%	18.6%	22.0%	64.8%	13.9%
Meropenem	11.1%							4.6%			
Nitrofurantoin			2.3%	3.7%		81.2%	100%				
Oxacillin									32.1%		
Penicillin				2.6%					81.6%		0%
Penicillin Oral											
Penicillin parenteral (Men)											
Penicillin parenteral (NonMen)											
Piperacillin	27.5%							13.1%			
Tetracycline				84.4%					24.4%		
Trimethoprim/Sulfamethoxazole		7.9%	37.2%		30.8%	16.2%	32.3%		7.7%	22.3%	
Vancomycin				0%					0%		0%

100% The highlighted non-susceptible antibiotics are due to intrinsically resistant to particular bacterial pathogen.

CPE Carbapenemase producing enterobacteriaceae

CRAB Carbapenem Resistant *Acinetobacter baumanii*

ESBL Extended-spectrum β-lactamases

MRSA/CA-MRSA Methicillin-resistant *Staphylococcus aureus* / Community associated MRSA

(1) Include *Enterococcus faecalis* & *Enterococcus faecium*

New Clinical Sessions

Minimally Invasive Centre	
Booking & Enquiry: 2608 3383	Time Schedule
Orthopaedics & Traumatology Dr. Lam Kin Wai, Micheal	Tue 11:30-14:30 Fri 10:00-13:00
Otorhinolaryngology Dr. Ngai Chi Man	Thu 09:00-13:00

Specialty Clinic – Obstetrics & Gynaecology	
Booking & Enquiry: 2608 3222	Time Schedule
Dr. Kwok Sui Yee, Karen	Thu 15:00-18:00 Sat 15:00-18:00

Union Hospital Polyclinic (Tseung Kwan O)	
Booking & Enquiry: 2721 0100	Time Schedule
Orthopaedics & Traumatology Dr. Lam Kin Wai, Micheal	Mon 10:00-13:00 Thu 16:00-18:30

New Doctor

Please extend a warm welcome to Dr. Ngai Chi Man for joining our Otorhinolaryngology team!

Dr. Ngai Chi Man
Specialist In Otorhinolaryngology

Regular Meeting

Mortality and Morbidity Meeting	
Date :	8 March 2023 (Wednesday)
Time :	8:30 am – 9:30 am
Co-ordinator :	**Dr. KWONG Kwok Hung, Peter** Specialist in General Surgery, Union Hospital
Venue :	Training Room, 8/F MIC, Hospital Building, Union Hospital
Booking & Enquiry:	2608 3151 (Quality Assurance & Training Department)

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